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Published in:
Psycho-Oncology

DOI:
10.1002/pon.6235

Publication date:
2023

Document Version
Publisher's PDF, also known as Version of record

Link to publication in Tilburg University Research Portal

Citation for published version (APA):
van Roozendaal, A. S., Schellekens, M. P. J., van Woezik, R. A. M., & van der Lee, M. L. (2023). Exploring the dynamic interconnectedness of protective and perpetuating factors of cancer-related fatigue. *Psycho-Oncology*. Advance online publication. https://doi.org/10.1002/pon.6235

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Download date: 09. Dec. 2023

Check for updates

Received: 30 June 2023 | Revised: 29 September 2023 | Accepted: 18 October 2023

DOI: 10.1002/pon.6235

WILEY

ORIGINAL ARTICLE

Exploring the dynamic interconnectedness of protective and perpetuating factors of cancer-related fatigue

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Funding information
Foundation Vrienden Integrale Oncologische Zorg (VIOZ)

Abstract

Objective: Approximately 25% of cancer patients suffer from cancer-related fatigue (CRF) after cancer treatment. CRF is a multi-factorial condition affected by several interrelated protective and perpetuating factors. As most studies merely assessed bivariate associations, more insight into the complex relationships among these constructs is needed. We applied the multivariate network approach to gain a better understanding of how patients' fatigue, perpetuating and protective factors are dynamically interconnected.

Method: Between February and August 2022, 30 cancer patients filled out a carefully developed ecological momentary assessment questionnaire (EnergyIn-Sight) five times a day for at least 21 days while being on the waitlist for psychological care for CRF. We performed a multi-level vector autoregression analysis to examine the interconnectedness among fatigue, protective factors (allowing rest, acceptance, and self-efficacy) and perpetuating factors (worrying, catastrophizing, and feeling guilty).

Results: In the contemporaneous network (concurrent associations), higher acceptance and self-efficacy were associated with lower fatigue, whereas all other factors were associated with higher fatigue. The strongest relationships were between worrying and feeling guilty and between acceptance and allowing rest. In the temporal network (lagged associations), fatigue was related to two factors: higher self-efficacy preceded lower fatigue, and higher fatigue preceded increased allowing rest.

Conclusions: Taking all included factors into account, the networks identified self-efficacy and allowing rest as key protective factors of CRF. Patients may benefit from psychological interventions that cultivate self-efficacy, as it seems to pave the way to reduced fatigue.

KEYWORDS
cancer, cancer-related fatigue, ecological momentary assessment, network approach, oncology, self-efficacy

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1 | BACKGROUND

Cancer-related fatigue (CRF) is among the most prevalent and debilitating side effects of cancer and its treatment. CRF is generally characterized by feelings of tiredness, weakness, and lack of energy, unlike anything patients have ever felt before.[1,2] Contrary to typical tiredness, CRF is neither proportional to recent activity, nor is it mitigated by adequate sleep or rest[3] causing patients to feel like their fatigue is beyond their control. CRF is experienced as a dynamic and unpredictable condition, with patients reporting sudden drops in energy levels, as well as a gradual build-up of their fatigue throughout the day.[4,5] CRF significantly impairs patients' quality of life.[5–7] Because CRF interferes with patients' overall health status, ability to work, and participation in daily activities, patients are often prevented from living a 'normal' life.[7–9] While almost all patients experience fatigue during treatment, in approximately 25% of patients fatigue persists for months to years after completing cancer treatment.[10] Although its exact etiology remains unclear, CRF is thought to arise from a complex interplay of clinical, physiological, environmental, and psychosocial factors.[8,10,11]

Research has identified several coping mechanisms which either maintain or exacerbate CRF (i.e. perpetuating factors) or which promote adaptive functioning in the face of CRF and can counteract perpetuating factors (i.e. protective factors).[12] To provide patients with the best possible care, we need to gain insight into how these perpetuating and protective factors are related to CRF and one another. Regarding protective factors, patients who are more accepting of their CRF show lower fatigue levels, suggesting that acceptance may protect patients from fatigue persistence.[4,6,13] Allowing oneself to rest may be another behavioral mechanism promoting adaptive functioning in the face of CRF, as patients often report that they cope with their fatigue by pacing themselves and by balancing activity and rest.[6,11] Self-efficacy, that is, one's confidence in their capability to influence one's fatigue, is also thought to promote adaptive health behaviors and mediate CRF severity.[14,15]

As for perpetuating factors, a direct link has been found between worrying and CRF, as worrying is thought to perpetuate CRF through endless pessimistic cognitions focused on physical health.[16,17] Another proposed perpetuating factor of CRF is catastrophizing, which is where one engages in an exaggerated negative evaluation of symptoms and imagines the worst possible outcome.[18,19] Catastrophizing is generally associated with increased symptom intensity and emotional distress, and catastrophic thinking about fatigue strongly predicts continuous elevated fatigue levels.[8,18] Feeling guilty is another factor that is expected to perpetuate one's fatigue. The idea of falling short of one's own and others' expectations can take up a lot of energy.[4,20]

Although these studies have offered valuable contributions to our understanding of which factors protect against or maintain fatigue, most of these studies used bivariate cross-sectional data and examined the relationship between CRF and perpetuating and protective factors independently of other factors. In line with patients' experiences, it is more likely that fatigue and its protective and perpetuating factors are interconnected and vary from moment to moment.[21,22] Following complexity theory of psychopathology, CRF can be understood as a dynamic pattern that emerges from interactions between interdependent biopsychosocial processes (symptoms, protective and perpetuating factors) in a complex adaptive system.[23] The network approach has the potential to capture this complex dynamic interplay among fatigue, protective and perpetuating factors. Thus, rather than viewing symptoms as manifestations of a common cause (i.e. you have trouble concentrating because you have CRF), in line with complexity science, the network approach conceptualizes symptoms and protective and perpetuating factors as mutually interacting and reinforcing elements of a complex dynamic system.[21] For example, fatigue can lead to social withdrawal, which may result in feelings of guilt, leading to catastrophic thinking, consequently triggering concentration problems. Studying the interconnectedness of protective and perpetuating factors of such a complex and dynamic condition like CRF requires intensive longitudinal data. Because it is not always feasible to collect intensive longitudinal data in clinical practice, it is clinically relevant to know about what complex and dynamic interrelations are generally found in patients suffering from CRF. Therefore, the present study employed group-level network analysis on ecological momentary assessment (EMA) data to shed light on how CRF and its protective and perpetuating factors are interrelated.

2 | METHODS

2.1 | Design

This study used data from the 'REFINE 2.0' project which was a prospective study using EMA data. The primary study aim of REFINE 2.0 was to examine the feasibility and effectiveness of implementing person-specific fatigue networks in the routine clinical practice of a mental health institute to help personalize treatment for CRF.[24] Ethical approval was obtained from the Ethical Review Board of Tilburg University (TSB_RP461). For the present study, we combined the EMA data of the participants to estimate dynamic group-level networks.

2.2 | Participants and procedure

To be eligible for inclusion, patients needed to (1) be 18 years or older; (2) be referred for mental healthcare at an institute specialized in Psycho-Oncology (the Helen Dowling Institute); (3) have had a cancer diagnosis; (4) experience fatigue as their primary problem, as determined by either a score of 35 or higher on the Checklist Individual Strength—Fatigue Severity subscale (CIS-FS)[25] or, in exceptional cases where patients scored lower than 35 on the CIS-FS, by the clinical judgment of a healthcare psychologist during the intake session.

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Participants were recruited between February and August 2022 at three locations of the Helen Dowling Institute in the Netherlands. Upon registration, all patients applying for psychological care at the Helen Dowling Institute are asked to fill out the Routine Outcome Monitoring (ROM) questionnaire, which encompasses several symptom questionnaires, including the CIS-FS. Based on their score, patients were invited to participate. When patients expressed interest in participation, they received an information letter. Prior to study commencement, we called all interested individuals to instruct them on the study's procedure and to discuss a starting date of their preference. After providing written informed consent, participants were sent a detailed handbook with study procedure instructions and they installed the EMA app (ethicadata.com) on their own smartphone. Participants filled out the EMA app while being on the waitlist for psychological care.

2.3 | Measures

Participants' demographic and clinical characteristics were derived from patients' files.

2.4 | Checklist individual strength—Fatigue severity subscale

The CIS-FS by Vercoulen and colleagues[25] was used to assess CRF. This 8-item fatigue severity subscale measures the subjective experience of fatigue, with questions such as: "physically, I feel exhausted".[26] Participants are asked to what extent they agree with statements on a 7-point scale, ranging from 1 ('yes that is true') to 7 ('no that is not true'). The cut-off score for severe CRF is 35 or higher, with scores ranging from 8 to 56.[26] The CIS-FS has a good reported internal consistency and test-retest reliability.[26]

2.5 | Ecological momentary assessment

During the 21-day EMA period, participants filled out the experience sampling app EnergyInSight five times a day, with each questionnaire taking approximately two minutes to fill out.[24] The questionnaires were sent at five quasi-random time intervals within three-hour time windows. To prevent dropout, notification timing was personalised to each participant's sleep-wake schedule. Questionnaires were required to be completed within 30 min after receiving the notification; otherwise they were recorded as missing.

Based on our quantitative (i.e., cross-sectional group-level network analysis) and qualitative research findings (i.e., meta-ethnography), the CRF literature, and our clinical expertise, we developed the EMA protocol Energy InSight.[6,13,20] For example, our group-level networks indicated illness acceptance and feeling hopeless as highly relevant factors of fatigue.[13] Therefore we included an item on acceptance and catastrophizing. From patients' experiences and our clinical expertise we know that resting after activity is a valuable coping strategy and feeling guilty can be a barrier in managing one's fatigue.[6,20] Therefore we added an item on allowing oneself to rest and feeling guilty to the EMA protocol. Next, in collaboration with EMA experts, we carefully developed items referring to present-moment experiences matching these variables. The Energy Insight app includes items on fatigue symptoms, positive and negative affect, social context, physical activity, and coping strategies of fatigue. After a proof-of-concept study, in which the suitability and usability of the EMA items, app and procedure were extensively assessed, these items were further finetuned, resulting in the present set of 20 items.[24]

To be included in the present analyses, participants needed to fill out a minimum of 75 EMA questionnaires, as a recent simulation study showed that with 75–100 assessments per person the network can include approximately 6 nodes for it to be reliable.[27] When participants missed too many EMA questionnaires, the assessment period was extended with the number of days necessary for reaching 75 observations. For the present study, we focused on the items assessing coping strategies because these provide insight into what patients do in response to the fatigue (e.g. allowing oneself to rest, catastrophizing about the fatigue) that helps attenuate or perpetuate fatigue. This insight could inform psychological treatment. As we were limited by the number of nodes, we were unable to include affect and physical activity.

Eventually, seven variables were included in the network models: fatigue, three perpetuating factors, and three protective factors of fatigue (see Table 1). Fatigue was measured by three EMA items measuring different dimensions of fatigue, as inspired by three subscales of the CIS-FS, namely: the physical dimension of fatigue ('physically I feel tired'), mental fatigue ('I am able to concentrate'), and the motivation to do things ('I feel like doing fun things'). The items 'concentration' and 'motivation' were reverse scored so that a higher score reflected a higher level of fatigue. The chronbach's alpha of this mean score was 0.70, showing an adequate inter-item reliability. Perpetuating factors were worrying about fatigue, catastrophizing that fatigue will never get better, and feeling guilty. Protective factors were allowing rest, accepting fatigue, and self-efficacy.

2.6 | Statistical Analysis

Prior to data analysis, the data analysis plan was registered on the online Open Science Framework (https://osf.io/537qd). First, we examined whether data showed sufficient variability and were stationary. To determine whether the included variables had sufficient variability, the mean squared successive difference (MSSD) was calculated for each item.[28] All items were found to have sufficient variability (MSSD >50). We then conducted the Augmented Dickey-Fuller (ADF) test to check whether variables were stationary.[29] Data are stationary when their statistical properties, such as the mean and variance, are constant over time. The ADF test demonstrated that all

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TABLE 1 Selected EMA items for the network models.

Factors	Variable	Item example	Mean, SD	Scale options
	Fatigue	Physically I feel tired	64.64, 22.36	0 = not at all; 100 = a lot
		I am able to concentrate	57.33, 22.95	0 = not at all; 100 = very well
		I feel like doing fun things	47.01, 27.54	0 = not at all; 100 = a lot
Perpetuating factors	Worrying	I worry about my fatigue	39.44, 29.71	0 = not at all; 100 = strongly
	Catastrophizing	I feel like my fatigue will never get better	51.03, 26.39	0 = not at all; 100 = strongly
	Feeling guilty	I feel guilty about not being able to do things because of my fatigue	44.09, 31.07	0 = not at all; 100 = a lot
Protective factors	Allowing rest	I allow myself rest	54.48, 25.68	0 = not at all; 100 = strongly
	Acceptance	I accept my fatigue	44.13, 25.91	0 = not at all; 100 = strongly
	Self-efficacy	I feel like I can influence my energy level	47.49, 24.24	0 = not at all; 100 = strongly

items were considered stationary (p value < 0.05), so all variables were included in the model.

Next, we used the R package 'imputeTS' version 3.2 to apply the Kalman Filter—an imputation method for time-series data—to perform imputation on missing observations.[30,31] When participants missed one or more full days, we decided to exclude these days from data analysis completely, rather than imputing the missing observations.

2.6.1 | Network estimation

Two moment-level group networks were estimated using the multilevel vector autoregressive (mlVAR) package (v0.5 in RStudio v1.4.1006): a contemporaneous network model and a temporal network model. In each network, selected variables such as fatigue are represented by so-called nodes. Associations between nodes are represented by edges. Green edges denote positive connections; red edges denote negative connections. Thicker and more saturated edges signal stronger connections between nodes. Based on the strongest correlation in the network, we set a maximum edge strength of 0.37 for all edges in the network models, ensuring that the thickness of the edges represented similar values in both models. All edges that were not significantly different from zero were not visible in the network graphs.[32] To derive results from our models, they were visually inspected and the strongest relations were interpreted.

The contemporaneous network shows the concurrent association between variables. Edges represent partial contemporaneous correlations between variables, after controlling for temporal nodes and all other nodes at the same timepoint. This means that, given all other nodes, two nodes that are connected by an edge are conditionally dependent. The temporal network shows how variables are predicted by variables at the previous time point (t-1) within the same day, including autoregressive effects. This network consists of partial directed correlations, demonstrating both the strength and directionality of associations between nodes, after controlling for all other nodes in the network.[21] This means that, at one time point, a variable is predicted by the same variable (auto-regressive effects) and all other variables (cross-lagged effects) at the previous time point. The links between nodes are shown with arrows, with an arrow from one node to another node depicting a cross-lagged effect, and an arrow directing to the same node depicting an autoregressive effect.

3 | RESULTS

3.1 | Study sample

A total of 143 individuals were approached for participation, of whom 46 people proved ineligible, 41 people did not respond, and 19 individuals refused to participate. Eventually, 37 individuals enrolled in the present study. One participant dropped out before data collection and six participants were excluded because they had an insufficient number of observations (19–48). The group of excluded participants appeared similar to the group of included participants. Sociodemographic and clinical information are reported in Table 2. Participants were on average 50.4 years old (SD = 9.7) and the majority was female (N = 23, 76.7%). Two participants did not meet the CIS-FS criterion of ≥35 but were included based on clinical impression of CRF.

The number of observations for the included 30 participants ranged from 68 to 101 before imputation (M = 87.7; SD = 10.0). Although we initially only wanted to include participants with at least 75 observations, we included five participants with only 68–73 observations. We considered the benefit of including additional participants to outweigh the disadvantage of the limited number of observations.

3.2 | Contemporaneous network model

The contemporaneous network is presented in Figure 1. A table with the contemporaneous directed correlation can be found in the supplementary material. Of 21 possible edges, 17 edges (81%) were

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TABLE 2 Sociodemographic and clinical characteristics of 30 cancer patients.

	N	(%)
Age [Mean (SD)]	50.4	(9.7)
Female gender	23	(76.7)
In a relationship	22	(73.3)
Children	24	(80.0)
Children living at home	14	(46.7)
Educational level[a]		
Low	11	(36.7)
Intermediate	2	(6.7)
High	17	(56.7)
Months since cancer diagnosis [Mean (SD; range)]	35.3	(38.2; range: 9–199)
Cancer type		
Breast	15	(50.0)
Haematological	5	(16.7)
Gynecological	3	(10.0)
Other[b]	7	(23.3)
Medical treatment[c]		
Chemotherapy	19	(63.3)
Radiotherapy	17	(56.7)
Surgery	16	(53.3)
Hormone treatment	10	(33.3)
Immunotherapy	7	(23.3)
Bone marrow transplant	2	(6.7)
Targeted therapy	1	(3.3)
Currently receiving medical treatment	6	(20.0)
Tumor with metastasis		
No	17	(56.7)
Yes	11	(36.7)
Unknown	2	(6.7)
Patients' impression of disease stage		
Little to no chance of survival	6	(20.0)
Reasonable chance of survival	5	(16.7)
In remission or cured	11	(36.7)
Unknown	8	(26.7)

[a]Low, primary and lower secondary education, intermediate, upper secondary education, high = higher vocational training/university.

[b]Other reported cancer types were: lung cancer, skin cancer, gastrointestinal cancer, male reproductive cancer, bone cancer.

[c]Percentages do not add up to 100 because patients followed multiple treatments.

significant and represented in the network. *Fatigue* was connected to all protective and perpetuating factors in the model. *Acceptance* and *Self-efficacy* were negatively associated with fatigue, which means that, while controlling for all other factors in the model, higher levels of *Acceptance* and *Self-efficacy* were associated with lower fatigue. For all other factors, higher levels of *Worrying*, *Catastrophizing*, *Feeling guilty*, and *Allowing rest* were associated with higher levels of fatigue. The strongest relations in the network were *Worrying—Feeling guilty* and *Acceptance—Allowing rest*. More worrying thus co-occurred with feeling more guilty and higher acceptance of one's fatigue co-occurred with allowing oneself more rest.

3.3 | Temporal network model

The temporal network is presented in Figure 2. A table with the partial directed correlations can be found in the supplementary material. Of 49 possible edges, 15 (31%) edges had an absolute edge weight above zero and were represented in the network. Autoregressive effects were found for all included nodes in the network. All nodes were most strongly predicted by their scores 3 hours prior (*t*-1). For example, *Fatigue* was most strongly predicted by patients' fatigue level at t-1. Whereas *Fatigue* was connected to all protective and perpetuating factors in the contemporaneous network, *Fatigue* was only connected to two factors in the temporal network. Higher *Fatigue* preceded higher levels of *Allowing rest*, but not vice versa. Furthermore, higher *Self-efficacy* preceded lower *Fatigue* 3 hours later. It is important to note that cross-lagged relationships were small and should thus be interpreted with caution.

4 | DISCUSSION

The present study applied network group analyses on EMA data to explore the dynamic interconnectedness of fatigue and its protective and perpetuating factors within patients seeking psychological help for their CRF. The contemporaneous group network revealed that fatigue was related to all protective and perpetuating factors in the model. We found that higher acceptance and self-efficacy were associated with lower fatigue levels, while higher levels of worrying, catastrophizing, feeling guilty, and allowing rest were associated with more fatigue. The temporal group network primarily showed autoregressive effects (e.g. fatigue was most strongly predicted by patients' fatigue level 3 hours prior). Only self-efficacy had a direct effect on fatigue in the temporal network, with higher self-efficacy at t-1 preceding lower fatigue 3 hours later. The temporal network also indicated that higher fatigue preceded higher levels of allowing rest.

Regarding protective factors, we found that the co-occurrence of acceptance and allowing rest was among the strongest

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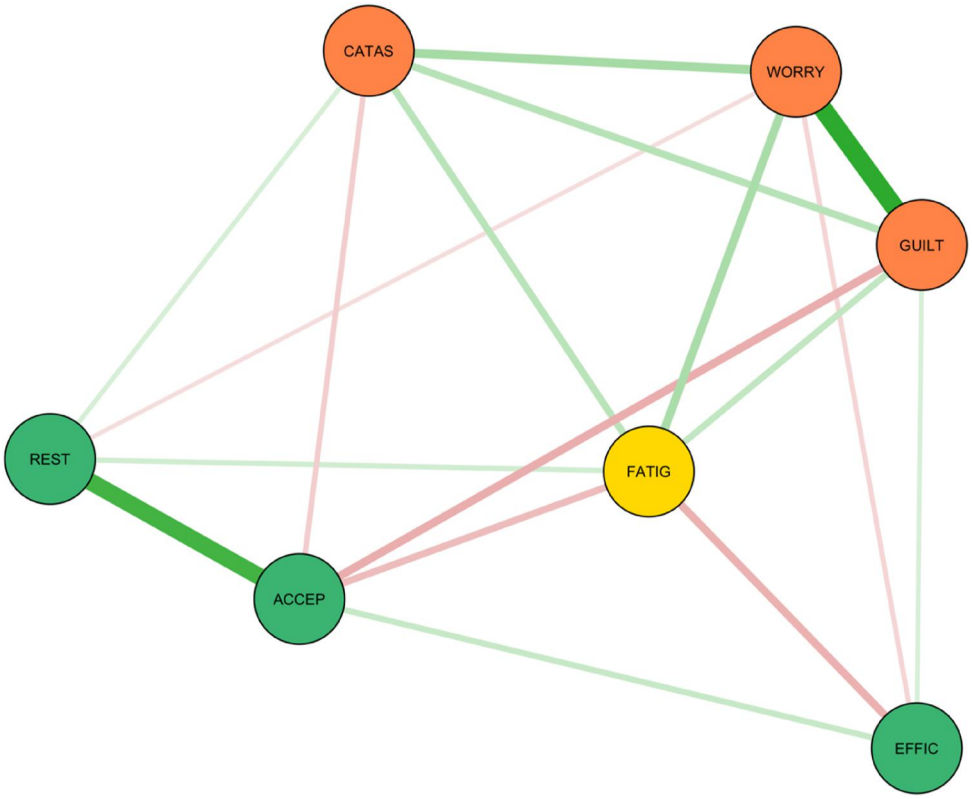

FIGURE 1 Contemporaneous Network - The network structure of perpetuating and protective factors of 30 cancer patients. Fatigue is depicted with a yellow node. Protective factors are depicted with green nodes and perpetuating factors with orange nodes. Positive and negative connections are denoted by green and red edges, respectively. The stronger a connection between two nodes, the thicker and more saturated the edge. Non-significant edges are not visible. ACCEP, accepting; CATAS, catastrophizing; EFFIC, self-efficacy; FATIG, fatigue; GUILT, feeling guilty; REST, allowing rest; WORRY, worrying.

relationships in the contemporaneous network. Previous studies suggest that acceptance of one's fatigue and current situation could translate into balancing one's activities, allowing oneself to rest more and to live life at a slower pace.[2,20] However, our temporal model showed that higher levels of allowing rest preceded higher levels of acceptance and not vice versa, suggesting that taking more time to rest could allow patients to reflect on and find ways to accept their current situation. Allowing rest was positively related to fatigue in the contemporaneous model, indicating that allowing more rest co-occurred with feeling more fatigued and/or the other way around. This may be explained by the temporal network, which showed that higher fatigue preceded allowing oneself to rest more, but not vice versa. Indeed, previous findings indicated that cancer patients take more time to rest when they feel more fatigued.[6] Interestingly, in the temporal network, allowing oneself to rest preceded higher acceptance of fatigue and lower catastrophizing. Thus, it could be that allowing rest in response to feeling fatigued acts as an indirect protective factor.

Self-efficacy was the only direct protective factor that preceded fatigue in the temporal network, with higher self-efficacy preceding lower fatigue 3 hours later. This finding reflects previous findings showing that better self-efficacy is associated with lower fatigue.[33] Potentially, those patients with greater self-efficacy are more likely to believe that their fatigue is adaptable, and consequently, are more persistent in their efforts to alleviate their fatigue, and as such lower their negative illness perceptions and improve their health-related quality of life.[34,35]

Regarding perpetuating factors, our findings demonstrated that higher feelings of guilt preceded increased worrying and vice versa, in both models. Previous research proposed that feelings of guilt may encourage worrying by directing one's attention toward negative self-information.[36] Similarly, by paying attention to negative information about the self, worrying about fatigue could also encourage feelings of guilt. Both of these factors co-occurred with increased fatigue. Previous research has demonstrated that feeling more fatigued can precede increased feelings of guilt about falling short,[4,20] and as lingering fatigue may remind cancer survivors of their illness, fatigue can precede more worrying behavior.[37] Conversely, worrying is thought to exacerbate CRF, as it can result in continuous pessimistic cognitions, leading to an uncontrollable negative cognitive cycle, which is often highly energy-consuming.[16,38] However, no direct relationship existed between either worrying or feeling guilty and fatigue in the temporal network.

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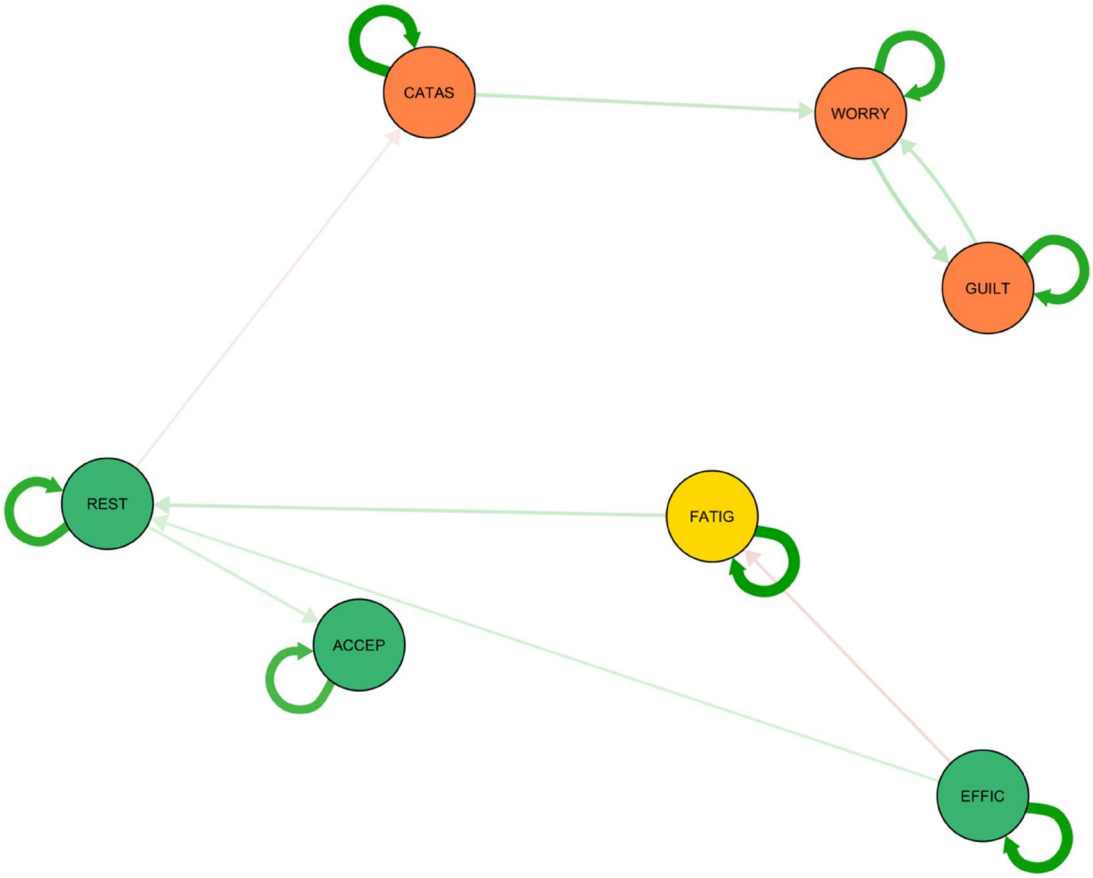

FIGURE 2 Temporal Network - The network structure of perpetuating and protective factors of 30 cancer patients. Fatigue is depicted with a yellow node. Protective factors are depicted with green nodes and perpetuating factors with orange nodes. Positive and negative connections are denoted by green and red edges, respectively. Non-significant edges are not visible. The stronger a connection between two nodes, the thicker and more saturated the edge. Arrows directed toward the same nodes indicate an autoregressive effect. ACCEP, accepting; CATAS, catastrophizing; EFFIC, self-efficacy; FATIG, fatigue; GUILT, feeling guilty; REST, allowing rest; WORRY, worrying.

4.1 | Study limitations

The current study knows several limitations. First, cross-lagged relationships in the temporal network model were small. Although it could be that there were indeed no or only weak relationships between nodes over time, another possibility could also be that the three-hour time difference between subsequent observations was not the best timeframe to capture the dynamic nature of the included nodes. The time lag for the current study was approximated based on clinical expertise with CRF dynamics, while also considering EMA burden (maximum of five assessments per day). Besides fatigue, we do not know the ideal time lag to capture the dynamics of the protective and perpetuating factors, nor how long it takes for these factors to perpetuate or attenuate fatigue. Requiring large-scale EMA studies, newly developed statistical methods can help determine the optimal time lag.[39,40] Second, with an average of 88 assessments per person, the number of included nodes was limited to 7 nodes for the network to be reliable.[27] For the present study, we chose to include 1 fatigue node and 6 coping strategies nodes. By increasing the assessment points per person, future research could explore the three dimensions (physical fatigue, mental fatigue, motivation) of fatigue separately to see what protective and perpetuating factors appear most relevant for the different dimensions of fatigue. Moreover, besides coping strategies, other factors (e.g. affect, physical activity and biological factors, such as inflammation and cortisol levels), could be added to the network to explore their relevance in perpetuating or attenuating fatigue. Third, women with breast cancer were overrepresented in this study. While this is in line with the characteristics of cancer patients seeking psychosocial support,[41] this might limit generalizability to patients with other cancer types. Fourth, we originally aimed to include 40 participants in our data analysis. However, more participants than initially expected did not meet the minimum number of required observations and six participants dropped out during the EMA period. A possible explanation for this lowered adherence is that, because the overarching project was set up to examine the feasibility and effectiveness of implementing EMA-based fatigue networks in routine clinical practice, the EMA process was automatized and the role of the researcher was limited as much as possible.

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4.2 | Clinical implications

Results of this study can help inform therapists what factors are generally important in protecting or perpetuating CRF and what factors may reinforce one another within patients. A key candidate appears self-efficacy. Cultivating the confidence that one is able to influence their fatigue seems to pave the way to diminished fatigue. Another important factor seems allowing rest. Helping patients to balance rest and activity in response to one's fatigue can help improve accepting one's fatigue and diminish catastrophizing about fatigue. Note that while balancing rest and activity is indeed positive, resting without being physically active might lead to physical deconditioning and perpetuate or even increase fatigue. Physical activity training has proven effective and is recommended in guidelines for treating CRF.[10,42] Therefore, healthcare professionals should not merely support patients to allow themselves to rest. Instead, they ought to encourage personalized physical activity and recommend rest and activity.

In conclusion, this study provided a group network of dynamically interconnected protective and perpetuating factors of fatigue in a group of cancer patients seeking psychological help. The network identified self-efficacy and allowing rest as key protective factors of CRF.

AUTHOR CONTRIBUTIONS

MS, RW and ML conceived the study. RW set up the study. RW collected the data with help from AR. AR analyzed the data with help from MS and RW. AR wrote the first draft with help from MS and incorporated the feedback from the other authors.

ACKNOWLEDGEMENTS

First, we would like to sincerely thank the patients for participating in our study. We would like to thank dr. Henriët van Middendorp for her guidance and valuable feedback on the thesis proposal and master thesis of the first author, which formed the basis of the present paper. Finally, we would like to acknowledge the VIOZ Foundation for their funding of the Refine 2.0 Implementation study.

CONFLICT OF INTEREST STATEMENT

We have no conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to cite this article: van Roozendaal AS, Schellekens MPJ, van Woezik RAM, van der Lee ML. Exploring the dynamic interconnectedness of protective and perpetuating factors of cancer-related fatigue. *Psychooncology*. 2023;1-9. https://doi.org/10.1002/pon.6235

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