Psychological coping factors associated with breast cancer-related fatigue: a systematic review of recent evidence for stages 0-III (2015-2021)

Michael Schaab

Faculty of Behavioral, Management and Social sciences (BMS), University of Twente

MSc Health Psychology and Technology

Dr. Christina Bode

Kim Wijlens MSc

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Abstract

Background and research objective: Cancer-related fatigue (CRF) is a common, distressing, and difficult to treat symptom for both breast cancer patients and survivors. This review investigates psychological coping factors, as defined in the Lazarus (1999) coping model, associated with breast CRF and how much evidence supports them.

Method: A comprehensive literature search was conducted in "PsycInfo", "Scopus", and "Pubmed" using variations of the keywords "Psychology", "Breast cancer", "Fatigue", and "Coping" using relevant keywords from the Lazarus (1999) model. Stage IV and/or metastatic breast cancer cases were excluded as well as articles discussing internal resources and predispositions. Seven articles with quantitative results published between January 2015 and April 2021 with a sample size of 100 or more breast cancer patients or survivors were included in the final sample. Sufficient inter-rater reliability between two raters was reached in the title, abstract and full-text scan.

Results: Sense of coherence and reassurance of worth were negatively associated with total breast CRF. Subjective/perceived stress, meaning focused coping, and breast-related stereotype threat were positively associated with total breast CRF. Reassurance of worth, nurturance, and optimism were negatively associated with mental fatigue. Optimism was also negatively associated with reduced motivation. All relationships were significant ($P<0.05$). No articles were found providing evidence for factors associated with severity and perceived interference, functioning, physical/sensory fatigue, and reduced motivation. A preliminary heuristic coping model was constructed based on the results.

Discussion and conclusion: This review provides a preliminary model that can provide insight into psychological coping factors associated with breast CRF, inspire further research and interventions, illustrate the gaps in current literature as well as the need for more research on the topic to solidify the model. Differing levels of evidence support each construct and are discussed in this review.

Keywords: Breast cancer, cancer-related fatigue, coping, psychology

Introduction

Breast cancer is one of the most prevalent illnesses and reported cases are rising. Breast cancer incidence data provided by Dutch cancer organizations report that, over the past four decades, the frequency of new cases has almost doubled in the Netherlands (NKR & IKNL, n.d.-a). Similar values are reported regarding prevalence (NKR & IKNL, n.d.-b). Mortality, however, has slightly declined in the same period and survivability rates have increased (NKR & IKNL, n.d.-c). While this statistic shows hope for survival of breast cancer, another problem is still prevalent (IKNL, n.d-a.). Nearly all women treated for breast cancer experience problems with their health after the treatment (IKNL, n.d-a.). There is a wide range of symptoms including fatigue, neuropathy, and problems with concentration and memory (IKNL, n.d-a). Knowledge about these symptoms is important to facilitate awareness and the organization of after-care (IKNL, n.d-a). It has become evident that more attention and knowledge about the side effects of cancer and its treatment is needed.

Fatigue has been recognized as one of the most prevalent and distressing side effects of cancer and cancer treatment (Lawrence et al., 2004, as cited in Bower et al., 2014). IKNL (n.d-b.) also state that for cancer patients in general fatigue is reported in all age groups and additionally has a chronic nature, hardly decreasing over time, with moderate to severe fatigue still being reported long after the cancer diagnosis (INKL, n.d.-b.). These factors make it increasingly clear that fatigue can become a severe problem for any patient regardless of age and can continue to be bothersome for long periods of time (INKL, n.d-b.). It also becomes increasingly evident that this problem is not just related to treatment when considering that after the breast cancer diagnosis more than two-thirds of those diagnosed report fatigue and more than a third of this group report quite a lot of fatigue (IKNL, n.d-b.). Fatigue is a common and distressing symptom related to breast cancer and its treatment and deeper insight into the problem and how to tackle it is needed.

Cancer-related fatigue (CRF)

CRF is defined by the NCCN 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” (NCCN, 2020). The experience of CRF has been described by breast cancer patients as an overwhelming exhaustion and lack of energy, unlike anything they have ever experienced, and being disproportionate to their activity or hours of sleep (Levkovich et al., 2019). Furthermore, this condition forces them to rest and lie down “until the storm passed”. This overwhelming fatigue that younger patients described as “Being imprisoned in the body of an 80-year-old” can lead to extreme feelings of helplessness and loss of control and quality of life in dealing with CRF (Levkovich et al., 2019). This problem is further

illustrated in studies finding strong correlations between the patient's subjective experience of fatigue and previously consistent data measures such as disruption of the patients sleep quality (Minton & Stone, 2012) indicating that, the subjective experience might disrupt much more than just the psychological state of the patient. CRF is a persistent, subjective symptom that causes a lot of distress, helplessness, and loss of control in breast cancer patients. Furthermore, it seems to extend beyond the psychological regarding its consequences, and a method of dealing with CRF is needed to ensure a good quality of life in breast cancer patients.

Treatment

Several treatment approaches have shown promise in alleviating breast CRF during and after treatment, such as interventions utilizing physical exercise or cognitive behavioural therapies (Buffart et al., 2014; Goedendorp et al., 2013). Thong et al., (2020) add that while interventions are available, there is no gold standard, and the current evidence base suggests exercise could be the best solution. Approaches revolving around physical activity however are not effective for all patients, and it heavily depends on what drives the patient's fatigue (Buffart et al., 2014).

Recent research has shown the promise of investigating the psychological factors behind breast CRF (Bootsama et al., 2020; Jiang et al., 2011a; Jiang et al., 2011b; Ruiz-Casado et al., 2021; Wang et al., 2013). A review on cancer-related fatigue (CRF) in breast cancer survivors underlined the importance of psychosocial factors such as depressive symptoms, lack of social support, social constraints, coping strategies, attitudes, and several others in influencing the development of fatigue (Ruiz-Casado et al., 2021). A meta-ethnography of qualitative research about patients suffering from chronic CRF found that dealing with the fatigue can lead patients to feel completely worthless, indecisive, and uncertain about their ability to cope with their fatigue (Bootsma et al., 2020). Moreover, while fatigue can be characterized by overwhelming bodily symptoms and/or sensations, the patients experience revealed a strong interconnectivity with mental symptoms. The perception of chronic CRF can additionally vary according to several psychological factors such as personality, vulnerability, coping mechanisms and how to utilize them in combatting stress, as well as the individual's general well-being, and social support (Bootsma et al., 2020). Jiang et al. (2011b) add to this with their findings that both objective and subjective social support, as well as utilization of social support were negatively correlated with breast CRF. In addition to this, several other studies on CRF found psychological characteristics of the patient, such as personality composition, and the patients coping profile to also have a positive influence on the breast cancer patients' fatigue (Jiang et al., 2011a; Wang et al., 2013). Research findings in the last ten years increase the consensus that psychological factors contribute significantly to breast CRF, and methods to utilize these factors could be a key part of finding a way to alleviate breast CRF.

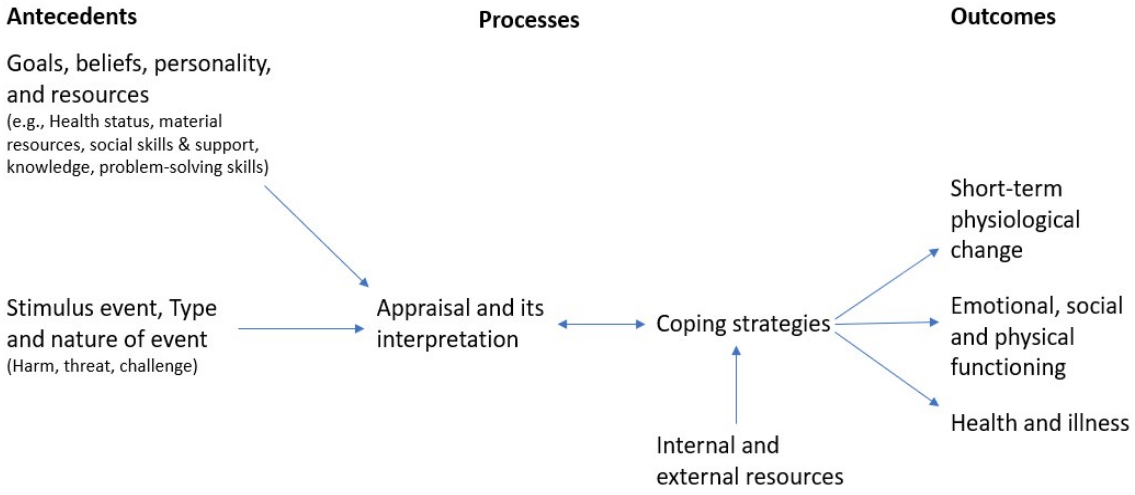
Psychological coping

CRF is not the only major source of psychological distress in the patient's life, with the breast cancer diagnosis itself already being a very stressful event, accompanied by several psychological symptoms, such as, shock, disbelief, denial, or despair (Stanton & Bower, 2015). Patients struggle to accept this new reality, and often perceive the diagnosis as a death sentence, in addition to worrying about the multitude of side-effects cancer and its treatment brings (Stanton & Bower, 2015). This issue does not stop after the diagnosis, and women with breast cancer often suffer from severe distress, anxiety, and depression during treatment and recovery (Schmid-Büchi et al., 2008). They also tend to feel limited in their role, fear the recurrence of breast cancer and suffer from overwhelming feelings of hopelessness and uncertainty (Schmid-Büchi et al., 2008). Ultimately, the role of psychology for breast cancer patients in being able to psychologically cope with their condition as well as their CRF is evident and needs to be considered in their treatment.

Coping is anything an individual does to minimize the effect of an actual, or perceived, stressor (Morrison & Bennett, 2016). Coping can target the 'objective' stressor or operate on an emotional level, aiming at reducing negative emotions (Morrison & Bennett, 2016). Coping tends to focus on the problem, emotions, or on ignoring or minimizing the threat of the stressor (Morrison & Bennett, 2016). The coping process (Figure 1) has been illustrated by Lazarus as made up of antecedents, processes, and outcomes (Lazarus, 1999, as cited in Morrison & Bennett, 2016). The individual's goals, beliefs, personality, and resources serve as psychological antecedents next to the actual stimulus event. These include factors such as knowledge, problem-solving skills, social skills & support but also non-psychological factors that can influence the process such as health status and material resources. The appraisal and interpretations of the stimulus event are affected directly by the antecedents in interaction with the individuals coping style and strategy. The coping strategies are then also again affected by the available internal and external resources to the individual's disposal. The outcomes resulting from this process are the individuals emotional, social, and physical functioning, health, and illness, as well as short-term physiological changes (Lazarus, 1999, as cited in Morrison & Bennett, 2016).

Figure 1

The coping process adapted from (Lazarus, 1999, as cited in Morrison & Bennett, 2016, p.342)



Interviews have shown that trying to cope with CRF on a cognitive and emotional level is important (Magnusson et al., 1999). Practicing acceptance and reducing the attention given to the feeling that fatigue is a problem is vital. This, however, was generally experienced as very difficult and thereby met with great frustration (Magnusson et al., 1999). A clearer picture of how to cope psychologically is necessary.

Recent studies on cancer patients in general found appraisals and cognitions about their disease such as their degree of acceptance, helplessness, and perceived benefits to be significantly associated with their fatigue and distress levels (Schellekens et al., 2020). The patient's coping style is also essential, such as helplessness relating to higher distress, whereas having a fighting spirit leading to reduced stress and increased QoL (Lashbrook et al., 2018). Further research strengthens this relationship with coping responses also often termed as 'Fighters' and 'Surrenders' depending on their attitude towards illness (Penner et al., 2020). Patients with a more positive, fighting, attitude tend to have better physical, emotional, and cognitive conditions in their social relations and an increased QoL (Penner et al., 2020). Acceptance behaviours and shifts in attention continue to be linked to positive psychological adjustment and additionally utilizing adaptive cognitive coping strategies rather than maladaptive ones led to the strongest psychological adjustment (Cheng et al., 2019; Li et al., 2017). Moreover, the flexibility of the patients coping strategy has been found to be important, and all coping strategies vary in usefulness depending on the context (Brannon & Feist, 2009; Lashbrook et al., 2018). These results indicate that having a comprehensive picture of how to psychologically cope with CRF could be an essential step in increasing patient well-being, quality of

life, and reducing psychological distress and related symptoms, due to the rising consensus, that psychological coping can be beneficial for breast CRF, as well as CRF in general.

Utilizing psychological coping to break the cyclic nature of CRF

Not only is psychological coping a potential solution for alleviating breast CRF but could even be considered essential due to the cyclic nature of breast CRF. A lot of psychological consequences of CRF can also be considered risk factors for breast CRF. These include low general well-being and poor mental health, but also baseline psychological distress, depression, a tendency towards pessimism and attention towards symptoms and the 'catastrophizing' of them (Abrahams et al., 2018; Thong et al., 2020). Fear is also an important factor (Thong et al., 2020), and can be facilitated by psychological factors such as low optimism and depressive symptoms (Stanton & Bower, 2015). Thereby, it seems individuals suffering from CRF could find themselves stuck in a cycle of psychological distress, with the consequences of their fatigue further increasing their CRF. This leads to the conclusion, that psychological coping with CRF could be an essential component of reducing breast CRF. However, so far, a comprehensive overview of psychological coping factors related to breast cancer fatigue in patients and survivors of breast cancer has not been established. Therefore, the question is asked: "Which psychological coping factors are associated with breast cancer-related fatigue and how much evidence supports the association?".

Method

Search plan

A comprehensive literature search was conducted utilizing the databases 'PsycInfo', 'PubMed', and 'Scopus'. The Search string (Table 1) consisted of the concepts 'Psychology', 'Breast cancer', 'Fatigue', as well as synonyms of fatigue, and variations of the concept 'Coping' as defined in Lazarus (1999).

Table 1

Search string

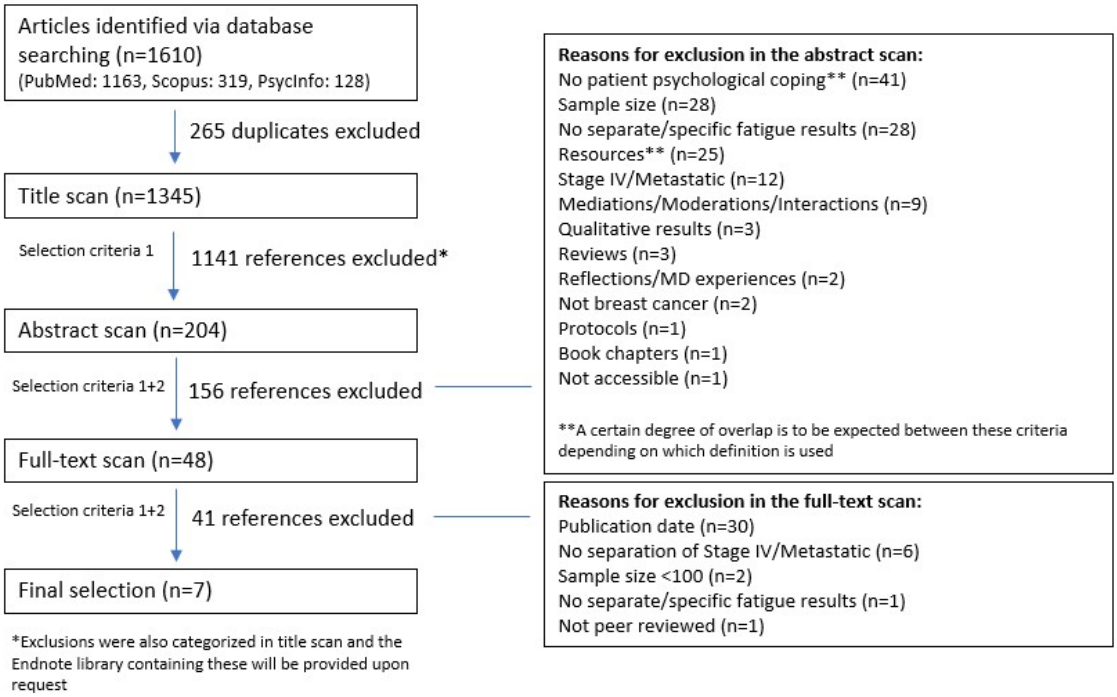
Concept	Syntax	
Psychology	psycholog*	AND
Breast cancer	(breast and cancer)	AND
Fatigue	(fatigu* OR exhaust* OR tire OR tiring OR tired)	AND
Coping (Lazarus, 1999)	(coping OR cope OR coped OR personality OR personalities OR goal* OR belief* OR believ* OR resource* OR apprais* OR interpret*)	

Study selection criteria

Identified articles need to fulfill the in- and exclusion criteria to be selected. Initially, duplicates are removed and then articles are excluded by their title. Corrections are included if the original article is as well. If they cannot be excluded by their title, they are marked unclear and included in the abstract scan. The research started broad (see selection criteria 1), but due to an overwhelming amount of literature to be read in full, a stricter selection was made in the abstract scan (see selection criteria 2). Finally, all articles still included after the abstract scan were included for the full-text scan. This process along with descriptions of exclusion in each phase are illustrated in figure 2.

Figure 2

Flow-chart of the study selection process



Selection criteria 1

The first selection criteria were applied in the title scan and required articles to not meet any of the following exclusion criteria and meet all inclusion criteria.

Exclusion criteria 1

Articles that meet the following criteria are excluded:

- All falsely included articles that do not refer to the topic of breast cancer
- Articles with a different predictor (not psychological coping as defined in Lazarus (1999)) and/or a different outcome (not breast CRF)
- Articles referring to behavioral lifestyle (Physical activity, yoga, massage, meditation, etc.) and medicine, biology, or treatment (Biological processes, drugs, surgery, etc.)
- Articles referring to the experience, perceptions, prevalence, general (care) needs or concerns, and/or categorization of fatigue rather than coping
- Articles referring to screening, assessment, or evaluation rather than the alleviation of fatigue
- Articles focusing solely on the caregivers/family/friends etc.

- Articles discussing nursing, care, or service and not how the patient can cope
- All evaluations and/or comparisons of specific interventions, therapies, rehabilitation programs, applications etc.
- Articles discussing research methods, as well as ethical reviews and papers
- Literature reviews and meta-analyses of all kinds

Inclusion criteria 1

Articles need to fulfill all the following criteria to be included:

- The article needs to discuss breast cancer-related fatigue
- The article needs to have specific mention of how the patient or survivor of breast cancer can psychologically cope with fatigue or mention how certain psychological factors are associated with fatigue
- The article needs to discuss theoretical evidence rather than the general efficacy of practical applications
- The article is required to be in English, Dutch, German, French, or Russian due to the linguistic ability of the research team
- The article needs to be publicly available, or accessible via the University of Twente library

Selection criteria 2

This research was conducted in the context of a master thesis, and following the completion of the abstract scan, it became evident that there is a broad range of literature available on this subject matter, and there would be too many full-text articles to be read and completed in a timely manner. The full library with all initial articles, and those kept following each scanning stage will be provided upon request by the researchers. Towards the aim of providing a comprehensive analysis in a timely manner, a selection was made to include a specific section of the available literature. Thereby, a second set of study selection criteria was additionally implemented to the first set of criteria.

Exclusion criteria 2

Articles that meet the following criteria are excluded:

- Articles regarding breast cancer patients with stage IV and/or metastatic breast cancer as defined by the American Joint Committee on Cancer (National Cancer Institute, n.d.). The reason why specifically this stage of disease was excluded was due to Vilhauer's (2011) findings that women with metastatic breast cancers felt marginalized, helpless, and silenced when visiting mixed-stage support groups. Their experiences in general were very different

than those of women with primary breast cancer who were afraid to face the idea of metastasis (Vilhauer, 2011). Therefore, it seems feasible to assume that information relevant for coping in the earlier stages might not be as relevant for later stages and a better solution might be to only look at results from specific stages. Stage IV cancer as defined by the American Joint Committee on Cancer typically involves the greatest tumor involvement and/or distant metastasis, which is directly invading another organ or viscera, major nerves, arteries, or bone (National Cancer Institute, n.d.). By excluding one of the four stages from this review, ensuring a smaller sample of literature, a timely completion was possible.

- Articles discussing cancer patients in general that include breast cancer patients, but do not give separate results for breast cancer patients
- The decision was made to narrow down which elements of the Lazarus (1999) model would be used for this review. The patients' internal resources, including general global health and quality of life, functioning, as well as psychopathologies, trauma, anxiety, depression, and mood, and related disorders were excluded. It is worth noting however, that perceived/subjective stress is treated as an element of the appraisal and interpretation, and thereby is not excluded as an internal resource. The reason for this was firstly to ensure that a feasible amount of literature was achieved for the full-text scan due to there being a vast amount of literature that fits within the frame of the Lazarus (1999) model. The reason why these specifically were excluded is because they were assumed to be harder to influence and could be seen more as predispositions that influence CRF rather than factors relevant for an individual to psychologically cope with CRF.
- Articles with fatigue as a predictor, or without separate and specific fatigue results, meaning that if fatigue is mentioned but no results regarding coping with it are reported
- Articles where fatigue or coping is the mediator, moderator, or interaction in a different context rather than predictor and outcome
- Due to a small sample of qualitative results, the decision was made to provide a solely quantitative analysis, thereby qualitative results are also excluded
- The literature is a book (chapters), study protocol, reflective paper, or MD experience
- All articles published prior to January 2015 and after April 2021 were excluded in the full-text scan

Inclusion criteria 2

All articles that are not excluded, will be included if they have a sample size of 100 or higher. This refers to the amount of participating breast cancer patients, thereby, if there are 50 patients and 50 healthy controls, the article is excluded.

Inter-rater reliability

Inter-rater reliability (IRR) was conducted to ensure reliable and reproducible results. This was done with PhD Candidate Kim Wijlens MSc at the University of Twente. Articles were exported from Endnote X9 into Microsoft Excel and randomized via the RAND function, by assigning random numbers and sorting by lowest numbers, exporting the lowest 10% back into the shared Endnote X9 library, which is then scanned by Kim. Screenshots and Microsoft Excel documents of the entire process are available and will be provided upon request. In the title scan an IRR of 86% was achieved, and all disagreements were discussed. Some articles could be agreed upon without clarification of the wording of the method section, and several other could not be agreed upon based on the title and required a re-scan of all titles in the category from the primary researcher to ensure their abstracts would be read. Using keywords from the articles that were disagreed on, roughly 300 titles were re-scanned by the primary researcher and 32 additional articles were included into the abstract scan. The remaining titles were then included into the abstract scan and the specific list can be provided upon request. The same process was conducted in the abstract with an initial IRR of 81%, which was then also brought to full agreement via discussion, adjustment of the methods section, re-scan of around 50 abstracts like those that were disagreed on by the primary researcher of which four additional articles were additionally included for the full-text scan. In the full-text scan, an IRR of 100% was reached.

Results

The final selection from the systematic review resulted in seven articles. The articles are presented based on their publication date below (Table 2-3). This review aimed at finding psychological coping factors associated with breast CRF in stage 0-III cases in accordance with the Lazarus (1999) coping model, and how much evidence supports them. Following the Lazarus model, excluding internal resources, the results would be structured in three groups: 1: goals, beliefs, personality, resources; 2: appraisal and its interpretation; and 3: coping strategies. However due to overlap between the first and third group, these were grouped together. Thereby, table 2 reports psychological coping strategies and beliefs and table 3 reports stress appraisals and interpretations. Initially, Table 2 was meant to also include results regarding personality and goals, however no studies discussing these in relation to breast CRF were found.

The first included study here (see Table 2; Study 1), a cross sectional descriptive study with a Norwegian population, aimed at evaluating the effect of social support in 160 early stage (I-II) breast cancer patients undergoing active curative treatment on cancer-related fatigue (Sørensen et al., 2020). They measured CRF with the Norwegian version of the fatigue questionnaire (FQ), measuring

physical (PF) and mental fatigue (MF). Social support was measured with the Norwegian version of the Social Provisions Scale (SPS), with the subscale's 'attachment', 'social integration', 'reassurance of worth', and 'nurturance' (Sørensen et al., 2020).

Next, a prospective multicentre cohort with longitudinal follow-up with a French population was included (see Table 2; Study 2) (Person et al., 2020). They discussed factors associated with the evolution of fatigue dimensions for breast cancer patients during the 2 years after surgery, measured with the French version of the Multidimensional Fatigue Inventory (MFI-20), containing the four dimensions: General and physical fatigue, mental fatigue, reduced activities, and reduced motivation. They investigated several factors, including the psychological coping factor optimism, measured with the life orientation test (LOT) in French. Their sample consisted of 459 stage I-IIIA newly diagnosed breast cancer patients having undergone breast surgery (Person et al., 2020).

The third article (see Table 2; Study 3) that was included was a cross-sectional descriptive evaluation of a randomized controlled trial in a Swedish population including 240 stage I-IIIA breast cancer patients scheduled for adjuvant chemotherapy (Hiensch et al., 2020). The psychological coping factor here is the patients sense of coherence (SOC), measured with the Swedish version of Antovosky's short 13-item questionnaire (SOC-13) including comprehensibility, manageability, and meaningfulness of one's experience of life. The SOC-13 was used to stratify groups and thereby investigate differences in cancer-related fatigue, measured with the Swedish version of the piper fatigue scale (PFS). The fatigue scale measures the four dimensions: behaviour/daily life, emotional/affective, sensory/physical, and cognitive fatigue (Hiensch et al., 2020).

The next included article (see Table 2; Study 4) discussed the symptom cluster of emotional distress, fatigue, and cognitive difficulties in a sample of 170 stage I-III breast cancer survivors one to twelve months post-surgery in an Israeli population (Levkovich et al., 2018). The variables of interest for this research concerning section 2 are emotional control, measured with the emotional control subscale for controlling depressed mood (CECS) and meaning-focused coping using the meaning in life questionnaire (MLQ). The study is of cross-sectional descriptive nature, and fatigue is measured with the fatigue symptom inventory (FSI), measuring severity and perceived interference. Questionnaires were administered in Hebrew and Arabic (Levkovich et al., 2018).

Finally, the last article in this section (see Table 2; Study 5) aimed at investigating breast-cancer related stereotype threat (BRST) and its connection to cancer-related symptoms, such as fatigue (Li et al., 2017). The study is of cross-sectional descriptive nature with a Chinese population, and measures fatigue with the Chinese version of the 13-item Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F) measuring functioning and fatigue. The sample comprises 131

stage I-III breast cancer patients with postmastectomy. BRST is measured with a yes/no question: "Do you think that disfigurement of your breast will decrease your womanliness?" (Li et al., 2017).

Table 2

Study characteristics of included studies for psychological coping factors and beliefs

NR*	Title; Author; Year	Study design; Population	Sample	CRF conceptualization and measurement	Outcomes
1	Social support in early-stage breast cancer patients with fatigue (Sørensen et al., 2020)	Cross-sectional descriptive study; Norwegian population	Stage I-II breast cancer patients undergoing active curative treatment (n=160)	Fatigue questionnaire (FQ), measuring physical (PF) and mental fatigue (MF)	Social support (SPS), measuring 'attachment', 'social integration', 'reassurance of worth', and 'nurturance'
2	Factors of the evolution of fatigue dimensions in patients with breast cancer during the 2 years after surgery (Person et al., 2020)	Prospective multicenter cohort with longitudinal follow-up; French population	Stage I-IIIA newly diagnosed breast cancer patients having undergone breast surgery (n=459)	Multidimensional Fatigue Inventory (MFI-20), measuring four dimensions: general and physical fatigue, mental fatigue, reduced activities, and reduced motivation	Optimism using the life orientation test (LOT)
3	Sense of coherence and its relationship to participation, cancer-related fatigue, symptom burden, and quality of life in women with breast cancer participating in the OptiTrain exercise trial (Hiensch et al., 2020)	Cross-sectional descriptive evaluation of a randomized controlled trial; Swedish population	Stage I-IIIA breast cancer patients scheduled for adjuvant chemotherapy (n=240)	Piper fatigue scale (PFS), measuring four dimensions: behavior/daily life, emotional/affective, sensory/physical, and cognitive	Sense of coherence (SOC) using Antonovsky's short 13-item questionnaire (SOC-13)
4	Symptom cluster of emotional distress, fatigue and cognitive difficulties among young and older breast cancer	Cross-sectional descriptive study; Israeli population	Stage I-III breast cancer survivors one-twelve months post-	Fatigue symptom inventory (FSI), measuring severity and perceived interference	The Emotional Control Subscale for controlling depressed mood (CECS); Meaning-focused coping using

NR*	Title; Author; Year	Study design; Population	Sample	CRF conceptualization and measurement	Outcomes
	survivors: The mediating role of subjective stress (Levkovich et al., 2018)		chemotherapy (n=170)		the Meaning in Life Questionnaire (MLQ
5	Breast-related stereotype threat contributes to a symptom cluster in women with breast cancer (Li et al., 2017)	Cross-sectional descriptive study; Chinese population	Stage I-III breast cancer patients minimum one week post (modified) radical mastectomy (n=131)	13-Item Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F), measuring functioning and fatigue	Breast-related stereotype threat (BRST) measured with a yes/no question: "Do you think that disfigurement of your breast will decrease your womanliness"

*Studies are assigned numbers based on publication date that are used in the following results

Next, table 3 summarizes the characteristics of studies included that discuss stress appraisals and/or interpretations. Firstly, a study already mentioned in the previous section (see Table 2; Study 4) (Levkovich et al., 2018), also was relevant here as it also measured subjective stress in their sample via the subjective stress scale (see Table 3; Study 4).

The second selected study (see Table 3; Study 6) aimed at researching depressive symptoms and inflammation as independent risk factors for fatigue in breast cancer survivors and measured their perceived stress with the Perceived Stress Scale (PSS) (Xiao et al., 2017). Fatigue was measured with the MFI-20, revolving around the four dimensions: general and physical fatigue, mental fatigue, reduced activities, and reduced motivation and a single item questionnaire capturing severity according to National Comprehensive Cancer Network (NCCN) guideline Version 2.2015. The study was of cross-sectional nature with an American population of 111 stage 0-III breast cancer patients post breast cancer surgery who received whole breast radiotherapy (Xiao et al., 2017).

The third study (see Table 3; Study 7) was a cross-sectional descriptive study investigating the association of fatigue with perceived stress in Chinese women with breast cancer (Ho et al., 2015). The sample comprised 133 stage I-III patients awaiting adjuvant radiotherapy. Fatigue was measured with the Chinese brief fatigue inventory, measuring severity and daily functioning. Stress was measured with the Chinese Perceived Stress Scale-10 (PSS-10) (Ho et al., 2015).

Table 3

Study characteristics of included studies for stress appraisals/interpretations

NR*	Title; Author; Year	Study design; Population	Sample	CRF conceptualization and measurement	Outcomes
4	Symptom cluster of emotional distress, fatigue and cognitive difficulties among young and older breast cancer survivors: The mediating role of subjective stress (Levkovich et al., 2018)	Cross-sectional descriptive study; Israeli population	Stage I-III breast cancer survivors one to twelve months post-chemotherapy (n=170)	Fatigue symptom inventory (FSI), measuring severity and perceived interference	Subjective Stress Scale
6	Depressive symptoms and inflammation are independent risk factors of fatigue in breast cancer survivors (Xiao et al., 2017)	Cross-sectional descriptive study; American population	Stage 0-III breast cancer patients post breast cancer surgery who received whole breast radiotherapy (n=111)	MFI-20, measuring four dimensions: general and physical fatigue, mental fatigue, reduced activities, and reduced motivation and a single item questionnaire capturing severity according to National Comprehensive Cancer Network (NCCN) guideline Version 2.2015	Perceived Stress Scale (PSS)
7	Association of Fatigue with Perceived Stress in Chinese Women with Early Stage Breast Cancer Awaiting Adjuvant Radiotherapy (Ho et al., 2015)	Cross-sectional descriptive study; Chinese population	Stage I-III breast cancer patients awaiting adjuvant radiotherapy (n=133)	Brief fatigue inventory, measuring severity and interference on daily functioning	Perceived Stress Scale-10 (PSS-10)

*Studies are assigned numbers based on publication date that are used in the following results

Next, because there are many differences between how fatigue is measured, in the following first the results for total/general fatigue are presented. In this section the composition of fatigue for each study and which measurement device was used is reported. Next, based on the order in which they

were initially found, a section for each sub-scale that was measured in the sample of literature is reported. The results of table 2 and 3 are now combined. Tables 4-8 summarize the results for fatigue in a concise and simplified way. The full tables with the exact numbers can be found in appendix 1. Significance was considered at $p<0.05$. Associations are considered positive when they increase fatigue and decrease functioning.

Total/General fatigue

In study one of Sørensen et al., (2020) no significant associations were found in a linear regression analysis between general social support and total fatigue, conceptualized as physical and mental fatigue (see Table 4; Study 1). Social support was measured with the SPS and measures the perceived level of attachment in the patient's social environment, the perceived level of reassurance of worth the patients received, how much nurturance they felt, and the level of perceived social integration of the patients. The only significant subscale was the one regarding 'Reassurance of worth' which had a significant negative association with total fatigue (B: -0.54; 95% CI: -1.03; -0.41; p:0.034) (Sørensen et al., 2020).

The second study collected data ten times over the course of two years resulting in three fatigue trajectories for total fatigue, composed from general and physical fatigue in their research, for newly diagnosed stage I-IIIA breast cancer patients having undergone breast surgery in a French sample. The three trajectories identified were: "No fatigue (19.2%)", "moderate, transient increasing fatigue (45,3%)" and "severe, transient increasing fatigue (35.5%)" (Person et al., 2020). No significant associations were found in a multivariate multinomial logistic regression analysis of factors associated with total fatigue for the no fatigue trajectory compared to the moderate or severe fatigue trajectories regarding optimism (see Table 4; Study 2) (Person et al., 2020).

In the third study, groups were stratified by SOC (see Table 4; Study 3) (Hiensch et al., 2020). SOC in their study was composed of the comprehensibility, manageability, and meaningfulness of one's experience of life. They found significant differences between the groups, with the strong SOC group (n=81) having less mean total fatigue than participants with weak-normal SOC (n=125) (Weak-normal: 3.0 ± 3.0; Strong: 1.8 ± 2.6; p: <0.01). Total fatigue was conceptualized as behaviour/daily life fatigue, emotional/affective fatigue, sensory/physical fatigue, and cognitive fatigue (Hiensch et al., 2020).

In the fourth study several bivariate associations between variables were reported including the significant positive associations of subjective stress (.46; $p<.001$) and meaning-focused coping (.17; $p<0.05$) with total fatigue, while the association of total fatigue with emotional control was non-significant (see Table 4; Study 4). In this study, total fatigue was conceptualized as severity and perceived interference (Levkovich et al., 2018).

Next, the fifth study (Li et al., 2017) with total fatigue composed of functioning and fatigue, compared groups with or without BRST based on the median, 25th and 75th percentile. They found significantly higher functioning, and thereby lower fatigue in the non-BRST group (see Table 4; Study 5) (Non-BRST: 40(34;47); BRST: 36(29;43); p:0.012). The significant association was also found to be positive in a multivariate logistic regression (OR:2.53; 95% CI:1.11; 5.81; p:0.028) (Li et al., 2017).

The sixth study also provided significant positive bivariate associations of subjective stress and total fatigue (see Table 4; Study 6), composed of severity and perceived interference (.633; $p<0.01$) (Xiao et al., 2017). The association was no longer significant in the multivariate model. In a mediation model subjective stress had a significant positive direct effect on fatigue when depressive symptoms were not in the model (B:1.30; $p<0.0001$) (Xiao et al., 2017).

Finally, the seventh study (Ho et al., 2015) conceptualized total fatigue as severity and perceived interference and found a significant positive association with perceived stress (0.43; $p<0.01$). A significant positive association was also found in a multiple regression (B(SE): 0.23 (0.04); 95% CI:0.16-0.30; Standardized B: 0.48; Adjusted R^2: 0.034; $p<0.001$).

Table 4

Summary of results: Total/general fatigue

Study	Fatigue composition	Evidence	
1 (Sørensen et al., 2020)	Physical + Mental	**Concept**	**Association**
		Social Provisions Scale (SPS) total	Non-significant
		Attachment	Non-significant
		Reassurance of worth	Negative
		Nurturance	Non-significant
		Social integration	Non-significant
		N=160	
		Level of evidence: Univariate linear regression analysis	
2 (Person et al., 2020)	General + Physical	**Concept**	**Association**
		Optimism	Non-significant
		N=346	
		Level of evidence: Multivariate multinomial logistic regression analysis	

Study	Fatigue composition	Evidence
3 (Hiensch et al., 2020)	Behavior/daily life + Emotional/affective + Sensory/physical + Cognitive	**Concept** / **Association** Sense of Coherence (SOC) / Negative N=206 Level of evidence: Stratified groups
4 (Levkovich et al., 2018)	Severity + Perceived interference	**Concept** / **Association** Subjective stress / Positive Emotional control / Non-significant Meaning-focused coping / Positive N=170 Level of evidence: Bivariate associations
5 (Li et al., 2017)	Functioning + Fatigue	**Concept** / **Association** Breast-related stereotype threat (BRST) / Negative N=131 Level of evidence: Group comparison and multivariate logistic regression
6 (Xiao et al., 2017)	Severity + Perceived interference	**Concept** / **Association** Subjective stress / Mixed results* N=111 Level of evidence: Bivariate associations, multivariate model, and mediation model *Bivariate associations showed a significant positive association. The association between subjective stress and fatigue was non-significant in the multivariate model. In a mediation model subjective stress had a significant direct positive effect on fatigue when depressive symptoms were not in the model

Study	Fatigue composition	Evidence	
7 (Ho et al., 2015)	Severity + Perceived interference	**Concept**	**Association**
		Perceived stress	Positive
		N=133 Level of evidence: Correlations and multiple regression	

Physical fatigue

Sørensen et al. (2020) investigated the association between physical fatigue and the SPS (see Table 5). The SPS measures the perceived level of attachment in the patient's social environment, the perceived level of reassurance of worth the patients received, how much nurturance they felt, and the level of perceived social integration of the patients. The results of a univariate linear regression analysis of this sample indicate that, no significant associations exist between the SPS concepts, as well as the scale in total, and physical fatigue (Sørensen et al, 2020).

Table 5

Summary of results: Physical fatigue

Study	Evidence	
1 (Sørensen et al., 2020)	**Concept**	**Association**
	Social Provisions Scale (SPS) total	Non-significant
	Attachment	Non-significant
	Reassurance of worth	Non-significant
	Nurturance	Non-significant
	Social integration	Non-significant
	N=160 Level of evidence: Univariate linear regression analysis	

Mental/Cognitive fatigue

No significant associations were found in a univariate analysis between general social support as measured by the SPS and mental fatigue in the first study (see Table 6; Study 1) (Sørensen et al., 2020). The SPS measures perceived levels of attachment in the patient's social environment, the perceived level of reassurance of worth the patients received, how nurtured they felt, and their perceived level of social integration. All subscales besides social integration independently were

significantly negatively associated with total fatigue (attachment: B: -0.54; 95% CI: -1.03; -0.41; p: 0.034, reassurance of worth: B: -0.54; 95% CI: -1.03; -0.41; P:0.034, nurturance: B: -0.54; 95% CI: -1.03; -0.41; p:0.034). Following multivariate analysis with these significant sub-scales, reassurance of worth (B: -0.54; 95% CI: -1.03; -0.41; p:0.034) and nurturance (B: -0.54; 95% CI: -1.03; -0.41; p:0.034) remained significant (Sørensen et al., 2020).

In the second study (Person et al., 2020) four fatigue trajectories were found for mental fatigue: "No fatigue (20.5%)"," low, transient fatigue (LTI) (38.3%)", "moderate, transient increasing fatigue (MTI) (34.6%)" and "severe, transient increasing fatigue (STI) (6.5%)". The results of a multivariate multinomial logistic regression analysis of factors associated with fatigue (see Table 6; Study 2) found significant negative associations with optimism for all fatigue trajectories in comparison to the no fatigue trajectory (LTI vs no fatigue: OR: 0.97; 95% CI: 0.95; 0.99; p: 0.008; MTI vs no fatigue: OR: 0.96; 95% CI: 0.94; 0.99; p: 0.003; STI vs no fatigue: OR: 0.93; 95% CI: 0.89; 0.97; p: 0.0009) (Person et al., 2020).

Table 6

Summary of results: Mental/cognitive fatigue

Study	Evidence	
1 (Sørensen et al., 2020)	**Concept**	**Association**
	Social Provisions Scale total	Non-significant
	Attachment	Mixed results*
	Reassurance of worth	Negative
	Nurturance	Negative
	Social integration	Non-significant
	N=160	
	Level of evidence: Multivariate linear regression analysis	
	*A negative association was found in a univariate linear regression, however in the multivariate regression the association was no longer significant	
2 (Person et al., 2020)	Low, transient increasing fatigue vs. no-fatigue	
	Concept	**Association**
	Optimism	Negative

Study	Evidence
	Moderate, transient increasing fatigue vs. no-fatigue **Concept** / **Association** Optimism / Negative Severe, transient increasing fatigue vs. no-fatigue **Concept** / **Association** Optimism / Negative N=344 Level of evidence: Multivariate multinomial logistic regression analysis

Reduced activities

Four trajectories were found for reduced activities in the second study (Person et al., 2020): "No reduced (10.9%)"," low, transient decreasing activities (LTD) (19.6%)", "moderate, transient decreasing activities (MTD) (51.8%)" and "severe, transient decreasing activities (STD) (17.6%)". No significant associations were found in a multivariate multinomial logistic regression analysis of factors associated with reduced activities for either trajectory for variables of interest compared to the no reduced activities trajectory (see Table 7) (Person et al., 2020).

Table 7

Summary of results: Reduced activities

Study	Evidence
2 (Person et al., 2020)	Low, transient decreasing activities vs. no-reduced **Concept** / **Association** Optimism / Non-significant Moderate, transient decreasing activities vs. no-reduced **Concept** / **Association** Optimism / Non-significant

Study	Evidence
	Severe, transient decreasing activities vs. no-reduced **Concept** / **Association** Optimism / Non-significant N=332 Level of evidence: Multivariate multinomial logistic regression analysis

Reduced motivation

Five trajectories were found for reduced motivation in the second study (Person et al., 2020): "No reduced (17%)", "decreasing (16.6%)", "increasing (11.5%)", "moderate, transient decreasing motivation (MTD) (38.8%)" and "severe, transient decreasing motivation (STD) (16.1%)". The results of a multivariate multinomial logistic regression analysis of factor associated with fatigue found significant negative associations with optimism for the STD trajectory in comparison to the no reduced motivation trajectory (see Table 8) (OR: 0.94; 95% CI: 0.90; 0.97; p: <0.0001).

Table 8

Summary of results: Reduced motivation

Study	Evidence
2 (Person et al., 2020)	Moderate, transient decreasing motivation vs. no reduction **Concept** / **Association** Optimism / Non-significant Severe, transient decreasing motivation vs. no reduction **Concept** / **Association** Optimism / Negative Decreasing motivation vs. no reduction **Concept** / **Association** Optimism / Non-significant

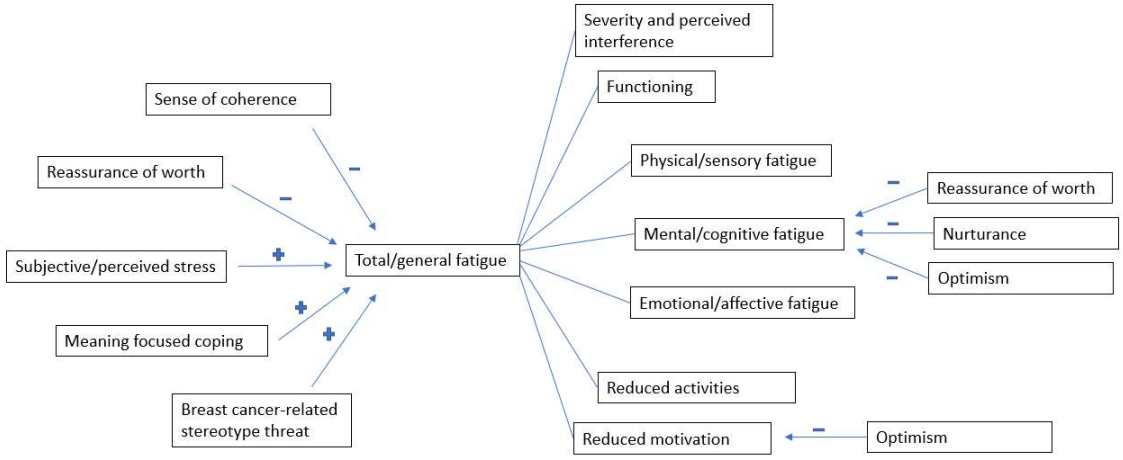
Study	Evidence
	Increasing motivation vs. no reduction **Concept** / **Association** Optimism / Non-significant N=328 Level of evidence: Multivariate multinomial logistic regression analysis

Preliminary model

The significant results from the seven included studies have been used to construct a preliminary heuristic breast-cancer related fatigue coping model (see Figure 3). Firstly, all significant results that were found are visualized. Next, the different conceptualizations used for fatigue, identified by the questionnaires used in each of the studies are added into the model, as well as all significant results that were found for each breast CRF sub-dimension. The arrows represent the direction of the association. A negative association (-) relates to increased fatigue and decreased functioning. A positive association (+) indicates decreased fatigue and increased functioning in association with the concept. It is to be noted that the heuristic model does not visualize the level of evidence, which can be found in the respective tables (see Tables 4-8).

Figure 3

Preliminary heuristic breast-cancer related fatigue coping model



Note: All relationships are significant at P<0.05

Discussion

The aim of this review was to identify psychological coping factors related to breast CRF and to document the level of evidence for the association. To do so, the Lazarus (1999) coping model was utilized to inform the search strategy and structure the results. Towards the later stages of the research fatigue and the sub-dimensions were used to structure the results instead, because it was seen as more practical.

The first notable result of this study was the fact that, a large amount of literature was found on the topic, leading to the necessity for this review to be narrowed. Thereby in this systematic review, a focus was made on personality factors, beliefs, goals, coping strategies and mechanisms, as well as appraisals and interpretations, including those related to stress i.e., subjective/perceived stress in the context of breast CRF research. To this end, several psychological coping factors were identified, and a preliminary coping model was constructed for breast CRF (see Figure 3). Stage IV and/or Metastatic cases were excluded, and secondly, predispositions such as psychopathologies, anxiety, depression, global QoL, psychological general health and functioning, and mood (disorders) were excluded in this review and the literature should be reviewed to get a more comprehensive picture of psychological coping for breast CRF.

Strong and consistent evidence

Subjective or perceived stress in relation to breast CRF was the most prevalent factor in this research, with three studies providing evidence regarding this relationship. All three studies report significant positive bivariate associations between the constructs, and in Ho et al. (2015), additionally significant positive multiple regression results strengthen the relationship. Xiao et al.'s (2017) study could not replicate these results in their multivariate model, however in a mediation model subjective stress had a significant positive direct effect, when depressive symptoms where not in the model. These results are in line with previous research which also found certain appraisals such attention towards symptoms and the catastrophizing of them, as well as baseline psychological distress and depression to be risk factors associated with CRF (Abrahams et al., 2018; Thong et al., 2020). More attention should be given to the interplay between subjective/perceived stress and depressive symptoms since this review excluded articles related to depression, however in one of the articles discussing subjective stress depressive symptoms had a important role to play on the influence of subjective stress on breast CRF. Regardless, the conclusion can be reached that subjective or perceived stress has a role to play in the psychological coping process with breast CRF and higher levels of subjective or perceived stress can be expected to associate with higher levels of breast CRF.

Despite there being only one study in this sample discussing it, the evidence for optimism is compelling, due to the longitudinal nature of the study with ten points of data collection over the course of two years (Person et al., 2020). To our knowledge this could be one of the most comprehensive studies about breast CRF and optimism. Comparing those participants who did not report mental fatigue with those reporting either low, moderate, or severe courses of mental fatigue, optimism significantly lowered the odds of having higher levels of mental fatigue. Thereby, regardless of the severity of mental fatigue, optimism seems to be a valuable psychological coping factor that can reduce breast CRF. Optimism also lowered the odds for experiencing a severe, decreasing, trajectory of reduced motivation. These results were not found for reduced activities or total fatigue, composed of general and physical in Person et al.'s (2020) research, indicating that other mechanisms might be at play for those dimensions of breast CRF. In contrast to these findings, however, is Jiang et al.'s (2011a) findings of correlations between optimistic coping and physical and emotional fatigue and not cognitive fatigue. Person et al. (2020) did not measure emotional fatigue, however it is surprising that in one study cognitive fatigue was insignificant, whereas physical was, and in the other study mental fatigue was significant. Regarding the findings about physical fatigue, in Person et al.'s (2020) research their conceptualization of physical fatigue was part of total fatigue, rather than a separate physical fatigue measurement, which could explain these results. It is also surprising that total fatigue was insignificant considering a plethora of research on breast CRF and CRF in general underlining the negative influence of pessimism, catastrophizing, and the protective potential of optimistic coping for total breast CRF (Abrahams et al, 2018; Jiang et al., 2011a; Thong et al., 2020). Nevertheless, despite there still being some confusion which elements and how exactly are influenced by optimism, it is clear that optimism is an important factor when coping with breast CRF psychologically.

No previous studies to our knowledge investigated reassurance of worth (as a social support sub-dimension) in the context of breast CRF, however Sørensen et al.'s (2020) research showed promising results for this construct as being a psychological coping factor associated with less breast CRF for both total, as well as less mental fatigue in a multivariate regression. Research by Jiang et al. (2011a) found that a support seeking coping style was negatively correlated with emotional and physical fatigue, thereby strengthening the relationship between coping factors related to social support as being helpful in reducing breast CRF. Jiang et al. (2011a), however did not find a significant correlation between the coping style and cognitive fatigue which might illustrate differences between support seeking coping styles and reassurance of worth. In a further study by Jiang et al., (2011b), there were negative correlations between breast CRF and social support, subjective support, objective support, and utilization of support. Next, another aspect of social

support, nurturance, was also identified as a psychological coping factor associated with less breast CRF, however different from reassurance of worth, it was only significant for mental fatigue. Again, to our knowledge no previous studies specifically discussed nurturance in the context of breast CRF, and this study can provide a basis for further research in the context of mental fatigue. In summary, it does seem that social support is an important psychological coping factors for breast CRF, and further research should expand upon the understanding of which aspects of social support affect which dimensions of breast CRF.

Weak and surprising results

The evidence for SOC being associated with less breast CRF comes from a study stratifying groups by their level of SOC (weak-normal vs. strong), and statistically testing the difference of their fatigue ratings, which was found to be significant (Hiensch et al., 2020). While this result is not enough to fully support this relationship, previous studies have found, that SOC significantly predicts distress, health status, quality of life, and has an influence on the coping strategies of women with breast cancer (Sarenmalm et al., 2013). Thereby, there does seem to be reason to believe that SOC is an important factor, however further studies specifically on breast CRF should be conducted to further explore and substantiate this relationship.

Several previously identified articles before this review was conducted found acceptance behaviours, shifts in attention, and adaptive coping strategies leading to increased psychological adjustment in cancer patients (Cheng et al., 2019; Li et al., 2017), as well as studies finding that coping strategies in general were important (varying to which degree), as well as the flexibility of the coping style (Brannon & Feist, 2009; Lashbrook et al., 2018). Thereby, the results that meaning focused coping was found be associated with more fatigue, is quite surprising, as it would rather be expected that meaning focused coping would help reduce breast CRF. However, it is to be noted that this coping style was only discussed in one article (Levkovich et al., 2018) and was a bivariate association. Therefore, to solidify the claim that, meaning-focused coping is destructive in the context of coping with breast CRF, more evidence is required.

To our knowledge the study by Li et al. (2017) was the first to investigate BRST in relation to breast CRF and brings compelling evidence on the subject matter. There were significant differences between groups, with the BRST group having lower functioning and higher fatigue, and additionally a multivariate logistic regression found the odds ratio to also be significantly higher for those with higher BRST. The question does arise however, whether one question is enough to measure the construct of BRST.

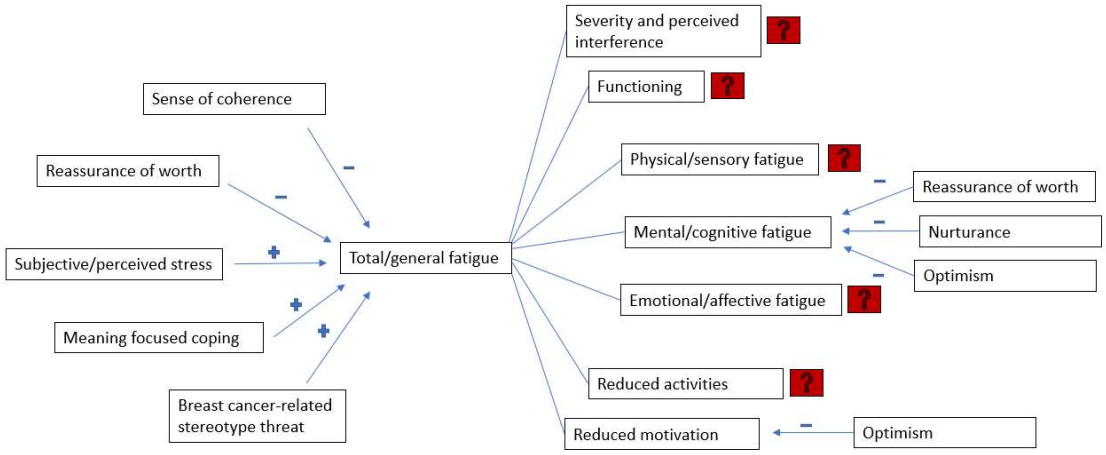
Missing results

Previous research had found personality factors to be related to breast CRF (Wang et al., 2013), and this research could not provide any support for these claims. It is however worth noting, that the original article of Wang providing evidence for influence of certain personality characteristics would have been included in this review, if the inclusion would have been broadened (i.e., to the last 10 years). However, this systematic review showed that no further research on personality and breast CRF was published in the last six years.

Despite identifying several sub-dimensions of breast CRF, for most of them no studies and thereby no evidence was found. These include physical/sensory fatigue, emotional/affective fatigue, severity and perceived interference, functioning, and reduced activities (see Figure 4). Moreover, internal resources and predispositions that were excluded due to time limitations such as quality of life and depression should be researched and incorporated into the model as well to solidify its usefulness as a psychological coping model with breast CRF.

Figure 4

Missing links in the preliminary heuristic breast-cancer related fatigue coping model



Limitations

It needs to be underlined that this review focused on a narrow area of coping due to the large amount of literature on the topic. Several factors relevant for coping with CRF such as general well-being, poor mental health, fear, depression (Abrahams et al., 2018; Thong et al., 2020) were not discussed in this review. Additionally, only including articles with samples above 100 ensured the reliability of the results, however, could also have caused lacking evidence. Furthermore, only articles from the last six years were included due to time limitations, due to this review being a master's thesis, thereby potentially missing important parts of the story published before that time

frame. These limitations did not allow for the construction of a full model in this review. Moreover, due to the massive amount of vocabulary related to psychology and coping it was difficult to include all possible variations. This is largely due to the state of psychological coping research, with Morrison & Bennett (2016) reporting that, over thirty definitions of coping exist, however that they consider the Lazarus mode to have had the most profound impact on the conceptualization of coping. Despite the search string being constructed with Lazarus (1999) model in mind, many alterations in vocabulary and other terms could still have broadened the results (e.g., attitude, self-efficacy etc.). Moreover, no core article could be found that really put the variables of interest together, and there was no real consistency in the use of the terminology of psychological coping. Thereby, it was also difficult to incorporate the findings into the structure of the heuristic model. In the end, the results were structured around fatigue and its sub-dimensions since this was most practical. Finally, stage IV and/or metastatic cases were excluded since based on Vilhauer's (2011) research it was hypothesized that differences in coping exist between primary and metastatic cases. This, however, could also have led to valuable results including all four stages being excluded. Further research should focus on psychologically coping for stage IV cases, as well as further investigating differences between the earlier and later stages. Moreover, there might also be differences in coping between the first three stages, and this idea should also be explored in future research.

Strengths

The research and search string are grounded in established health psychology theory (Lazarus, 1999). Moreover, the entire literature search was conducted very transparently with reasons for exclusion being provided in all three phases. Additionally, inter-rater reliability was conducted for the title, abstract and full-text scan and reached sufficient levels in all cases. Next, the disagreements were discussed and resolved, and if necessary, adaptions were made to the methods section. Thereby, based on the IRR this research should be considered reliable and reproducible. Lastly, all articles included in the analysis had a sample size of at least 100 participants, thereby again increasing the reliability of the results. Based on this review, we were able to present a heuristic model for CRF in breast cancer that did not exist in the literature, and to our knowledge there are not any other existing breast cancer fatigue models. Additionally, the level of evidence was noted in the results, and how this affects the model was discussed.

Implications for further research

Implications of this research are twofold. Firstly, this research can be used to inform interventions, therapy, and care development by gaining insight into evidence-based factors that can facilitate or hinder breast cancer related fatigue. Secondly, this research can inspire the funding and initiation of

a more full and comprehensive investigation into the topic, as well as research into factors that lack satisfactory evidence. Most important topics are incorporating the aspects of the Lazarus model that were excluded due to time limitations, investigating articles prior to January 2015, and conducting research on factors that lack multivariate and/or longitudinal results, as well as investigating coping for stage IV cases. Moreover, strictly following a model was difficult, and further research should consider only using models as inspiration rather than structural foundation to make things easier, and potentially allow for the discovery of knowledge not suitable for situation into specific models. Thereby, with a larger timeframe a full picture of all possible perspectives into this problem can be constructed, and further research on missing links in the model can be conducted to solidify a model to be used for psychologically coping with breast cancer-related fatigue.

Conclusion

Several psychological coping factors associated with breast CRF were identified in this review and were used to construct a preliminary heuristic coping model for breast CRF. Most of the findings are consistent with previous research on cancer-related fatigue and cancer-related outcomes in general. Differing levels of evidence were discussed that need to be considered when using this review as a basis for further research and/or practice. Moreover, due to the large literature base on this topic, further rigorous literature research, as well as research on the missing links in the model and research strengthening concepts with weak evidence is necessary to solidify the preliminary coping model proposed in this review.

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Appendix

Appendix 1

Table 3a

Total/general fatigue

Study	Fatigue composition	Evidence
1 (Sørensen et al., 2020)	Physical + Mental	Linear regression analysis: B / 95% CI / p SPS total: Non-significant Attachment: Non-significant Reassurance of worth: -0.54 / -1.03; -0.41 / 0.034 Nurturance: Non-significant Social integration: Non-significant N=160
2 (Person et al., 2020)	General + Physical	No significant evidence was found for optimism in a multivariate multinomial logistic regression analysis (Person et al., 2020)
3 (Hiensch et al., 2020)	Behavior/daily life + Emotional/affective + Sensory/physical + Cognitive	Groups stratified by Sense of Coherence (SOC): Weak-normal SOC (n=125) / Strong SOC (n=81) / P Fatigue: 3.0 ± 3.0 / 1.8 ± 2.6 / <0.01
4 (Levkovich et al., 2018)	Severity + Perceived interference	Bivariate associations Variable / Association with fatigue Subjective stress: .46**

	Emotional control	Non-significant
	Meaning-focused coping	.17*

N=170

*p<0.05 **p<.001

5 (Xiao et al., 2017) — Severity + Perceived interference

Bivariate associations

Variable	Association with fatigue
Subjective stress	.633*

N=111

*p<0.01

The association between subjective stress and fatigue was non-significant in the multivariate model

In a mediation model subjective stress had a significant direct effect on fatigue when depressive symptoms were not in the model (B: 1.30; p<0.0001)

6 (Li et al., 2017) — Functioning + Fatigue

Comparison of groups with and without breast-related stereotype threat (BRST) (Median (25^{th};75^{th} percentile)):

	Non-BRST (n=45)	BRST (n=86)	p
Fatigue	40 (34;47)	36 (29;43)	0.012

Multivariate logistic regression:

	OR	95% CI	p
BRST	2.53	1.11; 5.81	0.028

N=131

No significant results were found between the groups and participants who did not answer the BRST question

7 (Ho et al., 2015) — Severity + Perceived interference

Correlation (Ho et al., 2015)

Variable	Association with fatigue
Perceived stress	0.43*

N=133

*p<0.01

Multiple regression:

B (SE)	95% CI	β*	Adjusted R^2
0.23 (0.04)	0.16-0.30	0.48**	0.034

N=133

*Standardized B

**p<0.001

Appendix 2

Table 4a

Physical fatigue

Study	Evidence			
1 (Sørensen et al., 2020)	Linear regression analysis:			
		B	95% CI	p
	SPS total	Non-significant		
	Attachment	Non-significant		
	Reassurance of worth	Non-significant		
	Nurturance	Non-significant		
	Social integration	Non-significant		
	N=160			

Appendix 3

Table 5a

Mental/cognitive fatigue

Study	Evidence			
1 (Sørensen et al., 2020)	Linear regression analysis:			
		B	95% CI	p
	SPS total	Non-significant		

	Attachment	-0.23	-0.44; -0.02	0.034
	Reassurance of worth	-0.32	-0.53; -0.12	0.002
	Nurturance	0.15	0.03; 0.27	0.011
	Social integration	Non-significant		
	N=160			
	Multivariate linear regression analysis with the concepts significant in the linear regression:			
		B	95% CI	P
	Attachment	Non-significant		
	Reassurance of worth	-0.34	-0.60; -0.08	0.011
	Nurturance	.020	0.08; 0.31	0.001
	N=160			
2 (Person et al., 2020)	Multivariate multinomial logistic regression analysis:			
	Low, transient increasing fatigue vs. no-fatigue			
		OR	95% CI	p
	Optimism	0.97	0.95; 0.99	0.008
	Moderate, transient increasing fatigue vs. no-fatigue			
		OR	95% CI	p
	Optimism	0.96	0.94; 0.99	0.003
	Severe, transient increasing fatigue vs. no-fatigue			
		OR	95% CI	p
	Optimism	0.93	0.89; 0.97	0.0009

Appendix 4

Table 6a

Reduced activities

Study	Evidence
2 (Person et al., 2020)	No significant evidence was found for optimism in a multivariate multinomial logistic regression analysis (Person et al., 2020)

Appendix 5

Table 7a

Significant results for reduced motivation

Study	Evidence			
2 (Person et al., 2020)	Multivariate multinomial logistic regression analysis: Moderate, transient decreasing motivation vs. no reduction			
		OR	95% CI	P
	Optimism	Non-significant		
	Severe, transient decreasing motivation vs. no reduction			
		OR	95% CI	P
	Optimism	0.94	0.90; 0.97	<0.0001
	Decreasing motivation vs. no reduction			
		OR	95% CI	P
	Optimism	Non-significant		
	Increasing motivation vs. no reduction			
		OR	95% CI	P
	Optimism	Non-significant		