Using the patient perspective to personalize psycho-oncological care for chronic cancer-related fatigue

Tom Iepe Bootsma

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Proefschrift ter verkrijging van de graad van doctor aan Tilburg University
op gezag van de rector magnificus, prof. dr. W.B.H.J. van de Donk,
in het openbaar te verdedigen ten overstaan van
een door het college voor promoties aangewezen commissie
in de Aula van de Universiteit
op woensdag 15 november 2023 om 14.00 uur
door

Tom Iepe Bootsma,

geboren op 13 mei 1983
te Leeuwarden.

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The work presented in this thesis was carried out within the Helen Dowling Institute, Center for Psycho-Oncology, Bilthoven, The Netherlands.

This PhD research was funded by a grant from the Dutch Cancer Society (KWF Kankerbestrijding, grant number 10761) and Maarten van der Weijden Foundation, The Netherlands.

Financial support for the printing of this thesis was kindly provided by Tilburg University.

ISBN 978-94-6483-132-0

Printing: Ridderprint, www.ridderprint.nl
Lay-out: Publiss, www.publiss.nl
Cover design: Debbie Hesseling, The Fat Moose, www.thefatmoose.nl

“The variability is the law of life, and as no two faces are the same,
so no two bodies are alike, and no two individuals react and behave alike
under the abnormal conditions we know as disease”.
William Osler (1849-1919)

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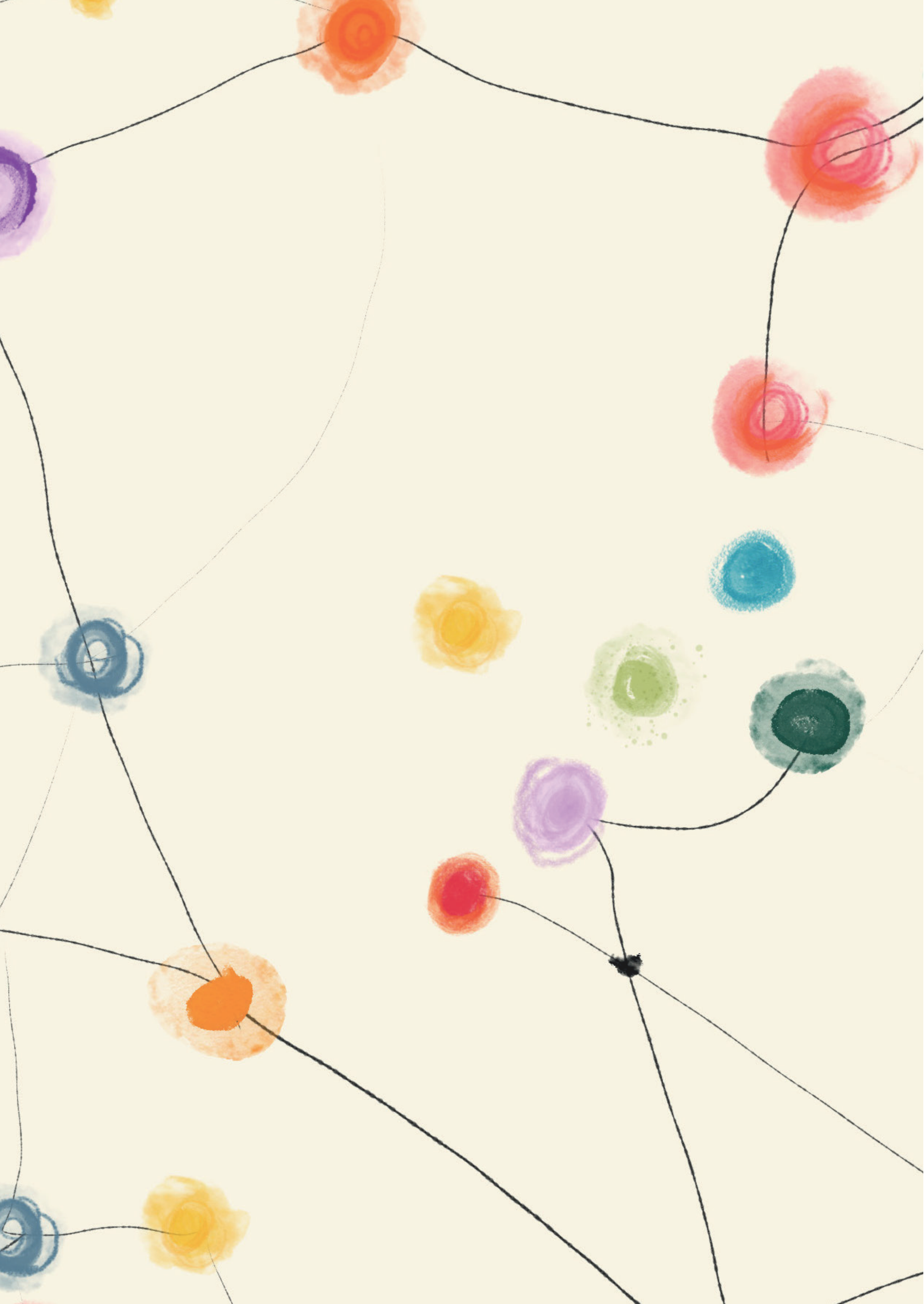


Chapter 1

GENERAL INTRODUCTION

GENERAL INTRODUCTION

Chronic cancer-related fatigue

Fatigue related to cancer and its treatment is the most prevalent and burdensome symptom among cancer patients.[1] The US National Comprehensive Cancer Network defines cancer-related fatigue in their guideline as:

*"*A distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment, that is not proportional to recent activity and interferes with usual functioning*"*.[2]

This experience of cancer-related fatigue and ways of responding can differ between individuals. Cancer-related fatigue can present itself during the cancer trajectory as an early symptom before diagnosis, during treatment, or after finishing treatment.[3,4] These intra-individual differences in cancer-related fatigue experiences and responses warrant a personalized treatment approach.

This thesis is part of the REFINE project. The REFINE project aims to take a person-centered approach to personalize psycho-oncological care for patients with chronic cancer-related fatigue (CCRF). In my thesis, I adopt the term CCRF for severe fatigue that is persistently present for at least three months after completion of the curative cancer treatment.[5] Although six months is often retained in research to define this chronic form of fatigue, I will use three months in this thesis as the lower limit. It seems better to start treatment for CCRF as soon as possible and prevent long-term and disabling problems. In this thesis, CCRF is approached as 'an illness of its own rights' related to the post-cancer experience.[6] Because of this central approach, this study involves an investigation of lived experiences of CCRF from a first-person perspective, which means through 'the eyes of the patient' in the context of the cancer experience. My thesis focuses on the patients' perspectives of experiencing and responding to CCRF to help therapists to use a person-centered approach to personalize psycho-oncological care.

The pathogenesis of CCRF remains inconclusive and probably involves several physiological and biochemical systems. The different hypothesis of underlying biological mechanisms originate from the central or peripheral nervous system and include cytokine dysregulation, hypothalamic-pituitary-adrenal (HPA) axis dysregulation, alterations in energy (ATP=Adenosine Triphosphate) and muscle metabolism.[1,3,7] One important example of an underlying mechanism related to the central nervous system is 'sickness behavior', which presents as co-occurring symptoms such as pain, sleep problems, lethargy, mood, and cognitive problems experienced during cancer treatment. This behavior is supposed to preserve energy to fight illness and promote healing process. This adaptive response to inflammation is activated through cancer and its treatment via cytokine signaling in the central nervous system. This neuroinflammation or cytokine dysregulation can become maladaptive and result in persistent CCRF.[3,8,9] However, these biological factors, for example inflammatory biomarkers associated with fatigue are not tested in clinical practice and/or utilized as targets in personalization of treatment for CCRF.[10] I will not further elaborate on the pathogenesis of CCRF because this thesis focuses on patients' experiences.

The scale of the problem

To gain more insight into the scale of this problem, we need to have a global estimation on how many cancer patients suffer from cancer-related fatigue and what life domains are involved. Therefore, I will first present some worldwide and national cancer statistics on incidence, prevalence, and survival rates. Secondly, I will zoom in on who will seek help with a referral to Dutch psycho-oncological care. Thirdly, I will present the average prevalence rates of different forms of cancer-related fatigue. Lastly, I will elaborate on the impacted life domains of CCRF.

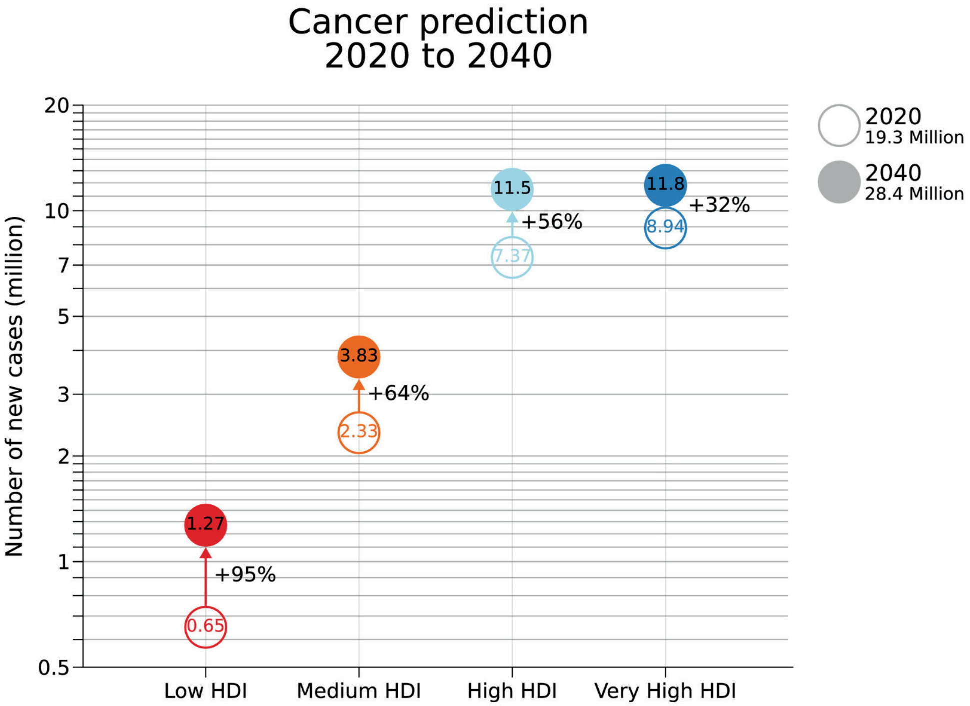
As the cancer population increases in the upcoming years, many more patients will suffer from cancer-related fatigue. **Figure 1** shows the burden of cancer with 19.3 million new cancer patients diagnosed in 2020 globally based on a human development index of different countries (i.e., a measure of human development: health, knowledge, and standard of living). In 2040 an increase of 47% with an estimated 28.4 million new cases is expected. In 2020 50.6 million cancer patients were alive worldwide with a diagnosis since 2015.[11]

In the Netherlands, 113,656 new cases were diagnosed in 2020 and the incidence is increasing because of population growth and ageing (**Figure 2**). **Figure 3** shows five-years prevalence of cancer in the Netherlands. In total 385,614 cancer patients were alive in 2020 who had a cancer diagnosis since 2015.[12] The five-year survival rates differ worldwide for different types of cancer and have overall increased up to 66% (diagnosis between 2011-2020) in the Netherlands in the past decades.[11,12]

The majority of cancer patients during or after cancer treatment (mean time since diagnosis: 37 months) who seek help with a referral to psycho-oncological care in the Netherlands experience a combination of fatigue, anxiety, and depressive symptoms.[13] Compared to the total Dutch cancer population, these patients are more often younger (mean age: 51 years old), female, and diagnosed with breast cancer.[13] Other characteristics of cancer patients who seek psycho-oncological help for their problems are highly educated, in a relationship, and having a paid job.[13]

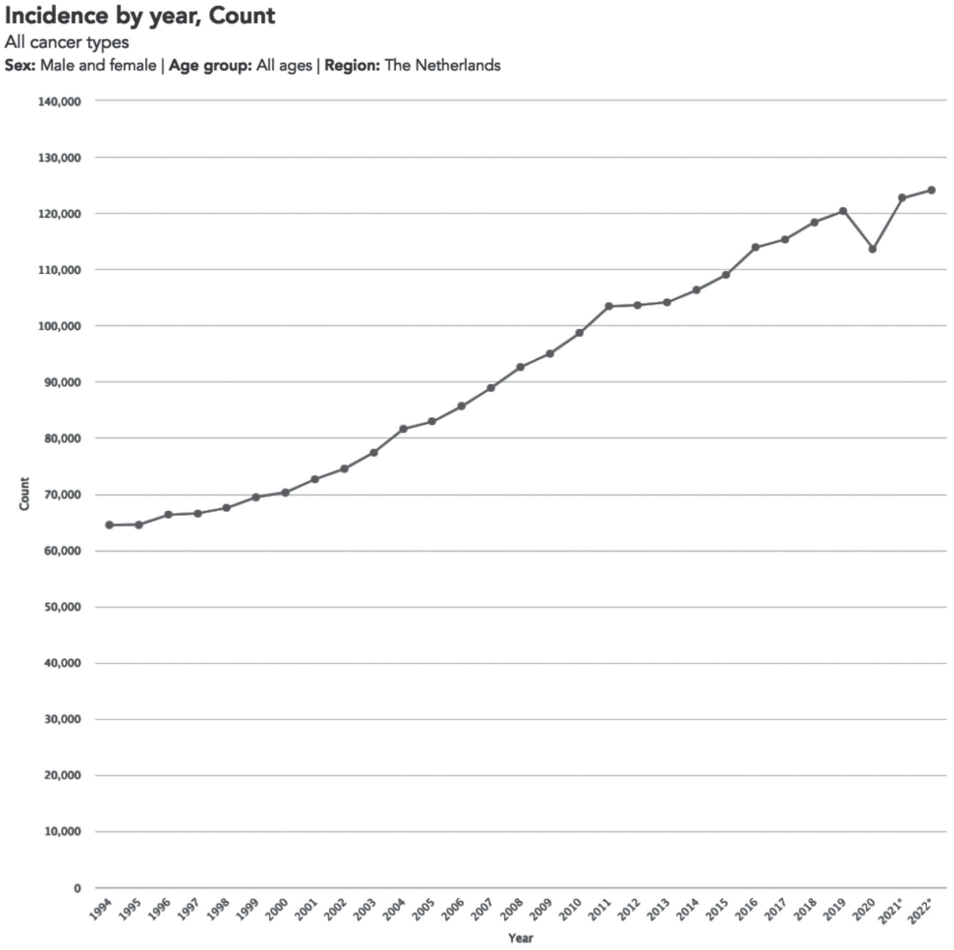
The prevalence rates of cancer-related fatigue vary across different types of cancer, treatment, and measurement method.[1,14] On average 40% of cancer patients report fatigue for the first time before diagnosis.[7,15] A larger patient group with prevalence rates between 80-90% suffer from increasing fatigue during active cancer treatment.[7,15–17] In two large multicenter studies approximately 20% and 29.2% of patients report severe fatigue undergoing active cancer treatment.[18,19] At least 25% of cancer patients still experience persistent severe fatigue, defined as CCRF, months to several years after cancer treatment.[20–22]

Figure 1: Burden of cancer worldwide in 2040



Projected Number of New Cases for All Cancers Combined (Both Sexes Combined) in 2040 According to the 4-Tier Human Development Index (HDI). Source: GLOBOCAN 2020.[11]

Figure 2: Incidence of cancer in the Netherlands



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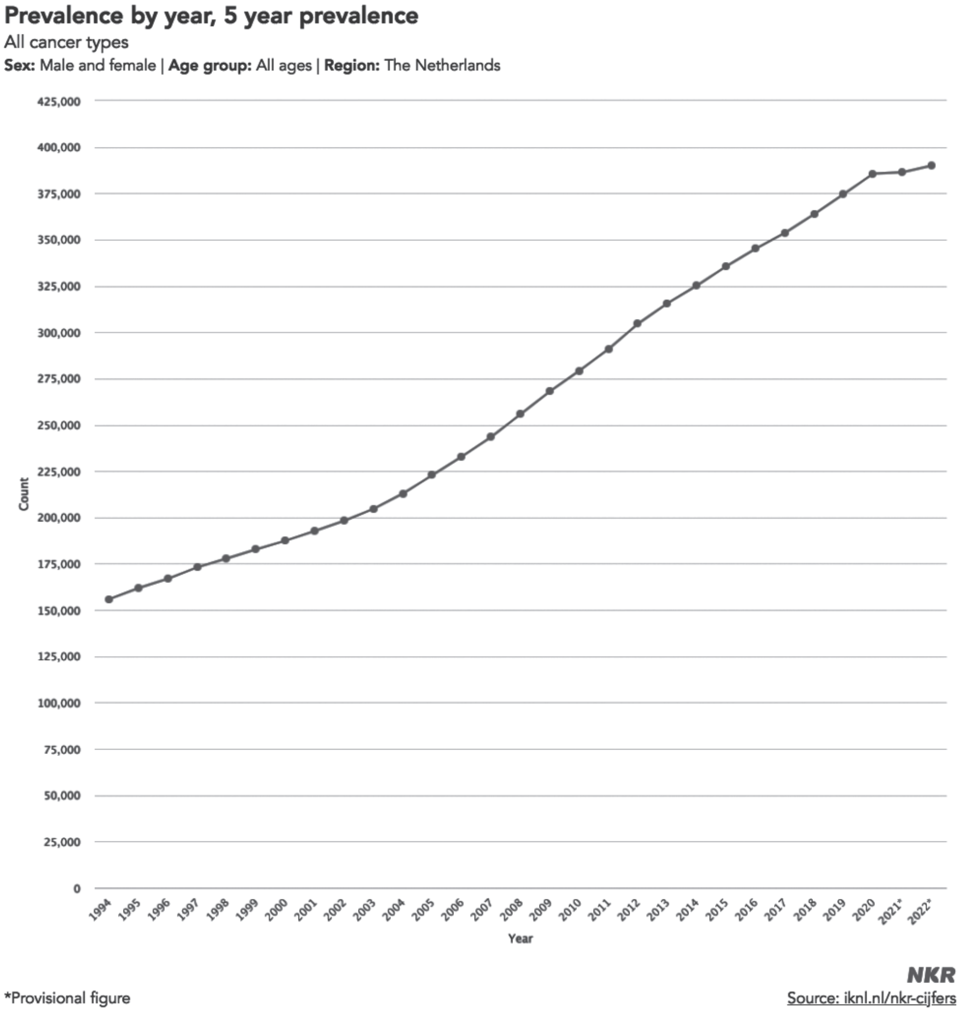
Source: iknl.nl/nkr-cijfers

Figure 3: Prevalence of cancer in the Netherlands



CCRF negatively impacts patients' daily lives and has different physical, emotional, cognitive, social, and economic effects.[23] Daily life activities such as walking, doing household chores, shopping, and preparing meals are more difficult because of experiencing CCRF.[21,23,24] Patients and their family members both experience anxiety and stress because CCRF causes inabilities to function, socialize, and practice enjoyable activities.[24,25] Many patients with CCRF experience a need to push themselves to do things, diminished motivation and interest in activities, and negative feelings.[23,24] Cognitive activities are more difficult because of concentration and memory problems.[23] The experience of CCRF also affects social activities and relationships because going out and spending time with friends is not always possible.[21,23,24] CCRF has a negative impact on the workability of patients and their caregivers.[23,26] The occupational effects patients with CCRF and their caregivers experienced are accepting fewer responsibilities, reducing working hours, and taking days off. Some patients and caregivers stopped working, went on disability or used unpaid family or medical leave time.[23] The growing group of patients that experience CCRF might also have a negative economic impact because of the expected increased medical and societal costs.[27] Due to the disruption of different physical, psychological, social, and spiritual aspects of wellbeing, the quality of life of patients with CCRF decreases.[24,28–30] In addition, a possible negative impact on survival, recurrence and mortality rates of cancer patients that suffer from CCRF is reported, which indicates the need for timely recognition and suitable treatment of CCRF.[31,32]

Difficulties with screening and diagnosis of CCRF in clinical practice

Despite the fact that CCRF is a common and disabling problem, in daily practice this problem is frequently overlooked and therefore patients with CCRF are under-reported, under-recognized, and under-treated by health professionals.[2,33] Health professionals use different unidimensional and multidimensional questionnaires with different subscales and timescales to measure the subjective experience of CCRF because there is no objective measure available.[34,35] According to clinical practice guidelines, cancer patients should be screened for fatigue and ability to carry out daily activities regularly during and after treatment by a clinical nurse specialist.[7]

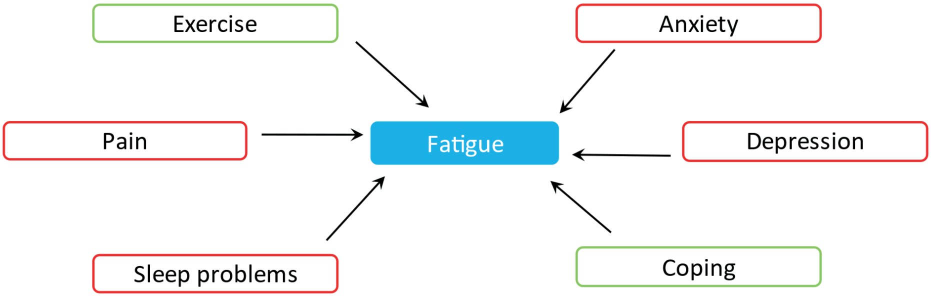
In 1998 a multidisciplinary workgroup named Fatigue Coalition proposed specific diagnostic criteria to define cancer-related fatigue as a syndrome of different symptoms: reduced energy, extra need to rest that is not in proportion to changes in activity level, and co-occurring physical, emotional and cognitive symptoms.[36] These symptoms are continuously or recurrently experienced and cause significant distress or impaired functioning in different areas. Fatigue is related to cancer or its treatment and has no other primary cause. For example, severe psychiatric comorbidity (e.g., major depressive disorder), or other diseases treatable with medication were excluded. Although these diagnostic criteria were evaluated as reliable and valid in a systematic review, in clinical practice, they remain under-utilized, and further research is needed to investigate their reliability.[37]

Another problem in clinical practice is that patients conceal their experiences in communication with their health professionals because of several unrealistic and negative beliefs about suffering from CCRF.[6,16] In the qualitative study of Penner, one patient reported CCRF as "a silent cry".[38] Patients may under-report CCRF because they belief it is an expected symptom that is untreatable.[39,40] Another belief patients have is that they will be seen as 'a complainer' and they avoid talking about CCRF: "I'm not complaining because I'm alive".[6] Patients can also keep silent because they belief that CCRF is a sign of recurrent or advancing disease and will interfere with the cancer treatment.[25,39] Health professionals may feel uncomfortable and not ask patients about CCRF because of different reasons such as lack of knowledge about effective and available treatments and time pressure in consults.[16,25,33,41] Differences may exist between patients' and health professionals' estimation of the impact of fatigue on quality of life. For example, health professionals may expect pain to have more impact than fatigue and underestimate the negative impact on quality of life. However, patients experience profound impact on daily life and functioning of CCRF in comparison with other cancer-related effects.[25]

Protective and risk factors of CCRF

Several factors, including protective and risk factors, could influence the severity of the experience of CCRF. Longitudinal studies reported that the experienced severity of CCRF varied over time and showed that fatigue that starts during treatment is the strongest predictor or risk factor for experiencing CCRF.[20,42–44] Studies from different disciplines (e.g., medical, epidemiological, behavioral, psychological, and neuroimmunology) investigated risk and protective factors for CCRF in a group of cancer patients. Researchers of these studies reported mixed evidence for the percentage of variance attributed to one or more individual risk factors and protective factors of CCRF. These studies often focused on specific physical or psychological risk and protective factors instead of a mix of all relevant factors. **Figure 4** shows an example of how current patient group research conceptualizes CCRF with different physical and psychological risk (i.e., anxiety, depression, pain, and sleep problems) and protective factors (i.e., exercise and coping).

Figure 4: Current conceptualization of CCRF



Less attention in research has been given to protective and behavioral factors that are helpful to respond to CCRF. Patients that adhere to lifestyle guidelines (e.g., weight, smoking, alcohol, diet, and physical activity) experienced less CCRF[45]. The effect of exercise and physical activity on lowering CCRF is most studied among cancer patients.[46–48] Other protective and behavioral psychological factors that help to respond to CCRF are: resilience, positive affect, psychological flexibility, and acceptance of illness.[46,49–51]

Most research focused on risk factors for experiencing CCRF. Several socio-demographic and clinical risk factors are linked to patients' personal or medical history and are not changeable or suitable as potential treatment targets. Although the list below might not be exhaustive, I will sum up potential risk factors for CCRF from previous research:

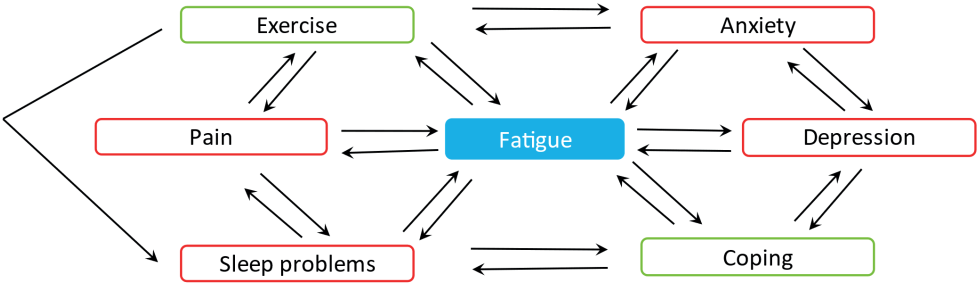
- Socio-demographic risk factors: younger age,[14] females,[14] absence of partner,[14] lower education level,[14] and occupational status (e.g., impaired return to work, work limitations, work output, and lower household income).[26]
- Clinical risk factors: cancer type (e.g., breast cancer and multiple myeloma),[14] shorter time since diagnosis,[14] higher stage of disease,[44,52] chemotherapy,[14,44] combination therapy (i.e., surgery, radiotherapy, chemotherapy with or without hormone therapy),[44] and one or more comorbidities.[14,52]
- Cognitive risk factors: cancer-related cognitive impairments (i.e., memory, executive functions, attention, and processing speed).[53]
- Psychological risk factors: distress (anxiety and depression),[10,30,43,48,52,54] history of childhood adversity,[1,10] history of major depressive disorder,[43] sleep disturbance,[10,20,43,55] maladaptive coping (e.g., fatigue catastrophizing and low self-efficacy),[20,56] negative illness perceptions (e.g., attribute more symptoms to illness and have poorer illness understanding),[57] and poor social support.[58]

- Physiological risk factors: inflammatory biomarkers (e.g., C-Reactive Protein (CRP),[59] IL-6,[59] sIL-6r,[59] IL-1ra,[59] Tumor Necrosis Factor (TNF)α,[59,60] soluble TNF receptor type II[10,59]), high body mass index (e.g., increased body fat and reduced lean mass),[10,60] physical inactivity (e.g., performance fatigability and low peak oxygen uptake),[20,60–62] and physical limitations (e.g., pain or neuropathy).[48,63]

However, previous research focused on different risk and protective factors at a patient group level; CCRF is a complex and multifactorial phenomenon.[3,64] Multiple protective and risk factors or co-occurring symptoms could influence the experience of CCRF.[1,3,7,8,60] These separate symptoms, for example fatigue, pain, insomnia, and depression, could form a 'multiple symptom concept' or 'symptom cluster'.[45,65–67] It is unclear if these factors cause fatigue or fatigue causes these factors, or both.[68] **Figure 5** shows an example of the conceptualization of CCRF as a complex and multifactorial problem. This figure visualizes the possible interrelatedness between different physical and psychological risk (i.e., anxiety, depression, pain, and sleep problems) and protective factors (i.e., exercise and coping).

Other studies identified profiles of cancer patients who experience different levels of CCRF accompanied with moderate distress or different physical activity levels, which further explored the heterogeneity of this patient group.[10,65,69] Future research should align with the complexity, multifactoriality, and heterogeneity of CCRF and use a multidisciplinary approach to look into the individual interconnectedness of risk and protective factors and dynamics over time to identify potential treatment targets.

Figure 5: Conceptualization of CCRF as complex and multifactorial problem



Treatment of CCRF

Up to now, effective behavioral guided interventions are available with specific working mechanisms that focus on treatable risk factors. These educational, psychosocial and physical activity (PA) interventions were investigated among specific patient groups in randomized controlled trials and include:

- Psycho-education focuses on improving the self-management of patients with CCRF to adapt and adjust to their current situation, and learn to recognize and better deal with distress.[70,71] Psycho-educational interventions, such as an activity/rest program can reduce psychological distress, and help to reduce CCRF and increase vitality.[71,72]
- Counseling and informing patients and their caregivers can improve understanding of CCRF, the multiple interacting psychosocial factors, and how to manage it.[71] Patients can learn to develop a personalized activity plan with energy preservation, task prioritizing, activity pacing, and task delegation of less important tasks. These strategies can improve the quality of life and reduce the subjective feelings of CCRF.[73]
- Cognitive behavioral therapy (CBT) is guided by a cognitive-behavioral therapist and addresses (a combination of) unhelpful cognitions, emotions, or behavior to change into helpful strategies to better deal with CCRF.[74,75] This therapy focuses on six factors: coping with cancer, fear of cancer recurrence, dysfunctional cancer-related thoughts and beliefs, sleep dysregulation, activity dysregulation, and lack of social support. Studies showed a clinically significant decrease in fatigue level and functional disability.[75–77]
- Mind-body interventions aim to better deal with stress accompanying fatigue and activity management. Mindfulness-based intervention (MBI) combines meditation techniques that focus on breath awareness, attention, and body awareness with psycho-education, CBT, and yoga exercises. In oncology, among the most used interventions are mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive behavioral therapy (MBCT).[78,79] Yoga is another form of mind-body intervention that uses body poses, meditation and breathing awareness and decreases fatigue severity and psychological distress.[71]
- PA and exercise interventions guided by an exercise professional have shown to be effective in reducing fatigue.[80–83] Walking in combination with aerobic and resistance exercises at home is recommended in patients with CCRF.[71] PA and exercises can have physical and psychological effects on reducing CCRF.

> The direct effects of PA are more muscle strength and better physical fitness to prevent physical deconditioning.[71] The indirect effects are positive feelings, the improvement of the immune system, and sleep.[71]

Multi-modal interventions that combine different aforementioned interventions are possible.[84] The treatments are provided in various modalities (e.g., face-to-face, individual or group, or web-based).[84–87] The use of web-based interventions has advantages for fatigued patients. Because practicing at home spares them from traveling to an institute, they can directly implement the lessons learned into their daily life.[79] Because there is a lack of consensus about the effectiveness of pharmacological and nutrition interventions, these are not yet recommended for patients with CCRF.[71,85]

Towards a person-centered approach to personalize psycho-oncological care for CCRF

Although several effective behavioral treatments are available, patients who suffer from severe CCRF with a devastating impact on their daily life need tailored psycho-oncological care. Randomized-controlled trials showed outcomes for effectivity at a group level instead of an answer to the question of: 'what is effective at an individual level?' Previous meta-analysis of randomized controlled trials showed the overall effects of different interventions on CCRF within specific patient groups. To determine the intra-individual heterogeneity in response to interventions and maximize the effect of an intervention on CCRF, the potential moderating effects of sociodemographic and clinical characteristics needs to be investigated. However, randomized controlled trials often lack power to identify differences in subgroups and meta-analysis lack detailed information on individuals.[83]

Two meta-analyses based on individual patient data investigated moderators of exercise and psychosocial interventions on fatigue and found that beneficial effects were consistent across subgroups based on socio-demographic and clinical characteristics.[83,88] The results of these studies are limited because of the lack of generalizability to other cancer patient populations and the analysis are based on single interactions, whereas these interactions are probably part of a network with multiple interactions between symptoms related to CCRF (See differences between **figure 4 and 5**). This individual symptom network of CCRF (N=1) needs to be explored to find the most effective intervention for the individual. Therefore, a major gap in research is that patients and health professionals both lack information for making a shared decision on what is the most suitable (combination of) treatment for CCRF at a certain moment during their post-cancer trajectory.

Recently, the focus of personalization in oncological clinical practice and research has switched from this aforementioned population-based Evidence-Based Medicine (EBM) toward biology-based Personalized and Precision Medicine (PM).[89] Therapists who use EBM decide on what patient care is needed based on their interpretation of the current best scientific evidence, while clinical intuition and patients' experiences are neglected.[90] Personalization of treatment according to PM is based on the individual genetic make-up and focuses on 'what you are' instead of 'who you are'. Furthermore, the research on underlying (genetic) causes of CCRF focused on genes that activate pro-inflammatory cytokines, which might also be complex to treat.[1] Person-Centered Medicine (PCM) that provides Person-Centered Care (PCC) is defined as: "medicine **of** the person as a whole with all its ill and positive aspects, **for** the person to fulfill the person's life project, **by** the person with clinicians presenting themselves as complete human beings, well-grounded on science and with high ethical aspirations, and **with** the person, family, and clinicians in collaboration as an equal partner". PCM and PCC conceptualize a person within their context, which corresponds with the words of philosopher Ortega y Gasset: "I am I and my circumstances".[90] Scientific evidence in PCM is not neglected but placed in a framework that incorporates personal and contextual factors.[90] To make a shared decision in person-centered psycho-oncological care, we need idiographic qualitative research that further unravels the values, meaning, and context of the subjective and individual experience of CCRF.

In the rest of this paragraph, I will present three gaps in current research on CCRF that will be addressed in this thesis. In the next paragraph, I will focus on the multidisciplinary and idiographic approach used in this thesis and explain how these gaps of knowledge need to be bridged in order to find a person-centered way to personalize psycho-oncological care for CCRF. The three gaps of current research encompass limited qualitative research, conceptual models and case conceptualization of CCRF:

- First, previous qualitative research has mainly focused on interviewing a specific group of patients (e.g., female breast cancer patients) who experienced fatigue during active cancer treatment.[91,92] To better understand the lived experience and habitual responses to persistent fatigue after cancer treatment, CCRF needs to be explored from a broader patient's perspective with a purposively selected sample to arrange diversity.
- Second, previous research has conceptualized CCRF into different models. For example, the biobehavioral model, in which risk factors of CCRF are classified into: predisposing, precipitating, and perpetuating factors.[4] Besides these risk factors for experiencing CCRF, protective factors in what is helpful to respond

to CCRF need to be further investigated. Another conceptual model example is the self-regulation model of illness representations of Leventhal, which addresses cognitive, emotional, and coping factors and how the individual understands CCRF.[93,94] However, these current conceptual models look into the influence of different factors on CCRF. An integrative model is lacking, because the interplay of these factors on each other is not taken into account. Therefore, a multifactorial network model for an individual patient is needed that visualizes how these risk and protective factors interact and could have a different impact on the level and pattern of fatigue over time.

- Third, psycho-oncological therapists, such as cognitive-behavioral therapists experience difficulties with the case conceptualization of CCRF. Therapists report a lack of clinical-relevant knowledge of the complexity and interrelations of the problem. They have to develop a working theory based on a combination of patient and therapeutic perspectives about what is the best treatment for the individual.[95] This theory of the individual patient entails interrelations between emotions, behaviors, cognitions, somatic states, and context to facilitate the personalization of treatment. A disadvantage of case conceptualization is the lack of a gold standard procedure for this complex problem-solving method, which results in low reliability between therapists. This method is also susceptible to recall bias because of the type of questions and the patient's memory determines the information. To improve case conceptualization at the start of treatment for CCRF in psycho-oncological practice, we need new ways of frequently daily measuring CCRF. These measurement methods reduce recall bias and enable using analysis to visualize the interrelated factors in an individual network model.

Idiographic approach

In this paragraph, I will briefly introduce the perspectives, theories, and methods used in this thesis to facilitate the personalization of psycho-oncological care for patients that seek help for CCRF. In the next paragraph, I will introduce the central research question and describe the details presented in the seven chapters of this thesis. In the last paragraph of this introduction, I will describe the research ethics and my role as a researcher.

Multidisciplinary approach

I will first introduce our multidisciplinary research team that consists of five members: Prof. Dr. Jenny Slatman (Professor in Medical and Health Humanities at Tilburg University), Prof. Dr. Marije van der Lee (Professor in Psycho-Oncology at Tilburg University, and Psychological therapist at Helen Dowling Institute), Dr. Melanie Schellekens (Senior researcher in Psycho-Oncology at Tilburg University and Helen Dowling Institute), Rosalie van Woezik, MSc (Research assistant in Psycho-Oncology at Helen Dowling Institute), and me Tom Bootsma (PhD researcher in Psycho-Oncology at Helen Dowling Institute and Tilburg University), who represent philosophical, psychological, medical, therapeutic, qualitative and statistical research backgrounds and have helped me to develop a holistic and broad view on CCRF. During the advisory board meetings with CCRF patient experts, CCRF researchers, psycho-oncological psychological therapists, and psycho-oncological physiotherapists, I had the opportunity to discuss my research proposals and preliminary results and open a critical reflection with these members from different multidisciplinary disciplines.

Phenomenological theories, approach and analysis

This thesis is based on idiographic research methodologies. Idiographic research focuses on the study of the individual with CCRF. As such, it can set the first step in a person-centered approach to personalize psycho-oncological care for CCRF. A qualitative form of idiographic research is the phenomenology of the body. Philosophers Husserl and Merleau-Ponty describe this embodiment theory.[96,97] A phenomenological research approach focuses on how ‘phenomena’ appear to our consciousness instead of the reality of things.[98] This interpretative approach aims to describe the meaning of the individual experiences and include both ‘what patients experience’ and ‘how patients experience it’.[99] Therefore, this phenomenological research approach with openly formulated research questions seems ideally suited to investigate lived experiences and helpful responses to CCRF.

In phenomenological research, several ways of approaching a patient’s body are explored.[100] In a healthy state, a body is absent and disappears from our attention. But if a patient experiences a chronic illness, the body appears as negatively present and a focal point of attention, which is called “dys-appearance” by Leder.[100] Medical professionals have a more instrumental or objectifying view on the patient’s body. Patients can also have this external view of their bodies. However, if a body is “ill” or “impaired” because of a chronic illness such as CCRF, a different view comes to the foreground that involves the internal view of embodiment based on lived experiences. To explore this internal view of different dimensions of the embodiment can facilitate patient-centered care for CCRF.[101]

Furthermore, a phenomenological approach can also illuminate the first-person perspective of what are helpful ways of responding to CCRF with identification of the process of habit formation based on the theory of Husserl and Wehrle.[97,102] From a psychological point of view, habits are repetitive ways of responding which are partially unconscious.[103] After cancer and its treatment patients' daily routines are disrupted through the potential impact of side effects such as CCRF, and the formation of new habits is required. More insight into this habit formation process can also help to provide patient-centered care for CCRF.

These phenomenological theories (e.g., embodiment, dys-appearance, and habit formation) of Husserl, Merleau- Ponty, Leder, and Wehrle were used as a theoretical framework to support the analysis of the qualitative data collected in this thesis. A starting point of this thesis is a meta-ethnography of Noblit and Hare, which was used to move beyond comparative and aggregative analysis and interpret the results of previous qualitative studies on experiencing and responding to CCRF after quality appraisal of the eligible studies.[104] The selection of studies and analysis of this interpretative review was a thorough, structured and careful process. Study selection, quality appraisal, and (part of) the analysis was performed by me and a second member of the research team.

In addition, I performed six semi-structured phenomenological interviews using a topic guide with open-ended questions to explore the lived embodied experiences and helpful responses to CCRF. Patients received a summary of their interview afterward, which we used as a member check for interpretation of the results to improve the internal validity.[105] Using the software program MaxQDA, I started the inductive analysis with nineteen interviews of the Fitter na Kanker (FNK) trial that evaluated experiences with two online treatments for CCRF. I followed a stepwise and case-by-case Interpretative Phenomenological Analysis (IPA) of Smith to analyze the complete sample of 25 participants.[106] The inductive analysis process was transparent, iterative, and stopped until saturation was attained. The qualitative analysis of all studies was for twenty percent doubled with a second member of the research team. Differences in coding were discussed until consensus was reached.

The identification of themes of the qualitative phenomenological studies was based on a codebook and discussed with our multidisciplinary research team. The final themes were cross-checked for interrelations and with the underlying interview data. I will present relevant quotes in all chapters to support our analysis and show the thick description. The quality criteria for qualitative research were used to present sufficient details in the published papers presented in the chapters of this thesis.[107]

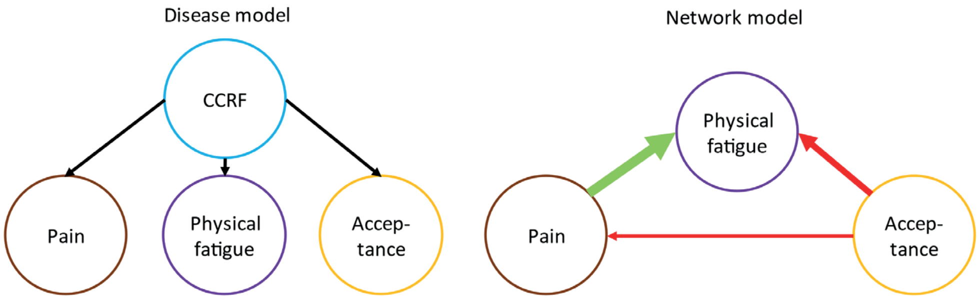
EMA data collection

A quantitative form of idiographic research I used in this thesis is Ecological Momentary Assessment (EMA), also named the Experience Sampling Method or abbreviated as ESM. EMA is a structured diary technique in which a participant receives questions (e.g., about symptoms, affect, and behavior) multiple times a day for multiple days on end in their daily living environment.[108] EMA can be used on a smartphone with notifications to complete a short questionnaire that is temporarily available. The use of EMA in clinical practice has several advantages: insight into prospective ecologically valid data, no recall bias of reporting in-the-moment experiences, it functions as an indicator of motivation to change during treatment, and empowers the patient to be involved in treatment.[108,109]

Network theory

A decade ago, the network theory was applied to psychopathology for the first time.[110] This network theory conceptualizes symptoms (e.g., pain and physical fatigue) and behavioral factors (e.g., acceptance) as interconnected elements of a complex network instead of focusing on one underlying cause as in the latent medical disease model (**Figure 6**). In medicine, a common cause of patients' symptomatology is often identifiable. However, in psychiatry or psychology, this latent medical disease model is less applicable to a mental disorder because of the difficulty in discovering biomarkers as the common cause of the underlying pathogenesis.[111] **Figure 6** shows that in the latent medical disease model one underlying factor explains the experience of CCRF, and interrelations between different factors are not taken into account.[111] The network theory is more in line with how a cognitive-behavioral therapist conceptualizes a mental disorder as systematic causal connections between cognitions, affect and behavior and provides a better fitting model to conceptualize CCRF with its different interacting protective and risk factors.[95]

Figure 6: Differences between disease model and network model of CCRF



The advantage of this theory is that using the corresponding network analysis on EMA data enables visualization of connections in a person-specific network between different, interrelated physical and psychological risk and protective factors. Furthermore, this theory helps to overcome the body-mind dualism, which separates physical and psychological factors.

Person-specific networks of CCRF

A patient's individual network is based on partial correlations between nodes represented as physical, mental, and behavioral factors. The positive or negative partial correlations between these nodes represented as edges in a network can differ in strength and direction.[110] For example, a patient with CCRF experiences physical fatigue because of pain and deals with these symptoms through acceptance. In the person-specific network of **figure 6** is the strongest, positive (green) directed connection visible between physical fatigue and pain, which means more pain results in more physical fatigue. Negative, directed (red) connections are visible between acceptance and pain and acceptance and physical fatigue in the network, which means that acceptance reduces the feelings of pain and physical fatigue. In a conversation with a psycho-oncological therapist, the context and the meaning of the relations between factors in a person-specific network can be further explored. In addition, they discussed how these important factors can be addressed during treatment. The person-specific networks presented in this thesis were analyzed with the software program R by Dr. Melanie Schellekens and Rosalie van Woezik MSc and discussed with the team before presented to patients and therapists.

Case and proof-of-concept study: personalization of psycho-oncological care for CCRF

In this thesis, the smartphone-based EMA data collection during waitlist and providing personalized descriptive and network feedback during psycho-oncological treatment for CCRF were evaluated by patients and therapists. I used a case study and proof-of-concept study design with different qualitative methodologies: cognitive walkthrough, think-aloud procedures, observations, and semi-structured interviews. In these studies, I used data triangulation because I collected data from multiple sources (EMA data, observations, and (think-aloud) interviews) and incorporated patients' and therapists' perspectives to increase the internal validity.[105] Before the start of the proof-of-concept and case study, I performed a cognitive walkthrough to check the procedure of the EMA app installation from a user's perspective and use my feedback to improve the study procedure.[112] The proof-of-concept study design was open for receiving feedback from the participants and improving the development of the EMA app and feedback reports during and after the study. Patients were invited to think aloud when using the EMA app and receiving the personalized descriptive and network feedback reports. Therapists were invited to think aloud when using instructions to interpret the person-specific network feedback of their patients. During these sessions, I listened, observed, and asked open questions. During the first or second treatment session with the patient and therapist the person-specific network feedback was provided, and I was present as observant. Questions of patients and therapists that were raised during the think-aloud sessions were answered in the debriefing.

Additionally, I performed semi-structured interviews to evaluate the use of EMA and personalized descriptive and network feedback reports with patients and therapists. The interviews were translated verbatim and I used the thematic analysis of Braun and Clark to analyze the transcripts case by case with MaxQDA software.[113] The analysis of the first of five participants and their therapist was doubled by a research team member and codes were discussed until consensus was reached. I prepared the process of development of themes by sharing a code book and organized a multi-disciplinary team discussion. The final themes were checked with the underlying data.

Research question and outline of thesis

As I mentioned before in this introduction, this thesis is part of the REFINE project, which combines patient-experiential knowledge with network theory to facilitate case conceptualization of psycho-oncological care for CCRF. The central research question of this thesis is: **in what way(s) can we personalize psycho-oncological care for patients with CCRF?**

To address this research question, **chapter 2** will start with a meta-ethnography of sixteen qualitative studies that provide an interpretative overview of what is knowledge from the patient perspective of CCRF. Indeed, to enhance the personalization of psycho-oncological care we first need to gain a deeper understanding of how (different) individual patients experience and respond to CCRF.

I used the overarching knowledge of the meta-ethnography to develop an interview guide and take the next step to improve the personalization of the psycho-oncological care for CCRF. I performed in-depth interviews to better understand the lived embodied experiences. In **Chapter 3**, I will present an interview study about experiences of 25 diverse participants with severe CCRF (N = 25). In this phenomenological study, I will use a theoretical-philosophical framework to explore how patients experience bodily disruptions of CCRF. These lived embodied experiences of patients could help to unravel the interrelated problems in their preferred wording and select and understand potential treatment targets in a personalized network.

More in-depth insight into the patient perspective of essential elements of responding to CCRF could further help to personalize psycho-oncological care. **Chapter 4** will present the results of a phenomenological interview study with the same mixed sample of 25 individuals that experienced severe CCRF (N = 25). In this interview study, I will focus on how patients respond to CCRF and facilitate adaptation. To target the complete spectrum of behavior during psycho-oncological care, I will illuminate the first-person perspective of responding to CCRF to gain insight into conscious and unconscious habitual processes.

This experiential knowledge of the meta-ethnography (**Chapter 2**) and the phenomenological interview study (**Chapters 3 and 4**) about lived embodied experiences and helpful habitual responses to CCRF were used to develop an EMA app, which we named *Energy InSight*. This name has a double connotation insight and in sight. Patients' and therapists' perspectives are needed to evaluate the usability and feasibility of the EMA app *Energy InSight* for personalization of treatment for CCRF in psycho-oncological practice.

Chapter 5 will describe a proof-of-concept study embedded in psycho-oncological care with five patients (N = 5) with CCRF and their therapists to evaluate the use of the smartphone-based EMA app *Energy InSight* for three weeks during the waitlist and personalized descriptive and network feedback. This explorative study will investigate how patients gain insight into CCRF by filling in the smartphone-based EMA app *Energy InSight* and receiving personalized feedback. In addition, I will evaluate patients' and therapists' perspectives on how these insights into CCRF could improve case conceptualization in psycho-oncological care for CCRF.

Chapter 6 will demonstrate a case study about the usability of providing feedback on moment-level and day-level symptom networks to a patient with CCRF who sought help in a center for psycho-oncology and completed the EMA app *Energy InSight* for 101 days during waitlist time. In this case study, I will provide personalized network feedback to one patient (N = 1) to explore whether this can help personalize psycho-oncological care and gain insight into how symptom dynamics change over time.

Finally, in **chapter 7**, I will summarize the results of this thesis and provide a critical reflection on the main results to put the findings in a broader perspective. Furthermore, I will discuss the methodological issues, implications for future research, and implications for clinical practice.

Research ethics and role of researcher

In the last paragraph of this introduction, I will describe the processes of ethical approval, patient consent, data collection, storage, and publishing. In addition, I will reflect on my role as a researcher and how I prepared conducting qualitative research of this thesis.

Ethical approval and patient consent

The three studies (i.e., interview, case, and proof-of concept study) presented in this thesis were approved beforehand by an ethical review board. The meta-ethnography did not need approval because I used data of previous qualitative studies. I have purposively selected participants to create a sample of patients with severe CCRF and differences in age, gender, relationship, cancer type, and (time since) treatment. Most participants were recruited at the Helen Dowling Institute (HDI), center for psycho-oncology after the consent of the treating psycho-oncological therapist. For the interview study, interview data of the FNK trial were re-analyzed, which was possible because participants had consented for using data in future research. Kanker.nl and some regional health professionals have assisted in recruiting participants with CCRF for the interview study of **chapters 3 and 4**. I have approached patients by telephone or e-mail and asked if they would like to receive a patient information sheet about the study. I explained participation is voluntary and has no impact on their treatment. After I received informed consent of the participant and the eligibility criteria were checked, patients were assigned a study number, and data collection started.

Data collection, storage, and publishing

The Fatigue Severity subscale of the Checklist Individual Strength (CIS-FS) was used to measure and monitor the fatigue level because this is a routine measurement in psycho-oncological care of the HDI. The cut-off for severe fatigue is 35 or above.[114] The paper-based informed consent forms and questionnaires with socio- and clinical demographics and fatigue/distress scores with a study number are securely and confidentially stored at the HDI in Bilthoven for ten (i.e., interview study) to fifteen (i.e., case and proof-of-concept study) years after the last paper of the REFINE project is published. All electronic data collected as part of this thesis and the key that identifies the participants with a study number are securely saved in study data packages on the HDI server. This study data are saved for ten (i.e., interview study) to fifteen (i.e., case and proof-of-concept study) years after the last paper of the REFINE project is published according to the regulations of Tilburg University. The interviews are not available publicly because the eligible patients consented that their data would be stored securely and confidentially. I used pseudonyms for patients in the interview study and in the tables of patients' and therapists' characteristics used in the studies, they are not recognizable as individuals. All papers presented in the chapters of this thesis were published open access and we pre-registered the data-analysis plans of the person-specific networks on Open Science Framework (OSF).

Reflection on my role as a researcher and preparation of conducting qualitative research

In qualitative research, the perspective of me as a researcher plays an important role in interpreting and analyzing the results. Because this thesis consists of qualitative research, I have to reflect on my role as a qualitative PhD researcher. I have a medical background and previous experience in qualitative and user experience research in the field of psycho-oncology. At the beginning of my project, I followed a course on conducting and analyzing qualitative research to become more familiar with interviewing and qualitative analyzing techniques. I learned about open questioning and asking follow-up questions to explore the lived experiences of patients. I used field notes for observations during and after the interviews to bracket my feelings, thoughts, and assumptions as a researcher. This bracketing is helpful to be aware of your position and reflect upon this influence because as a researcher embodied in the field of psycho-oncological research.[115] I will present some examples of field notes I made after the interview with participant Logan (REFINE, M, 61–70 year, >5 years CCRF) and his partner from the interview study (**chapters 3 and 4**):

"He talked a lot about his experiences with fatigue and how he found his ways of dealing with this fatigue".

"His partner is present before and after the interview and tells me that the check-ups in the hospital are still difficult, while he mentions that he gets used to it after ten years".

"He has a bit of crude humor and talks about fellow cancer sufferers ['kankerlijers' in Dutch]. He really enjoyed making jokes during the interview that put me on the wrong foot for a moment".

As a researcher, I adopted as much as possible a phenomenological stance of radical and bodily empathy during the interviews, which means that the experiences and bodily gestures of others are recognized, reflected upon, and appreciated.[115,116] This form of empathy helped me to keep an open mind to explore patients lived experiences and not express my thoughts and interpretations during the interview. During these interviews, I built trust and rapport with the participants to share positive and negative experiences.

At the start of my project, I was present during a treatment session with a therapist, client, and partner at the HDI. I became aware of the emotions that came up during this conversation, which helped me find a way to react to emotions during the interviews. I held a pilot interview with a cognitive-behavioral therapist that treated patients with CCRF at the HDI to test the formulation of the questions of my topic list used for the interview study about lived experiences with CCRF. I learned about the value of a break and moving around for a while during the interviews with fatigued patients.

I interviewed patients at home in their living environment at their preferred time, or if they preferred, they came over to the HDI for the interview. Before the interview, I introduced the purpose of the study and they could always skip a question if they don't want to talk about it or ask for a break at any moment. Sometimes a partner was present during (a part of) the interview. If patients had questions about care for CCRF during the interviews, I referred them to consult one of the therapists at the HDI. I recorded all interviews with two voice-recorders with the consent of the participants, and I removed these recordings after completing the anonymized transcription. The transcription process was supported by two research assistants.

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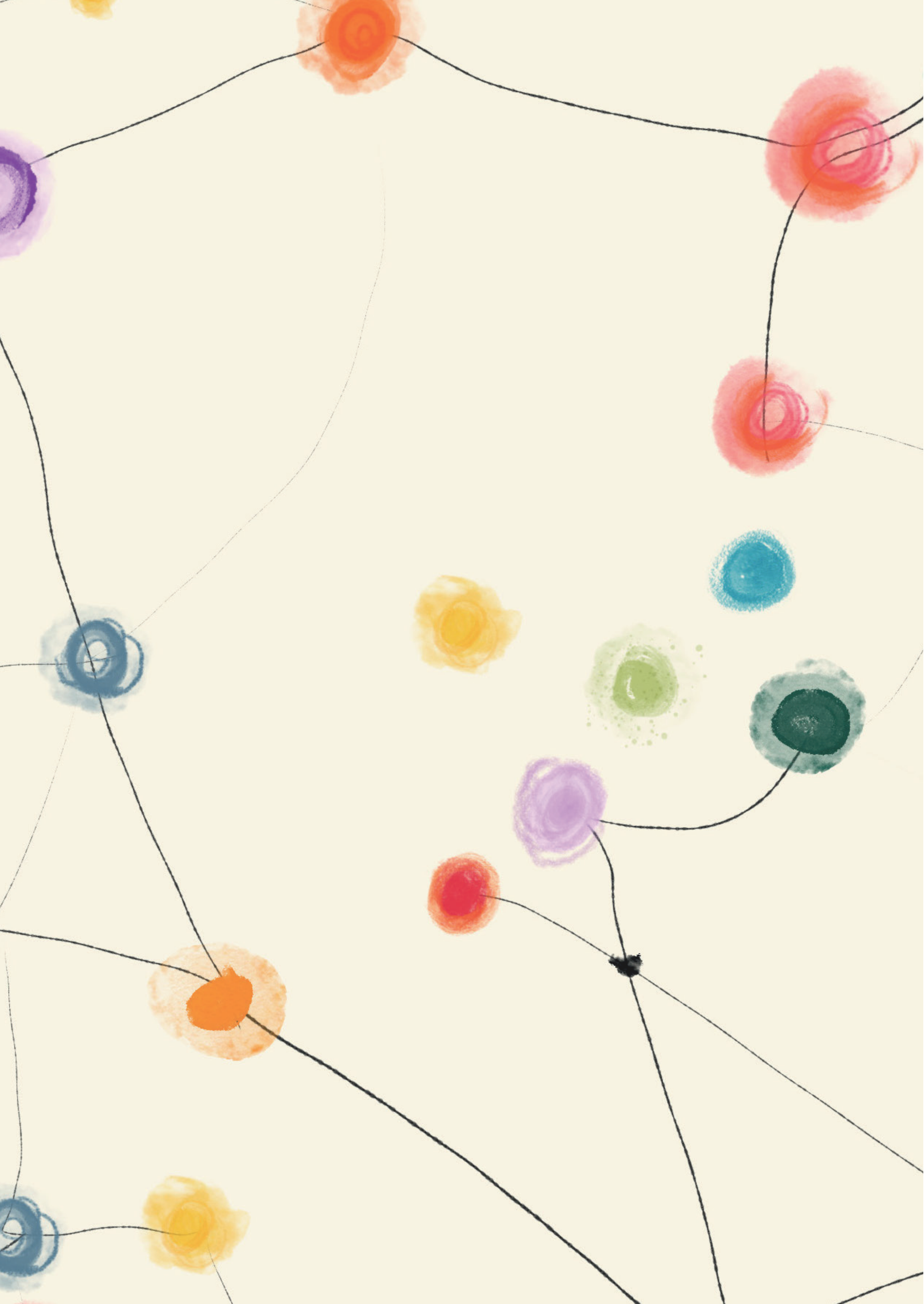


Chapter 2

EXPERIENCING AND RESPONDING TO CHRONIC CANCER-RELATED FATIGUE: A META-ETHNOGRAPHY OF QUALITATIVE RESEARCH

Bootsma TI, Schellekens MPJ, van Woezik RAM, van der Lee ML, Slatman J.
Experiencing and responding to chronic cancer-related fatigue: A meta-ethnography
of qualitative research. Psychooncology. 2020 Feb;29(2):241-250.

ABSTRACT

Objective

One of the most prevalent and disrupting symptoms experienced by cancer patients is chronic cancer-related fatigue (CCRF). A better understanding of the chronic nature of CCRF can provide valuable insights for theory and practice. The purpose of this meta-ethnography was to derive an overarching interpretative narrative on patients' experiences and responses to CCRF.

Methods

We conducted a comprehensive systematic literature search in five databases (05-03-2018). In addition, papers from reference lists were retrieved. Two researchers independently screened the papers for eligibility, and appraised quality (CASP-criteria). We followed the seven phases of meta-ethnography to extract, translate and synthesize first-order constructs (i.e., patients' views) and second-order constructs (i.e., authors' views) from the selected studies into third-order constructs (i.e., new interpretations).

Results

Of the 1,178 collected articles, 16 articles were included. Through synthesis, a new figure of six interrelated third-order constructs was developed: ***(1) embodied experience*** entails the dominating presence of the body; ***(2) (mis)recognition*** includes lack of recognition of CCRF by patients, relatives and health providers; ***(3) small horizon*** describes a resultant narrowed world; ***(4) role change*** encompasses adopting other life roles; ***(5) loss of self*** refers to the impact on one's identity*;* and ***(6) regaining one's footing*** describes the struggle against CCRF, adaptation to CCRF and finally acceptance of a "new normal with CCRF".

Conclusion

A new embodiment figure of CCRF with social (e.g., ***(mis)recognition***), spatial (e.g., ***small horizon***) and temporal dimensions (e.g., ***regaining one's footing***) was developed. This figure can help professionals to recognize CCRF, inform patients and personalize treatment.

BACKGROUND

Fatigue is one of the most prevalent and disrupting symptoms experienced by cancer patients.[1–6] The National Comprehensive Cancer Network (NCCN) has defined such fatigue as "a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment, that is not proportional to recent activity and interferes with usual functioning".[7] In approximately 25% of patients this fatigue is defined as chronic cancer-related fatigue (CCRF), because it persists for months to years after treatment completion.[6,8,9] CCRF is often accompanied by distress, interferes with daily activities and social relationships, and limits patient's quality of life.[10–13] In addition, CCRF is an important public health issue that incurs medical and societal costs.[14,15]

The patient perspective and experiential knowledge of qualitative studies provide a richness and depth that complements quantitative studies.[16] As such, it can help to gain a better understanding of what CCRF entails and to provide insight into how to best treat these patients.[17,18] Several qualitative studies have examined patients' experiences with fatigue in different cancer populations. For example, Levkovich et al. conducted interviews among breast cancer patients after chemotherapy and two main themes emerged: "Being imprisoned in the body of an 80-year-old" and "Family's bear-hug".[19]

Scott et al. (2009) analyzed patients' quotations and published a systematic review of qualitative studies focusing on fatigue across the cancer trajectory.[20] They concluded that patients often describe how fatigue affects their lives, rather than the sensations of fatigue.[20] Moreover, 'tiredness' does not capture the multidimensional character of the patient's fatigue experience.[20] So far, most qualitative reviews[20,21] have focused on experiences of fatigue in the acute phase of treatment, while the long-term chronic nature of this condition has remained less well understood. Therefore, a more detailed and up-to-date description of the chronicity of post-treatment fatigue is required.

Although previous qualitative research on CCRF provided valuable insights, the increasing number of new studies made it difficult for researchers and clinicians to appreciate which insights were most useful for further research or clinical practice. Thus far, qualitative reviews have performed comparative and aggregative analyses.[20,21] In order to personalize treatment for CCRF a more interpretative approach to analyze individual studies is needed. Therefore, we conducted a meta-ethnography to create an overarching interpretative narrative, while maintaining the integrity of the individual studies.[22–25] This meta-ethnography focused on how patients experience and respond to CCRF.

METHODS

Design

This study was based on Noblit and Hare's interpretative and iterative approach for conducting a meta-ethnography, modified with knowledge from practical examples in health care while utilizing the eMERGe guidance for reporting.[24–28] The seven phases used in this approach were followed: 1) formulating the research question; 2) searching and screening studies to decide what is relevant; 3) reading studies to become as familiar as possible with the conceptual content; 4) determining how studies are related through coding and comparing conceptual content; 5) translating the studies into one another; 6) synthesizing the translations; and 7) expressing the synthesis in a figure for use by health professionals.[23,24]

Search method and identification of the studies

Systematic comprehensive literature searches in Pubmed/Medline, EMBASE, CINAHL, PsycINFO and Web of Science were conducted by TB (05-03-2018) (**Table 1** for STARLITE criteria). Studies were included when they met the following eligibility criteria: 1) explored the experiences of adult patients with CCRF post-treatment; 2) used qualitative methodology to analyze data; and 3) were published in English or Dutch. **Table 1** shows exclusion criteria. Studies were first screened on title and abstract (TB and RW individually), followed by full-text screening (TB and MS individually). Discrepancies between selections were discussed until consensus was reached.

Quality appraisal

The selected papers were reviewed individually by TB and MS using the 10-item Critical Appraisal Skills Programme (CASP) checklist to assess whether the results were valid and reliable.[29] While the use of quality criteria is widely debated, we chose this commonly used appraisal tool to gain insight into the content and quality of the current evidence. The intention was not to reach consensus in scores on the CASP questions. The answer to each CASP question was counted by each researcher as fully addressed (3 points), partially addressed (2 points) and not addressed (1 point), leading to a score ranging from 10 to 30.

Data-analysis and synthesis

After reading and re-reading the included papers, first-order (i.e., patients' views on experiences) and second-order constructs (i.e., authors' interpretations of patients' views on experiences) of the selected studies were identified and listed with the help of the software program, MaxQDA 2018 (release 18.1.1). First-order constructs involve patients' understandings (quotes) of CCRF and were extracted from results section of the selected paper.[23,24] Second-order constructs involve the authors' interpretations (themes and concepts) of patients' understanding of CCRF and were usually extracted from the discussion and conclusion sections of the selected paper.[23,24] We created third-order constructs (i.e., new interpretations) by translating and synthesizing these first-order and second-order constructs.

Different constructs between and within studies were compared. As the content showed primarily similarities, a reciprocal translation was applied. Inconsistencies were handled by refutational translation. For example, third-order construct (mis)recognition encompassed both misrecognition and recognition. Thematic analysis started by listing constructs in conceptual categories of the most recently published and conceptually rich paper.[19] TB and RW independently listed the first- and second-order constructs of four different papers.[19,30–32] Subsequently, the construct list of these papers was compared to reach consensus, creating a final list with which the other papers were inductively analyzed. MS supervised this listing process.

Table 1: STARLITE principles applied to literature search

	Criteria	Results
S	**Sampling Strategy**	Comprehensive, Boolean search strategy
T	**Type of studies**	Qualitative study or qualitative research or nursing methodology research
A	**Approaches**	Electronic and reference lists
R	**Range of years**	No date limits (search 05-03-2018)
L	**Limits**	Language (English/Dutch), publication type (peer reviewed journal)
I	**Inclusions and exclusions**	Inclusion: 1) explored the experiences of adult patients with CCRF post-treatment; 2) used qualitative methodology to analyze data (i.e., oral and written descriptions of experiences and/or responses to CCRF); and 3) were published in English or Dutch; Exclusion: 1) patient sample (e.g., exclusively during treatment, exclusively advanced cancer, exclusively other condition (no cancer), children and adolescents, healthcare professionals); 2) other topic (no experiences); 3) methodology (e.g., quantitative study, meta-study, test of model); or 4) article type (e.g., abstract congress, thesis, commentary, brief report).
T	**Terms used**	Boolean search strategy (and/or) with keywords and synonyms: neoplasm or cancer or tumor, fatigue or tiredness and qualitative research for heading, topic, title and abstract
E	**Electronic sources**	Pubmed/Medline, EMBASE, CINAHL, PsycINFO, Web of Science

Group discussions were organized twice with a multidisciplinary team of TB (PhD student, MSc Medicine), MS (Postdoc researcher Psycho-Oncology), RW (Research assistant, Master student Behavioral Science), ML (Senior Researcher Psycho-Oncology and Psychologist treating patients with CCRF) and JS (Professor in Medical Humanities). TB, MS, ML and JS have extensive experience in conducting qualitative research in psycho-oncology. During our team discussions, we reflected on our own position and perspective to diminish bias.

Group discussions were based on merging conceptual categories (subthemes). Patients' experiences and responses to CCRF were approached as a whole and descriptions of temporal changes in these experiences and responses were taken into account. During the last group discussion, we adopted a line of argument synthesis and visualized the relations between third-order constructs (meta-themes) to complete the overarching narrative.[23,24] We cross-checked to determine whether the individual studies fitted these meta-themes.

RESULTS

Searches and study characteristics

The searches resulted in a total of 1,178 articles (**Figure 1**). After deduplication, title/abstract and full-text screening, 1,159 articles were excluded. Concurrence was reached to exclude four extra articles, based on article type (brief report)[33] or deductive qualitative methodology (secondary data-analysis or testing a model).[34–36] Finally, we included 16 studies in the meta-ethnography.[19,30–32,37–48] Study characteristics are summarized in **Table 2**. In total 705 patients, particularly women (29%-100% in reported study samples), were included in these studies. Patients of different ages, cancer types and stages (mainly breast cancer), and treatment phases participated. Four studies compared cancer patients to healthy subjects[39,40] or other patient groups.[38,41] Data of healthy subjects and other patient groups were excluded from analysis. Some studies were part of larger projects[31,44,45] or did not have qualitative data collection methods (e.g., blogs).[31,44,47,48] Quality appraisal by CASP criteria resulted in varying quality (scores 16-28 points) **(Table 3)**. All studies clearly described the aims of the research, and rationale for the qualitative methodology.[19,30–32,37–48] The majority, however, did not adequately consider the relationship between authors and participants.[31,32,37,39–47] None of the studies were excluded based on quality appraisal.

Figure 1: Flow diagram study selection

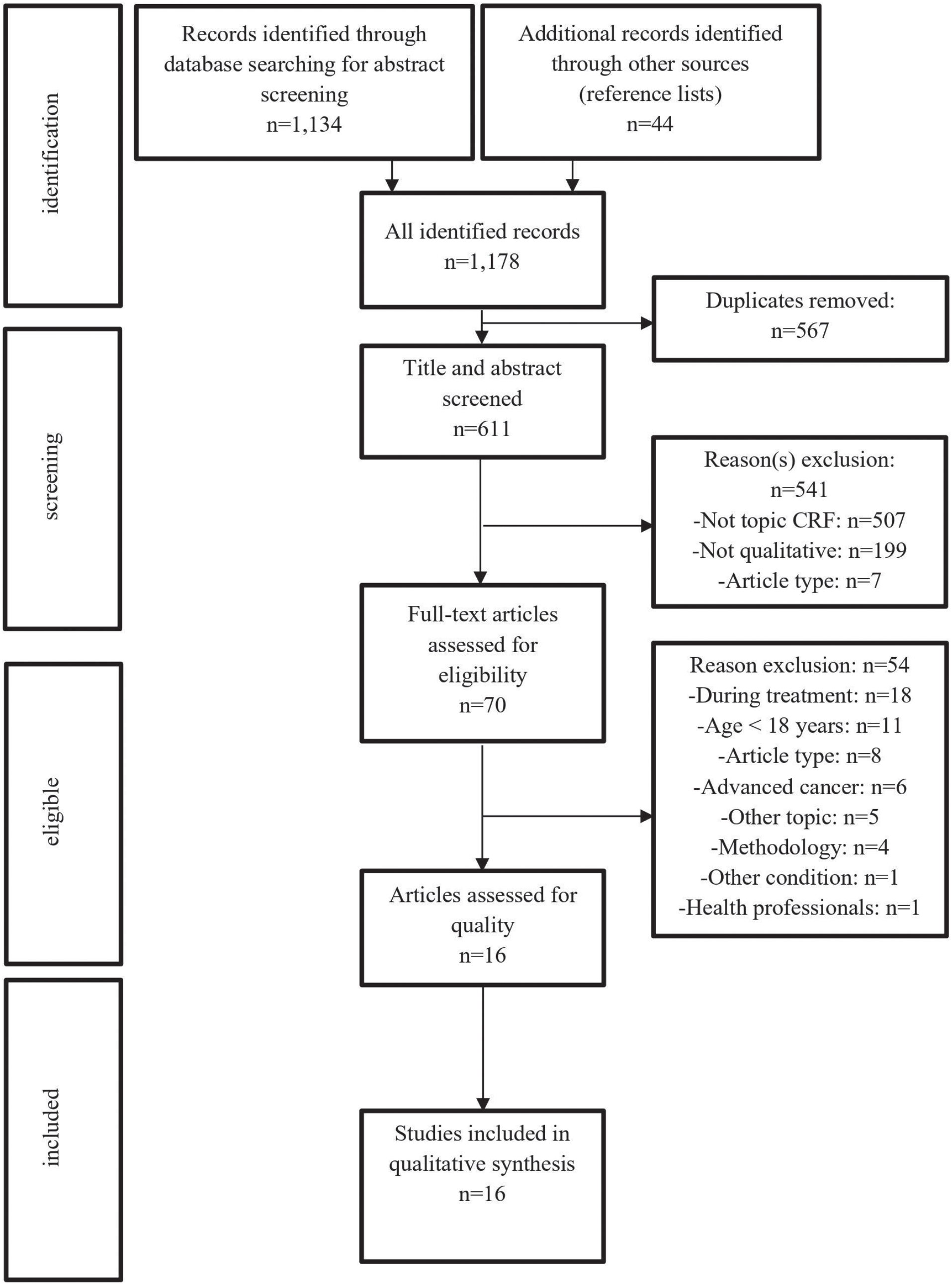


Table 2: Summary of study characteristics

Study	N (% females)	Age (range/SD)	Cancer type (stage)	Treatment	Treatment phase (time since diagnosis/ treatment)	Methods	Theoretical framework	Analysis	Aim
Glaus et al. (1996) Switzerland	20 (45%)	66 (42-81)	Mixed (14 different cancer types) (progressive/stable)	Chemo- and other therapy	On/post(†)	Interviews	Grounded theory	Content analysis & constant comparison	Explore fatigue (cancer/healthy subjects) and generate theory.
Pearce & Richardson (1996) UK	6 (†)	† (†)	† (†)	Chemo-therapy	On/post(†)	Interviews	Phenomenology	Method of Giorgi (1975)	Understand and describe the meaning of fatigue.
Ream & Richardson (1997) UK	9 (88%)	50 (29-59)	Breast, colon, non-Hodgkin's lymphoma, breast, rectal (metastasis yes/no)	Chemo-, radio-, therapy	On/post (>3 months since diagnosis)	Interviews	Phenomenology	Method of Moustakas (1994)	Capture a detailed description of fatigue (cancer/ chronic obstructive airways disease).
Holley (2000) USA	17 (29%)	59 (36-75)	Breast, head & neck, Non-Hodgkin's lymphoma, colon, non-small cell lung cancer, melanoma, gastro-eso-phageal, acute lymphocytic leukemia, squamous cell perineum, squamous cell tonsil (stage I-IV)	Chemo-, (high dose) radio-, bio-, therapy and peripheral stem cell transplant	On/post(†)	Interviews	Symbolic interactionism	Content analysis	Describe the experiences of fatigue, the common meanings, and the impact on patients' lives.

Study	N (% females)	Age (range/SD)	Cancer type (stage)	Treatment	Treatment phase (time since diagnosis/ treatment)	Methods	Theoretical framework	Analysis	Aim
Ream et al. (2003) UK/ Switzerland	15 (60%)	59 (46-73)	Breast, bowel, ovarian, lung, stomach, multiple myeloma, prostate (†)	Chemo- and other therapy	On/post(>1 year since diagnosis)	Focus groups	Thematic framework	Framework analysis	Explore patients' views on the current resources on the management of fatigue and providing recommendations for future development.
Gledhill (2005) France	24 (42%)	56 (38-78)	Mixed (local, regional and metastasis)	†	On/post (>3 months since diagnosis)	Interviews	Grounded theory	Thematic analysis	Explore differences in the representation of fatigue (cancer/ healthy subjects); identify the concepts, dimensions and terminology of (C)CRF and fatigue in healthy persons; examine strategies used in illness and health to overcome fatigue.

Study	N (% females)	Age (range/SD)	Cancer type (stage)	Treatment	Treatment phase (time since diagnosis/ treatment)	Methods	Theoretical framework	Analysis	Aim
Bennet et al. (2007) Australia	16 (100%)	56 (43-71)	Breast (stage I-II)	†	Post (>6 months since treatment)	Focus groups	Grounded theory	Multistage process: coding of symptom concepts; interpretation of data and axial coding	Describe characteristics of fatigue (cancer/ CFS).
Rosman (2009) The Netherlands	12 (100%)	46 (25-62)	Breast, Hodgkin's lymphoma, colon, non-Hodgkin's lymphoma, multiple myeloma, brain tumor (metastasis yes/no)	Surgery, chemo-, radio-, therapy, marrow bone trans-plantation	Post (>7 years since diagnosis)	Interviews	†	Thematic analysis	Describe how the symptom can be experienced as problematic and detail coping strategies that individuals use to live with it.
Tsai et al. (2010) Taiwan	15 (100%)	70 (65-82)	Breast (†)	Chemo-, radio-, hormonal therapy	On/post (>6 months since diagnosis)	Interviews	†	Content analysis	Explore fatigue experiences of older Taiwanese women.
Borneman et al. (2012) USA	252 (†)	60 (†)	Breast, lung, colon, prostate (stage I-IV)	†	On/post (>2 months since diagnosis	Open-ended question-naire	†	Content analysis	Describe patients' perceptions of the causes, relief, related symptoms, meaning, and suffering secondary to fatigue.

Study	N (% females)	Age (range/SD)	Cancer type (stage)	Treatment	Treatment phase (time since diagnosis/ treatment)	Methods	Theoretical framework	Analysis	Aim
Pertl et al. (2014) UK/Ireland	73 (80%)	51 (SD=11.5)	Breast, ovarian, lymphoma, leukemia, prostate, colon, lung, sarcoma, gastric, cervical (†)	†	Post (M=3 years and 4 months since treatment (SD=22 months))	Open-ended questionnaire	Pluralist approach Willig (2012); realist approach, social constructionist discourse analytic approach	Inductive thematic analysis, critical and Foucauldian discourse analysis,	Examine factors that contribute to the absence of a discourse of fatigue.
Cordero et al. (2015) USA/ Mexico	39(†)	†(†)	Breast, prostate (early/late stage)	†	On/post (>6 months since treatment)	Focus groups	†	Content analysis	Examine how Latino patients experience fatigue (cancer/prior to diagnosis).
Watson & Van Kessel (2016) New Zealand, Australia, USA , Pacific Islands	15 (73%)	34 (21-54)	Breast, Hodgkin's lymphoma, appendix, prostate, testicular, soft tissue sarcoma, osteo- sarcoma, non-Hodgkin's lymphoma (†)	†	Post (>9 months since treatment)	Online blogs	†	Thematic analysis	Explore fatigue via online blogs, with a focus on their experiences and personal explanations of fatigue.
Hodge et al. (2016) USA	132 (72%)	† (†)	† (†)	†	Post(†)	Focus groups	Grounded theory	Constructivist grounded theory techniques	Explore the experience of fatigue of American-Indian cancer survivors in the Southwest.

Study	N (% females)	Age (range/SD)	Cancer type (stage)	Treatment	Treatment phase (time since diagnosis/ treatment)	Methods	Theoretical framework	Analysis	Aim
Hagan et al. (2017) USA	47 (100%)	57 (32-73)	Ovarian, fallopian or primary peritoneal (recurrent disease)	†	On/post(M= 45.10; SD=37.79 months since diagnosis)	Symptom care plan	†	Descriptive content analysis	Describe cancer patients' goals and strategies for managing fatigue along with the process of individualizing both.
Levkovich et al. (2017) Israel	13 (100%)	52 (34-67)	Breast (stage I-III)	Surgery, chemotherapy	Post (>1 month since treatment)	Interviews	Phenomenology	Conventional content analysis	Explore the experience of fatigue, its effects, ways of coping and the role of family and social support.

†: missing items were not reported in studies

Table 3: CASP appraisal results

Study	CASP score† (reviewer 1)	CASP score† (reviewer 2)
Glaus et al. (1996)	27	28
Pearce & Richardson (1996)	21	21
Ream & Richardson (1997)	26	26
Holley (2000)	26	26
Ream et al. (2003)	21	20
Gledhill (2005)	18	18
Bennet et al. (2007)	20	22
Rosman (2009)	23	20
Tsai et al. (2010)	28	24
Borneman et al. (2012)	22	17
Pertl et al. (2014)	25	17
Cordero et al. (2015)	20	22
Watson & Van Kessel (2016)	26	22
Hodge et al. (2016)	23	18
Hagan et al. (2017)	25	16
Levkovich et al. (2017)	28	26

†: total sum scores of two authors in separate columns of 10 questions of CASP (question extensively addressed=3 points, partially addressed=2 points, and not addressed=1 point, minimum 10 points and maximum of 30 points. Q1: Was there a clear statement of the aims of the research?; Q2: Is a qualitative methodology appropriate?; Q3: Was the research design appropriate to address the aims of the research?; Q4: Was the recruitment strategy appropriate to the aims of the research?; Q5: Was the data collected in a way that addressed the research issue?; Q6: Has the relationship between researcher and participants been adequately considered?; Q7: Have ethical issues been taken into consideration?; Q8: Was the data analysis sufficiently rigorous?; Q9: Is there a clear statement of findings?; Q10 How valuable is the research?

Meta-themes

The first- (quotes in *italics*) and second-order (themes/concepts in normal font) constructs were translated in six new meta-themes: ***embodied experience*, *(mis)recognition, small horizon, role change, loss of self,*** and ***regaining one's footing*** (**Table 4**). Individuals differed in their experiences and responses. That is, not all individuals had all experiences/responses described in the meta-themes.

(1) Embodied experience

Patients' descriptions of CCRF were embodied, meaning that their experiences were predominated by bodily sensations or bodily symptoms,[38–40,44,45] such as "heavy limbs",[39] "legs like jelly or wobbly legs",[39] "feeling weak"[19,31,45,46] or "paralysis".[42] CCRF was often described as a whole body experience: "the body is worn-out",[39,40,46] "physically exhausted",[19,39,45] “body doesn’t want to go on”[30] or “body cannot heal, nor can it function well”.[46] One patient commented that her body could not carry her:

“It’s like the body can’t … carry you. It’s a real weakness … a bad feeling. And it’s simply … like you don’t have any energy, no energy for anything. Nothing, like you’re … you’re like a zombie; you just sit there … like a couch potato” F (Female), 67 (age), breast cancer (cancer type).[19 (p6)]

While several studies reported cognitive and affective symptoms of CCRF,[19,30–32,38–40,43,45–47] patients often described these symptoms as part of the body. For example, the metaphor *“the brain is out of function”* was commonly used to describe a cognitive sensation of tiredness in the head.[30,40,41]

Consequently, patients reported they became more aware of their bodies in various ways: *“the fatigue takes over every aspect of the body”*;[19] *“the feeling that the body dominated the mind”*;[39] or *“the whole body is shattered”*.[40] Other patients described CCRF as *“the betrayal of the body”* and *“trapped in an old, sick body”*.[19,39,41]

Patients’ experiences revealed that physical and mental symptoms of CCRF are strongly interrelated.[37,39,40,45–47] One patient described this relationship:

“Fatigue is a physical experience but there is also something psychological; if one thinks of being a death candidate, it’s not cheering you up” N/A (Identification Not Available).[40 (p87)]

(2) (Mis)Recognition

As CCRF is invisible, and healthy individuals also experience tiredness, so patients felt it was difficult to explain to others how intense CCRF is.[30,32,37–40,43,44,46,47] Consequently, others did not recognize patients’ experiences:[30,42–44,46,47]

“Because I look so much better than when I was having treatment, people think that I am back to prior fitness” F, N/A.[44 (p153)]

Patients also experienced being misunderstood by their friends and family.[30,43,44,46,47] One patient described how the family failed to remember the fatigue*:*

“My family is pretty good but they can easily forget how tired I can get as this is not obvious” F, N/A.[44 (p153)]

Patients often experienced a conflict between their own needs and the expectations around them.[19,47] Patients felt pressured to cease being sick and move on[44] and as a result, did not feel supported by their family and friends.[19,42,43,47] One patient reported about her unsupportive mother:

"My mum basically accused me of not trying hard enough to get over it" F, N/A.[44 (p156)]

Moreover, in some papers patients indicated that health care professionals did not recognize CCRF.[42,44] Because of a lack of objective medical parameters, health care professionals approached CCRF as a problem with *"no symptoms, no cause and no cure"*.[44] Therefore patients had negative experiences in communicating about CCRF with health care professionals and sometimes had the feeling they were not being heard or taken seriously.[44,45] This was primarily caused by a lack of awareness among health care professionals.[32,44] Patients voiced that for health care professionals CCRF is *"the least worrying side effect"* of cancer treatment, and as a result, *"comes at the bottom of the list"*.[32] This resulted in the management of CCRF being a low priority.[32]

Patients often did not get the right information about what they could expect in terms of CCRF after treatment.[32,44,46] Patients who were informed ahead of time appreciated the information that fatigue was a common experience and were then able to legitimize their fatigue.[32,43] One patient explained how better information improved recognition of CCRF:

"This material has helped a lot, it has given me good advice and especially I felt reassured that fatigue was not absurd or unusual but that others suffer from it as well" N/A.[32 (p105)]

Patients were reluctant to talk about their fatigue in general which contributed to the "misrecognition" of fatigue.[43,46,48] As patients were often not informed about CCRF by health care professionals, they did not recognize their symptoms of CCRF.[19,30,44,46] One patient described the misrecognition:

"*I have not been told that I have fatigue but I seem to be living with it- it varies a lot but I do believe it interferes with my daily life and the sense of needing to 'keep going' because 'it must be all in my head' because I've not really had any diagnosis, and this makes me feel worse when I am tired, because I feel silly"* N/A.[44 (p154)]

As a result of not being informed and prepared by health professionals for experiencing CCRF after cancer treatment, patients had pessimistic beliefs, for example CCRF is: *"untreatable"*,[45] *"inevitable"*,[43,45,47] *"sign of decline in health"*,[30] *"it is a sign of not being successfully recovered from cancer or cancer recurrence"*,[47] *"it indicates the body cannot heal nor function well"*,[46] *"it elicits concerns about survival"*,[31] or *"caused by the unknown"*.[31] Patients felt embarrassed, which further limited their willingness to discuss

CCRF with others.[19,39,43] Patients experienced a gap between expected "life after illness" and reality.[19] Furthermore, patients could lose control of their own story, due to the lack of conceptualization of the CCRF they felt in a "limbo between sickness and survivorship".[44] One patient expected the future to be limited by their fatigue:

"*I've settled in my mind that I'm going to get worse; I expect it to happen gradually, and I expect one of the ways it will show is that I will be more tired than I am now"* N/A.[37 (p114)]

On the other hand, in some studies, patients recognized fatigue as *"abnormal"* and *"pathological"* when it persisted after treatment[39,41,42] and sought medical help.[19,30–32,43–46,48] For some patients CCRF had become "an illness with its own rights".[39,42]

Patients with optimistic beliefs expected a future of normal pre-diagnosis levels of fatigue[37] or convinced themselves to be okay.[32] One patient reported:

"I don't think there's going to be any problem in the future" N/A.[37 (p114)]

(3) Small horizon

The physical, emotional, cognitive, and social consequences and limitations of CCRF resulted in a "small horizon" for some patients. It reduced their freedom and narrowed their scope of abilities. Patients were unable to regain their precancer activity level.[31,37,38,41,43] The various dysfunctions and inabilities included: reading,[39,41] getting out of bed,[19,31] moving,[42,45] walking,[39,40,45] climbing stairs,[39] carrying out household tasks,[38,39] praying,[30] working,[30,32,42] and socializing.[19,30–32,47] Thus, CCRF influences all kind of aspects of daily life and is seen as an "obstacle in daily life".[19,30,37,38,42,44]

These dysfunctions and inabilities were often accompanied by feelings of isolation or nonbelonging.[31,39,44] Patients used the following metaphors to describe their nonbelonging: *"gradual submersion"*, *"drowning*", and *"rising water"*.[39] Some patients wanted to be left alone and face their fatigue by themselves.[19,43,44]

Because of the struggle with dysfunctions and inabilities, the experience of CCRF had a major impact on patients' motivation to do things.[30,38,39,41] This loss of interest in enjoyable things and in life in general[30,38,39,46] contributed to the perception of "small horizon". One woman described this as a state of lethargy:

"*I don't sleep well. I lie awake for hours at night, and in the morning, I drag myself out of bed, straggle around taking endless catnaps, living in a state of lethargy, where just watching the clouds go by is my only interest. No reading, no pleasure in doing anything whatsoever,* *especially all those activities I so loved before I became ill and tired… and in the evening I never feel like going to bed. On the other hand I just fall asleep when and where I shouldn't in the day"* F, 62, leiomyosarcoma uterus.[39] (p299)

(4) Role change

The patients' suffering caused by CCRF interfered with responsibilities in daily life and performing life roles,[19,37,45,46] because of their inability to function normally at home and work.[38,41–43,47] Most patients became dependent upon others, who took over activities.[19,31,39,43] One problem related to suffering from CCRF and becoming dependent was the impact on the family role and family system,[19,30,31,37,41,43,46] which could result in stress and conflicts in families.[19,43] One woman described her role change in becoming a "limited mother":

"*I let go, you know … it's okay. It doesn't mean anything. True, you were used to running things … at first, it's some kind of contradiction, it's … it's a shock. You manage everything, then suddenly you feel … limited. Even your young child is bringing you a glass of water"* F, 43, breast cancer.[19] (p6)

Suffering from CCRF and becoming dependent also affected the partner role.[19,31] In this example the partner was supportive, and the patient was accepting help:

"*I actually felt like I was being led like a little girl … whose father is leading her [by the hand]"* F, 43, breast cancer.[19] (p7)

Partners could also be less supportive or even unsupportive. Patients indicated they experienced no closeness in their relationships, or even failure of marriage.[19,31] One patient described how her partner did not support her:

"He asked me if I could help him with something … I said—Me help you?! You need to help me! How can I help you? I can't … it was really difficult" F, 65, breast cancer.[19] (p7)

Patients' suffering from CCRF and losing their independency had a major impact and caused distress in their social support network.[19,30–32,38,40–44,46] Roles changed from helper to being helped:

"*I'm the type of person, when someone's ill or needy, or a friend needs something … I'm there right away … reporting for duty. Immediately. There's no way that someone needs something and I won't turn the world upside down to help them and … what happened actually, with my illness, is that … it's as if everyone I've ever helped, everyone I've spent time with … came to repay me"* F, 41, breast cancer.[19] (p7)

Furthermore, person's social well-being was disrupted[31] because of their inability to attend activities in community life.[46]

People with CCRF chose to cut back on their workload, to quit work or to retire from their work to have more time for themselves.[30,31,37,42,47] One patient described that suffering from CCRF prevented him from returning to work:

"I was determined to go back to work as soon as I possibly could. I mean I haven't a particularly hard job, but then I did it for a week and just had to, just couldn't do it anymore, and it really shocked me, that I felt so tired, so fatigued...so I think it would probably be quite handy to just make people aware of the fact that even though you are feeling quite well that the fatigue is going to get you, possibly will get you, and may well mean that you can't work" F, N/A.[32] (p106)

(5) Loss of self

People described their change as that from being a healthy person to being a patient with cancer, suffering a different and persistent fatigue compared to the fatigue they experienced precancer.[30] Patients described different feelings related to "loss of self", for example a lack of control,[19,30–32,38,39,44] loss of confidence,[39,41,44] worthlessness,[31,41] indecisiveness,[30,40] and uncertainty about the ability to cope with fatigue.[19,30,31,38–40] Patients also experienced a loss of purpose in life, for example, by losing their career plans.[31,44] In some cases, patients expressed an awareness of the finite nature of life:

"Hanging on to life by a thread of cotton", "walking along the razor's edge" or "along a tight rope" N/A.[39] (p304)

As a result of these feelings, including their small horizon and dependency, patients described a loss of self.[39,44]

"I was completely exhausted and in despair, living in a state of "absence", with regard to myself. My fatigue no longer served as an alert to the gravity of my condition. Rather, I came to tolerate it, unaware of the dangers due to my loss of lucidity. I felt ashamed of my powerlessness to face up to my fatigue, totally lost like a compass unable to find the North" F, 62, leiomyosarcoma uterus.[39] (p310)

Patients grieved for the person they had been and realized they could not go back to their "old self" before the cancer.[37–39,44] One patient quoted:

"I'm obviously not the man I was" N/A.[37] (p114)

Other patients commented on their changes in identity, for example from an active to an inactive person.[30,39,45] A frequently used metaphor for the change in identity, emphasizing the embodied experience of CCRF, was feeling an old sick person inside of them:[19,44,45]

"I feel like I'm in the body of an 80-year-old. That theoretically I know what my capabilities are, but ... in reality ... it's different. It's two different things. You know what you can do. But on the ... on the other hand, you don't. Now, it's ... exactly like an 80-year-old. Every single thing is 'a project'. I cook, I need to sit down and rest. Ten minutes, yes? Prepare something, need to sit down and rest. These are things that ... it's like being trapped in the body of an 80-year-old" F, 34, breast cancer.[19] (p5)

(6) Regaining one's footing

Regaining one's footing involves different successive approaches (struggling, adaptation and acceptance) in the process of finding a "new normal" with CCRF. The individual's perception of fatigue varied according to their personality, vulnerability, ways of coping with stressors, general wellbeing and social support.[31,38,40]

First, several patients described how they struggled against CCRF. They tried to fight it, continued their life roles, tried to fix it, distract themselves and even concealed their CCRF.[19,31,32,40,43–45,47,48] One patient told about her fight against CCRF:

"*I was very tired . . . I was tired, but my goal—my goal was to get through it as fast as I could. I pushed myself, I pushed myself, I pushed myself. Yeah, I was tired. I mean, I would be at work, I would have to put my head down or my sister used to work with me and I would tell her, 'You know what? I'm just going to go take a nap.' But I pushed myself, I pushed myself and I, I never gave up my heels"* F, N/A.[45] (p11)

After a phase of struggling, several patients used more adaptive responses to monitor and pace their activities. Monitoring of activities was used by patients to regain control of CCRF by exercising,[31,39,43,47,48] lifestyle changes,[30,31,43,47,48] keeping a diary,[32,48] or building their lives entirely on their fatigue experience.[42] One patient mentioned changing to a more regular lifestyle:

"*I have a very orderly and structured lifestyle. I don't do anything which has not been planned. Every day I get up at 9 o'clock, I read, I do my shopping; I always eat at 1 p.m. before having a nap until 4, then I watch a bit of TV, I eat at 6, lie down until 8, watch TV with my husband, then go back to bed at 10. It's a very regular life, but it suits me"* F, 62, Non-Hodgkin lymphoma.[42] (p32)

Several patients monitored their CCRF by being vigilant, recognizing and setting boundaries, listening to personal needs and listening to their bodies.[19,39,47,48] One patient explained:

"Fatigue taught me to listen to my body which is now so fragile" F, 48, Acute Lymphoblastic Leukaemia.[39 (p310)]

CCRF patients could pace themselves in different ways. Some patients focused on stopping doing an activity: having a break,[40] sitting or lying down to rest or sleep,[31,39,40,42,45,47,48] resting and waiting for it to pass[19,31,37,39,43] and avoiding physically straining activities.[30,42] Other patients re-shaped their daily lives: living their life day by day,[38,43] planning,[19,30,42,43,48] prioritizing,[19,30,43,48] reorganizing life and work,[19,30,42,43,47] and balancing activities.[19,46] One patient commented on how she lived at a slower pace:

"*If I'm more tired, it's not the end of the world, so I'll rest and do less. It's not the end of the world and it's possible to live at a slower pace than I was used to doing*" F, 60, breast cancer.[19 (p6)]

In this quote a patient reorganized life by quitting work because of CCRF:

"*I was a very active person, and I've gone from a very active life to . . . if I overexert, I'll tire myself out. I can't work for a couple reasons. First, the bank won't let me come back without a full medical release. Second, I wouldn't be able to do the job. You just have to adjust your lifestyle, and try to get the control back"* M (Male), 51, gastroesophageal cancer.[30 (p92)]

Finally, some patients accepted CCRF as a "new normal", by internalizing the current changes, trying to see positive aspects and finding balance.[19,31,37,43,47,48] One patient shared how she changed her attitude to accept her situation:

"*It's all about attitude really ... in altering what you can, accepting what you can't"* N/A.[37 (p114)]

As part of finding an "new normal" patients explored and reframed meaning by naming or assigning a cause to CCRF to give it a place in their life.[30,31,39,44] Some patients were informed by their health professionals to set goals and visualize strategies to overcome CCRF, to legitimize fatigue and get support from their family members.[32,42–44,46,48] One patient described the advantage of legitimization of fatigue:

"It is a matter of legitimisation to experience fatigue as a usual experience" N/A.[32 (p105)]

Table 4: Overview of constructs (first-, second-, third-order) and theme (sub- and meta-)

Third-order construct (meta-themes)	Merging categories (subthemes)	Second-order construct (examples)	First-order constructs (examples)
Embodied experience	Symptoms experienced in (whole) body	Bodily symptoms and sensations predominated[38–40,44,45]	*"Heavy limbs"*[39] *"Legs like jelly or wobbly legs"*[39] *"Feeling weak"*[19,31,45,46] *"Paralysis"*[42]
	Awareness of the body	Whole body experience[19,30,39–41,45,46] Cognitive and affective symptoms as part of the body[19,30–32,38–40,43,45–47]	*"The body is worn-out"*[39,40,46] *"Physically exhausted"*[19,39,45] *"Body doesn't want to go on"*[30] *"Body cannot heal, nor can it function well"*[46] *"The fatigue takes over every aspect of the body"*[19] *"The feeling that the body dominated the mind"*[39] *"The whole body is shattered"*[40] *"The betrayal of the body and trapped in an old, sick body"*[19,39,41] *"It's like the body can't … carry you. It's a real weakness … a bad feeling. And it's simply … like you don't have any energy, no energy for anything. Nothing, like you're … you're like a zombie; you just sit there … like a couch potato"* F, 67, breast cancer.[19] (p6) *"The brain is out of function"*[30,40,41]
	Interrelations of symptoms	Physical and mental symptoms spiral or vicious circle[37,39,40,45–47]	*"Fatigue is a physical experience but there is also something psychological; if one thinks of being a death candidate, it's not cheering you up"* N/A.[40] (p87)
(Mis)Recognition	Social misrecognition	Invisibility[30,42–44,46,47] and difficulty to explain[30,32,37–40,43,44,46,47]	*"Because I look so much better than when I was having treatment, people think that I am back to prior fitness"* F, N/A.[44] (p153)
		Misunderstanding,[30,43,44,46,47] conflict of needs and expectations,[19,47] pressure to move on[44], lack of support friends and family[19,42,43,47]	*"My family is pretty good but they can easily forget how tired I can get as this is not obvious"* F, N/A.[44] (p153)

Third-order construct (meta-themes)	Merging categories (subthemes)	Second-order construct (examples)	First-order constructs (examples)
	Medical misrecognition	Lack of objective parameters[42,44]	*“No symptoms, no cause and no cure”*.[44]
		Lack of communication,[44,45] lack of awareness[32,44] and low priority in management[32]	*“The least worrying side effect”*.[32] *“Comes at the bottom of the list”*.[32]
		Lack of information after treatment[32,44,46]	*“I have not been told that I have fatigue but I seem to be living with it- it varies a lot but I do believe it interferes with my daily life and the sense of needing to ‘keep going’ because ‘it must be all in my head’ because I’ve not really had any diagnosis, and this makes me feel worse when I am tired, because I feel silly”* N/A.[44] (p154)
	Medical recognition	Information provision[32,43]	*“This material has helped a lot, it has given me good advice and especially I felt reassured that fatigue was not absurd or unusual but that others suffer from it as well”* N/A.[32] (p105)
	Self-misrecognition	Lack of reporting[43,46,48] Lack of information[19,30,44,46] Pessimistic beliefs[30,31,43,45–47] Embarrassment[19,39,43] Gap between ‘life after illness’ and reality[19] “Limbo between sickness and survivorship”[44]	*“I’ve settled in my mind that I’m going to get worse; I expect it to happen gradually, and I expect one of the ways it will show is that I will be more tired than I am now”* N/A.[37] (p114) *“untreatable”,*[45] *“inevitable”,*[43,45,47] *“sign of decline in health”,*[30] *“it is a sign of not being successfully recovered from cancer or cancer recurrence”,*[47] *“it indicates the body cannot heal nor function well”,*[46] *“it elicits concerns about survival”*[31] or *“caused by the unknown”*.[31]
	Self-recognition	Recognition[39,41,42] Seek for help[19,30–32,43–46,48] “Illness with its own rights”[39,42] Optimistic beliefs[32,37]	*“Abnormal” and “pathological”*[39,41,42] *“I don‘t think there’s going to be any problem in the future”* N/A.[37] (p114) *“It would be very helpful to have after care on a regular basis to help cope with fatigue. And also awareness campaign so people who don’t have cancer may be able to understand that cancer doesn’t end when chemo ends*” N/A.[44] (p151)

Third-order construct (meta-themes)	Merging categories (subthemes)	Second-order construct (examples)	First-order constructs (examples)
Small horizon	Obstacle in daily life	Unable to live a productive life[31,37,38,41,43] Influences all kind of aspects of daily life[19,30,37,38,42,44]	*Reading,*[39,41] *getting out of bed,*[19,31] *moving,*[42,45] *walking,*[39,40,45] *climbing stairs,*[39] *carrying out household tasks,*[38,39] *praying,*[30] *working,*[30,32,42] *and socialising*[19,30–32,47]
	Isolation and not belonging	Loneliness[31,39,44] Wanted to be left alone and face fatigue by themselves[19,43,44]	*"Gradual submersion", "drowning*", and *"rising water"*[39]
	Loss motivation and interest	Impact on motivation to do things[30,38,39,41] Loss of interest in enjoyable things and in life in general[30,38,39,46]	*I don't sleep well. I lie awake for hours at night, and in the morning, I drag myself out of bed, straggle around taking endless catnaps, living in a state of lethargy, where just watching the clouds go by is my only interest. No reading, no pleasure in doing anything whatsoever, especially all those activities I so loved before I became ill and tired… and in the evening I never feel like going to bed. On the other hand I just fall asleep when and where I shouldn't in the day"* F, 62, leiomyosarcoma of uterus.[39] (p299)
Role change	Family role	Impact on family system[19,30,31,37,41,43,46] Dependency, others took over activities[19,31,39,43] Stress and conflicts[19,43]	"*I let go, you know … it's okay. It doesn't mean anything. True, you were used to running things … at first, it's some kind of contradiction, it's … it's a shock. You manage everything, then suddenly you feel … limited. Even your young child is bringing you a glass of water"* F, 43 breast cancer.[19] (p6)
	Partner role	Impact on partner of being dependent,[19,31] supportive,[19] less supportive and even unsupportive[19,31]	"*I actually felt like I was being led like a little girl … whose father is leading her [by the hand*]" F, 43, breast cancer.[19] (p7) *"He asked me if I could help him with something … I said—Me help you?! You need to help me! How can I help you? I can't … it was really difficult"* F, 65, breast cancer.[19] (p7)

Third-order construct (meta-themes)	Merging categories (subthemes)	Second-order construct (examples)	First-order constructs (examples)
	Social role	Impact on social relationships (distress in social support network,[19,30–32,38,40–44,46] social well-being disrupted,[31] inability to attend community life[46])	*“I’m the type of person, when someone’s ill or needy, or a friend needs something … I’m there right away … reporting for duty. Immediately. There’s no way that someone needs something and I won’t turn the world upside down to help them and … what happened actually, with my illness, is that … it’s as if everyone I’ve ever helped, everyone I’ve spent time with … came to repay me”* F, 41, breast cancer.[19] (p7)
	Work role	Impact on work (cut back on their workload, quit work, retire from work or prevent to return to work)[30,31,37,42,47]	*“I was determined to go back to work as soon as I possibly could. I mean I haven’t a particularly hard job, but then I did it for a week and just had to, just couldn’t do it anymore, and it really shocked me, that I felt so tired, so fatigued...so I think it would probably be quite handy to just make people aware of the fact that even though you are feeling quite well that the fatigue is going to get you, possibly will get you, and may well mean that you can’t work”* F, N/A.[32] (p106)
Loss of self	Feelings of loss	Lack of control,[19,30–32,38,39,44] Loss of confidence,[39,41,44] Worthlessness,[31,41] Indecisiveness,[30,40] Uncertainty in ability to cope with fatigue,[19,30,31,38–40] Loss of purpose in life and future,[31,44] Awareness of finite nature of life[39]	*“Hanging on to life by a thread of cotton”, “walking along the razor’s edge” or “along a tight rope”* N/A.[39] (p304)

Third-order construct (meta-themes)	Merging categories (subthemes)	Second-order construct (examples)	First-order constructs (examples)
	Identity change	No way back to “old self”[37–39,44] Active to inactive person[30,39,45] Feeling an “old sick person” inside[19,44,45]	*“I was completely exhausted and in despair, living in a state of “absence”, with regard to myself. My fatigue no longer served as an alert to the gravity of my condition. Rather, I came to tolerate it, unaware of the dangers due to my loss of lucidity. I felt ashamed of my powerlessness to face up to my fatigue, totally lost like a compass unable to find the North” F*, 62, Leiomyosarcoma uterus.[39 (p310)] “*I’m obviously not the man I was”* N/A.[37 (p114)] “*I feel like I’m in the body of an 80-year-old. That theoretically I know what my capabilities are, but … in reality … it’s different. It’s two different things. You know what you can do. But on the … on the other hand, you don’t. Now, it’s … exactly like an 80-year-old. Every single thing is ‘a project’. I cook, I need to sit down and rest. Ten minutes, yes? Prepare something, need to sit down and rest. These are things that … it’s like being trapped in the body of an 80-year-old”* F, 34, breast cancer.[19 (p5)]
Regaining one’s footing	Struggle against CCRF	Fight it, continued their life roles, tried to fix it, distract themselves, concealed their CCRF[19,31,32,40,43–45,47,48]	“*I was very tired . . . I was tired, but my goal—my goal was to get through it as fast as I could. I pushed myself, I pushed myself, I pushed myself. Yeah, I was tired. I mean, I would be at work, I would have to put my head down or my sister used to work with me and I would tell her, ‘You know what? I’m just going to go take a nap.’ But I pushed myself, I pushed myself and I, I never gave up my heels”* F, N/A.[45 (p11)]
	Adaptation to CCRF	Monitor activities to regain control (exercising,[31,39,43,47,48] lifestyle changes,[30,31,43,47,48] keeping a diary,[32,48] building their lives on their fatigue experience[42])	“*I have a very orderly and structured lifestyle. I don’t do anything which has not been planned. Every day I get up at 9 o’clock, I read, I do my shopping; I always eat at 1 p.m. before having a nap until 4, then I watch a bit of TV, I eat at 6, lie down until 8, watch TV with my husband, then go back to bed at 10. It’s a very regular life, but it suits me*” F, 62, Non-Hodgkin lymphoma.[42 (p32)]

Third-order construct (meta-themes)	**Merging categories (subthemes)**	**Second-order construct (examples)**	**First-order constructs (examples)**
		Monitor CCRF (being vigilant, recognizing and setting boundaries, listening to personals needs and listening to their bodies)[19,39,47,48]	*"Fatigue taught me to listen to my body which is now so fragile"* F, 48, Acute Lymphoblastic Leukemia.[39 (p310)]
		Pacing activities (stopping doing activities: having a break,[40] sitting or lying down to rest or sleep,[31,39,40,42,45,47,48] resting and waiting for it to pass[19,31,37,39,43] and avoiding physical straining activities[30,42])	*"If I'm more tired, it's not the end of the world, so I'll rest and do less. It's not the end of the world and it's possible to live at a slower pace than I was used to doing"* F, 60, breast cancer.[19 (p6)]
		Re-shaped their lives: living their life day by day,[38,43] planning,[19,30,42,43,48] prioritizing,[19,30,43,48] reorganizing life and work,[19,30,42,43,47] balancing activities.[19,46]	*"I was a very active person, and I've gone from a very active life to . . . if I overexert, I'll tire myself out. I can't work for a couple reasons. First, the bank won't let me come back without a full medical release. Second, I wouldn't be able to do the job. You just have to adjust your lifestyle, and try to get the control back"* M, 51, gastroesophageal cancer.[30 (p92)]
	Acceptance of CCRF	Internalizing current change in situation, trying to see positive aspects and finding new balance, change attitude[19,31,37,43,47,48]	*"It's all about attitude really ... in altering what you can, accepting what you can't"* N/A.[37 (p114)]
		Explore and reframe meaning (naming or assigning a cause to CCRF to give it place in their life,[30,31,39,44] set goals and visualize strategies to overcome fatigue, legitimize fatigue and get support from family members[32,42–44,46,48])	*"It is a matter of legitimisation to experience fatigue as a usual experience"* N/A.[32 (p105)]

Third-order construct (meta-themes)	Merging categories (subthemes)	Second-order construct (examples)	First-order constructs (examples)
Relations of meta-themes (embodied experience, (mis)recognition, small horizon, role change, loss of self, regaining one's footing)			*"I am at the age where people around me go out, party and have fun all the time. That's what college students do! ..... but I can't. Nobody understands that"* N/A.[47] (p4) (role change, small horizon and misrecognition). *"Functioning ... almost not at all. But with that, I didn't give up. I'm a person who doesn't give up ... so I sat more, rested more ... but I didn't give up."* F, 41, breast cancer.[19] (p6) (small horizon and regaining one's footing). *"I feel so tired. I don't know why I worry so much. More than one hundred days of worries and lack of sleeping my body condition get worse and worse…some of my children are not married yet; this means my duties are still unfulfilled"* F, N/A, breast cancer.[43] (p870) (embodied experience and regaining one's footing).

Relations of meta-themes

The six meta-themes we identified are interrelated. Central to all themes is the phenomenon of embodiment. Acknowledging that humans are primarily embodied beings – instead of composites of (disembodied) mind and body – embodiment refers to the fact that action, perception, orientation and cognition are based on our being embedded in a certain time and place, and social situation through our bodies. **Figure 2** captures the embodied dimension of CCRF. Fatigue is experienced in one's (entire) body, going together with loss of self. Role change and (mis)recognition are symbolized by the hands, "embodied tools" for intentional actions within one's social context. The small horizon behind the body, represents the narrowed world. Regaining one's footing is symbolized by the feet who seek to regain a new "optimum equilibrium" in one's world.[49 (p109)] How the various aspects of embodiment relate to one another depends on the individual patient. The following quote, for example, shows how role change, small horizon and (mis)recognition are interrelated in this respondent:

"I am at the age where people around me go out, party and have fun all the time. That's what college students do! ….. but I can't. Nobody understands that" N/A.[47 (p4)]

The embodied structure of CCRF involves social (e.g., ***(mis)recognition, role change***), spatial (e.g., ***small horizon***), and temporal (e.g., ***loss of self, and regaining one's footing***) dimensions.

DISCUSSION

Findings of synthesis

To our knowledge, this interpretative review is the first meta-ethnography based on sixteen qualitative studies that unraveled patients' perspective on the chronic nature of CCRF. The main finding of this synthesis is the embodied structure of CCRF that can be used in clinical practice for treating patients and in research for future development of measurement. Subsequently, a new figure was developed to visualize the valuable insights into how patients experience and respond to CCRF.

Previously, the onset of fatigue by patients undergoing treatment has been linked to paying explicit attention to the body as problematic and as an object.[50,51] In accordance with these studies, our results show that the awareness of the body in a negative way dominates patients' experience and is described as "old" and "sick". Although the human experience is always embodied, in everyday life the body is seldom a thematic object of experience, as there are less thoughts about the body and it dis-appears from attention.[52,53] Drawing on Leder's analysis of how one's own body can be either present or absent to oneself, the term "dys-appearance" (dys is a Greek prefix) is used to describe the situation when the body appears to the patient as "ill" or "bad".[52,53]

Because the body dys-appears while being chronically fatigued, it becomes the focal point of attention. The body loses its taken-for-granted dimension.[52] Consequently, the agency over one's body declines.[52] From a phenomenological point of view, it is claimed that whenever one's body appears obstinately in the foreground, one's possibilities to act and to endow meaning to one's situation, also defined as *"I can"*, shrink.[54] As a consequence of these reduced possibilities, the ability to adequately respond to the situation lessens.[54] Regaining one's footing, by contrast, implies that one is able to resume a certain renewed taken-for-granted view of one's body. Patients reported that pacing and monitoring activities helped to regain such a new equilibrium. In line with previous qualitative research[50] and meta-ethnographies in patients with cancer,[55] and chronic pain,[26] these strategies help patients to improve a sense of control and harmony with their altered bodies.

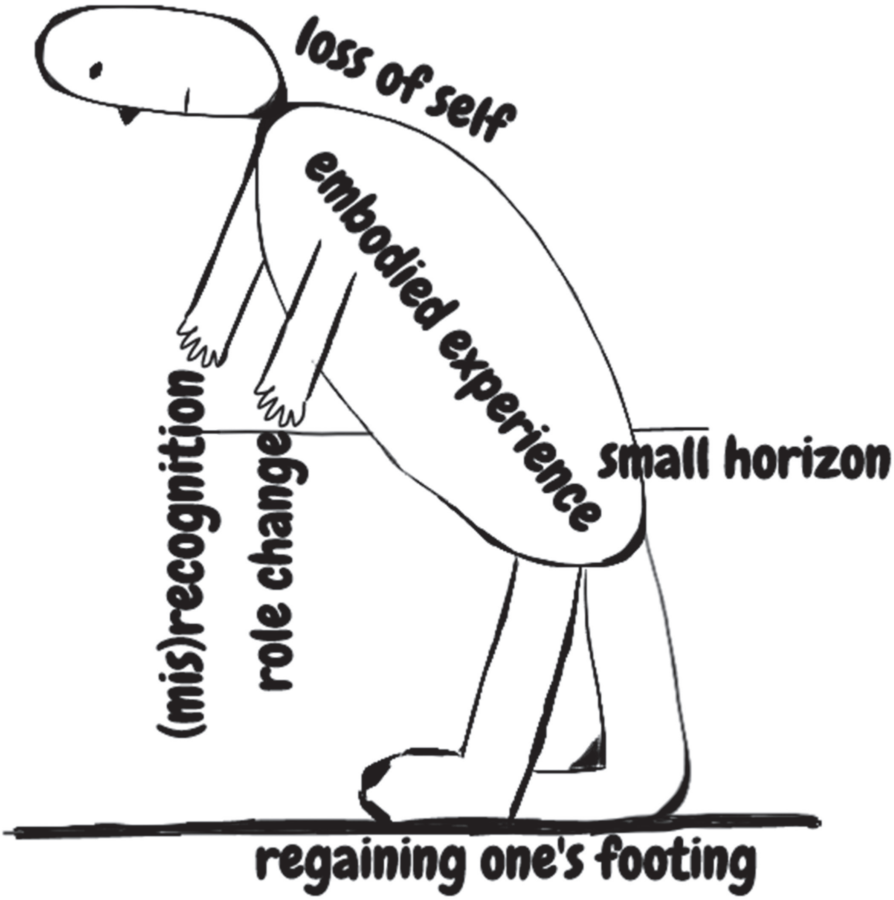
The individual experience and way of responding to CCRF is not static. The embodied experience of CCRF accompanied with loss of self could dominate and represent the illness state. Regaining one's footing entails learning to relate to CCRF in a different way and can help one to return to a healthy state. Paterson's shifting perspectives model of chronic illness demonstrated that this is a dialectical, constantly shifting process, in which either the illness (e.g., embodied experience) or wellness (e.g., regaining one's footing) perspective is in the foreground.[56]

In comparison to the NCCN definition of CCRF (Introduction),[7] our findings based on patients' individual experiences and responses, reflect a broadened context with embodiment and the related social, temporal, and spatial dimensions. Further research should focus more on how to measure embodied experiences and responses to CCRF. Currently, the EORTC QLQ-C30 is one of the questionnaires that captures some of these meta-themes (role change, small horizon, regaining one's footing) in the sub-scales on functioning (e.g., Role Functioning and Emotional Functioning).[57]

Study limitations

A potential limitation of this meta-ethnography is the inclusion of mixed cancer patients' samples: on-/post-treatment,[30–32,37–40,43,45,48] and curative/advanced stages of disease.[30,31,38–40,42,45,48] Only in the case where the authors reported patients' experiences during treatment, did we exclude these quotes from analysis. For disease stages, no distinction was made during analysis. We included studies with diverse demographics, although most studies focused on white, middle-aged, female breast cancer patients, shortly after treatment was finished.

Figure 2 Embodiment of CCRF



The systematic search strategy we conducted cannot exclude the possibility that some articles were missed. We tended to include a purposive and comprehensive sample of studies that allowed conceptual saturation to connect with the aim: develop an interpretative explanation of responses to CCRF. We included a broad range of qualitative data (e.g., interviews, blogs, open-ended questionnaires). Although some studies may have been of a bit lower quality, the content of all studies was valuable and informative to broaden the perspective on CCRF.

The starting point of the analysis was the newest and conceptually richest paper of Levkovich et al.[19] We could not initially discern whether or not this starting point affected the interpretation of concepts of other studies. However, as we conducted inductive analysis and cross-checked all studies afterwards, we expect the impact to be minimal.

Quality assessment revealed that one of the most frequent shortcomings was the lack of description of the relationship between researchers and participants.[31,32,37,39–47] Transparency in terms of the role of researchers and the ongoing critical reflection of their own biases is important in qualitative research, because of the level of subjectivity in this methodology. Future qualitative research should be attentive to the description of their methods section and should use, for example, the COREQ checklist.[58] The quality of the included studies impacts on the quality of the present results. However, by having carefully applied the meta-ethnography method, our results are considered to be reliable.

Clinical implications

The social, spatial and temporal dimensions underline CCRF's complex manifestation, which, ideally, requires a person-centered approach by health professionals.[59] During, as well as after, treatment, patients need information on CCRF and other side effects.[44,60,61] While not all educational interventions have the benefit of positively impacting the problem of fatigue, they do appear to have a moderating effect on reducing the related distress.[62] To prevent the false understanding of CCRF among patients, partners, family members, and health professionals several improvements are needed in providing: information, knowledge base, and education. Our first impression from clinical practice is that the figure can facilitate the communication between patients and health professionals. It can stimulate patients to discuss their problems, because they recognize their own experiences in the figure. By normalizing patients' experiences, they can regain a sense of control. The figure could also help advise patients on helpful strategies to manage CCRF. For example, by first explaining embodiment to the patient, therapy could focus on softening bodily dys-appearance and, as such, enable bodily dis-appearance.[63]

CONCLUSIONS

In conclusion, the main finding of this meta-ethnography is that patients' experiences and responses to CCRF are based on being embodied. Our findings emphasize the importance of informing patients to improve recognition and healthy responding to CCRF. In future qualitative studies, lived embodied experiences and helpful patterns of responding to CCRF could be further investigated in more heterogeneous samples, including more males and patients with different cancer types. To tailor treatment to the individual, insight into calculating the interrelationship between symptoms and ways of responding to CCRF is needed.[64]

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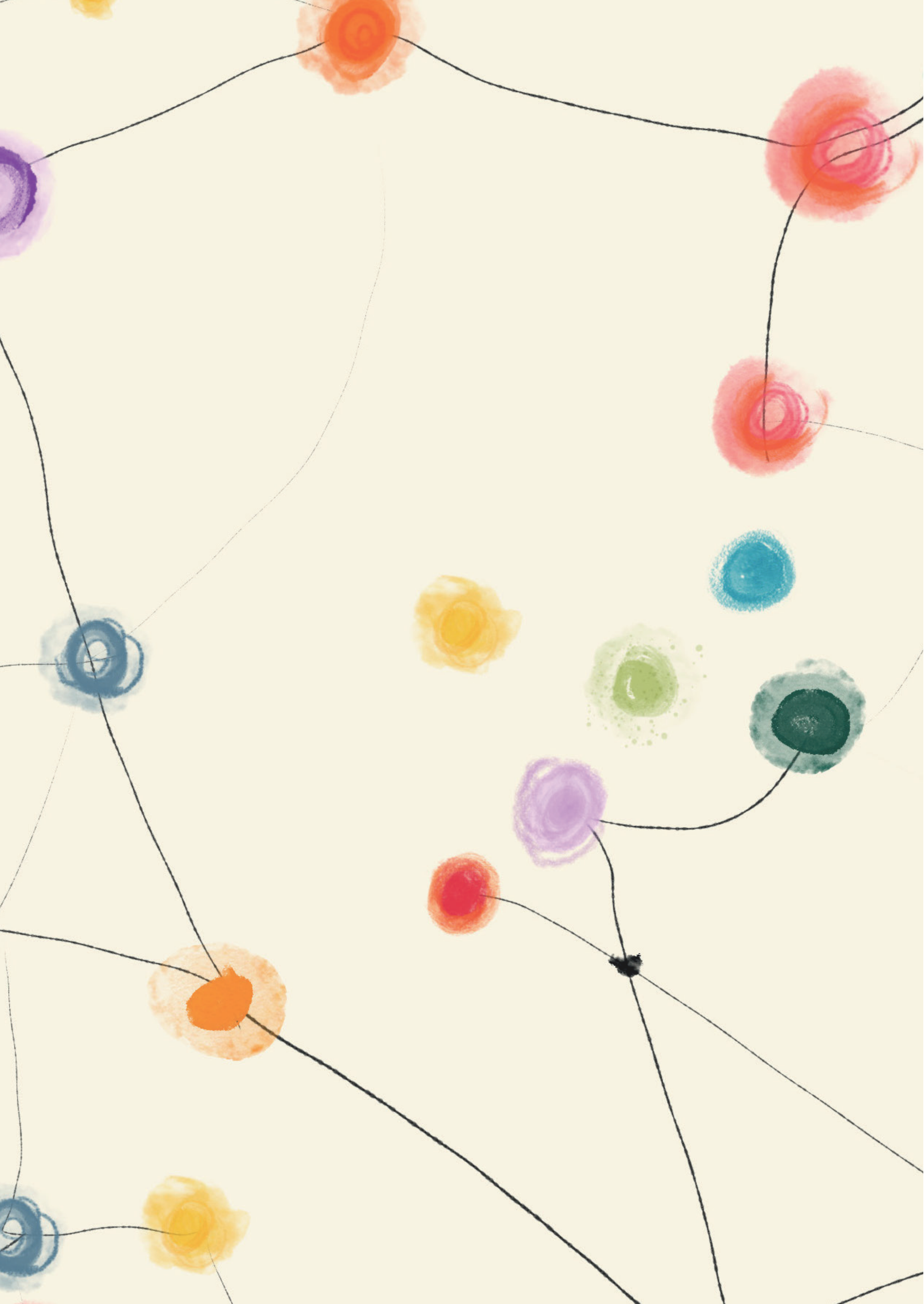

Chapter 3

NAVIGATING SEVERE CHRONIC CANCER-RELATED FATIGUE: AN INTERPRETATIVE PHENOMENOLOGICAL ANALYSIS

Bootsma TI, Schellekens MPJ, van Woezik RAM, van der Lee ML, Slatman J.
Navigating severe chronic cancer-related fatigue:
An interpretative phenomenological analysis. Psychol Health. 2021 Sep 2:1-24.

ABSTRACT

Objective

This article presents a phenomenological study on the embodied experiences of patients with chronic cancer-related fatigue (CCRF), aiming to better understand this complex phenomenon.

Design

Data collection consisted of individual interviews with 25 participants who suffered from severe CCRF for at least three months after cancer treatment was finished.

Main Outcome Measures

Against the theoretical background of philosophical phenomenology, we explored embodied experiences, incorporated temporal and spatial aspects of living with CCRF. We applied interpretative phenomenological analysis (IPA) to analyze the transcripts of the interviews.

Results

Using IPA, we identified four themes on how chronic fatigue is experienced post-cancer: ***(1) Worn out; (2) Diminishment of one's "I can"; (3) Invisibility;*** and ***(4) Regaining one's "I can***".

Conclusion

For clinical practice, these results imply that professionals could focus more on the role of the body and limitations of one's "I can" when treating CCRF. By studying these embodied CCRF experiences in individual patients, future research could help personalize and optimize treatment.

INTRODUCTION

Cancer-related fatigue is one of the most prevalent and disruptive symptoms experienced by cancer patients before, during and after treatment.[1,2] In the National Comprehensive Cancer Network (NCCN) guidelines cancer-related fatigue is defined as: “a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning”.[3] In at least one-quarter of all cancer patients, this fatigue becomes a chronic problem. When fatigue persists for at least three to six months after treatment, it often becomes chronic.[4–6] To make a clear distinction between fatigue during and after treatment, we use chronic cancer-related fatigue (CCRF) for fatigue post-treatment.[7] CCRF is an important public health issue due to the negative impact on patients’ lives, and incurring medical and social costs.[8] In clinical practice, it is strongly recommended to screen quickly for severe fatigue in newly diagnosed cancer patients to prevent it from being overlooked and become an under-reported, under-diagnosed and under-treated chronic problem.[3,9] In order to properly screen for CCRF, we first need to know more about patients’ experience with CCRF.

Suffering from CCRF is often accompanied with distress, impacts daily life and reduces the quality of life.[10–12] A recent study, applying network analysis to study symptoms among cancer patients seeking psychological care, showed evidence for the interrelatedness of CCRF with both risk factors (helplessness and physical symptoms) and protective factors (acceptance of illness) on a group level.[13] The complexity and interrelatedness of CCRF with other symptoms requires a better understanding and response to both the long-lasting physical cognitive, and emotional needs of these patients.[14]

Different psychological and exercise interventions are effective in reducing CCRF.[15–18] To date, there are also effective equivalents of these therapies available for patients with CCRF in an online form.[19] Despite this range of evidence-based treatment, it is not clear which type or combination of treatment works best for which patient.[15,19] Insight in how to tailor therapy to patients’ needs and characteristics will help to improve symptoms, reduce dropout, and can potentially reduce costs and improve implementation.[20–25]

A vital first step in the development of personalized therapy for CCRF is understanding this experience from the patient perspective.[26] The understanding of lived experiences entails the patients’ illness story, what the disorder means to the patient and goes beyond any objective, quantifiable and clinical data.[27] In addition, it reveals how patients feel, explain, interpret and understand their illness.[27,28] More insight into the subjective, lived experiences of CCRF could improve recognition and understanding of the severity of the problem in the communication between patients and professionals.[27,28] These insights could support professionals to be more empathic in their communication, provide useful information about future expectations at the right time and formulate their questions in a correct way.[29]

The richness and depth of qualitative research could help to understand patients' lived experiences.[30] A research method that could assist in tailoring treatment for CCRF is to ask for a more detailed description of experiences in the patients' own words. This method could help unravel if the interrelated problems a patient suffers from belong to one phenomenon or differentiate into distinctly different phenomena with different etiologies, and investigate the preferred word choice to determine possible targets for treatment.[31] For example, Dolgoy et al. (2019) identified new intervention targets by studying how people affected by cancer spontaneously described the nature and impact of fatigue. Besides the physical, emotional and functional consequences of CCRF, people also described how this fatigue impacted the sense of self and created feelings of uncertainty related to the onset, duration, impact and management of the fatigue. Based on these findings, the authors concluded that interventions addressing uncertainty and altered sense of self may be helpful to them.[32]

Previous studies emphasized the role of the body and bodily awareness in patients' experiences with CCRF.[33–36] A meta-ethnography, a review based on an interpretative analysis of sixteen qualitative studies showed that embodiment is a central phenomenon in experiencing and responding to CCRF.[37] The included qualitative studies showed limitations, such as small sample sizes, the inclusion of patients not only after but also during treatment that did not meet the duration criterion for chronic fatigue, and an overrepresentation of breast cancer patients. A detailed and comprehensive analysis of embodied experiences of CCRF in a mixed, larger sample after cancer treatment is lacking.

The present qualitative study explores the lived experiences of patients with severe CCRF. The lived experiences of CCRF could help to describe how the bodily disruption presents itself in the patients' life.[27,28] It starts with the question how patients experience these bodily disruptions of CCRF. The exploration is theoretically guided by the philosophical phenomenological account of disruptions in the experience of embodiment, time and space, and how these are related in patients that suffer from CCRF.[38–40] In our analysis CCRF is approached as a "chronic illness of its own rights",[41,42] within the context of the post-cancer experience.[33,43–46]

Theoretical framework

Phenomenology of the body, time, and space

A phenomenological approach enables us to describe the essence of CCRF by exploring it from the perspective of those who have experienced it.[47] It focuses on what we perceive rather than on the reality of things. This exploration of the meaning of experiences, consists of both what is experienced, and how it is experienced.[47,48] Perception is a basic element in using phenomenology to understand human experience, and an embodied activity itself.[38] According to the philosophical phenomenology of Merleau-Ponty, embodiment can be defined as "how we live in and experience the world through our bodies, especially through perception, emotion, language, movement in space, time and sexuality".[38,49] A phenomenological view of the body allows us to explore different dimensions of how CCRF disrupts a person's embodied being in the world, their experience of time, space, self, and relations to others.[38–40,50–53] The identification of all dimensions from different perspectives provides the opportunity for a comprehensive analysis of the lived experiences to gain a more complete insight into the disruption of this mind-body-world unity, which started with the cancer diagnosis.[33,43–46] This approach rejects mind-body dualism or other binaries because dualism is not helpful when exploring patients' experiences. The main goal is to use the framework to broaden the perspective of the patient's experience.

One's body can be experienced as the physical, objective body (*Körper*).[38,40] The material and social dimension of embodiment represent ways of experiencing this objective body from an "outside" or third-person perspective.[39] The material dimension expresses the body as a material thing in a causal relationship with the world. This bodily experience is often affected by the so-called gaze of the other.[54] Whenever one feels that one's body becomes subject of the gaze, one's focus may change from being engaged in projects in the world towards awareness of one's own body. Leder (1990) calls the thematization of one's body apart from itself as a material object: "dys-appearance". The social dimension illustrates that the material body is embedded in a social context. The other could treat the patient as an object instead of subject, which causes a split between the subjective, lived body and objective body. When patients adopt the perspective of the objectification of their body by the gaze of the other and become aware of themselves as "an alien thing", this can be described as "social dys-appearance".[55] Adjacent to the experience of the objective body, an objective way of experiencing time exists: the linear or outer time that refers to the time that can be measured by clocks, calendars etc.[50,56]

A second form of how one's body can be experienced, is as a lived, subjective body (*Leib*).[38,40] The representation of the affective and functional dimensions are ways of experiencing the subjective body from a "within" or a first-person perspective.[39] The affective dimension represents the chronically ill body as a bearer of (new) sensations. The functional dimension refers to the body as a seat of free movement, the possibility to act in the world, or put differently the "motor intentionality" or one's "I can".[38,40] Additionally, the subjective way of time-experience is the lived or inner time, defined as the ongoing stream of consciousness in which duration and temporality are experienced.[50,56] For example, waiting for a doctor's appointment could feel like hours even when the clock time is merely 30 minutes.

A chronic illness disrupts the possibility of action and changes the experience of both spatiality and temporality. First, in health one can move in and through space easily, while in illness space can seem restricted.[51] The lived space of the body is the situational spatiality in health. The body appears to oneself as a posture towards a certain task without a need to measure the geometrical distance surrounding a body, that is the positional spatiality.[57] The disruption of the lived body in case of chronic illness transforms the experience of the body as an orientational and intentional locus.[58] Because the situational spatiality is disturbed, the positional spatiality remains and a patient has to think before he or she acts.[57] This is reflected in the heightened sense of distance between oneself and surrounding things, because a loss of mobility. The same location previously considered as "near" is now seen as "far".[58] To overcome this loss of mobility and heightened sense of distance, patients with a chronic illness experience changes in the spatial arrangement of how to reach, open, or place things.[51] For example, chronically ill patients consider putting things within reach and strategically on the ground floor in their home to avoid taking the stairs because of their disabilities. Second, the introduction of a chronic illness, such as the persistence of CCRF after cancer,[43] into someone's life results in a disturbance of another time component, the biographical time, a disruption of previous lived experience.[51] Biographical time comprises all experiences, memories and emotions derived over a life-time and carried within the self.[51] When life is disrupted by a chronic illness, patients could experience feelings of alienation[59] because their body of the present and the future is compared to the body of the past and appears as "other" and "strange" to them, which could result in a loss of self.[51,52]

MATERIAL AND METHODS

In this qualitative study, part of the REFINE project for personalizing treatment for CCRF, initiated at the Helen Dowling Institute, mental health center for psycho-oncology in the Netherlands, 25 patients with severe CCRF participated. The guidelines of standards for reporting qualitative research (SRQR) were followed.[60] First, we re-analyzed semi-structured interviews with nineteen CCRF patients, who completed one of two web-based interventions in the randomized-controlled More Fit after Cancer trial (Fitter Na Kanker (FNK) trial).[7,61]

Participants of the FNK trial reported their lived experiences with CCRF. However, this exploration of lived experiences was less in-depth, because the open-ended interview questions focused on evaluating the interventions (**Table 1 Topic guide FNK trial**).

After re-analysis, the data provided insufficient answer to our research question: how do patients experience bodily disruptions of CCRF? Therefore, additional semi-structured interviews were required for a more in-depth exploration of the embodied experiences of CCRF. The first author developed a new topic guide with open-ended questions based on clinical expertise, literature and piloted it with a therapist experienced in treating patients with CCRF at the mental health center for psycho-oncology. Topics of this interview guide were experiences (descriptions, sensations, cognitions, patterns, attributions), consequences (daily life, body, self), actions (self, others, helping and hindering factors), and other important factors (**Table 2 Topic guide REFINE project**). Subsequently, six new patients were interviewed on their experiences with CCRF. Initially, the first interview was considered a pilot interview. As the questioning was positively evaluated, we included this interview in the analysis. We published a separate paper that focused on what helps patients in responding to CCRF.[62]

This study was approved by the Twente Medical Ethical Committee (P12-26) and the Research Ethics Committee of Tilburg School of Humanities and Digital Sciences (REC#2018/24) and was performed in accordance with the Declaration of Helsinki. Patients received an information letter and provided written informed consent. In some cases, the partner was present during (a part of) the interview. Field notes were taken during and after each interview. All interviews were audio-recorded and transcribed verbatim immediately after the interview by research assistants of the projects.

Interview data from FNK trial

To evaluate the web-based interventions of the FNK trial, 19 out of 22 selected patients were interviewed (December 2015 - March 2016) about their experiences with the programs: nine (partially) completed the physiotherapist-guided Ambulant Activity Feedback (AAF) and ten (partially) completed the psychologist-guided Mindfulness-Based Cognitive Therapy (eMBCT).[7] For the present qualitative analysis on lived embodied experiences, we particularly focused on patients' perception of interrelated symptoms, limitations, and impact on their daily life. For the FNK trial, participants were recruited via online and offline channels. Eligibility criteria were: 1) finished curative treatment at least three months ago (except hormonal treatment); 2) severely chronic fatigue score >=35 on Checklist Individual Strength (CIS) - fatigue severity subscale (FS);[63] 3) >19 years old and 18 years old at disease onset; 4) no current or former severe psychiatric comorbidity (i.e., suicidal ideation, psychosis or schizophrenia). The interviews took place at the patient's home and lasted on average 40 minutes. The two researchers who conducted the interviews had experience in the field psycho-oncology and/or qualitative research.

Table 1: Topic guide More Fit After Cancer (FNK) trial

1. Before discussing your experience with the therapy: Can you tell me something about the symptoms or things you suffered from before you started in this study?
   Prompt: fatigue, sleep, physical, anxiety, worrying, distress, work, social contacts, going out, family, household
2. Can you tell me something about your expectations before the start of the therapy?
   Prompt: positive expectations, doubt
3. What was your experience with the therapy?
   Prompt: positive and negative experiences
4. Can you tell me something about how you are doing now, after finishing treatment?
   Prompt: fatigue, sleep, physical, anxiety, distress, work, social contacts, family, household
5. In what way do you think the therapy has been helpful?
   Prompt: what and how?
6. Can you tell me something about how you experienced the contact with your therapist?
   Prompt: How was the contact? Did you feel comfortable? Do you think following the therapy without a therapist would have been possible too?
7. Can you tell me something about how you experienced the exercises?
   Prompt: Did the exercises help? With what and how? Was it pleasant or not? Where did you do the exercises? When did you do the exercises? What have you learned from the therapy? Do you still do the exercises? When? What exercises?
8. How did you experience receiving care via the computer?
   Prompt: Did everything work, or were there times things did not work? How did you experience the online environment? Usability? How did you play the audio files? On what device? How did you read the booklet? Printed or on a device?
9. Do you have any other comments about the therapy not yet discussed?
10. How was it to participate in this study?

Additional interviews REFINE project

The first author who conducted (August 2018 - January 2019) the additional interviews had prior experience in conducting qualitative research in the field of psycho-oncology. Interviews were held at the patients' preferred location: mental health center specialized in psycho-oncology, the patient's home, or online with a video-connection. The average duration of these interviews was 64 minutes. These patients were recruited by their health professionals in a mental health center specialized in psycho-oncology, a general practice, physiotherapy centers situated in urban and non-urban areas of a central part of the Netherlands, and via patient websites. In total 28 patients responded and we selected six participants that were all severely fatigued after completing cancer treatment and met the same eligibility criteria as used in the FNK trial. Recruitment of participants stopped when sufficient rich and thick personal accounts were collected to answer the research question.

Table 2: Topic guide REFINE project

1. How would you describe your fatigue? How is it to be tired? What do you feel when you are tired? What do you think when you are tired?
   Prompt: physical, mental, worrying, catastrophizing, cognitive and memory problems
2. I would like to know when you first suffered from this fatigue and how it has been going since then? Can you remember the moment the fatigue started? When did you first suffer from fatigue?
   Prompt: duration, pattern (duration, frequency), changes over time, changes during the day, comparison to pre-cancer fatigue
3. Maybe you have thoughts about what causes your fatigue? Why do you think you suffer from fatigue?
   Prompt: triggers, sensory stimuli, cause, nutrition, changes in sleep, fear (for recurrence), worrying, distress, physical activity
4. How does fatigue influence your daily life and social environment?
   Prompt: daily life, work, household, social life, partner/children/family
5. If you compare your life with fatigue with your life before the fatigue started, what has changed? How do you see yourself with fatigue?
   Prompt: changes in view of the body, changes in looking at yourself, changes in identity, changes in how others see or approach you?
6. When the fatigue started, how did you deal with the fatigue? In what ways could you influence the fatigue?
   Prompt: ways of dealing with fatigue, attributions, role of others (family, friends, acquaintances, others), to avoid/ be in situations?
7. What is helpful to you in dealing with fatigue?
   Prompt: protecting or helping factors, attention, acceptation, activity
8. What is not helpful in dealing with fatigue?
   Prompt: risk or unhelpful factors, go beyond boundaries
9. Do you have other experiences not yet discussed? What question about fatigue after cancer should I have asked to help understand it?
   Prompt: other factors or questions
10. In order to improve treatment for patients with fatigue, I would like to know what is important in dealing with fatigue. What is your most important advice to yourself, others, professionals to better learn to deal with the fatigue?
    Prompt: key topic, tips and tricks
11. How was it to participate in this study?

Because almost half of the interviewees (n = 8) of the FNK trial were middle-aged women with a history of breast cancer, purposive sampling (on age, gender, partner status, cancer type, and treatment) was applied to gain a broad scope of the lived experiences of CCRF patients. This resulted in a more diverse sample of in total 25 severely fatigued participants (**Table 3**). Eleven patients (44%) scored above the cut-off for depression screening (≥15) on the Hospital Anxiety and Depression Scale (HADS).[64,65]

Data-analysis

The interpretative phenomenological analysis (IPA)[66] started with the analysis of the interviews of the FNK trial. The first and third authors started with reading and re-reading the interviews. In the next step, they inductively coded the first five interviews with descriptive codes (MaxQDA software, version 18.2.0), while being supervised by the second and last author. This supervision included responding to questions and coaching during the coding process. The two researchers constantly compared and discussed the codes until they reached consensus. Increasingly less differences were found between the independent coding of the two authors. Therefore, after the first five interviews, the first author continued coding the remaining (20) interviews in the same way. All questions and inconsistencies during the coding process were discussed and decisions were recorded. Member checks were utilized for the six additional interviews of the REFINE project by sending a summary of findings to participants. All participants responded that they agreed with the content of the summary.

The code list was organized in seven main categories (i.e., experiences, metaphors, comparisons, beliefs, responses, helpful and unhelpful response) based on the interview data. We created six individual ‘CCRF experience profiles’ based on codes of the patients that participated in the REFINE project. We discussed these individual ‘CCRF experience profiles’ and the code list with the multi-disciplinary team of authors, who have clinical and qualitative research expertise in psycho-oncology. We excluded data from analysis that were related to partners who sometimes participated in the interview and data concerning the online therapy of the FNK trial.

Table 3: Participants‘ characteristics (N = 25)

Characteristic	Value
Female/male gender (n)	16/9
Age at interview (years; mean ± SD, range)	52.64 ± 12.86 (21-80)
In a relationship (n)	23
Children at home (n)	11
Education level (n)[a]	
-low	3
-intermediate	13
-high	9

Characteristic	Value
Currently employed (n)	
-job	10
-(partial) disabled	8
-no job/household	4
-retired	2
-scholar or student	1
Type of cancer(s) (n)[b]:	
-breast[c]	10
-hematological[d]	8
-digestive system	5
-head or neck	2
-male genitalia	2
-urinary tract	2
-bone or soft tissue	1
-brain and central nervous system	1
-skin	1
-gynecological	1
Treatment(s) (n)[b]:	
-surgery	20
-chemotherapy	18
-radiotherapy	15
-hormonal therapy	6
-immunotherapy	2
-bone marrow transplantation	1
Metastasis (n)	7
Comorbidities (n)[e]	12
Months since first diagnosis-interview, (M ± SD, range)	56.88 ± 45.11 (11-169)
Months since last treatment-interview, (M ± SD, range)	43.72 ± 35.96 (6-152)
Checklist Individual Strength (CIS) score[f], (M ± SD, range) Subscale: Fatigue Severity (FS)	43.0 ± 5.02 (35-52)
Hospital Anxiety Depression Scale (HADS) score[f], (M ± SD, range)	13.84 ± 5.39 (4-23)
Duration of severe fatigue (n)	
-3-5 months	1
-6-12 months	6
-1 year-2 years	6
-2-5 years	7
->5 years	5
Prior professional support for cancer (n)[g]	18

a: low=primary/lower secondary education; intermediate=upper secondary education; high=higher vocational training/university

b: numbers do not add up to 25 because multiple options are possible

c: one participant had another type of breast cancer for the second time and was counted twice

d: one participant had two different hematological diseases and was counted twice

e: comorbidities: diabetes, spine condition, pelvic disease, lung disease (asthma, bronchitis or CARA), thyroid disease, liver disease, ulcerative colitis, graft versus host disease, sleep apnea, neuropathic sensations, vertigo, tinnitus, PTSS, neurological disease, migraine and inflammatory bowel disease

f: baseline data T0a FNK trial

g: professional support: revalidation, general practitioner, spiritual counsellor, social worker, psychologist, institute for mental health care, institute for psycho-oncology, psychosomatic exercise therapy, physiotherapy and lifestyle program

The analytical process was case-by-case, inductive and iterative. Some examples of descriptive codes from the first part of the analysis included: “battery is low, need to recharge’ [metaphor] and “what I could I cannot do anymore” [comparison]. The next phases of analysis consisted of seven team discussions about the individual ‘CCRF experience profiles’ and code list. Together the authors extracted general patterns and themes from the code list. The results of the analysis were continuously checked with the underlying data (interviews). In the next group meetings, the theoretical framework was elaborated upon and applied to the code list to search for different patterns in the data.

In the latter phase of analysis, the authors searched for cross-case themes emerging from the different patterns. Four themes were identified about how chronic fatigue is experienced, what kind of functional limitations result from this fatigue, how the invisibility causes problems in social context and how patients adapt to the fatigue and its limitations. The analysis was completed by discovering dynamics and relations between the different themes within an individual patient.

RESULTS

Embodiment in CCRF: four different dimensions

In their descriptions of CCRF, the participants in our sample referred many times to their feelings of fatigue in their lives before cancer and reported differences in severity, timing, causality, and recovery between their pre- and post-cancer experiences of fatigue. Their experience of cancer and its treatment marked a change in their feelings of fatigue, functioning, and identity. Participants longed for their pre-cancer situation, which they experienced as a much better situation, in terms of how they felt and their level of functioning. Regarding their future, participants wondered whether they would keep suffering from CCRF and its limitations.

The process of experiencing CCRF is dynamic. That is, despite the chronic nature of CCRF, the fatigue experience changes over time and across social situations, with differing sensations and limitations. We identified four themes of patients’ experiences related to navigating CCRF. In this report, we explicitly quote twenty participants using pseudonyms (i.e., Amy, Brian, Britt, Christian, Daisy, Daniel, Finley, George, Isabelle, Jasmine, June, Kyra, Logan, Lynn, Oliver, Quinty, Rose, Samuel, Sebastian, and Zoe). Of course, our results are based upon the analysis of the interviews with all twenty-five participants. In all four themes different dimensions of experiencing embodiment, time and space were incorporated. ***(1) Worn out*** is an affective dimension that entails different descriptions of sensations (i.e., physical, emotional, sensory, and cognitive) of fatigue experienced over time in the patient's body (e.g., limbs and/or mind), which could result in a loss of self. ***(2) Diminishment of one's "I can"*** is a functional dimension that represents several limitations to move "freely" in time and space patients with CCRF experience in their lives. ***(3) Invisibility*** is a combination of a material and social dimension that describes the objectification of the experience of CCRF in their body in a social context. Objective time is used to indicate when they expect to be worn out. ***(4) Regaining one's "I can"*** is a functional dimension that refers to ways of adapting their active time and movement in space to the experience of CCRF, the functional limitations of one's "I can", and the material and social objectification of their bodies.

(1) Worn out

Participants used different synonyms to describe their feelings of CCRF, including tiredness and exhaustion. The commonly used word "fatigue" was not always appropriate to describe their feelings of chronic fatigue because this is often confused with the fatigue everyone experiences in their daily life. Daisy compared her feelings of exhaustion with experiences of fatigue after flu she had in her pre-cancer life:

"To be honest, that fatigue, I never had it so intense (…) Fatigue, normal is like recovering from the flu like I'm very weak, but this extreme fatigue, I did not know it before" [Daisy, FNK-MBCT, 51-60 year, 2-5 years CCRF].

These sudden moments of "really extremely exhausted" are not recognized or comparable to the feelings of fatigue that rarely occurred in their pre-cancer life. Most participants did not expect to experience chronic fatigue after treatment. Various combinations of superlative adjectives (e.g., total, extreme, overwhelming, intense, debilitating, or intangible) were frequently used to reinforce the meaning and express the intensity of their feelings.

Participants experienced difficulties to put their experiences with fatigue into words and sometimes used powerful metaphors to indicate the severity of CCRF. Examples of expressions included: "I am dog-tired", "I was drowning" or "I am 'totaled'" (i.e., like a car that is totaled).

Several participants expressed their experience of CCRF in terms of what they "lacked" in their current situation, that is "energy". The use of the word "lack" marked that before cancer, their energy level was in most cases not a problem. George experienced more problems with his energy levels after cancer treatment was finished:

"(…) I constantly have the feeling that I have somewhat less energy than an average person of my age. Actually, I always experienced this to some extent and I also noticed this during

my student life. And afterwards, after the first years of my disease and finishing chemotherapy etcetera, then you notice you have taken a huge hit" [George, FNK-MBCT, 31-40 year, >5 years CCRF].

However, some participants described this lack of "positive" feelings of being well-rested, recovered, energetic or fit, even at awakening, other participants had some moments of being more fit during the day or on some days.

In the descriptions of fatigue, a time indication was frequently used to express the chronicity of CCRF. Fatigue was experienced each and every day. Lynn described her complaints prior to the study:

Participant Lynn: "Uuuh extreme fatigue"

Researcher: "Yes… and uh in what way did you mean fatigue?"

Participant Lynn: "Yes when I woke up in the morning I wanted to go to bed again"

Researcher: "Yes, yes…"

Participant Lynn: "And actually the whole day oh how tired I am ohh phew I am tired" [Lynn, FNK-AAF, F, 61-70 year, 2-5 years CCRF].

While fatigue can be constantly present for some, for others it was more unpredictable and unexpected. Christian described how he experienced "fatigue attacks":

"It is possible, I mean in a weekend when you take it easy, you sleep in, I do that on Sundays, then you wake up at 11 a.m. ….and at 1 p.m. you get dressed and at 1 p.m. I totally collapse. (…) Then I really have to, well usually I go on the couch, lay flat for a moment. (…) Yes, then I say: "I just have to lay down for a moment", because the fatigue is so intense at that moment…but I am sometimes asleep for one hour" [Christian, FNK-MBCT, M, 61-70 year, 2-5 years CCRF].

Several patients reported that the severity of fatigue is a dynamic experience, because it fluctuated within and between days. Most patients indicated that they experienced more intense fatigue at the end of the day. They also mentioned how they could be extra fatigued during the day(s) after activity. Therefore, participants often needed to rest, either after activity or during "moments of being totally exhausted". During the day participants could suddenly fall asleep. Sebastian illustrated the time of sleeping is prolonged:

"Extremely fatigued, really like: I lie down in bed, then I had the feeling I sink into my bed as if I disappeared in the mattress and then I could sleep, well I was comatose. And then not just for one quarter, hours!" [Sebastian, FNK-AAF, M, 61-70 year, 1-2 years CCRF].

The depth of sleep was mentioned: "comatose" in this quote, other participants had similar experiences with a deeper sleep than before cancer. Contrarily, sometimes individuals had problems sleeping at night.

The feeling of CCRF is experienced by participants as being a part of their bodies, for example, "fatigue in your bones" and "the energy runs out of my legs". Some patients compared their fatigue to doing extreme physical activity: "climbing the Mount Everest" or "running a marathon". Different physical sensations were experienced. In several cases, the fatigue was predominantly felt in their limbs, which made their limbs feel "heavier and heavier" and resulted in difficulties standing on their feet, walking or climbing stairs. Because their body changed after cancer and treatment, patients reported that they experienced different symptoms (e.g., stiffness, pain, lymphedema) in their body related to fatigue. Some patients suffered from various chronic comorbidities (**Table 3**), which impacted their bodily experiences as well.

Although CCRF was their main symptom, patients also suffered from other (cancer-related) problems: sensory, cognitive, emotional, sleep (insomnia or hypersomnia), and physical difficulties. Isabelle illustrated how these different aspects were interrelated with her fatigue:

"It is often when I am at a birthday party, where the fatigue and sensory overload are related, and that's why I get a panic attack because previously I did not have this, so to say. Thus, it is all connected to one another" [Isabelle, REFINE, F, 21-30 year, 1-2 years CCRF].

Patients described several situations in which they are overstimulated: driving a car, multitasking, working, or going out. In this quote, June reported how difficult it is to process the various stimuli at once:

"(...) Memory, concentration, I am quickly…out of sorts. I cannot function in groups either. There were way too many, way too many stimuli too" [June, FNK-AAF, F, 61-70 year, 2-5 years CCRF].

This indicates how stimuli could have stronger effects post-cancer limiting their tolerance for processing stimuli. Some participants experienced particularly a lack of mental energy, sometimes combined with physical fatigue. These participants expressed sensations of their fatigue as: "in my head" or "absent-minded". They used metaphors, such as "I feel like I am hung-over" or "I feel like I am a heavily drunk driver". The effect of CCRF on participants' cognitive functions resulted in different cognitive problems (e.g., concentration, attention, memory, thinking, communication and understanding). Quinty commented:

"And that started maybe 5 years ago, I don't know exactly, but in any case, the consequence of fatigue, I see it as consequences, is also concentration problems" [Quinty, FNK-MBCT, F, 51-60 year, > 5 years CCRF].

Many patients experienced a loss of concentration which hindered their overall functioning, because they cannot be mentally active (e.g., working) anymore. In most respondents, the physical and mental limits of CCRF and cancer invoked various types of emotions and negative thoughts. They felt more vulnerable, worried more and experienced regularly (more) negative emotions (e.g., anger, sadness, depressive feelings, shame, and anxiety) than before cancer and its treatment. Emotions seemed to come more easily to the surface because most people felt frustrated about their fatigue and limitations in daily life. Some patients reported they did not recognize their fatigued bodies and their selves, which were reinforced by intense emotions, resulting in feelings of alienation. Zoe reported:

"I notice that it reinforces when I am tired, so fatigue is a sort of plus factor, which also makes me more depressed or sometimes very emotional all of a sudden. Thus, it all brings things closer to the surface, even more than usual. And then with that somewhat stronger fatigue, you sometimes think: I don't recognize myself" [Zoe, FNK-MBCT, F, 41-50 year, >5 years CCRF].

These feelings of becoming suddenly overwhelmed by intense negative emotions and severe fatigue were not recognized from before cancer and could make them feel like losing (control of) their selves.

(2) Diminishment of one's "I can"

CCRF confronted patients with several limitations. Before cancer, most patients were physically at 100%, whereas afterward their bodies were different and not completely recovered. Most patients were limited by and more aware of their bodily sensations, emotions, sensory stimuli and cognitions after cancer, losing trust in their bodies. As such, the complexity of CCRF also impaired patients' activities and social life. Several participants described how they were not always able to go out, function in a group or take care of children. Consequently, the suffering from CCRF indirectly affected participants' partners, family, and friends. Brian reported that his partner was just as much impacted by his disabilities as he was:

"(...) And for my wife, it is of course also, yes for her, my limitations become her limitations, because walking in the city alone is not the same as walking together (...)" [Brian, FNK-MBCT, M, 61-70 year, 1-2 years CCRF].

The fatigue limits activities. Close others had to take into account the patient's limitations and emotional reactions, and were required to take over certain tasks (e.g., driving a car or care for children), but it was usually impossible to take over all tasks.

Patients' daily schedules were disturbed and complicated because they actually felt they had no time to be fatigued. Because of CCRF, the time in which they were active was shortened, which results in unintended delay, or even the inability to perform everyday activities. For example, patients reported that more time is needed to get out of bed and get dressed. Almost all participants mentioned that they cannot do all of the things they used to do in one day. Rose reported that her daily activities are limited, which means that she is limited in her "I can":

"(...) because I am always tired, and that is really an understatement, I am really every day, at the end of the afternoon nearly exhausted (...), you face it every day. I can no longer do everything in my life that I would like to do (...)" [Rose, FNK-MBCT, F, 41-50 year, 1-2 years CCRF].

Patients experienced daily struggles with their activities, as they had to select one or two activities a day. Physical activity (e.g., doing sports, climbing stairs, lifting things) as well as mental activity (e.g., reading, watching movies) were limited. Patients were unable to move "freely" in time and space. Patients also expressed motivational problems, such as difficulties to start or make time for activities or travel. Jasmine reported about her motivational problems to start making dinner:

Picking up the piece where you left off, look. A household does indeed have things of which you say, yes at 5 am, I have to eat anyway, I will start making dinner. It is just that things that are common throughout the day, of which you think, oh yes, now I have to do that again" [Jasmine, REFINE, F, 71-80 year, 6-12 months CCRF].

The normal daily tasks were experienced as things that "have to be done" because everything took so much more time and effort, reducing their motivation. Patients tended to avoid or postpone things, or make up excuses in order to not being active throughout the day. They also experienced a diminished or lack of interest in activities. Activities were preferred at, and performed at, a lower intensity. They were unable to reach their pre-cancer working pace or training level.

Not only their present but the perception of their future life has become disrupted as well. Many patients started living day-by-day after cancer. Amy reported:

"Yes, it varies, sometimes it goes very well and I have cleaned the windows and sometimes that is just not possible. It just varies a lot. And you just have to accept that it happens and don't worry too much about it (...)" [Amy, FNK-MBCT, F, 51-60 year, 6-12 months].

In this example, acceptance without worrying helped to respond to the daily variations in the experience of CCRF. Other patients became more and more aware of the finite nature of life after cancer and were uncertain about their future. Because of its chronic nature and the impact on their functioning, almost all participants were worried and frequently raised the question: "Will the fatigue ever resolve?"

(3) Invisibility

The body of cancer patients could have different persistent changes and/or damages after cancer and its treatment. Patients could focus on their bodies as "an alien thing" because of the changed nature of their bodies or because of the negative attitude of others towards them, both resulting in objectification of their bodies. Some changes were visible on their bodies, such as lymphedema or scars from surgery. Others were invisible, such as the experience of pain or CCRF. This invisibility, the fact that others were unable to see CCRF, led to several problems. The interaction with others was impacted by CCRF. Many patients felt supported by their partner, friends and family, because they took over some activities, helped to protect their limits or just gave them the space they needed for a moment. In these situations, their loved ones recognized and asked about their feelings. On the other hand, some patients took the first step and communicated openly about their invisible fatigue and their possibilities in daily life with their close others, and asked for help if necessary. In these cases, there was a positive interaction between the patient and their loved ones. Other patients chose to contact new people that were unaware of their fatigue to avoid the judgment of others who do know about their medical situation. Other patients described how their family started to make decisions for the patients. However, after cancer treatment was finished, several participants reported a switch in the amount of positive attention they received from other people. While the experience of CCRF is still present, it is invisible to other people. As Britt described how she experienced the invisibility of CCRF as an extra disability:

"I'm only 10% of who I was, it's really absurd. And I look like nothing is wrong you know. That is also an extra disability" [Britt, FNK-AAF, F, 51-60 year, 1-2 years CCRF].

Several participants experienced a lack of social recognition because other people formulated the following questions, such as “Don’t you feel bored?”, “When will you be well?” and “Are you leaving already?” Other people, particularly, children expected them to be fit and active. Some patients understood these reactions and normalized these comments as they understood that healthy people could not recognize their experience of feeling extremely fatigued. Other patients felt ashamed and became more reluctant to show their feelings and talk about their fatigue experience:

“Yes and there, finally I come in such a modus that you do not even mention it [CCRF] anymore to other people (…) Yesterday, for example, I played tennis with my girlfriend, and my mother said: ‘Yes it is about time that you start doing something’. I said to my girlfriend: “So yes, instead of that, she could have said: ‘Ow how good of you that you started again’. Yes, that kind of support is very important for me to pick up my life again” [Oliver, REFINE, M, 41-50 year, 2-5 years CCRF].

Patients often did not feel acknowledged in their fatigue experience. Some patients did feel acknowledged by their health professionals, as they explained that their fatigue was caused by cancer and its treatment. Other patients experienced problems, because of the lack of recognition of professionals. Finley reported how the company doctor pushed him to return to work:

“When I visited the company doctor: ‘Why aren’t you working?’ He said to me: ‘You look great’. ‘Yes, even when I look so great, I don’t feel like that’. But try to explain to other people who don’t know what cancer and treatment means. Try to explain how you feel. You hit the wall. I went to another company doctor” [Finley, REFINE, M, 41-50 year, 6-12 months CCRF].

The company doctor misinterpreted the situation based on what was expected to be visible on the outside, which does not correspond to how the patients feels. Patients frequently reported similar situations with other people in which they “hit the wall”.

Besides the impact of social invisibility of CCRF, participants could also themselves focus on their bodies as “an alien thing” because of their awareness of bodily changes. Patients experienced their bodies as “ill”, “alien” or “older” and felt “betrayed” by their bodies. Logan described how, as a consequence, mind and body grew apart:

Well, this is the body I have to deal with. (…) Body and mind grow apart. The body ages but the mind stays young (…) Thus, body and mind grow apart, which is comparable to what you increasingly see in older people. They think of being 18 or 20 again and want to do things, *like when they were 30 and could do anything. But that is not possible anymore"* [Logan, REFINE, M, 61-70 year, >5 years CCRF].

Logan reported in the same interview how his body lost the taken-for-granted dimension:

"Before [cancer], you weren't concerned about your body. You were your mind, as the motor of activities and you could do everything and your body went along with it. At a certain moment, the body starts saying: 'stop, stop, stop' and it starts slowing down (...)" [Logan, REFINE, M, 61-70 year, >5 years CCRF].

This example illustrated how he experienced that his body has become a limiting factor for being and staying active. Their bodies suffered from severe fatigue for a certain amount of time during the day. In searching for an explanation of their fatigue, patients objectified their body and used objective time to refer to the moment of their fatigue started. Some patients could mention the objective time of 1-2 hours that they were able to be active and concentrated. Most patients also knew almost exactly at what time of the day they would be exhausted.

(4) Regaining one's "I can"

Patients became aware that: "this is the body you have to deal with" and realize that "you have to take into account that you will not reach your former level because your body has changed." Most patients anticipated on being fatigued. They would reduce the quality (i.e., intensity) and quantity (i.e., the number of) of their activities. Participants used different metaphors to express that they had to manage this complex situation through balancing their energy: "you have to break daily activities into pieces", "do not empty the tank at once" or "make sure that the man with the hammer does not hit you too hard". The experience of CCRF taught them to protect their limits, listen to their own needs and focus on what they can do. Sometimes they were forced to a timely stop of some of the daily activities that caused fatigue or to ask other people to help them.

Many patients searched for new ways to strengthen and move with their fatigued body, frequently supported by physiotherapists. Daniel commented on the need of physiotherapy:

"Eh, now yes, I had of course the physiotherapy for weight training as well. That was important. You need that. Because if you don't have that, you stay weak, like a cracked egg. And it is important that you endure. Of course the physiotherapist advised to go walking, go biking, because that's good for you, because then you get your muscles back. Thus uh, yes the support of the physiotherapist was essential" [Daniel, FNK-AAF, M, 41-50 year, 6-12 months CCRF].

Other participants practiced yoga or balance exercises. Their ways of moving around changed as well, both inside and outside their house. Kyra reported about her difficulties to climb the stairs and vacuuming at home:

"No, I can do the housework again, there have been periods when I was not able to do that, I was also very short of breath from fatigue, well then you should not walk behind a vacuum cleaner, because that doesn't work, and a lot of bending over and bending is not convenient and climbing stairs is still tiring, but nowadays it is possible again, but also in a dosed way, so with breaks. So if I want to vacuum the whole house, I do the attic and then I take a break and then I do two of three rooms on the first floor, break, and that's how I work down stairs" [Kyra, FNK-AAF, 51-60 year, 6-12 months CCRF].

Patients adapted their movements to their energy level. For example, biking or walking distance and pace were adapted to their situation, by taking breaks regularly. The public transport was rarely used. Driving a car or motor was not always possible and only possible for short distances, preferably outside the rush hours.

Most patients had to carefully plan and select their activities during the week and weekends because the time they could be active was shortened. Some participants mentioned that they preferred to plan their activities in the morning because during that moment of the day they felt more energetic. Patients reshaped their social life in response to their fatigue. Samuel described how he planned his social activities for the whole week:

"Yes, nowadays, it is mainly scheduling everything. I keep track of my appointments with an agenda, and dinner with friends is all in there. So, yes, I have a schedule for the week, so I know where to go and what to do. Like today, yes, I am free of activities, now you [researcher] are here for one hour, maybe longer. And afterward, I will rest for an hour" [Samuel, REFINE, M, 31-40 year, 2-5 years CCRF].

Most patients adapted their lives to their chronic fatigue experience and found new ways to function in daily life. The support of close others (also see Theme 3) facilitated this adaptation.

DISCUSSION

In this study, we explored the disruption of the lived body, lived time, lived space and lived social relations in patients suffering from CCRF. This chronic fatigue expressed itself in a broad array of experiences in patients who had finished their cancer treatment. We identified four interrelated themes that reinforce each other and illustrate the dynamic process of patients' bodily-felt experience of CCRF, which incorporated ***Worn out, Diminishment***

of one's "I can", Invisibility, and ***Regaining one's "I can"***. The chronically fatigued body is experienced from two perspectives: as a subject that is feeling and acting and as a material object that is felt and observed. These experiences of subject and object are closely intertwined. That is, patients experience the intense affective sensations of CCRF in close relationship to the functional limitations of one's "I can", and the consequences of the social invisibility of CCRF. Patients respond to these interrelated affective, functional, material and social dimensions of the CCRF experience by searching for new ways to adapt their lives towards CCRF in the process of regaining one's "I can".

Our interview data illustrated how bodily dys-appearance,[55] that is, awareness of the body as an object, is present in patients with CCRF. The chronically fatigued body is experienced as an obstacle ("ill", "alien", "older") and a limitation by losing its taken-for-granted position to act "free" in this world. Patients experience negative and intense bodily sensations, emotions, cognitions, and sensory stimuli that come to the foreground of their awareness and as such "stand in the way" of their functioning in daily life. These findings of bodily dys-appearance are similar to other qualitative studies on patients' experiences with CCRF and other chronic illnesses.[37,59,67]

The results showed that patients experience interrelations between the themes, and they report how their experience of CCRF can exacerbate. For example, when extremely fatigued (affective dimension), the body is negatively present in one's awareness (material dimension), limiting one's daily life functioning (functional dimensions). The mutual interaction and reinforcement of these affective, material and functional dimensions of CCRF is in line with embodied affectivity, which means that the body has a central position in how one perceives sensations and emotions, and how one's movement is affected.[68]

During the interview study, we observed that participants obviously struggle to put their experience of the invisible problem CCRF into words caused by the various feelings and potential cognitive problems. These difficulties to tell what they are feeling or explain this to others, could lead to miscommunication and misjudgment of the problem by close others and health professionals.[69] Leder used the term "social dys-appearance" when a disruption in communication exists that is affected by "the objectifying gaze of others".[55] The awareness of the body incorporates an intersubjective mode, because self-understanding always involves seeing oneself through the eyes of others.[55] The problem of CCRF is invisible to others and not explained by medical professionals. As such, the invisibility and differing expectations about fatigue after cancer can stigmatize and isolate patients.

Previous research on embodied experiences of cancer-related fatigue during and after treatment showed that regaining a sense of control could be an important aspect of boosting one's "I can".[37,70] For example, if a patient is better prepared for their chemotherapy and fatigue is recognized, the patient will experience more control, which can reduce the level of uncertainty and improve their wellbeing. In turn, this can facilitate patients in regaining one's "I can", which is not a disabling dimension, like the other themes, but a productive dimension that entails adaption.[39] The re-functioning results in a positive transformation of one's habitual identity that could facilitate new possibilities of perception, action, and self-understanding.[37,62] It helps to respond in a healthy way to CCRF.

The experiential changes of space were part of all the dimensions of embodied CCRF. Patients with CCRF experienced affective sensations and objectification of their bodies that influenced their functional limitations to move 'freely'. Because of their loss of mobility, caused by their chronically fatigued bodies and the heightened sense of distance similar to motor disorders,[58] transitions in spatial arrangement (e.g., taking an elevator instead of the stairs), driving a car (instead of using public transport) and walking or biking a short instead of a long-distance) were practiced to regain one's "I can".

Previous research showed that how a partner responds to chronic fatigue impacts the fatigue of the patient. For example, when patients and partners worry together about the fatigue and its limitations, patients will experience more fatigue.[71] Although we did not directly ask patients how fatigue influences their intimate relationships, several patients described how their partner was also affected by CCRF. Partners had to get used to the fact that patients were unable to do everything they used to do and need more time to rest. Open communication and support from partner, friends, and family appeared essential in regaining one's "I can".

Biographical, subjective, and objective time were used to refer to lived experience of CCRF. The frequently-made comparisons with pre-cancer fatigue experiences and activity levels are related to the disruption in biographical time.[51,52] Due to the affective sensations and functional limitations, patients experienced alienation of their bodies and a loss of their previous selves and expected a future with CCRF. Patients experienced different subjective time patterns that consisted of continuous experience of fatigue (e.g., omnipresent) and non-continuous experience of fatigue (e.g., fluctuations in severity). When patients describe how they perceive the cause of CCRF, objective time was used. Although patients tried to be attentive to objective time when planning activities, they could be overwhelmed by "fatigue attacks". Similar to patients with other chronic diseases, such as diabetes,[72] the chronically fatigued body has difficulties to improvise with time or to foresee what is needed. In a healthy situation, objective time is more structured around daily life and its activities,[51] while in the case of CCRF time is structured around moments of feeling less severely fatigued. Because of associated functional limitations, it took patients more time to carry out their daily life activities. The quality (e.g., reduced intensity), as well as, the quantity (e.g., fewer activities) of their activities had changed.

Strengths and limitations of the study

The small sample of 25 participants in total was homogeneous regarding characteristics of severe CCRF, that is, patients suffered from fatigue for at least three months after completion of treatment, and were active in seeking treatment for their fatigue. Nearly half of the sample suffered from severe depressive symptoms, while other severe psychiatric comorbidities were excluded. The experience of CCRF is often accompanied with anxiety and depressive symptoms.[13,73] Because we have investigated a diverse group of patients, we also reported a wide range of experiences and responses to CCRF. The open questions of the interviews started with the cancer experience and focused on experiences with CCRF, but we could not rule out that patients' answers were sometimes diffused with experiences of other comorbid conditions. We expect that the presence of partners during (part of the) interviews has led to more interaction and greater openness about the experiences. We cannot exclude that differences exist between patients with different cancer types and treatments. Another possible limitation is that the interviews were conducted by three different interviewers, but we expect that the influence was minimal because of the careful interpretative and inductive participant-oriented analysis process.[66,74] We performed member checks with six new participants and they all agreed with the descriptions, which improved the credibility of the data. Although the sample (N=25) was quite large for the idiographic analysis process, the IPA methodology was carefully performed throughout all case-by-case and cross-case stages of analysis.[66] During the analysis, we continuously checked if our interpretations were consistent with the underlying data. The philosophical framework we applied; enabled us to improve and direct the inductive analysis of the findings at a more in-depth level and put it into a broader context of chronically lived experiences.

Clinical implications

The present study provides new clinically important information on how patients experience CCRF. Patients use different words to express their experience with CCRF which could help professionals to better recognize, report and treat patients. These insights could also improve the understanding and communication between patients, close others, and professionals with a focus on softening bodily objectification and supporting them in their functioning.

Health professionals could ask patients questions about their experiences with CCRF to come to a shared decision with the patient on what therapy is most suitable. Questions could entail: what do you experience (intensity and interrelated symptoms), when do you experience CCRF (time and situation), what do you do about CCRF (when, how much, how, and future expectations), how is your social support, how do you deal with CCRF, and what is helpful?

Psycho-oncological care is a form of care that is lifeworld-led and focuses on the person as a whole and their significant others, which provides an existential view of well-being rather than focusing on one's illness. This type of care seems a promising way of helping patients handle the complex, dynamic, embodied problems that CCRF poses.[75–77] Because patients are easily fatigued after travelling, web-based interventions for CCRF could offer a valuable alternative.[61]

CONCLUSION

This interpretative phenomenological analysis has provided a window into the interrelated affective, functional, material, and social dimensions of the embodied experiences of CCRF and sheds light on the everyday world of those who live with it. This study shows that experiencing CCRF is a personal, complex and dynamic process that consists of different interrelated dimensions. This experiential knowledge adds additional embodied dimensions to the multidimensional problem CCRF and broadens the context with bodily, time, spatial and social aspects of how patients experience and communicate about CCRF. This information could help to design studies to measure individual patterns of fatigue to assist therapists to personalize effective treatment in clinical practice. We suggest more qualitative research in addition to quantitative methods is needed on this topic to explore how to best address the personal challenges individual patients with CCRF face daily in their social context.

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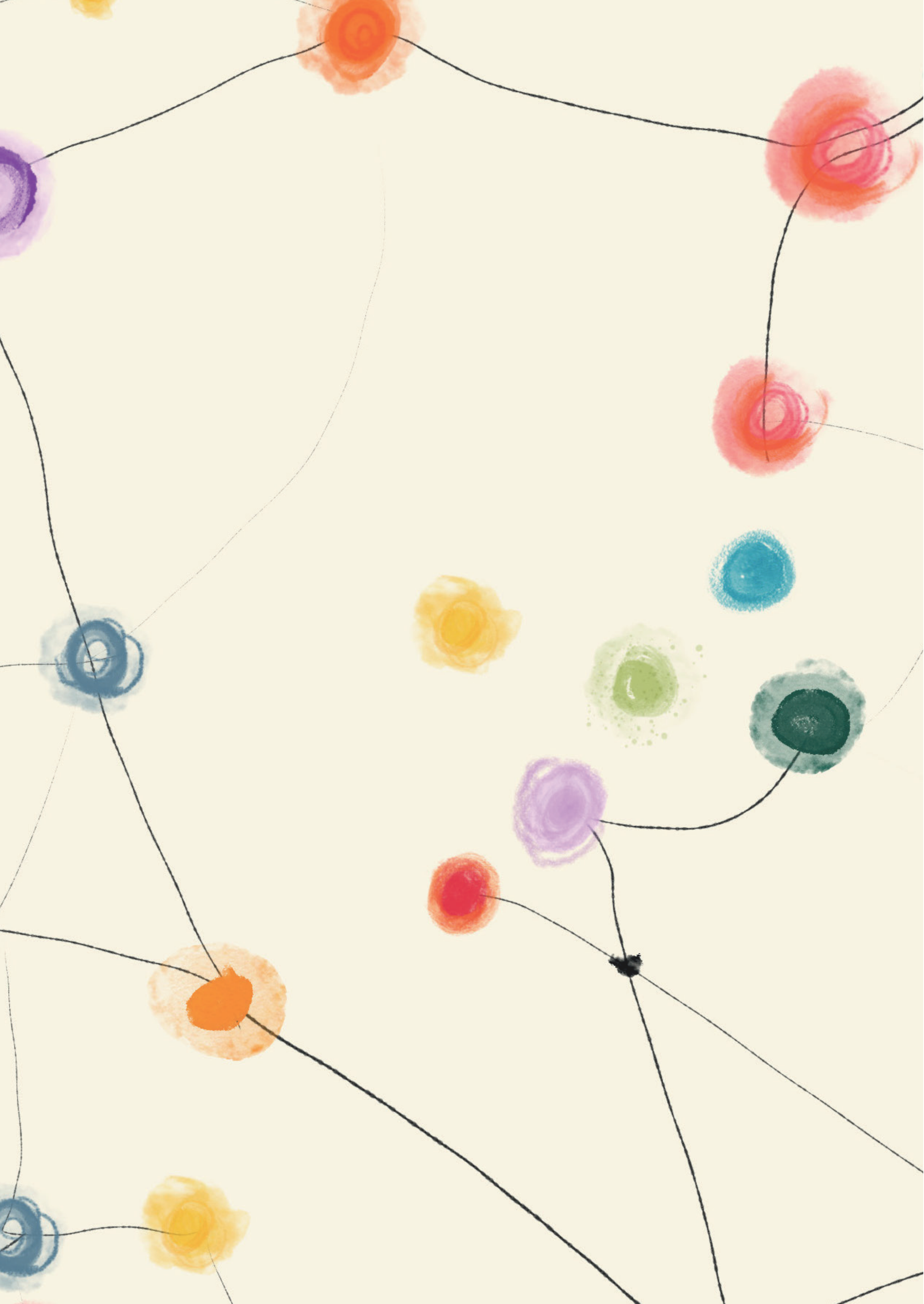

Chapter 4

FORMING NEW HABITS IN THE FACE OF CHRONIC CANCER-RELATED FATIGUE: AN INTERPRETATIVE PHENOMENOLOGICAL STUDY

Bootsma TI, Schellekens MPJ, van Woezik RAM, Slatman J, van der Lee ML. Forming new habits in the face of chronic cancer-related fatigue: An interpretative phenomenological study. Support Care Cancer. 2021 Nov;29(11):6651-6659.

ABSTRACT

Purpose

The growing group of patients who suffer from chronic cancer-related fatigue (CCRF) after cancer have helpful and less helpful ways of responding to this long-lasting and disruptive problem. This qualitative study aimed to gain insight in essential elements of how patients respond to CCRF, with a focus on helpful responses to facilitate adaptation.

Methods

We conducted semi-structured interviews with a purposive sample of 25 participants who experienced severe CCRF for at least three months. Participants were recruited via media, patient associations, meetings and health professionals until data saturation was attained. We used a topic guide with open-ended questions about lived experiences. Interpretative Phenomenological Analysis (IPA) was used for analysis of the transcripts.

Results

We identified five interrelated themes of how patients respond to CCRF: (***1) discovering physical and emotional boundaries; (2) communicating support needs; (3) reorganizing and planning activities and rest; (4) letting go of one's habitual identity;*** and ***(5) recognizing and accepting CCRF.***

Conclusion

This study highlights the development of new habits and positive beliefs in the face of CCRF and the importance of (social) support in this process. This experiential knowledge on helpful responses can be used to inform patients and their significant others and improve self-efficacy. Health professionals could use these insights to improve recognition of CCRF and personalize treatment.

INTRODUCTION

Approximately 25% of the cancer population experiences severe and disabling chronic cancer-related fatigue (CCRF) months to years after cancer treatment is finished.[1–4] Patients and their caregivers are often negatively impacted by the adverse physical, psychosocial and economic consequences of experiencing CCRF.[5] For example, fatigue as a chronic illness can affect the ability of the patient to engage in paid employment[6] and caregiver burden is high.[7,8] To date, various psychological and exercise interventions for CCRF exist and have been found effective in selected groups of cancer patients.[9–11] The variation in effectiveness of interventions for CCRF may also be down to a mixture of ineffective interventions or study designs that do not account for intra- and inter-individual variability in fatigue patterns. The question "what works best for whom?" needs to be addressed to support patients and therapists in the selection of the most effective intervention for alleviating CCRF. Further in-depth insight into the patient perspective on essential elements of responding to CCRF could help answer this question. Although the complex etiology is not fully understood, we expect that a variety of risk and protective factors can influence how people respond to CCRF over time.[12,13] So far, the literature has mainly focused on unhelpful responses to fatigue (e.g., dysfunctional cognitions, dysregulation of activity, negative social interactions).[8,14,15] In order to improve treatment of CCRF, more insight in helpful responses is needed to target the complete spectrum of behavior during therapy.

A relevant interrelated framework of personal, behavioral, and social factors to gain insight into patients' helpful responses to chronic illnesses, such as CCRF, is the THRIVE model.[16] One of the key factors of this model is the forming of new habits and breaking with unhelpful habits.[16–19] From a psychological perspective, habits are defined as repetitive behaviors that are partially automatically executed over time.[20] The experience of cancer and its possible side-effects during treatment has disrupted patients' daily routines. The persistence of CCRF after treatment prevents patients from restarting their daily routines, meaning they cannot do simple (automated) tasks in daily life at the same time and in the same way as before cancer.[5] The formation of new habits is required in this situation to improve self-management behaviors, such as exercising.[17,19,21] The THRIVE model emphasizes the importance of positive psychological beliefs (e.g., acceptance of illness and self-efficacy) in order to adhere to these new habits in the long-term.[22]

More insight into the formation of new habits and beliefs from a phenomenological perspective can inform us what conscious and unconscious processes are part of helpful responses in the face of CCRF. Therefore, we chose a phenomenological study design because this interpretative methodology can be applied to illuminate the first-person perspective of responding to CCRF. Responding to a chronic illness is expected to be a dynamic, complex, multifaceted, and ongoing process that is never fully completed.[16,23,24] The purpose of the present study is to gain insight in essential elements of how patients respond to CCRF, with a focus on helpful responding to facilitate adaptation.

METHODS

Study population

Participants were deemed eligible when they met the following criteria: 1) adults at time of cancer diagnosis; 2) experienced severe cancer-related fatigue (score ≥35 on Checklist Individual Strength - Fatigue Severity subscale[25]) for at least three months after finishing curative cancer treatment (except hormonal treatment); 3) had no current or former severe psychiatric comorbidity (i.e., suicidal ideation, psychosis or schizophrenia); and 4) were able to speak and read Dutch.

Recruitment

All participants were recruited within two research projects in the Netherlands. The first project is the More Fit after Cancer trial (Fitter Na Kanker (FNK) Trial) that selected 22 participants after (partial) completion of one of the two online interventions for CCRF: physiotherapist-guided Ambulant Activity Feedback (AAF) and psychologist-guided Mindfulness-Based Cognitive Therapy (eMBCT). In this study, nineteen participants agreed to participation in the interview study between December 2015 and March 2016. The second project is the REFINE project, in which 28 participants responded. Of the 28 responders, six participants were eligible and purposively sampled for participation in the interview study between August 2018 and January 2019.

In the FNK trial participants were recruited via advertisements in newsletters of patient associations, relevant websites, regional newspapers, social media and through oral presentations on various occasions for patients and/or caregivers. In the REFINE project participants were recruited via patient websites or their health professionals. The health professional provided the participants with information about the interview study and referred interested participants to the researcher. Willing participants of both projects were then contacted by a researcher of one of both projects, and both verbal and written informed consent was obtained. We stopped recruitment when saturation was attained, i.e., when no new information emerged from the interviews of the purposive selected sample during analysis.[24]

Semi-structured interviews

The semi-structured topic guides consisted of open-ended questions based on literature, clinical experience, and were pre-tested with a therapist with clinical expertise in treating patients with CCRF at the mental health institute for psycho-oncology. The first interviews with patients in both projects were seen as a pilot and evaluated as clear and concise. Therefore, no changes had to be made to the interview questions and these pilot-interviews were included in the analysis. The topic guide of the FNK trial focused on the evaluation of one of the two online interventions for CCRF **(See Table 1 Chapter 3)**. The topic guide of the REFINE project included experiences (descriptions, sensations, cognitions, patterns, attributions), consequences (daily life, body, self), actions (self, others, helping and hindering factors), and other important factors related to CCRF **(See Table 2 Chapter 3)**. Interviews were face-to-face and held at the participants' location of preference at either an institute for psycho-oncology, their home or online with a video-connection. Three researchers (two men, one woman), including the first author, conducted the interviews in both projects and had previous experience in psycho-oncology and/or qualitative research. The interviews were audio-recorded with a voice tracer and transcribed anonymously by one of the research assistants of the study projects. The duration of the interviews in the FNK trial was on average 40 minutes, and on average 64 minutes in the REFINE project. Member checks were utilized for the six additional interviews of the REFINE project by sending a summary of findings to participants to check that ways of responding to CCRF were correctly understood and to allow them the opportunity to respond. All participants agreed with the content of the summary.

Data-analysis

The first and third author independently coded the first five interviews of the FNK trial (MaxQDA software, version 18.2.0). Codes were discussed until consensus was reached. Because after five interviews less and less variation between codes existed, the first author openly coded the other twenty interviews case-by-case in the same inductive way. In case of uncertainties regarding the codes, the first author discussed this with the third author to reach consensus. We used the six steps of Interpretative Phenomenological Analysis (IPA) for the coding process.[24] The IPA is particularly useful to investigate the multidimensionality, dynamics, context, and subjectivity of CCRF.[24] The first step of coding according to IPA was reading and re-reading the transcripts to become familiar with the data. The second step was initial noting as the start of the open coding process. In the third step emergent themes about responding to CCRF were developed within the interviews. A selection of six categories (i.e., metaphors, beliefs, comparisons, responses, helpful and unhelpful responses) of the codebook were sorted in general maladaptive (e.g., move on, denial, and resistance) and adaptive (e.g., slow down, stop or reduce activities) subcategories. The complete codebook was used for interpretative analysis of lived experiences with CCRF for publishing a separate paper (**see Chapter 3**). In the fourth step, we searched for connections across the emergent themes and developed a cross-table with two general patterns in the coping process: adapting (individual/social) and letting go (individual/social). In the fifth step, we checked for completeness with the summary of the individual interviews. In the last step, we organized two team discussions to identify superordinate themes that describe both helpful and unhelpful responses. Discrepancies about identified themes between team members were discussed until consensus was reached. This multidisciplinary team included all authors who have clinical and/or qualitative research expertise in psycho-oncology.

RESULTS

Sample characteristics

In total 25 patients suffering from CCRF participated. Nine participants (partially) completed the AAF intervention. Ten participants (partially) completed the eMBCT intervention. Two participants reported that they were currently treated by a physiotherapist. Eleven patients (44%) scored above the threshold (≥15) on the Hospital Anxiety and Depression Scale, suggesting clinical levels of distress.[26–28] **Table 3 of Chapter 3** shows the characteristics of the participants.

Responses to CCRF

We identified five interrelated themes that characterize the dynamic and mutually reinforcing process of responding to CCRF: ***(1) discovering physical and emotional boundaries; (2) communicating support needs; (3) reorganizing and planning activities and rest; (4) letting go of one's habitual identity;*** and ***(5) recognizing and accepting CCRF.*** **Table 1** shows patients' quotes that support the five themes.

(1) Discovering physical and emotional boundaries

In the first period after experiencing CCRF, most patients used habits that were useful before their cancer diagnosis. For example, pushed themselves to do certain things in their daily life, tried to move on, and as a result, neglected their bodies and emotions. Moving on is characterized by speeding up activities and resisting CCRF. After a while, several patients stopped denying of the fact they suffered from CCRF and used different ways to tune into the emotions and sensations of their vulnerable bodies, afflicted by cancer and its treatment. For example, writing about their emotions, cognitions and CCRF experiences helped discover change and progression. This kind of self-monitoring led to new insights into how their body felt and gave them a choice in how to protect their boundaries. The protection of their boundaries is a dynamic process of trial and error. Patients described that they needed to learn deciding on the right moment for relaxation to prevent exhaustion.

(2) Communicating support needs

While discovering their physical and emotional boundaries, patients found it difficult to ask for help and tried to go on without support. However, most patients came to a point to accept they needed help and ask for the support of their close others. For example, patients openly communicated with their partner, friends, family, or colleagues about how they felt and what they could and could not do anymore. Most patients appreciated the support and empathic reactions they received from their social contacts. Some patients described how they tried to keep their CCRF silent when they met new people, because they were afraid of misunderstanding and negative reactions. When CCRF and the debilitating consequences for daily functioning persisted, most patients looked for more information on the internet, in books or apps and/or asked for professional support from their medical oncologist, a psychologist, or physiotherapist.

(3) Reorganizing and planning activities and rest

The experience of CCRF introduced a dysregulation in (social) activity, with patients being too active or too inactive. The time for rest was in all cases prolonged, for example, by sleeping more hours at night. Sometimes too much rest was taken, such as sleeping for hours during the day. As a result, patients did not experience an alleviation but an exacerbation of their feelings of CCRF. Becoming aware of their boundaries and communicating their support needs to others helped them to adapt their daily habits and search for more balance in activities and rest. Their activities were passively and actively clocked, structured, adjusted, or reduced, and alternated with time to rest. Patients reported examples of how they reorganized their daily activities: withdrawing from activities, taking time for themselves, going home earlier, and using ear plugs to avoid over-stimulation. Social activities lost their spontaneity and were planned. Patients prioritized the contact with close others and tended to stay at home instead of visiting someone. In cases of extreme fatigue, patients disengaged from their social life entirely and focused on resting. When exhaustion threatened their ability to do daily life activities, they found practical solutions. For example, some patients started using a disability parking card, cruise control in the car, an electric bike, or an elevator. The rush hours in traffic were avoided and a car was only used for short distances.

(4) Letting go of one's habitual identity

As patients learned more about their boundaries and adjusted their daily life accordingly, they were confronted with the fact the cancer and resulting CCRF had changed them. Some patients reported becoming more of an emotional person after cancer and preferring a different type of contact with others, with a focus on listening rather than talking and a need for in-depth conversations. Several (social) activities were not possible anymore. For example, some participants stopped working and had to let their significant others take over activities, such as taking care of children, driving the car, or cooking dinner. The letting go of old habits and becoming a less active person (in the evening or after activity) meant losing (part) of their old self.

(5) Recognizing and accepting CCRF

Most patients experienced negative emotions, unhelpful thoughts and beliefs that make it difficult to recognize and accept the unpredictable symptoms of CCRF. Some patients were able to let go of their negative emotions, unhelpful thoughts, and beliefs towards CCRF at certain moments throughout the day. If their social environment was accepting and understanding, it was easier to let go of their resistance against CCRF. The first step in this process was recognizing and acknowledging they suffered from CCRF. This awareness made it possible to accept that their situation was different from before cancer and they had to make the most of this "new normal". The formation of new habits such as discovering their boundaries, adjusting their daily life activities, and communicating their support needs have contributed to the acceptance of CCRF.

Interrelations of themes

The phenomenological approach showed that the identified themes are part of habit formation that starts at a pre-reflective level (i.e., prior to any conscious evaluation). One participant described the change in habits and adjustment to their new normal as an automatic process:

"Yes, unconsciously you devise things for yourself and yes that becomes routine and, in the meantime, you know, you don't even realize that you have planned or managed things like that because it eventually has become normal. It actually has become your life…" [male, 41-50 year].

The self-monitoring process of awareness of sensations and discovering physical and emotional boundaries is originated in the body and in relation to others by communicating support needs. These introspective and communicative ways of responding provide useful insights to reorganize one's activities and rest and vice versa. The letting go of old and unhelpful habits and beliefs initiates an identity change, which creates room for new habits and beliefs that facilitate acknowledging and accepting CCRF.

Table 1: Themes of responding to CCRF

(1) Discovering physical and emotional boundaries
"You will never reach your old level, so you have to keep in mind, maybe you will not reach that level ever again and be happy with what you can do. Yes, and in my case, I don't want to exaggerate, but it all turned out fine. Thus, I can do just about anything what I could do before. I can play tennis again, I can go out for an evening, I can study and I can handle work. But I uh, I have noticed that I should be aware of to the fact that I will go very quickly beyond my boundaries" [male, 31-40 years].
(2) Communicating support needs
"Yes, mainly my close friends and family notice this. And if I have a busy day at work and I'm unable to cook my meal without the risk of burning it than I can ask my sister if she would like to cook for me tonight" [male, 31-40 years].
(3) Reorganizing and planning activities and rest
"Whenever I sit on a chair, I drink my tea in 5 minutes and then I move on. I've learned that's not the way to do it. Instead, I get a puzzle, a Sudoku, then I solve the puzzle and remain seated for fifteen to twenty minutes" [male, 61-70 years].
(4) Letting go of one's habitual identity
"Yes, what is not helpful, is uh, doing sports [laughed] and yes, what shall I say, actually trying to pick up your old life. Of course, you return to life but not all activities you did before. That is not helpful actually. At least for me, that is counterproductive. I mean uh I can easily take my motorbike and so on but then I notice my concentration and I tried but it just doesn't work and that is counterproductive so I leave it there. I tried, but. Just like work, I tried 3 hours, but I couldn't keep up" [male, 41-50 years].
(5) Recognizing and accepting CCRF
"Well yes, specifically the fatigue comes up suddenly and it is actually not predictable when it will appear. Sometimes I am very busy and I do not feel it, and sometimes it's a very quiet day and then all of a sudden, kaboom. But it is also a very strange paralyzing fatigue, fatigue that normally disappears when you sit down, but this doesn't disappear. I still haven't discovered, now after 6 years, how I can make it better. It comes and goes. And on the one hand I accept it, because it is a part of me, and I don't know whether it is caused by the fact that I have had cancer or that it is caused by the chemo or the medications I still use. That I don't know. But I know that I have it and I accept it and on the other hand I think, no, I just don't accept it. Because I have to keep up in society, things are expected of me. And that makes it difficult to always accept it" [laughs a bit] [female, 41-50 years].

DISCUSSION

This study aimed to better understand how patients respond to CCRF in helpful ways. The processes of forming new habits and positive beliefs and breaking with unhelpful habits and negative beliefs appeared essential for a helpful way of responding. Body awareness helped patients to discover their physical and emotional boundaries and seek support, which in turn facilitated time-management between activities and rest. This change in habits created a change in identity, with new behavior and beliefs, which further aided patients to adhere to their new habits.

These findings are in line with other qualitative studies that found several comparable ways of responding to CCRF, such as support, activity management, identity change, and acceptance.[29,30] However, these qualitative studies did not investigate the habit formation process with use of helpful and less helpful ways over time. The discovering of physical and emotional boundaries is not covered sufficiently by other studies. Another difference is that while other qualitative studies focused on differences of responding to CCRF between persons, our results suggest also the possibility of differences within persons of responding to CCRF throughout the day and from day to day.

These results build on previous findings that responding to CCRF is embodied[31] and partly an automatic, repetitive habitual behavior that requires minimal forethought.[32] The identified themes of responding to CCRF closely fit the three levels of habit formation that were reported by Wehrle, based on Husserl's later works.[33,34] These active and passive levels of habit formation represent both conscious and unconscious processes in relation to one's previous experiences.[33] The first level of habit formation is defined as a style of experiencing based on a direct, unconscious reaction towards repeated individual experiences. The struggle against CCRF with unhelpful habits and beliefs, such as moving on and neglecting one's body are based on this primary unconscious reaction to CCRF and related to precancer experiences with fatigue. The second level of habit formation originates from the body and relates to previous embodied experiences (e.g., bodily memory) in active and passive ways. The themes "Discovering physical and emotional boundaries", "Communicating support needs" and "Planning and reorganizing activities and rest" are examples of the second bodily level of habit formation and indicate a learning process in relation to previous embodied experiences. For example, what the body experiences is central and related to previous experiences in the different self-monitoring processes patients use such as writing about experiences, clocking activities and taking care of their bodies. At first, these processes are more active before becoming aware of their bodies in more passive ways. The third level of habit formation is based on personal and conscious reflection to change and adhere to new habits. The themes "Letting go of one's habitual identity" and "Recognizing and accepting of CCRF" reflect this personal level of habit formation with development and adoption of new beliefs.

In the present study, we shed more light on what characterized the change of identity and how it plays a central role in responding to CCRF, by letting go of old habits and (social) activities and forming new ones. The changed habits of sleeping more, moving less, and changes in communication preferences make patients with CCRF sometimes unrecognizable for themselves and others, which has an impact on their identity.[33] This loss of self was reported by patients in several qualitative studies on CCRF.[31,35–37] Informing and involving the social environment (e.g., partner) on what it means to experience and cope with CCRF can facilitate this change in habits.[38]

Clinical implications and future research

This study offers in-depth insight into the central role of the body, identity, and dynamics of helpful and unhelpful responses in the face of CCRF that can be useful for improving self-management and development of personalized treatment. It depends on the individual patient whether self-management is sufficient to form new habits and beliefs or whether additional treatment is needed, and which (combination of) treatment(s) is preferred and most effective in reducing CCRF. These insights into responses to CCRF can facilitate patients and therapists in making a shared decision about the preferred (combination of) treatment(s).

Because many patients suffer from multiple interrelated symptoms after anticancer treatment is completed, a transdiagnostic or holistic perspective is preferred to treat these patients. For example, Kuba investigated a group of hematological cancer patients (≥2.5 years post diagnosis) and found that acceptance of one's present moment experiences is associated with lower levels of fatigue and subjective cognitive impairment.[39] Acceptance of CCRF is a central theme in our study and can be a potential target for interventions to deal with CCRF and other symptoms. Mindfulness-based interventions (MBIs) focus on enhancing bodily awareness by intentionally paying attention to present moment experiences, in an accepting, non-judgemental way.[40,41] Besides face-to-face and group interventions for treating CCRF, effective web-based interventions (e.g., online activity coaching, cognitive behavioral therapy (CBT), and mindfulness-based cognitive therapy (MBCT)) might be a valuable alternative for patients.[10,42,43] Health professionals should advise patients about the different options and refer patients to the treatment of preference.

Future research on CCRF could benefit from innovative methodologies such as the experience sampling method and network analysis to investigate inter-and intra-individual differences in experiencing and responding to CCRF and find an answer to the question: what works best for whom? Further qualitative research for developing and evaluating interventions is recommended that includes the caregivers' perspective because responding to CCRF is a mutual process.

Strengths and limitations

The IPA used in the present study goes beyond other existing qualitative studies on CCRF by exploring the central role of the body, interrelatedness and importance of social context in the evaluation of helpful responses in a purposive selected sample. Some limitations should be noted. First, patients' experiences were evaluated retrospectively on different times after cancer treatment was finished. Second, although a diverse clinical sample of patients with CCRF and several comorbidities participated, we should be cautious to generalize the results to individual cancer patients with other cultural backgrounds and differing comorbidities. Third, similar to other qualitative studies on CCRF,[31] the majority of participants had breast cancer which limits generalizability. At the same time, this is an adequate reflection of patients who seek psychological help for CCRF.[44] Fourth, although three different interviewers conducted the interviews, this impact is expected to be minimal, because of the self-reflection of interviewers and inductive participant-oriented analysis process of the rich data.[24,45]

CONCLUSIONS

The present study highlights the development and adherence of new habits and beliefs in the face of CCRF and the importance of (social) support in this process. This new experiential knowledge on self-monitoring, support-seeking, and time-management habits and acceptance of CCRF can help inform patients and their significant others about self-management in the face of CCRF and improve self-efficacy. Health professionals could use these insights in clinical practice to improve timely recognition and personalize treatment for patients with CCRF.

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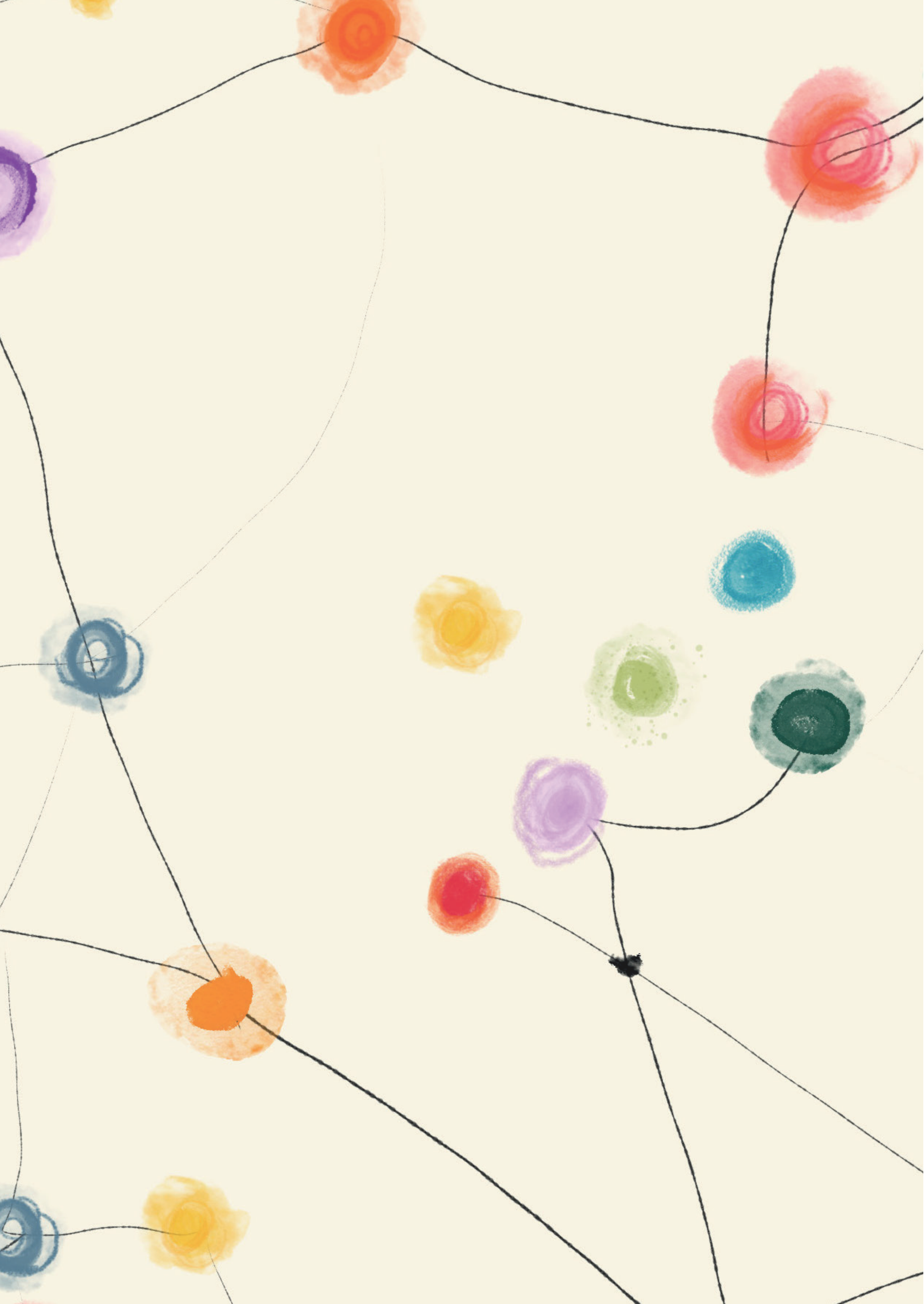


Chapter 5

USING SMARTPHONE-BASED ECOLOGICAL MOMENTARY ASSESSMENT AND PERSONALIZED FEEDBACK FOR PATIENTS WITH CHRONIC CANCER-RELATED FATIGUE: A PROOF-OF-CONCEPT STUDY

Bootsma TI, Schellekens MPJ, van Woezik RAM, Slatman J, van der Lee ML.
Using smartphone-based ecological momentary assessment and personalized
feedback for patients with chronic cancer-related fatigue:
A proof-of-concept study. Internet Interv. 2022 Aug 24;30:100568.

ABSTRACT

Introduction

Chronic cancer-related fatigue (CCRF) is a complex multidimensional problem warranting person-centered care. Providing patients and therapists personalized feedback based on network analysis applied to ecological momentary assessment (EMA) data could facilitate case conceptualization in psycho-oncological care. The aim was to explore patients' and therapists' experiences of using an EMA app and personalized feedback based on network theory to aid case conceptualization in psycho-oncological care.

Methods

A n = 5 proof-of-concept study was implemented in routine psycho-oncological care. We purposively selected adult cancer patients suffering from severe CCRF who were on the waitlist for psycho-oncological care. During a 3-week period, participants filled out the EMA app *Energy InSight* (fatigue, mood, activity, responding, and context) five times a day. Participants received a descriptive and network feedback report, which they reflected upon during the first therapy sessions. Thematic analysis was used to analyze user experiences.

Results

Patients experienced that filling out the *Energy InSight* app, as well as receiving descriptive and network-based personalized feedback provided them with insight into their CCRF. Although therapists experienced the discussion of network feedback as challenging, it facilitated the case conceptualization.

Discussion

Using EMA during waitlist for psychological care seemed feasible. Patients experienced beneficial effects from filling out the EMA app and talking over the personalized feedback reports, which in turn aided case conceptualization and personalized care. Based on this evaluation, an improved version of the *Energy InSight* app and a therapist training for providing network feedback is developed for implementation in psycho-oncological care.

INTRODUCTION

Chronic cancer-related fatigue

Fatigue is experienced as the most disruptive side effect of cancer and its treatment.[1] Approximately 25% of cancer patients suffer from chronic cancer-related fatigue (CCRF) months to years after cancer treatment is completed.[2,3] From the patient perspective, CCRF is an embodied experience with different interrelated dimensions (e.g., physical sensations, limited daily functioning, invisibility of fatigue) that vary across social situations, and throughout the day.[4] Patients with CCRF experience several limitations in their daily life. Along the way, learning new habits (e.g., reorganizing and planning of activities and rest) and adapting their beliefs (e.g., accepting their limits) helps them to deal with this long-lasting problem.[5] The dynamics, differences, and interrelations of experiences and responses to this complex problem require a person-centered approach.

What works best for whom?

Among effective behavioral interventions are mindfulness-based interventions (MBIs), cognitive behavioral therapy (CBT), and physical activity interventions (PAIs). Although these interventions have shown to be effective in treating CCRF, it is unknown what works best for whom.[6] Gaining insight into the needs and characteristics of individual patients can optimize the psycho-oncological care for CCRF patients.[7] Such a person-centered approach can help health professionals to make a shared and personalized decision with the patient on the most suitable treatment for CCRF.

Network approach and case conceptualization

The network approach to psychopathology as developed by Borsboom and Cramer (2013) has inspired the development of network methodology that can be used to empirically support case-conceptualization by visualization of a person-specific network.[8] This approach conceptualizes symptoms as causally connected elements of a complex dynamical system (e.g., sleep problems trigger fatigue and concentration problems, resulting in feelings of worthless and worrying, which can trigger a depressed mood), rather than viewing symptoms as the result of a latent disease (e.g., you feel depressed because you have a major depressive disorder).[8] Applying the network approach to psycho-oncology helps to shed more light on the interrelated co-occurring trans-diagnostic symptoms cancer patients often experience and overcome the deep-seated body and mind dualism.[9–11]

To date, therapists use case conceptualization as a basis for therapy and shared-decision making in clinical practice.[12] Therapists' experience and theoretical knowledge is combined with patients' characteristics and daily experiences to formulate a working hypothesis that, similar to the network approach, encompasses the identification of the patients' unique interrelations of emotions, behaviors, cognitions, somatic states, and context, in order to find the best suitable treatment for this individual. While this method can offer valuable insights for patients and therapists, its reliability appears insufficient because it is not feasible to empirically support the complexity of a case conceptualization. There is no golden standard for such a complex problem-solving procedure and it is sensitive to incomplete and biased retrospective information.[12]

Use of experience sampling method and personalized network feedback

A more reliable method to systematically collect data and analyze the interrelations of symptoms, emotions and behavior using the network approach is ecological momentary assessment (EMA). EMA is a structured data collection method in which a participant receives questions multiple times a day for multiple consecutive days about their present feelings, activities, and context in their daily living environment.[13] This results in a rich longitudinal dataset, making it possible to examine the interactions between symptoms and other factors in a detailed, ecologically valid manner at the level of the individual patient.[13] By applying network analysis, we can visualize the person-specific multidimensional and complex problem of CCRF. EMA is used in clinical research and practice to optimize treatment of different mental disorders (e.g., depression, psychosis) and has recently been introduced in psycho-oncology.[14–16] The use of EMA for patients who experience fatigue during and after cancer treatment has appeared usable and feasible.[15] So far, two studies investigated the use of smartphone-based EMA followed by personalized feedback for severely chronically fatigued cancer patients. In one case study, the most important predictors of fatigue were identified using time series analysis, which resulted in a different treatment plan.[17] This personalized treatment plan recommended treating these factors (e.g., fear of cancer recurrence) first during CBT. In another feasibility study, a personalized feedback report based on descriptive statistics and intensive longitudinal data analysis was provided to chronically ill adolescents who suffer from fatigue, and, if possible, discussed with the psychologist or physician to personalize treatment.[18] These studies provided limited or no insight in how patients and therapists experience working with such personalized feedback. In the present study, we will evaluate patients' and therapists' experiences and provide personalized feedback reports based on network theory and analysis to investigate personalization of psycho-oncological care for patients with CCRF.

Aim of study

This current qualitative study focuses on both patients' and therapists' experiences using smartphone-based EMA and personalized feedback in psycho-oncological care of CCRF. The primary aim was to examine to what extent and how a patient gains insight into CCRF by filling in the smartphone-based EMA and receiving personalized (network) feedback. The secondary aim was to explore how this insight can be used to help patients and therapists improve case conceptualization in psycho-oncological care for CCRF.

MATERIAL AND METHODS

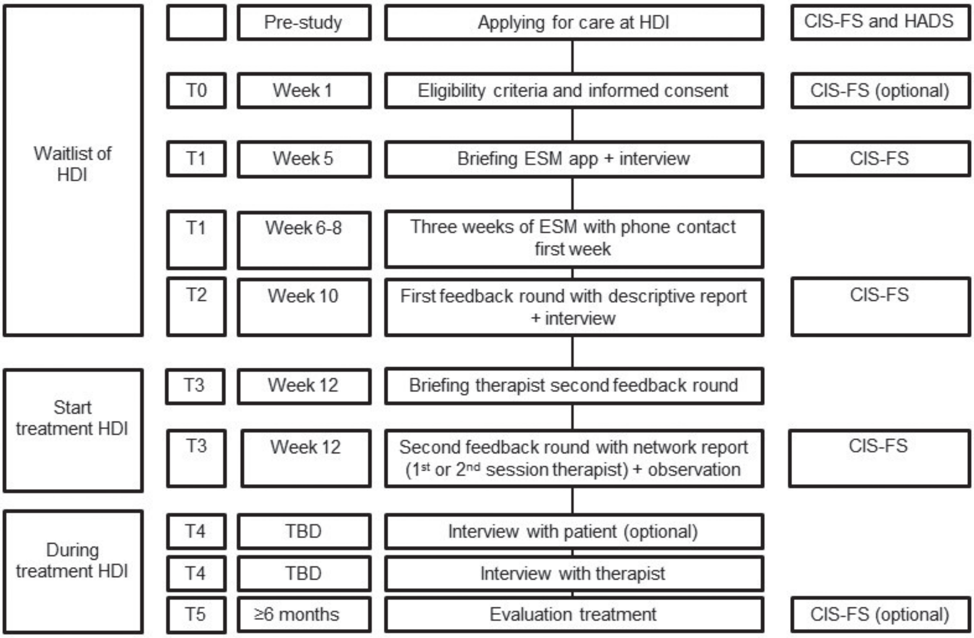
Study design

This n = 5 proof-of-concept study was part of the routine clinical care of the Helen Dowling Institute (HDI), a mental health care institute for cancer patients in the Netherlands. It was approved by the Medical Ethics Review Committee Brabant (P1935).

Study procedures

Figure 1 shows a flow chart of study procedures. Between September 2019 and February 2020, patients on the waitlist for HDI were consecutively selected for participation by their screening therapists (T0). Participants provided written informed consent. We checked the diversity of participants based on different demographic (i.e., gender, age, educational level, partner) and clinical characteristics (i.e., cancer type and (time since) treatment) and ensured sufficient time before the start of treatment to follow the study procedures. Eligibility criteria included: 1) adult patients ≥ three months since the end of curative cancer treatment; 2) severely fatigued (score ≥ 35 Checklist Individual Strength - Fatigue Severity subscale (CIS-FS));[19] 3) no current or former severe psychiatric comorbidity; 4) referred to HDI with treatment indication: CCRF; 5) sufficient Dutch language proficiency; and 6) own a mobile phone with an Android or iOS operating system. Participants received instructions by e-mail to install the EMA app on their mobile phone. During the first session (T1) with participants the installation of the EMA app was checked by TB and one participant used a loan phone because of technical problems. While being on the waitlist for psycho-oncological care, participants filled out the EMA items for three weeks (T1). Within a week, they received a personalized descriptive feedback report from the researcher (T2). Before discussing the network feedback with their client, therapists received instructions on interpreting the network figures. At the first or second treatment session, the therapist discussed the personalized network feedback report with the participant (T3). TB observed and evaluated patients' experiences with the EMA app (T1), the descriptive feedback report (T2), and the network feedback report (T3/T4). In addition, patients filled out questionnaires prior to the EMA period (T1), and before receiving the descriptive feedback (T2) report and the network feedback report (T3). TB collected qualitative user experience data from the therapists with the personalized feedback reports during the first phase of treatment (T3/T4).

Figure 1: Flow chart study procedures



Measures

Development EMA items app Energy InSight

The selection process of EMA items was guided by previous qualitative research on the patients' perspective on CCRF, group-level network studies on CCRF, and clinical expertise in treating patients with CCRF.[3–5,11,20,21] We selected items that we expected to vary momentarily and measured the experiences and responses to CCRF: fatigue-related symptoms, positive and negative mood, activity, coping with fatigue, and context **(Table 1)**.

The selected items were described elsewhere (**Chapter 6**).[22] The items were mainly positively framed, e.g., "energy" instead of "fatigue". Fatigue-related symptoms and mood items started with "I feel" or "I am" and were phrased momentarily. Activity and responses to CCRF were framed in terms of "in the past three hours" because that is the average time between two questionnaires. We organized two group meetings with patient experts, clinicians, and (EMA) researchers to discuss, refine, and validate the 24 selected questions of the EMA app named *Energy InSight (Dutch: Energie InZicht)*. The name *Energy InSight* comprises a double meaning: *Insight* and *in Sight*.

We used the custom-built smartphone app Ethica[23] to build in *Energy InSight* (**Figure 2**). TB pilot tested the questionnaire with patients and therapists and performed a cognitive walkthrough of *Energy InSight* and instructions.[24] Based on these findings, all documentation and *Energy InSight* were improved, validated, and finalized.

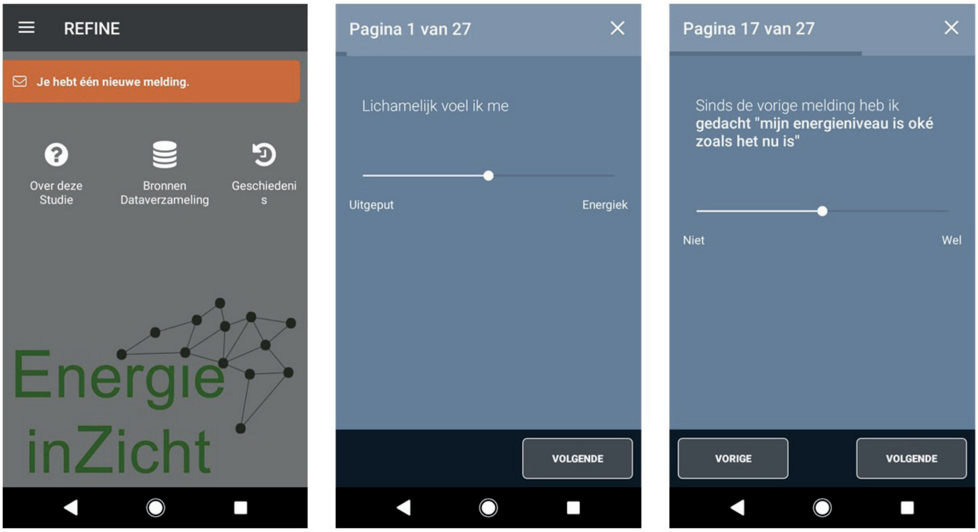
After evaluation with the first three participants, we decided to further refine *Energy InSigh*t and instructions. Participants reported that the extreme response options (exhausted-energetic) of the bipolar scale of the item "Physically I feel" were insufficiently recognized as an item about fatigue severity. We proceeded with the use of the word "fatigue" and a unipolar scale (not at all – a lot) for this item by the last two participants. We added one negative mood item "I feel anxious", because this was reported as missing. We added verbal instructions on what it means to be physically active (e.g., walking or biking) and mentally active (e.g., reading or administrative tasks) because participants had questions concerning the meaning of these items.

Following the briefing session, the three-week EMA study period (T1) started and the measurements were timed according to patients' sleep-wake schedule (i.e., average wake time during the week and in the weekend). Patients received five EMA prompts per day for at least three weeks at quasi-random time points (i.e., three-hour time windows). Two additional short questionnaires were sent at fixed time points in the morning (questions about sleep hours and quality) and evening (questions about energy level throughout the day, taking naps, and open comment field for personal remarks). Participants had a 30 minutes time frame to respond to the beep for the assessment (which took approximately three minutes to complete). In the last week, it was decided whether enough EMA (≥90 assessments) were filled out or whether an extension of a couple of days was needed to analyze reliable person-specific networks.[15,25]

Table 1: Items of EMA app *Energy InSight*

	Items	Scale options
Fatigue-related symptoms	**Momentary**	
1. Fatigue	Physically I feel	0 = Exhausted; 100 = Energetic
1. Fatigue (changed after 3 participants)	Physically I feel tired	0 = Not at all; 100 = A lot
2. Concentration	I am able to concentrate	0 = Not at all; 100 = Very well
3. Motivation	I feel like doing fun things	0 = Not at all; 100 = A lot
4. Pain	I am in pain	0 = Not at all; 100 = A lot
Positive mood	**Momentary**	
5. Happy	I feel happy	0 = Not at all; 100 = A lot
6. Enthusiastic	I feel enthusiastic	0 = Not at all; 100 = A lot
7. Relaxed	I feel relaxed	0 = Not at all; 100 = A lot
8. Curious	I feel curious	0 = Not at all; 100 = A lot
9. Content	I feel content	0 = Not at all; 100 = A lot
Negative mood	**Momentary**	
10. Frustrated	I feel frustrated	0 = Not at all; 100 = A lot
11. Agitated	I feel agitated	0 = Not at all; 100 = A lot
12. Down	I feel down	0 = Not at all; 100 = A lot
13. Insecure	I feel insecure	0 = Not at all; 100 = A lot
14. Guilty	I feel guilty	0 = Not at all; 100 = A lot
15. Anxiety (added after 3 participants)	I feel anxious	0 = Not at all; 100 = A lot
Activity	**In the past three hours…**	
16. Physically active	I was physically active	0 = Not at all; 100 = A lot
17. Mentally active	I was mentally active	0 = Not at all; 100 = A lot
Coping with fatigue	**In the past three hours…**	
18. Pondering	I thought about my energy level	0 = Not at all; 100 = A lot
19. Allowing rest	I took into account my energy level by allowing myself rest (other than sleeping)	0 = Not at all; 100 = A lot
20. Accepting	I thought “my energy level is okay right now”	0 = Not at all; 100 = Strongly
21. Hopeless	I had the idea “my energy level will never improve”	0 = Not at all; 100 = Strongly
22. Control	I had the idea “I could influence my energy level”	0 = Not at all; 100 = Strongly
Context	**Momentary**	
23. Location	I am	1) At home 2) Elsewhere
24. Alone	I am alone	1) Yes 2) No
25. Company	I am with	1) Partner 2) Children 3) Family 4) Friends 5) Colleagues 6) Health professionals 7) Unknown persons 8) Other

Figure 2: EMA app *Energy InSight*



Je hebt één nieuwe melding.

Lichamelijk voel ik me

Sinds de vorige melding heb ik **gedacht "mijn energieniveau is oké zoals het nu is"**

Presenting personalized feedback reports

RvW constructed a personalized descriptive and network feedback reports, including verbal and visual feedback. The tone of the text of both reports was descriptive and informative, without giving advice. We continuously improved lay-out, explanation and visualization of figures.

The descriptive report included 1) Fatigue level during the day and throughout the 3-week period in relation to Physical Activity, 2) Concentration level during the day and throughout the 3-week period in relation to Mental activity, 3) Level of Positive and Negative Feelings during the day and throughout the 3-week period, and 4) Context and Company in relation to Fatigue. We used different figures: bar charts, graphs, pie charts, and plots.

The network report included the visual display of network models. In a network model, the *nodes* represent the variables (e.g., symptoms, mood) and the *edges*, which are the lines between two variables, represent a positive or negative association (e.g., a partial correlation between two variables). A thicker and more saturated *edge* means a stronger positive or negative connection between two *node*.[8] The feedback report included 1) a contemporaneous network based on partial contemporaneous correlations among items and 2) a temporal network based on partial directed correlations including autoregressive and cross-lagged effects. For a description of data analysis, see the preregistered data analysis plan at the Open Science Framework (https://osf.io/7z69j/) and our case study (**Chapter 6**).[22]

Additional questionnaires

As part of routine clinical care, patients filled out the Hospital Anxiety Depression Scale (HADS)[26] to assess psychological distress (cut-off ≥15) and CIS-FS[19] to assess fatigue severity (cut-off ≥35). In addition, the CIS-FS[19] was used to monitor whether fatigue severity did not increase during EMA period.

Qualitative user experience methods

TB used think-aloud procedures, semi-structured interviews, and observations to assess the user experiences. He has a medical background and previous experience with qualitative and user experience research in psycho-oncology. He took field notes and observed during all study procedures. Sessions were recorded and transcribed verbatim.

Patients were invited to think aloud when using *Energy InSight* (T1) and looking into their descriptive feedback report (T2). Therapists were invited to think aloud when evaluating the instructions during the briefing of the personalized network report (T3). They were encouraged to make both positive and negative comments during their review and pretending that the researcher is not present. If the participant or therapist was quiet for a while, the first author intervened by prompting an open-ended question, for example “What are your thoughts right now?” to maintain the flow of the conversation.

Patients’ and therapists’ experiences with *Energy InSight* and personalized feedback reports were evaluated with semi-structured interviews **(See Table 2)**, which were held at the patients’ home or HDI. After the COVID-19 lockdown regulations in March 2020, all patients had completed T1. The study procedures (T2/T3) with patients and therapists took place online (Teams), and they received all materials by e-mail or post. Patients were instructed that it was not recommended to read their personalized feedback reports before the session and to keep their personalized feedback reports at hand during the online sessions (T2/T3). We used video connections during these online sessions to observe patients and therapists. The semi-structured interviews (T4) were held through telephone or the video platform Teams.

Table 2: Topic Guides

Topic guide T1 post-interview think-aloud user experiences patients EMA app
Experiences
-What were your first experiences with the EMA app (*Energy InSight*)?
-Did you experience any problems or notice other things?
Design
-How do you evaluate the design of the app?
-How do you evaluate the colors and symbols of the app?
Functionality
-How do you evaluate the functions of the app?
-Did you notice other things?
Motivation and expectations
-What is your motivation to participate in the EMA study?
-What are your expectations of the EMA study?
First impression descriptive feedback report
-Presentation of descriptive feedback report. What is your first impression?

Topic guide 1 T2 user experiences patients EMA app
Positive and negative experiences app
-How was your experience with using the EMA app? (prompts: relation, reaction, filling in)
-What do you like?
-What do you dislike?
Changes after use of the EMA app
-Has something changed as result of using the EMA app?
-What has changed? (prompts: insights, CCRF, responding to CCRF, relation with body, identity, behavior)
Effects on daily life and social context
-What was the effect of filling in the EMA app on your daily life? (prompt: effect on or disturbance of daily life)?
-What was the effect of filling in the EMA app when you were with others? (prompt: partner, children)
Expectations of using app
-To what extent did the use of the EMA app meet your expectations? (prompt: expectations post-interview briefing)
Questions of app
-How do you evaluate the questions of the EMA app?
-Did you miss any questions in the EMA app?
Current fatigue experience
-How is your fatigue experience right now?
Other experiences
-Do you have any other comments related to the EMA app?
Expectations of network feedback
-What are your expectations of the network feedback discussion with the therapist next time?

Topic guide 2 T2 user experiences patients descriptive feedback report

Experiences and expectations

-How was your experience to read the personal descriptive report?
-What were your experiences with the descriptive feedback report?
-How much did the personal feedback report meet your expectations?

Content report

-What do you like in the report?
-What do you dislike in the report?
-What was most interesting in the report?
-What was least interesting in the report?
-How do you prefer to receive this report?
-What could be improved, adapted or what did you miss in the report?

Effect

-What were the effects?
-What is your take home message from the descriptive feedback report?

Topic guide T4 user experiences patients network feedback report

Experiences receiving network feedback

-How did you experience the discussion of the personal network feedback report with your therapist?
-How did you experience receiving the feedback in a face-to-face session?
-What can be improved or adapted or what did you miss?

Content report

-What were your experiences with the content of the network feedback report?
-How much did the personal network feedback report meet your expectations?
-What do you like in the report?
-What do you dislike in the report?
-What was most interesting in the report?
-What was least interesting in the report?
-Did you have unanswered questions about the report?

Effect and treatment

-What were the effects of the network feedback report?
-What is your take home message from the network feedback report?
-To what extent was the network feedback report of additional value compared to the descriptive feedback report?
-What was the effect of receiving the results of the app on the decision of the treatment?

Topic guide T4 user experiences therapists feedback reports
Briefing and expectations
-What were your expectations of the use of the network report before the briefing?
-How did you experience the instructions during the briefing about the use of the network report for the treatment of this participant?
-How did you experience the method of instructions (e.g., instructions, summary, reports, instructions researchers, order, method: face-to-face, mail, training?)
-How did you evaluate the moment of receiving instructions?
-What can be improved or adapted or what did you miss? (use of words, instructions networks and connections?)
Experiences discussion network report during treatment
-What were your expectations of the treatment session during which the network report was discussed?
-How did you experience the discussion of the network report with the participant?
-How did you evaluate the moment of discussion of the report?
-What do you like or dislike (for the therapist as well as the patient)?
Use of reports during treatment
-How much did the use of the network report during treatment meet your expectations?
-What were your experiences with the use of the network report (in combination with the descriptive feedback report) during treatment?
-What was useful and relevant from the network report?
-What was not useful and not relevant from the network report?
-How much did you use the first feedback report? (e.g., useful/relevant)
Effect of use reports during treatment
-What was the effect of the network report (for the therapist as well as the patient) (e.g., insight main problems)
-What was the effect of use of the network report on personalizing the therapy?
-What was the effect of use of the network report on treatment decision?
-To what extent was discussing the network report during therapy of additional value?

Qualitative data analysis

Data collection and analysis were an iterative process. The six phases of inductive thematic analysis were followed, based on a realist method to report experiences, meanings and reality of participants.[27] In the first within-case analysis phase, TB and RvW started with reading and rereading the transcripts of the first participant in chronological order. In the second phase, transcripts of all study time points (T1-T4) were openly coded with MaxQDA (Plus 2020 student version 20.1.0) and a coding framework was developed and continuously adapted.[28] The codes were discussed until consensus was reached. The first author continued with open inductive coding of all the sessions (T1-T4) of the four other participants in consecutive order. In the third cross-case analysis phase, the codes were organized into potential themes in the codebook. In the fourth phase, these themes were checked with the interview data. In the fifth phase, two group sessions with the multidisciplinary team were organized to identify final themes. In the sixth phase, the manuscript was written with selection of extracts in relation to the research questions and we decided to present one box with presentation of a participant to illustrate the case conceptualization process.

RESULTS

Participants and their therapists

A total of eleven patients were purposively selected from the HDI waiting list. Two patients were ineligible because they had no mobile phone or received active cancer treatment. Four patients declined participation because they expected it would take too much time (n = 2) or experienced improvement of their symptoms during the waitlist (n = 2). Five eligible patients signed informed consent and were assigned to four different therapists. The characteristics of the five participants are summarized in **Table 3**. To protect the participants anonymity, we use pseudonyms. The therapists (three women, one man) were aged between 52 and 63 years and had varying work experience as a therapist (2-25 years) and in the field of psycho-oncology (0-8 years).

Compliance

All five participants completed the study period (**Table 3**). The average overall compliance rate was 85%. It took participants on average 5 to 10 minutes to answer the EMA questions after receiving the prompt.

Cross-case insights of patients and therapists

Table 4 shows how patients experienced using *Energy InSight* and receiving personalized feedback reports. The use of *Energy InSight* resulted sometimes in negative reactions of others and increased awareness of their present experiences. The *Energy InSight* app and the descriptive feedback report provided visibility and acknowledgment of suffering from CCRF. The discussion of both feedback reports was emotionally confronting for patients and resulted in the identification of their main problems. The network feedback was of additional value to the descriptive feedback because it led to recognition of the (inter)relations of their main problems with other issues. Using *Energy InSight* and its feedback provided individual insights into CCRF, opened a dialogue about their main problems, and initiated steps to behavioral change to learn to better respond to CCRF **(Table 4)**.

Table 3: Characteristics of five participants

Characteristics	Sylvia	James	Maria	Cassie	William
Age	31-40	71-80	51-60	51-60	61-70
In a relationship	Yes	Yes	Yes	No	Yes
Educational level	High	High	Low	High	Intermediate
Employment	Fully disabled	Retired	Part-time job	Partly disabled	Sick leave
Tumor type (+Metastasis)	Gynecological +M	Urogenital	Breast	Breast	Urogenital
Time since diagnosis (months)	28	11	49	36	21
Treatment	Surgery, chemotherapy	Surgery, chemotherapy	Surgery, chemo-, radio-, hormonal therapy	Surgery, radio-, hyperbaric-oxygen therapy	Surgery
Time since end of treatment (months)	14	3	29	26	21
Comorbidity	Bowel, musco-skeletal, renal disease	No	No	Thyroid, muscoskeletal disease	Depression, Herpes Zoster
Medication use with fatigue as potential side-effect	Yes	Yes	Yes	Yes	Yes
Prior professional support cancer and/or fatigue	Yes	Yes	No	Yes	No
Start severe fatigue	Since treatment (1-2 year)	Since treatment (6-12 months)	Since treatment (2-5 year)	Since treatment (1-2 year)	Before diagnosis (2-5 years)
HADS (pre-study)	13	9	21	16	25
CIS-FS (pre-study)	49	50	40	46	53
CIS-FS (T0)				41	50
CIS-FS (T1)	42	39	28	37	53
CIS-FS (T2)	39	23	33	37	51
CIS-FS (T3)	45	22	23	33	51
CIS-FS (T5)	37	24	32	24	50
EMA duration (days)	21	24	22	22	21
Compliance (n/N (%))	99/110 (90)	96/119 (81)	91/112 (81)	92/110 (84)	95/105 (90)
Latency time (M, (SD))	6.16 (7.44)	7.43 (7.45)	9.89 (8.48)	8.71 (7.44)	4.88 (7.12)
Main problem treatment after EMA study	CCRF	Coping with cancer	Fear of recurrence	CCRF	CCRF

Table 4: Themes of patients' and therapists' experiences

Patients' experiences	Using *Energy InSight*	Personalized descriptive feedback report	Personalized network feedback report
Negative reactions	Negative reactions and questions of others (Sylvia, James, Cassie)		
Awareness	Self-awareness of body, (dis-)abilities and feelings (Sylvia, Maria, Cassie and William)		
Visibility and acknowledgment of CCRF	Visibility and acknowledgment of CCRF (Cassie and William)	Visibility and acknowledgment of their main problems (all participants)	
Emotional confrontation		Positive emotional confrontation with their current experiences (Sylvia, Maria, Cassie and William)	Emotional confrontation with their current experiences (Sylvia, Maria, Cassie)
Identification and recognition of CCRF		Identification of their main problems (all participants)	Identification and recognition of their main problems in relation to other issues (all participants)
Initiation to change	First steps to behavioral change (Sylvia and Cassie)	Next steps to behavioral change (Sylvia and Maria)	Set goals or change direction for treatment (all participants)
Therapists' experiences		Limited use of descriptive reports (therapist of Maria and William)	Insightful, useful and "accelerator" in treatment (therapist of Maria, Cassie and William) Refinement of main problems (therapist of James, Maria, Cassie and William) Difficulty to discuss network associations (all therapists) Gap between translation of abstract network towards practical use in treatment (therapist of Sylvia and James)

Additionally, **table 4** shows how therapists experienced the use of personalized feedback supporting their treatment. On the one hand, therapists mentioned difficulties with discussing network feedback that were related to lack of statistical background (abstract network), lack of experience as therapist, lack of background knowledge of participant (first treatment session). But on the other hand, they reported the potential of feedback to aid case conceptualization and accelerate treatment by translation of network figures towards practical use in treatment.

The feedback reports showed differences in daily and weekly symptom levels and associations in the networks. These differences were reflected in treatment choice. Cassie, Sylvia, and William started with different psycho-oncological treatments for CCRF and their experiences will be presented in the results section. James' and Maria's treatment changed after discussion of feedback because they learned from the network visualization that CCRF was not their main problem. Cassie's case is presented in **Table 5**. For extensive description of Sylvia's case, see **Chapter 6**.[22]

Table 5: Case illustration of Cassie

Cassie's had no specific motivation to participate other than she was always open to research.

After completion of the EMA period, Cassie reported she realized that fatigue plays a major role in her daily life, while other problem, such as sleep, negative feelings, and fear of recurrence improved. Cassie mentioned a change in habitual behavior. She restarted to plan activities and rest that she learned during group therapy in the hospital.

The descriptive feedback report provided insight into her experiences of the last three weeks. Cassie concluded that her fatigue was more extreme than she had expected (**Figure 3**). She reported that reading the personalized descriptive feedback report was emotionally confronting in a good way, and she gained insights into her problems from the report but did not know what to improve.

Together with her therapist Cassie explored the meaning of the contemporaneous network and found out she responded differently to CCRF at work in the morning and at home in the afternoon (**Figure 4**). Control over her energy level appeared an important node, which was positively connected with allowing rest and feelings of hopelessness (i.e., fatigue will never improve). Cassie realized that in the afternoon at home her energy level is lower and it is more difficult to take her rest when she takes care of her adult son. In those moments, she feels the fatigue will never get better. Cassie started eMBCT to search for more helpful ways to deal with CCRF. Based on the feedback report, her therapist would focus on setting boundaries and taking rest during therapy.

Figure 3: Average fatigue level from day to day of Cassie

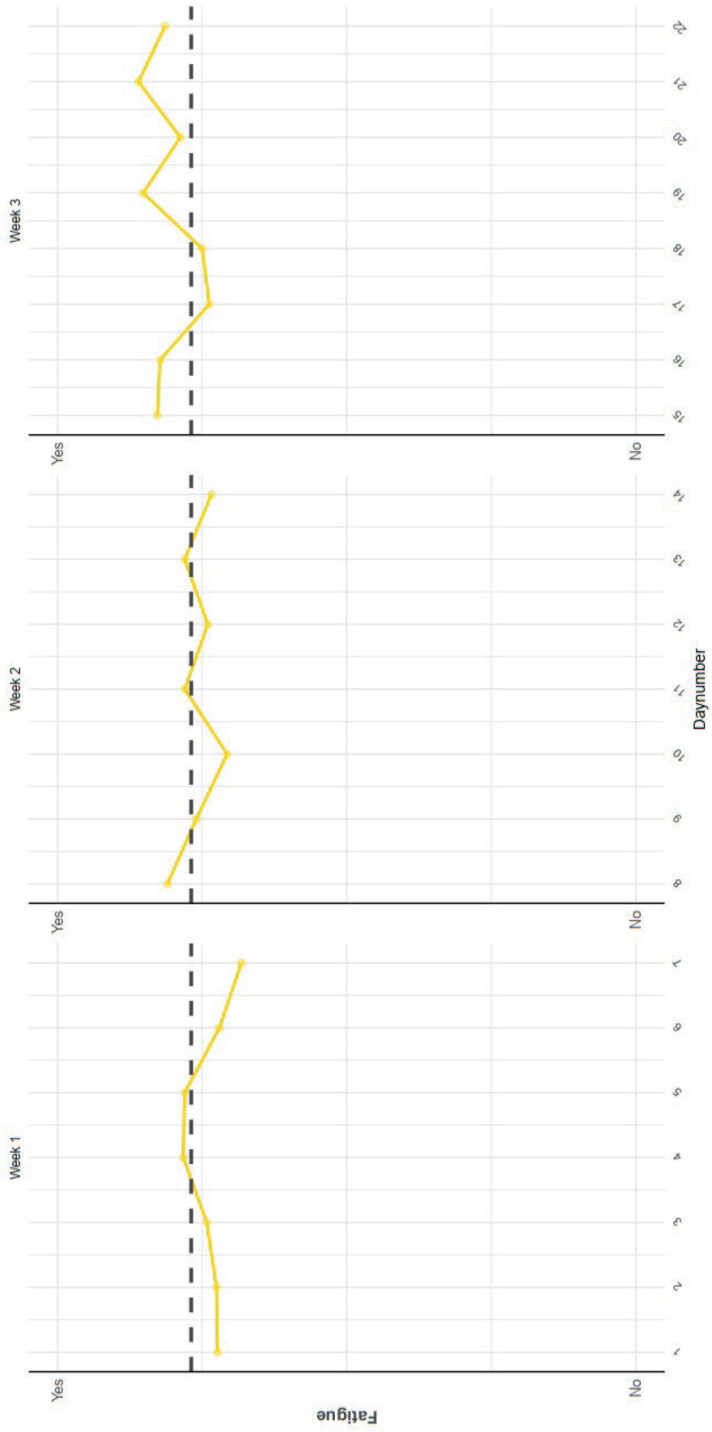
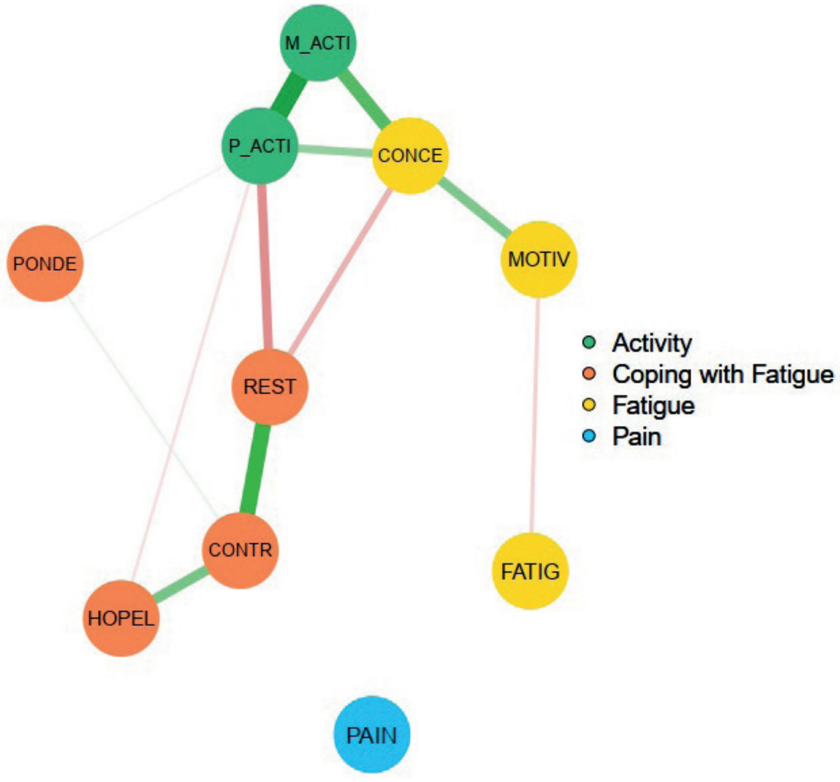


Figure 4: Contemporaneous network of Cassie



A connection between two nodes in this network is based on partial contemporaneous correlation. The stronger a connection between two nodes, the thicker and more saturated the edge. Positive and negative connections are denoted by green and red edges, respectively. FATIG = Fatigue; CONCE = Concentration; MOTIV = Motivation; PAIN = Pain; P_ACTI = Physically active; M_ACTI = Mentally active; PONDE = Pondering; REST = Allowing rest; HOPEL = Feeling hopeless; CONTR = Feeling in control.

Patients’ experiences using *Energy InSight*

Filling out *Energy InSight* was overall positively evaluated, although some participants reported that it was disturbing during conversations with others because they did not want to miss a questionnaire.

Participants experienced an increased awareness of their bodies, feelings, and (dis)abilities. Furthermore, responding to *Energy InSight* increased visibility of their problems with energy levels and led to acknowledgment.

William: “*Yes, you’ll actually start noticing what you hadn’t noticed before. That’s pretty… like for me, at the moment, I’m not seeing myself making any progress. At a certain point I felt like it was producing a lot of the same answers, so you’ll feel like you’re not actually progressing. And that, yeah, that hits harder, let’s put it that way. (…) However, that was also actually a positive experience, because it makes you realize that that is what’s going on”.*

This awareness, visibility and acknowledgment could help set the first steps to change their behavior in favor of responding to CCRF.

Sylvia: *“This app really forced me to pay attention to my energy levels, which I believe to be a good thing. You really need to take an honest look at yourself and reflect on what you are really feeling and what is going on. I believe that that alone had an effect, resulting in me hitting the brakes and listening to my own body more often”.*

Patients’ experiences personalized descriptive feedback report

Participants got more insight in their fatigue experience through the descriptive feedback. It helped visualize the fatigue, which usually remains invisible. Patients described they would share the report with relatives or close friends to increase understanding of their experiences. The personalized descriptive report helped to identify or confirm their main problems.

Cassie: *“The level of fatigue is very high I see. And if you see this curve, I expected more association between physical activity and fatigue. Mental activity and concentration that is also something I noticed. Because of concentration I have trouble reading certain stuff. I recognize this in the report. It is very clear, what my experiences were in three weeks”.*

This report was experienced as a positive emotional confrontation with their current experiences and prepared them to set next steps for behavioral change. Patients were looking forward to starting their therapy and handling CCRF.

William: *"Well yeah naturally it's never really pleasant to hear that you've come less far than you previously thought. So that does make you aware of your current situation. I didn't expect that, if I'm honest. But it is good to be aware of your situation, because then you know that you need to put in more effort. And the helplines are open, so I hope that this report can be used to make it easier and faster to diagnose and start the right treatment"*.

Patients' experiences personalized network feedback report

Participants evaluated the network report as having additional value compared to the descriptive feedback because of the visualization of the relations among symptoms.

Sylvia: *"Yes, I am convinced that the network report has additional value. The descriptive report was, in my opinion, a visualization of the data without relations and the interpretation to give personal meaning. For example, in the morning, you experience a higher level of fatigue than in the evening. This report shows good results but is mainly descriptive. And in the network report, you can see connections or no connections. And I think it's more on the side of interpretation and the real meaning of these things. I think that is really an addition."*

During the open discussion of the personalized network report with the therapist in the first or second treatment session, the meaning of (the relations of) their main problems presented in the contemporaneous and temporal networks were explored and mostly recognized. The discussion of the personal meaning of the personalized network report was again experienced as an emotional confrontation with their current experiences. Discussing the network report helps patients realize they can play an active role in managing their fatigue. It was helpful to set a treatment goal.

Cassie: *"Well, the fact that I can influence it [energy level]. Yes, I can work with it [energy level] and or play with it [energy level]. I have to look at it [energy level]"*.

Therapists' experiences with personalized feedback reports

Therapists experienced discussing the network feedback report with their patients as insightful, useful and "an accelerator" in the treatment process.

Cassie's therapist: *"What it brought me is that I gained insights into things I can work on with my client. Because I know what the issues are. So I don't have to look around. I can directly start with therapy"*.

Despite the briefing session, therapists experienced some difficulty with discussing the network associations with the patient. While therapists thought the feedback reports were helpful in refining the main problems, some therapists experienced a "gap" between the abstract network report and applying this during treatment.

Sylvia's therapist: *"At this moment there is no clear relationship in the network with the main problem fatigue. I keep in mind that guilt is a problem and ruminating. But to structure the treatment according to the CBT model of fatigue after cancer as I am used to do, it does not completely match".*

DISCUSSION

Principal findings

A three-week EMA period, while being on the waitlist for psycho-oncological care for CCRF appeared feasible. The EMA monitoring and feedback reports provided patients new insights into their main problems. In turn, these insights can aid patients and therapists in case conceptualization and setting goals for psycho-oncological treatment. Because the feedback reports showed that the complex CCRF network was indeed person-specific, this approach seems well suitable for case conceptualization of patients that suffer from CCRF and/or other psychological problems.

Patients' experiences

Patients' findings of gaining awareness, new insights into CCRF and initiating behavior change are in line with previous qualitative studies. These studies investigated experiences with EMA and personalized network feedback for the treatment of depression, showing improved coping with the disorder, facilitated communication between patients and clinicians, and informed treatment direction.[14,29,30] In addition, our patients reported less desirable effects of EMA, such as filling in the questionnaire on "automatic pilot" and receiving negative comments from others. Fortunately, our patients did not experience increased fatigue symptoms due to EMA, which has been reported in previous studies among patients with mental disorders.[31] However, we should be aware of the burden EMA puts on patients and that the data can be emotionally confronting and challenging to interpret by patients. Involving their therapist and discussing the networks together; can help patients deal with the feedback and increase their insight.

Therapists' experiences

The evaluation among therapists showed several advantages of the personalized feedback reports based on EMA, i.e., they can help refine the main problems and work as an accelerator in treatment. These advantages are similar to the findings from other qualitative studies.[29] Therapists in our research, however, mentioned some difficulties interpreting network associations with patients and integrating them into treatment. To overcome these difficulties, it could be helpful to train therapists with feedback about the interpretation of network associations in clinical practice.[29]

Strengths and limitations

We used data triangulation with multiple sources of data (i.e., observations and (think-aloud) interviews) and incorporated patients' and therapists' perspectives to increase the internal validity of this study.[28] All included participants completed the study. A possible explanation for the successful compliance might be the context in which patients responded to the EMA app.[32] Participants mentioned that filling out the questionnaires while being on the waitlist is beneficial for motivation. The EMA data collection empowered patients to change their behavior and become actively involved in their treatment.[33] Based on the positive experiences of five patients and their therapists in this proof-of-concept study, EMA and discussing personalized feedback seems usable in psycho-oncological practice, however, we should be aware of several limitations. First, although we used purposive selection of participants on the waitlist who suffered from CCRF, in the end, two cases were treated for other psychological problems. Evidently, the findings of this qualitative research, based on a small sample, cannot be generalized. To investigate the effectivity of the use of personalized (network) feedback in the CCRF population a larger quantitative study is warranted. Second, while the EMA items were carefully selected and both patients and therapists considered the items as important in relation to CCRF, we might have missed some potentially relevant items. Offering patients the opportunity to add an item they consider relevant for their CCRF might be a valuable next step in using personalized feedback of network models in clinical practice.[14]

Recommendations for implementation in psycho-oncological practice and future research

In order to implement *Energy InSight* and personalized feedback in psycho-oncological practice, we need to further automatize the process of data collection and generating feedback reports. Using automated apps, therapists can easily run a script and generate a personalized feedback report for their patients. To further improve user-friendliness for patients, the automated personalized feedback might be incorporated into the EMA app.

The *Energy InSight* app could be connected with actigraphy measurements, to gain a more objective sense of physical activity. Such data would be interesting to use in PAIs and help patients balance their activity and rest.

Based on therapists' experiences, training is recommended to improve the knowledge and take into account precautions of interpretation of network associations.[34]

All therapists and patients agreed that the best moment to discuss the feedback and optimally aid case conceptualization is a second face-to-face treatment session. In this second session, there should be sufficient time to reflect on the meaning of the personalized feedback. Moreover, patients experience no stress for meeting their therapist for the first time and uncertainty about the possibilities for treatment, and the therapist knows the patients' background for interpretation of the networks. Future studies could focus on the feasibility and efficacy of EMA and automated personalized feedback compared to usual psycho-oncological care in a larger sample of patients with CCRF. By using activity trackers and other wearables, the personalized could be extended beyond psychosocial care and also include PAIs. These studies could benefit from a reduction of the EMA items and use only momentarily items to prevent recall bias and include more items in temporal networks.

CONCLUSIONS

Based on patients' and therapists' experiences presented in this proof-of-concept study, using *Energy InSight* combined with personalized (network) feedback seems a feasible and usable method in psycho-oncological care for patients with CCRF. The use of *Energy InSight* during the waitlist and personalized feedback with a discussion of the personal meaning of interrelated problems at the start of treatment can provide insights to refine the main focus and direction of the treatment.

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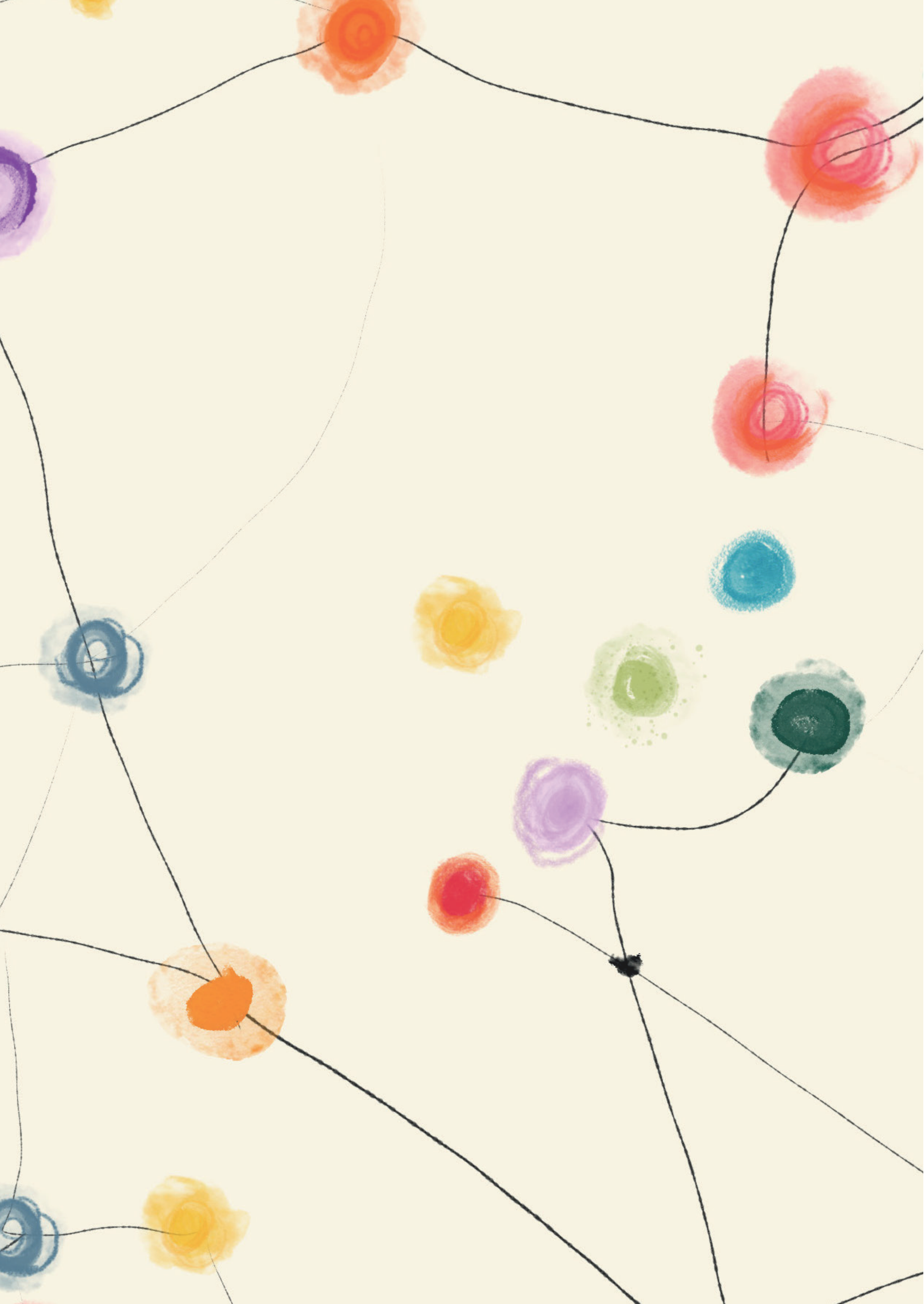


Chapter 6

PERSONALIZING PSYCHOLOGICAL CARE FOR CHRONIC CANCER-RELATED FATIGUE: A CASE STUDY ON SYMPTOM DYNAMICS

Schellekens MPJ, Bootsma TI, van Woezik RAM, van der Lee ML.
Personalizing Psychological Care for Chronic Cancer-Related Fatigue:
A Case Study on Symptom Dynamics. J Pers Oriented Res. 2021 Aug 26;7(1):1-13.

ABSTRACT

Approximately 25% of cancer patients suffer from chronic cancer-related fatigue (CCRF), which is a complex, multifactorial condition. While there are evidence-based interventions, it remains unclear what treatment works best for the individual patient. Psychological network models can offer a schematic representation of interrelations among fatigue and protective and perpetuating factors for the individual patient. We explored whether feedback based on these individual fatigue networks can help personalize psychological care for CCRF. A 34-year-old woman with CCRF was referred to our mental healthcare institute for psycho-oncology. During the waitlist period, she filled out an experience sampling app for 101 days, including five daily assessments of fatigue, pain, mood, activity and fatigue coping. The interplay between items was visualized in network graphs at the moment-level and day-level, which were discussed with the patient. For example, acceptance of fatigue in the past three hours was associated with less hopelessness and less fatigue in the following moment. At the day-level, acceptance was also being associated with less fatigue, less hopelessness, a better mood, and more motivation to do things. The patient recognized these patterns and explained how unexpected waves of fatigue can make her feel hopeless. This started a dialogue on how cultivating acceptance could potentially help her handle the fatigue. The patient would discuss this with her therapist. Feedback based on individual fatigue networks can provide direct insight into how one copes with CCRF and subsequently offer directions for treatment. Further research is needed in order to implement this in clinical practice.

INTRODUCTION

Fatigue is one of the most prevalent and disrupting side effects of cancer and its treatment. It is characterized by feelings of weakness, exhaustion, and lack of energy. This fatigue differs from typical tiredness as it is not alleviated by rest or sleep, nor is it proportional to recent exertion[1]. In approximately 25% of patients, fatigue persists for months to years after completion of cancer treatment.[2] This persisting fatigue is defined as chronic cancer-related fatigue (CCRF). The unpredictable nature of CCRF with sudden drops in energy makes it difficult for patients to live their lives. CCRF is associated with reduced quality of life and heightened distress.[2,3] It interferes with patients' ability to work, their daily life activities, and social relationships.[4,5]

Despite its prevalence and disrupting effects, the etiology of CCRF remains poorly understood. Evidence suggests CCRF is a complex multifactorial condition, affected by a range of physiological (e.g., inflammation), clinical (e.g., comorbidities, cancer treatment), and psychosocial factors (e.g., distress).[2,6] For example, during cancer treatment fatigue often co-occurs with symptoms such as pain, sleep problems, loss of appetite and withdrawal, collectively known as cytokine-induced sickness behaviors.[7] Sickness behavior is an adaptive response to inflammation and is believed to preserve energy resources to fight illness and promote healing processes,[7] which is very helpful during cancer treatment. Due to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and other underlying physiological mechanisms, fatigue can persist long after completion of cancer treatment.[8] While before cancer, patients had a general sense of how much rest was needed after exertion, now they have no idea whether and when they will recover from CCRF, making it very difficult to determine when to be active and when to rest.

So far, qualitative research has provided some insight into the unpredictable nature of fatigue throughout the day and from day to day.[5,9] Patients suffering from CCRF usually report a continuous level of fatigue throughout the day with sudden appearances of exhaustion, often forcing the patient to lie down until the fatigue passes.[9,10] Patients also experience changes in fatigue at the day-level, with some days of energy, while on others there is none.[5] While these studies provide some understanding of the course of CCRF, in order to help patients to get more grip on their fatigue, we need to gain more insight into what factors affect CCRF, both throughout the day and from day to day.

Following the multifactorial etiology of CCRF, several types of treatments have proven effective in coping better with CCRF. These include both psychosocial interventions (e.g., cognitive behavioral therapy, mindfulness-based cognitive therapy) as well as physical activity interventions (e.g., exercise interventions, activity coaching).[11–13] While these interventions have proven to be effective in reducing CCRF, it is unknown what intervention is most suitable for the individual patient. In order to unravel what treatment works best for whom, we need to help patients gain more insight into the factors that worsen or relieve their CCRF.[2]

Based on the literature, our clinical experience, and qualitative and quantitative research on CCRF,[5,14] we developed an experience sampling app, termed '*Energy InSight*', to unravel the perpetuating and protective factors of the individual patient's CCRF. The experience sampling method (ESM) is a structured diary technique, in which a participant receives questions multiple times a day for multiple days on end about their thoughts, feelings, activities, and context in their daily living environment.[15,16] This results in an intensive longitudinal dataset, making it possible to examine the interactions between symptoms, cognitions, emotions, and behavior in a detailed, ecologically valid manner at the level of the individual patient.[15] Such a rich dataset provides the opportunity to examine the interaction between fatigue and related factors on different time frames, allowing more insight into the elusive course of fatigue throughout the day and from day to day.

Despite concerns about the burden this method puts on patients, ESM has already shown promising first results concerning feasibility and usefulness in psycho-oncology research.[17] On a small scale, ESM has already found its way into clinical practice as a personalized screening tool in the field of depression and psychosis research.[18,19] Research suggests that as patients are actively involved in collecting data and gain insight into the personal, contextualized dynamics of their daily life, ESM contributes to self-management and patient empowerment.[18,20,21]

A new way to make sense of this intensive longitudinal data and to gain insight into an individual's symptom dynamics is the network approach. The network approach to mental disorders theorizes disorders as causally connected symptoms in a network structure.[22] Thus, rather than viewing symptoms as manifestations of a common cause (e.g., you feel depressed because you have a depressive disorder), symptoms are conceptualized as elements of a complex dynamical system (e.g., sleep problems can trigger fatigue and concentration problems, resulting in feelings of worthlessness and loss of enjoyment, which in turn can trigger a depressed mood). Consequently, such a network of strongly interconnected symptoms can fulfill the criteria of a mental disorder.[23] Due to the self-sustaining nature, it can be difficult to get out of such a malfunctioning state, potentially explaining the chronic nature of certain disorders. Next to symptom measures, other theoretically relevant nodes can be included in the network to reveal the nature of the complex relationships and core mechanisms involved in disorders.[24] As such, the network approach seems very well suited to apply to a complex, multi-factorial condition, such as CCRF. By adding perpetuating and protective factors of CCRF to the network, we can gain more insight into what worsens or relieves a person's fatigue. The network approach is supported by network analyses that offer a visual display of (causal) relationships between symptoms, cognitions, emotions and behavior.[25] These visualized person-specific networks are rather intuitive and easy to understand for researchers, therapists and laypersons alike, and therefore have the potential to be used in providing personalized feedback as well as supporting personalized interventions.

Only a handful of studies have explored the application and effectiveness of ESM-derived personalized feedback on daily life dynamics.[26–30] For example, Van Roekel and colleagues (2017) demonstrated that personal lifestyle advice (based on descriptives and network graphs of daily life activities, social context, and pleasure ratings) resulted in higher positive affect and pleasure ratings among anhedonic young adults, compared to those not receiving feedback.[26] Two case studies also explored the potential of providing feedback on symptom dynamics by using network analysis to inform treatment. Bak and colleagues (2016) showed how the dynamic symptom network of a patient with schizophrenia provided increased insight into relapse and recovery, facilitating the patients' treatment.[27] Moreover, Kroeze and colleagues (2017) described how the symptom network of a patient with treatment-resistant anxiety and depressive symptoms provided increased insight into the patient's symptom dynamics, which was valued as useful by the patient and therapist and facilitated a new direction in treatment.[28] In sum, adding ESM-derived feedback to standard care seems feasible and has the potential to improve treatment in psychological healthcare.

Aim of the present study

This case study aimed to explore the usability of providing feedback on symptom networks to a patient who sought help for CCRF in a mental health care institute for psycho-oncology. We explored whether the network provided new insights into CCRF and whether these insights helped to personalize treatment. To gain more insight into how symptom dynamics change over time, based on reported changes throughout the day and from day to day,[5,9] we explored explore both moment-level as well as day-level networks.

METHODS

Design and procedure

This case study was part of an n = 5 proof-of-concept study in which we developed the experience sampling app *Energy InSight*, assessed its feasibility, and explored whether it contributed to psychological care for CCRF. This study was approved by our ethical review board METC Brabant (P1935). Patients suffering from CCRF who were referred to the Helen Dowling Institute, a mental healthcare institute for psycho-oncology in the Netherlands, were invited to participate. After providing written informed consent, patients received instructions and installed the ESM app on their own smartphone. They filled out the app while they were on the waitlist for psychological care. During the 21-day ESM period, patients received notifications at five quasi-random time intervals (i.e., three-hour time windows) a day, and two questionnaires at a fixed time point in the morning and evening. The timing of the measurements was adjusted to the patients' sleep-wake schedule. Patients had to fill out the measurements within 30 minutes after the notification, otherwise, it was considered missing. During the first or second treatment session patients discussed the fatigue networks with their therapist. In our proof-of-concept study, we have described in more detail how patients and therapists experience the ESM app *Energy InSight* and the resulting network reports (**Chapter 5**).[31]

One of these participants, who we will name Sylvia, was motivated to fill out the app for 100 days. This provided enough power to explore not only how fatigue and other factors affect each other from moment to moment, but also from day to day. Assessments for 100 days were deemed sufficient as simulation studies have shown adequate performance for estimating eight-node networks using 50 observations.[25] With 100 assessments and a 15% dropout rate, which is common in ESM studies among cancer patients,[17] we expected to be able to estimate reliable networks of Sylvia's ESM data. Like the other participants in the proof-of-concept study, Sylvia received the 21-day feedback at the first meeting with her therapist. Before the second meeting with her therapist, she finished filling out the app for 100 days. After 100 days, the first and second author discussed with Sylvia the moment-level and day-level networks, which she later discussed with her therapist.

Case presentation

Sylvia was a 34-year-old woman who was referred to the Helen Dowling Institute, a mental healthcare institute for psycho-oncology. She suffered from severe fatigue (score of 49, which is way above the severe fatigue cut-off of ≥35 on Checklist Individual Strength –

Fatigue Severity subscale[32]) for over a year by then. Two years prior she was diagnosed with ovarian cancer with bone metastases. The tumor was removed through surgery. Next, she received four rounds of chemotherapy, followed by two surgeries to remove the affected rib and vertebra. After one year of curative treatment, leading to chemotherapy-induced kidney failure, she received medical follow-up consultations every few months by an oncologist. She also suffered from inflammatory bowel disease and inflammatory rheumatism since her teenage years. She lives together with her partner, had a university education and was fully incapacitated for work since her cancer diagnosis. Previously, she worked fulltime as a project leader.

While she had always struggled with fatigue due to her comorbidities, throughout her cancer treatment the fatigue worsened dramatically. Sylvia described she had particular trouble concentrating when she felt tired. When she tried to read a newspaper or do her administration, she could get headaches and become nauseous. This severely limits her daily life activities. Her experience of fatigue was rather similar from day to day. Usually, she had trouble starting the day, which usually took her a few hours. Fatigue increased throughout the day, with a dip in the late afternoon. She usually took a nap by then because she was unable to do any of her activities. She did, however, also experience unexpected waves of extreme fatigue that did not seem to be related to previous activities. During those moments, it was difficult to get through the day. Furthermore, when she had a particularly busy activity, for example, when she went to a party, she had trouble dealing with all the stimuli and social interactions at once. As a result, she would be extra fatigued for the following two to three days.

ESM assessment

Based on quantitative (i.e., network analysis on group-level) and qualitative research findings (i.e., meta-ethnography), we developed the ESM app *Energy InSight*. For example, based on group-level networks,[14,33] we decided to include items on acceptance of fatigue and a sense of control over fatigue in the app. Moreover, based on patients' experiences of fatigue being intertwined with emotions (e.g., guilt) and pain, as shown in the meta-ethnography[5] we added items on emotions and pain to the app. This resulted in a selection of 24 items that were assessed 5 times a day in a period of 100 days. For the network modeling items on social context (location, company, type of company) were excluded, resulting in 21 items (see **Table 1** for an overview of the items).

Table 1: The selected nodes from the ESM app (n=447) per network

	Item	Scale options	M	(SD)	NW*
Fatigue	Physically I feel	0 = Exhausted; 100 = Energetic	39.68	20.15	1 - 2
Concentration	I am able to concentrate	0 = Not at all; 100 = Very well	48.22	26.72	1 - 2
Motivation	I feel like doing fun things	0 = Not at all; 100 = A lot	65.71	23.96	1 - 2
Pain	I am in pain	0 = Not at all; 100 = A lot	40.96	31.04	1 - 2
Positive mood					1
- Happy	I feel happy	0 = Not at all; 100 = A lot	74.06	20.28	2
- Enthusiastic	I feel enthusiastic	0 = Not at all; 100 = A lot	76.56	21.02	2
- Relaxed	I feel relaxed	0 = Not at all; 100 = A lot	59.17	31.65	2
- Curious	I feel curious	0 = Not at all; 100 = A lot	86.22	15.22	2
- Content	I feel content	0 = Not at all; 100 = A lot	45.08	25.56	2
Negative mood					1
- Frustrated	I feel frustrated	0 = Not at all; 100 = A lot	39.20	28.93	2
- Agitated	I feel agitated	0 = Not at all; 100 = A lot	40.96	31.04	2
- Down	I feel down	0 = Not at all; 100 = A lot	24.03	21.44	2
- Insecure	I feel insecure	0 = Not at all; 100 = A lot	42.89	25.96	2
- Guilty	I feel guilty	0 = Not at all; 100 = A lot	25.82	26.69	2
	In the past three hours…				
Physically active	I was physically active	0 = Not at all; 100 = A lot	47.02	37.04	1
Mentally active	I was mentally active	0 = Not at all; 100 = A lot	46.80	34.96	1
Pondering	I thought about my energy level	0 = Not at all; 100 = A lot	84.22	25.40	1
Allowing rest	I took into account my energy level by allowing myself rest (other than sleeping)	0 = Not at all; 100 = A lot	69.27	32.27	1
Accepting	I thought “my energy level is okay right now”	0 = Not at all; 100 = Strongly	41.90	24.78	1
Hopeless	I had the idea “my energy level will never improve”	0 = Not at all; 100 = Strongly	46.05	25.52	1
Control	I had the idea “I could influence my energy level”	0 = Not at all; 100 = Strongly	57.37	28.92	1

* NW1 = Network 1. Contemporaneous network; NW2 = Network 2. Temporal network.

Fatigue

Three items were used to assess different dimensions of fatigue: the physical level of fatigue (“Physically I feel… [exhausted to energetic]”), mental fatigue in the form of concentration difficulties (“I am able to concentrate”), and the motivation to do things (“I feel like doing fun things”). The item on physical fatigue was reverse scored such that a higher score reflected more fatigue.

Pain

Pain was assessed with the item “I am in pain”.

Mood

Mood was assessed with 10 affect items. Example items were “I feel content” and “I feel agitated”. In order to improve the interpretability of the contemporaneous network, which included all 21 items, affect items were aggregated into ‘positive mood’ (happy, enthusiastic, relaxed, curious, content) and ‘negative mood’ (frustrated, agitated, down, insecure, guilty).

Activity

Activity was assessed with two items: “In the past three hours I was physically active” and “In the past three hours I was mentally active”. Items were phrased in terms of ‘the past three hours’ because the average time between assessments was three hours.

Coping with Fatigue

Five items assessed thoughts and behaviors concerning fatigue. These included pondering about the fatigue (“In the past three hours I thought about my energy level”), allowing oneself to rest when fatigued (“In the past three hours I took into account my energy level by allowing myself rest (other than sleeping)”), accepting the level of fatigue as is (“In the past three hours I thought ‘my energy level is okay right now’”), feeling hopeless about one’s fatigue (“In the past three hours I had the idea ‘my energy level will never improve’”), and feeling in control of the fatigue (“In the past three hours I had the idea I could influence my energy level”). Items were phrased in terms of ‘in the past three hours’ because the average time between beeps was three hours.

Statistical analysis

The data analysis plan was pre-registered online at Open Science Framework at the start of data collection (https://osf.io/wf8vc/). We estimated two moment-level network models: (1) A contemporaneous network model including all variables. To improve the readability of the contemporaneous network, we summarized the 10 mood items into two aggregated mood variables: positive mood and negative mood; and (2) A temporal network model including the fatigue, pain and mood variables. See **Table 1** for an overview of the variables per network. The temporal network model only contained fatigue, pain and mood variables as these items relate to the present moment. To prevent confusion regarding the interpretation, we left out items referring to the past three hours (i.e., coping with fatigue and activity variables). Besides these moment-level network models, we also ran these network models at the day-level. For these network models, we used the average scores per day of each variable. Variables for the network models were selected based on sufficient variability (i.e., Mean Squared Successive Difference (MSSD) >50). In this case, the variability of all 21 variables proved sufficient. In the moment-level temporal networks we did not allow the first response of the day to regress on the last response of the previous day.

Network Estimation

The contemporaneous and temporal networks were estimated using the R package graphicalVAR. In the contemporaneous network, ‘‘nodes’’ represent the selected variables while ‘‘edges’’ (i.e., links connecting two nodes) represent the partial contemporaneous correlations. In partial correlation networks the association between two nodes is estimated while controlling for all other nodes. This means that when an edge is present between two nodes, they are conditionally dependent given all other nodes.

A temporal network is based on partial directed correlations. In this model, a variable at a certain time point is predicted by the same variable at the previous time point (autoregressive effects) and all other variables at the previous time point (cross-lagged effects). The connections between nodes are depicted with arrows. An arrow from one node to another depicts a cross-lagged effect, while an arrow directing to the same node depicts an autoregressive effect.

The graphicalVAR package uses penalized maximum likelihood estimation to estimate model parameters, while simultaneously controlling for parsimony.[34,35] The graphical-VAR package estimates 2,500 different models, varying 50 levels of parsimony in the contemporaneous network and 50 levels of parsimony in the temporal network. Bayesian information criterion (BIC) model selection is used to select the best fitting model. This means that edges that are likely to be spurious are removed from the model, leading to networks that are simpler to interpret.[36,37]

The estimated models are displayed in network graphs. The stronger a connection between two nodes, the thicker and more saturated the edge. Based on the strongest connection, we have set a maximum edge strength of .55 for all network models to ensure that the thickness of the edges is comparable between models. Positive and negative connections are denoted by green and red edges, respectively. The networks were visually inspected and interpreted based on the strongest connections among variables.

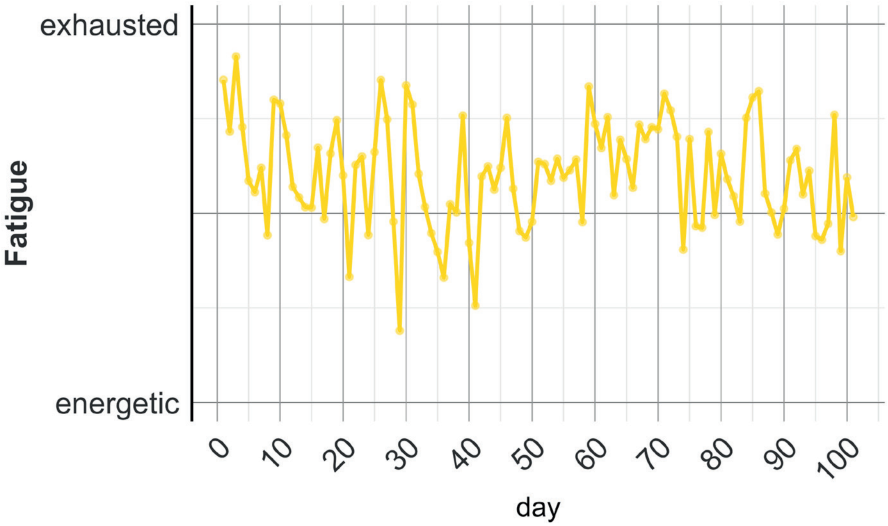
RESULTS

In a detailed personalized feedback report, the course of fatigue, moment-level and day-level network plots were presented to the patient and discussed with her by the first two authors after 101 days. Sylvia explained how she had no trouble filling out the app. She filled out 445 of the 501 assessments (88.8% compliance). Sylvia described how filling out the app for 101 days helped her to become more aware of her body. By answering the items every three hours, she actively monitored her energy level and sensed her boundaries more easily. This awareness allowed her to choose to rest in time and not overexert herself.

Course of Fatigue

On average, the level of fatigue increased throughout the day with a peak in the evening. Sylvia recognized this. She described how she often woke up tired and that the fatigue worsened with ever activity she did. The average level of fatigue varied greatly from day to day with a majority of “fatigue” days and some days of “energy” (**Figure 1**).

Figure 1: Average fatigue level from day to day



Moment-Level Contemporaneous Network

The contemporaneous moment-level network (**Figure 2**) included three items that were strongly connected to other items: Motivation, Acceptance, and Allowing Rest. Regarding Motivation, there were connections with Fatigue, Concentration, and Positive Mood. This suggests that when Sylvia was looking forward to doing fun things, she felt less fatigued, was better able to concentrate and experienced more positive emotions at that moment. Sylvia recognized this pattern in the sense that when she felt less fatigued, she could undertake more and felt happier and more content.

Acceptance was connected to Fatigue and Hopelessness. This suggests that when she thought ‘the fatigue will never get better’ in the past three hours, she was less okay with her energy level in the past three hours, and she experienced more fatigue in the following moment. Sylvia described how unexpected waves of fatigue could make her feel hopeless. She found it interesting that acceptance connected hopelessness with fatigue. Sylvia saw this as an opportunity. Becoming more aware of the changes in her fatigue, and being okay with her energy level for what it was, could help her deal more effectively with the fatigue and potentially decrease it.

Allowing Rest (other than sleep) was connected to Pondering about one’s fatigue level, having a sense of Control over one’s fatigue level and Physical Activity. Sylvia explained how filling out the app already helped her to relax more. For example, she usually would rest by doing the dishes. Now she realized that taking a good rest by doing nothing, just drinking a cup of tea, helped her to relax more, which gave her a sense of control over her fatigue. Interestingly, Allowing Rest was not directly related to Fatigue.

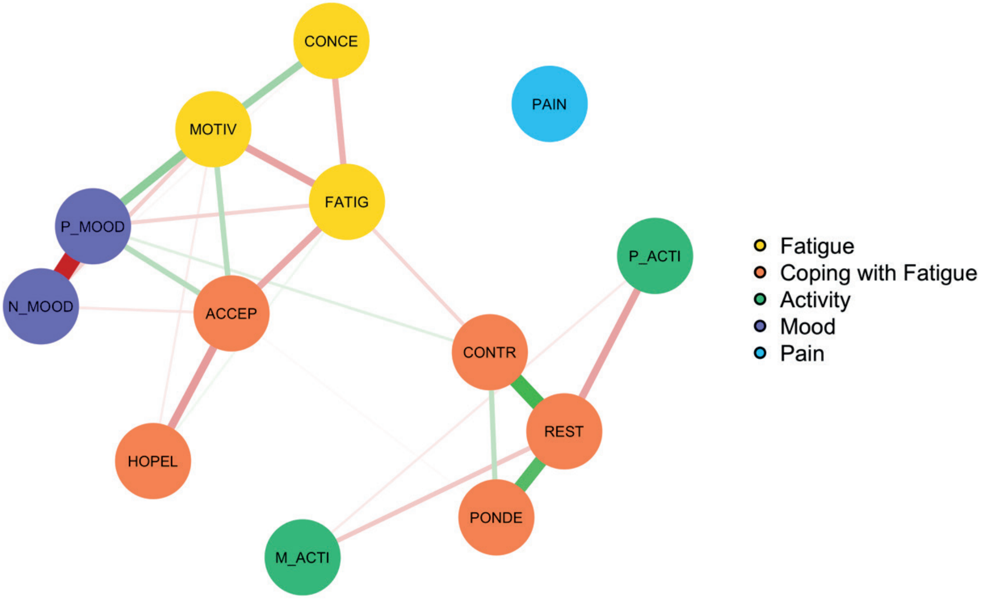
At the first meeting with her therapist, Sylvia had received feedback from the 21-day report. The connections in the moment-level contemporaneous network model based on the first 21 days were similar to the 101-day report, with the exception of Acceptance. In the 21-day report no connection was found between Acceptance and Fatigue.

Day-Level Contemporaneous Network

The day-level contemporaneous network (**Figure 3**) was rather similar to the moment-level contemporaneous network. When visually inspecting the strongest connections among symptoms, the main difference concerned the connections of Acceptance with other nodes. Similar to the moment-level networks, Acceptance was connected to Hopelessness and Fatigue. In addition, the day-level network also showed connections of Acceptance with

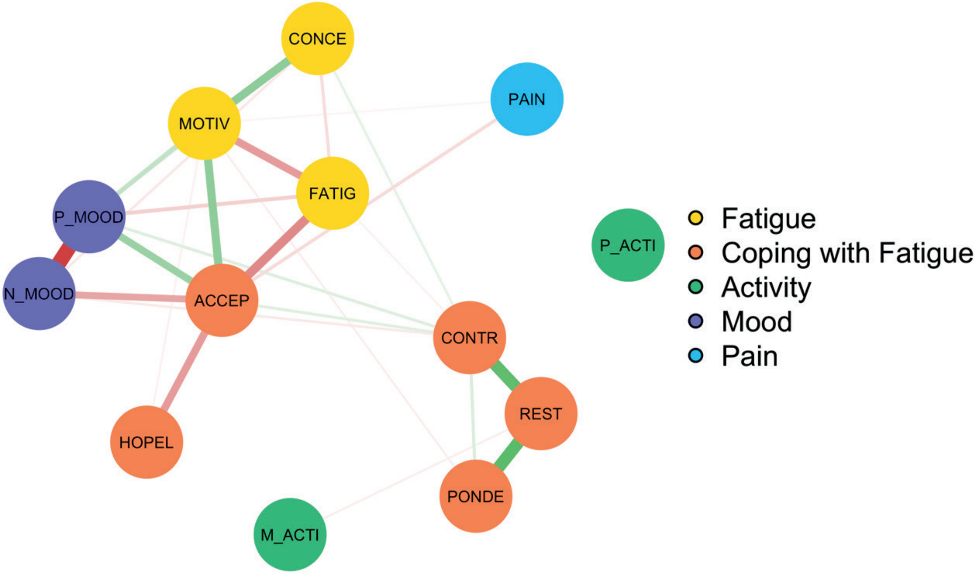
Negative Mood, Positive Mood and Motivation. This suggests that when Sylvia accepted her fatigue level for what it was on a certain day, she felt less hopeless regarding her fatigue, was in a less negative and more positive mood, felt more motivated to do things and experienced less fatigue that day. Sylvia recognized this and explained that when she was okay with her fatigue level, she generally felt better throughout the day.

Figure 2: Moment-level contemporaneous network



Note. The stronger a connection between two nodes, the thicker and more saturated the edge. The weakest connection was -0.0086 (ACCEP-PONDE) and the strongest connection was -.5129 (P_MOOD-N_MOOD). Positive and negative connections are denoted by green and red edges, respectively. FATIG = Fatigue; CONCE = Concentration; MOTIV = Motivation; PAIN = Pain; P_MOOD = Positive mood; N_MOOD = Negative mood; P_ACTI = Physically active; M_ACTI = Mentally active; PONDE = Pondering; REST = Allowing rest; ACCEP = Accepting; HOPEL = Feeling hopeless; CONTR = Feeling in control.

Figure 3: Day-level contemporaneous network



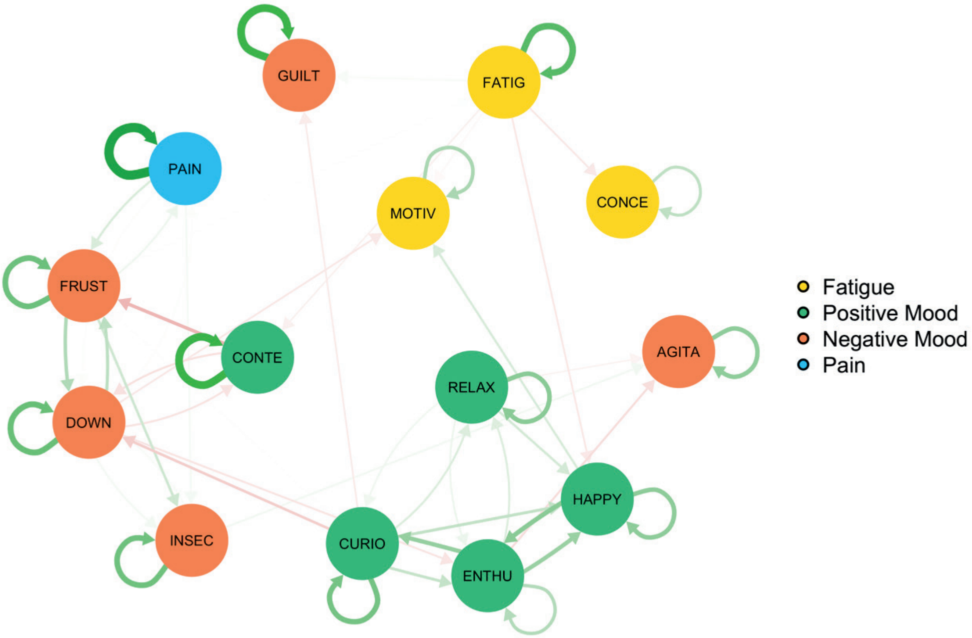
Note. The stronger a connection between two nodes, the thicker and more saturated the edge. The weakest connection was -0.0180 (MOTIV-PAIN) and the strongest connection was -.4332 (P_MOOD-N_MOOD). Positive and negative connections are denoted by green and red edges, respectively. FATIG = Fatigue; CONCE = Concentration; MOTIV = Motivation; PAIN = Pain; P_MOOD = Positive mood; N_MOOD = Negative mood; P_ACTI = Physically active; M_ACTI = Mentally active; PONDE = Pondering; REST = Allowing rest; ACCEP = Accepting; HOPEL = Feeling hopeless; CONTR = Feeling in control.

Moment-Level Temporal Network

The temporal network (**Figure 4**) included autoregressive effects of Fatigue, Pain, feeling Guilty, and feeling Content. This means that, for example, when Sylvia was fatigued at one moment, she was more likely to be fatigued in the next moment (i.e., approximately 3 hours later). Sylvia described how fatigue and pain were the two main chronic symptoms she suffered from. She also recognized the feelings of guilt. She explained that when she was fatigued or in pain, she felt guilty about not taking good care of herself.

The connections of the moment-level temporal network of the 21-day report were similar to the connections found in the 101-day report, with the exception of pain. As pain did not show sufficient variability (MSSD <50) in the first 21 days, it was not included in the network.

Figure 4: Moment-level temporal network including Fatigue, Pain and Mood

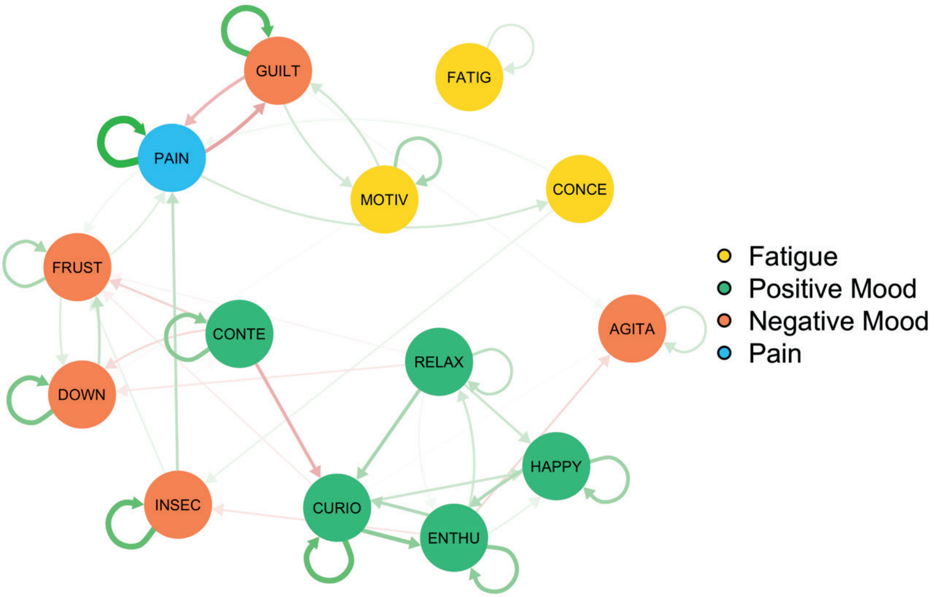


Note. The stronger a connection between two nodes, the thicker and more saturated the edge. The weakest connection was -0.0031 (HAPPY-GUILT) and the strongest connection was -.5458 (PAIN). Positive and negative connections are denoted by green and red edges, respectively. FATIG = Fatigue; CONCE = Concentration; MOTIV = Motivation; PAIN = Pain; P_MOOD = Positive mood; HAPPY = Happy; ENTHU = Enthusiastic; RELAX = Relaxed; CURIO = Curious; CONTE = Content; FRUST = Frustrated; AGITA = Agitated; DOWN = Down; INSEC = Insecure; GUILT = Guilty.

Day-Level Temporal Network

Similar to the moment-level network, Pain and Guilt showed strong autoregressive effects in the day-level network (**Figure 5**). In addition, also feeling Curious and feeling Insecure showed autoregressive effects. At the day level, this means that, for example, when Sylvia experienced pain one day, she was likely to feel pain the next day. In contrast with the moment-level network, fatigue did not show a strong autoregressive effect at the day-level. This suggests that yesterday's fatigue was not a strong predictor of today's fatigue. Sylvia did not immediately recognize this and explained how attending a party could leave her tired for multiple days on end.

Figure 5: Day-level temporal network



Note. The stronger a connection between two nodes, the thicker and more saturated the edge. The weakest connection was -0.0093 (MOTIV-DOWN) and the strongest connection was -.4656 (PAIN). Positive and negative connections are denoted by green and red edges, respectively. FATIG = Fatigue; CONCE = Concentration; MOTIV = Motivation; PAIN = Pain; P_MOOD = Positive mood; HAPPY = Happy; ENTHU = Enthusiastic; RELAX = Relaxed; CURIO = Curious; CONTE = Content; FRUST = Frustrated; AGITA = Agitated; DOWN = Down; INSEC = Insecure; GUILT = Guilty.

Experiences with feedback

While the temporal networks did not show connections between nodes over time, they portrayed some autoregressive effects. The contemporaneous network models provided insight into how we could create the best circumstances to help Sylvia handle her fatigue better throughout the day. Helping her to accept her fatigue level may help her handle her fatigue better and improve her wellbeing. Sylvia thought the network models were useful as they provided a deeper insight into what factors were important to her fatigue. All in all, she thought the networks were easy to understand and experienced the process of filling out the app and receiving feedback on the networks as positive.

Sylvia had already started cognitive behavioral therapy (CBT) with her therapist when she received feedback on the 101-days report. Based on the 21-day network report, feeling guilty about not taking good care of herself was already one of the main targets in treatment. The

100-day report confirmed these findings. In contrast to the 21-day report, both the moment-level and day-level contemporaneous network models of the 101-day report showed the importance of accepting her fatigue. Sylvia thought that a practice that helped her to become more aware of her fatigue level could help her accept her fatigue level better. Sylvia would take this up with her therapist.

DISCUSSION

This case study showed how personalized feedback based on network graphs of ESM data can provide insight into the symptom dynamics of CCRF and provide opportunities for personalizing psychological treatment. From clinical practice and qualitative research, we know that fatigue changes throughout the day but also from one day to the next.[5,9] Sylvia also experienced this and was therefore motivated to fill out the ESM app for 100 days. This allowed us to assess both moment-level and day-level networks, gaining more insight into the elusive course of fatigue.

Filling out the ESM app for 101 days was feasible for our severely fatigued patient. She became more aware of her body and her boundaries. Sylvia thought the network models based on ESM data were useful as they provided insight into what factors were important to her fatigue. Interestingly, the moment-level networks based on 101 days provided additional insight beyond the networks based on the initial 21 days. Including more assessments helps estimating more reliable networks,[25] potentially revealing connections that are not visible with less assessments. In Sylvia’s case, we found a connection between acceptance and fatigue after 101 days, which was not present after 21 days. Feeling more acceptant of her fatigue in the past three hours was associated with less fatigue in the following moment. The day-level network models were rather similar to the moment-level network models, suggesting that the factors were robustly associated with fatigue. That is, at the day-level, more acceptance was also associated with less fatigue and less hopelessness as well as with a more positive mood and more motivation to do things. These findings suggested that Sylvia could benefit from treatment that helps cultivate acceptance.

One difference between the moment-level and day-level temporal networks was the autoregressive effect of fatigue. While fatigue from three hours ago predicted present-moment fatigue, yesterday’s fatigue was not such a strong predictor of today’s fatigue. The day-level network did not provide other insights beyond the moment-level network. More research is needed to examine whether the additional insight provided by day-level networks outweigh the burden of filling out the app for 100 rather than 21 days in clinical practice.

The present study provided insight into changes in CCRF throughout the day and from day to day. Although CCRF is chronic and experienced as continuously present, in this case, fatigue appeared to increase over the course of a day and varied from day to day. Sylvia even experienced a few days of energy. However, in order to gain more insight into the course and symptom dynamics of CCRF we need to explore what time lag is the most optimal to study CCRF. The currently chosen time lag of approximately three hours between assessments was roughly based on our clinical experience with changes in CCRF and the burden of a maximum number of 5 assessments per day. Newly developed statistical methods can help determine the optimal time lag.[38,39] A large-scale ESM study is needed with more assessments per day, allowing us to determine the optimal time lag, and assess the extent of inter-individual differences.

The idiographic findings on the central role of acceptance are in line with recent findings from our cross-sectional group-level network model among 342 cancer patients seeking psychological care.[14] In this study, we examined the interconnectedness among symptoms (anxiety, depression, fatigue) and risk and protective factors, showing that acceptance of illness appeared to be the most centrally embedded factor in the network, meaning it had more and stronger connections with other symptoms (e.g., less anxiety) and factors (e.g., less helplessness) in the network than other factors. Moreover, a recent meta-analysis of 78 studies demonstrated how acceptance of cancer is related to lower distress, anxiety and depression.[40] These findings emphasize the importance of coming to terms with one's illness in the adjustment to cancer. Acceptance involves a non-judgmental and compassionate attitude towards one's experiences,[41] thereby reducing the struggle with the realities of the illness and actively soothing one's stress system.[42]

Methodological issues

While this case study demonstrates a successful portrayal of how network models can facilitate personalizing psychological treatment for CCRF, the following methodological issues should be taken into account. First, as in any case study, the generalizability of the findings is limited as the network models are specific for this patient. It should be noted that the participant was a highly educated woman very motivated to gain insight in her CCRF. However, the present findings did show that the network models can provide interpretable and useful information, which is generalizable to other patients. By going beyond the usual severity scores, studying the unique patterns of connectivity among symptoms can facilitate the development of a personalized treatment plan.

Furthermore, the selection of relevant nodes is highly important for network models as results may differ depending on which symptoms are chosen for inclusion in network analyses. We might not have included all potentially relevant variables for this person, using the standardized questions of the *Energy InSight* ESM app. However, the selection of the *Energy InSight* items was based on patients' experiences with CCRF,[5] group-level network models in fatigued cancer patients,[14] and the CCRF literature. Moreover, Sylvia considered the items in the network as highly relevant. Offering patients the opportunity to add an item they consider relevant for their CCRF might be a valuable next step in using personalized feedback of network models in clinical practice.[19]

Unfortunately, not all items could be included in the temporal networks as some items referred to the present moment (fatigue, mood, pain), while others referred to the past three hours (coping with fatigue, activity). A good alternative would be to only include items that can be framed in terms of the present moment. For example, the item on acceptance refers to the past three hours in the present study, but could also be framed in terms of the present moment (i.e., "I consider my energy level as okay right now"). This will allow us to include the coping with fatigue items into the temporal network. Moreover, it makes full use of the in-the-moment reports that are unique to ESM and prevent memory bias.[16]

CONCLUSION

Network models of the symptom dynamics of a single patient provided recognition of important factors (e.g., allowing rest, feelings of guilt) and new insight into coping with CCRF (e.g., acceptance of fatigue) that can be helpful in treatment. Furthermore, filling out the ESM app for 100 days was feasible for our patient, who suffered from severe CCRF and provided additional insight on top of the feedback based on the initial 21 days. Further research is needed to determine whether the benefit of day-level networks outweighs the burden of prolonged ESM assessment.

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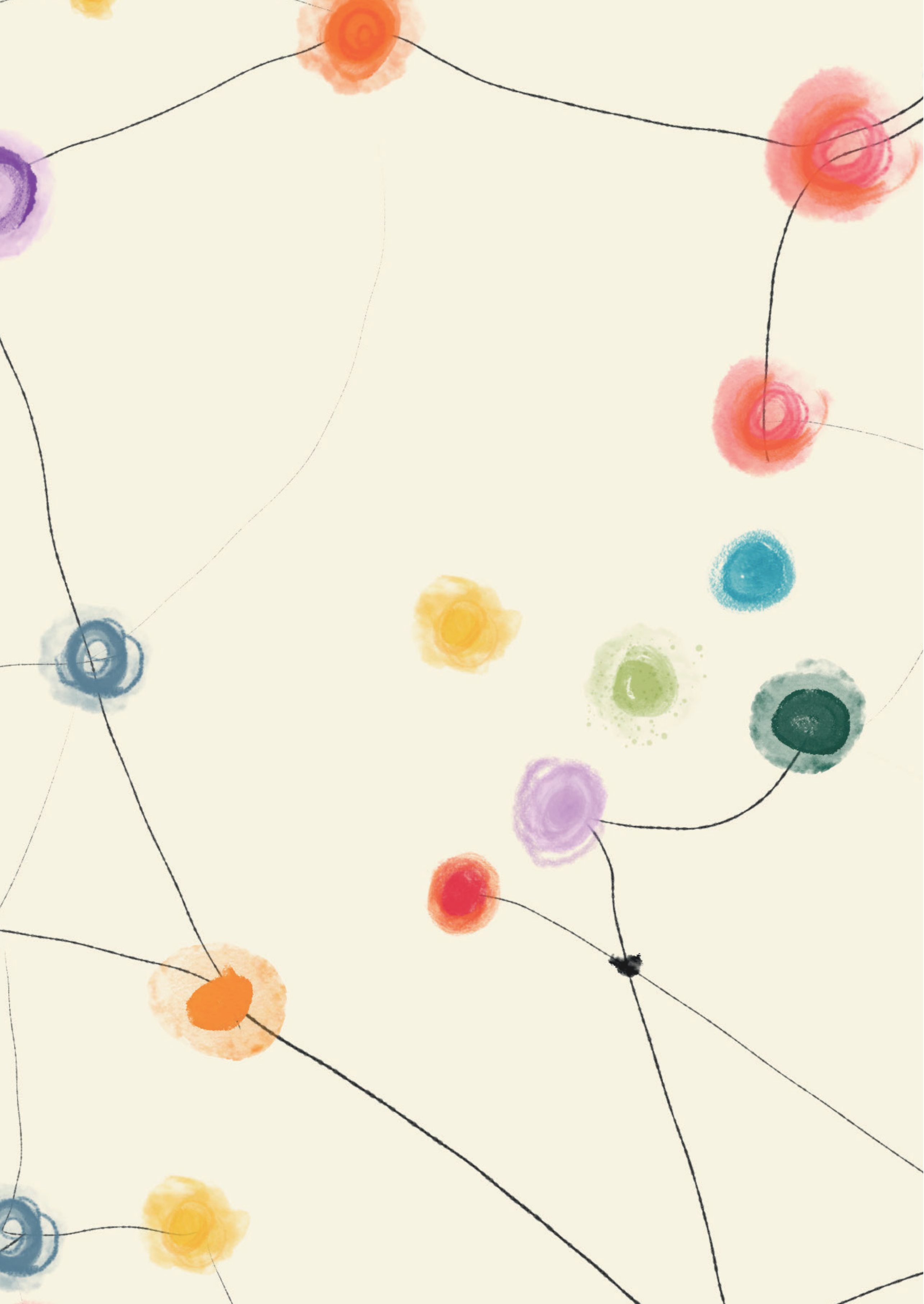

Chapter 7

SUMMARY ENGLISH AND GENERAL DISCUSSION

SUMMARY ENGLISH

Principal findings

In this thesis, I explored the patient perspective on CCRF. I used idiographic and phenomenological methodologies to investigate how patients experience and respond to CCRF. This experiential knowledge of CCRF combined with network theory applied to EMA data are used to find an answer to the central research question: **in what way(s) can we personalize psycho-oncological care for patients with CCRF?**

In the following paragraphs, I summarize the findings of five studies. The summary is followed by a critical reflection on the main results of this thesis to put them in a broader context, a discussion of the methodological strengths and limitations of the presented idiographic research, and an outline of the recommendations for clinical psycho-oncological practice and future research.

Chapter 2: Experiencing and responding to chronic cancer-related fatigue: A meta-ethnography of qualitative research

Chapter 2 consists of a meta-ethnography of qualitative studies, which included patients who suffered from CCRF. The aim of this meta-ethnography was to create an overarching interpretative narrative that focused on how patients' experience and respond to CCRF.

I performed a comprehensive systematic literature search. Of the 1178 selected studies, I included sixteen qualitative studies after deduplication and abstract and full-text screening. These studies included 705 patients (majority women) with different ages, cancer types (mainly breast cancer), stages, and (phase of) treatment(s). The quality of the included studies was variable according to the appraisal with the CASP criteria for qualitative research.[1] I followed the seven phases of meta-ethnography first described by Noblit and Hare to extract and translate the first-order constructs (patients' interpretations) and second-order constructs (authors' interpretations) from the studies and synthesize these into third-order constructs (new interpretations).[2]

This interpretative qualitative review that focused on how patients experience and respond to CCRF showed an embodied structure of CCRF. I developed a figure of embodied CCRF (see **figure 2** in **Chapter 2**) that consists of six interrelated third-order constructs with social, spatial and temporal dimensions:

1. ***Embodied experience:*** the negative awareness of the body;
2. ***(Mis)Recognition:*** the lack of recognition by patients, relatives and health professionals (social dimension);

3. ***Small horizon:*** a narrowed world perspective (spatial dimension);
4. ***Role change:*** adopting other life roles (social dimension);
5. ***Loss of self:*** the impact on identity (temporal dimension);
6. ***Regaining one's footing:*** the process of responding to CCRF by struggling, adapting and accepting (temporal dimension).

These findings can help health professionals to recognize CCRF and take a person-centered approach. My first impression from psycho-oncological care practice is that the figure can be used as a tool to facilitate the communication between patients and health professionals. This can lead to recognition and normalization of the central problems, which can help patients to regain a sense of control.

Chapter 3: Navigating severe chronic cancer-related fatigue: An interpretative phenomenological analysis

In **Chapter 3**, I conducted semi-structured face-to-face interviews with adult participants who suffered from severe CCRF for at least three months after completion of cancer treatment. The purposively selected sample included a homogeneous sample of 25 participants. The aim of this interview study was to better understand the lived experiences of patients with severe CCRF. In this interview study, I used a theoretical framework of philosophical phenomenology to explore how patients with CCRF experience disruptions in embodiment, time, and space and how these are related.[3–5] For qualitative analysis of the interviews, I followed the six steps of the IPA method of Smith.[6]

After discussion with our multidisciplinary research team, I identified four interrelated themes that expressed different dimensions of the embodied experience of CCRF:

1. ***Worn out:*** how CCRF is an overwhelming dynamic experience with different sensations (i.e., physical, emotional, sensory, and cognitive) in one's body (e.g., limbs and/or mind), and could result in a loss of self (affective dimension);
2. ***Diminishment of one's "I can":*** how time and space to move 'freely' is restricted by the bodily experience of CCRF and impairs one's activities and social life (functional dimension);
3. ***Invisibility:*** how the body with CCRF becomes an object within a social context because others cannot see CCRF (social and material dimension);
4. ***Regaining one's "I can":*** how one can adapt active time and movement in space to the embodied experience of CCRF, one's limitations in functioning, and objectification of one's body in a social context (functional and productive dimension).

This phenomenological interview study showed that experiencing CCRF is a personal, complex, and dynamic process that consists of interconnected affective, social, material, functional, and productive dimensions.

Chapter 4: Forming new habits in the face of chronic cancer-related fatigue: An interpretative phenomenological study

In **Chapter 4**, I used the same interview sample of 25 participants with severe CCRF from **Chapter 3** and focused on the question of what is helpful in responding to CCRF to facilitate adaptation. I followed the six steps of the IPA method of Smith:[6]

I identified five interrelated themes of the dynamic and mutually reinforcing habitual process of responding to CCRF:

1. ***Discovering physical and emotional boundaries:*** a learning process of self-monitoring focused on how one's body feels to protect boundaries and prevent exhaustion;
2. ***Communicating support needs:*** ways of searching for information and asking for (professional) help;
3. ***Reorganizing and planning activities and rest:*** finding a new way to balance activities and rest in one's life;
4. ***Letting go of one's habitual identity:*** stopping with old habits and changing one's role into a less active person;
5. ***Recognizing and accepting CCRF:*** how the formation of new habitual ways to respond to CCRF creates room for new beliefs such as acceptance of one's CCRF.

This phenomenological interview study provided insight into what is helpful while responding to CCRF. In this process of habit formation, breaking with unhelpful habits and negative beliefs is essential.

Chapter 5: Using smartphone-based ecological momentary assessment and personalized feedback for patients with chronic cancer-related fatigue: A proof-of-concept study

A quantitative form of idiographic research is ecological momentary assessment (EMA), also called the experience sampling method. EMA is a structured diary technique, in which a participant receives questions (e.g., symptoms, affect, behavior) multiple times a day for multiple days on end in their daily living environment.[7] Based on the findings from **chapters 2-4** described above and from the perspective of the network theory as introduced in the **first**

chapter, together with my colleagues, I developed the *Energy InSight* app, an EMA app specifically targeted at assessing CCRF idiographic as interrelated phenomenon.

In **Chapter 5**, I conducted a proof-of-concept study implemented in routine psycho-oncological care with five participants on the waitlist for psychological treatment for severe CCRF and their therapists. Participants completed EMA questions (i.e., fatigue, mood, activity, coping with CCRF, and context) of the *Energy InSight* app on their mobile phone five times a day for a three-week period. In the following week they received personalized descriptive feedback from the researcher and during the first session with their therapist they discussed the network feedback together.

The aims were to explore 1) to what extent and how a patient gained insight into CCRF by filling in the smartphone-based EMA and receiving personalized (network) feedback, and 2) how this insight can help patients and therapists improve the case conceptualization process in psycho-oncological care for CCRF. I used think-aloud interviews, semi-structured interviews, and observations to explore the user experiences of patients and their therapists. I performed inductive thematic analysis of the transcripts[8]. Based on patients' and therapists' experiences in this proof-of-concept study, using EMA data collection and discussing descriptive and network feedback seems feasible and usable to personalize and improve psycho-oncological care for CCRF.

Patients' experiences (N=5):

The qualitative findings showed that using the EMA app (*Energy InSight)* for some patients resulted in negative reactions from others and increased the awareness of the body, (dis) abilities, and feelings. Using the EMA app (*Energy InSight)* and receiving the descriptive feedback report enabled for everyone visibility and acknowledgment of their main problem. The discussion of the descriptive and network feedback was emotionally confronting in a positive way for most patients. The descriptive and network feedback helped all patients to identify and recognize interrelated problems of CCRF. Using the EMA app (*Energy InSight*), followed by the descriptive feedback initiated for some patients a change in their behavior to respond to CCRF in helpful ways. The discussion of the network feedback report helped all patients to set treatment goals or change treatment direction.

Therapists' experiences (N=4):

The qualitative findings demonstrated that some therapists reported limited use of the descriptive reports. Most therapists evaluated the network feedback as insightful, useful, and an accelerator in treatment to identify the main problems. However, exploring network associations and translating the findings to practical use in psycho-oncological care was challenging for all therapists.

Chapter 6: Personalizing psychological care for chronic cancer-related fatigue: A case study on symptom dynamics

In **Chapter 6**, I presented a case study to illustrate how feedback on person-specific networks can provide new insight into CCRF and how these insights can aid personalization of psychological treatment of CCRF. This case was part of the proof-of-concept study (**Chapter 5**).

A 34-year-old woman with CCRF as her main problem was referred to a mental health institute for psycho-oncology. During the time on the waitlist, she completed the EMA questionnaire (*Energy InSight*) with 24 questions about fatigue, mood, activity, coping with fatigue, and context five times a day. She was willing to fill out the EMA app for 101 days. This allowed us to explore both moment-level and day-level partial (directed) correlation networks and to gain more insights into how symptom dynamics can change over time.

The interplay between symptoms, cognitions and behavior was visualized in the person-specific moment-level and day-level networks, which were discussed with the patient. For example, accepting fatigue was an important node in the moment-level and day-level contemporaneous network. In the moment-level network, acceptance of fatigue in the last three hours had a connection with less hopelessness in the past three hours and less fatigue in the following moment.

In the day-level contemporaneous network, acceptance was associated with less fatigue, less hopelessness, better mood, and more motivation to do things on the same day. The patient recognized this pattern. She explained that the unpredictability of CCRF can make her feel hopeless.

These findings opened a dialogue with the patient about the importance of acceptance in responding to fatigue. She discussed these findings with her therapist. This case study demonstrated how symptom networks can provide insights into how to better respond to fatigue and might help to find a direction for treatment.

GENERAL DISCUSSION

Reflection on main findings

Adopting a phenomenological and network perspective on CCRF

In this thesis, I used qualitative phenomenological and quantitative idiographic network research methodologies that worked complementary in exploring the experiences and responses to CCRF on an individual level. I took four steps during the REFINE project and will use these steps to describe what I learned from adopting a phenomenological and network perspective on CCRF. In this description, I will address the gaps of knowledge mentioned in the introduction: a narrowed perspective on CCRF, the lack of integrative conceptualization of CCRF (including protective factors), and difficulties with communication and case conceptualization of CCRF by patients and therapists.

(1) As the starting point of the REFINE project, I took a broad view on CCRF by conducting an interpretative meta-ethnography of existing qualitative studies.[2] From the patients' perspective, the qualitative data showed that the body plays a central role in the experiences and responses to CCRF. However, in medical practice, the patient's body is often approached as a machine, which is in line with the body and mind dualism. This distinction between body and mind was first introduced in Western philosophy by Descartes in the 17th century,[9] and since the 19th century largely applied in Western medicine. In this biomechanical model of the body, a patient is simplified into separate, individual body parts aimed to diagnose and treat disease.[10] In the case of a patient with CCRF, there is no objective gold standard to diagnose, and there are different treatment options, which hampers the communication and makes this model difficult to apply.

Therefore, I used a phenomenological perspective to approach a person with a severely fatigued body. With this holistic approach, a patient with CCRF is seen as whole or an integrated body (instead of body parts) within an environmental context.[10] This holistic approach is also similar to how patients experience and respond to CCRF, which impacts all aspects of their lives and are represented in social, spatial, and temporal dimensions of embodied CCRF, as identified in the meta-ethnography. Compared to previous qualitative reviews on CCRF that used aggregative, comparative and descriptive analysis, the interpretative results of the meta-ethnography provide new insight into the interrelated dimensions of CCRF.[11,12]

(2) As a second step of the REFINE project, I used a philosophical phenomenological theoretical framework to analyze interview data of patients with severe CCRF.[3–5] Using these in-depth interviews, I fully explored the lived embodied experiences and helpful and

unhelpful habitual responses to CCRF within a social context. This in-depth exploration provided a phenomenological and embodied perspective on CCRF. The interview study reported that experiences and responses vary between individuals. These intra-individual differences warrant an idiographic approach. Based on these results, I conceptualize CCRF as a personal, multidimensional, interrelated, complex, and dynamic problem.

However, these new interrelated existential embodied dimensions are not completely captured by the different unidimensional and multidimensional questionnaires used for measuring CCRF. The variety in the content of these questionnaires to measure CCRF is for some part due to a lack of consensus about the conceptualization to define this complex problem.[13] In research with large patient groups, retrospective questionnaires are ideal and frequently used to present generalizable results. However, these quantitative questionnaire tools only measure unequivocal information about CCRF and cannot interpret the different ways one's severely fatigued body is experienced over time.[14] Additionally, questionnaires entail a number of items that measure a particular aspect of one's fatigue (i.e., subscales of fatigue dimensions) on a predefined timescale (i.e., last week) with numerical response options. In this way, the embodied experience of CCRF is questioned without its lived context and separated from its interrelated social, temporal, and spatial dimensions.[14]

The network theory provides a better way to conceptualize CCRF in line with how patients experience these interrelated dimensions of CCRF as a so-called vicious cycle. This theory was first introduced in psychology in 2013 by Borsboom and Cramer and conceptualizes a mental disorder as a complex dynamic system of multiple interacting factors.[15] This network perspective offers a new way to better understand CCRF. For example, a patient in the phenomenological interview study reported that fatigue is a plus factor that makes her more depressed and more emotional all of a sudden. The network theory focuses on these functional interrelations between these different experiential factors instead of assuming one (unknown) underlying mechanism or cause.[9]

(3) In the third step of the REFINE project, I integrated knowledge from this phenomenological and network perspective, previous (network) research on CCRF, and clinical and patient expertise to select and formulate momentary and retrospective items for the development of the EMA app *Energy InSight.*[16,17] Embodied (e.g., physical fatigue) and habitual (e.g., allowing rest) experiential dimensions of CCRF expected to change throughout the day were included. In line with the person-centered care perspective also health-promoting factors such as acceptance of CCRF, which was reported as helpful by patients in the meta-ethnography (**Chapter 2**) and phenomenological interview study (**Chapter 4**) were added to the EMA app *Energy InSight.*[18] In the case study of

Chapter 6, the person-specific moment-level and day-level networks showed how acceptance of fatigue was helpful in dealing more effectively with CCRF in daily life. Our network group-level study demonstrated similar findings concerning the importance of acceptance of illness for patients who sought psycho-oncological care for fatigue, anxiety and/or depression.[16] A recent study of Lewson et al. indicated that patients who completed cancer treatment and suffered from more severe symptom levels (i.e., fatigue, sleep disturbance, anxiety, and depressive symptoms) discontinued meaningful daily activities and experienced less acceptance of cancer and their cognitions, emotions, and symptoms.[19] Therefore, acceptance of cancer and CCRF seems an important focus during treatment of patients with CCRF.

(4) In the last step of the REFINE project, I used the network perspective to visualize the complex interconnectivity between different symptoms, cognitions, emotions, and behavioral responses to CCRF. Such interactions may be initiated by underlying biological, psychological, and social mechanisms.[20] In the proof-of-concept study (**Chapter 5**), therapists used these person-specific networks for an individual meaning-making exploration process of interrelations between different dynamic experiential embodied and habitual dimensions of CCRF. The previous qualitative findings from the meta-ethnography (**Chapter 2**) and phenomenological interview study (**Chapters 3 and 4**) helped in the dialogue between patients and therapists to interpret the strongest network connections of the person-specific network and put their lived experiences into the context of daily life. Based on network theory and analysis, it was dependent on the individual how these perpetuating and protective factors were interrelated and what connections were most important.[21] In this way, the network perspective addressed the complexity and individual heterogeneity of how patients experience CCRF in addition to information about the severity of CCRF from the CIS-FS questionnaire and descriptive feedback report.[15,22,23] This network and descriptive feedback visualized the severity and relations of the invisible problem CCRF. This visibility of CCRF in the feedback reports overcomes difficulties such as concealment of particular experiences in communication between patients and therapists. This idiographic method at the start of lifeworld-led psycho-oncological care for CCRF corresponds with the shift in care towards a holistic and individual approach using mobile health technology and personalized feedback that focuses on individual transdiagnostic symptom dynamics irrespective of a particular diagnosis.[22,24,25]

Towards a new way of measuring CCRF

In this paragraph, I will discuss how our results fit in with the broader literature on EMA and reflect critically on two psychometric aspects of EMA: validity and measurement reactivity. I presented our proof-of-concept study with the EMA app (*Energy InSight*) in **Chapter 5**. During three weeks, patients with CCRF on the waitlist for psycho-oncological care received five notifications during the day to complete the EMA questionnaire (*Energy InSight*) within half an hour. The use of EMA during waitlist time appeared feasible because none of the participants dropped out and had an overall high compliance rate. The qualitative evaluation with patients and therapists reported mainly positive user experiences with EMA and receiving personalized feedback. One of these five cases presented in the case study (**Chapter 6**) succeeded the study period with from 21 days to 101 days (five notifications per day) to investigate also day-level personalized networks. Our study findings are in line with the scoping review of Kampshoff et al. which concluded that EMA in the field of oncology seems useful and feasible but is currently under-utilized despite its good potential.[26] This review was based on twelve small and observational EMA studies with different outcomes. Five studies had as the primary outcome fatigue during and after treatment to gain a better understanding of daily patterns of fatigue.[27–31] In addition, two recent EMA studies of Nap-Van der Vlist et al. and Harnas et al. provided personalized feedback to patients with CCRF after EMA data collection using a different EMA questionnaire and EMA study protocol. Both studies reported similar positive user experiences.[32,33] Therefore, the promising results of these first EMA studies with patients with CCRF will guide future psycho-oncological research in the direction of how to optimally use EMA and personalized feedback to personalize treatment.[34]

1. EMA validity

Despite the potential and promising results of these previous EMA studies on CCRF, the use of EMA faces some methodological boundaries. I will start to discuss on how we took two psychometric aspects into account in our proof-of-concept and case study (**Chapters 5 and 6**): EMA validity and measurement reactivity. In the limitations section of this discussion, I will provide more information on other boundaries of EMA data collection.

During the start-up of the proof-of-concept study (**Chapter 5**), we organized two multidisciplinary team meetings with patient experts, clinicians, and (EMA) researchers to improve node validity. This process consisted of selecting the adequate nodes for a network and evaluating their quality of assessment.[35] I performed pilot testing with a patient expert before start of data collection. Besides symptoms which are the basis of most networks, positive and negative affect, helpful and unhelpful cognitive and behavioral responses to CCRF were included, because these were all expected to dynamically interact with each other.[35] The EMA items were short and neutral and formulated in patients' words to avoid response bias.[36] We used the word "energy" instead of "fatigue" in the included items of EMA app *Energy Insight* to reduce the risk of negative reactivity.

Although the EMA items of the app (*Energy InSight*) showed face validity because they were subjectively viewed to measure CCRF by experts (i.e., patients, therapists, researchers), two other important forms of validity need more attention in EMA research.[37,38] Firstly, content validity that is the degree to which the measure captures the whole construct (CCRF) with all its facets and needs to be qualitatively evaluated.[37] Secondly, construct validity that refers to the degree to which the EMA tool measures the complex construct (CCRF) that it claims or aims to measure.[37,39] However, no objective measure of CCRF exists, only a comparison with retrospective questionnaires on CCRF can be made, which measure other information.[40]

To date, most researchers select their own set of EMA items as was shown in the two previously published EMA studies on CCRF. The authors of these studies did not report on content validity.[32,33] Our EMA questionnaire (*Energy Insight*) was open to modifications during and after the proof-of-concept study (**Chapter 5**). I performed a qualitative user evaluation on content validity of EMA items, which resulted in a change in items (i.e., adding item feeling anxious and changing the first item physically I feel with adding the word “tired” to improve recognition and measurement of fatigue), response options (i.e., no bipolar scale with exhausted/energetic to measure fatigue), and instructions (i.e., explanation of what is physically and mentally active).

EMA guidelines to improve design and methods including psychometric aspects need to be developed.[34] These guidelines might recommend on how to select nodes for a network. To properly model a phenomenon such as CCRF, a network needs to be minimally complete and include only necessary and separate identifiable nodes that are sufficiently distinct from each other and exclude unnecessary and overlapping nodes.[35] For content validity of patient-reported outcomes (PROs), COSMIN criteria were introduced that could be applied to EMA as well. These criteria recommend reporting on relevance for the construct of use (i.e., for target population and context of use), comprehensiveness (i.e., including all key concepts), and comprehensibility (i.e., instructions, items and response options) of EMA items to the users.[37,41] The focus of the EMA user evaluation in our proof-of-concept study (**Chapter 5**) was more on comprehensiveness and comprehensibility, although also recognizability and importance of nodes were checked during the discussion of the personalized network feedback report. This proper content validity of the EMA questionnaire (*Energy InSight*) is expected to be a basis of good construct validity.[37,38]

2. *Measurement reactivity*

When interpreting the present findings of the proof-of-concept study (**Chapter 5**), in which patients completed the EMA questionnaire (*Energy InSight*) several times a day for a couple of weeks to collect sufficient data for network analysis, it seems to be more burdensome than treatment as usual without these assessments.[42] Another psychometric aspect related to this longitudinal data collection is measurement reactivity, which means any change in the participant due to the EMA measurement.[43] I will discuss the expected influence of three different forms of measurement reactivity: changes in the underlying construct CCRF (e.g., fatigue level), changes in the behavior (e.g., avoiding physical activity during study period), and changes in the EMA response behavior (e.g., other responses to EMA items over time).[44] Measurement reactivity is important to take into account and could bias EMA findings and decrease ecological validity of EMA assessment.[44] Therefore, I monitored their fatigue levels with the CIS-FS questionnaire, which reduced for all patients during study period of the proof-of-concept study. Patients also did not report that using the EMA app increased their fatigue levels. There is also no evidence for changes in reported symptom level in other EMA studies with different patient groups.[44,45] Some patients of the proof-of-concept study (**Chapter 5**) reported changing their behavior while filling out the app. For example, taking more rest because they became more aware of their fatigue while filling out the app. This potential change in behavior during self-monitoring of CCRF with the EMA app might have an effect on the results presented in the personalized descriptive and network feedback reports. The last form of measurement reactivity is the change in EMA response behavior and is caused by a habituation effect. Because participants become better in responding to EMA about how they feel on the scale with less use of extremes, which might improve the quality of the findings over time.[44] Another effect on EMA response behavior is the fatigue or boredom effect, which was mentioned by one participant of the proof-of-concept study (**Chapter 5**) as responding on automatic pilot and could lead to more homogeneous responses to EMA.[44]

Experiences with smartphone-based EMA and personalized feedback about CCRF integrated into psycho-oncological care

Recently, a cultural shift towards the increased importance of patient engagement in therapeutic process started. Patient empowerment means patients' ability to meet their needs, solve their problems, and mobilize necessary resources to feel in control of their lives.[46] This involves being active in both self-management and shared-decision making. A good example is the active involvement of patients in EMA data collection and the evaluation of personalized feedback during the proof-of concept and case study, which motivates and contributes to co-creating a treatment process.[24,46–48]

Importantly, the proof-of-concept and case study findings showed that the self-monitoring process of the EMA data collection helped patients with CCRF to gain insight into their main problems. Responding to EMA items could be seen as an intervention or clinical tool on its own that could result in increased awareness of, reflection about, and insight into problems.[21] Furthermore, patients of the proof-of-concept study reported that EMA data collection activates them to get started with how to better handle their fatigue. This theme 'initiation of behavioral change' might be an indicator of patients' motivation for psycho-oncological treatment.[47] This motivation of participants to use smartphone-based EMA during the waitlist was mentioned in the interviews of the proof-of-concept study and even more reflected in the attrition and compliance rates of all study participants.

Additionally, personalized feedback could improve patient empowerment because it might facilitate communication between patients and health professionals and further enhance motivation for treatment and shared-decision-making.[24] An advantage of using the EMA app during waitlist and providing feedback at the start of psycho-oncological care for CCRF is the practical use for a shared decision on the treatment direction and set treatment goals. Because this type of care, organized as lifeworld-led care with a holistic and well-being focus, psycho-oncological therapists can use the individual network exploration with their patients in the case conceptualization process to personalize treatment.[21,49]

In this way, personalization of psycho-oncological care is based on individual experiences and lived context instead of generalized results between groups.[24] This shared-decision process is enriched with individual EMA data, which empowers and motivates the patient to participate in this process as an equal partner.[24] The therapist acts as a coach with their therapeutic knowledge and the patient is the expert on their lived experiences.[24] The presented network feedback invited patients to perceive their fatigue as a complex dynamic system in which several protective and perpetuating factors are connected with fatigue.[21] The descriptive reports showing the course of different (combination of) variables over time were an additional source of information.[21] This collaborative and explorative method might possibly accelerate and improve psycho-oncological care for CCRF.[50]

We provided no specific advice in the personalized descriptive and network reports patients received at the start of psycho-oncological care. Therapists were instructed to guide the dialogue with explorative questions about the correlational interpretation of networks. Therapists translated the findings into treatment goals and practical tools that can help patients to respond to CCRF. Due to methodological limitations of network modeling, recently researchers have warned for the risk of overinterpreting person-specific networks in clinical practice. Similar to our procedure, they recommend therapists to ask explorative questions about the networks to guide the case conceptualization.[21,22] In addition, the meaning-making of the network connections in a dialogue between patients and therapists could be experienced as a (positive) emotional confrontation by patients. Therefore, this careful approach to openly discuss network associations seems appropriate for patients that suffer from severe CCRF and comorbidities who were referred to psycho-oncological practice.

Besides patients' experiences with EMA data collection and personalized feedback, therapists' experiences were evaluated in the proof-of-concept study. The four therapists reported positive experiences: insightful, useful, accelerator of treatment, and refinement of main problems. In the survey study of Piot et al. therapists reported similar experiences such as gaining insight into the context specificity of symptoms, triggers, and the severity and frequency of symptoms as most useful aspects of EMA.[42] However, translating the abstract network to what can help the patient was also experienced as challenging for therapists in the proof-of-concept study. These results are in line with the study of Frumkin et al. who evaluated the feasibility and utility of person-specific networks among psychological treatment-seeking patients and therapists and found a more tempered response of therapists for its use.[51] Frumkin et al. raised the point that the sparseness of the models may have influenced the attitude towards usefulness of the person-specific network models in clinical practice.[51] In the proof-of-concept study, therapists explored networks of different density from patients with CCRF. Previously, dense networks were hypothesized to reflect the severity of disease. With more research being done in this field, this hypothesis has not been confirmed and it is unknown what the relation is between density of the network and severity of the disease.

Strengths and limitations of idiographic research

In this thesis, I used complementary idiographic methodologies with their own strengths and limitations to find a new way to personalize psycho-oncological care for patients with CCRF. The major strength of incorporating the patient voice was the iterative development process of the EMA questionnaire (*Energy InSight*) that provided after applying the network perspective new therapeutic insights on how individual patients experience and respond to CCRF.

Quality of qualitative research

Most studies of this thesis were (partly) based on qualitative research. To improve the quality of the meta-ethnography presented in **Chapter 1**, I used EMERGE guidelines for reporting all the steps from the seven phases, according to Noblit and Hare.[2,52] In addition, I assessed the quality of sixteen qualitative studies with CASP criteria beforehand.[1] To evaluate the quality of the phenomenological interview study presented in **Chapters 3 and 4**, I took into account the four broad principles of Yardley (i.e., sensitivity to context, commitment to research process and rigor, transparency and coherence of research, and impact and importance).[6,53] To increase the internal validity of the proof-of-concept and case study presented in **Chapters 5 and 6**, I used data triangulation to collect data from different sources (i.e., participant observations and (think-aloud) interviews), and incorporated both patients' and therapists' voices.

Limitations of qualitative research

Despite these strengths, we should be aware of some limitations. On one side, the broad interpretative analysis of the meta-ethnography (**Chapter 2**) and interpretative phenomenological analysis of the interview study (**Chapters 3 and 4**) were based on participant's ability to openly and adequately discuss their lived experiences of CCRF with different interviewers. On the other side, these qualitative analyses were based on my skills as a qualitative researcher to reflect on, analyze, and discuss the interpretation of these findings with our multidisciplinary research team.[54]

Due to the study design of the proof-of-concept study with five diverse cases guided by four different therapists, it was not possible to reach data saturation for the thematic analysis and this resulted in a less complete view of user experiences with EMA data collection and personalized feedback reports. Moreover, take caution when interpreting the predominantly positive evaluation of the motivated participants in the study sample of the proof-of-concept study (selection bias). Some patients refused participation because of the expected burden of assessments. During implementation in psycho-oncological care, the adherence and experiences with EMA data collection might be less beneficial.

The idiographic research methods used in this thesis facilitated case conceptualization and gained individual profound insights into CCRF, but cannot make general claims for a larger population with CCRF.[6,54,55] Therefore, quantitative studies with a larger group of participants are needed to investigate if this new way of case conceptualization with EMA data collection and personalized feedback may lead to increased efficacy of psycho-oncological care for the population of people suffering from CCRF (e.g., reduced treatment time).

Limitations of EMA data collection

The EMA questionnaire (*Energy InSight*) contained 24-25 items about fatigue-related symptoms, positive and negative affect, activity, coping with fatigue, and context. Other EMA pilot studies recommended 20-30 items in a personalized questionnaire purposed for case conceptualization and not overburden patients with too many assessments.[21] At the same time, we need to consider a minimum number of assessments to have sufficient power to model a reliable person-specific network. In three cases of the proof-of-concept study, we extended the study period by one to three days to reach this minimum number of assessments needed for network analysis, which was an extra burden for the patient. The EMA data collection of the proof-of-concept and case study were based on previous simulation studies of Epskamp that estimated reliable networks of eight nodes with 50 observations per person.[56] A recent simulation study of Mansueto et al. showed that it is advisable to reduce the number of nodes to six nodes with 75 of 100 observations for estimating reliable temporal networks.[57] These new insights into including reduced maximum nodes for reliable networks show that our personalized networks in the feedback reports based on previous simulation studies included possibly too many nodes and in future network research it is recommended to include maximal six nodes in temporal networks.[56,57]

The sampling design of the proof-of-concept study consisted of a three-week period with a measurement frequency of five times a day on semi-random time points. In situations with other people present or at work, it was not always possible to respond to the EMA questionnaires, which increases the risk that some particular situations were not sampled.[58] However, the advantage of this relative unpredictability of the timing of assessments (compared to a fixed sampling scheme) makes them unavoidable, maintains the daily life routines, and reduces bias in the selection of relevant moments of subjective experiences.[36] The delay to respond was set up to 30 minutes in line with other studies to diminish the risk of self-selection and recall bias, and it took around 5-10 minutes to respond from the moment the signal was received.[36] Patients reported that this time was sometimes too short for answering the questionnaire.

A key feature of the use of EMA is to capture dynamic and momentary states in daily life.[36] We used different timeframes of the selected EMA items (*Energy InSight*): symptom, affect, and contextual items were momentarily (i.e., here-and-now) and activity and coping items were retrospectively (i.e., past three hours) assessed. The difference in timeframe might influence the answers.[58] The advantage of the use of momentary items is that the risk on recall bias is minimized. However, we expected that the retrospective items (i.e., activity and coping) occurred less frequently, were ongoing or difficult to assess in the moment and could be missed when assessed momentarily. Therefore, a question over a longer time interval will provide a better insight into these variables.[36] A disadvantage of the use of retrospective questions is the risk on retrospective biases, especially by cancer patients who also might experience memory problems.[36]

We ordered the items always in the same way. We started with momentary questions, followed by retrospective questions, and ended with contextual questions. This order with most transitory constructs first (i.e., fatigue-related symptoms and affect) and context at the end may prevent that more momentary items are influenced by the previous items.[36] Patients recommended improving the questionnaire and presenting the questions in a random way. This random order of questions avoids completing the EMA questionnaire on automatic pilot and sequence effects that could bias the data because negative affect influences the response to the other questions.[36] For randomization of the order of the questions, it is recommended to keep the same group of questions with the same timeframe and response options together.[36] Although the risk of recall bias is reduced with EMA, the subjective self-report method is susceptible to other forms of bias: social desirability, cognitive biases and cultural norms.[58] For example, social desirability in responding to behavior items in a way that is viewed positive by others. For example, be more often physically active than actually is the case.[36,59] Therefore, it is sometimes better to use also objective sensor-based activity or ambulatory physiological measures or a combination.[36,47]

Recommendations for patients, health professionals, and psycho-oncological care

Based on the qualitative results presented in this thesis about new ways to personalize psycho-oncological care for CCRF, I will provide several recommendations for psycho-education and self-management, education of health professionals, personalization of psycho-oncological care, and transdiagnostic implications.

Psycho-education and self-management of CCRF

Patients need to be well-informed before, during, and after cancer treatment about the possible embodied experiences and responses to CCRF. The embodiment figure, a product of the meta-ethnography, could be presented as a poster in waiting rooms from hospitals and psycho-oncological care practices, or as an image in information leaflets, or on websites with patient information. Based on our experience of this poster in the waiting room of the HDI, this figure can help patients in recognizing and understanding the different aspects of their CCRF experience. Furthermore, this can help patients to start communicating with their health professionals and caregivers about their experience with CCRF and the need for support to regain a sense of control. Patients could also learn what is helpful and not helpful in responding to CCRF. For example, protecting physical and emotional boundaries, reorganizing and planning activities and rest, and accepting are helpful ways of responding to CCRF. Partly based on the findings of the meta-ethnography (**Chapter 2**) and interview study (**Chapters 3 and 4**), the website https://fitterbijziekte.nl/kanker/ was developed, which provides useful patient information with several practical advices, and informs them when to talk to a professional.

Education of health professionals about CCRF

Health professionals could benefit from the embodiment figure of the meta-ethnography and the insight into differences in the wording of patients' experiences to better recognize, report, and treat CCRF and improve their communication with patients. Health professionals should interpret and integrate the subjective lived experience of CCRF and the bodily signs with the medical diagnosis to timely refer to psycho-oncological care if needed.[60] Furthermore, they need to improve their knowledge on what is helpful and unhelpful in responding to CCRF. For example, health professionals could advise patients on how to protect physical and emotional boundaries, reorganize and plan activities and rest, communicate support needs, and foster acceptance of CCRF.

Personalized psycho-oncological care for CCRF

The use of EMA data collection and personalized feedback helps to better understand the individual processes of experiencing and responding to CCRF. These insights can be used to improve case conceptualization by therapists. This might in clinical psycho-oncological practice result in a better informed shared-decision on the type of and/or focus of treatment. Based on therapist experiences, it seems important for therapists to first learn more about a patient's background. Therefore, a second treatment session instead of a first treatment session seems more appropriate to evaluate the personalized network feedback. A next step in personalization is to ask patients before start to add a personal item related to their CCRF from, for example, from an EMA repository (e.g., https://www.esmitemrepository.com/).[61]

Because therapists experienced exploring and interpreting network associations with patients as challenging, a training about interpreting and discussing the feedback is highly recommended.[21,42,50] This training could include information about network theory and how to interpret positive and negative network associations in personalized networks. Important points are: 'correlation is not the same as causation' and 'networks are only part of reality'. Examples of practical tips to discuss are: how to communicate with patients about networks, how to explore network associations with explorative questions if patients recognize associations, and how to discuss an example of how this works for them.[21] The EMA data collection and the development of personalized feedback need to be further automatized for implementation in psycho-oncological practice.

Transdiagnostic implications

The embodied, interrelated, dynamic experiences and helpful and unhelpful responses to CCRF might also be recognized by patients with other chronic illnesses who experience chronic fatigue. For example, chronic fatigue is also experienced by patients suffering from stroke, renal dialysis, long-Covid, chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME), fibromyalgia, multiple sclerosis, ankylosing spondylitis, auto-immune diseases, and inflammatory diseases. While cancer is a life-threatening disease, most of these chronic diseases are not. Previous qualitative studies on patients with different chronic conditions suffering from chronic fatigue found themes similar to our findings: weariness as an unfamiliar bodily experience, unpredictability, uncontrollability, invisibility, and difficulties to describe fatigue.[62]

Recommendations for future research

Effectivity of EMA and personalized feedback in psycho-oncological care for CCRF

The case and proof-of-concept study showed promising results on the feasibility and usability of smartphone-based EMA and personalized network feedback. However, several research questions remain still unanswered. First evidence suggests that EMA itself could be considered as an intervention with benefits for patients.[63] Therefore, the question about the best moment of use in the cancer trajectory is raised: whether the use of EMA as intervention tool during cancer treatment prevents or reduces CCRF? Because experiencing fatigue during treatment is a strong predictor for CCRF, personalization also means providing treatment at moments of high risk and high symptom levels.[64]

Another important clinical question: whether the clinical added value of EMA and personalized feedback for patients and therapists of generating additional and useful insights into CCRF outweighs the costs of time investment and efforts of both? To find an answer to this question, future research could investigate the effectivity and cost-effectiveness of smartphone-based EMA data collection and personalized feedback to aid case conceptualization in a larger group of patients with CCRF referred to clinical psycho-oncological practice. A randomized controlled trial is recommended which compares a patient group with psycho-oncological care for CCRF as usual, a patient group with EMA data collection without personalized feedback and a patient group with EMA data collection and personalized feedback on treatment outcomes of reducing CCRF and treatment time.

To conduct a larger EMA study, a reduction and revision of the EMA questionnaire (*Energy InSight*) to less items and adding an optional personal question is needed. This will improve adherence and estimate reliable networks. These items could be formulated momentarily to reduce the risk of cognitive bias and enable to include all items in the same network analysis.[21] The integration of different qualitative and quantitative idiographic research methodologies with an active and central role of patients, if possible, as co-researcher is recommended for future psycho-oncological research on the personalization of psycho-oncological care for CCRF. For example, patients can help to formulate items more specifically, which can improve their compliance to EMA data collection.[21,22]

A relevant methodological question is: what is the optimal time lag for measuring CCRF? Patients' experiences suggested that CCRF might change from moment to moment, from day to day, or from week to week. The time lag between two measurements used in the proof-of-concept study was three hours. In the case study, besides moment-level, day-level networks were explored. Future large-scale EMA studies need to investigate whether this is the optimal time lag to detect changes in the experience of CCRF and look into intra-individual differences.[65]

Add objective activity and sleep measures to EMA

In the EMA study, we only included a subjective retrospective physical activity measure without sensor-based data or ambulatory physiological measures. Quality of sleep and taking naps during the day were only reported by patients of the proof-of-concept and case study in the morning and evening questionnaires and were not included in their personalized feedback reports. It is common knowledge that sleep and activity impact the experience of CCRF,[66] although it might be difficult to incorporate in network analysis due to different measurement time frames. Patients might benefit from descriptive feedback on their sleep and activity habits. Because PA interventions are also highly recommended for patients with CCRF, future research needs to investigate the reliability of the use of these objective measures in routine clinical practice and how they relate to network analysis.[66]

Caregivers' perspective of CCRF

Although some caregivers participated during patients' interviews, I did not include caregivers' perspective in the analysis. However, the qualitative findings from the phenomenological interview study reported about patients experiencing (mis)recognition, the invisibility of the problem in a social context and communicating support needs, which shows how important the role of caregivers is in dealing with CCRF. Dyadic research on cancer patients and their partners advises a mutual constructive communication strategy to develop adaptive coping strategies for dealing with cancer and CCRF.[67,68] In future research on CCRF, we need to investigate the caregivers' perspective and their active involvement in psycho-oncological interventions that focus on treating patients with CCRF.

CONCLUDING REMARKS

In conclusion, this thesis, which is part of the REFINE project, provides new insights into the different interrelated dimensions of lived embodied experiences and helpful and unhelpful habitual responses to CCRF. The body plays a central role in how patients experience and respond to CCRF. The network approach used for personalization of psycho-oncological care for CCRF is based on individual heterogeneity, and thus, enables to investigate within-person effects, such as how CCRF is experienced in one person over time. Based on patients' and therapists' evaluation, the use of smartphone-based EMA data collection with the newly developed *Energy InSight* questionnaire during the waitlist followed by personalized (network) feedback seems usable and feasible to improve personalization of psycho-oncological care. The ecologically valid EMA data collection and receiving personalized descriptive and network feedback might help patients and their therapists to learn more about day-to-day dynamics between person and context. This might facilitate the shared-decision on treatment direction and the main focus of treatment during case conceptualization at start of psycho-oncological care for CCRF.

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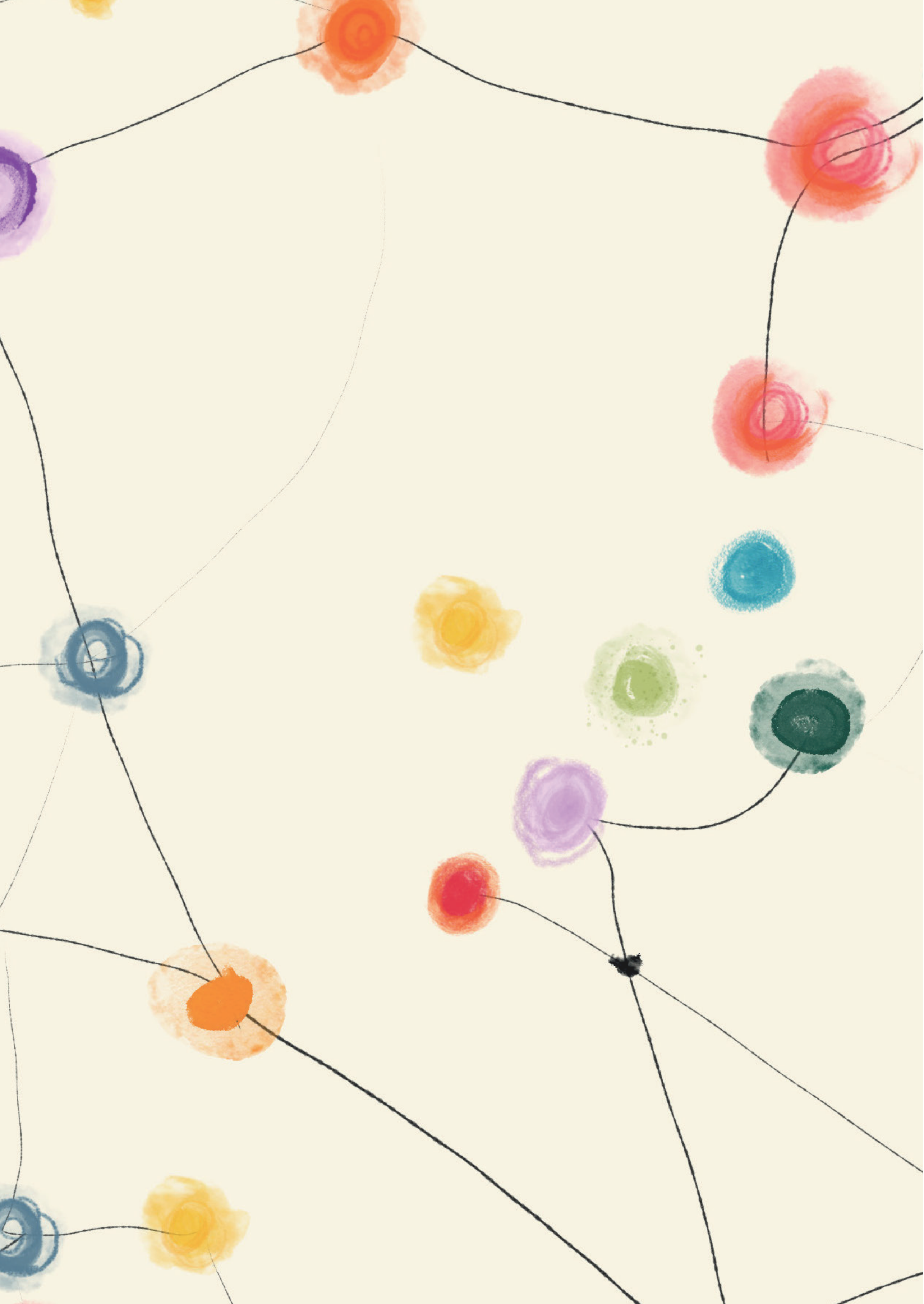

Chapter 8

NEDERLANDSE SAMENVATTING (SUMMARY IN DUTCH)

NEDERLANDSE SAMENVATTING

Hoofstuk 1: Algemene introductie

Chronische kanker-gerelateerde vermoeidheid en behandeling

Een veelgebruikte definitie voor kanker-gerelateerde vermoeidheid is: 'een onaangenaam, aanhoudend, subjectief gevoel van lichamelijk, emotionele en/of cognitieve vermoeidheid of uitputting dat gerelateerd is aan kanker of aan de behandeling ervan, dat niet is gerelateerd aan verrichte inspanning en interfereert met het dagelijks functioneren'.[1] Deze vermoeidheid kan voor de diagnose, tijdens en na de behandeling voor kanker optreden.[2] Omdat er individuele verschillen bestaan in ervaringen en omgaan met deze vermoeidheid, is een persoonsgerichte benadering om de behandeling te personaliseren aanbevolen.

Dit proefschrift is onderdeel van het REFINE-project met als doel een persoonsgerichte benadering te ontwikkelen om de psycho-oncologische zorg voor chronische kanker-gerelateerde vermoeidheid na kanker (CKV) te personaliseren. CKV wordt in dit proefschrift gebruikt voor ernstige chronische kanker-gerelateerde vermoeidheid, die blijvend aanwezig is ten minste drie maanden na afronding van de curatieve behandeling voor kanker en zal benaderd worden als een ziekte gerelateerd aan de eerdere ervaringen met kanker.[3,4] Het patiënten-perspectief over hoe CKV ervaren wordt en hiermee omgegaan wordt staat centraal in dit proefschrift, zodat een persoonsgerichte benadering samen met therapeuten ontwikkeld kan worden om de psycho-oncologische zorg voor CKV te personaliseren.

Hoewel er waarschijnlijk verschillende fysiologische en biochemische systemen betrokken zijn bij het ontstaan van CKV, is de exacte oorzaak vooralsnog onduidelijk, waardoor het ook nog niet goed mogelijk is om de behandeling hierop te richten.[2,5]

Ongeveer een kwart van de mensen met kanker ervaart CKV maanden tot zelfs jaren nadat de behandeling voor kanker is afgerond.[6–8] Met de groei van de populatie die gediagnosticeerd wordt met kanker zal deze groep met CKV in Nederland en wereldwijd ook verder groeien.[9,10] Mensen die verwezen worden naar psycho-oncologische zorg in Nederland hebben vaak last van een combinatie van verschillende klachten zoals vermoeidheid, angst en depressieve symptomen.[11] CKV heeft een negatieve invloed op het dagelijks leven en verschillende fysieke, emotionele, cognitieve, sociale en economische gevolgen, waardoor ook de kwaliteit van leven afneemt.[12,13] In de klinische praktijk wordt CKV door zorgprofessionals vaak over het hoofd gezien ondanks dat er diagnostische criteria zijn opgesteld.[14] Een ander probleem is dat patiënten vaak hun ervaringen met CKV in de communicatie met zorgprofessionals verbergen vanwege onrealistische en negatieve overtuigingen over CKV.[3,15] Zorgprofessionals kunnen zich ook oncomfortabel voelen of bewust niet vragen naar CKV om verschillende redenen, zoals gebrek aan kennis over beschikbare behandelingen of tijdsdruk.[3]

Verschillende factoren, waaronder beschermende en risicofactoren kunnen van invloed zijn op CKV. Vermoeidheid tijdens de behandeling van kanker is de sterkste voorspeller voor het ervaren van CKV.[8] Onderzoek naar CKV richt zich vaak op een specifieke risicofactor of beschermende factor in plaats van alle relevante factoren bij elkaar. Er is ook minder aandacht voor beschermende en gedragsfactoren zoals leefstijlfactoren en psychologische factoren die behulpzaam kunnen zijn in omgaan met CKV.[16–19] CKV kan beter gezien worden als een complex en multifactorieel fenomeen, waarbij per individu verschillende factoren van invloed zijn op deze vermoeidheid en/of deze vermoeidheid van invloed is op verschillende factoren.[2,20,21] Er zijn verschillende effectieve behandelingen beschikbaar met specifieke werkingsmechanismes die zich richten op behandelbare risicofactoren. Deze psychosociale en beweeginterventies zijn onderzocht onder specifieke patiëntengroepen in gerandomiseerde studies.[22] Combinaties van verschillende behandelingen zijn ook mogelijk en deze kunnen in verschillende vormen worden aangeboden.[23]

Naar een persoonsgerichte benadering om de psycho-oncologische zorg voor CKV te personaliseren

Hoewel er verschillende effectieve gedragsinterventies beschikbaar zijn, hebben patiënten die ernstige CKV ervaren met een grote negatieve impact op hun dagelijks leven psycho-oncologische zorg op maat nodig. Gerandomiseerde onderzoeken en meta-analyses naar CKV hebben onvoldoende antwoord kunnen geven op de vraag ‘wat is effectief voor het individu?’[24] Een individueel symptoomnetwerk van CKV (N=1) kan mogelijk helpen in de gedeelde besluitvorming om de meest effectieve behandeling voor het individu te vinden.

Recent is de focus van de op een groep gebaseerde geneeskunde op basis van wetenschappelijk bewijs (Evidence Based Medicine=EBM) verplaatst naar de op biologie gebaseerde, gepersonaliseerde precisiegeneeskunde (Personalized and Precision Medicine=PM) voor personalisatie in de klinisch-oncologische praktijk en onderzoek.[25] Bij EBM wordt gekeken naar het sterkste wetenschappelijke bewijs zonder rekening te houden met klinische intuïtie en patiënten-ervaringen.[26] Bij PM wordt gekeken naar de genetische basis en richt men zich op ‘wat je bent’ in plaats van ‘wie je bent’. Bovendien, het onderzoek naar onderliggende (genetische) oorzaken van CKV richt zich op genen die pro-inflammatoire cytokinen activeren, dat lijkt ook ingewikkeld om te behandelen.[1] Persoonsgerichte geneeskunde (Person-Centered Medicine=PCM) die persoonsgerichte zorg (Person-Centered Care=PCC) biedt, richt zich op de persoon als geheel en zijn omgeving, waarbij ook van wetenschappelijk bewijs gebruik wordt gemaakt binnen een kader van persoonlijke en contextuele factoren.[26]

Om een gedeeld besluit te kunnen nemen in persoonsgerichte psycho-oncologische zorg, is er idiografisch kwalitatief onderzoek nodig dat kijkt naar de waarden, betekenis en context van deze subjectieve en individuele ervaring met CKV.

Er zijn drie kennislacunes in onderzoek naar CKV die overbrugt moeten worden om een persoonsgerichte manier te vinden om de psycho-oncologische zorg te personaliseren:

(1) beperkt kwalitatief onderzoek naar CKV voornamelijk bij borstkankerpatiënten tijdens behandeling voor kanker;[27,28]

(2) gebrek aan multifactoriële conceptualisatie van CKV waarbij verschillende factoren van invloed op elkaar kunnen zijn en ook beschermende factoren meegenomen worden;[29–31]

(3) suboptimale casusconceptualisatie door psycho-oncologische therapeuten voor het gezamenlijk kiezen van de beste behandeling voor CKV. Dit betekent dat therapeuten een werktheorie proberen te formuleren op basis van patiënten- en therapeuten-perspectief over wat de beste behandeling is voor het individu.[32] De complexiteit van het probleem CKV met onderlinge verbanden met onder andere emoties, gedrag, cognities en context, moeite met herinneren van deze verbanden door de patiënt en een gebrek aan gouden standaard maken dit proces van casusconceptualisatie ingewikkeld.

Idiografische benadering

Een multidisciplinair onderzoeksteam en adviesraad hielpen mij om een holistische en brede kijk op CKV te ontwikkelen en kritisch te reflecteren. Dit proefschrift is gebaseerd op idiografische onderzoeksmethodes. Idiografisch onderzoek richt zich op onderzoek naar het individu met CKV, waardoor het een eerste stap kan zetten in de richting van persoonsgerichte benadering van personaliseren van psycho-oncologische zorg voor CKV.

Een kwalitatieve vorm van idiografisch onderzoek is fenomenologie van het lichaam gebaseerd op de ‘embodiment theorie’ van de filosofen Husserl en Merleau-Ponty.[33,34] Fenomenologie richt zich op ‘wat’ en ‘hoe’ patiënten een fenomeen ervaren, waardoor het geschikt is om geleefde ervaringen en behulpzame manieren van omgaan met CKV te onderzoeken.[35,36] In geval van een chronische ziekte als CKV staat het lichaam op een negatieve manier op de voorgrond en worden nieuwe gewoontes gevormd om beter om te kunnen gaan met CKV.[37,38] Inzichten hierin kunnen helpen in persoonsgerichte zorg voor CKV. Verschillende fenomenologische theorieën over belichaming en gewoontevorming zijn gebruikt om de analyse van de kwalitatieve data te ondersteunen.[33,34,37,39]

Een kwantitatieve vorm van idiografisch onderzoek is ‘Ecological Momentary Assessment’ (EMA). Deze methode is een gestructureerde dagboektechniek, waarbij de deelnemers vragen ontvangen (bijv. over symptomen, gevoel en gedrag) meerdere keren per dag voor meerdere dagen achter elkaar in hun dagelijkse leefomgeving.[40] EMA heeft verschillende voordelen: inzicht in longitudinale data uit het dagelijks leven van patiënten (ecologische validiteit), geen herinneringsbias bij ervaringen in het moment, een indicator van motivatie tijdens behandeling en empowerment van patiënten om betrokken te zijn bij hun behandeling.[40,41]

De netwerkbenadering werd tien jaar geleden voor het eerst toegepast bij psychopathologie.[42] Deze theorie ziet symptomen en gedragsfactoren als samenhangende elementen van een complex netwerk in plaats van de focus op één onderliggende oorzaak volgens het latente medische ziektemodel. In geneeskunde is een onderliggende oorzaak vaak aanwijsbaar, terwijl voor mentale aandoeningen dit veel moeilijker is.[43] De netwerktheorie is ook meer in overeenstemming met hoe cognitieve gedragstherapeuten een mentale stoornis zien met onderlinge relaties tussen gedachten, gevoel en gedrag.[32] Daarnaast past het beter bij de multifactoriële conceptualisatie van CKV, maakt het analyse van EMA-data mogelijk en is er geen onderscheid tussen lichaam en geest.

In dit proefschrift worden individueel vermoeidheidsnetwerken getoond die gebaseerd zijn op partiële correlaties tussen knopen die fysieke, mentale en gedragsfactoren voorstellen. Deze netwerkanalyses werden verricht met behulp van softwareprogramma R door dr. Melanie Schellekens en Rosalie van Woezik MSc en besproken binnen het onderzoeksteam. De positieve en negatieve partiële correlaties tussen knopen zijn verbindingen in een netwerk en kunnen verschillen in sterkte en richting.[42] In een gesprek tussen en patiënt en psycho-oncologisch therapeut kunnen de context en betekenis van deze verbindingen in een individueel vermoeidheidsnetwerk onderzocht worden om te kijken hoe de behandeling hierop gericht kan worden.

Onderzoeksvraag en hoofstukindeling van proefschrift

In dit proefschrift, onderdeel van het REFINE-project, wordt de ervaringskennis van patiënten met CKV gecombineerd met netwerkbenadering om casusconceptualisatie in psycho-oncologische zorg voor CKV te verbeteren. De centrale onderzoeksvraag van dit proefschrift is: **op welke manier(en) kunnen we de psycho-oncologische zorg voor patiënten met chronische kanker-gerelateerde vermoeidheid personaliseren?**

In dit proefschrift is het patiënten-perspectief van CKV onderzocht met behulp van interpretatieve review (meta-etnografie) van bestaande kwalitatieve literatuur naar het ervaren van en omgaan met CKV (**hoofdstuk 2**), een fenomenologische interviewstudie naar belichaamde ervaringen met CKV (**hoofdstuk 3**) en nieuwe helpende gewoontes voor het omgaan met CKV (**hoofdstuk 4**), een proof-of-concept (**hoofdstuk 5**) en casestudie (**hoofdstuk 6**) naar gebruik van EMA op de mobiele telefoon en ontvangen van gepersonaliseerde feedback door patiënten met CKV om psycho-oncologische zorg te personaliseren. **Hoofstuk 7** bevat een kritische reflectie om de resultaten in een breder kader te plaatsen. Ook worden er methodologische beperkingen besproken, evenals implicaties voor toekomstig onderzoek en de klinische praktijk.

Ethiek en rol als onderzoeker

Er is toestemming gevraagd bij een ethische commissie voor start van de interview-, proof-of-concept en casestudies en de onderzoeksdata zullen op een veilige manier opgeslagen blijven gedurende de daarvoor geldende termijnen bij het Helen Dowling Instituut (HDI). Deelnemers aan de studie werden geworven bij het HDI via hun behandelend therapeut. Voor de interviewstudie ook via een oproep bij Kanker.nl en regionale zorgprofessionals. Na ontvangen van informed consent en check van de inclusiecriteria, startte de dataverzameling.

Bij het uitvoeren van kwalitatief onderzoek speelt het perspectief van mij als onderzoeker een belangrijke rol in het interpreteren en analyseren van de resultaten. Ik heb een medische achtergrond en ben geschoold als kwalitatief onderzoeker in de psycho-oncologie voor en tijdens mijn promotietraject. Ik heb een empathische houding aangenomen en veldaantekeningen gemaakt tijdens en na de interviews om bewust te zijn van mijn eigen gevoelens, gedachten en aannames als onderzoeker. De interviews vonden plaats thuis in hun eigen leefomgeving op een gewenst tijdstip of als ze daar de voorkeur aan gaven bij het HDI. Partners waren soms aanwezig tijdens (een deel van) de interviews. Van alle interviews zijn opnames gemaakt die zijn verwijderd na transcriberen.

De belangrijkste bevindingen

Hoofdstuk 2: Ervaren van en omgaan met CKV: Een meta-etnografie van kwalitatief onderzoek

Hoofdstuk 2 bestaat uit een meta-etnografie van kwalitatieve studies met patiënten die CKV ervaren. Het doel van deze meta-etnografie is om een overkoepelend overzicht te ontwikkelen dat zicht richt op hoe patiënten CKV ervaren en hiermee omgaan.

Ik heb een uitgebreide systematische zoekstrategie naar literatuur uitgevoerd. Van de in totaal 1178 studies, heb ik zestien studies geïncludeerd na ontdubbelen en screenen van de samenvattingen en de volledige artikelen. Deze studies bevatten in totaal 705 patiënten (meerderheid vrouwen) van verschillende leeftijden en met verschillende vormen van kanker (voornamelijk borstkanker), stadia van kanker en (fase van) behandeling(en). De kwaliteit van de studies die zijn meegenomen werd getoetst aan de hand van de CASP-criteria.[44] Ik heb de zeven fases van de meta-etnografie gevolgd die voor het eerst zijn beschreven door Noblit en Hare om eerste-orde constructen (interpretaties van patiënten) en tweede-orde constructen (interpretaties van auteurs) eruit te halen en te vertalen om derde-orde constructen (nieuwe interpretaties) te vormen.[45]

Deze interpretatieve kwalitatieve review toonde een belichaamde structuur van CKV. Ik heb een figuur van belichaamde CKV (zie **figuur 2** van **hoofdstuk 2**) ontwikkeld dat bestaat uit zes derde-orde constructen met sociale, ruimtelijk en temporele dimensies die onderling met elkaar samenhangen:

1. ***De belichaamde ervaring:*** op een negatieve manier bewust zijn van het lichaam;
2. ***(Geen) Erkenning:*** gebrek aan erkenning van patiënten, naasten en zorgprofessionals (sociale dimensie);
3. ***De smalle horizon:*** een kleinere leefwereld (ruimtelijke dimensie);
4. ***Rolverandering:*** aannemen van andere levensrollen (sociale dimensie);
5. ***Verlies van zelf:*** de impact op identiteit (temporele dimensie);
6. ***Vaste grond terugvinden:*** het proces van omgaan met CKV door worsteling, aanpassen en accepteren (temporele dimensie).

Deze bevindingen kunnen zorgprofessionals helpen om CKV te herkennen en een persoonsgerichte benadering toe te passen. Mijn eerste indruk van de psycho-oncologische praktijk is dat het figuur kan helpen als middel om te communicatie tussen patiënten en zorgprofessionals te vergemakkelijken. Dit kan leiden tot herkennen en normaliseren van de belangrijkste problemen, dat kan patiënten helpen om een gevoel van controle terug te krijgen.

Hoofdstuk 3: Ervaren van ernstige CKV: Een interpretatieve fenomenologische studie

In **hoofdstuk 3** heb ik semigestructureerde interviews afgenomen met volwassenen met ernstige CKV ten minste drie maanden na afronding van de behandeling voor kanker. Deze doelgericht geselecteerde homogene groep bestond uit 25 deelnemers met CKV. Het doel van deze interviewstudie was om de geleefde ervaringen van patiënten met CKV beter te begrijpen. In deze interviewstudie heb ik een theoretische kader gebaseerd op filosofische fenomenologie gebruikt om te onderzoeken hoe patiënten met CKV veranderingen in belichaming, tijd en ruimte ervaren en hoe deze aan elkaar gerelateerd zijn.[33,34,46] Voor kwalitatieve analyse van de interviews, volgde ik de interpretatieve fenomenologische analyse methode (IPA) van Smith.[47]

Na discussie met ons multidisciplinaire onderzoeksteam heb ik vier thema's die onderling met elkaar samenhangen geïdentificeerd, waarbij verschillende dimensies van de belichaamde ervaring van CKV naar voren komen:

1. ***Uitgeput***: hoe CKV een overweldigende dynamische ervaring is met verschillende sensaties (zoals fysieke, emotionele, zintuiglijke en cognitieve) in iemands lichaam (bijv. ledematen of hoofd) en kan resulteren in verlies van identiteit (affectieve dimensie);
2. ***Vermindering van iemands "ik kan"***: hoe tijd en ruimte om 'vrij' te bewegen beperkt is door de belichaamde ervaring van CKV en iemands activiteiten en sociale leven beperkt (functionele dimensie);
3. ***Onzichtbaarheid***: hoe het lichaam met CKV een object wordt in sociale context omdat anderen CKV niet kunnen zien (sociale en materiële dimensie);
4. ***Herstel van iemands "ik kan"***: hoe actieve tijd en beweging in de ruimte aangepast kan worden aan de belichaamde ervaring met CKV, iemands beperkingen in functioneren, het object worden van iemands lichaam in een sociale context (functionele en productieve dimensie).

Deze fenomenologische interviewstudie toonde dat ervaren van CKV een persoonlijk, complex en dynamisch proces is dat bestaat uit affectieve, sociale, materiële, functionele en productieve dimensies die met elkaar samenhangen.

Hoofdstuk 4: Het vormen van nieuwe gewoontes in de omgang met CKV: Een interpretatieve fenomenologische studie

In **hoofdstuk 4**, gebruikte ik dezelfde groep van 25 geïnterviewden met ernstige CKV uit **hoofdstuk 3** en richtte ik me op de vraag wat kan helpen in het omgaan met CKV om aanpassing te vergemakkelijken. Ik volgde voor analyse de IPA-methode van Smith:[47]

Ik identificeerde vijf dynamisch samenhangende en elkaar onderling versterkende thema's voor het vormen van nieuwe gewoontes in de omgang met CKV:

1. ***Ontdekken van fysieke en emotionele grenzen:*** een leerproces van zelfmonitoring gericht op hoe iemands lichaam voelt om grenzen te bewaken en uitputting te voorkomen;
2. ***Communiceren over behoeften aan ondersteuning***: manieren om te zoeken naar informatie en vragen om (professionele) hulp;
3. ***Herorganiseren en plannen van activiteiten en rust***: het vinden van manieren voor balans van activiteiten en rust in iemands leven;

4. **Loslaten van iemands gewoonte-identiteit**: stoppen met oude gewoontes en veranderen van iemands rol in een minder actief persoon;
5. ***Herkennen en accepteren van CKV***: hoe het vormen van nieuwe gewoontes in de omgang met CKV ruimte maakt voor nieuwe overtuigingen, zoals het accepteren van iemands CKV.

Deze fenomenologische interviewstudie geeft inzicht in wat helpt in de omgang met CKV. In het proces van vormen van nieuwe gewoontes is het stoppen met gewoontes die niet helpend zijn en negatieve overtuigingen essentieel.

Hoofdstuk 5: Gebruiken van 'ecological momentary assessment' op de mobiele telefoon en gepersonaliseerde feedback voor patiënten met CKV: Een proof-of-concept studie

Een kwantitatieve vorm van idiografisch onderzoek is 'ecological momentary assessment' (EMA), ook wel 'experience sampling method' genoemd. EMA is een gestructureerde dagboekmethode waarbij de deelnemer vragen ontvangt (bijv. over symptomen, gevoelens, gedrag) meerdere keren per dag meerdere dagen achter elkaar in de dagelijkse leefomgeving.[40] Gebaseerd op de bevindingen van **hoofdstuk 2-4** hierboven beschreven en vanuit het perspectief van de netwerktheorie geïntroduceerd in **hoofdstuk 1**, heb ik samen met mijn collega-onderzoekers, de app *Energie InZicht* ontwikkeld, een EMA-app die zich specifiek richt op het meten van het onderling samenhangende fenomeen CKV bij het individu.

In **hoofdstuk 5**, heb ik een proof-of-concept studie uitgevoerd binnen de huidige psycho-oncologische zorg met vijf deelnemers die op de wachtlijst voor psychologische behandeling voor CKV stonden en hun therapeuten. Deelnemers vulden de EMA-vragen (over vermoeidheid, gevoelens, activiteiten, omgaan met CKV en context) van de *Energie InZicht* app vijf keer per dag gedurende een periode van drie weken in op hun mobiele telefoon. In de daaropvolgende week ontvingen ze gepersonaliseerde descriptieve feedback van de onderzoeker en tijdens de eerste sessie met hun therapeut bespraken ze de netwerkfeedback samen.

De doelen waren om te onderzoeken 1) in hoeverre en hoe kan een patiënt inzicht krijgen in CKV door het invullen van de EMA-app (*Energie InZicht*) op de mobiele telefoon en het ontvangen van gepersonaliseerde (netwerk) feedback, en 2) hoe kan dit inzicht patiënten en therapeuten helpen om het proces van casusconceptualisatie te verbeteren in psycho-oncologische zorg voor CKV. Ik gebruikte hardop-denk-interviews, semigestructureerde interviews en observaties om de gebruikerservaringen van patiënten en hun therapeuten te onderzoeken. Ik voerde een inductieve thematische analyse uit van de transcripten.[48] Gebaseerd op de ervaringen van patiënten en therapeuten uit deze proof-of-concept studie, lijkt het gebruik van EMA-dataverzameling en bespreken van descriptieve en netwerkfeedback haalbaar en bruikbaar om de psycho-oncologische zorg voor CKV te personaliseren en te verbeteren.

Patiënten-ervaringen (N=5)

De kwalitatieve bevindingen toonden dat het gebruik van de EMA-app (*Energie InZicht*) voor sommige patiënten resulteerde in negatieve reacties van anderen en toegenomen bewustzijn van het lichaam, (on)mogelijkheden, en gevoelens. Het gebruik van de EMA-app (*Energie InZicht*) en ontvangen van descriptieve feedback zorgde voor zichtbaarheid en erkenning van het belangrijkste probleem bij iedereen. Het bespreken van het descriptieve en netwerkrapport was een emotionele confrontatie op een positieve manier voor de meeste patiënten. Het descriptieve en netwerkrapport hielp alle patiënten om de onderling met CKV samenhangende problemen te identificeren en te herkennen. Het gebruik van de EMA-app (*Energie InZicht*), gevolgd door de descriptieve feedback maakte het voor sommige patiënten mogelijk om hun gedrag te veranderen in de omgang met CKV op een behulpzame manier. Het bespreken van het netwerkfeedback-rapport hielp alle patiënten om hun behandeldoel te stellen of de behandelrichting aan te passen.

Therapeuten-ervaringen (N=4)

De kwalitatieve bevindingen van sommige therapeuten toonden een beperkt gebruik van het descriptieve rapport. De meeste therapeuten evalueerden de netwerkfeedback als inzichtrijk, bruikbaar, en een versneller in de behandeling om het kernprobleem te identificeren. Hoewel het bespreken van de netwerkverbindingen en vertalen naar praktische handvatten in de psycho-oncologische praktijk voor alle therapeuten uitdagend was.

Hoofdstuk 6: Personaliseren van psycho-oncologische zorg voor CKV: Een casestudie over samenhangende symptomen

In **hoofdstuk 6,** presenteer ik een casestudie om te illustreren hoe feedback over persoonsgerichte netwerken inzicht in CKV kan geven en hoe deze inzichten kunnen helpen bij het personaliseren van de psychologische behandeling van CKV. Deze casus was onderdeel van de proof-of-concept studie (**Hoofdstuk 5**).

Een 34-jarige vrouw met CKV als belangrijkste probleem werd verwezen naar een ggz-instelling voor psycho-oncologische zorg. Tijdens de tijd op de wachtlijst, vulde zij de EMA-vragenlijst (*Energie InZicht*) in met 24 vragen over vermoeidheid, gevoelens, activiteit, omgaan met vermoeidheid, en context vijf keer per dag. Ze was bereid om de vragenlijst gedurende 101 dagen in te vullen. Dit maakte het mogelijk om zowel moment-level als dag-level partieel (gerichte) correlatie netwerken te onderzoeken en meer inzicht te krijgen in hoe de samenhang tussen symptomen over de tijd kan veranderen.

Het samenspel tussen symptomen, gedachten en gedrag werd zichtbaar gemaakt in individuele moment-level en dag-level netwerken, die werden besproken met de patiënt. Bijvoorbeeld, 'accepteren van vermoeidheid' was een belangrijke knoop in de moment-level en dag-level netwerken op hetzelfde moment. In het moment-level netwerk hing 'accepteren van vermoeidheid' in de afgelopen drie uur samen met minder 'hopeloosheid' in de afgelopen drie uur en minder 'vermoeidheid' in het volgende moment.

In het dag-level netwerk op hetzelfde moment, was 'acceptatie' verbonden met minder 'vermoeidheid', minder 'hopeloosheid', meer 'positieve gevoelens', en meer 'motivatie om dingen te doen' op dezelfde dag. De patiënt herkende dit patroon. Zij legde uit dat de onvoorspelbaarheid van CKV haar een hopeloos gevoel gaf.

De bevindingen maakte het belang van acceptatie in het omgaan met vermoeidheid bespreekbaar met de patiënt. Ze besprak deze bevindingen met haar therapeut. De casestudie toonde hoe symptoomnetwerken inzicht kunnen geven in hoe beter met vermoeidheid om te gaan en zouden kunnen helpen in het vinden van een behandelrichting.

ALGMENE DISCUSSIE

Kritische reflectie van belangrijkste bevindingen

Een fenomenologisch en netwerkperspectief over CKV aannemen

In dit proefschrift, heb ik kwalitatieve fenomenologische en kwantitatieve idiografische netwerk onderzoeksmethodes gebruikt die elkaar aanvulden om ervaringen en omgaan met CKV op een individueel niveau te kunnen onderzoeken. Ik beschrijf welke vier stappen ik heb gebruikt, wat ik ervan heb geleerd en hoe dit heeft bijgedragen aan de kennislacunes uit de introductie: beperkt kwalitatief onderzoek naar CKV, gebrek aan multifactoriële conceptualisatie van CKV en suboptimale casusconceptualisatie door psycho-oncologische therapeuten.

(1) Als eerste stap ontwikkelde ik een brede kijk op CKV door een interpretatieve meta-etnografie van bestaande kwalitatieve studies.[45] Vanuit het patiënten-perspectief toonde deze kwalitatieve data dat het lichaam een centrale rol speelt in het ervaren en omgaan met

CKV. In de medische praktijk wordt het lichaam gezien als machine met een scheiding van lichaam en geest. In dit biomechanische model bestaat het lichaam uit onderdelen om de ziekte te diagnosticeren en te behandelen.[49] Omdat er geen gouden standaard bestaat om CKV te diagnosticeren en er verschillende behandelingen mogelijk zijn, verstoort dit de communicatie en is dit model niet goed toepasbaar. Daarom heb ik een fenomenologisch perspectief gebruikt om een persoon met een ernstig vermoeid lichaam te benaderen. Met deze holistische benadering wordt een patiënt met CKV als geheel gezien.[49] Deze holistische benadering komt overeen met hoe patiënten CKV ervaren en hiermee omgaan.

(2) Als tweede stap gebruikte ik een filosofisch fenomenologisch theoretisch kader om interviewdata van patiënten met ernstige CKV te analyseren.[33,34,46] De belichaamde ervaringen en behulpzame en niet-behulpzame gewoontes in omgaan met CKV binnen een sociale context werden onderzocht. Gebaseerd op deze resultaten, stel ik CKV voor als een persoonlijk, multidimensionaal, onderling samenhangend, complex en dynamisch probleem.

Hoewel vragenlijsten naar CKV nuttig zijn en vaak gebruikt worden om resultaten te generaliseren voor grote groepen patiënten, geven ze onvoldoende inzicht in de verschillende manieren waarop het ernstig vermoeide lichaam wordt ervaren over de tijd.[38] De netwerktheorie is een betere manier om CKV te conceptualiseren en ook vanuit patiënten-perspectief te zien hoe verschillende dimensies kunnen samenhangen in een zogenaamde vicieuze cirkel.[42,50]

(3) In de derde stap heb ik alle opgedane kennis van het fenomenologisch en netwerkperspectief, eerder (netwerk) onderzoek naar CKV, en klinische en patiënten-expertise geïntegreerd om momentane en retrospectieve items te formuleren voor de ontwikkeling van de EMA-app *Energie InZicht*. Dimensies over belichaamde ervaringen (bijv. fysieke vermoeidheid) en gewoontes (bijv. rust nemen) die zeer waarschijnlijk veranderen door de dag heen werden geïncludeerd.[51,52] Ook behulpzame factoren zoals accepteren van CKV werden meegenomen op basis van eigen en ander onderzoek.[52,53]

(4) In de laatste stap gebruikte ik het netwerkperspectief om de complexe samenhang tussen verschillende symptomen, gedachtes, emoties en manieren van omgaan met CKV te visualiseren. In de proof-of-concept studie, gebruikten therapeuten de gepersonaliseerde vermoeidheidsnetwerken om betekenis te geven aan samenhang tussen dynamische belichaamde ervaringen en gewoontes in omgang met CKV van het individu. De netwerktheorie en netwerkanalyse maakte het mogelijk om per individu naar belangrijke factoren te kijken die samenhangen in aanvulling op de ernst van CKV op basis van de CIS-FS vragenlijst en het descriptieve rapport.[32] Het inzichtelijk maken van het onzichtbare probleem CKV kan helpen in de communicatie tussen patiënt en therapeut. Deze idiografische aanpak bij de

start van op de leefwereld gerichte psycho-oncologische zorg voor CKV is kenmerkend voor verschuiving naar een holistische en individuele benadering die gebruik maakt van mobiele technologie en breder kijkt naar samenhang van transdiagnostische symptomen zonder koppeling aan een specifieke diagnose.[54,55]

Naar een nieuwe manier van meten van CKV

In de proof-of-concept studie (**hoofdstuk 5**) kregen patiënten met CKV op de wachtlijst voor psycho-oncologische zorg gedurende drie weken vijf keer per dag een melding om de EMA-vragenlijst (*Energie InZicht*) binnen een half uur in te vullen. Het gebruik van EMA tijdens de wachtlijst bleek haalbaar omdat niemand uitviel en veel vragenlijsten werden beantwoord. De gebruikerservaringen van patiënten en therapeuten met EMA en gepersonaliseerde feedback waren overwegend positief. Een patiënt heeft de vragenlijst 101 dagen ingevuld om dag-level persoonlijke vermoeidheidsnetwerken te onderzoeken. De bevindingen zijn in overeenstemming met een review van Kampshoff dat EMA binnen de oncologie bruikbaar en haalbaar is maar nog onvoldoende ingezet wordt ondanks de goede mogelijkheden.[56] Ook twee recente EMA-studies van Nap-Van der Vlist en Harnas gebruikten gepersonaliseerde feedback voor patiënten met CKV.[57,58] Daarom zal vanwege deze positieve bevindingen toekomstig psycho-oncologisch onderzoek zich gaan richten op onderzoek naar optimaal gebruik van EMA en gepersonaliseerde feedback om de behandeling te personaliseren.

Ondanks de positieve resultaten van gebruik van EMA bij CKV, zijn er ook methodologische beperkingen van de proof-of-concept en casestudie (**hoofdstuk 5 en 6**), waarvan ik hier twee psychometrische aspecten zal bespreken: validiteit en meting reactiviteit. De andere studiebeperkingen worden verderop besproken.

(1) EMA-validiteit: Wij startten met het zorgvuldig selecteren van de knopen voor het netwerk van CKV met multidisciplinaire expertmeetings en een pilot-test met een ervaringsdeskundige (knoop- en indruksvaliditeit).[59] We zouden ook rekening moeten houden met twee andere vormen van validiteit: inhouds- en constructvaliditeit.[60] Inhoudsvaliditeit gaat over de mate waarin het hele construct (CKV) met al zijn onderdelen wordt gemeten en kwalitatief wordt onderzocht.[60] Constructvaliditeit gaat over de mate waarin het complexe construct (CKV) gemeten wordt.[60] Richtlijnen om bij de ontwikkeling van een EMA-protocol rekening te houden met deze psychometrische aspecten moeten ontwikkeld worden.[61] Wij hebben tijdens de proof-of-concept studie de inhoudsvaliditeit van de EMA-items geëvalueerd en verwachten dat dit de basis vormt voor goede constructvaliditeit.[60]

(2) Meting reactiviteit: Er zijn verschillende vormen van meting reactiviteit: verandering in het onderliggende construct (CKV) bijv. (bijv. van vermoeidheid), verandering in gedrag (bijv. geen fysieke activiteit tijdens studieperiode) en verandering in EMA-invulgedrag (bijv. andere antwoorden invullen gedurende de tijd).[62] Meting reactiviteit is belangrijk om rekening mee te houden omdat dit bias kan geven van de bevindingen en de ecologische validiteit kan verminderen.[62] In de proof-of-concept studie werd de mate van vermoeidheid gemeten met de CIS-FS vragenlijst en geen toename gerapporteerd. Dit komt overeen met andere studies.[63,64] Sommige patiënten rapporteerden een verandering van gedrag tijdens het invullen van de app die mogelijk invloed kan hebben op de gepersonaliseerde feedback. Ook kunnen er veranderingen in het invulgedrag zijn opgetreden door gewenning minder extremen invullen of door verveling op de automatische piloot gaan invullen en meer dezelfde antwoorden geven.[63]

Ervaringen met EMA op mobiele telefoon en gepersonaliseerde feedback over CKV geïntegreerd in psycho-oncologische zorg

Het is steeds belangrijker om als patiënt betrokken te zijn bij het therapeutisch proces. Empowerment betekent als patiënt zelf de mogelijkheid hebben om te voldoen aan behoeften, problemen op te lossen en om hulp te vragen zodat er een gevoel van controle is over het eigen leven.[65] Een goed voorbeeld van actieve betrokkenheid van patiënten is de EMA-dataverzameling en het bespreken van gepersonaliseerde feedback in de proof-of-concept en casestudie, dat motiveert en draagt bij aan het co-creëren van het behandelproces.[55]

Zelfmonitoring met EMA gaf inzicht in de belangrijkste problemen en was een interventie op zichzelf om beter met CKV om te kunnen gaan. Het starten van een gedragsverandering is een indicator van motivatie voor psycho-oncologische zorg en kwam ook terug in de goede respons op de vragenlijsten van alle deelnemers.[41] Daarnaast kan de gepersonaliseerde feedback het empowerment van patiënten verbeteren omdat het de communicatie vergemakkelijkt tussen patiënten en zorgprofessionals en verder de motivatie voor behandeling en gedeelde besluitvorming versterkt. Door het gebruik tijdens de wachtlijst kan het in de praktijk direct ingezet worden voor het bepalen van de behandelrichting en behandeldoelen te stellen tijdens casusconceptualisatie om de psycho-oncologische zorg te personaliseren.[32]

Op deze manier is personaliseren gebaseerd op individuele ervaringen en geleefde context in plaats van gemiddelde resultaten van een groep.[55] Het gedeelde besluitvormingsproces is verrijkt met individuele EMA-data die patiënten empoweren en motiveren om als gelijke partner deel te nemen aan het proces.[55] De therapeut is de coach met therapeutische kennis en de patiënt is de expert van geleefde ervaringen. De gepersonaliseerde feedback geef inzicht in de samenhang van factoren met vermoeidheid en het verloop van vermoeidheid over de tijd.[32] Deze manier van terugkoppeling kan mogelijk de psycho-oncologische zorg versnellen en verbeteren.[66]

Er werd geen advies gegeven in de feedbackrapporten van de proof-of-concept en casestudie. Therapeuten werden geïnstrueerd om verdiepende vragen te stellen over de verbindingen in het netwerk en zelf de bevindingen te vertalen naar behandeldoelen en praktische handvatten. Dit helpt ook om over-interpretatie te voorkomen, wat een risico is van het gebruik van netwerken. Het betekenis geven aan netwerkverbindingen samen met de therapeut kan ook emoties oproepen, waardoor voorzichtigheid is geboden.

De vier therapeuten uit de proof-of-concept studie evalueerden het gebruik van gepersonaliseerde feedback als inzichtgevend, bruikbaar, versneller in behandeling en verfijning van de belangrijkste problemen vergelijkbaar met ervaringen van therapeuten in de studie van Piot.[67] Ook vonden de therapeuten het een uitdaging om de abstracte netwerken te vertalen naar wat een patiënt kan helpen, wat overeenkomt met de studie van Frumkin.[68]

Sterke punten en beperkingen van idiografisch onderzoek

In dit proefschrift gebruikte ik idiografische onderzoeksmethodes die elkaar aanvullen met hun eigen sterke punten en beperkingen om een nieuwe manier te vinden om psycho-oncologische zorg voor patiënten met CKV te personaliseren.

Het sterkste punt was om het patiënten-perspectief mee te nemen in de iteratieve ontwikkeling van de EMA-vragenlijst (*Energie InZicht*) die na toepassen van het netwerkperspectief nieuwe therapeutische inzichten presenteerde over hoe patiënten CKV ervaren en hiermee omgaan.

Kwaliteit van kwalitatief onderzoek

De meeste studies van dit proefschrift zijn (deels) gebaseerd op kwalitatief onderzoek. Ik gebruikte de EMERGE-richtlijnen om de zeven fases van Noblit en Hare van de meta-etnografie in **hoofdstuk 1** te beschrijven.[45,69] Ik gebruikte de CASP-criteria om de kwaliteit van de zestien studies te beoordelen.[44] Voor de interpretatieve fenomenologische studies van **hoofdstuk 3 en 4** werden de principes van Yardley gebruikt voor het uitvoeren van goed kwalitatief onderzoek.[47,70] Om de interne validiteit van de proof-of-concept en casestudie te vergroten gebruikte ik data-triangulatie om data van verschillende bronnen te verzamelen en zowel het patiënten als therapeuten perspectief mee te nemen.

Beperkingen van kwalitatief onderzoek

De uitkomsten meta-etnografie (**hoofdstuk 2**) en interpretatieve fenomenologische interviewstudies (**hoofdstuk 3 en 4**) zijn gebaseerd op open en adequaat de geleefde ervaringen met CKV te bespreken met de verschillende interviewers en mijn vaardigheden als kwalitatief onderzoeker om te reflecteren, analyseren en de bevindingen te interpreteren met ons multidisciplinair onderzoeksteam.

Vanwege het studiedesign van de proof-of-concept studie met vijf patiënten die begeleid werden door vier verschillende therapeuten was het niet mogelijk om data te verzamelen tot verzadiging voor de thematische analyse. Dit kan zorgen voor een minder compleet overzicht van de gebruikerservaringen. Ook moet voorzichtig omgegaan worden met de voornamelijk positieve ervaringen van de gemotiveerde patiënten, omdat ook patiënten hebben geweigerd deel te nemen vanwege de verwachte last aan vragenlijsten. Tijdens implementatie in psycho-oncologische zorg moet rekening gehouden worden met dat het minder gunstig kan uitpakken voor deelnemers.

De idiografische onderzoeksmethodes gebruikt om casusconceptualisatie te verbeteren gaven nieuwe individuele inzichten in CKV, maar kunnen geen uitspraken doen voor de totale patiëntenpopulatie met CKV.[47,71] Daarvoor zijn kwantitatieve studies nodig met grotere groepen patiënten om te onderzoeken of deze nieuwe manier van casusconceptualisatie met EMA-dataverzameling en gepersonaliseerde feedback kan leiden tot meer efficiënte zorg (bijv. kortere behandeltijd).

Beperkingen van EMA-dataverzameling

De EMA-vragenlijst (*Energie InZicht*) bevatte 24-25 items over vermoeidheid-gerelateerde symptomen, positieve en negatieve gevoelens, activiteit, omgaan met vermoeidheid en context. Andere EMA-pilot studies raden 20-30 items aan voor casusconceptualisatie om patiënten niet te belasten met te veel vragen.[32] Een minimumaantal vragenlijsten is nodig om voldoende power te hebben voor analyse van een betrouwbaar persoonlijk netwerk met een nog beperkter aantal knopen op basis van meest recente simulatiestudies.[72]

Het design van de proof-of-concept studie bestond uit drie weken met vijf keer per dag op semi-random tijdsmomenten een vragenlijst. In situaties met andere mensen of op werk, was het niet altijd mogelijk om de vragenlijst in te vullen, dat maakt het risico dat sommige momenten niet worden meegenomen groter.[73] Toch is het voordeel van deze relatieve onvoorspelbaarheid van de timing van de vragenlijsten (vergeleken met een vast schema) dat ze onvermijdbaar zijn, gedurende de dagelijkse routines opkomen en vermindert dit bias van selecteren van relevante momenten van subjectieve ervaringen.[74] De tijd om te reageren was 30 minuten, gelijk aan andere studies, om het risico op zelfselectie en herinneringsbias te verminderen.[74] Het kostte 5-10 minuten om te reageren vanaf ontvangst van het signaal. Dit was soms te kort om de vragenlijst te beantwoorden.

Een belangrijk kenmerk van het gebruik van EMA is om dynamische en momentane veranderingen in het dagelijks leven te monitoren.[74] Wij hebben verschillende tijdsframes gebruikt van de geselecteerde EMA-items (*Energie InZicht*): symptomen, gevoelens en contextuele items werden momentaan (hier en nu) en items over activiteit en coping retrospectief (gedurende de laatste drie uur) geformuleerd. Het verschil in tijdsframe kan de antwoorden beïnvloeden.[73] Het voordeel van momentane items is dat er minder risico is op herinneringsbias. Hoewel we verwachten dat de retrospectieve items minder vaak voorkomen, langer duren en moeilijker te meten zijn in het moment kunnen ze gemist worden wanneer momentaan gemeten.[74] Een nadeel van retrospectieve items is herinneringsbias, vooral bij kankerpatiënten met mogelijk geheugenproblemen.[74]

De volgorde van de items was altijd hetzelfde: eerst momentane vragen, gevolgd door retrospectieve vragen en eindigen met contextuele vragen. Deze volgorde met het meest veranderende construct eerst en context aan het einde kan voorkomen dat de momentane items worden beïnvloed door de vorige items.[74] Patiënten riepen op om de vragen in een random manier te presenteren. Dit voorkomt vragen op de automatische piloot invullen en effecten van volgorde die bias kunnen introduceren dat een negatief effect heeft op de antwoorden op de andere vragen.[74] Voor randomisatie van de volgorde is het aanbevolen om dezelfde groep met vragen met hetzelfde tijdsframe en antwoordopties bij elkaar te houden.[74] Hoewel het risico op herinneringsbias kleiner is met EMA is deze subjectieve zelf-reportmethode gevoelig voor andere vormen van bias: sociale wenselijkheid, cognitieve vormen van bias en culturele normen, bijvoorbeeld sociale wenselijkheid van antwoorden op gedragsitems op een manier die positief gezien wordt door anderen.[73] Daarom is een combinatie met objectieve maten van activiteit of fysiologische maten soms beter.[74]

Aanbevelingen voor patiënten, zorgprofessionals en psycho-oncologische zorg

Psycho-educatie en zelfmanagement van CKV

Patiënten zouden goed geïnformeerd moeten worden voor, tijdens en na de behandeling van kanker over de mogelijke belichaamde ervaringen en manieren van omgaan met CKV. Het belichaamde figuur van CKV, onderdeel van de meta-etnografie kan hierbij helpen om te herkennen en te begrijpen wat de verschillende aspecten zijn. Ook kan dit helpen om te communiceren met zorgprofessionals en naasten over de ervaring met CKV en wat nodig is om een gevoel van controle terug te krijgen. Bijvoorbeeld fysieke en emotionele grenzen bewaken, herorganiseren en plannen van activiteiten en rust zijn behulpzame manieren van omgaan met CKV.

Educatie aan zorgprofessionals over CKV

Zorgprofessionals kunnen voordeel hebben bij het gebruik van het belichaamde figuur van CKV uit de meta-etnografie en inzicht krijgen in verschillende bewoordingen die patiënten gebruiken voor hun ervaringen, zodat ze het signaleren, behandelen en de communicatie met patiënten kan verbeteren. Zorgprofessionals kunnen de subjectieve geleefde ervaringen met CKV en de lichamelijke signalen gebruiken om de diagnose CKV te stellen en te verwijzen naar psycho-oncologische zorg indien nodig.[75] Ook zouden ze hun kennis kunnen verbeteren van wat helpt en niet helpt in het omgaan met CKV. Zorgprofessionals kunnen bijvoorbeeld patiënten adviseren hoe ze hun fysieke en emotionele grenzen kunnen bewaken, activiteiten en rust kunnen herorganiseren en plannen, zorgbehoeftes kunnen aangeven en acceptatie van CKV kunnen bevorderen.

Gepersonaliseerde psycho-oncologische zorg voor CKV

Het gebruik van EMA-dataverzameling en gepersonaliseerde feedback kan helpen om het individuele proces van ervaren en omgaan met CKV beter te begrijpen. Deze inzichten kunnen helpen om de casusconceptualisatie te verbeteren. In de psycho-oncologische praktijk kan dit helpen bij een beter geïnformeerde gedeelde besluitvorming over de soort en focus van de behandeling. Het is belangrijk voor therapeuten om eerst de patiënt te leren kennen, waardoor een tweede behandelafspraak meer geschikt is om de gepersonaliseerde feedback rapporten te bespreken. Een volgende stap is om patiënten te vragen om zelf een item gerelateerd aan CKV toe te voegen aan de EMA-app *Energie InZicht*.

Omdat het betekenis geven en interpreteren van netwerkverbindingen met patiënten als uitdagend wordt ervaren door therapeuten, is een training sterk aanbevolen.[32] Deze training kan informatie geven over de netwerktheorie en hoe positieve en negatieve verbindingen in een netwerk geïnterpreteerd kunnen worden.[32] Belangrijke punten zijn: 'correlatie is geen causaliteit' en 'netwerken zijn een deel van de werkelijkheid'.[32] De EMA-dataverzameling en ontwikkeling van rapporten moet verder geautomatiseerd worden voor implementatie in de psycho-oncologische praktijk.

Transdiagnostische implicaties

De belichaamde, onderling samenhangende, dynamische ervaringen en behulpzame en onbehulpzame manieren van omgaan met CKV kunnen herkend worden door patiënten met andere chronische ziektes die chronische vermoeidheid ervaren. Hoewel kanker een levensbedreigende ziekte is, zijn de meeste chronische ziekten dat niet. Eerder kwalitatief onderzoek naar verschillende chronische ziektes met vermoeidheid vond vergelijkbare thema's: vermoeidheid als een onbekende belichaamde ervaring, onvoorspelbaarheid, oncontroleerbaarheid, onzichtbaarheid en moeite om chronische vermoeidheid te omschrijven.[76]

Aanbevelingen voor toekomstig onderzoek

Effectiviteit van EMA gepersonaliseerde feedback in psycho-oncologische zorg voor CKV

De proof-of-concept en casestudie toonden veelbelovende resultaten met betrekking tot haalbaarheid en bruikbaarheid van EMA-dataverzameling op mobiele telefoon en ontvangen van gepersonaliseerde feedback. Toch blijven een aantal onderzoeksvragen onbeantwoord. Ten eerste: zou het gebruik van EMA als interventie tijdens de behandeling van kanker CKV kunnen voorkomen of verminderen? Een andere belangrijke klinische vraag is of de klinische meerwaarde van gebruik EMA en gepersonaliseerde feedback voor patiënten en therapeuten voor aanvullende en nieuwe inzichten opweegt tegen de kosten van tijdsinvestering en moeite van beiden? Een gerandomiseerd onderzoek is aanbevolen waarbij psycho-oncologische zorg als gebruikelijk, wordt vergeleken met EMA met en zonder gepersonaliseerde feedback om te onderzoeken of CKV en behandeltijd afnemen. Om een grotere studie te doen, zou de EMA-vragenlijst (*Energie InZicht*) gereduceerd en gereviseerd kunnen worden met minder items en mogelijke toevoeging van een persoonlijk belangrijk item. Ook zouden de items uitsluitend momentaan geformuleerd kunnen worden om herinneringsbias te verminderen en alle items te kunnen includeren in dezelfde netwerkanalyse.[32] Een actieve rol voor patiënten in het personaliseren van psycho-oncologische zorg is belangrijk. Een andere belangrijke methodologische vraag is: wat is het optimale tijdsinterval voor het meten van CKV? Toekomstige grootschalige EMA-studies zouden kunnen onderzoeken wat het optimale tijdsinterval is om veranderingen in CKV te meten.[77]

Toevoegen van objectieve activiteit- en slaapmetingen aan EMA

In dit proefschrift zijn geen objectieve maten voor activiteit en slaap meegenomen, maar hebben we dit retrospectief uitgevraagd. Het is bekend dat slaap en activiteit van invloed zijn op het ervaren van CKV,[22] maar het blijft moeilijk om dit mee te nemen in netwerkanalyses vanwege verschillende tijdsframes. Het kan allebei teruggekoppeld worden in de descriptieve feedback. Omdat beweeginterventies belangrijk zijn voor patiënten met CKV,[22] kan verder onderzocht worden welke objectieve maten belangrijk zijn en hoe deze zich verhouden tot netwerkanalyse.

Perspectief van naasten over CKV

Hoewel sommige partners aanwezig waren tijdens de interviews, is het perspectief van naasten niet meegenomen in de analyse. Wel kwam het belang van naasten naar voren uit de fenomenologische interviewstudie over miskenning van CKV, onzichtbaarheid van CKV in sociale context en communiceren van ondersteuningsbehoeften. Toekomstig onderzoek bij CKV zou zich kunnen richten op het perspectief van naasten en de actieve rol in psycho-oncologische interventies voor CKV.

CONCLUSIE

Dit proefschrift, dat onderdeel is van het REFINE-project, geeft nieuwe inzichten in verschillende dimensies van geleefde belichaamde ervaringen en helpende en niet-helpende manieren van omgaan met CKV die onderling met elkaar samenhangen. Het lichaam staat centraal in hoe patiënten CKV ervaren en ermee omgaan. De netwerkbenadering die gebruikt wordt om de psycho-oncologische zorg voor CKV te personaliseren is gebaseerd op verschillen binnen individuen, en maakt het dus mogelijk om te onderzoeken hoe een individu CKV ervaart in verloop van tijd. Na evaluatie met patiënten en therapeuten, lijkt het gebruik van de EMA-dataverzameling (*Energie InZicht)* tijdens de wachtlijst gevolgd door gepersonaliseerde netwerkfeedback bruikbaar en haalbaar om het personaliseren van psycho-oncologische zorg te verbeteren. Dit zou de gedeelde besluitvorming over de behandelrichting en het hoofddoel van de behandeling tijdens casusconceptualisatie bij start van de psycho-oncologische zorg kunnen vergemakkelijken.

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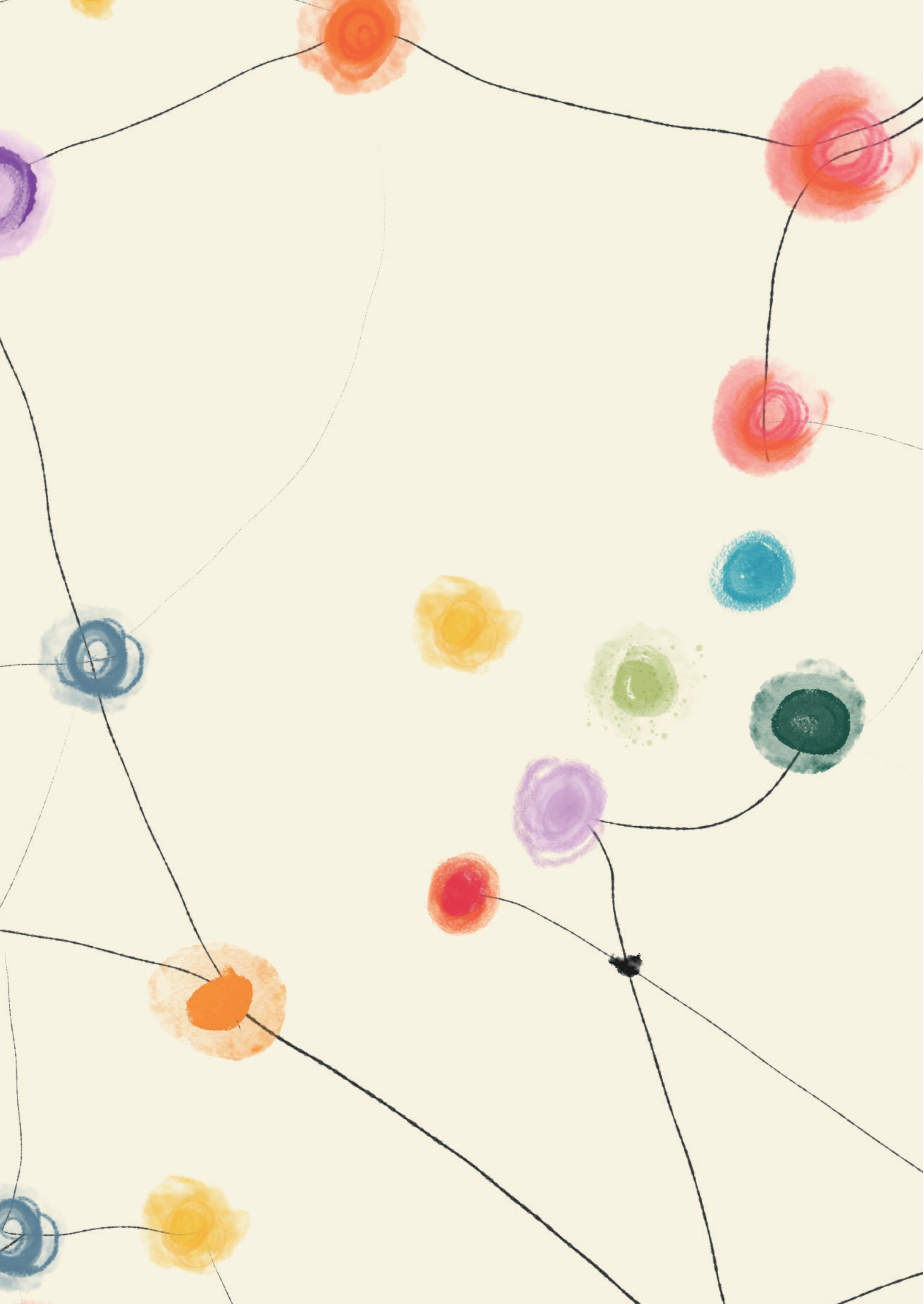


Chapter 9

CURRICULUM VITAE

CURRICULUM VITAE

Tom Iepe Bootsma is op 13 mei 1983 geboren te Leeuwarden. Hij groeide op in Friesland en verhuisde op zijn zestiende naar Den Helder, waar hij zijn gymnasiumdiploma bij scholengemeenschap Nieuwediep behaalde in 2001. Hierna werd hij ingeloot voor de studie Geneeskunde bij de Universiteit Leiden en in het jaar daarop behaalde hij zijn propedeuse. Hij voltooide tijdens zijn opleiding twee wetenschapsstages, waarbij zijn interesse in wetenschappelijk onderzoek werd gewekt. In 2008 behaalde hij zijn doctoraalexamen Geneeskunde.

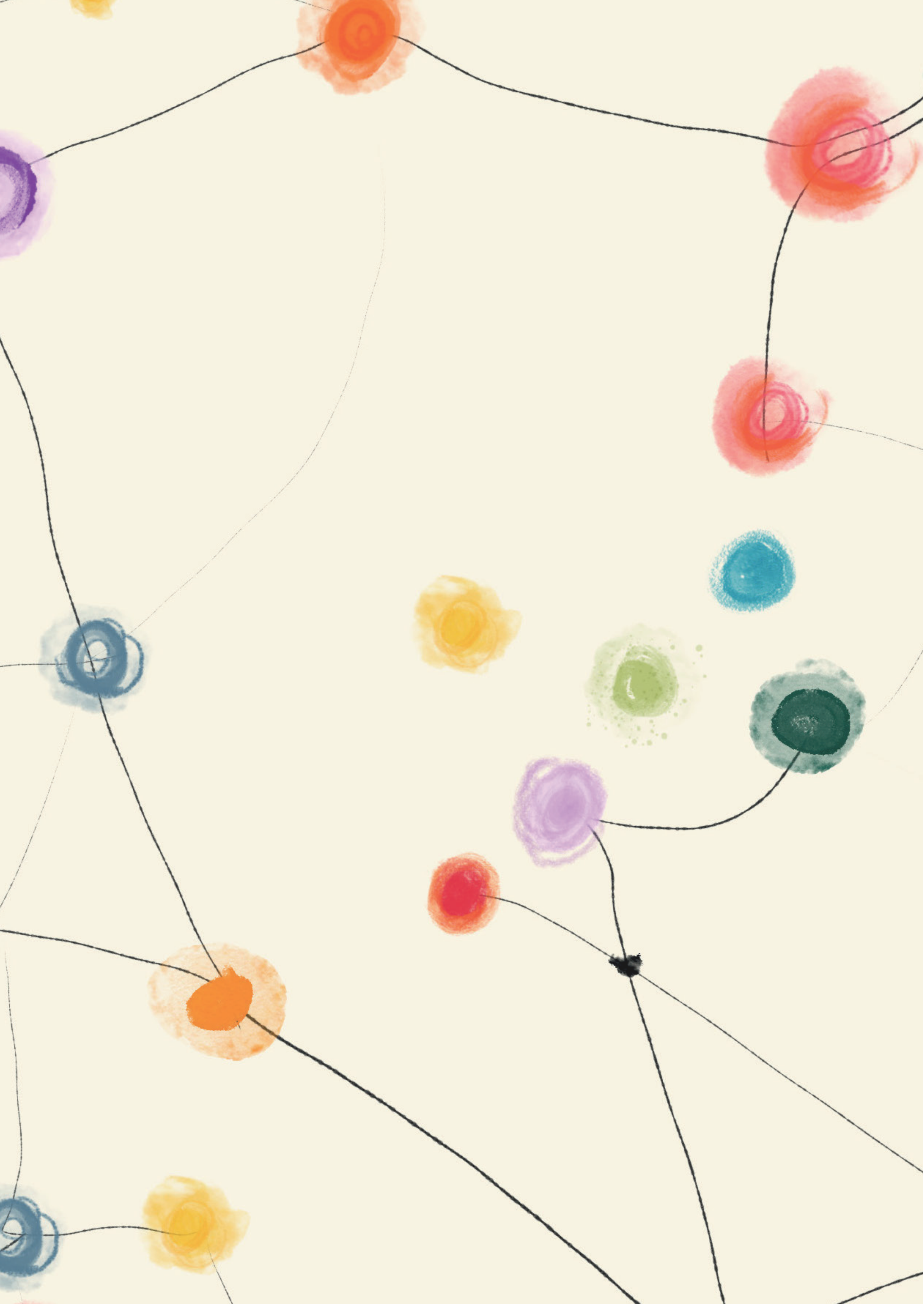
Zijn carrière in het onderzoek naar kanker startte in 2008 bij Stichting Kinderoncologie Nederland (SKION) in Den Haag waar hij werkte als datamanager. Van 2010 tot 2012 heeft hij als (centraal) datamanager gewerkt voor Integraal Kanker Centrum Nederland (IKNL). In 2013 werkte hij als studiecoördinator van verschillende klinische trials op de afdeling hematologie in het UMC Utrecht.

Van 2013 tot 2015 kreeg hij een functie als onderzoeksmedewerker voor projecten naar late effecten van (Non)-Hodgkin lymfoom en zaadbalkanker bij prof. dr. Floor van Leeuwen op de afdeling Psychosociaal Onderzoek en Epidemiologie van het Antoni van Leeuwenhoek. In 2016 volgde een functie als junior onderzoeker bij prof. dr. Eveline Bleiker op dezelfde afdeling en dr. Arjen Witkamp van het UMC Utrecht. In oktober 2017 werd een informatieve website gelanceerd voor mannen met borstkanker, hun naasten en zorgprofessionals (www.mannenmetborstkanker.nl).

Naast zijn werk in het onderzoek heeft hij in 2015 de post-HBO opleiding tot vitaliteitscoach bij Atma Instituut in Amersfoort voltooid. Ook was hij gedurende tien jaar als vrijwilliger actief in de functie van coördinator voor patiëntenorganisatie Transvisie en COC Leiden voor transgenders en hun naasten. Hij coördineerde en organiseerde activiteiten, voorlichtingen, ziekenhuisbezoeken en individuele gesprekken. Hij nam deel aan focusgroepen voor ontwikkeling van medische en psychosociale zorgstandaarden voor genderzorg en keuzehulpen voor genitale operaties en fertiliteit. Hij werkte aan verschillende onderzoeksvoorstellen en presenteerde hierover op internationale congressen.

In 2017 startte hij zijn promotieonderzoek bij het Helen Dowling Instituut en School of Humanities and Digital Sciences van Tilburg University waarvan dit proefschrift het resultaat is. Hij presenteerde zijn werk op verschillende nationale en internationale congressen. In 2019 won hij de poster-award bij het NVPO-congres met een poster-pitch over de meta-etnografie uit **hoofdstuk 2** van dit proefschrift.

Sinds februari 2021 is hij terug bij het Antoni van Leeuwenhoek en werkt hij als postdoctoraal onderzoeker in de onderzoeksgroep van prof. dr. Winette van der Graaf en dr. Olga Husson. Hij is studiecoördinator van een internationale EORTC-studie om de kwaliteit van leven te meten bij sarcoompatiënten. Daarnaast is hij ook betrokken bij verschillende studies met sarcoompatiënten die op verschillende manieren behandeld zijn, jongvolwassenen met kanker en mannen met borstkanker. Hij is bezig om zijn eigen onderzoekslijn op te zetten.



Chapter 10

LIST OF PUBLICATIONS

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Bootsma TI, Schellekens MPJ, van Woezik RAM, Slatman J, van der Lee ML. Using smartphone-based ecological momentary assessment and personalized feedback for patients with chronic cancer-related fatigue: A proof-of-concept study. Internet Interv. 2022 Aug 24; 30: 100568. doi: 10.1016/j.invent.2022.100568. PMID: 36072334; PMCID: PMC9441302.

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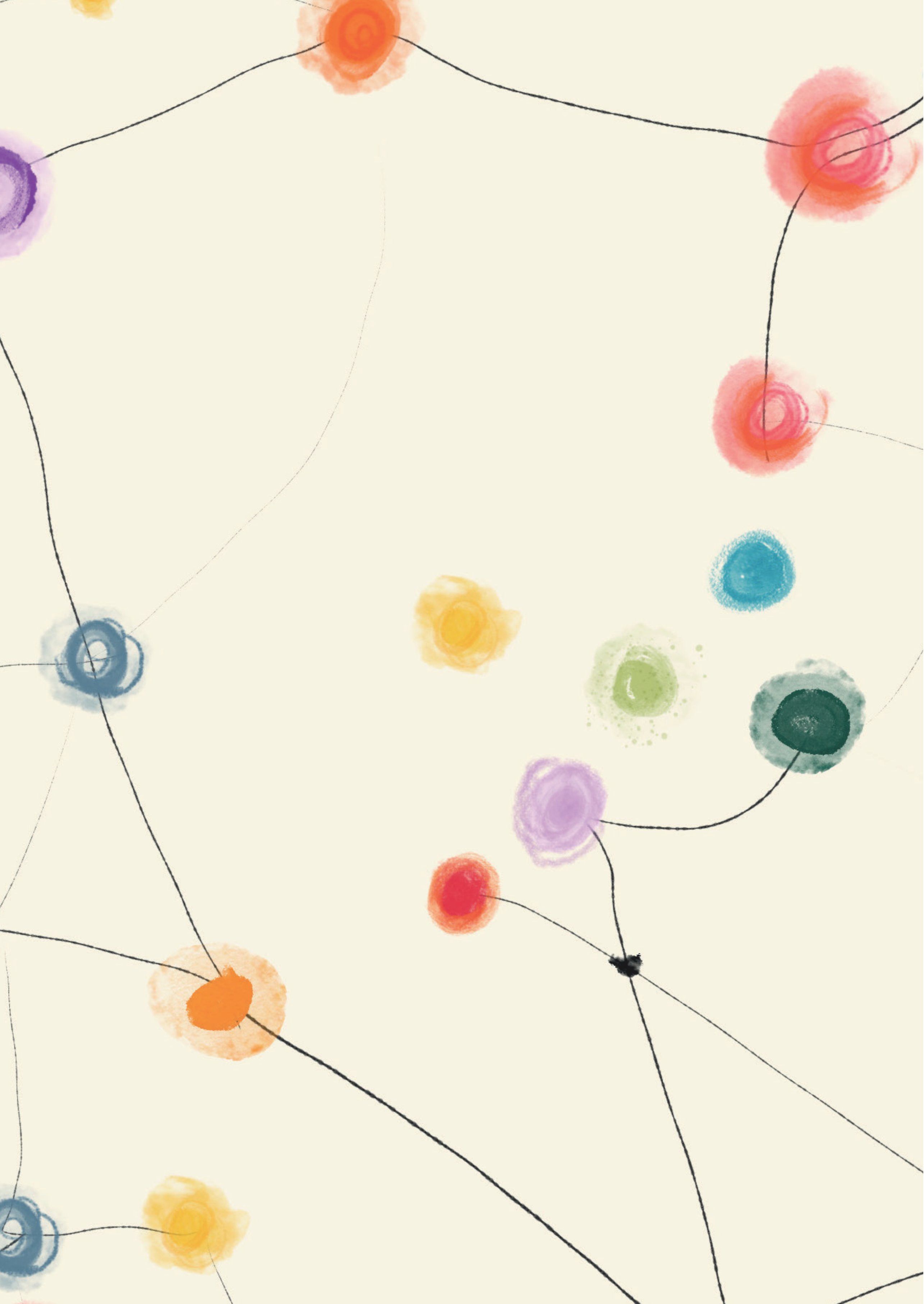

Chapter 11

DANKWOORD
(ACKNOWLEDGMENTS)

MIJN ELFSTEDENTOCHT

Mijn promotietraject was een echte Elfstedentocht. Daarom bestaat dit proefschrift dan ook uit 11 hoofdstukken, waarvan dit het laatste hoofdstuk is om nog even terug te blikken en goed af te sluiten. Misschien komt mijn eigen ervaring met extreme vermoeidheid na één van de Elfstedenfietstochten ook het dichtste bij hoe chronische kanker-gerelateerde vermoeidheid (CKV) ervaren wordt. Sommigen van de geïnterviewden met CKV in dit proefschrift gebruikten namelijk zelf ook de vergelijking met het doen van een intensieve en langdurende sportactiviteit. Zo'n Elfstedentocht als metafoor voor een proefschrift schrijven betekent ook dat er vele supporters zijn onderweg en het ook ongewis blijft hoelang deze tocht exact zal duren. Ik wil daarom iedereen bedanken die in welke vorm dan ook heeft bijgedragen tijdens dit intensieve proces om te komen tot 'mijn boekje'.

Het begint natuurlijk allemaal met het bemachtigen van 'een startkaart'. Hoewel ik toen al een andere nieuwe baan had, was de wens om te promoveren groot. De vacaturetekst en laptop gingen mee in de koffer na Frankrijk en na aanmoediging van mijn partner Paul werd de sollicitatiebrief in één keer geschreven op het terras van de stacaravan op een camping aan de Côte d'Azur. Een eerste en tweede gesprek volgden op de mooie locatie van het Helen Dowling Instituut in Bilthoven en ik mocht starten. Bijkomend groot voordeel was dat ik op de nieuwe racefiets naar mijn werk kon gaan als training voor alle fietselfstedentochten die ik elk jaar op tweede Pinksterdag heb gereden.

In de eerste plaats wil ik alle participanten zowel patiënten met CKV als psycho-oncologische therapeuten van het Helen Dowling Instituut die aan de studies van mijn proefschrift hartelijk danken voor het delen van hun rijke ervaringen en inzichten. Ik ben ontzettend dankbaar voor alles wat jullie met me wilden delen. Jullie vormen de basis van het onderzoek in dit proefschrift.

Goed trainen is belangrijk om een Elfstedentocht te kunnen fietsen en dat gaat niet zonder blessures en goede coaches. In de eerste week van mijn promotietraject raakte ik helaas geblesseerd aan mijn rug door het meetillen van een brancard. De eerste weken heb ik toen vooral staand artikelen gelezen. De eerste maanden van mijn promotietraject zijn we op zoek gegaan naar een goede coach passend bij het onderwerp. Hoewel er bij start van mijn promotie dus nog geen promotor beschikbaar was voor het project, kan ik mij gelukkig prijzen met de begeleiding door twee promotoren: prof. dr. Jenny Slatman, prof. dr. Marije van der Lee en co-promotor: dr. Melanie Schellekens. Bijzonder om te melden is dat de eerste kennismaking met prof. dr. Jenny Slatman online plaatsvond via Skype bij prof. dr. Marije van der Lee thuis onder het genot van een kopje thee.

Prof. dr. Jenny Slatman dank dat je mij als externe promovendus wilde begeleiden. Jouw filosofische kijk en toepassing van theorieën over belichaming heeft mijn promotieonderzoek verrijkt. Je opmerkingen over taal waren altijd raak. De body reading groep waarbij verschillende filosofische teksten en leesboeken werden besproken en lunches met de andere PhD's en postdocs van jouw onderzoeksgroep in Tilburg waren altijd zeer de moeite waard.

Prof. dr. Marije van de Lee dank voor het bedenken en schrijven van de subsidie voor het REFINE-project, waarbij de patiënt en netwerktheorie centraal staan. Wat mooi dat je nu ook mijn promotor bent als professor. Jouw klinische blik en rijke onderzoekservaring met patiënten met CKV maakten het verschil in dit praktijkgericht onderzoek. Jij bracht onderzoekers bij elkaar en zorgde voor een goed klimaat om te presteren niet alleen inspanning maar ook ontspanning met lunchwandelingen en gezelligheid met elkaar tijdens het VGCT-congres, de week voor de ontwikkeling van app *Energie Inzicht* in Tilburg, de retraite met de cognitiegroep en de schrijfweek.

Dr. Melanie Schellekens dank dat je mijn dagelijks begeleider was en wij de passie voor het wielrennen delen. Jouw brede onderzoekservaring, structuur en kritische blik hebben mijn schrijven en presenteren naar een hoger niveau getild. Ik heb hier ontzettend veel van mogen leren. Het was ontzettend bijzonder om nauw samen te werken aan het REFINE-project en met elkaar en de deelnemers tot mooie resultaten te komen en het project ook weer een vervolg heeft mogen krijgen. Ik bewonder hoe je jouw passie voor het onderzoek combineert met het moederschap van Noor.

Ik wil de leden van leescommissie bestaande uit prof. dr. Jim van Os, prof. dr. Tom Smeets, prof. dr. Hanneke van Laarhoven en dr. Marjolein de Boer bedanken voor het beoordelen van mijn proefschrift en het voeren van een levendige discussie tijdens mijn verdediging.

Ik wil KWF en Maarten van der Weijden hartelijk bedanken voor de financiering van het REFINE-project. Het was een grote eer dat ons project is geselecteerd in 2018 tijdens de eerste elfstedenzwemtocht. Ik wil alle leden van de wetenschappelijke adviesraad bedanken voor hun input tijdens de door ons georganiseerde bijeenkomsten van het REFINE-project. Jullie feedback was altijd waardevol en bood ons nieuwe inzichten om het onderzoek nog beter te kunnen uitvoeren. Ik wil Tilburg Experience Sampling Center (TESC) toen nog onder leiding van Angélique Cramer en Loes Keijsers voor het delen van hun expertise. Ik wil alle betrokken collega's van Tilburg University bedanken voor het meedenken over de vragen voor de app *Energie InZicht* tijdens de week waar wij onze resultaten presenteerden in februari 2019 op de campus.

Ik wil het Helen Dowling Instituut onder leiding van Hanneke Haanraadts en Anette Pet tijdens mijn promotietraject bedanken voor de aanmoedigingen, mooie werkplek en de prettige sfeer. De kleine, vertrouwde en warme setting maakte het mogelijk voor mij om als persoon te groeien. Ik ben Annemiek werkzaam als cognitief gedragstherapeut bij het HDI die helaas heel plotseling is overleden dankbaar voor haar hulp bij het ontwikkelen van de interviewguide en goede tips hoe om te gaan met ernstig vermoeide mensen. Ik ben Mahmoed een van de systeemtherapeuten van het HDI dankbaar dat ik een behandelgesprek mocht bijwonen. Zonder goed vervoer haal je ook de finish niet, ik prijs me gelukkig dat ik de HDI-auto mocht ik lenen om de deelnemers thuis te bezoeken en voor de afspraken in Tilburg. De prijsvraag voor het bedenken van de naam voor de EMA app: *Energie InZicht* werd gewonnen door oud-collega Karlijn Bouts.

Ik wil alle (oud)medewerkers van het HDI bedanken voor hun gezelligheid tijdens de lunches in het keukentje, de medewerkersdagen, de sinterklaasvieringen en de HDI-events. De borrels op de vrijdagmiddag waren ook een hele goede manier om het weekend te starten. Marijke en Martine jullie waren er ook bijna altijd bij en wat hebben we het gezellig gehad!

Het REFINE-project was een opvolger van het Fitter na Kanker-onderzoek. Ik ben dankbaar dat ik het interviewmateriaal van Fieke en Joost mocht gebruiken. En ook dat Marije me wegwijs heeft gemaakt in de data van het Fitter na Kanker-onderzoek.

De afdeling wetenschappelijk onderzoek werd steeds groter en gezelliger. Eltica dank voor je interesse in mijn onderzoek en wat goed dat je de stap hebt gezet om je eigen weg te kiezen. Yvonne het was ontzettend fijn om samen een PhD te kunnen doen bij het HDI. Ik wil je bedanken voor alle steun tijdens mijn project. Rosalie jouw ondersteuning in mijn promotietraject was enorm van transcriberen tot netwerkanalyses en wat fijn dat je vandaag achter me staat als paranimf. Het was altijd een plezier om samen te werken. Laura ik was al overtuigd van je enthousiasme om een PhD te combineren met praktijkervaring bij het HDI tijdens je sollicitatie en ik wens je nog veel succes. Sophie wat een herkenning in persoonlijke ervaringen en natuurlijk ook met het afronden van een PhD naast een baan als postdoc. Ik hoop dat jij ook snel mag promoveren. Anne en Berend allebei ontzettend bedankt voor jullie hulp bij het transcriberen van de lange interviews voor de proof-of-concept studie. Pascalle en Martijn het was bijzonder om ook jullie onderzoeksplannen mee te krijgen en dank voor jullie interesse in mijn promotietraject. En Martijn natuurlijk ook voor zijn interesse in het fietsen. Ik wacht nog op de HDI-toertocht! Het was ook altijd gezellig op de onderzoekskamer met Sanne, Anne, Laurine, Wiep, Sanne en Shaniqua.

De body reading group onder leiding van prof. dr. Jenny Slatman heeft mij kennis doen nemen van brede filosofische literatuur en contact geïnitieerd met de andere leden van de onderzoeksgroep: Elise, Sanne, Ingeborg, Hans-Georg, Irene, Sanneke, Annelies, Monica, en anderen die hierbij aanwezig waren. Ik heb veel van jullie mogen leren. Elise het is fijn dat wij contact hebben gehouden in het staartje van de PhD en ervaringen hebben kunnen uitwisselen. Ik hoop dat je ook snel mag promoveren. Sanne wij delen dezelfde interesses en dat schept een band. Ik vond het leuk om af en toe bij je op de kamer te zitten. Ik wens je veel succes met de afronding van je PhD. De lunches tijdens de bezoeken aan Tilburg University waren altijd heel gezellig en ook het laatste teamuitje in 2022 in Tilburg.

Na initiatief van de KWF-werkgemeenschap Psychosociale Oncologie zijn de vermoeidheidsonderzoekers een aantal keer per jaar samengekomen op verschillende werklocaties (AmsterdamUMC, locatie AMC, Prinses Máxima Centrum, HDI) en online om eigen werk te presenteren en te kijken naar mogelijke samenwerkingen. Ik wil alle collega's bedanken die hierbij aanwezig waren en hun werk hebben gedeeld.

In februari 2021 kwam ik terug bij het Antoni van Leeuwenhoek in de ondezoeksgroep van prof. dr. Winette van der Graaf en dr. Olga Husson. Ik wil Olga en Winette bedanken voor deze mooie positie binnen hun onderzoeksteam. Ook voor het vertrouwen, support en de ruimte die ze mij gegeven hebben om mijn proefschrift af te ronden. Het is een groot plezier om met jullie te mogen werken. Ik wil al mijn lieve (oud-)collega's bedanken voor hun aanmoedigingen voor het afronden van mijn proefschrift: Martha, Renske, Deborah, Silvie, Dide, Vivian, Daan, Cas, Milou, Lina, Catarina, Emily, Simone, Evelyne, Carla, Asiye, Danielle, Anke, Esther, Mies, Noelle, Emma, Robin en alle studenten die een scriptie bij ons schrijven of hebben geschreven. Ik kijk er ontzettend naar uit om met jullie te blijven samenwerken en mijn eigen projecten te mogen starten volgend jaar.

Mijn vrienden wil ik allemaal bedanken voor de momenten van ontspanning en de steun tijdens mijn promotietraject. Ik weet dat mijn tijd die ik met jullie kon doorbrengen beperkt is geweest afgelopen jaren. Simon jij hebt altijd achter me gestaan en bedankt dat ik altijd bij je terecht kon om mijn ervaringen met promoveren te delen. Siem, Dennis en Aike ik heb genoten van onze afspraken en natuurlijk het kampeerweekend tijdens coronatijd in de Betuwe. Ik ben trots dat we nu allemaal een mooie carrière aan het opbouwen zijn. Casper wat fijn dat ik toen we een week in Tilburg aan het werk waren om de app (*Energie InZicht*) te ontwikkelen bij jou mocht logeren en dat vond je hond ook haha. Ik heb genoten van onze relaxte afspraken. Ik ben blij dat jij als paranimf vandaag achter me staat. Raymon ontzettend bedankt voor het proeflezen van mijn proefschrift. We hebben regelmatig afgesproken om ergens te eten en onze gesprekken zijn altijd goed. Jean dank voor je steun en fijn dat we zo regelmatig even contact hebben. Hester en Milou mijn studiegenoten en vriendinnen fijn dat we nog altijd contact hebben om af en toe wat leuks te doen en bij te kletsen. Sietske dank voor onze mooie vriendschap en het fijne contact wat we hebben.

Natuurlijk ook mijn oud-collega's met wie ik altijd contact heb onderhouden en interesse in mijn werk hebben getoond. Gabey we kennen elkaar nu al sinds 2013 toen ik voor het eerst bij het AVL kwam en hoe bijzonder is het dat we sindsdien contact hebben onderhouden. Ik ben blij dat ik nu weer terug in het AVL ben en we regelmatig even koffie kunnen drinken. Dank voor al jouw steun tijdens mijn promotietraject. De AVL PSOE groep met wie ik heb gewerkt op de altijd gezellige onderzoekskamer voordat ik bij het HDI kwam: Harmke, Karen, Sandra, Saskia, Kim, Inge, Marietta, en Marieke wat fijn dat we nog steeds af en toe contact hebben en ik kijk terug op gezellige etentjes in Amsterdam.

Heit en mem wil ik bedanken voor de kans die ze mij hebben gegeven om te mogen studeren. Mijn broeder Bart, hoewel we allebei in een ander werkveld werken, delen we een passie voor wetenschappelijk onderzoek. Wat mooi dat jij en Emily nu samen een gezin vormen. Mijn neefje Rens is al een echte boekenwurm en ik lees hem graag voor. Misschien kunnen we in de toekomst samen fietsen. Lieve beppe ik draag voor altijd jouw naam en ik kom het boekje bij je brengen. Je zal vast zoals altijd zeggen dat het echt iets voor me is onderzoek naar kanker doen en wat zul je trots zijn op je oudste kleinzoon. Het is bijzonder hoe je met pake vroeger altijd onze ontwikkeling hebt gestimuleerd. Pake deelde ook de liefde voor het fietsen met mij. Hoe mooi is het dat ik vandaag op jullie trouwdag mijn proefschrift mag verdedigen.

Mijn schoonouders wil ik bedanken voor de leuke vakanties en de borrels op zondagmiddag waar alles besproken kon worden. Mijn zwager Bas wil ik bedanken voor zijn interesse in mijn werk en schoonzus Debby voor het mooie ontwerp van de cover van mijn proefschrift. Mijn nichtje Lowietje wat hebben wij het leuk gehad in Frankrijk op vakantie om samen de schildpadden te voeren en te vissen naar eendjes.

Voor een Elfstedentocht heb je een goede fiets nodig, maar voor het schrijven van een proefschrift een goede computer. Ik ben mijn schoonvader Paul dankbaar voor het beschikbaar stellen van zijn IMac. De IMac mag nu met pensioen omdat het proefschrift klaar is.

Als laatste wil ik mijn lieve partner Paul bedanken. Het afleveren van een proefschrift is niet niks. Fijn dat je altijd naast me stond bij de hoogtepunten van papers die geaccepteerd werden, maar ook mij de tijd hebt gegeven om het proefschrift af te kunnen maken. Ik ben blij met de liefde die we voor elkaar voelen. Ik hou van jou.

Nu is het tijd voor feest!