Systematic Reviews

The Effectiveness of Psychological Interventions for Fatigue in Cancer Survivors: Systematic Review of Randomised Controlled Trials

--Manuscript Draft--

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Abstract:	Background Fatigue is a common symptom in cancer patients that can persist beyond the curative treatment phase. This systematic review evaluated the effectiveness of psychological interventions for cancer-related fatigue in post-treatment cancer survivors. Methods We searched relevant online databases and sources of grey literature. Randomised controlled trials (RCTs) evaluating psychological interventions in adult cancer patients after the completion of treatment, with fatigue as an outcome measure, were included. Two review authors extracted data independently from the selected studies and assessed the methodological quality using the Cochrane Collaboration Risk of Bias Tool. Results Thirty-three psychological interventions were identified. The sample size of the included studies varied between 28 and 409, with 4,525 participants overall. Twenty-three of the included studies reported a significant effect of the interventions on reducing fatigue in cancer survivors. Most interventions focused on psychoeducation, mindfulness, cognitive or behaviour therapy-oriented strategies. However, studies differed widely in terms of measurement tools used to assess fatigue, mode, duration and frequency of the intervention delivery. Conclusions This review showed some tentative support for psychological interventions for fatigue after cancer treatment. However, as the RCTs were heterogeneous in nature and the number of high quality studies was limited, definitive conclusions are not yet possible. With the growing need for stage-specific research in cancer, this review sought to inform current practice and to summarise the existing evidence base of randomised controlled trials in the area. Registration PROSPERO registration number: CRD42014015219
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Response to Reviewers:	26 Sept 2019 Dear Paul Shekelle, MD Systematic Reviews Thank you for your comments on our manuscript "The Effectiveness of Psychological Interventions for Fatigue in Cancer Survivors: Systematic Review of Randomised Controlled Trials" (SYSR-D-19-00062R1). We are delighted that it is potentially acceptable for publication in Systematic Reviews. In the latest draft we have assessed the quality of the evidence across studies, using the GRADE framework. Changes to the text have been made to the methods, result and discussion section (highlighted in red in marked version of manuscript). We have also added this in the section on “Changes to the protocol” as we had not said that we would do such an assessment in our previously published protocol. Regarding the numbers the PRISMA flow diagram, we apologise for the typo. We have changed this to state that there were n=23 studies form the 2015 search and n=10 studies from the 2018 search. The total number of studies is therefore 33. We thank you for pointing this out. If you have any other requirements or recommendations, please let us know. We look forward to receiving your response. Best wishes, Dr Teresa Corbett
Additional Information:	
Question	**Response**
Covering letter concerning your manuscript	Dear Editor: Enclosed please find our manuscript entitled The Effectiveness of Psychological Interventions for Fatigue in Cancer Survivors: Systematic Review of Randomised Controlled Trials, which we wish to submit for consideration for publication in Systematic Reviews. The review outlined in this paper aims to build upon a Cochrane review conducted by Goedendorp et al (2009) to assess the effectiveness of psychosocial interventions for fatigue in people during cancer treatment. In recent years, an emphasis has been placed on recognising the needs of those post-cancer treatment, with some persistent symptoms (such as fatigue) lasting into longer-term survivorship. To our knowledge, this is the first review to assess psychological interventions for fatigue in those after the completion of curative treatment. We found that there is some evidence of a reduction in fatigue associated with psychosocial interventions. However, this review highlights the need for high-quality design and enhanced reporting of studies evaluating the effectiveness of psychological interventions for CrF in post-treatment cancer survivors. We feel that it is particularly appropriate for your journal because you have previously published the review protocol (Corbett, T., et al., Protocol for a systematic review of psychological interventions for cancer-related fatigue in post-treatment cancer survivors. Systematic reviews, 2015. 4(1): p. 174.) All authors have read and approved the final version of this manuscript, which is not under consideration elsewhere. Please address all correspondence concerning this manuscript to Dr Teresa Corbett (t.k.corbett@soton.ac.uk) Thank you in advance for considering our submission and we look forward to learning of the outcome of its review. Sincerely, Dr Teresa Corbett
Is this study a clinical trial?<hr><i>A clinical trial is defined	No

by the Word Health Organisation as 'any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes'.</i>	

The Effectiveness of Psychological Interventions for Fatigue in Cancer Survivors: Systematic Review of Randomised Controlled Trials

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ABSTRACT

Background: Fatigue is a common symptom in cancer patients that can persist beyond the curative treatment phase. This systematic review evaluated the effectiveness of psychological interventions for cancer-related fatigue in post-treatment cancer survivors.

Methods: We searched relevant online databases and sources of grey literature. Randomised controlled trials (RCTs) evaluating psychological interventions in adult cancer patients after the completion of treatment, with fatigue as an outcome measure, were included. Two review authors extracted data independently from the selected studies and assessed the methodological quality using the Cochrane Collaboration Risk of Bias Tool.

Results: Thirty-three psychological interventions were identified. The sample size of the included studies varied between 28 and 409, with 4,525 participants overall. Twenty-three of the included studies reported a significant effect of the interventions on reducing fatigue in cancer survivors. Most interventions focused on psychoeducation, mindfulness, cognitive or behaviour therapy-oriented strategies. However, studies differed widely in terms of measurement tools used to assess fatigue, mode, duration and frequency of the intervention delivery.

Conclusions: This review showed some tentative support for psychological interventions for fatigue after cancer treatment. However, as the RCTs were heterogeneous in nature and the number of high quality studies was limited, definitive conclusions are not yet possible. With the growing need for stage-specific research in cancer, this review sought to inform current practice and to summarise the existing evidence base of randomised controlled trials in the area.

Registration: PROSPERO registration number: CRD42014015219

Keywords

Cancer; psychological; survivorship; fatigue; post-treatment; cancer-related fatigue; psychooncology; review; narrative review.

Highlights

- The majority of treatments comprise standard components of CBT, mindfulness and/or psychoeducation. Studies comparing active psychological therapies are scarce. There is insufficient high quality evidence to recommend psychological treatment as having possible benefit for cancer-related fatigue in post-treatment cancer survivors. There is no reported evidence of adverse effects.
- The majority of the evidence is for the treatment of fatigue in those with breast cancer but there is insufficient evidence to indicate if the treatments are more effective for one type of cancer over another.
- The interventions appear to have had some impact on mood, self-efficacy to cope with fatigue and quality of life/functional impact of fatigue. However, there appeared to be little impact of the interventions on pain. Interventions designed specifically for CrF did not tend to assess sleep variables.
- With wide-ranging heterogeneity in study design and measures used to assess the outcomes, it is difficult to evaluate which format or elements reduce fatigue after cancer treatment. Furthermore, the optimum time to intervene after treatment has ended is not clear.

BACKGROUND

Cancer-related fatigue (CrF) is commonly defined as "a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer and/or cancer treatment that is not proportional to recent activity, and significantly interferes with usual functioning"[1]. There is little understanding of the underlying aetiology of CrF [2] but it is considered a multidimensional symptom that is comprised of physical, mental, and emotional aspects [1, 3, 4].

There is limited evidence of the effectiveness of pharmacological interventions for the management of CrF [5]. However, some reviews of non-pharmacological interventions have indicated that psychological and activity-based interventions may be effective [2, 6]. Interventions that incorporate restorative approaches, supportive-expressive techniques, and cognitive-behavioural psychosocial interventions may reduce levels of CrF [6, 7]. In this review, we have focused on psychological therapies designed to improve functioning and/or reduce the physical and psychological impact of CrF.

Psychological interventions such as cognitive-behavioural therapy (CBT) aim to influence or change cognitions, emotions, behaviours, or a combination of these [8]. Interventions which target these processes may improve symptom management in CrF [9]. These therapies may increase knowledge, improve emotional adjustment, and enhance quality of life, and have also been associated with improved coping skills, physical health and functional adjustment [6, 10]. Patients and healthcare professionals have been reported to have high expectations of, and relatively positive attitudes towards, psychological therapies [10].

There is some evidence that psychosocial interventions are effective in reducing fatigue in patients undergoing active treatment for cancer[8]. While biological insults such as cancer or cancer treatment may lead to fatigue symptoms during the treatment phase of those with

cancer, behavioural and cognitive variables may prolong fatigue during to post-treatment phase[1]. However, it is still unclear whether psychological interventions are helpful for managing fatigue in post-treatment cancer survivors beyond the early diagnostic and treatment phase [11]. Consequently, there is a need to conduct a critical review of the literature pertaining to psychological interventions in post-treatment cancer survivorship.

Objectives

This review systematically reviews and synthesizes the evidence from randomised controlled trials (RCTs) investigating the effectiveness of psychological interventions for persistent fatigue in people after the completion of cancer treatment.

METHODS

The review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (registration number: CRD42014015219) and the protocol has been published[12]. The review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [13].

Criteria for considering studies for this review

Types of studies

RCTs comparing psychological treatments with no intervention (i.e. usual care or wait list controls), attention controls, or another intervention for CrF. Studies were included regardless of treatment intensity or duration, mode of treatment delivery (e.g. individual, group) or medium of treatment (e.g. in-person, online). We did not impose date restrictions. Studies found in the grey literature were included if a full-text paper in English was available, either through databases or through contact with the study authors.

Types of participants

Adults 18 years and older who had completed treatment for cancer regardless of gender, tumour type, and type of medical treatment received.

Types of interventions

We included studies that evaluated the effect of psychological therapies in the management of CrF. Interventions including psychotherapy and psycho-education were included. These interventions included those that provided advice or information (verbal, written, audio-visual or computer delivered material) in order to help people understand and manage CrF, strategies such as cognitive restructuring, coping skill development, meditation, or relaxation techniques. Studies that combined psycho-behavioural and non-psychological methods were included only if the study had a predominant emphasis on a psychological element in the design. Studies were excluded if they did not employ a psychotherapeutic rationale or theory in the intervention design[12].

Types of outcome measures

Studies were required to have "fatigue" as an outcome of interest. In line with Goedendorp et al [8], studies were included if fatigue was measured with a questionnaire designed specifically to evaluate fatigue. Fatigue subscales that were part of a broader quality-of-life measure were also included, if specific fatigue-related data were available. Fatigue could also be measured with a visual analogue scale (VAS) or as part of a symptom list and scored as 'present' or 'absent'. Fatigue could be measured in terms of characteristics such as intensity, distress, duration, frequency, or as dimensions such as physical fatigue, mental fatigue, or general fatigue.

Secondary outcomes included:

- Functional impact of fatigue (self-report questionnaires measures assessing the impact of fatigue on daily functioning)

- Fatigue self-efficacy (self-reported scales of control or self-efficacy in relation to fatigue)
- Mood (self-reported scales of depression, and/or anxiety, or distress)
- Global quality of life (self-report questionnaires measures assessing the impact of fatigue on quality of life).

Information sources:

The following electronic databases were searched: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL PsycINFO, Web of Science, and CancerLit. Alterations were made to the search strategies as appropriate for each database. An example search strategy can be seen in Table 1 (See Appendix 3. For further details of the search strategies used). The original search was conducted on October 6th and 7th 2015 and was updated on the 22nd and 23rd of January 2018. Studies from 2014- 2018 were assessed for inclusion based on the criteria followed in the original search.

Unpublished and ongoing trials were identified by checking appropriate databases of current ongoing clinical research studies. Grey literature was searched using the OpenGrey database (www.opengrey.eu), which includes technical or research reports or doctoral dissertations. Conference papers from annual American Society of Clinical Oncology (ASCO) or International Psycho Oncology Society World Congress (IPOS) conferences were also searched. Other published, unpublished, and ongoing trials were identified by checking trials and protocols published on the following clinical trials registers and websites.

• World Health Organization International Clinical Trials Registry Platform (WHO ICTRP; www.who.int/ictrp/en).

• metaRegister of Controlled Trials (mRCT; www.controlled-trials.com/mrct/).

• ClinicalTrials.gov (www.clinicaltrials.gov).

• www.cancer.gov/clinicaltrials.

Search methods for identification of studies

Insert Table 1. Sample Search Strategy: Details of the terms searched in CINAHL database

Data collection and analysis

One review author (TC) conducted the initial search before screening titles. Titles that were clearly not relevant to this review were removed. Three review authors (TC, EC and BMG) independently screened the remaining titles and abstracts for their eligibility for inclusion. Ineligible studies were excluded at this stage, with each author recording the reason for rejection. Full-text copies were retrieved and screened if the title and abstract did not provide sufficient information concerning the inclusion criteria for this review. Copies of all studies that possibly or definitely met the inclusion criteria were also retrieved. Disagreements between the reviewers were resolved by discussion, with the involvement of another reviewer where agreement could not be reached (DD). Multiple reports of the same study were included as a single study, with each study identified by the lead author of the primary results paper.

Data extraction and management

Review authors (TC, EC, AG and BMG) extracted data independently from the studies using a specifically designed data extraction form (see Table 2.). Authors were contacted where further clarity regarding the study was required, or in order to obtain additional data.

Assessment of risk of bias in included studies

The risk of bias of each trial was assessed as high risk, low risk, or unclear risk as per recommendations provided in Chapter 8 of the Cochrane Hand book for Systematic Reviews

of Interventions[14]. Further details regarding the risk of bias domains was provided in the study protocol[12].

Quality of the Evidence

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process was used to assess the evidence for the primary comparison of 'Psychological Interventions compared to usual care for Fatigue in cancer survivors'.

RESULTS

Figure 1 depicts the PRISMA flow diagram of studies identified and excluded at each stage of the review. The initial literature search of seven databases in 2015 resulted in 4,212 potentially relevant articles. Following exclusion of duplicates, 3, 285 articles remained. The titles and abstracts of these articles were screened and 60 full-text articles were selected to be retrieved and reviewed in detail. Following review of the full-text papers, a further 37 studies were excluded and 23 RCTs fulfilled all eligibility criteria for inclusion.

The updated search in 2018 resulted in 8,540 potentially relevant articles. Once duplicates and studies prior to 2014 were removed, 3,362 studies published were assessed for inclusion. Thirty-four full-text articles were reviewed, eight of which had already been included or were follow-up studies associated with papers included in the original review. Ten new papers were added to the review.

In total, 33 RCTs fulfilled all eligibility criteria for inclusion. A full description of these studies can be seen in Table 2 and Table 3.

In cases where more than one paper was published relating to the same study, the papers were as assigned to one study. Five articles were found in the grey literature and full-texts were not available online. Study authors of each of these papers were contacted. Three study authors

provided full-texts in preparation for publication. The other two papers were excluded at this point, as full-texts were not available. No articles were found in snowball search.

Insert Figure 1. the PRISMA flow diagram of studies identified and excluded at each stage of the review.

Description of Included studies

Data were extracted from the included papers (See Table 2. for a description of the included studies). The 33 RCTs reported data on 4,486 cancer survivors (2,196 intervention and 2,290 controls). The majority of studies were conducted in the United States [15-30]. Six were carried out in the Netherlands [31-36], three in the United Kingdom [37-39]. The remainder were conducted in Australia,[40, 41] Canada [42, 43], Germany [44], France [45, 46] and Korea [47, 48].

Participants

As per the inclusion criteria for this review, studies were required to include only those who have completed active medical treatment prior to taking part in the research. However, there was little consistency across the studies regarding the timing of the intervention in relation to time elapsed since completion of cancer treatment.

Interventions

Details of interventions can be seen in Table 2, including content, strategies employed, mode of delivery, duration, who delivered the intervention and the comparison or control group used. Twelve studies reported on the effects of a CBT intervention [19, 21, 23, 26, 28, 32, 33, 35, 37, 41, 43, 48], of which six were focused specifically on CBT for insomnia (CBT-i) [19, 23, 26, 28, 37, 43] . Over half of these (n=5) were studies on CBT-I [19, 23, 28, 37, 43]. Two of the CBT interventions were combined with physical activity [35, 41]. Other studies incorporated CBT strategies into the intervention. Dolbeault et al [45] reported on a psycho-

educational intervention based on CBT and another study reported on a trial of Cognitively-Based Compassion Training[20]. Van der Lee et al used a combination of CBT and mindfulness strategies in a trial on mindfulness-based cognitive therapy[34].

Seven studies [17, 18, 24, 25, 27, 39, 49] reported on mindfulness-based interventions. Two of the studies were specifically aimed at CrF[24, 39], and 3 were focused on cancer [17, 27, 49].

Bruggeman-Everts [31] compared Ambulant Activity Feedback (AAF) and psychologist-guided Web-based mindfulness-based cognitive therapy groups to a psychoeducational group, showing that the psycho-education group was least effective at reducing fatigue. Other interventions included a patient education program [44], a physical activity behaviour change intervention[29], and a combined Psycho-education and physical activity intervention [46]. Health coaching and Motivational interviewing was employed in 2 studies [16, 47]. Freeman et al., 2015 tested an Imagery-based intervention [22]. Three studies reported on lifestyle interventions [15, 40] [50] and one online intervention aimed to enhance self-efficacy to manage problems associated with cancer-related fatigue following primary cancer treatment [38].

Control group

There was substantial heterogeneity in the comparison groups used within the trials. See Table 2 for further details

Outcomes

Primary outcomes

A variety of different measures were used to assess fatigue. The Brief Fatigue Inventory (BFI) was used in five studies [15, 18, 23, 38, 48] and the Functional Assessment in Cancer

Therapy - Fatigue (FACIT-F) was used in five studies [17, 21-23, 40]. Five studies used the Fatigue Symptom Inventory (FSI) [18, 24, 27, 29, 37] and the Multidimensional Fatigue Inventory (MFI) was used in 4 studies[34, 35, 43, 46]. Ritterband [28] used the short form of the Multidimensional Fatigue Symptom Inventory-Short Form(MFSI-SF). The Schwartz Cancer Fatigue Scale was used in one study[16]. Four studies [31-33, 36] employed the Checklist Individual Strength (CIS). The remaining studies used fatigue subscales of broader multi-dimensional measures. Three studies assessed fatigue using two different questionnaires. Yun et al [48] used both the BFI and the Fatigue Severity Scale (FSS), whereas another study used the BFI in conjunction with the FACIT-F [23]. The third study used both the Fatigue Assessment Questionnaire (FAQ) and fatigue subscale of the EORTC-QLQ-C30 [44].

Secondary outcomes

Secondary outcomes of interest to this review were specified a prioi in the study protocol [12] and are summarised in Appendix 1. These included mood (self-reported scales of depression, and/or anxiety, or distress); global quality of life and functional impact of fatigue (self-report questionnaire measures assessing the impact of fatigue on quality of life and daily functioning); and fatigue self-efficacy. Most of the studies included a measure of mood, either as an outcome or a control variable. However, the mood outcomes were assessed by a wide range of psychometric tools which assessed various dimensions of mood including stress, depression, anxiety, and distress. Many of the studies also included a measure of global quality of life (QoL) and functional impact of fatigue. Only two of the studies assessed self-efficacy in relation to coping with fatigue [38, 46].

In the review process, other frequently reported secondary outcomes that were not outlined in the review protocol were identified as relevant to this review. These outcomes of interest

were Insomnia or sleep quality and pain. Studies that assessed sleep quality or insomnia tended to be designed with the aim of impacting insomnia or quality of life after cancer treatment.

As with the measures used to assess fatigue, a variety of measures were used to assess mood-related variables, with some studies including more than one measure of mood. The most commonly used measures were the Hospital Anxiety and Depression Scale (HADS) [51], The Patient Health Questionnaire (PHQ) [52](a measure of depression severity) and The Profile of Mood States (POMS) [53] (a measure of psychological distress). The State-Trait Anxiety Inventory (STAI) [54] was also used.

The two most commonly used scales to assess quality of life were the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) [55] and the Functional Assessment of Cancer Therapy—General (FACT-G) [56]. In the study protocol, the reviewers aimed to delineate the concepts of "global quality of life" and "functional impact of fatigue" [12].However, in line with Luckett et al. [57], this was not deemed appropriate in the final review. Both types of measures assess physical, emotional, social, and functional/role scales. The QLQ-C30 provides brief scales for cognitive functioning, financial impact, and a range of symptoms either not assessed by the FACT-G or else subsumed within its well-being scales. The FACT-G includes both symptoms and concerns within each scale [57]. The Medical Outcomes Study (MOS) [58], Sickness Impact Profile (SIP) [59], the SF-12 [60] and the M.D. Anderson Symptom Inventory (MDSAI) [61]were also used.

A variety of outcome measures were also used to assess sleep quality or insomnia. The Insomnia Severity Index (ISI) [62] was the most commonly used. Other measures included the Women's Health Initiative Insomnia Rating Scale (WHIIRS) [63]and the Pittsburgh Sleep

Quality Index (PSQI) [64]. Broader QoL measures that assessed insomnia/sleep quality included the MDSAI [61] and the EORTC QLQ-C30 [55].

Risk of bias assessment

The included studies were assessed for risk of bias using the Cochrane 'Risk of Bias' Tool [14]. Some aspects of the studies were not reported with sufficient detail to assess bias and therefore were rated as unclear risk of bias for domains where insufficient information was provided. Further details are presented in Appendix 2.

Random sequence generation (selection bias)

Most studies described the process of allocating participants between study groups randomly, providing details about the method of randomization employed. Eight studies did not describe random sequence generation in enough detail to allow a definite judgment.

In the majority of studies (n=24), the method of allocation concealment either was not described or not described in sufficient detail to allow a definite judgment.

Blinding (performance bias and detection bias)

Most of the trials included in this review were at high risk of performance bias because, owing to the nature of the intervention, it was not possible to blind the trial personnel and participants. In a number of the studies were not described in sufficient detail to allow a definite judgment as to whether or not outcome assessors were blinded about the group allocation of participants.

Incomplete outcome data (attrition bias)

All studies provided some details of study attrition. Many of the studies (n=19) were at a low risk of attrition bias, with good completion rates.

Selective reporting (reporting bias)

The majority of studies were at a low risk of reporting bias as, based on the information provided by the trial authors and study protocols (where available), it was unlikely that there was selective reporting of the primary and secondary outcomes. Sixteen of the trials were provided trial registration details.

Other bias

Most trials were deemed to be at a low risk for other biases such as potential bias due to baseline differences, inappropriate influence of the study sponsor, and early stopping for benefit [12].

Quality of the Evidence

We employed the GRADE approach to assess the evidence for the primary comparison of 'Psychological Interventions compared to usual care for Fatigue in cancer survivors'. As seen in Table 4, the majority of the evidence relating to psychological interventions for fatigue is of low quality, largely due to the finding that the available evidence is too heterogeneous to pool across studies. Further, it due to incomplete reporting of methods, it was difficult to ascertain risk of bias in studies. There is little evidence that directly answers the questions of interest for different types of psychological therapies.

Insert: Table 4 Grade evidence summary

Effects of interventions

In the published protocol, we had planned to conduct a meta-analysis, if it was deemed clinically meaningful and appropriate to do so[12]. However, given the heterogeneity in participant groups, study design, study comparators and measures used, we synthesised data narratively, as a meta-analysis would have been inappropriate.

Comparison 1: Psychological interventions (all types) vs usual care

Primary outcome: Fatigue

Eleven psychological interventions reported a significant effect of the intervention on an outcome of fatigue, compared to a waitlist control or usual care [18, 24, 25, 27, 28, 32, 33, 37, 43, 44, 47].

Secondary Outcomes:

1. **Global quality of life (QoL) /functional impact of fatigue**

   Global QoL/functional impact of fatigue was assessed in 19 of the 22 studies that compared a psychological intervention to a waitlist control or usual care. Thirteen of these 19 studies demonstrated a significant improvement compared to the control group, in at least one measure of QoL /functional impact of fatigue [24, 25, 32-34, 36, 37, 39, 43-46, 48]. One study reported that participants assigned to the intervention group had significantly lower physical well-being compared to the control group at follow-up[20]. The remaining studies did not report any Group X Time interaction effects [16, 27, 28, 38, 40].

2. **Fatigue self-efficacy**

   Two studies assessed Fatigue self-efficacy. Bower et al [18]used the fatigue subscale of the HIV self-efficacy questionnaire and reported that Intervention group participants were significantly more confident than control group participants about their ability to manage fatigue and its impact on their lives at follow-up [18]. Foster et al assessed fatigue using the Perceived Self-efficacy for Fatigue Self-management (PSEFSM). Initial evidence of improved fatigue self-efficacy at T1 in the intervention group was not maintained at final follow-up[38].

3. **Mood**

   Mood was assessed over time in 18 of the 22 studies that compared a psychological intervention to a waitlist control or usual care. Ten of these reported significant improvements compared to the control group, in at least one measure of mood over time[20, 24, 25, 27, 37, 43-45, 48].

4. **Sleep/ insomnia**

Sleep/ insomnia was assessed over time in 12 of the 22 studies that compared a psychological intervention to a waitlist control or usual care. Nine of these reported significant improvements compared to the control group, in at least one measure of sleep quality or insomnia symptoms over time[15, 17, 24, 25, 27, 28, 37, 43, 44]. Three of these studies were designed to specifically target insomnia or sleep disturbance- all were effective for reducing fatigue [28, 37, 43].

Subgroup analysis and investigation of heterogeneity

In the original protocol, we specified that we would explore effects by subgroups of specific psychological intervention type (e.g. cognitive behavioural therapy) vs usual care.

Comparison 2: Subgroups of specific psychological intervention type (e.g. cognitive behavioural therapy) vs usual care

Cognitive-behavioural therapy vs Usual Care

Five studies reported on the effects of a CBT intervention compared to waitlist control or usual care [28, 32, 33, 37, 43], of which three were focused specifically on CBT for insomnia (CBT-i) [28, 37, 43].

Primary outcome: Fatigue

Each of the five CBT studies reported significant effect of the intervention on fatigue over time [28, 32, 33, 37, 43]. Two other studies incorporated CBT strategies into the intervention. Dolbeault et al [45] reported a significant effect on fatigue of a psycho-educational intervention based on CBT. Another study reported no significant differences between groups on a trial of Cognitively-Based Compassion Training[20]. Van der Lee et al reported a significant effect of intervention over time using a combination of CBT and mindfulness strategies in a trial on mindfulness-based cognitive therapy[34].

Secondary Outcomes:

1. **Global quality of life /functional impact of fatigue**

   Four of the five CBT studies reported significant effect of the intervention over time at least one measure of Global QoL /functional impact of fatigue [28, 32, 33, 37, 43]. Savard et al reported a significant group-time interaction global quality of life using the EORTC QLQ-C30[43].Using the Functional Assessment of Cancer Therapy Scale– general FACT-G, Espie et al [37] reported that CBT was associated with increased physical and functional QoL compared to the control group, at post-treatment and at follow-up. Using the SIP-8, both Prinsen et al [33]Gielissen et al[32] stated that the intervention condition reported a significantly greater decrease than patients in the waiting list condition in functional impairment. Ritterband et al [28] reported that the group x time interaction for either the physical or mental subscale of the SF-12 was not significant.

   Using the EORTC core quality of life questionnaire (EORTC QLQ-C30), Dolbeault et al reported greater improvement in emotional functioning, role functioning, and global health status scales in the CBT-based psycho-educational intervention group compared with the control group. Group × time interaction effects were non-significant for the other subscales of the EORTC [45]. Using the SIP-8, van der Lee et al reported that six months after the intervention, the mean well-being score at post measurement was significantly higher in the mindfulness-based cognitive therapy intervention group than in the waiting list group corrected for pre-treatment level of well-being.[34]. Conversely, participants assigned to Cognitively-Based Compassion Trainingh had significantly lower physical well-being compared to the control group at follow-up[20].

2. **Fatigue self-efficacy**

None of the five CBT studies assessed fatigue self-efficacy.

3. Mood

Mood was assessed over time in 4 of the 5 studies that compared a CBT intervention to a waitlist control or usual care[28, 32, 37, 43]- three of these reported a significant effect of the intervention on mood[32, 37, 43]. Gielissen et al [32] assessed psychological distress using the Symptom Check List 90 and found that participants in the intervention condition reported a significantly greater decrease in psychological distress (95% CI, 12.7 to 30.4, $p<0.001$) than patients in the waiting list condition. Using the Hospitals Anxiety and Depression Scale [HADS], Espie et al[37] reported that CBT participants had reduced symptoms of anxiety, and depression relative to the control group (Anxiety 95% CI -0.92 to -0.12 p= 0.011; Depression 95% CI -0.99 to -0.19 p=0.004). Also using the HADS, Savard et al[43] reported significant group-time interactions on scores of anxiety ($P < .05$) and depression ($P < .05$). In contrast, Ritterband et al[28] reported that the group x time interaction was not significant (p=.09) on the total HADS score.

Dolbeault et al [45] reported that a greater reduction of negative affect and improvement in positive affect was demonstrated in the intervention group compared with the control group. Significant group x time interactions indicated a positive effect of the intervention on anxiety, measured using the State-Trait Anxiety Inventory. Psychological adjustment - assessed with the Profile of Mood States (POMS) - demonstrated group x time interactions in favor of the intervention on anxiety, anger and depression. No effect of the intervention group was evidenced on The Mental Adjustment to Cancer Scale (MAC).

Dodds et al [20] reported that compared to controls, at follow-up, participants assigned to the CBCT group demonstrated had significantly lower levels of perceived

stress in the past week (−1.6, 95 % CI −3.1, −0.2)- assessed using the Perceived Stress Scale (PSS-4). The Cognitive and Affective Mindfulness Scale—Revised (CAMS-R 10) demonstrated enhanced mindful presence in participants assigned to the CBCT group compared to controls, at follow-up (3.1, 95 % CI 0.4, 5.8). There was no significant impact of the intervention on the other mood scales at final follow-up (week 12): Brief Center for Epidemiologic Studies—Depression questionnaire (CES-D-10), Fear of Cancer Recurrence Inventory (FCRI), the Impact of Events Scale—Revised (IES-R) or UCLA Loneliness Scale Version 3 (R-UCLA).

4. Sleep/ insomnia

Sleep/ insomnia was assessed over time in 4 of the 5 studies that compared a CBT intervention to a waitlist control or usual care[28, 37, 43, 45]- three of these reported significant improvement compared to the control group, in at least one measure of sleep quality or insomnia symptoms over time[28, 37, 43]

Using the Insomnia Interview Schedule Insomnia Severity Index, Savard et al[43] reported significant group-time interactions for all self-reported sleep variables, except for total sleep time. These included sleep efficiency, total wake time, sleep onset latency, wake after sleep onset.

Ritterband et al [28] also employed the Insomnia Severity Index and reported a significant group x time interaction effect with the intervention group showing a significant improvement in insomnia severity from pre- to post-assessment, compared to the control group. These improvements were also clinically significant. Sleep Diary Variables were also used to assess sleep sleep efficiency, sleep onset latency, wake after sleep onset and total sleep time. A significant group x time interaction was found for sleep efficiency and sleep onset latency with medium-to-large treatment effects (d=.72 and d=.67 respectively). There was not a significant group x time interaction

for wake after sleep onset, time in bed, number of awakenings or total sleep time. The intervention group also showed significantly more improvements than those in the control group on soundness of sleep and feeling restored, with large effect sizes (1.21 and 1.35, respectively).

Espie et al[37] also used sleep diaries to assess difficulty initiating (SOL) and maintaining (WASO) sleep. Changes in total sleep time were not statistically significant, but improvements were seen in the CBT group WASO, SOL, and Sleep efficiency scores. CBT was associated with median reduction in insomnia symptoms of almost 1 hour (SOL+WASO) compared with no change in the control group.

Dolbeault et al [45] reported that no effect of the intervention group was evident over time, assessed using the EORTC QLQ-C30 sleep.

Mindfulness-based interventions

Six studies compared mindfulness-based interventions to waitlist control or usual care, [17, 18, 24, 25, 27, 39]. Two of the studies were specifically aimed at CrF [24, 39]and Another 2 were specifically focused on cancer [17, 27].

Primary outcome: Fatigue

Four of the studies on mindfulness-based interventions reported a significant effect of intervention on fatigue over time [18, 24, 25, 27]. One of the effective studies one was specifically aimed at CrF [24] and one was specifically focused on cancer[27].The effective findings were not maintained at final follow up in one of the studies[18].

Secondary Outcomes:

1. **Global quality of life /functional impact of fatigue**

   Four of the mindfulness assessed Global QoL /functional impact of fatigue [24, 25, 27, 39]. Three reported significant effect of the intervention over time on at least one

measure of Global QoL /functional impact of fatigue[24, 25, 39]. Hoffman et al[39] employed the breast-specific quality of- life scale FACT-B and the FACT-ES scale for endocrine symptoms and reported that mean scores in the intervention group were greater at both 8 and 12 weeks compared with the control group for all six measures (except social well-being which was significant at 8 weeks only). Using the WHO five-item well-being questionnaire (WHO-5), Hoffman et al also reported significant increases in the intervention group compared with controls at both timepoints[39]. The authors also noted that increased hours of formal mindfulness classroom and home practice in the intervention group was associated with improved scores in FACT-ES, FACT-B, FACT physical well-being and WHO-5 at 12 weeks. Johns et al assessed functional status using the Sheehan Disability Scale (SDS) and reported that the MBSR group demonstrated significantly lower functional disability scores than the control group at final follow-up with a large effect size (d =-1.22)[24]. Lengacher et al used the M.D. Anderson Symptom Inventory (MDASI)[25]. They reported significant improvements in favour of MBSR(BC)) in the symptom interference items (i.e., general activity, work (including work around the house) relations with other people, walking) and Housework, and Relationships. Using the Medical Outcomes Study Short-Form 36 (SF-36, v.2), Reich et al [27], reported that Group × Time interaction was not significant for either mental or physical health.

2. **Fatigue self-efficacy**

Bower et al used the fatigue subscale of the HIV self-efficacy questionnaire and reported that Intervention group participants were significantly more confident than control group participants about their ability to manage fatigue and its impact on their lives at follow-up [18].

3. **Mood**

Mood was assessed over time in each of the six studies that compared mindfulness-based interventions to waitlist control or usual care, [17, 18, 24, 25, 27, 39]. - three of these reported a significant effect of the intervention on mood [24, 25, 27]. In the study by Reich et al [27, 65], patients in the MBSR(BC) group showed significantly greater improvements in anxiety (P = .007) assessed using the State-Trait Anxiety Inventory, and FORs (overall and problems; P < .01), as measured using the Concerns About Recurrence Scale. Results for depression (measured using CES-D) showed that participants assigned to MBSR(BC) tended to report greater improvement than those in usual care; however, this trend did not reach statistical significance. The authors confirmed that improvement in both the cluster of psychological symptoms (anxiety, depression, perceived stress and QOL, emotional well-being) (P = 0.007) was related to assignment[27]. Lengacher et al [25]assessed mood, enjoyment of life, distress, and sadness, using the MDASI[61]. The MBSR(BC) intervention showed an improvement in mood, but not in distress or sadness. Johns et al [24]assessed anxiety using the Patient Health Questionnaire Generalized Anxiety Disorder Scale- the MBSR group demonstrated significantly lower anxiety scores than the control group with a large effect size (d =-0.98).Depression scores (measured using PHQ-8) were also significantly lower with large differences at final follow-up (d =-1.71)[24].
Using the Beck Depression Inventory-II (BDI-II), Bower et al [18]found that a significant Group x time interaction at post-treatment was not maintained at 3 month follow-up. Stress decreased over the assessment period in both groups, as measured using the Perceived Stress Scale (PSS). Hoffman et al [39] reported statistically significant improvements in outcome in the MBSR group compared with control group at both 8 and 12 weeks (for POMS total mood disturbance. The subscales of anxiety, depression showed these effects only at 8 week follow-up. Anger was

significantly improved at 12 weeks but not at 8 weeks. The authors found that increased hours of formal mindfulness classroom and home practice in the MBSR group was associated with improved scores in POMS total mood disturbance[39]. Using the State Trait Anxiety (STAI), Blaes et al [17] found no significant difference between groups in anxiety despite a trend towards improvement for MBCR.

4. **Sleep/ insomnia**

Sleep/ insomnia was assessed over time in three studies that compared mindfulness-based interventions to waitlist control or usual care - two of these reported a significant effect of the intervention on sleep/insomnia over time[17, 24]. Two of the studies assessed sleep quality using the Pittsburgh Sleep Quality Index (PSQI). Blaes et al [17]reported that total sleep quality improved in those who received MBCR compared to those in the control group – this was maintained at 4 months. Conversely, Bower et al [18] reported no significant effects for subjective sleep quality. Johns et al [24]used the Insomnia Severity Index and reported that sleep disturbance was significantly improved for intervention group compared with the control condition at both follow-up points.

Other psycho-social interventions vs usual care

The eight remaining interventions incorporated psycho-education, motivational strategies and lifestyle and behaviour change approaches [15, 16, 38, 44, 46, 48, 50].

Primary outcome: Fatigue

A patient education program was reported to have improved fatigue [44], while a combined Psycho-education and physical activity intervention showed that participants in the intervention group showed greater improvement in fatigue, but this was not a significant

effect [46]. Health coaching was found to lead to a significant reduction on fatigue at 12 months but not at 3 months[47] and an intervention employing Motivational interviewing showed no significant differences between groups at 6 months[16]. Lifestyle interventions did reported mixed findings regarding their impact on fatigue, with one [15, 40] reporting no significant differences between groups and one a significant effect of intervention at 6 months that was not maintained at 12months[50]. An online intervention that aimed to enhance self-efficacy to manage problems associated with cancer-related fatigue following primary cancer treatment reported no significant changes in fatigue[38].

Secondary Outcomes:

1. **Global quality of life /functional impact of fatigue**

   Seven of the trials on other psycho-social interventions reported on Global QoL /functional impact of fatigue [16, 38, 44, 46, 48, 50]. Four reported significant effect of the intervention over time on at least one measure of Global QoL /functional impact of fatigue[36, 44, 46, 48]. Using the SF-36, Bennett et al [16] noted Group × Time interaction was not significant for either mental or physical health. Fillion et al[32] reported marginal Group X Time interaction effects for physical quality of life in favour of the intervention group using the Medical Outcomes Study Short Form 12-Item Health Survey (SF- 12). While mental quality of life showed no interaction or main effects, both conditions improved overtime. Conversely, There was no effect on the intervention on mental well-being.

   Three studies used the EORTC core quality of life questionnaire (EORTC QLQ-C30). In the study by Reif et al[44], all functional and symptom scale values as well as single items values increased significantly in the intervention compared to the control group. Willems et al also reported that the intervention was effective in increasing emotional and social functioning at 6months [36], however these findings were not

maintained at 12months[50]. Similarly, Yun et al[48] reported a significantly greater increase in global QOL and in emotional, cognitive, and social functioning scores of EORTC QLQ-C30 scales. However, significance was lost on the emotional, and social functioning scores after Bonferroni corrections were applied for 15 multiple comparisons. Using the Functional Assessment of Cancer Therapy Scale– general FACT-G, Foster et al [38] did not report a significant effect of the intervention over time on the Fact-G measure.

2. **Fatigue self-efficacy**

   Foster et al did not reported improved fatigue self-efficacy at final follow-up[38].

3. **Mood**

   Mood was assessed in 6 of the 7 studies reporting on other psycho-social interventions [15, 38, 44, 46, 48, 50]. Yun et al [48]reported that the web-based intervention group had clinically more meaningful improvement than the control group in HADS anxiety score. However, a statistically significant greater decrease in HADS was lost after Bonferroni corrections were applied. Willems et al reported that another online intervention was effective in reducing HADS depression scores at 6months[36], but at 12 months from baseline, the intervention group no longer differed from the control group [50]. Reif et al [44] also used the HADS and reported Group X time interactions in favor of the intervention group for both anxiety and depression. Both Foster et al [38]and Bantum et al [15]reported a non-significant difference in groups in change over time using the Patient Health Questionnaire (PHQ-8). Fillion et al [46] reported that no interaction effects for Emotional distress (POMS anxiety + depression) were found.

4. **Sleep/ insomnia**

Sleep/ insomnia was assessed in 3 of the 7 studies reporting on other psycho-social interventions [15, 44, 48]. Reif et al reported an improvement in the intervention group, compared to the control group using the EORTC QLQ-C30 insomnia subscale[44]. Using the Women's Health Initiative Insomnia Rating Scale (WHIIRS), Bantum et al [15] reported that the intervention group showed reduced insomnia from baseline to 6 months compared to the control group. Finally, Yun et al [48] did not report a significant effect of the intervention on scores on the Medical Outcome Study–Sleep Scale (MOS-SS) Sleep Quality Index I and II.

Further investigation of heterogeneity in trials comparing psychological interventions (all types) vs usual care

In the original protocol, we hypothesised that each of the factors below has the potential to have a clinically meaningful effect on the response to a psychological intervention among fatigued post-treatment cancer survivors.

1. Intervention for specific cancer type only vs intervention for any cancer type
2. In-person interventions vs remote interventions
3. Interventions specifically designed to treat fatigue after cancer treatment vs interventions not specific for fatigue

We performed narrative assessment of the influence of these factors on the primary outcomes. This narrative synthesis did not reveal any clear patterns in the findings based on differential influences of these factors on the effect of psychological interventions on fatigue.

Comparison 3. Intervention for specific cancer type only vs intervention for any cancer type

In a previous Cochrane review [8] it was noted that many of the studies of fatigued cancer patients during cancer included only breast cancer patients. Nine of the effective interventions in this review only included breast cancer patients. Seven studies that focused

on breast cancer did not report a reduction in fatigue. Of 17 the studies with mixed samples, 13 reported a significant reduction in fatigue. However, breast cancer patients were often overrepresented in the studies of mixed samples. For example, one study [47] noted that over 60% of their sample had had breast cancer. Most studies included participants who had received a variety and combinations of cancer treatments (e.g. surgery, chemotherapy, radiotherapy). In one study [16], the authors specified that targeted patients were those who had received only radiotherapy.

Comparison 4. In-person interventions vs remote interventions

Sixteen of the 22 trials compared that compared a psychological intervention to waitlist control or usual care were delivered in a group setting [17, 18, 20, 24, 25, 27, 33, 34, 37, 39, 43-47], with 11 of these reporting a reduction in fatigue over time [18, 24, 25, 27, 33, 34, 37, 43-45, 47]. The majority of the group interventions had 6-9 weekly 1-2.5 hour sessions. Six included some homework or home practice [18, 20, 24, 25, 27, 39], with 4 of these studies reporting an effective reduction on fatigue[18, 24, 25, 27].

Two of the twenty-two trials that compared psychological interventions to waitlist control or usual care of the interventions involved individual face-to-face sessions- both of these were effective [32, 39]. One [47] of the 2 studies [46, 47] that offered telephone support were effective at reducing fatigue. A combination in-person/ telephone showed a reduction in fatigue at 3 months that was not maintained at 6 months[16]. Five of the studies reported on an online intervention [15, 28, 38, 48, 50]. The duration of these interventions varied from 6 weeks [15, 28, 38] to 6 months [50]. All of the interventions were stand-alone interventions and two reported a significant reduction in fatigue at final follow-up [28, 48, 50]

Comparison 5. Interventions specifically designed to treat fatigue after cancer treatment vs interventions not specific for fatigue

This review sought to interventions that were specifically designed to treat fatigue after cancer treatment and interventions not specific for fatigue. Nine of the twenty-two trials that compared psychological interventions to waitlist control or usual care were interventions specific for fatigue [17, 24, 32-34, 38, 44, 46, 48]. Of the nine studies on interventions specific for fatigue, 5 assessed fatigue as part of inclusion criteria ([24, 34, 38, 44, 48]. Only one of these 6 studies did not report a significant effect on fatigue [38]. Two of the 4 studies interventions specific for fatigue that did not assess fatigue as part of inclusion criteria were effective [32, 33]. Three studies were specific interventions for insomnia or sleep disturbance- all were effective for reducing fatigue [28, 37, 43]. The remaining studies aimed to address lifestyle and quality of life or physical activity. Of these 6 studies were effective in reducing fatigue [16, 18, 25, 45, 47, 50] at at least one follow- up point. However, the effect of the intervention on fatigue was not maintained in two of these studies at final follow-up [16, 18, 25, 45, 47, 50].

DISCUSSION

The aim of this review was to provide an overview of psychological interventions for fatigue after the completion of cancer treatment, and to evaluate the effectiveness of these interventions. In our search, 33 psychological interventions were identified, in which the effect on fatigue was tested in a RCT. The sample size of the included studies varied between 28 and 409, with 4,525 participants overall. As with a previous review of interventions during treatment [8], the individual studies suggested that there is some evidence that psychological interventions are effective in reducing fatigue in cancer survivors. Twenty-three of the included studies reported a significant effect of the interventions on fatigue. However, the

overall quality of the evidence about psychological interventions for fatigue after the completion of cancer treatment is low.

Given the heterogeneity in participant groups, study design, study comparators and measures used, we synthesised data narratively. Most interventions focused on psychoeducation, skills training, goal-setting, self-monitoring, problem-solving, identification of maladaptive cognitions and emotion-focused coping strategies. Interventions also integrated behaviour therapy-oriented strategies including stimulus control and other techniques, targeting physical activity, sleep and stress management. However, studies differed widely in terms of mode, duration and frequency of the intervention delivery. This has also been reported in other reviews of non-pharmacological interventions for fatigue [66]. There were also differences in the extent of contact across the different interventions. It was not possible to establish if certain types of intervention were superior for reducing fatigue or if there was potentially an influence of heterogeneous specific disease sites and cancer treatments. These issues have previously been reported in other studies [4, 11, 67].

Heterogeneity across the studies was also due to different definitions of fatigue criteria, various assessment tools and there were a number of different self- report measures used in the studies. As such, the same construct may not have been measured [68], as some tools were uni-dimensional, while others addressed the multi-dimensional nature of fatigue. Some of these measures were subscales of broader quality of life measures. Further, a number of these measures were designed specifically for cancer patients, while others were generic fatigue measures. Previous research has suggested that the lack of recommendations regarding fatigue measurement may be detrimental to research [68].

The strengths of this review includes the large number of studies included, a rigorous literature search based on a pre-published protocol; the use of independent raters; use of

standard tools for reporting reviews and assessing bias in studies; and the presentation of a number of different variables that may be associated with intervention effectiveness. We are not aware of any studies that we have missed but acknowledge the potential for incomplete retrieval of identified research that may be a limitation of our review.

A number of limitations reduced our ability to make strong recommendations about any of the intervention strategies. In some studies, it was difficult to assess when exactly participants completed cancer treatment prior to participating in the study. As noted in similar reviews [68-70], the generalisability of the findings are limited due to the high proportion of studies that focused specifically on breast cancer or recruited a disproportionate number of breast cancer survivors. The majority of studies did not specifically target fatigue or screen for fatigue as part of inclusion criteria as recommended in existing guidelines [1, 6, 66]. Few studies described the cancer treatment received by participants in detail, such as, types of treatments and total duration. In terms of trial design, most studies did not report on the adherence of participants to the intervention treatment, adverse effects or integrity checks that may allow further inferences to be made about the quality of the studies. Blinding of participants is often not possible to achieve in studies of this nature. However, as noted in other reviews of fatigue [67], it is troublesome that a number of studies did not ensure blinding of outcome assessment given the subjective and self- reported nature of the outcomes. Many aspects of trial procedures were not reported in sufficient detail to adequately assess risk of bias in all domains of all included trials. Trials with negative results might not have been published at all, and therefore may have been missed during our search.

Conclusion

This review showed that there is some tentative support for psychological interventions for fatigue after cancer treatment based on the findings of individual studies. However, the RCTs were heterogeneous in nature and the number of high quality studies was limited. Due to this

heterogeneity, it is difficult to draw firm conclusions from the findings of this review. These findings demonstrate the need for the publication of more detailed descriptions of complex interventions, promoting methodological rigour and transparency in the design and throughout the trial process [71, 72]. Future trials need to consider the multidimensional nature of CrF in order to improve our understanding of this complex symptom [67].

ABBREVIATIONS

AMG	AnnMarie Groarke
ASCO	American Society of Clinical Oncology
BFI	Brief Fatigue Inventory
BMG	Brian E. McGuire
CIS	Checklist Individual Strength
CrF	cancer-related fatigue
DD	Declan Devane
EC	Emma Carr
EORTC	European Organisation for Research and Treatment of Cancer
FACIT-F	Functional Assessment in Cancer Therapy - Fatigue
FACT	Functional Assessment of Cancer Therapy
FAQ	Fatigue Assessment Questionnaire
FSI	Fatigue Symptom Inventory
FSS	Fatigue Severity Scale
HADS	Hospital Anxiety and Depression Scale
IPOS	International Psycho-Oncology Society World Congress
ISI	Insomnia Severity Index
JW	Jane Walsh
MDSAI	M.D. Anderson Symptom Inventory
MeSH	Medical Subject Headings
MFI	Multidimensional Fatigue Inventory
MFSI-SF	Multidimensional Fatigue Symptom Inventory-Short Form
MOS	Medical Outcomes Study
NCCN	National Comprehensive Cancer Network
PHQ	Patient Health Questionnaire
PICO	Participants, Interventions, Comparisons, Outcome(s)
POMS	The Profile of Mood States
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSQI	Pittsburgh Sleep Quality Index
QOL	quality of life
RCT	randomised controlled trial

SF-12	Medical Outcomes Study Short Form 12-Item Health Survey
SIP	Sickness Impact Profile
STAI	State-Trait Anxiety Inventory
TC	Teresa Corbett
VAS	visual analogue scale
WHIIRS	Women's Health Initiative Insomnia Rating Scale
WHO ICTRP	World Health Organization International Clinical Trials Registry Platform

DECLARATIONS

Changes to the protocol

1. Secondary outcomes of interest to this review were specified *a prioi* in the study protocol. However, in the review process, other frequently reported secondary outcomes were identified as relevant to this review. These outcomes of interest were Insomnia or sleep quality and pain. We have included these outcomes in the review.
2. In the published protocol, we had planned to conduct a meta-analysis, if it was deemed clinically meaningful and appropriate to do so[12]. However, given the heterogeneity in participant groups, study design, study comparators and measures used, we synthesised data narratively, as a meta-analysis would have been inappropriate.
3. Due to this heterogeneity were also performed narrative assessment to explore effects by subgroups of specific psychological intervention type (e.g. cognitive behavioural therapy) vs usual care.
4. Narrative assessment was also used to summarise the influence of these factors on the primary outcomes.
    a. Intervention for specific cancer type only vs intervention for any cancer type
    b. In-person interventions vs remote interventions
    c. Interventions specifically designed to treat fatigue after cancer treatment vs interventions not specific for fatigue
5. A GRADE table has been added at the request of the editor

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Authors' contributions
TC carried out initial background research and conceived of the study. TC also drafted the manuscript. EC, TC and BMG carried out screening process. TC and DD rated the quality of evidence using GRADE. BMG and DD have helped in drafting the manuscript or revising it critically for important intellectual content. AMG and JW have made substantial contributions to conception and design of the project, including revising the manuscript. All authors have given final approval of the version to be published.

Insert Table 2 Details of the interventions included in the review

Insert Table 3 Summary of Findings for the Main Comparisons

1. Bower, J.E., et al., *Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical oncology clinical practice guideline adaptation.* Journal of Clinical Oncology, 2014. **32**(17): p. 1840.
2. Berger, A.M., et al., *Screening, evaluation, and management of cancer‐related fatigue: Ready for implementation to practice?* CA: a cancer journal for clinicians, 2015. **65**(3): p. 190-211.
3. Du, S., et al., *Patient education programs for cancer-related fatigue: a systematic review.* Patient education and counseling, 2015. **98**(11): p. 1308-1319.
4. O'Higgins, C., et al., *The pathophysiology of cancer-related fatigue: current controversies.* Supportive Care in Cancer, 2018: p. 1-12.
5. Finnegan-John, J., et al., *A systematic review of complementary and alternative medicine interventions for the management of cancer-related fatigue.* Integrative cancer therapies, 2013. **12**(4): p. 276-290.
6. Mustian, K.M., et al., *Comparison of pharmaceutical, psychological, and exercise treatments for cancer-related fatigue: a meta-analysis.* JAMA oncology, 2017. **3**(7): p. 961-968.
7. Jacobsen, P.B., et al., *Systematic review and meta-analysis of psychological and activity-based interventions for cancer-related fatigue.* Health Psychology, 2007. **26**(6): p. 660.
8. Goedendorp, M.M., et al., *Psychosocial interventions for reducing fatigue during cancer treatment in adults.* The Cochrane Library, 2009.
9. Adam, R., C. Bond, and P. Murchie, *Educational interventions for cancer pain. A systematic review of systematic reviews with nested narrative review of randomized controlled trials.* Patient education and counseling, 2015. **98**(3): p. 269-282.

10. Newell, S.A., R.W. Sanson-Fisher, and N.J. Savolainen, *Systematic review of psychological therapies for cancer patients: overview and recommendations for future research.* Journal of the National Cancer Institute, 2002. **94**(8): p. 558-584.
11. Minton, O., et al., *Cancer‐related fatigue and its impact on functioning.* Cancer, 2013. **119**: p. 2124-2130.
12. Corbett, T., et al., *Protocol for a systematic review of psychological interventions for cancer-related fatigue in post-treatment cancer survivors.* Systematic reviews, 2015. **4**(1): p. 174.
13. Moher, D., et al., *Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement.* Annals of internal medicine, 2009. **151**(4): p. 264-269.
14. Higgins, J., *Green S. Cochrane handbook for systematic reviews of interventions Version 5.1. 0. The Cochrane Collaboration.* Confidence intervals, 2011.
15. Bantum, E.O.C., et al., *Surviving and thriving with cancer using a Web-based health behavior change intervention: randomized controlled trial.* Journal of medical Internet research, 2014. **16**(2).
16. Bennett, J.A., et al., *Motivational interviewing to increase physical activity in long-term cancer survivors: a randomized controlled trial.* Nursing research, 2007. **56**(1): p. 18-27.
17. Blaes, A.H., et al., *Mindfulness-based cancer recovery in survivors recovering from chemotherapy and radiation.* Journal of Community and Supportive Oncology, 2016. **14**(8): p. 351-358.
18. Bower, J.E., et al., *Mindfulness meditation for younger breast cancer survivors: a randomized controlled trial.* Cancer, 2015. **121**(8): p. 1231-1240.
19. Dirksen, S.R. and D.R. Epstein, *Efficacy of an insomnia intervention on fatigue, mood and quality of life in breast cancer survivors.* Journal of advanced nursing, 2008. **61**(6): p. 664-675.
20. Dodds, S.E., et al., *Feasibility of Cognitively-Based Compassion Training (CBCT) for breast cancer survivors: a randomized, wait list controlled pilot study.* Supportive care in Cancer, 2015. **23**(12): p. 3599-3608.
21. Ferguson, R.J., et al., *A randomized trial of videoconference‐delivered cognitive behavioral therapy for survivors of breast cancer with self‐reported cognitive dysfunction.* Cancer, 2016. **122**(11): p. 1782-1791.
22. Freeman, L.W., et al., *A randomized trial comparing live and telemedicine deliveries of an imagery‐based behavioral intervention for breast cancer survivors: reducing symptoms and barriers to care.* Psycho‐Oncology, 2015. **24**(8): p. 910-918.
23. Heckler, C.E., et al., *Cognitive behavioral therapy for insomnia, but not armodafinil, improves fatigue in cancer survivors with insomnia: a randomized placebo-controlled trial.* Supportive Care in Cancer, 2016. **24**(5): p. 2059-2066.
24. Johns, S.A., et al., *Randomized controlled pilot study of mindfulness‐based stress reduction for persistently fatigued cancer survivors.* Psycho‐Oncology, 2015. **24**(8): p. 885-893.
25. Lengacher, C.A., et al., *Mindfulness based stress reduction in post-treatment breast cancer patients: an examination of symptoms and symptom clusters.* Journal of behavioral medicine, 2012. **35**(1): p. 86-94.
26. Matthews, E.E., et al. *Cognitive behavioral therapy for insomnia outcomes in women after primary breast cancer treatment: a randomized, controlled trial*. in *Oncology nursing forum*. 2014. Oncology Nursing Society.
27. Reich, R.R., et al., *Mindfulness-based stress reduction in post-treatment breast cancer patients: immediate and sustained effects across multiple symptom clusters.* Journal of pain and symptom management, 2017. **53**(1): p. 85-95.

28. Ritterband, L.M., et al., *Initial evaluation of an Internet intervention to improve the sleep of cancer survivors with insomnia.* Psycho- Oncology, 2012. **21**(7): p. 695-705.
29. Rogers, L.Q., et al., *Effects of a multicomponent physical activity behavior change intervention on fatigue, anxiety, and depressive symptomatology in breast cancer survivors: randomized trial.* Psycho- oncology, 2017. **26**(11): p. 1901-1906.
30. Rogers, L.Q., et al., *Physical activity and health outcomes three months after completing a physical activity behavior change intervention: persistent and delayed effects.* Cancer Epidemiology and Prevention Biomarkers, 2009. **18**(5): p. 1410-1418.
31. Bruggeman-Everts, F.Z., et al., *Effectiveness of two web-based interventions for chronic cancer-related fatigue compared to an active control condition: results of the "Fitter na kanker" randomized controlled trial.* Journal of medical Internet research, 2017. **19**(10).
32. Gielissen, M.F., et al., *Effects of cognitive behavior therapy in severely fatigued disease-free cancer patients compared with patients waiting for cognitive behavior therapy: a randomized controlled trial.* Journal of Clinical Oncology, 2006. **24**(30): p. 4882-4887.
33. Prinsen, H., et al., *The role of physical activity and physical fitness in postcancer fatigue: a randomized controlled trial.* Supportive Care in Cancer, 2013. **21**(8): p. 2279-2288.
34. van der Lee, M.L. and B. Garssen, *Mindfulness- based cognitive therapy reduces chronic cancer- related fatigue: a treatment study.* Psycho- Oncology, 2012. **21**(3): p. 264-272.
35. van Weert, E., et al., *Cancer-related fatigue and rehabilitation: a randomized controlled multicenter trial comparing physical training combined with cognitive-behavioral therapy with physical training only and with no intervention.* Physical therapy, 2010. **90**(10): p. 1413-1425.
36. Willems, R.A., et al., *Short- term effectiveness of a web- based tailored intervention for cancer survivors on quality of life, anxiety, depression, and fatigue: randomized controlled trial.* Psycho- oncology, 2017. **26**(2): p. 222-230.
37. Espie, C.A., et al., *Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer.* Journal of clinical oncology, 2008. **26**(28): p. 4651-4658.
38. Foster, C., et al., *A web-based intervention (RESTORE) to support self-management of cancer-related fatigue following primary cancer treatment: a multi-centre proof of concept randomised controlled trial.* Supportive Care in Cancer, 2016. **24**(6): p. 2445-2453.
39. Hoffman, C.J., et al., *Effectiveness of mindfulness-based stress reduction in mood, breast-and endocrine-related quality of life, and well-being in stage 0 to III breast cancer: a randomized, controlled trial.* J Clin Oncol, 2012. **30**(12): p. 1335-1342.
40. Reeves, M., et al., *The Living Well after Breast Cancer™ Pilot Trial: A weight loss intervention for women following treatment for breast cancer.* Asia- pacific Journal of Clinical Oncology, 2017. **13**(3): p. 125-136.
41. Sandler, C.X., et al., *Randomized evaluation of cognitive-behavioral therapy and graded exercise therapy for post-cancer fatigue.* Journal of pain and symptom management, 2017. **54**(1): p. 74-84.
42. Carlson, L.E., et al., *Randomized controlled trial of mindfulness-based cancer recovery versus supportive expressive group therapy for distressed survivors of breast cancer.* J Clin Oncol, 2013. **31**(25): p. 3119-3126.

43. Savard, J., et al., *Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects.* Journal of Clinical Oncology, 2005. **23**(25): p. 6083-6096.
44. Reif, K., et al., *A patient education program is effective in reducing cancer-related fatigue: a multi-centre randomised two-group waiting-list controlled intervention trial.* European journal of oncology nursing, 2013. **17**(2): p. 204-213.
45. Dolbeault, S., et al., *The effectiveness of a psycho‐educational group after early‐stage breast cancer treatment: results of a randomized French study.* Psycho-Oncology: Journal of the Psychological, Social and Behavioral Dimensions of Cancer, 2009. **18**(6): p. 647-656.
46. Fillion, L., et al., *A brief intervention for fatigue management in breast cancer survivors.* Cancer nursing, 2008. **31**(2): p. 145-159.
47. Yun, Y.H., et al., *A randomized controlled trial of physical activity, dietary habit, and distress management with the Leadership and Coaching for Health (LEACH) program for disease-free cancer survivors.* BMC cancer, 2017. **17**(1): p. 298.
48. Yun, Y.H., et al., *Web-based tailored education program for disease-free cancer survivors with cancer-related fatigue: a randomized controlled trial.* Journal of Clinical Oncology, 2012. **30**(12): p. 1296-1303.
49. Carlson, L.E., et al., *Randomized‐controlled trial of mindfulness‐based cancer recovery versus supportive expressive group therapy among distressed breast cancer survivors (MINDSET): long‐term follow‐up results.* Psycho-Oncology, 2016. **25**(7): p. 750-759.
50. Willems, R.A., et al., *Long-term effectiveness and moderators of a web-based tailored intervention for cancer survivors on social and emotional functioning, depression, and fatigue: randomized controlled trial.* Journal of Cancer Survivorship, 2017. **11**(6): p. 691-703.
51. Zigmond, A.S. and R.P. Snaith, *The hospital anxiety and depression scale.* Acta psychiatrica scandinavica, 1983. **67**(6): p. 361-370.
52. Spitzer, R.L., J.B. Williams, and K. Kroenke, *Patient Health Questionnaire: PHQ*. 1999: New York State Psychiatric Institute.
53. Lorr, M. and D.M. McNair, *Profile of mood states-bipolar form*. 1988: Educational and Industrial Testing Service San Diego, CA.
54. Spielberger, C.D., et al., *State-trait anxiety inventory (STAI).* BiB, 2010. **1970**: p. 180.
55. Aaronson, N.K., et al., *The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology.* JNCI: Journal of the National Cancer Institute, 1993. **85**(5): p. 365-376.
56. Cella, D.F., et al., *The Functional Assessment of Cancer Therapy scale: development and validation of the general measure.* J Clin Oncol, 1993. **11**(3): p. 570-579.
57. Luckett, T., et al., *Choosing between the EORTC QLQ-C30 and FACT-G for measuring health-related quality of life in cancer clinical research: issues, evidence and recommendations.* Annals of Oncology, 2011. **22**(10): p. 2179-2190.
58. Stewart, A.L., R.D. Hays, and J.E. Ware, *The MOS short-form general health survey: reliability and validity in a patient population.* Medical care, 1988. **26**(7): p. 724-735.
59. Bergner, M., et al., *The Sickness Impact Profile: development and final revision of a health status measure.* Medical care, 1981: p. 787-805.
60. Ware Jr, J.E., M. Kosinski, and S.D. Keller, *A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity.* Medical care, 1996. **34**(3): p. 220-233.

61. Cleeland, C.S., et al., *Assessing symptom distress in cancer patients: the MD Anderson Symptom Inventory.* Cancer: Interdisciplinary International Journal of the American Cancer Society, 2000. **89**(7): p. 1634-1646.
62. Morin, C.M., *Insomnia: Psychological assessment and management*. 1993: Guilford Press.
63. Levine, D.W., et al., *Reliability and validity of Women's Health Initiative Insomnia Rating Scale.* Psychological assessment, 2003. **15**(2): p. 137.
64. Buysse, D.J., et al., *The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research.* Psychiatry research, 1989. **28**(2): p. 193-213.
65. Lengacher, C.A., et al., *Examination of broad symptom improvement resulting from mindfulness-based stress reduction in breast cancer survivors: a randomized controlled trial.* Journal of clinical oncology, 2016. **34**(24): p. 2827.
66. Hulme, K., et al., *Fatigue interventions in long term, physical health conditions: A scoping review of systematic reviews.* PloS one, 2018. **13**(10): p. e0203367.
67. Bennett, S., et al., *Educational interventions for the management of cancer‐related fatigue in adults.* Cochrane Database of Systematic Reviews, 2016(11).
68. Pearson, E., et al., *Interventions for cancer‐related fatigue: a scoping review.* European journal of cancer care, 2018. **27**(1): p. e12516.
69. Kelley, G.A. and K.S. Kelley, *Exercise and cancer-related fatigue in adults: a systematic review of previous systematic reviews with meta-analyses.* BMC cancer, 2017. **17**(1): p. 693.
70. Johnson, J.A., et al., *A systematic review and meta-analysis of randomized controlled trials of cognitive behavior therapy for insomnia (CBT-I) in cancer survivors.* Sleep medicine reviews, 2016. **27**: p. 20-28.
71. Craig, P., et al., *Developing and evaluating complex interventions: the new Medical Research Council guidance.* International journal of nursing studies, 2013. **50**(5): p. 587-592.
72. Hoffmann, T.C., et al., *Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide.* Bmj, 2014. **348**: p. g1687.

Availability of data and materials

The dataset supporting the conclusions of this article is included within the article (and its additional file(s)).

Table 1. Sample Search Strategy: Details of the terms searched in CINAHL database

	Search term
1	'cancer survivors' OR 'neoplasm'/exp OR neoplasm OR surviv* OR 'cancer'/exp OR cancer OR 'remission'/exp OR remission OR 'post treatment'
2	psychology OR psych*or AND behaviour AND therapy OR hypnosis OR relaxation OR imagery OR cognition OR psychotherapy OR cognit*
3	fatigue OR asthenic OR asthenia OR exhaustion OR exhausted OR 'loss of energy' OR 'loss of vitality' OR weary OR weariness OR weakness OR apathy OR apathetic OR lassitude OR lethargic OR lethargy OR sleepy OR sleepiness OR drowsy OR drowsiness OR tired OR tiredness
4	“randomized controlled trial” OR controlled OR clinical OR trial OR 'random assignment'
5	1 AND 2 AND 3 AND 4

Table 2 Details of the interventions included in the review

Study	Content	Strategies	Time since treatment	Mode	Duration	Delivered by	Control group
Bantum 2014	Multiple health behaviour change program.	Skills building; information; encouragement; action planning; building self-efficacy; improving diet; increasing exercise; stress management via relaxation training;· processing and communicating emotional experiences; fatigue management	Had completed primary treatment within last 5 years	Online	6 x weeks	Cancer survivors mentored by the principal investigators.	Waitlist control
Bennett 2007	Motivational interviewing	Careful listening; summarising; feedback; barrier identification; affirmation; building self-efficacy	Had completed primary treatment at least 6 months prior to the study	In-person/ Telephone	3 x 10-minute MI sessions. 20-minutes per phone call	Physical activity counsellor and master's-prepared research assistant	Usual care
Blaes 2016	Mindfulness based cancer recovery programme was used.	A range of Mindfulness meditaion techniques practiced during group sessions , Expected to practice home meditaion for 45 minutes a day, keep a log of home practice sessions along with doing mindfulness readingand reflective exercises	Had completed primary treatment at least 6 months prior to the study	Group	8 weekly 2.5 hour classess and a full day silent retreat	University Faculty trained and certified in MBCR programme	Waitlist control
Bower 2015	Mindfulness	Information; mindfulness; relaxation; meditation; gentle movement exercises (e.g., mindful walking); psychoeducation; problem solving; working with difficult thoughts and emotions; managing pain; cultivation of loving kindness.	Had completed primary treatment at least 3 months prior to the study	Group	6 weekly x 2-hour sessions. Daily home-practice 5-20 minutes.		Waitlist control
Bruggeman-Everts 2017	Two different Web-based interventions aimed at reducing	AAF: involves taking notice of the Personal Digital Assistant messages, responding to these messages by changing physical	Had completed primary treatment at	Online	3/ hours per week, 9 weeks	AAF : pyshiotherapist	Compared two different guided Web-

	CCRF: (1) Ambulant Activity Feedback (AAF), and (2) Web-based Mindfulness-Based Cognitive Therapy (eMBCT)	activity, reading the weekly feedback from the physiotherapist, reporting experiences, and replying to the feedback by email. eMBCT: reading the weekly information, doing mindfulness exercises while listening to the MP3 files, filling out logs with their experiences, reading the weekly feedback of the therapist, and replying to this feedback by email weekly	least 3 months prior to the study			& eMBCT: psychologist	based interventions compared to an unguided active control condition receiving psycho-educational emails
Carlson 2016	Mindfulness -based cancer recovery programme (MBCR) VS Supportive expressive group therapy	Both based on existing available programmes. Mindfulness conscious awareness cultivated through training in mindfulness meditation and gentle yoga practices. SET facliitated mutual support, enhancing emotional expresiveness and coping, detoxifying feelings around death	Had completed primary treatment at least 3 months prior to the study	Group	8 weekly sessions of 90 minutes each plus a 6 hour workshop (total of 18 hours)	Research Assistants	Compared two empirically supported group interventions: mindfulness-based cancer recovery (MBCR) and supportive-expressive group therapy (SET). These were also compared to a minimal-treatment control condition that was a 1-day didactic stress

							management seminar.
Dirksen 2008	CBT- insomnia	Stimulus control instructions;· sleep restriction therapy; sleep education and hygiene; cognitive strategies; sleep diaries; discussing progress.	Had completed primary treatment at least 3 months prior to the study	Group	2-weeks pre-treatment 6-weeks x treatment : 4 x week classes (1-2 hour) and 2 x week telephone (15 mins) 2-weeks post-treatment	Master's level Registered Nurse therapist	Education
Dodds 2015	Cognitively-based compassion training	CBCT was delivered in eight weekly, 2-h classes through didactics, class discussion, and guided meditation practice. Participants were asked to meditate at least three times per week using audio recordings of guided meditations (average length 30 min), and to maintain a practice log.	Treated with adjuvant systemic chemotherapy within the past 10 years	Group and individual	8 weekly 2 hour classes and home meditaion 3 times a week	The interventionist was a clinically trained Ph.D. social work researcher and experienced 20-year meditator fulfilling requirements for CBCT teacher certification of the Emory University-Tibet Science Initiative (ETSI).	Waitlist control

Dolbeault 2009	Psycho-educational group based on CBT	Self-monitoring; problem-solving; cognitive restructuring; communicate; relaxation.	Had completed primary treatment at least two weeks prior to the study (within the last year)	Group	8 weekly x 2-hour sessions,	Led by 2 therapists, either psychologists or psychiatrists trained in group therapy and BCT	Waitlist control
Espie 2008	CBT- insomnia	Stimulus control; sleep restriction; cognitive therapy strategies.	Had completed primary treatment at least four weeks (1 month) prior to the study	Group	5 weekly, 50-minute sessions.	Cancer nurses, mentored by clinical psychologist	Usual care
Ferguson 2016	CBT-MAAT: cognitive behavioral therapy, Memory and Attention Adaptation Training	The 4 MAAT components include: 1) education, 2) self-awareness training to identify, 3) stress management and self-regulation, 4) cognitive compensatory strategies training	Had completed primary treatment at least 6 months prior to the study	Videoconference device	8 visits of 30 to 45 minutes	clinical psychologist	Compared cognitive behavioural therapy (CBT) Memory and Attention Adaptation Training (MAAT), with an attention control condition.
Fillion 2008	Psycho-education and physical activity	Relaxation skills; coping strategies; links between thoughts, emotions, and fatigue; self-regulation techniques (e.g., self-recording and goal setting); decrease passive coping strategies (e.g., behavioural and social disengagement and naps);	Completed their initial cancer treatment no longer than 2 years before enrolment	Group	4 weekly group meetings of 2.5-hours and 1 x short telephone	Kinesiologist, trained research nurses,	Usual care

		increase awareness of the benefits of exercise; adherence techniques; reinforcement self-efficacy, motivation, and positive outcomes.			booster session (5-15 minutes)		
Foster 2016	Self-efficacy to manage CrF	Defines CRF (possible causes and effects); goal setting and planning; diet, sleep, exercise, home life and work; thoughts and feelings; strategies for talking to others; patient stories; self-monitoring; feedback; automated weekly emails; reminders.	Any time point following primary cancer treatment (within last 5 years)	Online	6 weeks.	online	Waitlist control
Freeman 2015	Imagery-based intervention	Education on the mind–body connection; impact of mental imagery and the sensate experience on physiological processes; apply learning and receive peer-feedback; identify maladaptive 'passive imagery' (e.g., automatic thoughts focused on fear/loss of control); create adaptive 'active imagery' (e.g., thoughts focused on empowering, meaning–making themes); practice 'targeted imagery'; monitor the effects of imagery on mind–body health.	At least 6 weeks after completing cancer treatment	Group/ tele-medicine	5 weekly 4-hour group sessions (live delivery or telemedicine delivery). First 4 sessions separated into 3 modules (25-minutes didactic education; 25-minutes of group interaction; 20–30 minutes guided imagery). Brief (<10 min) weekly	Licensed professional counsellor, and a family medicine physician	Compared live and telemedicine deliveries of an imagery-based behavioural intervention. Also had a waitlist control condition.

					phone calls during intervention delivery and for 3 x months post-treatment.		
Gielissen 2006	CBT	Focused on six perpetuating factors (six modules) of post-cancer fatigue, which were based on existing literature and experience in clinical practice: Coping with the experience of cancer; fear of disease recurrence; dysfunctional cognitions concerning fatigue; dysregulation of sleep and activity; focus on low social support and negative social interactions.	Had completed primary treatment at least 1 year prior to the study	Individual	Number of sessions was determined by the number of modules used and whether the goal of the therapy was reached. 5-26 x 1-hour therapy sessions over 6-month period (M = 12.5 sessions; SD= 4.7 sessions).	3x therapists with previous CBT experience with patients with chronic fatigue	Waitlist control
Heckler 2016	CBT- insomnia	sleep hygiene guidelines; study medication instructed to take the study medication (armodafinil or placebo) in a split dose (7–9 am and 12–2 pm) for a total of 47 days	Had completed primary treatment at least four weeks (1 month) prior to the study	Individual	7 weeks ; CBT-I sessions 1, 2, and 4 were in person (30–60 min in duration), and sessions 3, 5,		Compared CBT-I to a wakefulness-promoting agent, armodafinil

					6, and 7 (15–30 min in duration) were by phone		
Hoffman 2012	Mindfulness for CRF	Body scan; sitting/ walking/ compassion meditation; gentle hatha yoga; psycho-education related to CrF; class discussion; bedtime body scan; information (relationship of stress and fatigue, influence of the perception of exhaustion on subsequent diminished physical activity and that physical activity is helpful with CrF); mindful communication practice.	Had completed primary treatment at least 2 months prior to the study (completed their initial cancer treatment no longer than 2 years before enrolment)	Group	7 weeks x 2-hour classes; Guided home practices (20 min)	MBSR teaching experience	Waitlist control
Johns 2014	MBSR-CRF	body scan, sitting meditation, gentle hatha yoga, walking meditation, and compassion meditation; protocol was adapted for the cancer context, a practice that has precedent in previous studies ; MBSR-CRF adaptations included 2-h classes, seven classes instead of eight, no retreat, brief psycho-education related to CRF, and shorter guided home practices (20 min) to accommodate fatigued participants; however, all of the core content of the standard MBSR curriculum was included. Recordings of guided meditations of body scan, sitting meditation, gentle hatha yoga	Had completed primary treatment at least 3 months prior to the study	group	7 x 2-h classes; guided home practices (20 min)	instructor had 6 years of MBSR teaching experience, completing all components of professional training leading to eligibility for MBSR Teacher Certification Review (phase 4, Oasis	Waitlist control

		with chair adaptations, and compassion meditation were created by the facilitator for home practice.				Institute at the Center for Mindfulness in Medicine, Health Care and Society	
Lengacher 2012	Mindfulness	Awareness of thoughts and feelings through meditation practice (sitting and walking meditation, body scan, and gentle hatha yoga); informal mindfulness meditation; educational material related to relaxation, meditation, and the mind–body connection; pay attention and observe responses during stressful situations; group support sessions on emotional/ psychological responses and physical symptoms; discussion of barriers to the practice of meditation and application of mindfulness in daily situations; supportive interaction between group members.	Had completed primary treatment within 18 months prior to study	Group	6 weekly, 2-hour sessions; Formal exercises (15–45 min per day, 6 x days per week; increased per week); Informal home practice; 1x day x 8-hour silent retreat.	Licensed clinical psychologist trained in MBSR	Usual care
Matthews 2014	CBT- insomnia	Treatment rationale; conceptual model of insomnia; sleep restriction; stimulus control; sleep schedule; sleep hygiene; cognitive therapy: altering dysfunctional beliefs about sleep and the impact of sleep loss on daytime functioning; sleep titration and treatment gains; relapse prevention and skills to cope with setbacks.	Had completed primary treatment at least four weeks (1 month) prior to the study	Group/ individual 3 x sessions in person 2x sessions via telephone.	5 weekly sessions: Session 1: 60 mins; Session 2, 3 and 6: 30–45 minutes; Session 4 and 5 (Telephone): 15–20 minutes.	An advanced practice nurse with specialized training in CBTI	Active behavioural placebo treatment (BPT).

Prinsen 2013	CBT for post-cancer fatigue.	Information on coping with the experience of cancer; fear of disease recurrence; dysfunctional cognitions concerning fatigue; dysregulation of sleep; dysregulation of activity; discussion of low social support and negative social interactions; tailored physical activity program of walking or cycling; gradually replace physical activities by other activities.	Had completed primary treatment at least 1 year prior to the study	Group	12–14 (50 min) individual sessions in 6 months. Two daily sessions of tailored physical activity program	Psychologists	Waitlist control
Reeves 2017	Combined approach of increasing physical activity, reducing energy intake and behavioral therapy,	received a detailed workbook, self-monitoring diary, digital scales, pedometer, calorie-counter book and up to 16 telephone calls over the intervention	Any time point following primary cancer treatment	telephone-delivered	6 months: Telephone calls (weekly for 6 weeks followed by 10 fortnightly calls)	lifestyle coaches, who were accredited practicing dietitians trained in exercise promotion and motivational interviewing	Usual care
Reich 2017	MBSR (BC)	1) educational material related to relaxation, meditation, the mind-body connection, and a healthy lifestyle for survivors, 2) practice of meditation in group meetings and homework assignments, and 3) group processes related to barriers to the practice of meditation and supportive group interaction. training in formal meditation techniques (sitting meditation, body scan, gentle Hatha yoga, and walking meditation), along with informal	Had completed primary treatment within previous two weeks (completed their initial cancer treatment no longer than 2	group	Six-week, two-hour per week sessions; practice the meditative techniques for 15–45 minutes per day	Psychologist trained in MBSR; Intervention sessions conducted by a single instructor were monitored weekly by a research assistant, who	Waitlist control

		techniques of integrating mindfulness into daily life activities. BCS were requested to formally and informally practice the meditative techniques for 15–45 minutes per day and to record their practice times in a daily diary. A manual and compact discs were provided to guide home practice.	years before enrolment)			recorded time and delivery of the components of the two-hour class sessions on a fidelity checklist.	
Reif 2012	Patient education program	Problem solving; goal setting and evaluation; other cognitive techniques; behaviour therapy-oriented strategies and techniques; diary-keeping; perform exercises and implement lifestyle changes.	Any time point following primary cancer treatment	Group	6 weekly 90-minute sessions. 2 x additional meetings after 3 and 6 months.	Nurses/ psychologist	Waitlist control
Ritterband 2012	CBT- insomnia	Introduction and rationale; sleep restriction; stimulus control; sleep hygiene; identify and restructure unhelpful beliefs about sleep; relapse prevention; high degree of individual tailoring and feedback; interactive elements; automated emails; encourage adherence.	Had completed primary treatment at least four weeks (1 month) prior to the study	Online	Access to Shuti for 9 weeks (6 week programme). Each core: 45 and 60 minutes.	NA	Waitlist control
Rogers 2017	Physical activity behaviour change intervention	Self-efficacy; outcome expectations; behavioural capability; observational learning; self-control; social support; personal behavioural modification plan; overcoming exercise barriers; emotional coping (including stress management); exercise benefits; task self-efficacy by gradual advancement of the exercise prescription; self-monitoring with daily activity log; overcoming exercise barriers	Had completed primary treatment at least 2 months prior to the study	Group/ individual	12-week programme: 6 group sessions during the first 8 weeks; 12 individual exercise sessions during the	trained facilitators Psychologist/ exercise specialist	Provided publically available, printed materials

		experienced by the participant; self-monitoring; use of the behavioural modification plan; providing positive reinforcement; setting up for maintenance			first 6weeks; 3 individual counselling sessions during the final 6 weeks.		
Sandler 2017	CBT and GET (Graded exercise) or education	Activity pacing, graded exercise,psychoeducation, sleep wake management, cognitive retraining, 3 optional CBT modules = coping , depression and anxiety management	Had completed primary treatment at least 3 months prior to the study	individual	12 weeks 5 45minute sessions with exercise therapist and 6 to 8 x 55 minute sessions with psychologist conduced fortnightly	Clinical Psychologist and Exercise Physiologist	Education
Savard 2005	CBT- insomnia	Stimulus control therapy; sleep restriction; cognitive restructuring; sleep hygiene; fatigue and stress management	Had completed primary treatment at least four weeks (1 month) prior to the study	Group	8 weekly sessions of approximately 90 minutes	Master-level psychologist.	Waitlist control
Van Der Lee 2012	MBCT	Skills that enhance the ability to raise awareness to present experiences; information and instructions about various themes; home practice (CDs with breathing instruction and awareness exercises).	Had completed primary treatment at least 1 year prior to the study	Group	9 week group therapy, weekly sessions (2.5 hours); 1 x 6 hour session; 1 x 2.5 hours follow-up session 2 x months after	Both therapists had followed MBSR training with Kabat Zinn.	Waitlist control

					the 9th session. Total duration = 28.5 hours.		
Van Weert 2010	CBT and physical activity	Self- management, goal setting, monitoring; norms and decision making, action, self-reflection; self-efficacy: mastery of experiences and perceived success, modelling, social persuasion, physiological feedback; discussion of irrational illness perceptions; finding effective and adaptive solutions to stressful problems; dysfunctional cognition, emotions, and behaviours; discussing distress, exercise physiology, and relaxation; homework assignment, and relaxation exercises; individual fitness goal-aerobic training muscle strength training, and information; information on the benefits of exercise; illustrative "model of fatigue,"; restore the balance between demand and capacity during tasks and activities.	Had completed primary treatment at least 3 months prior to the study	Group	1hour twice a week for 12 weeks (24 hours individual physical training and 24 x hours of group sports and games). 24 hours CBT (once a week, 2 x hours per session).	2 x physical therapists experienced in the delivery of physical training interventions to patients with cancer. CBT was supervised by 2 x psychologists.	Compared physical training combined with cognitive behavioural therapy with physical training alone and with no intervention.
Willems 2016	Psychosocial and lifestyle support	Self-management training; return-to-work; fatigue; anxiety and depression; social relationship and intimacy issues; physical activity, diet, smoking cessation; general information on the most common residual symptoms	Had completed primary treatment at least four weeks (1 month) prior to the study (within the last year)	Online	6 months	Stand-alone online	Waitlist control

Yun 2017	Health coaching	physical activity, dietary habits, and distress management: individual tele-coaching: a TTM-based health education booklet and workbook for cancer survivors, 2) a workshop for empowerment of patients' leadership skills, and 3) TTM-based telephone coaching with a health coaching manual (repeated assessment of stage of change, and planning how to achieve target health levels in accordance with their preferences and abilities)	Completed their initial cancer treatment no longer than 2 years before enrolment	Group/ individual tele-coaching	1-h health education workshop 3-h leadership workshop individual coaching by telephone for a 24-week period (intervention only)- 16 sessions of tele-coaching were conducted: 30 min per week for 12 sessions, 30 min per 2 weeks for 2 sessions, and 30 min per month for 2 sessions were offered for the intervention group.	Health partners: long-term cancer survivors who formed partnerships with cancer patients and helped them achieve the target levels set for their health behaviors. Health master coaches: health professionals who mentored and supervised health partners.	Usual care
Yun 2012	CBT	Based on 2008 National Comprehensive Cancer Network & on the transtheoretical model (TTM) of health behaviour change	Completed their initial cancer treatment no	Online	12 weeks	Independent research	Usual care

		and social cognitive theory as developed by Bandura or on cognitive behavioural therapy (CBT). Personally tailored sections based on the TTM model; physical activity; sleep hygiene; pain control; general introduction; energy conservation; nutrition; distress management; self-assessment and graphic reports; health advice; online education, caregiver monitoring and support; health professional monitoring.	longer than 2 years before enrolment			coordinator (nurse)	

Table 3 Summary of Findings for the Main Comparisons

Study	Measure used to assess fatigue	Total	n-intervention	n Control	Final follow-up	Finding
Bantum 2014	Brief Fatigue Inventory (BFI)	303	156	147	6 months	p=0.56 Effect size= 0.17 (Calculated by taking the differences of the means at 6 months predicted from the model, including adjustment factors, divided by the standard deviation for the difference computed from the within and between subject variance components.) Control group, • Baseline (n=176); mean (95% CI)= 40.8 (38.9-42.8) • Month 6 (n=156) ; mean (95% CI)= 40.7 (38.7-42.8) Intervention group • Baseline (n=176) ; mean (95% CI)= 39.0 (37.0-40.9) • Month 6 (n=147) ; mean (95% CI)= 36.4 (34.2-38.5)
Bennett 2007	Schwartz Cancer Fatigue Scale	56	28	28	6 months	On average, the level of fatigue status for all participants was 15.20 at baseline and declined 4.22 points (27%) across the study. Group × Time interaction for fatigue was significant [Λ =0.78, $F(2,37) = 5.24$, p =0.010]. However, inspection of the graph showed this was an artifact of 3-month measures, whereas values at baseline and **at 6 months showed no significant differences between groups**, leading to the conclusion that the significant effect of the interaction was the result of measurement error.
Blaes 2016	Functional Assessment in cancer Therapy-Fatigue (FACT-F)	42	28	14	4 months	There was an improvement in fatigue in both groups with time. Mean improvement from baseline to 4 months was 6.8 for the MBCR group and 1.3 for controls (p = 0.19). There was **no statistically significant difference in improvement in fatigue for two groups**.
Bower 2015	Fatigue Symptom Inventory	71	39	32	3 months	Mindfulness led to significant improvements in fatigue (p = 0.007), from pre- to post-intervention. **No group differences in change from baseline to 3-month follow-up p=0.57**
Bruggeman-Everts 2017	Checklist Individual Strength -	167	55	112	9 weeks	AAF = eMBCT = psycho-education $\chi2(4)=27.63$, P<.001 AAF = psycho-education $\chi2(2)=28.28$, P<.001 eMBCT = psycho-education $\chi2(2)=10.89$, P=.004 AAF = eMBCT $\chi2(2)=2.19$, P=.34

	Fatigue Severity [CIS-FS] subscale					Multiple group latent growth curve analysis, corrected for individual time between assessments, showed that fatigue severity decreased significantly more in the AAF and eMBCT groups compared to the psychoeducational group.
Carlson 2013 (2016)	POMS	271	113	158	6 and 12 months later.	Group-by-time effect at intervention (6months): p=0.001 95% CI −0.45 [−0.70;−0.20] **Group-by-time effect at follow-up (12 months) p= 0.76**
Dirksen 2008	Profile of Mood States Fatigue/Inertia Subscale (POMSF/I)	72	34	38	2 weeks	Statistically significant pre- to post-treatment change (P<0.05). From pre- to post-treatment, the CBT-I group improved on fatigue. Statistically significant interaction effects were found for fatigue At post-treatment, a trend was noted towards lower fatigue [t(70) = 1·87, P = 0·07].
Dodds 2015	Medical Outcomes Study Short Form 12-Item Health Survey (SF-12)	28	16	12	4-week	Improvement in fatigue/vitality From baseline to study week 8 = 5.5, 95% CI [1.5; 9.6]; 1-month FU 0.3 95% CI [−4.2; 4.9] **no significant differences at the 4- week follow-up.**
Dolbeault 2009	POMSF/I and EORTC Fatigue	167	81	86	6 months	Comparison of change scores between randomization arms (Group: n=81; Control: n=87) POMS Fatigue • Group: E1 Mean (SD) 10.01 (7.38) ; E3 Mean (SD) 6.86 (5.58) ; Intra-subject p= -0.069 Eta^2= 0.02 • Control: E1 Mean (SD) 8.78 (6.85); E3 Mean (SD) 8.87 (6.84) Inter-subject p= 0.370 Eta^2= 0.01 • **Time X group p= 0.000 Eta^2= 0.07** EORTC Fatigue • Group: E1 Mean (SD) 2.24 (0.81) ; E3 Mean (SD) 2.08 (0.73) Intra-subject p= 0.834 Eta^2= 0.00 • Control E1 Mean (SD) 2.09 (0.68) ; E3 Mean (SD) 2.14 (0.77) • Inter-subject p= 0.408 Eta^2= 0.00

						• **Time X group p= 0.036 Eta²= 0.03** **A greater reduction of negative affects and improvement in positive affects and in quality of life functional or symptom scales were observed in the TG compared with the CG. This concerned the POMS fatigue (7% of the variance explained by the model including the time/group interaction term) and the EORTC QLQ-C30 fatigue (3%).**
Espie 2008	FSI	150	100	50	6 months	p< 0.001 (Standardized Effect =-0.82) CBT participants had reduced symptoms of fatigue relative to TAU. **FSI Interference** **Post-Treatment** • Standardized Effect - 0.81 • 95% CI -1.20 to-0.42 • *P*< 0.001 **6-Month Follow-Up** • Standardized Effect - 0. 82 • 95% CI -1.22 to-0.42 • *P*< 0.001
Ferguson 2016	Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F]	47	27	20	2 months	Memory and Attention Adaptation Training (MAAT) and Supportive Therapy (ST) participants did not differ with regard to fatigue (FACIT-F) at the post-treatment (F (1,28), 0.072; p =0.79) or 2-month ((F (1,28), 2.35; p =0 .14). The Cohen's d effect sizes for, fatigue at the 2-month follow-up time point suggested that MAAT participants demonstrated sustained clinical gains compared with ST participants (0.46)
Fillion 2008	Multidimensional Fatigue Inventory	87	44	43	3 months	Marginal Group x Time interaction effects: p=0 .07; Cohen d= 0.36 Significant Time main effects: p=0 .0001; Cohen d= 0.69 Significant Group main effects: p=0 .03; Cohen d= 0.49 Results showed that participants in the intervention group showed greater improvement in fatigue.
Foster 2015	Brief Fatigue Inventory (BFI)	159	83	76	12 weeks	T1 Group effect (95 % CI) 0.514 (−0.084, 1.112) p= 0.09 T2 Group effect (95 % CI) 0.106 (−0.427, 0.638) p= 0.70
Freeman 2015	FACIT-Fatigue and Scale (FACIT-F, version 4)	118	71	47	3 months	Group effect p-value= 0.002 Time effect p-value= 0.084 Group × time effect p-value= 0.321

						The Bonferroni method was used to correct for multiple comparisons, and alpha was adjusted to 0.01. Linear multilevel modeling analyses revealed less fatigue, cognitive dysfunction, and sleep disturbance for Live Delivery and Telephone Delivery compared with WL across the follow-up (p's<0.01). Changes in fatigue, cognitive dysfunction, sleep disturbance, and health-related and breast cancer-related QOL were clinically significant. There were no differences between LD and TD.
Gielissen 2006	Fatigue severity subscale of the CIS	98	50	48	6 months	Patients in the intervention condition reported a significantly greater decrease than patients in the waiting list condition in fatigue severity (difference, 13.3; 95% CI, 8.6 to 18.1)
Heckler 2016	Brief Fatigue Inventory (BFI)/ FACIT-F	96	47	49	7 weeks (post intervention)	CBT and placebo P= 0.0005 (95 % CI) [−2.22, −0.74] CBT and placebo P= <0.0001 (95 % CI) [5.57, 12.90] CBT-I effect (95% CI) for BFI was −1.00 (−1.64, −0.37), P=0.0024, meaning that CBT-I led to a mean change one unit less than no CBT-I. The CBT-I effect (95 % CI) for FACIT-Fatigue was 7.16 (3.68, 10.64), P<0.0001, meaning that CBT-I led to a mean change seven units higher than no CBT-I. No statistically significant change between post-intervention and follow-up; P=0.294 (BFI), P=0.145 (FACIT-Fatigue).
Hoffman 2012	pOMSF/I	214	103	111	12-14 weeks	There were statistically significant differences between treatment groups for POMS fatigue *P= 0* .002 [8 weeks only] Difference Between Groups at T2 Adjusted for Baseline Mean= -2.68; 95% CI= [-4.31 to -1.04] Difference Between Groups at T3 Adjusted for Baseline Mean= -1.84 95% CI= [-3.45 to -0.22] Interaction time X treatment group, *P* .324
Johns 2014	Fatigue Symptom Inventory	35	18	17	1 month	significantly greater improvements in fatigue interference than wait-list controls. The magnitude of the effect of MBSR on this and other fatigue outcomes including fatigue severity and vitality was large at the end of the intervention and 1 month later. improvements in all

						symptoms were maintained for at least 6 months beyond the completion of the MBSR course for both groups after their respective courses. T2 FSI interference p*=<0.001 Pooled SD= 1.73 Effect size=-1.43 95% CI effect size=[1.96, -0.90] FSI severity p*=<0.001 Pooled SD= 1.64 Effect size=-1.55 95% CI effect size=[- 2.09, -1.01] T3 FSI interference p*=<0.001 Pooled SD= 2.01 Effect size=-1.34 95% CI effect size=[1.88, -0.81] FSI severity p*=<0.001 Pooled SD=1.51 Effect size=-1.54 95% CI effect size= [-2.10,-0.97]
Lengacher 2012	Symptom Inventory (MDASI)	84	41	43	6 Week	p<0.5 P (between-group post-assessment) p= 0.05 At post-intervention, the MBSR(BC) group showed greater improvement across symptoms, and especially symptom interference items, compared to the control group. For the MBSR(BC) group, statistically-significant reductions (P<0.01) were observed for fatigue.
Matthews 2014	Piper Fatigue Scale	56	30	26	6 Week	p= 0.76 d= 0.2 No group differences in improvement were noted relative to fatigue.
Prinsen 2013	Checklist Individual Strength (CIS-fatigue)	37	23	14	6 months	CBT resulted in a significantly larger decrease in fatigue severity compared to a period of waiting for therapy. After 6 months of follow-up, patients who underwent CBT, with a mean of 12.0±5.0 individual sessions, showed a significantly larger change in fatigue scores than patients in the waiting list group (p<0.001, respectively −49.0±23.0 % and −16.4±25.0 %). Baseline to follow-up (within group) p<0.001 p=0.022
Reeves 2017	FACIT	90	45	45	6-month	Only the intervention arm showed significantly improved Fatigue- Mean change (95% CI)= 3.0 (0.7, 5.3) p<0.01 Intervention – usual care- No statistically significant intervention effects were observed Mean difference (95% CI)= 1.1 (−2.4, 4.5)

						p= 0.527
Reich 2017/ Lengacher 2016	Fatigue Symptom Inventory	303	155	148	12 Weeks	MBSR(BC) demonstrated greater symptom improvement in fatigue (severity and interference; p <0 .01). Effect sizes (Cohen's d) were between 0.27 and 0.23. A majority of improvements in fatigue occurred during the MBSR(BC) training, with little change occurring during the follow-up period (6 to 12 weeks). Fatigue—severity (FSI) p= 0.002 T2 week d= 0.33 95% CI [0.13 to 0.54] T3 week d=0.27 95% CI 12 0.07 to 0.47 Fatigue—interference (FSI) p= 0 .006 T2 week d=0.3 95% CI [0.10 to 0.51] T3 week d=0.23 95% CI [0.02 to 0.43]
Reif 2013	Fatigue Assessment Questionnaire (FAQ) and Fatigue subscale of the EORTC-QLQ-C30	234	120	114	6 months	FAQ : Significant reduction in intervention group: (F = 76.510, p < 0.001, η2= 0.248). The control group showed almost no change in CRF levels over time. In the repeated measures ANOVA, this difference was statistically significant for the group by time interaction (F = 76.51, p < 0.001). The partial η2of 0.248 indicates a large effect. QLQ-C30 fatigue subscale: the IG showed a reduction from 75.37 (19.39) to 40.74 (30.60) while the values in the CG remained about the same (F = 57.837, partial η2= 0.2, p < 0.001). This finding confirms the results of the FAQ.
Ritterband 2012	Multidimensional Fatigue Symptom Inventory- Short Form (MFSI-SF)	28	14	14	9 weeks	p < 0.01 Overall adjusted ES (d)= 1.16 A significant group × time interaction was found for the overall measure of fatigue, MFSI-SF ($F_{1,26}$ = 13.88, p<0.01). Participants in the Internet group had significantly improved fatigue scores from 22.86 to 9.50 (t(13) = 3.63, p<0.01); control participants' scores did not improve over time, changing from 13.71 to 19.79 (t(13) = − 1.64, p = 0.12). Several MFSI-SF subscales also had significant group × time interactions, including general fatigue ($F_{1,26}$ = 9.46, p<0.01), mental fatigue ($F_{1,26}$ = .65, p<0.01), and vigor

						($F_{1,26}$ = 14.79, p<0.01), with Internet participants showing improvements compared with control participants in all cases. Although some subscales lacked significant group × time interactions (physical fatigue, p = 0.11; emotional fatigue, p = 0.08), adjusted ES for the fatigue variables ranged from a low of 0.47 to a high of 1.63, indicating a SHUTi treatment effect for fatigue.
Rogers 2017	Fatigue Symptom Inventory	222	110	112	3 months	BEAT Cancer significantly reduced fatigue intensity at both time points (mean between group difference [M] = −0.61; 95% CI = −1.04 to −0.19; effect size [d] = −0.32; P = .004 at M3 and M = −0.46; 95% CI −0.89 to −0.03; d = −0.26; P = .038 at M6). Significant and greater reductions in fatigue interference occurred (M = −0.84; 95% CI = −1.26 to −0.43; d = −0.40; P < .001 at M3 and −0.66; CI −1.08 to −0.24; d = −0.35; P = .002 at M6).
Sandler 2017		46	22	24	24 weeks	Fatigue severity improved in all subjects from a mean of 5.2 (-3.1) at baseline to 3.9 (-2.8) at 12 weeks, suggesting a natural history of improvement. Clinically significant improvement was observed in 7 of 22 subjects in the intervention group compared with 2 of 24 in the education group (P < 0.05) The whole cohort reported improvements in fatigue scores between baseline and 12 weeks (Mdiff = −1.27; 95% CI −2.52 to −0.03; p < 0.05) and 24 weeks (Mdiff = −1.51; 95% CI −2.84 to −0.18; p < 0.05). Change scores differed significantly in favour of the intervention (M = 2.55, SD = 3.77; t(36) = −2.56; p < 0.05) at 12 weeks in comparison to the education arm (M = 0.10; SD = 2.55) but **not at follow up (Mdiff = 1.56; 95% CI –3.77 to 0.48; p = 0.13).** These groupwise changes indicate an effect size in the CBT/GET group of d = 0.79, compared with d = 0.04 in the education arm.
Savard 2005	Multidimensional Fatigue Inventory (MFI)	57	27	30	12 months	Pooled data revealed significant differences between pre- and post-treatment on fatigue ($F_{1,158}$ = 11.70; P < .001), No significant difference was detected between post-treatment and the follow-up evaluations.

						Therapeutic effects were well maintained up to 12 months after the intervention and generally were clinically significant. Pooled Data (n =57) 3-month follow-up : adjusted mean= 2.33; 95% CI= 2.15 to 2.51 6-month follow-up: adjusted mean = 2.25; 95% CI= 2.07 to 2.43 12-month follow-up: adjusted mean = 2.18 ; 95% CI= 1.98 to 2.38
Van Der Lee 2012	Multidimensional Fatigue Inventory (MFI)- General fatigue	83	59	24	6 months	p< 0.001 At post-treatment measurement the proportion of clinically improved participants was 30%, versus 4% in the waiting list condition (X^2 (1) =56.71; p=0.007). The mean fatigue severity score at post-measurement was significantly lower in the intervention group (95%CI =33.2–37.9) than in the waiting list group (95% CI= 40.0–47.4) controlled for pre-treatment level of fatigue. The effect size for fatigue is 0.74 (d= (mean post intervention–mean post control)/pooled SD). The treatment effect was maintained at 6-month follow-up. At follow up 39% of the participants in the intervention group showed clinically relevant improvement in fatigue severity.
Van Weert 2010	Multidimensional Fatigue Inventory (MFI)- General fatigue	209	76	133	12 weeks	In comparison with the WLC group, the PT group showed more reduction in 4 domains of fatigue, whereas the PT+CBT group showed more reduction in one domain only. Finally, the results showed that physical training combined with CBT and physical training alone were equally effective in reducing fatigue. Thus, CBT did not seem to contribute additional positive effects on fatigue to the benefits of physical training. PT+CBT (WLC= Reference) Between-Group Change General fatigue (95% CI) =-1.3 (-3.1 to 0.4) Physical fatigue (95% CI) =-2.7 (-4.5 to -1.0) P<0.01. Mental fatigue(95% CI) =-0.5 (-2.3 to 1.2) Reduced motivation(95% CI) =-0.6 (-2.1 to 1.0) Reduced activation(95% CI) =-0.9 (-2.6 to 0.8)

Willems 2017	Fatigue severity subscale of the CIS	409	188	221	6 months 12months	The intervention was effective in reducing fatigue (B =-4.36, p = 0.020, d = 0.21). Adjusted: 6 months p= 0.030 95% CI [−7.87 to −0.39] (d=0.21) Adjusted: 12 months p= 1.000 95% CI [−3.88 to 3.88] (d=0.04) Between- group differences at 12 months from baseline on emotional (p = .611, d = 0.04) were non-significant The intervention group remained fairly stable in fatigue between 6 and 12 months from baseline, but the control group slightly improved over time, leading to non-significant group differences at 12 months from baseline.
Yun 2017	EORTC QLQ-C30 fatigue score	174	57	117	12 months	From baseline to 12 months, the LP group, relative to the UC group, showed a significantly greater decrease in the EORTC QLQ-C30 fatigue score (*p* = 0.065) 3 months: p= 0.214 12 months: pvalue= 0.010**
Yun 2012	Brief Fatigue Inventory (BFI) and Fatigue Severity Scale (FSS)	273	136	137	3months	BFI: p < 0.01 95% CI -1.04 to-0.27 Cohen's d= 0.29 FSS: p < 0.01 95% CI -0.78 to -0.21 Cohen's d=0.27 Compared with the control group, the intervention group had an improvement in fatigue as shown by a significantly greater decrease in BFI global score (-0.66 points; 95% CI -1.04 to-0.27) and FSS total score (-0.49; 95% CI, -0.78 to -0.21).

Table 4 Grade evidence summary

Outcomes	№ of participants (studies)	Certainty of the evidence	Explanations
Psychological Interventions compared to usual care for Fatigue in cancer survivors			
Follow up: range 2 weeks to 1 years **Intervention**: Psychological Interventions **Comparison**: usual care	2918 (22 RCTs)	⊕⊕◯◯ LOW [a,b]	a. Downgraded x 1 level for risk of bias due to all studies having high or unclear risk of performance bias. Many aspects of trial procedures were not reported in sufficient detail to adequately assess risk of bias in all domains of all included trials (e.g. unclear risk of selection bias in 18/22 studies, unclear risk of detection bias in16/22). b. Downgraded x1 level for indirectness of evidence as many studies were combined interventions, which limit our ability to draw conclusions in relation to our research question relating solely to the effectiveness of psychological interventions. Generalizability of the findings are limited due to the high proportion of studies that recruited only/mostly breast cancer survivors. The majority of studies did not specifically target fatigue or screen for fatigue as part of inclusion criteria as recommended in existing guidelines. In some studies, it was difficult to assess when exactly participants completed cancer treatment prior to participating in the study. High levels of heterogeneity in sample and methods.
Subgroups of specific psychological intervention type (e.g. cognitive behavioural therapy) vs usual care			
CBT interventions compared to usual care for Fatigue in cancer survivors Follow up: range 1 months to 1 years	648 (8 RCTs)	⊕⊕◯◯ LOW [a,b]	a. Downgraded x 1 level for risk of bias due to high/ unclear risk due to incomplete outcome data (attrition bias) in 5 of 8 studies Many aspects of trial procedures were not reported in sufficient detail to adequately assess risk of bias. b. Downgraded x1 level for indirectness of evidence as high levels of heterogeneity in sample and methods that limit the generalizability of the findings- While CBT was incorporated in all interventions to some degree, it was delivered in a variety of settings, modes and assessed in different ways. For example, 3 x studies were not CBT interventions but were based on CBT strategies and 3x studies were focused specifically on CBT for insomnia.

Mindfulness-based interventions compared to usual care for Fatigue in cancer survivors Follow up: range 1 months to 4 months	749 (6 RCTs)	⊕⊕◯◯ LOW [a, b]	a. Downgraded x 1 level for risk of bias due to high or unclear risk of performance bias in all studies. Many aspects of trial procedures were not reported in sufficient detail to adequately assess risk of bias. b. Downgraded x1 level for indirectness of evidence as high levels of heterogeneity in sample and methods that limit the generalizability of the findings- While mindfulness was incorporated in all interventions to some degree, it was delivered in a variety of settings, modes and assessed in different ways.
Other psycho-social interventions compared to usual care for Fatigue in cancer survivors Follow up: range 3 months to 12 months	1521 (8 RCTs)	⊕⊕◯◯ LOW [a, b]	a. Downgraded x 1 level for risk of bias due to high or unclear risk of performance bias in all studies Some aspects of trial procedures were not reported in sufficient detail to adequately assess risk of bias b. Downgraded x1 level for indirectness of evidence as high levels of heterogeneity - While all were psychological interventions, they were vastly different in sample and methods. Further, 4 x studies were lifestyle interventions that incorporated other interventions such as physical activity and dietary changes.

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Appendix 1 Summary of Findings for Secondary outcomes.

Study ID	Outcome	Outcome Measure	Finding
Bantum 2014	Mood	Patient Health Questionnaire (PHQ-8): depression	In the subgroup analyses looking at differences between survivors with diagnoses ≤ 2 and >2 years prior to enrollment, there were no significant differences, although there were suggested trends seen for depression (*P*=.09), such that people who were greater than 2 years post treatment improved slightly more on those measures (data not presented in paper). Depression (PHQ) Control group, mean (95% CI) Baseline (n=176): 7.7 (7.0-8.3) Month 6 (n=156): 7.1 (6.4-7.7) Intervention group, mean (95% CI) Baseline (n=176): 6.5 (5.9-7.1) Month 6 (n=147): 6.1 (5.4-6.7) *p*= 0 .69 Effect size Month 6= 0.19 (Calculated by taking the differences of the means at 6 months predicted from the model, including adjustment factors, divided by the standard deviation for the difference computed from the within and between subject variance components.)
	Insomnia or sleep quality	Women's Health Initiative Insomnia Rating Scale (WHIIRS)	Significant interactions between condition group and time were found for insomnia. The intervention group experienced an improvement from baseline to 6 months compared to the control group: reduced insomnia (9.6 to 9.2 compared to 9.6 to 10.1, *P*=.03). In the subgroup analyses looking at differences between survivors with diagnoses ≤ 2 and >2 years prior to enrollment, there were no significant differences, although there were suggested trends seen for insomnia (*P*=.07), such that people who were greater than 2 years post treatment improved slightly more on those measures (data not presented in paper). Insomnia (WHIIRSe) Control group, mean (95% CI) Baseline (n=176): 9.6 (9.1-10.1) Month 6 (n=156): 10.1 (9.6-10.7) Intervention group, mean (95% CI) Baseline (n=176): 9.6 (9.1-10.1) Month 6 (n=147): 9.2 (8.7-9.8)

			p=0 .03 Effect size Month 6= 0.20 (Calculated by taking the differences of the means at 6 months predicted from the model, including adjustment factors, divided by the standard deviation for the difference computed from the within and between subject variance components.)
Bennett 2007	Global quality of life / Functional impact of fatigue	(SF-36, v.2) Physical Component Summary (PCS) and Mental Component Summary (MCS; Ware, 2005)	Mental Component Summary Results of the Level 1 MLM model showed that both the intercept (B = 45.65, p <.001) and the linear slope (B = 3.12, p <.01) were significantly different from zero. On average, the level of mental health status for all participants was 45.65 at baseline and increased 6 points (13%) across the study. There was significant individual variation in both the intercept and the slope to be explained in a Level 2 model; however, that model showed that group assignment was not associated significantly with variation around the mean slope. Physical Component Summary (PCS) Results of the Level 1 MLM model showed that both the intercept (B = 42.98, p <.001) and the linear slope (B = 1.57, p <.001) were significantly different from zero. On average, the level of physical health status for all participants was 42.98 at baseline and increased 3 points (7%) across the study. As there was no significant individual variation in the slope to be explained in a Level 2 model, an ANOVA analysis of group mean trajectory adequately represented the data. That analysis showed that the Group × Time interaction was not significant for physical health, [Wilk's lambda [LAMBDA] =.89, F(2,38) = 2.42, ns].
Blaes 2016	Sleep	Pittsburgh Sleep quality index	At the 2-month assessment, sleep quality (PSQI, range 0-21, <5 = poorer sleep quality) in the MBCR group improved from the baseline 8.9 to 6.4, compared with the wait-list group (baseline 7.2 to 7.6); and at 4 months after course completion, it was 6.1 compared with 7.8, respectively (P = .03).
	mood-anxiety	State Trait Anxiety (STAI)	There was a trend toward improvement in the anxiety scores (STAI, range 20-80, higher score = greater anxiety) in the MBCR group compared with the wait-list group at 2 months (31.8 vs 39.4, respectively; P = .07) and 4 months (32.8 vs 40.7; P = .10).
Bower 2015	Fatigue self-efficacy	Fatigue subscale of the HIV self-efficacy questionnaire	Bower et al used the fatigue subscale of the HIV self-efficacy questionnaire and reported that Intervention group participants were significantly more confident than control group participants about their ability to manage fatigue and its impact on their lives at follow-up [1].
	Mood	Beck Depression Inventory-II (BDI-II) and Perceived Stress Scale (PSS)	MAPS intervention led to significant reductions in perceived stress (P = .004) and marginal reductions in depressive symptoms (P = .094) Depressive symptoms: CES-D Baseline, n = 71 MAPS Group 14.50 ± 1.58 Control Group 19.25 ± 1.75 Postintervention, n = 65 MAPS Group 9.99 ± 1.64 Control Group 18.47 ± 1.80

<table>
<tr><td></td><td></td><td></td><td>p=0.095
3-Month Follow-Up, n = 59
MAPS Group 14.17 ± 1.70 Control Group 17.92 ± 1.82
p=0.664

PSS
Baseline, n = 71
MAPS Group 18.05 ± 0.99 Control Group 18.42 ± 1.12
Postintervention, n = 65
MAPS Group 14.25 ± 1.04 Control Group 19.15 ± 1.14
p=0.004
3-Month Follow-Up, n = 59
MAPS Group 17.42 ± 1.09 Control Group 18.21 ± 1.16
p=0.796</td></tr>
<tr><td></td><td>Insomnia or sleep quality</td><td>Pittsburgh Sleep Quality Index (PSQI)</td><td>PSQI Baseline, n = 71
MAPS Group 8.13 ± 0.62 Control Group 8.39 ± 0.70
Postintervention, n = 65
MAPS Group 6.48 ± 0.65 Control Group 8.70 ± 0.71
p=0.015
3-Month Follow-Up, n = 59
MAPS Group 7.27 ±0.67 Control Group 7.86 ± 0.72
p=0.647</td></tr>
<tr><td>Bruggeman-Everts 2017</td><td>Mental health</td><td>HADS & the Positive and Negative Affect Schedule</td><td>
<table>
<tr><th>Outcome</th><th>Condition</th><th>Intercept at T0_b(I)</th><th>Linear slope factor (S)</th><th>Two-tailed Pvalue of linear slope (P)</th></tr>
<tr><td>HADS</td><td>AAF</td><td>13.237 (0.921)</td><td>-0.076 (0.017)</td><td><.001</td></tr>
<tr><td></td><td>eMBCT</td><td>13.903 (0.771)</td><td>-0.110 (0.022)</td><td><.001</td></tr>
<tr><td></td><td>Psycho-education</td><td>14.579 (1.012)</td><td>-0.083 (0.024)</td><td><.001</td></tr>
<tr><td>PA</td><td>AAF</td><td>31.762 (0.939)</td><td>0.101 (0.022)</td><td><.001</td></tr>
<tr><td></td><td>eMBCT</td><td>28.995 (0.932)</td><td>0.156 (0.026)</td><td><.001</td></tr>
<tr><td></td><td>Psycho-education</td><td>29.422 (1.091)</td><td>0.128 (0.027)</td><td><.001</td></tr>
<tr><td>NA</td><td>AAF</td><td>20.330 (0.931)</td><td>-0.068 (0.023)</td><td>0.003</td></tr>
</table>
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	eMBCT	20.718 (0.914)	-0.071 (0.032)	**0.03**
	Psycho-education	20.805 (1.215)	-0.082 (0.029)	**0.004**

Carlson 2016 | Mood disturbance (primary) | POMS(anxiety, depression, anger, vigor, fatigue, confusion.) Calgary Symptoms of Stress Inventory

Outcomes	Intervention Group × Time					Follow-up Group × Time			
	Est	se	*t*	*p*	*d* [CI]	Est	se	*t*	*p*
POMS									
Anxiety	−1.23	0.46	−3.02	**0.003**	**−0.39 [−0.64;−0.14]**	0.04	0.08	0.48	0.63
Depression	−1.58	0.59	−2.72	**0.01**	**−0.33 [−0.58;−0.08]**	0.10	0.12	0.86	0.39
Anger	−1.13	0.44	−2.62	**0.01**	**−0.35 [−0.60;−0.10]**	0.13	0.13	1.56	0.12
Vigor	0.88	0.41	2.14	**0.03**	**0.30 [0.05;0.55]**	0.01	0.08	0.14	0.89
Fatigue	−1.44	0.42	−3.45	**0.001**	**−0.45 [−0.70;−0.20]**	−0.03	0.08	−0.30	0.76
Confusion	−0.95	0.30	−3.13	**0.0002**	**−0.39 [−0.64;−0.14]**	0.02	0.06	0.26	0.79
Total mood disturbance	−6.29	1.80	−3.49	**0.001**	**−0.39 [−0.64;−0.14]**	−0.06	0.31	−0.19	0.85

	QoL (secondary)	FACT-B Functional Assessment of Cancer Therapy - Breast module

FACT-B	Intervention Group × Time					Follow-up Group × Time			
	Est	se	*t*	*p*	*d* [CI]	Est	se	*t*	*p*
Physical well-being	0.51	0.29	1.73	**0.09**	**0.22 [−0.03;0.47]**	0.02	0.05	0.41	0.68
Social well-being	0.43	0.29	1.49	0.14	0.17 [−0.08;0.42]	−0.11	0.06	−1.89	**0.06**
Emotional well-being	0.53	0.25	2.13	**0.03**	**0.27 [0.02;0.52]**	−0.02	0.04	−0.51	0.61
Functional well-being	0.64	0.28	2.28	**0.02**	**0.27 [0.02;0.52]**	−0.03	0.05	−0.65	0.52
Breast cancer symptom scale	0.26	0.32	0.79	0.43	0.10 [−0.15;0.35]	−0.04	0.06	−0.74	0.46
Total	2.00	0.98	2.03	**0.04**	**0.22 [−0.03;0.47]**	−0.14	0.16	−0.86	0.39

Dirksen 2008 | Global quality of life / Functional impact of fatigue | Functional Assessment of Cancer Therapy-Breast (FACT-B) (version 4)

	Mean	**sd**	**Mean**	**sd**	**Effect size**
Functional Assessment of Cancer Therapy-General					

			CBT-I: 83·3; 11·9; 91·6; 15·0; 0·26 CC: 84·8; 9·2; 87·7; 14·7 Functional Assessment of Cancer Therapy- Breast CBT-I: 108·5; 14·8; 118·8*; 11·9; 0·37 CC: 109·0; 20·0; 113·1*; 18·2 FACT-B physical well-being CBT-I: 22·0; 5·6; 24·8*; 3·3; 0·14 CC: 23·1; 4·1; 24·3*; 3·8 FACT-B social well-being CBT-I: 22·1; 4·9; 23·3; 3·9; 0·38 CC: 22·2; 6·1; 21·4; 5·9 FACT-B emotional well-being CBT-I: 20·1; 2·8; 20·8; 2·3; 0·06 CC: 20·4; 3·1; 20·6; 4·0 FACT-B functional well-being. CBT-I: 19·1; 4·0; 22·7*; 4·2; 0·27 CC: 19·1; 4·7; 21·5*; 4·7
	Mood	• the State-Trait Anxiety Inventory (STAI) (state (STAI-S) and a trait anxiety scale (STAI-T)) • the Center for Epidemiologic Studies-Depression Scale (CES-D).	**Mean; sd; Mean; sd; Effect size** State-Trait Anxiety Inventory (state) CBT-I: 30·2; 8·7; 29·0; 8·8; 0·42 CC: 31·8; 9·3; 33·7; 13·3 State-Trait Anxiety Inventory (Trait) CBT-I: 36·5; 10·2; 32·9*; 7·8; 0·24 CC: 36·1; 9·3; 35·0; 9·4 Center for Epidemiologic Studies-Depression Scale CBT-I: 11·6; 7·3; 7·8*; 7·3; 0·15 CC: 10·9; 7·8; 9·1; 9·7
Dodds 2015	Mood Pain	Five subscales of the Fear of Cancer Recurrence Inventory (FCRI) Impact of Events Scale—Revised (IES-R) Revised UCLA Loneliness Scale Version 3 (R-UCLA)	Outcome; Intervention–control (95 % CI); ; ; 1-month FU (*N* = 11); Post; 1-month FU Perceived stress; **5.1 (3.0)**; **−1.2 (−2.5, 0.2)**; **−1.6 (−3.1, −0.2)*** Depression; 5.5 (5.0); −3.7 (−6.3, −1.1)**; −1.3 (−4.2, 1.6) FCR: triggers; 12.5 (5.8); −2.2 (−6.0, 1.6); 1.7 (−2.4, 5.8) FCR: severity; 13.7 (8.5); −0.9 (−2.9, 1.2); 0.6 (−1.7, 2.8) FCR: psychological distress; 3.3 (4.5); −0.1 (−1.5 1.3); 0.4 (−1.2, 2.0)

		Brief Center for Epidemiologic Studies—Depression questionnaire (CES-D-10) Medical Outcomes Study Short Form 12-Item Health Survey (SF-12)	FCR: functioning impairments	1.7 (2.7)	−1.3 (−2.5–0.1)*	1.3 (−0.1, 2.7)
			FCR: insight	1.1 (2.1)	−0.3 (−0.8, 0.2)	−0.3 (−0.9, 0.3)
			Traumatic stress: intrusion	0.5 (0.3)	−0.1 (−0.3, 0.2)	−0.1 (−0.3, 0.2)
			Traumatic stress: avoidance	0.7 (0.8)	−0.3 (−0.6, −0.02)*	0.1 (−0.2, 0.4)
			Traumatic stress: hyperarousal	0.4 (0.4)	−0.1 (−0.3, 0.2)	−0.003 (−0.3, 0.3)
			Traumatic stress: global	1.6 (1.3)	−0.4 (−1.0, 0.2)	0.04 (−0.6, 0.7)
			Loneliness	37.9 (16.6)	−2.9 (−7.7, 2.0)	−2.5 (−7.9, 3.0)
			Bodily pain	52.0 (7.0)	2.0 (−3.1, 7.0)	−1.9 (−7.5, 3.8)
			Physical well-being	**54.0 (4.9)**	**−0.1 (−3.2, 2.9)**	**−4.3 (−7.7, −0.9)***
			Mental well-being	46.5 (10.4)	2.0 (−2.4, 6.5)	4.4 (−0.6, 9.3)
Dolbeault 2009	Global quality of life / Functional impact of fatigue Mood Insomnia or sleep quality Pain	EORTC QLQ-C30 and breast cancer module (EORTC QLQ-BR23). State-Trait Anxiety Inventory Profile of Mood States (POMS) The Mental Adjustment to Cancer Scale (MAC) EORTC QLQ-C30 sleep EORTC pain	In both groups changes were observed over time in the STAI trait and state anxiety scores, the POMS anxiety, anger, confusion, depression and global scores, the MAC helplessness–hopelessness and anxious preoccupations scores, in the EORTC QLQ-C30 scores for physical, emotional, cognitive and social functioning, dyspnoea, sleep and financial difficulties, and in the QLQ-BR23 body image, future prospects and breast symptom scores. Controlling for a time effect, significant group/ time interactions indicate a positive effect of the intervention on anxiety, our primary outcome measure. This was evidenced for the STAI state and trait anxiety scales, explaining 6% and 4% of the variance in the STAI-state and STAI-trait anxiety scores, respectively Found positive results on other variables identified as secondary outcome measures. A greater reduction of negative affect and improvement in positive affect and in quality of life functional or symptom scales were observed in the TG compared with the CG. This concerned the POMS anxiety and global scores (8% of the variance explained by the model including the time/group interaction term), scores for fatigue (7%), anger (5%), interpersonal relationships (4%), vigor (3%) and depression (2%) and the EORTC QLQ-C30 scores, emotional functioning (9%), role functioning (3%), global health status (3%) and fatigue (3%). In contrast, no effect of the PEG was evidenced on the MAC scale or on the POMS confusion scores.			
Espie 2008	Global quality of life / Functional impact of fatigue	Functional Assessment of Cancer Therapy Scale–general FACT-G	CBT participants had increased physical and functional QOL relative to TAU. Correlations between changes in SE from baseline to post-treatment after CBT and changes in statistically significant QOL measures were low. **FACT Physical** Post-Treatment Standardized Effect= 0.58 Post-Treatment 95% CI= - 0.19 to 0.97 Post-Treatment *p*=0.004* 6-Month Follow-Up Standardized Effect= 0.74			

			6-Month Follow-Up 95% CI=- 0.34 to 1.14 6-Month Follow-Up *p* <0 .001† **FACT Social** Post-Treatment Standardized Effect= 0.42 Post-Treatment 95% CI= 0.03 to 0.81 Post-Treatment *p*=0.036 6-Month Follow-Up Standardized Effect= 0.13 6-Month Follow-Up 95% CI= -0.27 to 0.53 6-Month Follow-Up *p*=0.529 **FACT Emotional** Post-Treatment Standardized Effect= 0.38 Post-Treatment 95% CI= -0.01 to 0.78 Post-Treatment *p*=0.057 6-Month Follow-Up Standardized Effect= 0.16 6-Month Follow-Up 95% CI= - 0.25 to 0.57 6-Month Follow-Up *p*=0. 444 **FACT Functional** Post-Treatment Standardized Effect= 0.86 Post-Treatment 95% CI= 0.47 to 1.25 Post-Treatment *p*<0 .001† 6-Month Follow-Up Standardized Effect= 1.17 6-Month Follow-Up 95% CI= 0.77 to 1.57 6-Month Follow-Up *p*<0 .001† *Significant at 5% after adjustment for multiple comparisons within each time point using the Hochberg procedure. †Significant at 1% after adjustment for multiple comparisons within each time point using the Hochberg procedure.
	Mood	Hospitals Anxiety and Depression Scale [HADS]	CBT participants had reduced symptoms of anxiety, and depression relative to TAU. Correlations between changes in SE from baseline to post-treatment after CBT and changes in statistically significant QOL measures were low. HADS **Anxiety**

			Post-Treatment Standardized Effect= -0.57 Post-Treatment 95% CI= -0.96 to -0.18 Post-Treatment *p*=0.005* 6-Month Follow-Up Standardized Effect= -0.52 6-Month Follow-Up 95% CI=-0.92 to-0.12 6-Month Follow-Up *p*=0.011* **Depression** Post-Treatment Standardized Effect= -0.67 Post-Treatment 95% CI= -1.06 to -0.28 Post-Treatment *p*=0.001† 6-Month Follow-Up Standardized Effect= -0.59 6-Month Follow-Up 95% CI= -0.99 to -0.19 6-Month Follow-Up *p*=0.004* *Significant at 5% after adjustment for multiple comparisons within each time point using the Hochberg procedure. †Significant at 1% after adjustment for multiple comparisons within each time point using the Hochberg procedure.
	Insomnia or sleep quality	PSQI, Epworth sleepiness (baseline only) and sleep diary assessed the central insomnia dimensions of difficulty initiating (SOL) and maintaining (WASO) sleep.	At post-treatment, CBT was associated with median reduction in SOL of 16 minutes (95% CI, 10 to 22 minutes), and in WASO of3 8 minutes (95% CI, 28 to 59 minutes), the corresponding median reductions following TAU were 0 minutes (95% CI, -8.5 to 6.6) and 2 minutes (95% CI, -15 to 9). Effect sizes were moderate to large and were both highly statistically significant (*p*= 0.001). TST also increased by a median of 16 minutes (95% CI, -1 to 30) with CBT compared with 5 minutes (95% CI, -14 to 24) after TAU, but the difference between arms was not statistically significant. SE increased by 10% (95% CI, 9% to 12%) after CBT; the change in the TAU was 0% (95% CI, -3% to 3%). This effect size was large and highly statistically significant. This pattern of results generally held at 6 months post-treatment. Effect sizes were somewhat reduced for WASO, SOL, and SE but remained moderate and statistically significant (*p*=0.001). Changes in TST again were not statistically significant. In summary, CBT was associated with median reduction in insomnia symptoms of almost 1 hour (SOL + WASO) compared with no change following TAU. Post-treatment and follow-up SE of 85% is commonly regarded as the lower limit of normal sleep. A higher proportion of CBT participants achieved this criterion, 51% (51 of 100) versus 34% on TAU (17 of 50; *p*=0.008); at 6 months this difference was no longer significant (44%; 44/100 of patients on CBT; 48%; 24 of 50 on TAU; *p*= 0 .966).
Ferguson 2016	QoL/self-reported function	FACTCog Impact on Quality of Life scale	On the FACT-Cog Impact on Quality of Life scale, MAAT and ST participants did not differ at the posttreatment (*F* (1,28), 0.187; *P* = .67) or 2-month follow-up (*F* (1,28), 1.19; *P* = .28) time points, but a moderate effect size was observed at the 2-month follow-up, with MAAT participants reporting higher QOL (*d* = 0.43). On other QOL measures, MAAT and ST participants did not differ with regard to general function at either the posttreatment (*F* (1,28), 0.236; *P* = .63) or 2-month follow-up (*F* (1,28), 1.14; *P* = .295) time points.

			However, the Cohen's *d* effect sizes for function, at the 2-month follow-up time point suggested that MAAT participants demonstrated sustained clinical gains on this QOL measures compared with ST participants (general function, 0.50).
	general anxiety and depression	Depression Anxiety Stress Scales-21 [DASS-21]	With respect to anxiety about cognitive problems in daily life (MIA-A), the MAAT and ST participants did not differ at the posttreatment follow-up time point (*F*(1,28), 0.089; *P* = .77). However, at 2-month follow-up, there was a trend toward MAAT participants having decreased anxiety regarding cognitive problems (*F*(1,28), 3.53; *P* = .07), with a large effect size noted (*d* = .90) However, the Cohen's *d* effect sizes for anxiety at the 2-month follow-up time point suggested that MAAT participants demonstrated sustained clinical gains on this measures compared with ST participants (DASS-21 anxiety scale, 0.55). MAAT and ST participants did differ at a statistically significant level with regard to depression at baseline. This suggests that ST participants were more depressed and thus could have had more cognitive problems affecting results.
Fillion 2008	Global quality of life / Functional impact of fatigue	Medical Outcomes Study Short Form 12 Menopause-Specific Quality of Life Questionnaire	Marginal Group × Time interaction effects (ANCOVA) emerged for physical quality of life, and significant Group and Time main effects were obtained for physical quality of life. Simple effect contrasts revealed a significant Group difference at T1 for physical quality of life. That is, women who received the intervention showed a significantly higher level of physical quality of life immediately after the intervention (T1) compared with women in the control group. The same analyses conducted on mental quality of life showed no interaction or main effects, thus demonstrating that both conditions improved in a similar manner on mental quality of life overtime (P > .05). However, an ad hoc simple effect contrast revealed a significant effect at follow-up, F1,83 = 4.37, P = .04 indicating that the experimental group's mental quality of life improvement was more important than that of the control group.
	Mood	Profile of Mood States: combined anxiety and depression subscales	A reduction in emotional distress (ie, combined Profile of Mood States depression/anxiety items) was predicted both immediately after the intervention and at follow-up. A mixed-model ANCOVA (adjusting for physical menopausal symptoms) on emotional distress was conducted. No interaction or Time main effects for emotional distress emerged, meaning that, overall, the participants' level of distress did not change over time. However, a Group main effect was revealed. When examining pairwise comparisons, emotional distress significantly differed at follow-up (Control M = 13.13, SD = 5.44; Experimental M = 11.15, SD = 3.85), thus revealing that the participants exposed to the intervention experienced less distress (ie, less combined depression and anxiety symptoms) at 3-month follow-up compared with those in the control condition.
	Pain	Brief Pain Inventory	Not reported
Foster 2015	Global quality of life / Functional impact of fatigue	Functional Assessment of Cancer Therapy—General (FACT-G) and Personal Wellbeing Index (PWI)	

	Time point	**Mean (SD)**		**Group effect (95 % CI)**	***P***
		RESTORE	**Comparator**		
	T0	64.9 (17.2)	63.0 (19.8)	–	–

<table>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>Personal Wellbeing Index (range 0–100)[a]</td><td>T1</td><td>65.3 (19.1)</td><td>64.6 (18.6)</td><td>0.622 (−3.437, 4.682)</td><td>0.76</td></tr>
<tr><td></td><td>T2</td><td>63.8 (21.8)</td><td>65.1 (24.1)</td><td>0.244 (−5.687, 6.175)</td><td>0.94</td></tr>
<tr><td>FACT-G (range 0–108)[a]</td><td>T0</td><td>72.9 (16.2)</td><td>71.4 (17.8)</td><td>–</td><td>–</td></tr>
<tr><td></td><td>T1</td><td>74.1 (18.0)</td><td>76.9 (17.4)</td><td>−2.206 (−5.503, 1.091)</td><td>0.19</td></tr>
<tr><td></td><td>T2</td><td>75.0 (19.4)</td><td>78.7 (18.5)</td><td>−3.034 (−6.639, 0.571)</td><td>0.10</td></tr>
</table>
</td></tr>
<tr><td></td><td>Fatigue self-efficacy</td><td>Perceived Self-efficacy for Fatigue Self-management (PSEFSM)</td><td>
There is evidence of improved fatigue self-efficacy at T1 (0.514, 95 % CI [−0.084, 1.112], P = 0.09), in the RESTORE group though the impact is lost by T2
<table>
<tr><th></th><th>Time point</th><th colspan="2">Mean (SD)</th><th>Group effect (95 % CI)</th><th>P</th></tr>
<tr><th></th><th></th><th>RESTORE</th><th>Comparator</th><th></th><th></th></tr>
<tr><td>Fatigue self-efficacy (range 1–11)</td><td>T0</td><td>5.376 (1.930)</td><td>5.373 (2.048)</td><td>–</td><td>–</td></tr>
<tr><td></td><td>T1</td><td>6.421 (1.781)</td><td>5.904 (2.107)</td><td>0.514 (−0.084, 1.112)</td><td>0.09</td></tr>
<tr><td></td><td>T2</td><td>6.439 (2.228)</td><td>6.294 (2.207)</td><td>0.106 (−0.427, 0.638)</td><td>0.70</td></tr>
</table>
</td></tr>
<tr><td></td><td>Mood</td><td>Patient Health Questionnaire (PHQ-9)</td><td>
<table>
<tr><th></th><th>Time point</th><th colspan="2">Mean (SD)</th><th>Group effect (95 % CI)</th><th>P</th></tr>
<tr><th></th><th></th><th>RESTORE</th><th>Comparator</th><th></th><th></th></tr>
<tr><td>PHQ-9 (range 0–27)</td><td>T0</td><td>9.77 (5.50)</td><td>8.96 (5.66)</td><td>–</td><td>–</td></tr>
<tr><td></td><td>T1</td><td>8.41 (5.58)</td><td>7.74 (5.82)</td><td>−0.452 (−1.761, 0.858)</td><td>0.50</td></tr>
<tr><td></td><td>T2</td><td>8.59 (6.37)</td><td>6.82 (5.50)</td><td>0.676 (−0.880, 2.231)</td><td>0.40</td></tr>
</table>
</td></tr>
<tr><td>Freeman 2015</td><td>Global quality of life / Functional impact of fatigue</td><td>Medical Outcomes Study 36-item short form survey (SF-36)
FACT-B</td><td>
<table>
<tr><th></th><th colspan="2">Live Delivery n = 48</th><th colspan="2">Telemedicine Delivery n = 23</th><th colspan="2">Waitlist Control n = 47</th><th>Group Effect</th><th>Time Effect</th><th>Group* Time Effect</th></tr>
<tr><th></th><th>M</th><th>SD</th><th>M</th><th>SD</th><th>M</th><th>SD</th><th>p-value</th><th>p-value</th><th>p-value</th></tr>
<tr><td>SF-36 PCS</td><td></td><td></td><td></td><td></td><td></td><td></td><td>0.154</td><td>0.529</td><td>0.111</td></tr>
<tr><td>Baseline</td><td>47.20</td><td>8.60</td><td>46.54</td><td>8.48</td><td>45.24</td><td>10.23</td><td></td><td></td><td></td></tr>
<tr><td>1 Month</td><td>48.81</td><td>9.84</td><td>48.64</td><td>9.05</td><td>43.49</td><td>11.34</td><td></td><td></td><td></td></tr>
</table>
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			3 Months	50.54	8.49	46.95	8.04	45.44	10.24			
			Group LSM, SE*	48.32	0.91	49.93	1.36	46.81	0.91			
			SF-36 MCS							0.020	0.612	0.661
			Baseline	42.45	10.50	43.45	8.03	42.41	10.04			
			1 Month	48.51	8.72	49.25	7.97	46.50	10.40			
			3 Months	49.80	8.04	50.84	7.58	43.29	12.75			
			Group LSM, SE*	48.77	1.24	49.40	1.86	44.30	1.25			
			FACT-B							0.076	0.003	0.208
			Baseline	22.63	5.98	22.09	4.03	20.32	6.06			
			1 Month	25.32	5.97	24.84	5.29	22.32	6.08			
			3 Months	26.18	5.83	27.21	4.22	22.72	5.20			
			Group LSM, SE*	24.66	0.57	26.03	0.85	23.66	0.58			
			There was no group effect on PCS, MCS, or FACT-B, though means were in the expected direction. There were no group*time effects that reached the adjusted alpha level of 0.011									
	Mood	Psychological distress : Brief Symptom Inventory-Global Severity Index (BSI-GSI)		**Live Delivery n = 48**		**Telemedicine Delivery n = 23**		**Waitlist Control n = 47**		**Group Effect**	**Time Effect**	**Group* Time Effect**
			BSI-GSI							0.051	0.120	0.032
			Baseline	53.98	7.75	51.77	7.81	55.51	7.26			
			1 Month	48.88	8.31	49.32	8.58	52.20	8.44			
			3 Months	46.80	7.82	49.26	7.34	53.02	8.95			
			Group LSM, SE*	48.24	1.02	47.81	1.59	51.51	1.03			
			There was no group effect on BSIGSI though means were in the expected direction. Though there were no group*time effects that reached the adjusted alpha level of 0.011, there was a group*time effect on BSIGSI scores at the $p < 0.05$ level ($p = 0.032$). Pairwise comparisons of groups at each time point revealed that neither TD or LD differed from WL at the 1-month follow-up (p's > 0.3), both LD ($p = 0.011$) and TD ($p = 0.004$) reported lower BSIGSI than WL at the 3-month follow-up, and TD and LD did not differ from one another at either time point (p's > 0.7).									

<table>
<tr><td></td><td>Insomnia or sleep quality</td><td>Pittsburgh Sleep Quality Index (PSQI)</td><td>
<table>
<tr><th></th><th colspan="2">Live Delivery n = 48</th><th colspan="2">Telemedicine Delivery n = 23</th><th colspan="2">Waitlist Control n = 47</th><th>Group Effect</th><th>Time Effect</th><th>Group* Time Effect</th></tr>
<tr><td>PSQI</td><td></td><td></td><td></td><td></td><td></td><td></td><td><0.001</td><td>0.346</td><td>0.303</td></tr>
<tr><td>Baseline</td><td>8.79</td><td>4.11</td><td>8.30</td><td>3.74</td><td>9.96</td><td>4.74</td><td></td><td></td><td></td></tr>
<tr><td>1 Month</td><td>6.12</td><td>3.74</td><td>5.95</td><td>3.47</td><td>9.18</td><td>4.61</td><td></td><td></td><td></td></tr>
<tr><td>3 Months</td><td>6.70</td><td>3.83</td><td>5.53</td><td>2.46</td><td>9.74</td><td>4.32</td><td></td><td></td><td></td></tr>
<tr><td>Group LSM, SE*</td><td>7.09</td><td>0.36</td><td>6.04</td><td>0.54</td><td>8.74</td><td>0.37</td><td></td><td></td><td></td></tr>
</table>
Using a Bonferroni correction for multiple QOL comparisons (alpha = 0.011), there was an effect of group on PSQI (p's ≤ 0.002). There were no group*time effects that reached the adjusted alpha level of 0.011.</td></tr>
<tr><td>Gielissen 2006</td><td>Global quality of life / Functional impact of fatigue</td><td>Sickness Impact Profile-8 (SIP-8).</td><td>The proportion of patients with clinically significant improvement on functional impairment was significantly higher in the intervention condition than in the waiting list condition. Patients in the intervention condition reported a significantly greater decrease in functional impairment (difference, 383.2; 95% CI, 197.1 to 569.2) than patients in the waiting list condition.</td></tr>
<tr><td></td><td>Mood</td><td>Psychological distress was measured by the Symptom Check List 90</td><td>Patients in the intervention condition reported a significantly greater decrease in psychological distress (difference, 21.6; 95% CI, 12.7 to 30.4) than patients in the waiting list condition.</td></tr>
<tr><td>Heckler 2016</td><td colspan="2">No secondary outcomes reported</td><td></td></tr>
<tr><td>Hoffman 2012</td><td>Global quality of life / Functional impact of fatigue</td><td>Functional Assessment of Cancer Therapy-Breast (FACT-B)
FACT, Functional Assessment of Cancer Therapy

Functional Assessment of Cancer Therapy-Endocrine Symptoms (FACT-ES)</td><td>After adjustment for the outcome measurement made at T1, there were statistically significant treatment effects for FACT-ES, FACT-B, physical well-being, social well-being, emotional wellbeing, and functional well-being. Mean scores in the experimental group compared with the control group were greater at both T2 and T3 for all six measures (except social well-being which was significant at T2 only). For emotional well-being, there was some evidence that treatment effects at T3 were statistically significantly greater that at T2. No other interactions were statistically significant.

After adjustment for T1 measurements, there were statistically significant increases in the WHO-5 in the experimental group compared with controls, and these were apparent at T2 and T3.

For the WHO-5, the minimum clinically important difference has been suggested to be a change of 10% on standardized percentage scores, which are obtained by multiplying the raw scores by four. The adjusted mean</td></tr>
</table>

		WHO five-item well-being questionnaire (WHO-5)	differences, expressed as standardized percentage scores, were 8.04% at T2 and 8.60% at T3. These scores were close to the minimum clinically important difference of 10%

Outcome Measure	**Experimental Group (n = 103)**			**Control Group (n = 111)**			**Difference Between Groups at T2 and T3 Adjusted for Baseline**	
	N	**Mean**	**SD**	**N**	**Mean**	**SD**	**Mean**	**95% CI**
FACT-ES								
T1	102	127.02	18.84	107	127.08	23.20	NA	
T2	102	134.97	19.26	107	127.37	23.58	7.65	3.95 to 11.36
T3	102	135.34	19.54	107	127.42	21.26	7.98	4.46 to 11.49
Interaction time × treatment group, *P*							.814	
Treatment group main effect, *P*							**< .001**	
FACT-B								
T1	101	96.57	17.22	106	96.68	21.05	NA	
T2	101	103.56	17.91	106	96.84	21.14	6.81	3.48 to 10.14
T3	101	103.78	17.85	106	96.22	19.43	7.65	4.61 to 10.68
Interaction time × treatment group, *P*							.493	
Treatment group main effect, *P*							**< .001**	
FACT PWB								
T1	102	21.88	4.29	111	21.89	4.35	NA	
T2	102	22.86	4.22	111	21.84	4.54	1.03	0.19 to 1.87
T3	102	22.97	4.34	111	21.67	4.87	1.31	0.49 to 2.12
Interaction time × treatment group, *P*							.521	
Treatment group main effect, *P*							**.002**	
FACT SWB								
T1	102	17.59	5.91	109	18.78	6.01	NA	
T2	102	18.36	5.65	109	18.26	5.88	1.06	0.17 to 1.94
T3	102	18.09	5.81	109	18.30	5.75	0.71	−0.24 to 1.65
Interaction time × treatment group, *P*								.436
Treatment group main effect, *P*								.032
FACT EWB								
T1	102	16.91	3.84	109	15.97	4.58	NA	
T2	102	18.14	3.82	109	16.59	4.40	0.93	0.09 to 1.78

			T3	102	18.59	3.75	109	16.28	4.42	1.72	0.86 to 2.57
			Interaction time × treatment group, *P*						**.042**		
			Treatment group main effect, *P*						**.001**		
			FACT FWB								
			T1	102	17.83	5.03	110	17.65	5.83	NA	
			T2	102	19.46	5.27	110	17.41	6.06	1.91	0.87 to 2.95
			T3	102	19.45	5.32	110	17.53	5.37	1.80	0.77 to 2.83
			Interaction time × treatment group, *P*						.804		
			Treatment group main effect, *P*						< .001		
			WHO-5								
			T1	103	13.04	4.48	111	12.53	4.68	NA	
			T2	103	14.91	4.23	111	12.60	4.92	2.01	1.00 to 3.01
			T3	103	15.08	4.62	111	12.65	4.30	2.15	1.16 to 3.15
			Interaction time × treatment group, *P*							.768	
			Treatment group main effect, *P*							**< .001**	

Mood | **POMS**

There were statistically significant differences between treatment groups for POMS total mood disturbance, anxiety, depression, anger, vigor, fatigue, and confusion. The T1-adjusted mean differences and 95% CIs at T2 and T3 suggested statistically significant lowermood-state scores in the experimental group than in the control group at both measurement occasions except for depression (T2 only), anger (T3 only), and confusion (T2 only). There were no statistically significant interactions between treatment group and measurement occasion.

Outcome Measure	Experimental (n = 103)		Control (n = 111)		Difference Between Groups at T2 and T3 Adjusted for Baseline	
	Mean	SD	Mean	SD	Mean	95% CI
Total score						
T1 total mood disturbance	43.65	34.73	49.23	39.37	NA	
T2 total mood disturbance	30.02	31.60	48.08	39.89	−15.30	−23.75 to −6.86
T3 total mood disturbance	29.83	34.19	45.47	35.67	−12.91	−21.02 to −4.81
Interaction time × treatment group, *P*					558	
Treatment group main effect, *P*					**< .001**	
Subscales						
T1 tension/anxiety	13.16	7.20	13.42	7.24	NA	
T2 tension/anxiety	10.32	7.0	13.36	7.20	−2.93	−4.67 to −1.20
T3 tension/anxiety	10.33	7.02	12.73	6.59	−2.30	−3.96 to −0.63

			Interaction time × treatment group, *P*					.493	
			Treatment group main effect, *P*					**< .001**	
			T1 depression/dejection	12.79	10.76	15.70	12.79	NA	
			T2 depression/dejection	10.0	9.95	14.96	13.23	−3.39	−6.06 to −0.71
			T3 depression/dejection	10.34	10.32	14.10	11.60	−2.32	−4.86 to 0.22
			Interaction time × treatment group, *P*					.365	
			Treatment group main effect, *P*					**.017**	
			T1 anger/hostility	10.75	8.08	11.60	8.62	NA	
			T2 anger/hostility	8.78	7.57	11.11	8.88	−1.96	−3.96 to 0.05
			T3 anger/hostility	7.87	6.72	11.04	8.95	−2.69	−4.44 to −0.95
			Interaction time × treatment group, *P*					.458	
			Treatment group main effect, *P*					**.005**	
			T1 vigor/activity	−14.31	6.53	−14.06	6.19	NA	
			T2 vigor/activity	−15.91	6.0	−13.57	6.61	−2.21	−3.67 to −0.75
			T3 vigor/activity	−16.23	6.63	−13.47	6.22	−2.63	−4.12 to −1.15
			Interaction time × treatment group, *P*					.606	
			Treatment group main effect, *P*					**< .001**	
			T1 fatigue/inertia	11.17	6.64	11.75	7.20	NA	
			T2 fatigue/inertia	8.71	6.10	11.62	7.16	−2.68	−4.31 to −1.04
			T3 fatigue/inertia	9.27	6.90	11.39	6.73	−1.84	−3.45 to −0.22
			Interaction time × treatment group, *P*					.324	
			Treatment group main effect, *P*					**.002**	
			T1 confusion/bewilderment	10.11	5.58	10.65	5.57	NA	
			T2 confusion/bewilderment	8.13	4.71	10.33	5.30	−1.91	−3.01 to −0.81
			T3 confusion/bewilderment	8.24	5.32	9.63	4.31	−1.09	−2.20 to 0.01
			Interaction time × treatment group, *P*					.141	
			Treatment group main effect, *P*					**.002**	
Johns 2014	Global quality of life / Functional impact of fatigue	Functional status: Sheehan Disability Scale (SDS)	Functional disability scores were lower in the MBSR group at T2 (d = −0.45), although not statistically different (p = 0.25); however, at T3 the MBSR group demonstrated significantly lower functional disability scores than controls (p = .0013) with a large effect size (d = −1.22).						
	Mood	Patient Health Questionnaire Generalized	Depression scores were significantly lower (p < .001) for MBSR than controls with large differences at T2 (d = −1.30) and T3 (d = −1.71). Sleep disturbance was significantly improved for MBSR compared to the control condition at both						

<table>
<tr><td></td><td></td><td>Anxiety Disorder Scale and Depression severity: PHQ-8.</td><td colspan="2">T2 (d = −0.74) and T3 (d = −1.00). Anxiety scores were lower in the intervention group at T2 than for the control group (d = −0.47), although not statistically different (p = 0.10). By T3, however, the MBSR group demonstrated significantly lower anxiety scores than the control group (p = 0.002) with a large effect size (d = −0.98).</td></tr>
<tr><td></td><td>Insomnia or sleep quality</td><td>Sleep disturbance: Insomnia Severity Index</td><td colspan="2">The MBSR group demonstrated significantly greater improvement than the control group in fatigue interference as measured against the Bonferroni-corrected significance level of p < .00278 at T2 and T3. Effect sizes (d) for group differences (adjusted for baseline levels) in fatigue interference were large at both time points, ranging from −1.43 at T2 to −1.34 at T3.</td></tr>
<tr><td>Lengacher 2012</td><td>Global quality of life / Functional impact of fatigue</td><td>M.D. Anderson Symptom Inventory (MDASI)</td><td colspan="2">
<table>
<tr><td></td><td colspan="3">Control</td><td colspan="3">MBSR(BC)</td><td>P</td></tr>
<tr><td></td><td>Baseline</td><td>6-Week post-assessment</td><td></td><td>Baseline</td><td>6-Week post-assessment</td><td>P</td><td>(between-group post-assessment)</td></tr>
<tr><td>Trouble remembering</td><td>2.9(2.7)</td><td>2.0(2.2)</td><td>.03</td><td>2.1(2.7)</td><td>1.3(1.9)</td><td>.05</td><td>.07</td></tr>
<tr><td>Drowsy</td><td>2.6(2.7)</td><td>1.9(2.0)</td><td>.13</td><td>2.2(2.1)</td><td>1.4(2.2)</td><td>.04</td><td>.05</td></tr>
<tr><td>Numbness</td><td>1.6(2.5)</td><td>1.4(2.7)</td><td>.34</td><td>1.8(2.4)</td><td>1.1(1.8)</td><td>.07</td><td>.46</td></tr>
<tr><td>Dry mouth</td><td>1.5(2.5)</td><td>1.1(2.1)</td><td>.08</td><td>1.0(1.6)</td><td>.68(1.6)</td><td>.12</td><td>.60</td></tr>
<tr><td>Shortness of breath</td><td>1.1(2.4)</td><td>.83(1.8)</td><td>.57</td><td>0.7(1.1)</td><td>.48(1.1)</td><td>.15</td><td>.21</td></tr>
<tr><td>Lack of appetite</td><td>1.0(2.1)</td><td>.73(1.6)</td><td>.11</td><td>0.5(1.2)</td><td>.25(.78)</td><td>.15</td><td>.06</td></tr>
<tr><td>Nausea</td><td>0.4(1.7)</td><td>.02(.15)</td><td>.11</td><td>0.2(0.6)</td><td>.05(.22)</td><td>.20</td><td>.53</td></tr>
<tr><td>Vomiting</td><td>0.1(0.5)</td><td>0.0(0.0)</td><td>.32</td><td>0.0(0.0)</td><td>.03(.16)</td><td>.32</td><td>.31</td></tr>
<tr><td>General activity</td><td>2.1(3.2)</td><td>1.6(2.4)</td><td>.41</td><td>2.1(2.6)</td><td>.68(1.3)</td><td>.001</td><td>.12</td></tr>
<tr><td>Housework</td><td>2.4(3.2)</td><td>1.5(2.3)</td><td>.03</td><td>2.0(2.7)</td><td>.57(1.3)</td><td>.002</td><td>.02</td></tr>
<tr><td>Walking</td><td>2.2(3.3)</td><td>1.0(1.8)</td><td>.02</td><td>1.5(2.6)</td><td>1.1(2.2)</td><td>.14</td><td>.46</td></tr>
<tr><td>Relationships</td><td>1.8(3.0)</td><td>.98(1.8)</td><td>.11</td><td>1.3(2.1)</td><td>.45(1.4)</td><td>.004</td><td>.05</td></tr>
</table>
</td></tr>
<tr><td></td><td>Mood</td><td>MDASI mood, enjoyment of life, distress, and sadness</td><td colspan="2">
<table>
<tr><td></td><td colspan="3">Control</td><td colspan="3">MBSR(BC)</td><td>P</td></tr>
<tr><td></td><td>Baseline</td><td>6-Week post-assessment</td><td></td><td>Baseline</td><td>6-Week post-assessment</td><td>P</td><td>(between-group post-assessment)</td></tr>
<tr><td>Distress</td><td>2.2(2.8)</td><td>1.4(2.2)</td><td>.01</td><td>1.7(2.5)</td><td>.82(1.5)</td><td>.02</td><td>.11</td></tr>
<tr><td>Sadness</td><td>2.1(2.8)</td><td>1.2(2.1)</td><td>.003</td><td>2.1(2.6)</td><td>.98(1.8)</td><td>.05</td><td>.35</td></tr>
<tr><td>Mood</td><td>2.4(3.2)</td><td>1.6(2.4)</td><td>.04</td><td>1.8(2.4)</td><td>.70(1.5)</td><td>.005</td><td>.04</td></tr>
<tr><td>Enjoyment of life</td><td>2.3(3.1)</td><td>1.3(2.1)</td><td>.008</td><td>1.6(2.2)</td><td>.63(1.6)</td><td>.003</td><td>.06</td></tr>
</table>
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<table>
<tr>
<td></td>
<td>Insomnia or sleep quality</td>
<td>MDASI sleep disturbance and MDASI drowsiness</td>
<td>the MBSR(BC) group showed greater improvement across symptoms, and especially symptom interference items, compared to the control group. For the MBSR(BC) group, statistically-significant reductions (P < .01) were observed for disturbed sleep.
<table>
<tr><td></td><td colspan="3">Control</td><td colspan="3">MBSR(BC)</td><td>P</td></tr>
<tr><td></td><td>Baseline</td><td>6-Week post-assessment</td><td></td><td>Baseline</td><td>6-Week post-assessment</td><td>P</td><td>(between-group post-assessment)</td></tr>
<tr><td>Disturbed sleep</td><td>3.1(3.3)</td><td>2.1(2.9)</td><td>.01</td><td>3.2(3.0)</td><td>1.9(2.5)</td><td>.009</td><td>.98</td></tr>
<tr><td>Drowsy</td><td>2.6(2.7)</td><td>1.9(2.0)</td><td>.13</td><td>2.2(2.1)</td><td>1.4(2.2)</td><td>.04</td><td>.05</td></tr>
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</tr>
<tr>
<td></td>
<td>Pain</td>
<td>MDASI pain</td>
<td>
<table>
<tr><td></td><td colspan="3">Control</td><td colspan="3">MBSR(BC)</td><td>P</td></tr>
<tr><td></td><td>Baseline</td><td>6-Week post-assessment</td><td></td><td>Baseline</td><td>6-Week post-assessment</td><td>P</td><td>(between-group post-assessment)</td></tr>
<tr><td>Pain</td><td>1.8(2.2)</td><td>1.9(2.6)</td><td>.73</td><td>2.0(2.3)</td><td>1.4(1.8)</td><td>.04</td><td>.61</td></tr>
</table>
</td>
</tr>
<tr>
<td>Matthews 2014</td>
<td>Global quality of life / Functional impact of fatigue</td>
<td>European Organisation for the Research and Treatment of Cancer Quality of Life</td>
<td>No group differences in improvement were noted relative to QOL</td>
</tr>
</table>

<table>
<tr><td></td><td></td><td>Questionnaire– Core 30 (EORTC QLQ-C30)</td><td></td></tr>
<tr><td></td><td>Mood</td><td>Hospital Anxiety and Depression Scale (HADS)</td><td>No group differences in improvement were noted relative to mood.</td></tr>
<tr><td></td><td>Insomnia or sleep quality</td><td>Sleep parameters extracted from the diary included SL, SE, WASO, TST, and number of nocturnal awakenings.

The Insomnia Severity Index</td><td>Sleep efficiency and latency improved more in the CBTI group than the BPT group; this difference was maintained during follow-up. Women in the CBTI group had less subjective insomnia, greater improvements in physical and cognitive functioning, positive sleep attitudes, and increased sleep hygiene knowledge.</td></tr>
<tr><td>Prinsen 2013</td><td>Global quality of life / Functional impact of fatigue</td><td>Sickness Impact Profile-8 (SIP-8)</td><td>Functional impairment was not significantly different between the intervention and the waiting list group at baseline. The change score in functional impairment (SIP-8) was significantly different between the CBT and the waiting list group (respectively −73.0 ± 28.1 % and −9.5 ± 47.1 %).</td></tr>
<tr><td>Reeves 2017</td><td>Global quality of life / Functional impact of fatigue</td><td>SF-36</td><td>The between-group intervention effects for other secondary outcomes were not statistically significant. Statistically significant improvements were observed within both arms in physical QoL scores and all body image subscales apart from social barriers. Neither arm changed significantly in mental QoL.
<table>
<tr><td></td><td colspan="2">Baseline mean (SD)</td><td colspan="2">Mean change (95% CI)†</td><td colspan="2">Intervention – usual care†,‡</td><td></td></tr>
<tr><td></td><td>Intervention</td><td>Usual care</td><td>Intervention</td><td>Usual care</td><td>Mean difference (95% CI)</td><td>P</td></tr>
<tr><td>Quality of Life (SF-36)</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Physical component (0–100)</td><td>46.1 (8.8)§</td><td>45.1 (10.4)¶</td><td>3.4 (1.4, 5.4)**</td><td>4.0 (1.9, 6.1)***</td><td>0.4 (−3.7, 2.9)</td><td>0.821</td></tr>
<tr><td>Mental component (0–100)</td><td>49.4 (8.5)§</td><td>50.5 (10.4)¶</td><td>2.1 (−1.1, 5.3)</td><td>0.4 (−2.7, 3.5)</td><td>0.3 (−3.8, 4.5)</td><td>0.869</td></tr>
<tr><td>Treatment-related side-effects</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
</table>
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</table>

			Fatigue (FACIT) (0–52): 41 (34, 46)††; 43 (31, 47)¶; 3.0 (0.7, 5.3)**; 1.5 (−1.0, 4.0); 1.1 (−2.4, 4.5); 0.527 Body Image (BIRS) Total (32–160): 81.6 (19.6)¶; 82.8 (20.8)††; −8.6 (−13.0, −4.1)***; −10.5 (−15.6, −5.4)***; 1.8 (−6.0, 9.7); 0.639 Strength and health (12–60): 32.9 (9.2)¶; 33.7 (8.1)††; −4.4 (−6.6, 2.2)***; −4.5 (−6.8, 2.2)***; −0.9 (−2.8, 4.5); 0.627 Social barriers (9–45): 18.5 (6.6)¶; 18.8 (7.9)††; −1.6 (−3.4, 0.2); −3.5 (−5.5, −1.6)***; 1.9 (−0.7, 4.6); 0.149 Appearance and sexuality (11–55): 30.2 (7.6)¶; 30.3 (8.7)††; −2.6 (−4.6, −0.7)**; −3.1 (−5.6, −0.7)*; −0.3 (−3.8, 3.2); 0.866
Reich 2017	Global quality of life / Functional impact of fatigue	Medical Outcomes Studies Short-Form General Health Survey (SF-36) M.D. Anderson Symptom Inventory	

Cluster Psychological	MBSR(BC)			UC		
	Mean	SD	*n*	Mean	SD	*n*
Emotional well-being (SF-36)						
Baseline	63.83	17.42	167	68.57	18.32	155
Week 6	70.87	18.02	152	69.36	18.78	145
Week 12	71.33	19.41	153	72.71	19.13	146

From baseline to six weeks, the model demonstrated evidence of MBSR(BC) effectiveness in the psychological (anxiety, depression, perceived stress and QOL, emotional well-being) (P = 0.007) clusters. participants who received the MBSR(BC) training improved more than those who did not at the six-week time point.

standardized regression coefficients (β) for psychological symptoms (.17), effect sizes of 0.35

	Mood	CES-D Perceived Stress Scale State-Trait Anxiety Inventory Concerns About Recurrence Scale	

Cluster Psychological	MBSR(BC)			UC		
	Mean	SD	*n*	Mean	SD	*n*
Depression (CESD)						
Baseline	10.87	6.89	167	10.04	6.46	155
Week 6	8.12	5.45	154	8.82	6.05	146
Week 12	8.66	6.26	155	8.95	6.80	148
Anxiety (STAI)						
Baseline	38.62	12.30	167	35.86	11.29	155
Week 6	30.62	12.80	159	31.76	13.20	152
Week 12	31.82	12.10	155	32.99	13.40	148
Stress (PSS)						

<table>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>Baseline</td><td>17.57</td><td>7.71</td><td>167</td><td>15.39</td><td>7.62</td><td>155</td></tr>
<tr><td>Week 6</td><td>20.19</td><td>5.06</td><td>156</td><td>20.21</td><td>5.33</td><td>151</td></tr>
<tr><td>Week 12</td><td>12.90</td><td>7.75</td><td>158</td><td>12.89</td><td>8.20</td><td>154</td></tr>
</table>

From baseline to six weeks, the model demonstrated evidence of MBSR(BC) effectiveness in both the psychological (anxiety, depression, perceived stress and QOL, emotional well-being) (P = 0.007) clusters. participants who received the MBSR(BC) training improved more than those who did not at the six-week time point.

standardized regression coefficients (β) for psychological symptoms (.17), effect sizes of 0.35</td></tr>
<tr><td></td><td>Insomnia or sleep quality</td><td>Pittsburgh Sleep Quality Index</td><td>
<table>
<tr><td></td><td>MBSR(BC)</td><td></td><td></td><td>UC</td><td></td><td></td></tr>
<tr><td></td><td>Mean</td><td>SD</td><td>n</td><td>Mean</td><td>SD</td><td>n</td></tr>
<tr><td>Sleep (PSQI)</td><td colspan="6"></td></tr>
<tr><td>Baseline</td><td>9.12</td><td>5.04</td><td>165</td><td>8.25</td><td>4.23</td><td>155</td></tr>
<tr><td>Week 6</td><td>7.26</td><td>4.47</td><td>148</td><td>7.52</td><td>4.11</td><td>145</td></tr>
<tr><td>Week 12</td><td>7.08</td><td>4.42</td><td>150</td><td>7.02</td><td>4.12</td><td>145</td></tr>
<tr><td>Drowsiness (MDASI)</td><td colspan="6"></td></tr>
<tr><td>Baseline</td><td>3.14</td><td>3.10</td><td>167</td><td>2.92</td><td>3.14</td><td>155</td></tr>
<tr><td>Week 6</td><td>2.32</td><td>2.46</td><td>152</td><td>2.61</td><td>2.97</td><td>145</td></tr>
<tr><td>Week 12</td><td>2.16</td><td>2.85</td><td>152</td><td>2.33</td><td>2.78</td><td>147</td></tr>
</table>
</td></tr>
<tr><td></td><td>Pain</td><td>Brief Pain Inventory</td><td>Pain (P = 0.97) cluster improvement was not related to assignment.

<table>
<tr><td>Cluster Pain</td><td>MBSR(BC)</td><td></td><td></td><td>UC</td><td></td><td></td></tr>
<tr><td></td><td>Mean</td><td>SD</td><td>n</td><td>Mean</td><td>SD</td><td>n</td></tr>
<tr><td>Quality of life (SF-36)</td><td colspan="6"></td></tr>
<tr><td>Baseline</td><td>62.44</td><td>27.52</td><td>167</td><td>62.74</td><td>24.68</td><td>155</td></tr>
<tr><td>Week 6</td><td>65.76</td><td>26.18</td><td>152</td><td>66.24</td><td>24.76</td><td>145</td></tr>
<tr><td>Week 12</td><td>68.43</td><td>27.76</td><td>153</td><td>70.36</td><td>22.70</td><td>146</td></tr>
<tr><td>Severity (BPI)</td><td colspan="6"></td></tr>
<tr><td>Baseline</td><td>11.30</td><td>10.12</td><td>167</td><td>9.69</td><td>8.60</td><td>155</td></tr>
<tr><td>Week 6</td><td>9.59</td><td>9.44</td><td>157</td><td>8.28</td><td>8.16</td><td>151</td></tr>
<tr><td>Week 12</td><td>8.46</td><td>9.41</td><td>161</td><td>8.66</td><td>8.40</td><td>155</td></tr>
</table>
</td></tr>
</table>

<table>
<tr>
<td>Reif 2012</td>
<td>Global quality of life / Functional impact of fatigue</td>
<td>EORTC QLQ-C30</td>
<td>Secondary outcomes also showed significant improvements in all measures, including quality of life (F = 29.607, p < 0.001, η2 = 0.113)
<table>
<tr><th></th><th>Group</th><th>Pre-intervention</th><th>Post-intervention</th><th>Follow-up at 6 months</th><th colspan="2">Group × time</th><th>Partial eta-squared</th></tr>
<tr><th></th><th></th><th>Mean (SD)</th><th>Mean (SD)</th><th>Mean (SD)</th><th>F</th><th>p</th><th>Group × time</th></tr>
<tr><td rowspan="2">Global Health Status (range: 0–100)</td><td>IG</td><td>44.17 (18.32)</td><td>57.08 (22.93)</td><td>63.82 (21.67)</td><td rowspan="2">29.607</td><td rowspan="2"><0.001</td><td rowspan="2">0.113</td></tr>
<tr><td>CG</td><td>43.06 (18.97)</td><td>40.35 (19.16)</td><td>39.91 (18.57)</td></tr>
<tr><td rowspan="2">Physical functioning (range: 0–100)</td><td>IG</td><td>59.28 (20.92)</td><td>72.33 (19.28)</td><td>78.55 (20.55)</td><td rowspan="2">32.432</td><td rowspan="2"><0.001</td><td rowspan="2">0.123</td></tr>
<tr><td>CG</td><td>58.60 (19.92)</td><td>57.48 (22.74)</td><td>56.78 (24.15)</td></tr>
<tr><td rowspan="2">Role functioning (range: 0–100)</td><td>IG</td><td>41.39 (25.20)</td><td>59.58 (29.36)</td><td>69.58 (28.96)</td><td rowspan="2">33.906</td><td rowspan="2"><0.001</td><td rowspan="2">0.128</td></tr>
<tr><td>CG</td><td>39.18 (23.46)</td><td>37.86 (26.17)</td><td>38.16 (27.93)</td></tr>
<tr><td rowspan="2">Emotional functioning (range: 0–100)</td><td>IG</td><td>37.64 (24.89)</td><td>58.82 (26.42)</td><td>68.96 (27.14)</td><td rowspan="2">51.826</td><td rowspan="2"><0.001</td><td rowspan="2">0.183</td></tr>
<tr><td>CG</td><td>37.28 (24.92)</td><td>36.77 (25.81)</td><td>33.77 (25.37)</td></tr>
<tr><td rowspan="2">Cognitive functioning (range: 0–100)</td><td>IG</td><td>41.25 (24.82)</td><td>60.97 (28.21)</td><td>68.61 (28.92)</td><td rowspan="2">48.974</td><td rowspan="2"><0.001</td><td rowspan="2">0.174</td></tr>
<tr><td>CG</td><td>42.25 (26.16)</td><td>39.77 (27.20)</td><td>36.70 (27.17)</td></tr>
<tr><td rowspan="3">Social functioning (range: 0–100)</td><td>IG</td><td>37.08 (28.04)</td><td>58.33 (31.53)</td><td>66.11 (32.40)</td><td rowspan="3">31.282</td><td rowspan="3"><0.001</td><td rowspan="3">0.119</td></tr>
<tr><td>CG</td><td>39.62 (31.39)</td><td>37.86 (31.14)</td><td>35.09 (28.60)</td></tr>
<tr><td>CG</td><td>61.11 (36.28)</td><td>64.33 (34.84)</td><td>66.67 (33.77)</td></tr>
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</tr>
<tr>
<td></td>
<td>Mood</td>
<td>Hospital Anxiety and Depression Scale (HADS-D)</td>
<td>Secondary outcomes also showed significant improvements in all measures, including anxiety (F = 33.194, p < 0.001, η2 = 0.125), and depression (F = 24.604, p < 0.001, η2 = 0.096)</td>
</tr>
</table>

			<table><tr><td></td><td>Group</td><td>Pre-intervention Mean (SD)</td><td>Post-intervention Mean (SD)</td><td>Follow-up at 6 months Mean (SD)</td><td>Group × time *F*</td><td> *p*</td><td>Partial eta-squared Group × time</td></tr><tr><td>Anxiety scale (range: 0–21)</td><td>IG</td><td>9.16 (3.92)</td><td>6.73 (4.40)</td><td>5.32 (4.39)</td><td>33.194</td><td><0.001</td><td>0.125</td></tr><tr><td></td><td>CG</td><td>9.51 (3.98)</td><td>9.47 (3.94)</td><td>9.81 (4.43)</td><td></td><td></td><td></td></tr><tr><td>Depression scale (range: 0–21)</td><td>IG</td><td>8.32 (3.85)</td><td>6.09 (4.72)</td><td>5.04 (4.71)</td><td>24.604</td><td><0.001</td><td>0.096</td></tr><tr><td></td><td>CG</td><td>8.71 (3.58)</td><td>8.77 (3.88)</td><td>8.86 (4.01)</td><td></td><td></td><td></td></tr></table>
	Insomnia or sleep quality	EORTC QLQ-C30 insomnia subscale	<table><tr><td></td><td>**Group**</td><td>**Pre-intervention** **Mean (SD)**</td><td>**Post-intervention** **Mean (SD)**</td><td>**Follow-up at 6 months** **Mean (SD)**</td><td>**Group × time** ***F***</td><td> ***p***</td><td>**Partial eta-squared** **Group × time**</td></tr><tr><td>Insomnia (range: 0–100)</td><td>IG</td><td>64.44 (33.12)</td><td>45.83 (37.44)</td><td>38.89 (36.24)</td><td>22.727</td><td>**<0.001**</td><td>0.089</td></tr><tr><td></td><td>CG</td><td>61.11 (36.28)</td><td>64.33 (34.84)</td><td>66.67 (33.77)</td><td></td><td></td><td></td></tr></table>
Ritterband 2012	Global quality of life / Functional impact of fatigue	SF-12	<table><tr><td>Variable</td><td>Internet Participants (n=14) Mean (SD)</td><td> Pre-Post ES (d)*</td><td>Control Participants (n=14) Mean (SD)</td><td> Pre-Post ES (d)*</td><td>$F_{1,26}$</td><td>*P* Value</td><td>Overall Adjusted ES (d)</td></tr><tr><td>SF-12: Mental</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Pre</td><td>43.02 (13.51)</td><td>0.48</td><td>46.86 (7.95)</td><td>0.00</td><td>3.14</td><td>0.09</td><td>0.48</td></tr><tr><td>Post</td><td>48.51 (8.73)</td><td></td><td>46.82 (10.06)</td><td></td><td></td><td></td><td></td></tr><tr><td>SF-12: Physical</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Pre</td><td>48.96 (10.36)</td><td>0.15</td><td>45.56 (7.22)</td><td>−0.06</td><td>0.44</td><td>0.52</td><td>0.21</td></tr><tr><td>Post</td><td>50.36 (9.76)</td><td></td><td>44.96 (10.34)</td><td></td><td></td><td></td><td></td></tr></table> Regarding the SF-12, a measure of quality of life, the group x time interaction for the mental subscale was not significant (*p*=.09), but the adjusted ES indicated a small-to-medium treatment effect (d=.48). On the physical subscale of the SF-12, the group x time interaction also did not reach significance (*p*=.52), but the adjusted ES indicated a small treatment effect for SHUTi (d=.21).

<table>
<tr>
<td></td>
<td>Mood</td>
<td>The Hospital Anxiety and Depression Scale (HADS)</td>
<td>On the total HADS score, a measure of anxiety and depression, the group x time interaction was not significant (p=.09). However, the adjusted effect sizes for the total was d=.52; and the subscales, depression and anxiety, were d=.54 and d=.42, respectively. Regarding the SF-12, a measure of quality of life, the group x time interaction for the mental subscale was not significant (p=.09), but the adjusted ES indicated a small-to-medium treatment effect (d=.48). On the physical subscale of the SF-12, the group x time interaction also did not reach significance (p=.52), but the adjusted ES indicated a small treatment effect for SHUTi (d=.21).
<table>
<tr><th rowspan="2">Variable</th><th colspan="2">Internet Participants (n=14)</th><th colspan="2">Control Participants (n=14)</th><th rowspan="2">$F_{1,26}$</th><th rowspan="2">P Value</th><th rowspan="2">Overall Adjusted ES (d)</th></tr>
<tr><th>Mean (SD)</th><th>Pre-Post ES (d)*</th><th>Mean (SD)</th><th>Pre-Post ES (d)*</th></tr>
<tr><td colspan="8">HADS: Total</td></tr>
<tr><td>Pre</td><td>14.64 (7.45)</td><td rowspan="2">0.73</td><td>14.00 (5.19)</td><td rowspan="2">0.21</td><td rowspan="2">3.18</td><td rowspan="2">0.09</td><td rowspan="2">0.52</td></tr>
<tr><td>Post</td><td>9.93 (5.53)</td><td>12.64 (6.01)</td></tr>
<tr><td colspan="8">HADS: Depression</td></tr>
<tr><td>Pre</td><td>5.21 (3.58)</td><td rowspan="2">0.63</td><td>5.43 (2.65)</td><td rowspan="2">0.09</td><td rowspan="2">2.08</td><td rowspan="2">0.16</td><td rowspan="2">0.54</td></tr>
<tr><td>Post</td><td>3.21 (2.42)</td><td>5.14 (4.02)</td></tr>
<tr><td colspan="8">HADS: Anxiety</td></tr>
<tr><td>Pre</td><td>9.43 (4.29)</td><td rowspan="2">0.70</td><td>8.57 (3.27)</td><td rowspan="2">0.28</td><td rowspan="2">3.15</td><td rowspan="2">0.09</td><td rowspan="2">0.42</td></tr>
<tr><td>Post</td><td>6.71 (3.85)</td><td>7.50 (2.98)</td></tr>
</table>
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<tr>
<td></td>
<td>Insomnia or sleep quality</td>
<td>Pittsburgh Sleep Quality Index</td>
<td>There was a significant group x time interaction effect with the Internet group showing a marked improvement in insomnia severity from pre- to post-assessment, and the control group showing no significant change (F1,26=22.8; p<.01). More specifically, the Internet group dropped from an ISI score of 17.1 at pre-assessment to 8.2 at post-assessment, (t(13)=10.15, p<.01), while the control group showed no significant change: ISI of 15.9 at pre-assessment and 14.4 at post-assessment, (t(13)=1.24, p=0.2;). Per Cohen's guidelines [54], the adjusted ES indicates a large SHUTi treatment effect for insomnia severity (d=1.85). Gains made by participants who used SHUTi were also clinically significant. At baseline, 9 out of 14 participants (64%) in each group had ISI scores in the "clinically significant" range of insomnia, as defined by an ISI score of greater than 14. The remaining five participants in each group all had ISI scores in the "subthreshold insomnia" range (ISI score in the range of 8 to 14); no participant had an ISI score in the "no insomnia" range (ISI <8). After using SHUTi, only 2 of the 14 (14%) Internet participants still had "clinically significant" levels of insomnia symptoms (ISI >14), compared to 8 of 14 control participants (57%). In addition, 7 of 14 (50%) Internet participants had ISI scores in the "no insomnia" range, compared to just 2 of 14 (14%) control participants.</td>
</tr>
</table>

Sleep Variable and Period	Internet Participants (n=13)		Control Participants (n=13)		$F_{1,24}$	*P* Value	Overall Adjusted ES (d)
	Mean (SD)	Pre-Post ES (d)*	Mean (SD)	Pre-Post ES (d)*			
Sleep Efficiency, %							
Pre	72.16 (9.56)	1.05	75.55 (14.13)	0.33	11.45	< 0.01	0.72
Post	85.67 (6.50)[a]		79.75 (11.45)[b]				
Total Sleep Time, min							
Pre	361.62 (68.36)	0.46	362.46 (73.39)	0.14	2.11	0.16	0.32
Post	396.05 (49.64)		373.05 (63.60)				
SOL, min							
Pre	48.42 (32.37)	0.83	40.73 (30.57)	0.16	5.18	0.03	0.67
Post	19.88 (16.79)[a]		35.23 (22.31)				
WASO, min							
Pre	55.88 (30.52)	0.72	47.54 (31.25)	0.50	1.03	0.32	0.22
Post	31.99 (21.76)		30.99 (19.72)				
Time In Bed, min							
Pre	498.69 (47.45)	0.63	481.04 (58.58)	0.23	2.56	0.12	0.40
Post	461.42 (39.55)		467.31 (42.56)				
Awakenings, no.							
Pre	2.64 (1.19)	0.69	1.98 (.51)	0.26	3.05	0.09	0.43
Post	1.87 (.90)		1.69 (.59)				
Soundness of sleep, scale score[c]							
Pre	2.55 (.61)	1.42	2.85 (.43)	0.21	9.34	< 0.01	1.21
Post	3.38 (.59)[a]		2.98 (.69)				
Restored, scale score[d]							
Pre	2.38 (.38)	1.51	2.82 (.54)	0.16	11.95	< 0.01	1.35
Post	3.21 (.60)[a]		2.91 (.58)				

<table>
<tr><td>Rogers 2017</td><td>Mood</td><td>Hospital Anxiety and Depression Scale</td><td>Adjusted linear mixed-model analyses demonstrated significant effects of BEAT Cancer vs usual care on depressive symptomatology (M3 M = −1.3; CI = −2.0 to −0.6; d = −0.38; P < .001), and anxiety (M3 M = −1.3; CI = −2.0 to −0.5; d = −0.33; P < .001). BEAT Cancer effects remained significant at M6 for all outcomes (all P values <.05; d = −0.21 to −.35).

<table>
<tr><td></td><td></td><td>Unadjusted Means</td><td></td><td colspan="2">Adjusted<u>a</u> Between-group Differences Estimated Least Square Mean with (95% CI); P Value</td></tr>
<tr><td></td><td>Baseline mean (SD)</td><td>Month 3 mean (SD)</td><td>Month 6 mean (SD)</td><td>BEAT Cancer vs usual care at month 3 (postintervention)</td><td>BEAT Cancer vs usual care at month 6 (3 mo postintervention)</td></tr>
<tr><td>Depression</td><td></td><td></td><td></td><td>−1.3 (−2.0 to −0.6); <.001</td><td>−0.7 (−1.4 to −0.0); .042</td></tr>
<tr><td>BEAT Cancer</td><td>4.8 (3.3)</td><td>3.0 (2.6)</td><td>3.5 (3.3)</td><td></td><td></td></tr>
<tr><td>Usual care</td><td>4.7 (3.5)</td><td>4.3 (3.1)</td><td>4.3 (3.5)</td><td></td><td></td></tr>
<tr><td>Anxiety</td><td></td><td></td><td></td><td>−1.3 (−2.0 to −0.5); <.001</td><td>−0.8 (−1.5 to −0.0); .044</td></tr>
<tr><td>BEAT Cancer</td><td>7.1 (3.9)</td><td>5.6 (3.4)</td><td>5.8 (3.9)</td><td></td><td></td></tr>
<tr><td>Usual care</td><td>7.0 (3.9)</td><td>6.8 (3.5)</td><td>6.5 (3.7)</td><td></td><td></td></tr>
</table>
</td></tr>
<tr><td>Sandler 2017</td><td>Mood</td><td>Sphere Psychological health subscale</td><td>There was no statistically significant change in mood disturbance designated on the PSYCH subscale of the SPHERE over time for the whole sample (F(2,44) = 2.42; P = 0.10) (Fig. 4). In addition, no significant difference was found between groups at end treatment (MEdu = 0.50, SD = 1.62; MInt = 0.65, SD = 2.83; t(44) = −0.23; P = 0.82) or follow-up (MEdu = 0.33, SD = 1.68; MInt = 0.88, SD = 2.41; t(44) = −0.92; P = 0.36).</td></tr>
<tr><td></td><td>Functional status</td><td>The 36-item Short Form Health Survey (SF - 36; RAND)</td><td>A clinically significant improvement in fatigue was observed in 7 of 22 participants in the intervention arm compared with 2 of 24 in the education arm (P < 0.05; χ2) at end treatment. In support of this response designation, these participants had a mean improvement in functional status (role limitation physical—SF-36; M = 34.72 and SD = 35.50) compared with nonresponders (M = 6.89; SD = 17.22; t(43) = 3.4; P < 0.01). By follow-up, 5 of 22 participants in the intervention arm and 6 of 24 in the education arm reported a clinically significant improvement. From the education arm, two participants deteriorated (by 1 SD) at end treatment and four participants at follow-up. No participants from the intervention arm reported deterioration.

Consistent improvements in physical functioning status (SF-36) were observed in all participants between baseline and 12 week (Mdiff = 12.45; 95% CI 3.43–21.48; P < 0.01) and 24 weeks (Mdiff = 14.40; 95% CI 3.86–24.93; P < 0.05). Similarly, improvements in fatigue were mirrored in the interviewer-designated outcomes via the SCIN, with significant decreases in scores from baseline to 12 weeks (Mdiff = −4.05; 95% CI −5.42 to −2.69; P < 0.001) and 24 weeks (Mdiff = −5.23; 95% CI −6.51 to −3.95; P < 0.001). No significant differences in the change scores of physical functioning were observed between the groups at any time point</td></tr>
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<table>
<tr><td></td><td>Sleep Disturbance</td><td>Pittsburgh Sleep Quality Index</td><td>An improvement in global sleep scores was observed (F(2,34) = 8.20; P < 0.01) between baseline and end treatment (Mdiff = −2.07; 95% CI −3.43 to −0.72; P < 0.01) and sustained at follow-up 24 weeks (Mdiff = 1.80; 95% CI −3.07 to −0.52; P < 0.01). Insomnia also decreased, evidenced by reductions in the mean time taken to fall asleep (F(2,41) = 4.89; P < 0.05) between baseline and end treatment (Mdiff = −10.62; 95% CI −19.34 to −1.91; P < 0.05), which was maintained at follow-up (Mdiff = 10.49; 95% CI −19.00 to −2.03; P < 0.05). Participants also rated their overall sleep quality as better between baseline and end treatment (Mdiff = −1.73; 95% CI −2.89 to −0.57; P < 0.01) and at follow-up (Mdiff = −1.57; 95% CI −2.66 to −0.49; P < 0.001). No significant difference in global sleep change scores was evident between the education (M = 1.52; SD = 2.96) and intervention groups (M = 2.26; SD = 3.85) at postintervention (t(35) = −0.66, P = 0.51) or follow-up (MEdu = 1.51, SD = 3.37; MInt = 2.18; SD = 2.36; t(37) = −0.69, P = 0.49).</td></tr>
<tr><td>Savard 2005</td><td>Global quality of life / Functional impact of fatigue</td><td>European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30+3)</td><td>Significant group-time interactions were obtained on scores of global quality of life ($F_{1,48}$ = 5.69; P < .05). A priori contrasts revealed significant time effects in the global quality-of-life scale ($F_{1,48}$ = 16.27; P < .001), whereas no significant time effect was found on any variable in the control condition.

Pooled data revealed significant differences between pre- and post-treatment on the global quality-of-life scale (F1,159 = 15.63; P < .0001). No significant difference was detected between post-treatment and the follow-up evaluations.

<table>
<tr><th>Variable</th><th></th><th>Cognitive-Behavioral Therapy (n = 27)</th><th></th><th>Waiting-List Control (n = 30)</th><th></th></tr>
<tr><th></th><th>Mean</th><th>95% CI</th><th>Mean</th><th>95% CI</th><th>Mean</th><th>95% CI</th></tr>
<tr><td>QLQ-C33 (global)</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Prewaiting</td><td>—</td><td>—</td><td>67.08</td><td>60.10 to 74.06</td><td>—</td><td>—</td></tr>
<tr><td>Pretreatment*</td><td>52.88</td><td>45.80 to 59.96</td><td>70.10</td><td>63.18 to 77.02</td><td>61.49</td><td>56.55 to 66.43</td></tr>
<tr><td>Post-treatment</td><td>67.56</td><td>60.07 to 75.05</td><td>74.93</td><td>68.01 to 81.85</td><td>71.24</td><td>66.14 to 76.34</td></tr>
<tr><td>3-month follow-up</td><td>70.79</td><td>62.81 to 78.77</td><td>75.68</td><td>68.39 to 82.97</td><td>73.23</td><td>67.82 to 78.64</td></tr>
<tr><td>6-month follow-up</td><td>69.83</td><td>61.85 to 77.81</td><td>73.77</td><td>66.26 to 81.28</td><td>71.80</td><td>66.33 to 77.27</td></tr>
<tr><td>12-month follow-up</td><td>75.51</td><td>66.67 to 84.35</td><td>73.47</td><td>65.98 to 80.96</td><td>74.49</td><td>68.71 to 80.27</td></tr>
</table>
</td></tr>
<tr><td></td><td>Mood</td><td>Hospital Anxiety and Depression Scale.</td><td>Significant group-time interactions were obtained on scores of anxiety ($F_{1,45}$ = 5.19; P < .05) and depression ($F_{1,48}$ = 4.14; P < .05). A priori contrasts revealed significant time effects in the treatment condition on anxiety ($F_{1,46}$ = 4.77; P <</td></tr>
</table>

.05), and the depression ($F_{1,49}$ = 9.03; *P* < .01) scale, whereas no significant time effect was found on any variable in the control condition.

Pooled data revealed significant differences between pre- and post-treatment on anxiety (F1,150 = 11.10; P < .001), depression (F1,146 = 11.87; P < .001). No significant difference was detected between post-treatment and the follow-up evaluations on any of these variables.

		Cognitive-Behavioral Therapy (n = 27)		**Waiting-List Control (n = 30)**		
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
HADS-A						
Prewaiting	—	—	6.57	5.14 to 8.00	—	—
Pretreatment*	8.61	7.14 to 10.08	7.21	5.90 to 8.52	7.91	6.93 to 8.89
Post-treatment	7.23	5.74 to 8.72	5.99	4.68 to 7.30	6.61	5.61 to 7.61
3-month follow-up	5.86	4.37 to 7.35	5.66	4.29 to 7.03	5.76	4.74 to 6.78
6-month follow-up	5.34	3.83 to 6.85	5.71	4.30 to 7.12	5.52	4.48 to 6.56
12-month follow-up	6.19	4.52 to 7.86	4.78	3.37 to 6.19	5.48	4.38 to 6.58
HADS-D						
Prewaiting	—	—	2.83	1.93 to 3.73	—	—
Pretreatment*	4.64	3.74 to 5.54	2.62	1.82 to 3.42	3.63	3.02 to 4.24
Post-treatment	2.90	1.96 to 3.84	2.29	1.49 to 3.09	2.60	1.97 to 3.23
3-month follow-up	2.66	1.72 to 3.60	1.99	1.15 to 2.83	2.33	1.70 to 2.96
6-month follow-up	2.37	1.45 to 3.29	1.83	0.95 to 2.71	2.10	1.45 to 2.75
12-month follow-up	2.41	1.35 to 3.47	1.68	0.82 to 2.54	2.04	1.35 to 2.73

<table>
<tr><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td>Insomnia or sleep quality</td><td>The Insomnia Interview Schedule
Insomnia Severity Index
And sleep diary
sleep onset latency
sleep onset
total wake time
total sleep time
sleep efficiency
use of sleep-promoting medications</td><td>Significant group-time interactions were obtained on all sleep variables, with the exception of total sleep time: sleep efficiency ($F_{1,52}$ = 22.59; P < .0001), total wake time ($F_{1,52}$ = 22.77; P < .001), sleep onset latency $F_{1,53}$ = 4.16; P < .05), wake after sleep onset ($F_{1,52}$ = 16.70; P < .001), ISI-P ($F_{1,52}$ = 25.31; P < .0001), ISI-C ($F_{1,52}$ = 79.37; P < .0001), and ISI-SO ($F_{1,48}$ = 4.54; P < .05). A priori contrasts revealed significant time effects on all variables in the treatment condition and all variables with the exception of two in the control condition (sleep onset latency and wake after sleep onset). Significant time effects found in the control condition were always of a lower magnitude compared with those of the treatment condition. For instance, sleep efficiency increased from 69.5% to 84.4% at post-treatment in the experimental condition, whereas it increased only from 71.1% to 74.5% in the control condition during the waiting period. An analysis was conducted to investigate whether hypnotic use at pretreatment had a moderating role in the effect of CBT on subjective sleep measures at post-treatment. No significant hypnotic use-group-time interaction was found on any of these sleep variables (P from .28 to .93).</td></tr>
<tr><td>Van Der Lee 2012</td><td>Global quality of life / Functional impact of fatigue</td><td>Sickness Impact Profile.
Dutch Health and Disease Inventory questionnaire</td><td>
<table>
<tr><td>Functional impairment</td><td colspan="2">Follow up</td><td colspan="2">Difference with baseline</td><td colspan="2">Difference with post-measurement</td></tr>
<tr><td></td><td>Mean</td><td>SD</td><td>95% CI</td><td>p</td><td>95% CI</td><td>p</td></tr>
<tr><td>MBCT (N= 56)</td><td>11.9</td><td>12.9</td><td>1.4 to 8.4</td><td>0.01</td><td>1.5 to 4.8</td><td>0.30</td></tr>
<tr><td>Well-being MBCT (N = 56)</td><td>54.2</td><td>9.2</td><td>9.8 to 5.4</td><td>0.00</td><td>4.2 to 0.4</td><td>0.02</td></tr>
</table>
Six months after the intervention, participants reported significantly functional impairment than at baseline. Treatment effects at postmeasurement were maintained for functional impairment.</td></tr>
<tr><td></td><td>Mood</td><td>Hospital Anxiety Depression Scale

**Control variable</td><td>About a quarter of all participants (25.8%) scored above the cut-of score of the HADS at baseline. A Chi-square test revealed no differences in percentage of depressive cases between the intervention and the waiting-list control group: (p 5 0.371).</td></tr>
<tr><td></td><td>Insomnia or sleep quality</td><td>Sleep Quality Scale—SQS

**Control variable</td><td>One-third of all participants (30.6%) suffered from sleep disturbances (25% in the waiting-list control group; 32% in the intervention group). A Chi-square test revealed no differences in percentage of cases of sleep disturbance between the intervention and the waiting-list control group (p 5 0.718).</td></tr>
<tr><td>Van Weert 2010</td><td colspan="3"></td></tr>
<tr><td>Willems 2016</td><td>Global quality of life / Functional impact of fatigue</td><td>EORTC QLQ-C30</td><td>
<table>
<tr><td></td><td>Mixed models (n = 414)</td><td>Imputed data (n = 462)</td></tr>
</table>
</td></tr>
</table>

		95% CI	*p*	p_{fdr}	*d* [95% CI]	95% CI	*p*
Emotional functioning							
6 months	Crude	0.18–6.25	.038	.038	−0.15 [−0.34 –0.05]	−0.77–5.48	.139
	Adjusted	0.02–6.07	.049	.049		−1.15–5.00	.221
12 months	Crude	−0.35–5.93	.081	.661	−0.08 [−0.28 –0.12]	−3.01–3.56	.871
	Adjusted	−0.47–5.78	.096	.384		−3.43–3.11	.923
Social functioning							
6 months	Crude	0.41–6.87	.027	.037	−0.15 [−0.35 –0.04]	−2.22–4.96	.453
	Adjusted	0.35–6.66	.030	.048		−2.45–4.53	.562
12 months	Crude	−1.97–4.73	.421	.661	−0.02 [−0.22 –0.18]	−6.57–0.54	.096
	Adjusted	−1.97 – 4.59	.435	.580		−6.80–0.10	.057

	Mood	Hospital Anxiety and Depression Scale (HADS)	

		Mixed models (*n* = 414)				Imputed data (*n* = 462)	
		95% CI	*p*	p_{fdr}	*d* [95% CI]	95% CI	*p*
	Adjusted	−1.97 – 4.59	.435	.580		−6.80–0.10	.057
Depression							
6 months	Crude	−0.90–−0.11	.011	.037	0.21 [0.01–0.40]	−0.93–−0.10	.014
	Adjusted	−0.86–−0.07	.021	.048		−0.82–−0.00	.049
12 months	Crude	−0.70–0.10	.145	.661	0.10 [−0.11–0.30]	−0.60–0.23	.375
	Adjusted	−0.66 – 0.16	.227	.454		−0.50–0.33	.684
	Adjusted	−4.90–2.88	.611	.661			

Yun 2017	Mood	PTGI/ Hospital Anxiety and Depression Scale (HADS)	The LP group showed a significantly greater decrease in the HADS anxiety score (*p* = 0.025).

		Unadjusted estimates, mean (SD)		**Adjusted analysis for intervention vs usual care[a]**		
		Intervention group	**Control group**	**Intervention group**	**Control group**	***P*value[1)]**
HADS						

			Anxiety	Baseline	5.7 (3.4)	5.9 (3.1)			
				3 months	5.0 (3.0)	6.1 (3.1)	5.2 (0.2)	6.0 (0.3)	**0.025****
				12 months	5.1 (3.0)	5.8 (2.9)	5.2 (0.3)	5.7 (0.4)	0.228
			Depression	Baseline	6.4 (3.5)	6.1 (3.1)			
				3 months	5.5 (3.3)	5.4 (2.8)	5.6 (0.2)	5.6 (0.3)	0.986
				12 months	5.4 (3.4)	5.6 (3.1)	5.3 (0.3)	5.7 (0.4)	0.428
	Global quality of life / Functional impact of fatigue	EORTC Quality of Life Questionnaire (EORTC QLQ-C30)	A significantly greater increase in the social functioning score of the EORTC QLQ-C30 (p = 0.018), and a significantly greater decrease in the appetite loss (p = 0.048) and financial difficulties scores (p = 0.036) of the EORTC QLQ-C30 from baseline to 3 months. From baseline to 12 months, the LP group, relative to the UC group, showed a significantly greater decrease in the EORTC QLQ-C30 fatigue score (p = 0.065)						

		Unadjusted estimates, mean (SD)		**Adjusted analysis for intervention vs usual care[a]**		
		Intervention group	**Control group**	**Intervention group**	**Control group**	***P*value[1)]**
EORTC QLQ-C30						
Functional scales						
Global health status	Baseline	64.5 (19.9)	63.4 (18.7)			
	3 months	67.7 (18.7)	65.7 (17.5)	67.0 (1.6)	66.0 (2.3)	0.705
	12 months	70.1 (17.1)	65.3 (17.9)	69.0 (1.6)	66.0 (2.2)	0.269
Physical functioning	Baseline	78.6 (13.5)	77.9 (11.1)			
	3 months	80.0 (12.1)	78.4 (12.0)	79.4 (0.9)	79.3 (1.3)	0.942
	12 months	82.9 (13.1)	78.2 (12.4)	81.9 (1.2)	78.7 (1.6)	0.123
Role functioning	Baseline	79.4 (21.4)	77.9 (19.8)			
	3 months	80.9 (18.1)	77.3 (18.4)	80.3 (1.5)	78.5 (2.2)	0.497
	12 months	82.7 (19.8)	79.9 (18.9)	80.9 (1.8)	81.1 (2.4)	0.958
Emotional functioning	Baseline	76.8 (19.4)	73.0 (23.0)			
	3 months	78.0 (19.1)	74.5 (16.5)	76.7 (1.5)	75.3 (2.2)	0.602
	12 months	78.0 (19.9)	75.9 (18.3)	76.2 (1.9)	77.7 (2.4)	0.625
Cognitive functioning	Baseline	76.7 (19.9)	72.6 (20.9)			
	3 months	80.1 (17.2)	72.5 (20.2)	77.6 (1.4)	75.1 (2.4)	0.322

				12 months	78.1 (14.9)	76.5 (19.2)	76.8 (1.6)	78.4 (2.1)	0.552
			Social functioning	Baseline	75.8 (26.8)	73.1 (23.4)			
				3 months	85.4 (19.3)	76.3 (20.2)	84.8 (1.8)	77.4 (2.5)	0.018
				12 months	85.3 (19.5)	78.2 (22.4)	84.8 (2.2)	79.0 (2.9)	0.123

	Insomnia or sleep quality	EORTC Quality of Life Questionnaire (EORTC QLQ-C30) Medical Outcome Study–Sleep Scale (MOS-SS) Sleep Quality Index I and II			**Unadjusted estimates, mean (SD)**		**Adjusted analysis for intervention vs usual care[a]**		
					Intervention group	**Control group**	**Intervention group**	**Control group**	***P*value[1)]**
			EORTC QLQ-C30						
			Symptom scales						
			Insomnia	Baseline	28.8 (30.0)	30.3 (28.9)			
				3 months	24.1 (24.50	26.7 (26.9)	25.0 (2.1)	25.7 (3.1)	0.850
				12 months	26.2 (27.9)	32.0 (27.2)	27.6 (2.5)	29.1 (3.4)	0.732
			The MOS-SSS	Baseline	65.6 (20.9)	65.6 (20.6)			
				3 months	66.3 (21.1)	67.9 (19.3)	66.9 (1.4)	65.7 (2.0)	0.621
				12 months	66.6 (21.1)	68.0 (19.7)	67.1 (1.7)	65.3 (2.4)	0.535

	Pain	EORTC Quality of Life Questionnaire (EORTC QLQ-C30)			**Unadjusted estimates, mean (SD)**		**Adjusted analysis for intervention vs usual care[a]**		
					Intervention group	**Control group**	**Intervention group**	**Control group**	***P*value[1)]**
			EORTC QLQ-C30						
			Symptom scales						
			Pain	Baseline	15.4 (19.2)	21.4 (19.0)			
				3 months	11.9 (16.0)	19.6 (19.6)	13.6 (1.5)	17.4 (2.1)	0.146
				12 months	13.1 (17.6)	19.7 (21.4)	15.5 (1.8)	16.2 (2.3)	0.810

Yun 2012 | Global quality of life / Functional impact of fatigue | EORTCQLQ-C30

the intervention group experienced a significantly greater improvement in global quality of life (5.22; 95% CI, 0.93 to 9.50)

Outcome	Intervention Group (n = 136)				Control Group (n = 137)				Group Difference*		Adj *P* *	Effect Size†
	Baseline		Change at3 Months		Baseline		Change at3 Months					
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	95% CI		

			EORTC-C30
			Global health status/QOL: 61.15, 19.41, 7.60, 19.42, 59.79, 19.17, 2.62, 19.59, 5.22, 0.93 to 9.50, **.017**, 0.26
			Functional scales
			Physical: 72.01, 15.11, 6.86, 11.92, 72.80, 16.05, 4.57, 13.38, 2.13, −0.45 to 4.72, .106, 0.18
			Role: 71.45, 24.76, 6.50, 19.37, 72.51, 23.45, 4.01, 20.16, 1.90, −2.02 to 5.83, .340, 0.13
			Emotional: 70.16, 21.31, 5.02, 17.98, 67.21, 21.77, 1.64, 18.58, 4.69, 0.69 to 8.69, **.022**, 0.19
			Cognitive: 73.41, 19.18, 5.15, 16.29, 69.59, 23.04, 0.73, 18.62, 6.09, 2.23 to 9.94, **.002‖**, 0.25
			Social: 76.84, 23.50, 7.97, 21.75, 76.28, 22.75, 3.04, 19.62, 4.73, 0.53 to 8.93, **.027**, 0.24
	Mood	HADS	the intervention group experienced a significantly greater decrease in HADS anxiety score (-0.90; 95% CI,-1.51 to --0.29)

Outcome	Intervention Group (n = 136)				Control Group (n = 137)				Group Difference*		Adj *P* *	Effect Size †
	Baseline		Change at3 Months		Baseline		Change at3 Months					
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	95% CI		
HADS score												

Anxiety	6.42	3.83	−0.79	2.79	6.52	3.86	0.11	2.59	−0.90	−1.51 to −0.29	**.004**	0.33
Depression	5.65	3.09	−0.39	3.08	5.73	3.30	−0.12	2.81	−0.28	−0.93 to 0.36	.387	0.09

Insomnia or sleep quality — Medical Outcome Study–Sleep Scale (MOS-SS) Sleep Quality Index I and II

Outcome	Intervention Group (n = 136)				Control Group (n = 137)				Group Difference*		Adj *P* *	Effect Size†
	Baseline		Change at3 Months		Baseline		Change at3 Months					
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	95% CI		
MOS-SS												
Sleep Quality Index I	31.52	15.70	−3.11	12.58	33.33	17.82	−1.58	10.67	−2.04	−4.53 to 0.44	.106	0.13
Sleep Quality Index II	32.16	16.01	−3.08	12.11	33.76	18.02	−1.40	11.37	−2.04	−4.57 to 0.49	.114	0.14

Pain — Brief Pain Inventory

Outcome	Intervention Group (n = 136)				Control Group (n = 137)				Group Difference*		Adj *P* *	Effect Size†
	Baseline		Change at3 Months		Baseline		Change at3 Months					
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	95% CI		
BPI score												

			Severity	2.12	1.76	−0.45	1.46	2.35	2.00	−0.42	2.00	−0.13	−0.49 to 0.22	.458	0.01
			Interference	1.86	1.96	−0.49	1.76	2.02	2.16	−0.27	1.75	−0.28	−0.63 to 0.06	.110	0.13

Appendix 2. Risk of Bias Assessment

Bantum 2014

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomized using a random number table
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	Low risk	(<20%) Roughly 14% (13.9%, 49/352) of participants who were randomized did not provide any data at 6 months, which did not differ by condition (11.4%, 20/176 and 16.5%, 29/176) for control and intervention, respectively).
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported. Trial registered: Clinicaltrials.gov NCT00962494
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias

Bennett 2007

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"a physical activity counselor assigned each participant to either the intervention or the control group according to a computer-generated randomization scheme."
Allocation concealment (selection bias)	Unclear risk	"assignments were placed in sealed envelopes prior to study."
Blinding of participants and personnel (performance bias)	High risk	"The physical activity counselor who conducted the MI intervention was not blinded to group assignment."
Blinding of outcome assessment (detection bias)	High risk	"The physical activity counselor who conducted the outcome measurements was not blinded to group assignment."
Incomplete outcome data (attrition bias)	Low risk	<20% attrition from both arms at follow-up
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported

Other bias	Unclear risk	The trial appears to be free of other problems that could put it at a high risk of bias
Blaes 2016		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization was done by a SAS random number generator.
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	Unclear risk	Not specified. (Faculty delivered the intervention)
Blinding of outcome assessment (detection bias)	Unclear risk	Blinding of outcome assessors not specified
Incomplete outcome data (attrition bias)	Low risk	3/27 MBCR; 2/13 CONTROL One participant withdrew from the study because of progressive disease.
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported Trial registered: Clinicaltrials.gov NCT01601548
Other bias	Unclear risk	The trial appears to be free of other problems that could put it at a high risk of bias
Bower 2015		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not specified
Allocation concealment (selection bias)	Unclear risk	condition assignments were kept in sealed envelopes in the research office,
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	Low risk	Follow up of 92% at the primary endpoint. 83% completed the 3-month follow-up questionnaire
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported. Trial registered Clinicaltrials.gov NCT01558258.
Other bias	Unclear risk	Participants were recruited through invitations to women who had enrolled in an earlier study

Bruggeman-Everts 2017

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomized via a computerized tool: an embedded automated randomization function
Allocation concealment (selection bias)	Unclear risk	Researchers could neither influence nor predict the outcome of the randomization process.
Blinding of participants and personnel (performance bias)	High risk	Neither researchers, participants, nor therapists were blind to treatment, as the medical ethical committee insisted that we announced the minimal intervention as our control group.
Blinding of outcome assessment (detection bias)	Low risk	independent statistician (RvdS) was blind to allocation while checking all analyses.
Incomplete outcome data (attrition bias)	High risk	Proportion of participants who dropped out the intervention before completing 6 weeks of the protocol, was 18% (11/62) in the AAF condition, 38% (21/55) in the eMBCT condition, and 6% (3/50) in the psycho-education condition.
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported. Trial registered: Trialregister.nl NTR3483
Other bias	Unclear risk	The trial appears to be free of other problems that could put it at a high risk of bias

Carlson 2016

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Women were assigned randomly using the Research Randomiizer website(http://www.randomizer.org/) 2:2:1 (2 conditions and a control group) by the Statistician
Allocation concealment (selection bias)	Low risk	Central allocation by random generator used by Statistician
Blinding of participants and personnel (performance bias)	Unclear risk	At the time of initial assessment, participants as well as RAs were blind to condition.
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	High risk	165 women completed their pre-intervention and post-intervention assessment (MBCR: 74 + 13 = 87; SET: 73 + 5 = 78), 65% of the original sample. At 6 months, 130 women completed the follow-up assessment (51.5%), and 128 women completed the 12-month follow-up assessment (50.8%).
Selective reporting (reporting bias)	Unclear risk	All outcomes pre-specified by authors reported.

		Trial registered Clinicaltrials.gov NCT00390169
		The follow up study assessed a broader range of outcome measures than the primary study
Other bias	Unclear risk	The trial appears to be free of other problems that could put it at a high risk of bias

Dirksen 2008

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A random numbers table.
Allocation concealment (selection bias)	Unclear risk	Not specified- assigned to treatment groups by the research assistant
Blinding of participants and personnel (performance bias)	High risk	"The research assistant was not blinded to the group assignment"
		Participants: due to the nature of the intervention content, participants could not have been blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	Low risk	<20% attrition
Selective reporting (reporting bias)	Low risk	All outcomes specified in methods reported in results
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias

Dodds 2015

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization was performed by the study biostatistician using stratified block randomization using random block size, as implemented in the ralloc module of the Stata statistical software package
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	Unclear risk	Study participants were blinded to group assignment until completion of all baseline assessments. The interventionist delivering CBCT could not be blinded.
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	High risk	Of the 33 randomized participants, 22 had follow-up data (67 %, 95 % CI 48, 82 %), slightly less than the targeted proportion of 70 %.

Selective reporting (reporting bias)	Unclear risk	No published protocol but reported everything they said they would in the paper
Other bias	Unclear risk	No correction was made for multiple comparisons
Dolbeault 2009		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization by sealed letter was performed at each site, with a readjustment of the number of subjects in each group after every eighth subject.
Allocation concealment (selection bias)	Unclear risk	a readjustment of the number of subjects in each group after every eighth subject
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	High risk	Patients who missed four group sessions were excluded from the analyses. Completed in treatment group n = 81 (79 %) Completed in control group n = 87 (86 %) lack of complete data for one-fifth of the patients, who did not complete the questionnaires at all three evaluation times
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes reported
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias
Espie 2008		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Centralized computer-based registration/randomization service available within the Cancer Research UK Clinical Trials Unit, Glasgow.
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Due to the nature of the intervention, it was not possible to blind participants or therapists to allocation.
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified

Incomplete outcome data (attrition bias)	Unclear risk	Not specified
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias
Ferguson 2016		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer randomization to treatment type (MAAT or ST) was performed for participant numbers
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Computer randomization was performed and was revealed to the participant after baseline assessment
Blinding of outcome assessment (detection bias)	Low risk	The psychometrist responsible for all assessments remained blind to each participant's assigned treatment condition throughout the study.
Incomplete outcome data (attrition bias)	Unclear risk	7/20 participants dropped out of ST and 5/27 withdrew from MAAT. Reasons for withdrawal included an inability to commit time, personal problems (eg, family illness), or moving. The final sample for analyses was 22 participants for MAAT and 13 participants for ST.
Selective reporting (reporting bias)	Unclear risk	All outcomes pre-specified by authors reported
Other bias	Unclear risk	The trial appears to be free of other problems that could put it at a high risk of bias
Fillion 2008		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The sequence of randomization was computer generated, after a preliminary stratification, according to the adjuvant treatments received.
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Not possible in this study
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	Low risk	(<20%) 3 x control group lost to follow up; 4 x experimental group lost to follow up

Selective reporting (reporting bias)	High risk	Pain outcomes pre-specified by authors not reported
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias

Foster 2015

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A statistician independently generated a random allocation sequence, using 'R' for each NHS Centre, and participants were randomised in blocks of four [20].
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias)	Low risk	Statisticians and members of the research team not involved in recruitment were blinded during analysis.
Incomplete outcome data (attrition bias)	High risk	36% attrition
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported. Trial registered ISRCTN67521059.
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias

Freeman 2015

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Assignment by adaptive randomization (minimization) was balanced by age, gender, stage, chemotherapy, surgery, radiation, and hormone use.
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	Unclear risk	<20%
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported

Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias
Gielissen 2006		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Random assignment was done by means of a sequence of labeled cards contained in sealed, numbered envelopes prepared by a statistical adviser.
Allocation concealment (selection bias)	Unclear risk	Envelopes prepared by a statistical adviser. The envelopes were opened by the researcher (M.G.) in the presence of the patient.
Blinding of participants and personnel (performance bias)	Unclear risk	Not possible in this study
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	High risk	Experimental group: 9 lost to follow-up (<20%) Control group: 12 lost to follow-up (44 out of 56… 20% = 11 people)
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias
Heckler 2016		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A computer-generated randomization schedule with a block size of eight, stratified by city and sex, was used to assign participants to one of four groups (from other paper: Roscoe JA, Garland SN, Heckler CE, Perlis ML, Peoples AR, Shayne M, Savard J, Daniels NP, Morrow GR (2014) Randomized placebo-controlled trial of cognitive behavioral therapy and armodafinil for insomnia after cancer treatment. J Clin Oncol. doi: 10.1200/JCO.2014.57.6769)
Allocation concealment (selection bias)	Low risk	Random assignment was conveyed to a pharmacist, who provided the study coordinator with the appropriate study medications.
Blinding of participants and personnel (performance bias)	Unclear risk	All study personnel and subjects were blinded regarding medication (armodafinil, placebo) assignment but not CBT-I (yes, no) condition. Random assignment was conveyed to a pharmacist, who provided the study coordinator with the appropriate study medications.

Blinding of outcome assessment (detection bias)	Low risk	All study personnel and subjects were blinded regarding medication (armodafinil, placebo) assignment but not CBT-I (yes, no) condition.
Incomplete outcome data (attrition bias)	High risk	29 (30 %) of the 96 randomized eligible subjects did not provide post-intervention data.
Selective reporting (reporting bias)	Unclear risk	All outcomes pre-specified by authors reported. Trial registered Clinicaltrials.gov NCT01091974.
Other bias	Unclear risk	The original grant application was approved, with modafinil 100 mg twice per day as the active medication. A switch to A 50 mg twice per day was made at the suggestion of Cephalon, which manufactured both medications and supplied the drug and matching placebo
Hoffman 2012		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random assignment was performed by operations director of the organization, who was independent from the study, by using an externally computer generated randomization program in blocks of four, which ensured allocation concealment because no clinician/researcher could anticipate or direct the allocation of participants.
Allocation concealment (selection bias)	Unclear risk	“No clinician/researcher could anticipate or direct the allocation of participants.”
Blinding of participants and personnel (performance bias)	High risk	The clinician-researcher conducting the study and delivering MBSRcould not be blinded to the allocation of participants to either the treatment or control group
Blinding of outcome assessment (detection bias)	Low risk	Anonymized data were collected by a research assistant who was blinded to group assignment and independent from MBSR deliver
Incomplete outcome data (attrition bias)	High risk	There were three instances (two patients in the intervention group and one patient in the control group) in which more than 20%of data was missing from participants at T1, and thus, according to rules set by the questionnaire manuals, their data was excluded because it was too sparse to analyze.
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias
Johns 2014		
Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	The randomization sequence was generated by coin toss in blocks of four by the principal investigator.
Allocation concealment (selection bias)	Low risk	Research assistants and participants were blinded to the randomization sequence using sequentially numbered and sealed envelopes.
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias)	Unclear risk	All outcomes were self-reported on study questionnaires and therefore not subject to bias by assessor interpretation.
Incomplete outcome data (attrition bias)	Low risk	No drop-out
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported. Trial registered Clinicaltrials.gov NCT01247532
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias
Lengacher 2012		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	A two-armed randomized controlled design, with randomization stratified by stage of cancer (0, I, III, and III) and treatment received (radiation treatment only or radiation treatment and chemotherapy), was used to randomly assign enrolled participants to either an MBSR(BC) group or a wait-listed control group.
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	Unclear risk	patients were not blinded to treatment group,
Blinding of outcome assessment (detection bias)	Unclear risk	Data on measures of presence of symptoms (MDASI), patient demographics, and clinical history were collected at baseline (1 week prior to the MBSR (BC) intervention) and within 2 weeks after the 6-week MBSR(BC) intervention. Participant randomization was done after baseline assessments were complete.
Incomplete outcome data (attrition bias)	Low risk	1 per group loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias
Matthews 2014		

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Adaptive randomization program, controlling for age, insomnia severity, recruitment site, and breast cancer stage (Matthews, Cook, Terada, & Aloia, 2010).
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Participants, but not the study therapist, were blind to treatment condition.
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	Low risk	2 loss to follow up in each group
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias
Poulsen 2013		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random assignment was done by means of a sequence of labelled cards contained in sealed, numbered envelopes prepared by a statistical adviser. The envelopes were opened by the psychologists in the presence of the patient. Randomization took place per patient
Allocation concealment (selection bias)	Low risk	The envelopes were opened by the psychologists in the presence of the patient. Randomization took place per patient
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias)	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	High risk	Control: 0 loss to follow-up Experimental: 27 lost to follow-up (>20%)
Selective reporting (reporting bias)	High risk	Functional impairment not in original protocol. Trial registered Clinicaltrials.gov NCT01096641.
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias
Reeves 2017		

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomization sequence and group allocation were generated by a staff member not involved with the study using a computer-generated random number sequence, with block sizes of six.
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias)	Low risk	Data were collected by research staff, blinded to randomization assignment, at baseline and 6 months.
Incomplete outcome data (attrition bias)	High risk	5/45 INTERVENTION DROPOUT 11/45 CONTROL (24%)
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported
Other bias	Unclear risk	One reported adverse event (musculoskeletal injury) was attributable to the intervention.

Reich 2017

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not clear: "were randomly assigned to either a six-week MBSR(BC) program or usual care." Participants were randomly assigned at a one-to-one ratio to MBSR(BC) or UC with waitlisted MBSR(BC). An SPSS macro (version 17.0; SPSS, Chicago, IL) was used to create a stratified block randomization scheme,(C.A. Lengacher, R.R. Reich, C.L.Paterson, et al.Examination of broad symptom improvement due to Mindfulness-Based Stress Reduction for Breast Cancer Survivors: a randomized controlled trialJ Clin Oncol, 34 (2016), pp. 2827-2834)
Allocation concealment (selection bias)	Unclear risk	Method of randomisation not clear
Blinding of participants and personnel (performance bias)	High risk	Blinding to group assignment after the baseline assessment by the assessors was not possible with use of the waitlisted control design. (C.A. Lengacher, R.R. Reich, C.L.Paterson, et al.Examination of broad symptom improvement due to Mindfulness-Based Stress Reduction for Breast Cancer Survivors: a randomized controlled trialJ Clin Oncol, 34 (2016), pp. 2827-2834)
Blinding of outcome assessment (detection bias)	Unclear risk	not clear

Incomplete outcome data (attrition bias)	Low risk	152/167 (92%) participants in the intervention group and 147/155 (94%) in the usual care group completed
Selective reporting (reporting bias)	Unclear risk	All outcomes pre-specified by authors reported. Trial registered Clinicaltrials.gov NCT01177124.
Other bias	Unclear risk	The trial appears to be free of other problems that could put it at a high risk of bias

Reif 2012

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation lists were used for concealed allocation by central telephone calls.
Allocation concealment (selection bias)	Low risk	concealed allocation by central telephone calls.
Blinding of participants and personnel (performance bias)	High risk	Patients and tutors could not be blinded to treatment allocation for practical reasons.
Blinding of outcome assessment (detection bias)	Low risk	data entry and analysis was performed by blinded researchers
Incomplete outcome data (attrition bias)	Low risk	6% loss to intervention, 15% loss to control
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported. Trial registered Clinicaltrials.gov NCT00552552
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias

Ritterband 2012

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Random group assignment was based on a computer-generated randomization schedule managed by the project coordinator
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	participants received an email with notification of their assignment to either the experimental (Internet) or waitlist control group.
Blinding of outcome assessment (detection bias)	Unclear risk	Not specified

Incomplete outcome data (attrition bias)	Low risk	No dropout
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported
Other bias	Unclear risk	Drs. Ritterband and Thorndike are equity holders of BeHealth Solutions, Inc, which is negotiating a license for the software described in this paper.

Rogers 2017

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	randomization was based on computer-generated numbers in blocks of 4 within each recruiting site.
Allocation concealment (selection bias)	Low risk	Randomization occurred in the order in which the participants completed baseline testing with study staff being unaware of the randomization until the moment the randomization result was revealed by opening an opaque sealed envelope.
Blinding of participants and personnel (performance bias)	High risk	participant blinding to study group was not possible,
Blinding of outcome assessment (detection bias)	Low risk	data entry and management were performed by individuals blinded to the participant's group allocation
Incomplete outcome data (attrition bias)	Low risk	222 participants completed baseline testing and were randomized (110 to BEAT Cancer and 112 to usual care). Retention was similar in both groups (97% at M3 and 96% at M6).
Selective reporting (reporting bias)	Unclear risk	All outcomes pre-specified by authors reported. Trial registered Clinicaltrials.gov NCT00929617 Original protocol (written in 2009) proposed assessing depression and anxiety as sources of physical activity self-efficacy [2]. In this paper these are reported as health outcomes because “updated literature reviews indicate a significant burden of suffering caused by psychosocial symptoms and a clear knowledge gap regarding the ability of behavior change interventions to translate exercise training benefits.”
Other bias	Unclear risk	Only one related serious adverse event occurred (intervention group; pelvic stress fracture). Related expected adverse events in the BEAT Cancer group included back or lower extremity musculoskeletal pain or injury (n = 14), heart rate monitor rash (n = 1), fall while walking (n = 1), breast reconstruction (n = 3), and chest pain during treadmill fitness test (n = 1). Related adverse events in the UC group included arm tingling (n = 1) during the treadmill test and knee tendonitis (n = 1) [3].

Sandler 2017

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	randomly allocated (computer-generated sequence)
Allocation concealment (selection bias)	Unclear risk	Allocation was concealed from the coordinator until intervention commencement.
Blinding of participants and personnel (performance bias)	High risk	Personnel, were not blind to allocated interventions
Blinding of outcome assessment (detection bias)	Unclear risk	Insufficient nformation to judge of risk on blinding of outcome assessments. An independent psychologist who was blinded to group allocation conducted the Semistructured Clinical Interview for Neurasthenia (SCIN)
Incomplete outcome data (attrition bias)	Low risk	2/24 control and 3/22 intervention. A total of five participants discontinued because of work or family commitments. All participants completed baseline self-report questionnaires allowing an intention-to-treat analysis to be conducted.
Selective reporting (reporting bias)	Unclear risk	All outcomes pre-specified by authors reported. Trial registered Australian New Zealand Clinical Trials Registry ACTRN12611000338965
Other bias	High	Only provided 70% of the original statistical power estimate, and Type II error is therefore plausible. The protocol steering committee provided a waiver for one participant who had completed adjuvant therapy 17 months before being screened.

Savard 2005

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not clear: "randomly assigned"
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Not possible

Blinding of outcome assessment (detection bias)	Unclear risk	Not specified
Incomplete outcome data (attrition bias)	Low risk	<20%
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified by authors reported
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias

Van Der Lee 2012

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	First, the researcher used SPSS syntax to randomly select 12 participants out of all eligible candidates in file at that moment.
Allocation concealment (selection bias)	High risk	Not concealed
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias)	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	(<20%) Intervention: 82% completed T2 questionaire; Control: 97% completed T2 questionaire
Selective reporting (reporting bias)	High risk	HADs means not reported

van Weert 2010

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization was conducted at the group level by an independent researcher using a randomization list.
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	High risk	Therapists could not be blinded, as they had to schedule the intervention sessions. Until the first session, participants were blinded to the intervention they were allocated to receive
Blinding of outcome assessment (detection bias)	High risk	Main investigators were not blinded to group assignment
Incomplete outcome data (attrition bias)	Low risk	<20% for all groups
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes reported.

Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias
Willems 2016		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	the computer randomly assigned
Allocation concealment (selection bias)	Unclear risk	Fully automated
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias)	Low risk	Fully automated
Incomplete outcome data (attrition bias)	Low risk	<20%
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported. Trial registered Dutch Trial Register (NTR3375)
Other bias	Unclear risk	Change to protocol: Originally, this criterion was set to 6-52 weeks [13]. After recruitment, we noted that participants were included outside this criterion. The lower limit of 6 weeks was set so participants had had a sufficient recovery period after treatment before participating in the study; the upper limit of one year was set to include participants highest in their distress. Since participants voluntarily participated and can decide whether they are able to participate and levels of distress are still high 56 weeks after treatment [22], we adjusted this criterion to 4-56 weeks. This led to an additional 13 participants in the control condition and 7 in the intervention condition.
Yun 2017		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	With the aid of a computerized random number generator (SAS 9.1.3, Proc plan), we randomly assigned eligible participants, two-to-one, to the intervention or the usual care group. To minimize the effects of potentially confounding variables on outcomes, we performed block randomization with 8 strata defined by type of cancer (breast, stomach, colon, or lung) and number of behavior goals practiced at the study entry (0 or 1 out of 3 defined possible behaviors).
Allocation concealment (selection bias)	Unclear risk	not clear
Blinding of participants and personnel (performance bias)	High risk	Masking:None (Open Label)

Blinding of outcome assessment (detection bias)	Unclear risk	not clear
Incomplete outcome data (attrition bias)	High risk	In the LP group, 115 (69.3%) participants completed the 12-month course at 3 months and 117 (70.5%) at 6–12 months. In the UC group, 60 (73.2%) participants completed the course at 3 months and 57 (71.3%) at 12 months.
Selective reporting (reporting bias)	Low risk	All outcomes prespecified by author reported Trial registered Clinicaltrials.gov NCT01527409
Other bias	Unclear risk	The trial appears to be free of other problems that could put it at a high risk of bias

Year 2012

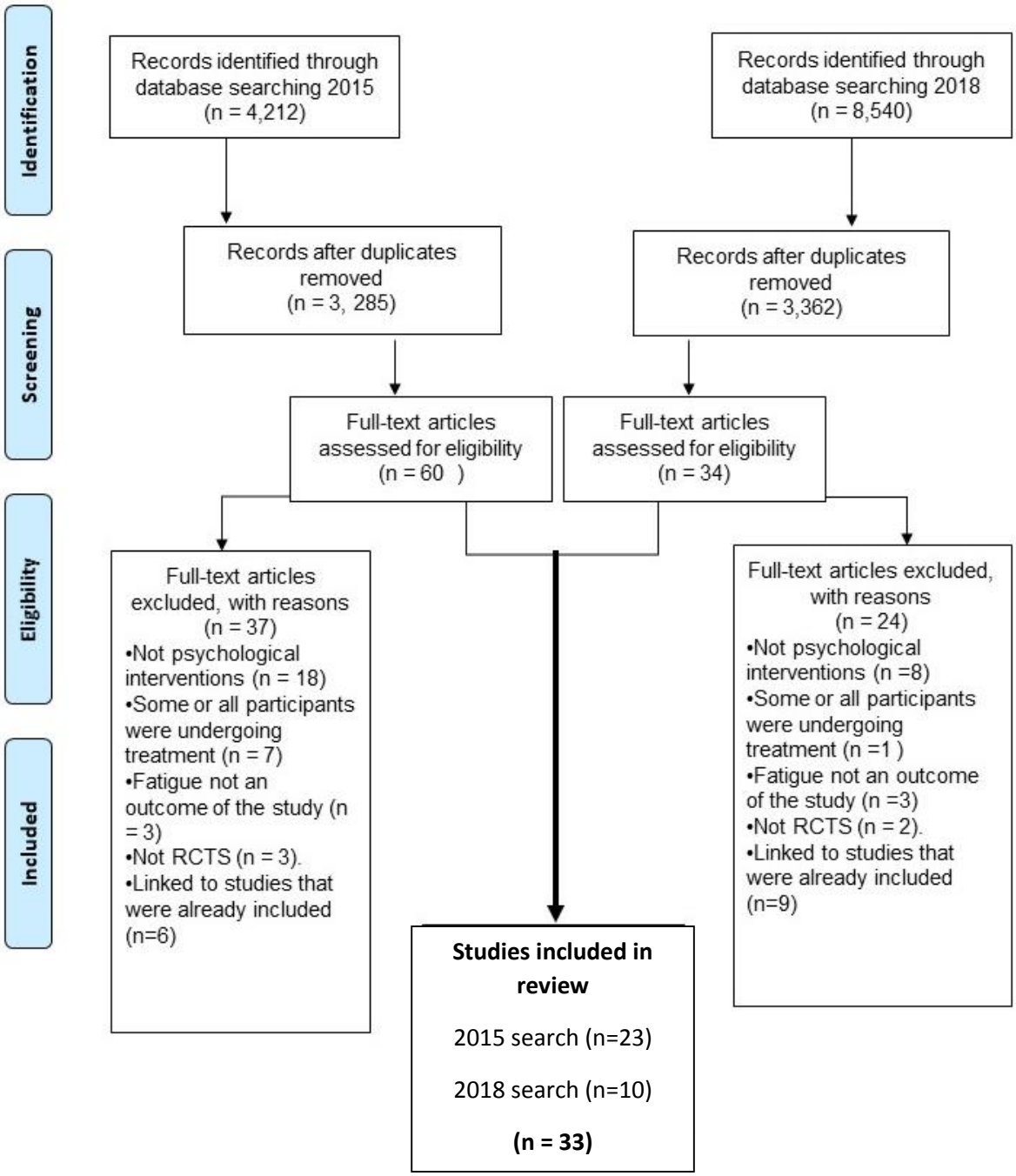
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	An independent statistician generated a randomization table with NQuery Advisor 6.01 (Statistical Solutions, Saugus, MA) and used the table to assign each patient to either the intervention group or the usual care group.
Allocation concealment (selection bias)	Unclear risk	Independent statistician used the table to assign each patient to either the intervention group or the usual care group.
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias)	Low risk	An independent research coordinator (nurse) managed both groups
Incomplete outcome data (attrition bias)	Low risk	23 of 136 loss to follow-up on intervention arm
Selective reporting (reporting bias)	Low risk	All outcomes prespecified byy authors reported. Trial registered Clinicaltrials.gov NCT01228773
Other bias	Low risk	The trial appears to be free of other problems that could put it at a high risk of bias

Appendix 3. Search strategies used in this review

	Ovid MEDLINE(R); Embase; CancerLit
	Search Terms
S5	S1 AND S2 AND S3 AND S4
S4	(randomized controlled trial or controlled clinical trial or 'random assignment').mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy]
S3	(fatigue or asthenia or asthenic or asthenia or (exhaustion or exhausted) or 'loss of energy' or 'loss of vitality' or (weary or weariness or weakness) or (apathy or apathetic or lassitude or lethargic or lethargy) or (sleepy or sleepiness or drowsy or drowsiness) or (tired or tiredness)).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy]
S2	(Psych* or Behav* or Therap*or hypnosis or relaxation or imagery or cogniti*).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy]
S1	('cancer survivors' or neoplasm or survivor or cancer or remission).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy]
	EBSCOhost Research Databases **CINAHL Plus with Full Text; Psychinfo**
	Search Terms
S5	S1 AND S2 AND S3 AND S4
S4	(randomized controlled trial or controlled clinical trial or “random assignment”)
S3	(fatigue or asthenia or asthenic or asthenia or (exhaustion or exhausted) or “loss of energy” or “loss of vitality” or (weary or weariness or weakness) or (apathy or apathetic or lassitude or lethargic or lethargy) or (sleepy or sleepiness or drowsy or drowsiness) or (tired or tiredness))
S2	Behav* OR Therap* or hypnosis or relaxation or imagery or cognition or psych* or cognit*
S1	'cancer survivors' or neoplasm or survivor or cancer or remission
	Web of Science
	Search Terms
S5	#4 AND #3 AND #2 AND #1
S4	**TOPIC:** ((randomized controlled trial or controlled clinical trial or “random assignment”))

S3	**TOPIC:** ((fatigue or asthenia or asthenic or asthenia or (exhaustion or exhausted) or “loss of energy” or “loss of vitality” or (weary or weariness or weakness) or (apathy or apathetic or lassitude or lethargic or lethargy) or (sleepy or sleepiness or drowsy or drowsiness) or (tired or tiredness)))
S2	**TOPIC:** (Behavi* or Therap* or hypnosis or relaxation or imagery or psych* or cognit*)
S1	**TOPIC:** ('cancer survivors' or neoplasm or survivor or cancer or remission)

2



Prisma

Manuscript with changes marked

26 Sept 2019

Dear Paul Shekelle, MD
Systematic Reviews

Thank you for your comments on our manuscript "The Effectiveness of Psychological Interventions for Fatigue in Cancer Survivors: Systematic Review of Randomised Controlled Trials" (SYSR-D-19-00062R1). We are delighted that it is potentially acceptable for publication in Systematic Reviews.

In the latest draft we have assessed the quality of the evidence across studies, using the GRADE framework. Changes to the text have been made to the methods, result and discussion section (highlighted in red in marked version of manuscript). We have also added this in the section on "Changes to the protocol" as we had not said that we would do such an assessment in our previously published protocol.

Regarding the numbers the PRISMA flow diagram, we apologise for the typo. We have changed this to state that there were n=23 studies form the 2015 search and n=10 studies from the 2018 search. The total number of studies is therefore 33. We thank you for pointing this out.

If you have any other requirements or recommendations, please let us know.
We look forward to receiving your response.

Best wishes,

Dr Teresa Corbett