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Effects of Mindfulness-Based Interventions on Fatigue in Cancer Survivors: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

This systematic review and meta-analysis was designed to determine the efficacy of mindfulnessbased interventions (MBIs) in improving fatigue-related outcomes in adult cancer survivors. Randomized controlled trials (RCTs) were identified from PubMed, MEDLINE, PsycINFO, CINAHL, Web of Science, and EMBASE databases and reference lists of included studies. Separate random-effects meta-analyses were conducted for fatigue and vitality/vigor. Twenty-three

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studies reporting on 21 RCTs (N=2,239) met inclusion criteria. MBIs significantly reduced fatigue compared to controls at post-intervention (g=0.60, 95% CI[0.36, 0.83]) and first follow-up (g=0.42, 95% CI[0.20, 0.64]). Likewise, MBIs significantly improved vitality/vigor at post-intervention (g=0.39, 95% CI[0.25, 0.52]) and first follow-up (g=0.35, 95% CI[0.03, 0.67]). The evidence grade was low due to risk of bias, substantial heterogeneity, and publication bias among studies. MBIs show promise in improving fatigue and vitality/vigor in cancer survivors. More rigorous trials are needed to address current gaps in the evidence base.

Graphical abstract



Keywords

mindfulness; cancer; fatigue; vitality; vigor; randomized controlled trial; systematic review; metaanalysis

1. Introduction

Many of the estimated 43.8 million cancer survivors worldwide suffer from debilitating effects of cancer and its treatments [1]. These effects include both psychological (e.g., depression, anxiety) and physical symptoms (e.g., pain, fatigue) [2, 3]. Fatigue is one of the most prevalent and distressing symptoms reported by 25–99% of patients undergoing active cancer therapy [4, 5]. Moderate to severe levels of fatigue persist for 22–33% of survivors in the months and years following cancer treatment [6]. Fatigue profoundly interferes with survivors' activities and mood [6, 7] and is often associated with other disruptive symptoms (e.g., sleep disturbance, pain, anxiety, depressive symptoms) [8, 9], attentional disturbance [10, 11], and impaired health-related quality of life [7, 12]. Fatigue is also associated with increased healthcare utilization [13], significant disability [13–15], and financial burden resulting from disability [7, 16–18].

One treatment for fatigue with rapid growth in popularity in the past two decades is mindfulness-based intervention (MBI). Through training in mindfulness meditation, individuals learn to focus attention on present-moment experiences with an attitude of open

curiosity and acceptance, resulting in less reactivity to difficult internal experiences [19]. While Mindfulness-Based Stress Reduction (MBSR) was the first and arguably the most popular manualized MBI [20, 21], several other MBIs (e.g., Mindfulness-Based Cognitive Therapy [MBCT] [22], Mindfulness-Based Cancer Recovery [MBCR] [23], Mindfulness-Based Art Therapy [MBAT] [24], Mindful Awareness Practices [MAP] [25]) have been tested in cancer for psychological and physical symptoms, including fatigue [26].

Although MBIs are listed as evidence-based treatments for fatigue in clinical practice guidelines, the strength of the recommendations varies across guidelines. MBSR, for example, has the highest-level evidence (category 1) in the National Comprehensive Cancer Network guidelines [27] and lower level evidence in the American Society of Clinical Oncology [28, 29] and Canadian Association of Psychosocial Oncology [28, 29] guidelines (category 2A), with the Oncology Nursing Society designating MBSR as "likely to be effective" but with insufficient evidence to be "recommended for practice" [30]. These inconsistent recommendations reflect weaknesses in current analyses of available evidence. Although several recent meta-analyses of MBIs in cancer have included fatigue among the outcomes, most only examined breast cancer [31–35], several were exclusive to MBSR [31–33, 36], and none included all of the MBI types examined in the present review. Further, most meta-analyses did not: (1) examine the distinct constructs of fatigue and vitality/vigor separately [37], (2) systematically assess evidence quality, such as with the "Grading of Recommendations Assessment, Development and Evaluation" (GRADE) approach [38], or (3) analyze MBIs' effects at follow-ups beyond post-intervention.

The primary aim of the current systematic review and meta-analysis was to evaluate the efficacy of MBIs on fatigue and vitality/vigor in adult cancer survivors to inform clinical practice guidelines. We included fatigue (measured by scales assessing tiredness, exhaustion, and need for rest) and vitality/vigor (measured by scales assessing energy and active levels of functioning), as they are common outcomes in fatigue trials in cancer; however, we analyzed the effects separately given that these are distinct constructs [37]. We compared the efficacy of MBIs with that of usual care/wait-list controls or active treatment controls at post-intervention and the first available follow-up, when applicable. The effects of potential moderators (e.g., gender, age, intervention type) were also examined. The GRADE approach was used to assess evidence quality. The present review is the largest and most inclusive meta-analysis to assess MBI's impact on fatigue in cancer while providing a rigorous examination of study quality.

2. Materials and Methods

2.1. Search Strategy

This review followed the recommendations of the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement [39]. The protocol is registered in the PROSPERO database (CRD42020113022). A systematic literature search was conducted using PubMed [Cancer subset], MEDLINE, PsycINFO, CINAHL, Web of Science, and EMBASE databases from inception until December 2019. Each database was searched with a combination of keywords related to (a) *cancer* or *neoplasm*, (b) *fatigue* or *vitality/vigor*, and (c) *mindfulness-based intervention* (truncated keywords such as mindful* were used to

capture full terms and phrases such as mindfulness-based therapy, mindfulness meditation, and Mindfulness-Based Stress Reduction). A complete list of search terms can be found in Table 1. Reference lists and forward citations of selected eligible articles were also examined to identify any studies that may have been missed in systematic database searches.

2.2. Inclusion and Exclusion Criteria

Eligibility criteria were applied in three phases: (1) title screening, (2) abstract screening, and (3) full-text screening. Inclusion criteria included: (1) adult sample (18 years of age) of cancer survivors (with any type or stage of cancer; on active cancer treatment or post-treatment); (2) randomized controlled trials (RCTs) testing a mindfulness-based behavioral intervention (e.g., MBSR, MBCT) where the main intervention component was guided mindfulness meditation, (3) intervention outcomes of fatigue or vitality/vigor assessed at baseline and one or more times post-intervention with sufficient data to calculate an effect size (corresponding authors were contacted for needed data if not provided in the publication), and (4) peer-reviewed studies with results published in English. Studies were excluded if the MBI did not have mindfulness as the main component (e.g., Acceptance and Commitment Therapy; studies primarily focused on yoga).

2.3. Study Selection

Figure 1 shows a flowchart of study selection. The second author (WLT) conducted the search. Two independent reviewers (SAJ and WLT) applied study eligibility criteria in three phases: (1) screened all titles and excluded articles that clearly did not have a focus on fatigue in cancer survivors or were not empirical, (2) screened selected abstracts and excluded those that clearly did not have a focus on MBIs, were not empirical, and/or did not assess fatigue or vitality/vigor, and (3) screened the full-text articles of the remaining citations. Disagreements were resolved by consensus.

2.4. Coding

A pair of reviewers from our team (SAJ, ES, PVS, JLC, TLT, MLS, MTF) individually extracted data from each paper using a standardized template created specifically for our review. Any disagreements were reconciled by consensus among the pairs with discrepancies resolved by judgment from the first author (SAJ). Data extracted included: authors, year of publication, sample size, treatment status, cancer type(s), cancer stage(s), intervention arms/details, study setting, outcomes, measures, eligibility criteria, baseline characteristics, assessment time points, and unadjusted means/SDs (effect sizes) for fatigue and/or vitality/vigor outcome(s) at each time point. Other extracted data included clinical trial registration, eligibility criteria based on clinically significant fatigue, mention of a theoretical framework underlying the intervention, interventionist qualifications, specification of mindfulness home practice assignments and completed practice time, documented assessment of MBI fidelity, and reporting on adverse effects of MBIs.

2.5. Risk of Bias Assessment

Risk of bias was assessed for the 23 included papers using the Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0) [40]. Each included paper was

independently reviewed by a pair of co-authors (SAJ, ES, PVS, JLC, TLT, MLS, MTF) for risk of bias, who then met in pairs to establish consensus for each risk of bias domain. Discrepancies were resolved by judgment from the first author (SAJ) in consultation with

2.6. Quality of Evidence Assessment

the senior author (KLR) when needed.

The GRADE system was used to rate the overall quality of evidence of the meta-analytic results [38]. GRADE assessment goes beyond risk of bias, which addresses internal validity of the included studies, to instead reflect the general confidence in the overall effect size. GRADE uses a baseline rating of high for RCTs. This rating can be downgraded to moderate, low, or very low based on five assessment criteria: risk of bias, inconsistency of the results, indirectness, imprecision, and publication bias. The ratings were determined by two authors (SAJ and ES) who established consensus for ratings for each GRADE criterion.

2.7. Meta-analytic Method

Effect sizes were standardized weighted mean differences based on Hedges's *g*, correcting for bias due to small sample sizes, for continuous measures of fatigue or vitality/vigor. Separate analyses were conducted for fatigue and vitality/vigor at post-intervention and first follow-up.

We calculated the standardized pre-post effect sizes using the formula $d = (_T - _C)/SD_P$, where $_T$ and $_C$ are the mean pre-post change scores for the treatment and control conditions, and SD_P is the pooled post-treatment standard deviation. This indicates the degree to which the intervention group changed compared to controls in standard deviation units.

Using Comprehensive Meta-Analysis software (Version 3.0), we corrected *d* for small sample sizes, resulting in Hedges's *g*. According to Lipsey and Wilson [41], effect sizes from 0.00 to 0.32 are considered small, 0.33 to 0.55 are considered moderate, and 0.56 and above are considered large. Effect sizes were weighted by the inverse standard error and presented with 95% confidence intervals (CI). To obtain a summary statistic, effect sizes were pooled across studies using the inverse variance random-effects model [42]. When studies reported more than one relevant effect size for either fatigue or vitality/vigor, the average effect size was used so that only one result for either fatigue or vitality/vigor was included in the analyses per sample. A positive effect size value was chosen to represent the effect size in the hypothesized direction.

Heterogeneity of effect sizes was examined using *Cochran's Q* and I^2 statistics. A *Q* statistic of less than .10 was considered as evidence of significant heterogeneity. We described I^2 values of 25%, 50%, and 75% as low, moderate, and high levels of heterogeneity, respectively. We examined potential publication bias using Begg's funnel plots [43] with Duval and Tweedie's trim-and-fill adjustment [44], as well as Egger's test of asymmetry and Rosenthal's fail-safe N. In addition, we conducted sensitivity analyses based on study quality.

We examined the effects of potential moderators, including participant gender composition (% female), mean age of the sample, type of MBI (MBSR vs. other), type of control condition (active control vs. non-active control [waitlist/usual care]), intervention dose (total number of intervention hours including retreat hours), drop-out rate, and time between post-intervention and first follow-up assessment (in months). Effects of potential moderators were examined with meta-regression analyses using a restricted maximum likelihood model. We examined each moderator independently to maximize the number of studies included in the analyses.

3. Results

3.1. Studies Included

The electronic database search identified 575 records. After excluding duplicates, 242 records were extracted for title and abstract screening. A total of 105 records were excluded based on title screening, with an additional 89 excluded based on abstract screening. Thus, 48 records were selected for full-text screening of which 29 records were excluded. We reviewed reference lists of the 19 included publications and found 4 additional eligible publications resulting in 23 eligible publications selected for meta-analyses. Of the 23 records examined for coding, 15 records included sufficient information for analyses. We contacted authors of the remaining 8 records and received sufficient data for all of these records. Overall, 23 records with sufficient information were included in effect size calculations [22–25, 45–63].

3.2. Study Characteristics

In total, 23 research papers describing results of 21 independent RCTs were included in the analyses. Seventeen of the included studies assessed fatigue, 11 assessed vitality/vigor, and 6 assessed both fatigue and vitality/vigor. The characteristics of the included studies are presented in Table 2. The included trials involved 2,239 cancer survivors, with a mean sample size of 106.6 (range: 24–322). The mean percentage of females across studies was 92.8% (range: 70.6–100%). The mean age of the samples was 53.4 (range: 42.8–58.0). The mean percentage of participants with breast cancer was 77.9% (range: 0–100%). Approximately half of the studies implemented original or adapted MBSR (K = 10, 47.6%). Most RCTs included a waitlist/usual care control (K = 15, 71.4%). The mean intervention dose was 18.9 hours (range: 9–36 hours). A total of 15 RCTs included one or more follow-up assessments beyond post-intervention, with a mean follow-up time of 3.1 months (range: 0.9–6.2 months).

3.3. MBI Study Quality

The characteristics of MBIs are presented in Table 3. Protocols of approximately half of the included studies were registered (K= 12, 52.2%) [23, 25, 45, 46, 51, 53–56, 62–64]. Only 5 studies (21.7%) screened participants for inclusion based on clinically significant fatigue [22, 46, 51, 60, 64], and only 5 studies [25, 45, 51, 56, 64] used a rigorous fatigue measure recommended for clinical trials [65, 66]. Monti and colleagues were the only researchers who described the theoretical framework underlying their MBI [24]. Nine studies (39.1%) reported that the interventionists who delivered the MBI had earned certification as a

mindfulness teacher. Fewer than half of the included studies (K = 11, 47.8%) described the frequency and amount of mindfulness home practice suggested between class sessions [25, 45, 48, 49, 51, 54, 61, 63, 64], and this ranged from 5–45 minutes per day, 3–7 days per week. Most of these studies (K = 9, 81.8%) reported participants' home practice time [25, 45, 48, 49, 51, 54, 61, 63, 64]. A minority of studies (K = 7, 30.4%) used MBI fidelity monitoring, with only one study reporting fidelity outcomes [64]. The large majority of included reports (K = 21, 91.3%) did not report on adverse effects of MBIs; however, the 2 studies that did report noted no adverse effects [51, 62].

3.4. Effect Sizes Post-Intervention

3.4.1. Effect Sizes.—A total of 18 publications describing 17 RCTs with independent effect sizes were included in the meta-analysis of change in fatigue from pre- to post-intervention (see Figure 2 for forest plots). The pooled effect size for improving fatigue was large and significant in favor of MBIs (Hedges's g = 0.60, 95% *CI*[0.36, 0.83]; see Table 4 for results). A total of 11 studies were included in the meta-analysis of change in vitality/vigor from pre- to post-intervention. The pooled effect size for improving vitality/vigor was moderate and significant in favor of MBIs (Hedges's g = 0.39, 95% *CI*[0.25, 0.52]).

3.4.2. Heterogeneity.—There was evidence of large heterogeneity between studies for changes in fatigue (Q = 74.99, p < 0.001, $I^2 = 78.66\%$). In contrast, no significant heterogeneity was detected for changes in vitality/vigor (Q = 11.46, p = 0.323, $I^2 = 12.74\%$).

3.4.3. Publication Bias.—For fatigue, a sensitivity analysis was conducted excluding two outlier effect sizes [50, 59, 60]. Omitting these studies resulted in a moderate effect in favor of MBIs (Hedges's g = 0.43, 95% CI[0.28, 0.59]). For both fatigue and vitality/vigor, the fail-safe number exceeded the criterion for robustness of results. However, Egger's regression tests showed evidence of asymmetry in the funnel plots for both outcomes (see Supplemental Figure 1 for funnel plots). Using the trim and fill method, one study was located in the funnel plot of effect sizes for fatigue. Adjusting the effect size for the missing study yielded a Hedges's g of 0.53 (95% CI [0.27, 0.80]) for fatigue. Similarly, using the trim and fill method, four studies were located in the funnel plot of effect sizes for vitality/ vigor. Adjusting the effect size for the missing studies yielded a Hedges's g of 0.31 (95% CI [0.16, 0.46]) for vitality/vigor. Sensitivity analyses omitting studies with poor study quality [24, 45, 56, 58, 60] resulted in a Hedges's g of 0.55 (95% CI [0.31, 0.78], K = 14) for fatigue and a Hedges's g of 0.42 (95% CI[0.26, 0.58], K = 9) for vitality/vigor. Taken together, these results suggest that studies showing an advantage of MBI over controls for both fatigue and vitality/vigor were more likely to be published than studies favoring controls.

3.5. Effect Sizes at First Follow-up

3.5.1. Effect Sizes.—A total of 12 studies reported follow-up fatigue data (beyond post-intervention) for MBIs and controls, with an average follow-up period of 2.8 months beyond post-intervention (range: 0.9–6.0 months; see Figure 2 for forest plots). There was a moderate effect on fatigue in favor of MBIs at follow-up (Hedges's g = 0.42, 95% *CI*[0.20, 0.64]; see Table 4). Six studies reported follow-up vitality/vigor data (beyond post-

intervention) for MBIs and controls, with an average follow-up period of 3.5 months (range: 0.9-6.2 months). There was a moderate effect on vitality/vigor in favor of MBIs (Hedges's *g* = 0.35, 95% *CI*[0.03, 0.67]).

3.5.2. Heterogeneity.—There was evidence of moderate heterogeneity between studies for changes in fatigue (Q = 33.60, p < 0.001, $I^2 = 67.27\%$) and vitality/vigor at follow-up (Q = 12.42, p = 0.029, $I^2 = 59.75\%$).

3.5.3. Publication Bias.—For fatigue, the fail-safe number exceeded the criterion for robustness of results. Even though Egger's regression tests showed evidence of asymmetry in the funnel plot suggesting potential publication bias, the trim and fill method did not suggest any missing studies for fatigue at follow-up (see Supplemental Figure 1 for funnel plots). In contrast, the fail-safe number was below the criterion for robustness of results for vitality/vigor (see Table 4). Egger's regression test, however, showed no evidence of asymmetry in the funnel plot. Moreover, the trim and fill method did not suggest any missing studies for vitality/vigor at follow-up. Sensitivity analyses omitting studies of poor quality [24, 45, 56, 58, 60] resulted in a Hedges's *g* of 0.36 (95% *CI*[0.14, 0.58], *K*=9) for fatigue and a Hedges's *g* of 0.40 (95% *CI*[0.00, 0.80], *K*=5) for vitality/vigor. Together, these results suggest the possibility of a publication bias for studies favoring MBI over control for both fatigue and vitality/vigor at follow-up.

3.6. Exploring Potential Moderators

Table 5 presents results of the meta-regression analyses. These results should be interpreted with caution as we had a limited number of studies in the meta-regression analyses. Thus, statistical power may have limited our ability to detect significant differences between subgroups [67].

3.6.1. Gender.—Gender composition of the sample (i.e., percent female) did not significantly moderate the intervention effects on fatigue or vitality/vigor at post-intervention or follow-up.

3.6.2. Age.—Age was a significant moderator of the intervention effect on fatigue at post-intervention. We found that for every 1-year increase in age, the intervention effect in favor of MBIs was weakened by 0.08 (b = -0.08, 95% *CI*[-0.16, -0.01]). However, age did not significantly moderate the intervention effects on fatigue at follow-up or on vitality/vigor at post-intervention or follow-up.

3.6.3. Type of MBI.—Type of MBI (i.e., MBSR vs. non-MBSR) did not significantly moderate the intervention effects on fatigue or vitality/vigor at post-intervention or follow-up.

3.6.4. Type of Control Condition.—Type of control condition (i.e., active vs. waitlist/ usual care control) did not significantly moderate the intervention effects on fatigue or vitality/vigor at post-intervention or follow-up.

3.6.5. Intervention Dose.—Intervention dose did not significantly moderate the intervention effects on fatigue or vitality/vigor at post-intervention or follow-up.

3.6.6. Drop-out Rate.—Drop-out rates at post-intervention and follow-up did not significantly moderate the intervention effects on fatigue at post-intervention or follow-up. However, drop-out rates at post-intervention and follow-up significantly moderated intervention effects on vitality/vigor at post-intervention and follow-up; for every 1% increase in the drop-out rate, the intervention effect in favor of MBI was weakened by 0.01 at post-intervention and follow-up (b = -0.01, 95% *CI*[-0.02, -0.004], b = -0.01, 95% *CI*[-0.03, -0.001], respectively).

3.6.7. Follow-up Time.—Time between post-intervention and follow-up assessment in months did not significantly moderate the intervention effects on fatigue or vitality/vigor at follow-up.

3.7. Risk of Bias Assessment

As shown in Figure 3, most included RCTs were categorized as being at low risk of bias with respect to randomization sequence generation and incomplete outcome data (K = 14, 60.9% and K = 13, 56.5%, respectively). Allocation concealment and blinding of outcome assessment often went unreported (K = 15, 65.2% and K = 19, 82.6%, respectively) in the included studies. Risk of bias was high for blinding of participants/personnel in all included studies (K = 23, 100%). Likewise, the majority of studies (K = 13, 56.5%) were evaluated as being at high risk of bias in the domain of selective reporting.

3.8. Quality of Evidence

Based on GRADE [38], the quality of evidence for fatigue and vitality/vigor at postintervention and follow-up were all rated as low, indicating a low level of confidence in the effect estimates. The level of evidence was downgraded to low primarily due to concerns regarding risk of bias and publication bias (see Supplementary Tables 1 and 2 for GRADE ratings).

4. Conclusions

The present meta-analysis provides an updated synthesis of the current evidence for MBIs targeting fatigue and vitality/vigor in cancer survivors and identifies research gaps that warrant attention. Results suggest that MBIs show promise in reducing fatigue and improving vitality/vigor at post-intervention and an average of 3–4 months later. Effects were large for fatigue at post-intervention and moderate at first follow-up. Effects were moderate for vitality/vigor at both time points. Given notable overall risk of bias, publication bias, and heterogeneity of findings, the quality of the evidence supporting these findings was low. Although current recommendations of MBIs for fatigue are mixed, overall, results support tentative recommendations for MBIs in clinical practice guidelines for fatigue in cancer survivors.

Our meta-analysis provides the most comprehensive and rigorous examination of the evidence regarding MBI for fatigue in cancer survivors. To date, nine meta-analyses of MBIs

in cancer have included fatigue among the outcomes [31-36, 68-70]. Of these, only four were prospectively registered to support transparency and replication [31, 32, 68, 69]. Only two assessed the quality of the evidence (e.g., GRADE), and these meta-analyses only included five [32] and six [69] RCTs, respectively. The majority of the meta-analyses were breast cancer specific [31-35]. Finally, the meta-analyses included 2 to 14 studies compared to 21 independent studies in the present meta-analysis (17 assessing fatigue and 11 assessing vitality/vigor). The effect sizes of MBI for fatigue in published meta-analyses ranged from 0.28–0.89 at post-intervention (mean SMD = 0.57; median and mode = 0.50). Only three meta-analyses reported an effect beyond post-intervention [32, 34, 69]. Among these three, the effect sizes ranged from 0.19 to 0.40. Our effect sizes for fatigue were 0.60 at post-intervention and 0.42 at first follow-up, comparable to those found in other meta-analyses.

Across studies included in our review, participant characteristics were generally homogeneous (e.g., 92.8% female, 77.9% breast cancer, mean ages 42.8-58.0 years). This homogeneity may have contributed to largely null findings when examining possible moderators of MBI's effects. Further, some studies failed to report relevant demographic, medical, and procedural variables, resulting in reduced statistical power for some of the moderation analyses. Inconsistent moderation effects of age and post-intervention drop-out rate were found. Age moderated the fatigue effect at post-intervention, with younger participants reporting a stronger effect from MBIs. However, this effect did not occur at first follow-up and was not found for vitality/vigor. MBI's effect on vitality/vigor became weaker at both time points as the drop-out rate increased; however, this effect was not found for fatigue. It is possible that more symptomatic participants were more likely to drop out, thereby reducing intervention effects on vitality/vigor. The lack of a significant moderation effect for control condition type (i.e., active vs. waitlist/usual care control) on fatigue and vigor/vitality also warrants discussion. Several of the active controls offered minimal guidance on fatigue management to create an expectation of therapeutic benefit. This may explain why the magnitude of change in fatigue and vigor/vitality was similar across both control condition types.

Included RCTs had a number of strengths and weaknesses in their rigor. Strengths included low refusal rates (mean=30%) and high retention (mean=90% post-intervention and 86% at first follow-up). In addition, the sample size was 100 in nine trials. In terms of weaknesses, only five of the included studies [22, 46, 51, 60, 64] screened for fatigue as an inclusion criterion as recommended in existing guidelines [28]. Additionally, most studies (14/21, 66.7%) used a waitlist/usual care control group. Relative to active comparison groups, no-treatment controls often produce the largest effect size in favor of the experimental treatment [71]. The measurement of fatigue is another limitation, with some studies measuring fatigue severity, interference, or a combination of both. Notably, few of the included studies (5/21, 23.8%) [25, 45, 51, 56, 64] used a fatigue measure recommended for clinical trials based on strong psychometric properties and user-friendliness [65]. Most studies also did not report on the adherence of participants to MBI, adverse effects, or outcomes of fidelity monitoring that may allow further inferences to be made about study quality. Several aspects of trial procedures were not reported in sufficient detail to adequately assess risk of bias. The common lack of outcome assessor blinding is particularly problematic, given the self-

reported nature of the outcomes. Finally, trials have mainly focused on breast cancer survivors, despite the ubiquity of fatigue across cancer types [72, 73].

Our findings point to a number of important directions for future research. Future MBI trials for fatigue should target those most in need by establishing a threshold of fatigue severity for eligibility as assessed by a rigorous measure of fatigue, perhaps coupled with an objective measure (e.g., fatigability). Additionally, MBI warrants testing in more diverse samples with respect to gender, race/ethnicity, age, and cancer type. Comparing MBIs to other behavioral interventions for fatigue (e.g., physical activity, cognitive-behavioral therapy) is another important future direction. Further studies are also needed to determine the long-term effectiveness of MBIs for fatigue in cancer. Only one of the included studies reported a follow-up assessment beyond 6 months post-intervention [23]. As our meta-analysis showed a decline in effect size during short-term follow-up, booster sessions warrant examination in future research. Testing theory-driven mechanisms that may explain the effect of MBIs on fatigue in cancer survivors is another priority for future research. Beyond clinical trials, future meta-analytic reviews of MBIs for fatigue in cancer could be strengthened by including both published and unpublished literature in this area. Our meta-analytic review may be affected by the file drawer problem (i.e., publication bias) because we only considered published articles for inclusion to ensure that studies had been peer-reviewed.

In conclusion, although MBIs show promise in the treatment of fatigue and improving vitality/vigor, further methodologically robust trials are required to definitively examine their long-term efficacy. Use of rigorous screening and outcome measures of fatigue across studies will strengthen the evidence base. Furthermore, comparisons of MBIs to other tested fatigue interventions are needed. Such research will ultimately reduce suffering and disability in the large population of cancer survivors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

• Fatigue is a prevalent and disruptive symptom for many cancer survivors.

- Mindfulness-based interventions (MBI) have been tested to reduce fatigue in cancer.
- Meta-analyses tested the efficacy of MBIs in cancer for fatigue and vigor/ vitality.
- MBIs significantly improved fatigue and vigor/vitality compared to controls.
- Evidence grade was low due to risk of bias, heterogeneity, and publication bias.

Vitae.

- Shelley A. Johns is a board certified clinical health psychologist and associate professor at Indiana University School of Medicine where she conducts randomized controlled trials to improve symptom management in adults with cancer. Dr. Johns' research primarily focuses on testing behavioral interventions to address fatigue, fear of recurrence, depression, and anxiety in cancer survivors.
- Will L. Tarver is an assistant professor at The Ohio State University College of Medicine. Dr. Tarver's research focuses on health information technologies and their potential to improve care coordination for people with cancer, including those who are part of underserved populations.
- Ekin Secinti is a PhD candidate in the clinical psychology doctoral program at Indiana University – Purdue University Indianapolis (IUPUI). Her program of research broadly focuses on how medical patients and their family caregivers cope with symptoms. Her recent work has focused on social processes and acceptance-based coping in relation to mental health in adults with cancer and their family caregivers.
- Catherine E. Mosher is an associate professor in the Department of Psychology at IUPUI, where she directs a behavioral oncology laboratory. Dr. Mosher's primary research interests are in developing, evaluating, and disseminating psychosocial interventions for cancer patients and their family caregivers, as well as identifying predictors of health outcomes in these populations.
- Patrick V. Stutz has been a clinical research specialist at Indiana University School of Medicine for three years assisting with research in behavioral oncology. A certified clinical research professional (CCRP) through the Society of Clinical Research Associates (SoCRA), he assists the first author in grant writing, study startup, recruitment, data collection, data cleaning, and manuscript preparation.
- Jennifer L. Carnahan is a geriatrician and assistant professor at Indiana University School of Medicine. Dr. Carnahan's research centers on improving care for adults with dementia in nursing homes, with emphasis on care transitions from skilled nursing facilities to home.
- Tasneem L. Talib is a clinical research coordinator at Indiana University School of Nursing, where she assists with grant and manuscript writing. Dr. Talib is also an assistant teaching professor in the department of Educational Psychology at Ball State University, where she teaches courses in Human Growth and Development and Adolescent Psychology.
- Mackenzie L. Shanahan is a PhD candidate in the clinical psychology doctoral program at IUPUI. She conducts research in the area of expectations, including hope and optimism, and clinical pain.

- Micah T. Faidley is an alumnus of IUPUI Department of Psychology. During his summer internship at Regenstrief Institute, Inc., he worked closely with the first author to extract data from eligible studies in the present review.
 - Kelley M. Kidwell is an associate professor in the Department of Biostatistics at the University of Michigan School of Public Health. Dr. Kidwell's research centers on the design and analysis of clinical trials, especially sequential multiple assignment randomized trials. She collaborates in many clinical areas and populations, including cancer, mental health, and rare diseases.
- Kevin L. Rand is an associate professor in the IUPUI Department of Psychology, where he teaches and conducts research on personality, stress, and coping. Clinically, Dr. Rand applies existential psychotherapy principles in conjunction with cognitive-behavioral techniques to improve health outcomes for adults and adolescents with conditions like cancer and chronic pain.

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Figure 1.

Systematic review flowchart.

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itudy name	iedaes's Sl	S <u>ta</u> andard	itistics fo	Lower U	jdy Ipper			Hedges	's g and 95% CI				Study name	100		Sta	istics for	each st	udy			Hed	ges's g and	195% CI
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laes (2016)	0.204	0.396	0.156	-0.571 0	3.979	0.515	0.606		-				Carlson (2016)		0.097	0.167	0.028	-0.231	0.424	0.580	0.562	1	-	- 1
ower (2015)	0.613	0.252	0.063	0.120	1.106	2.438	0.015						Dodds (2015)		0.649	0.381	0.145	-0.097	1.396	1.705	0.088		-	
uggeman-Evens (2017)	0.044	0.220	0.048	0.213	1.074	2.928	0.003						Hoffman (2012)		0.329	0.137	0.019	0.060	0.598	2 399	0.016			-
here (2019)	0.008	0.273	0.025	0.528	0.644	0.079	0.030						Johns (2015)		1.080	0.355	0.128	0.385	1 776	3.045	0.002			
affman (2012)	0.348	0 137	0.019	0.079	0.617	2 533	0.011		T				Jahma (2016)		0.640	0.044	0.000	0.170	1 120	0.000	0.000			100
ing (2016)	3.486	0.639	0.409	2.233	4.739	5.454	0.000				>		Joins (2010)	100170	0.040	0.244	0.000	0.000	0.700	2.004	0.000			
ohrs (2015) Severity & Interference	1.507	0.377	0.142	0.769 :	2.245	4.003	0.000			-			Kenne Sarenmai	n (2017)	0.363	0.166	0.035	-0.006	0.732	1.820	0.054			
ohms (2016) Sevenity & Interference	0.164	0.239	0.057	-0.304 /	0.632	0.687	0.492						Lengacher (2008		0.391	0.221	0.049	-0.042	0.824	1.700	0.077			
engacher (2012)	0.411	0.221	0.049	-0.023 /	0.844	1.856	0.063						Monti (2006)		0.485	0.207	0.043	0.080	0.891	2.346	0.019			-
engacher (2016) Severity & Interference	0.355	0.116	0.014	0.127	0.583	3.050	0.002						Monti (2013)		0.153	0.178	0.032	-0.196	0.503	0.858	0.391			
iu (2019)	0.989	0.209	0.043	0.581	1.398	4.745	0.000		_	-			Speca (2000)		0.462	0.215	0.046	0.040	0.884	2.147	0.032			-
ahmani (2014 & 2015)	3.665	0.667	0.445	2.358	4.972	5.496	0.000				>		Zernicke (2014)		0.627	0.273	0.074	0.092	1.161	2.297	0.022		-	-
xeca (2000)	0.216	0.213	0.045	-0.201 0	0.633	1.014	0.311								0.387	0.068	0.005	0.254	0.520	5.710	0.000			•
an der Lee (2012)	0.772	0.247	0.061	0.287	1.256	3.122	0.002			-														
itek-Januesek (2019)	0.102	0.170	0.029	-0.232 0	0.435	0.598	0.550		-												-2.0	0 -1.00	0.00	1.00
micke (2014)	0.283	0.268	0.072	-0.241 0	3.807	1.058	0.290																	
	0.599	0.120	0.014	0.384	3,834	4,985	0.000	4	-													Favors Cont	rol F	avors Mindfu
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Studies with Patigue as an Outcot y name a (2016) or (2015) grama-Evrits (2017) son (2016) ma (2019) ma (2019) to (2018) Soventy & Interference spacer (2016) Seventy & Interference spacer (2016) Seventy & Interference spacer (2016) Seventy & Interference (2016) Seventy & Interference State (2016) Seventy & Interference State (20	ne iedgest's 9 0.217 0.116 0.081 1.022 0.225 1.022 0.231 0.2331 0.331 0.331 0.419	F Stan andard V 0.357 0.258 0.258 0.258 0.258 0.258 0.258 0.258 0.259 0.137 0.201 0.175 0.113	Fatigu fariance 0.127 0.066 0.048 0.075 0.019 0.075 0.019 0.075 0.019 0.075 0.019 0.031 0.013 0.013	IE FOI Imit L Lower U Imit L 0.482 (0.183 - 0.484 (0.339 (0.183 - 0.484 (0.043 (0.045	LOW- 1097 1097 1098 1099	-Up 0.609 0.450 0.070 0.310 0.310 0.310 2.504 2.504 2.504 2.504 2.504 2.504 2.504 3.705	Value 0.543 0.055 0.055 0.056 0.056 0.036 0.009 0.004 0.009 0.004 0.009 0.004 0.009 0.004 0.009 0.004 0.009 0.004 0.009 0.009 0.009 0.009 0.009 0.009 0.009 0.0000 0.0000 0.0000 0.0000 0.000000	Hedger	75 g and 95% CI		2.00	d)	Study name Carlson (2016) Dodds (2015) Hoffman (2012) Johns (2016) Montil (2013)	Hedges's 9 0.013 0.024 0.390 1.497 0.243 0.185 0.350	Standarr error 0.25 0.41 0.33 0.37 0.24 0.22 0.16	Statistic Varian 0.0.01 0.0.1 0.1 1.1 <td>Vita s for ex con line 67 -0. 68 -0. 19 0. 41 0. 58 -0. 52 -0. 26 0.</td> <td>lity/V ach stu 494 (780 (120 (761 2 229 (034 (</td> <td>/igor int 0.521 0.659 2.234 0.615 0.631 0.667</td> <td>Follov 0.052 0.058 2.831 1.009 0.813 2.168</td> <td>v-up 0.959 0.954 0.005 0.000 0.313 0.416 0.030 -2</td> <td>He 2.00 -1.00 Favors Co</td> <td>dges's g a</td> <td>and 95% Cl</td>	Vita s for ex con line 67 -0. 68 -0. 19 0. 41 0. 58 -0. 52 -0. 26 0.	lity/V ach stu 494 (780 (120 (761 2 229 (034 (/igor int 0.521 0.659 2.234 0.615 0.631 0.667	Follov 0.052 0.058 2.831 1.009 0.813 2.168	v-up 0.959 0.954 0.005 0.000 0.313 0.416 0.030 -2	He 2.00 -1.00 Favors Co	dges's g a	and 95% Cl

Figure 2.

Forest plots for the intervention effect on (a) fatigue at post-intervention, (b) vitality/vigor at post-intervention, (c) fatigue at follow-up, and (d) vitality/vigor at follow-up.



Figure 3.

Low risk of bias

Risk of bias summary of authors' judgments for each included study and risk of bias graph of authors' judgments as percentages across all included studies.

Table 1.

Operationalization of the search terms by topic.

Торіс	Search Terms
Cancer	Cancer, neoplasm
Fatigue	Fatigue, vitality, vigor, vigour
Mindfulness-based interventions	Mindful [*] , meditat [*] , MBSR, MBCT, MBCR

Note:

"*" represents truncations. Search terms within each category are combined with OR. Search terms between categories are combined with AND. Some terms were truncated.

essment	Fatigue outcome Measure)	atigue FACT- b	atigue -SI)	atigue verity JIS- S) ^{a,b}	atigue POMS) b igor POMS) b	ancer elated atigue SRF :ale)
come ass	ime q tt(s) (N	E E		н	F. V. 6 V. V. 6 V (F. V. 0 V	。 、、、、3 。 、、、3 。 、 、、、3
Out	Foll t up t poin	Post- inter mos. post- inter	Post- inter mos. post- inter	Post- inter mos. post- inter	Post- inter mos. post- post- inter	Post- inter mos. post- inter
ention	Control (s)	Waitlist	Waitlist	Home- based AAF; 3 hours/ week for 9 weeks PE emails; 10 min/week for 9 weeks	SET; 12 weekly 1.5-hour sessions SMS; ** 1. day minimal attention waitlist	Qigong; 12 weekly 2-hour sessions
Interv	MBI	MBCR; 8 weekly 2.5- hour sessions + 8-hour retreat	MAPs; 6 weekly 2- hour sessions	Web-based eMBCT; 4 hours/week for 9 weeks	MBCR; 8 weekly 1.5- hour sessions + 6-hour retreat	Unspecified Mindfulness interv. 12 weekly 2- hour sessions
	Origin	United States	United States	The Netherlands	Canada	Taiwan
thnicity [N [%)]	Control(s)	NR	White: 25 (78.1%) Black: 1 (3.1%) Asian: 5 (15.6%) Other: 1 (3.1%)	NR	NR	NR
Race/ E (MBI	NR	White: 29 29 (74.4%) Black: 1 (2.6%) Asian: 3 (7.7%) Other: 6 (15.4%)	N	NR	NR
listribution) female]	Control(s)	12 (85.7%)	32 (100.0%)	44 (80.0%; AAF); 40 (80.0%; PE)	118 (100.0%)	24 (88.9%)
Gender o [N (%	MBI	26 (92.9%)	39 (100.0%)	39 (70.9%)	134 (100.0%)	23 (92.0%)
an age	Control(s)	57	47.7	56.45 (AAF); 56.54 (PE)	54.14	53.74 ^b
Me	MBI	55	46.1	51.36	55.12	54.04 ^b
ıple size	Control(s)	14	32	62 (AAF); 50 (PE)	118	27
San	MBI	28	39	55	134	25
	Fatigue eligibility criterion	NA	AA	35 CIS- FS	NA	NA
	Sample	Any cancer type (69.0% breast), stage I-III, 6 mos. post-curative tx	Breast cancer, stage 0-III dx at age 50, 3 mos. to 10 years post-tx (excl. hormone therapy)	Any cancer type (47.3% breast), 3 mos. post- curative tx (excl. (excl. hormone therapy)	Breast cancer, stage 0-IV, 3 mos. post-tx (excl. hormone therapy), score 4 Distress Thermometer	Any cancer type (65.4% breast), stage I-III, 1 mo. post-curative tx
	Author, year	9 Blaes, 2016 <i>Crit Rev Oncol</i>	S 100 100 <i>Hematol.</i> Author manusc	ript; available in PMC 202	Carlson, 2016 Abuil 01	Cheng, 2019

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Table 2.

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Characteristics of the included studies

assessment	Fatigue outcome (Measure)	Vitality (SF-12)	Fatigue (POMS) Vigor (POMS)	Fatigue (QLQ- C30)	Fatigue (FSI) ^{ab} Vitality (SF-36) ^b	Fatigue (FSI) ^a Vitality (SF-36)	Vitality (SF-36)
Outcome	Follow- up time point(s)	Post- interv. 1 mo. post- interv.	Post- interv. 1 mo. post- interv.	Post- interv.	Post- interv. 1 mo. post- interv.	Post- interv. 6 mos. post- interv.	Post- interv.
ention	Control(s)	Waitlist	Waitlist	Waitlist	Waitlist	PES; 8 weekly 2- hour sessions	Self- guided MBSR; 2 hours/ week for 8 week or 0
Interv	MBI	CBCT; 8 weekly 2- hour sessions + booster 1 mo. post- interv.	Original MBSR: 8 weekly 2- hour sessions (session 1 and 8 were 2.25 hours) + 6-hour retreat	Adapted MBAT; 12 weekly 45- minute sessions	Adapted MBSR; 7 weekly 2- hour sessions	Adapted MBSR; 8 weekly 2- hour sessions	Adapted MBSR; 8 weekly 2- hour sessions
	Origin	United States	United Kingdom	South Korea	United States	United States	Sweden
thnicity [N %)]	Control(s)	White: 12 (75.0%) Other: 4 (25.0%)	NR	NR	White: 13 (76.5%) Other: 4 (23.5%)	White: 23 (63.9%) Other: 13 (36.1%)	NR
Race/ E (MBI	White: 11 (91.7%) Other: 1 (8.3%)	NR	NR	White: 15 (83.3%) Other: 3 (16.7%)	White: 27 (77.1%) Other: 8 (22.9%)	NR
listribution) female]	Control (s)	16 (100.0%)	111 (100.0%)	12 (100.0%)	16 (94.1%)	31 (86.1%)	52 (100.0%; S-MBSR); 52 (100.0%; UC)
Gender d [N (%)	MBI	12 (100.0%)	103 (100.0%)	12 (100.0%)	17 (94.4%)	33 (94.3%)	62 (100.0%)
an age	Control(s)	55.8	50.1	51.42	55.7	56.4	57.2 (S- MBSR); 57.2 (UC)
Me	MBI	54.7	49.0	51.75	58.8	56.9	57.2
nple size	Control(s)	16*	111 *	12	17	36	52 (S- MBSR); 52 (UC)
Sar	MBI	12 *	103 *	12	18	35	62
	Fatigue eligibility criterion	NA	NA	NA	4 FSI- SC	4 FSI- SC	NA
	Sample	Breast cancer, stage F-IV, 10 years post- adj. systemic chemo	Breast cancer, stage 0-III, 2 mos. to 2 years post-tx (excl. hormone therapy)	Breast cancer, stage 0-III, <2 years post- curative tx	Any cancer type (86% breast), stage LIV, 3 mos. post-tx (excl. hormone therapy)	Breast or colorectal cancer (85% breast), stage 0-III, 3 mos. post-rx (excl. hormone therapy)	Breast cancer, post- adj. chemo and/or radiation
	Author, year	5015 Crit R	, Hoffman, 2012 2012 <i>ev Oncol Hematol.</i> Author	9105 مەر manuscript; av	silable in PMC 202	2 April 01.	Kenne Sarenmalm, 2017

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sessment	Fatigue outcome (Measure)	Vitality SF-36) ^b	Fatigue symptom cluster (MDASI)	TsI) FSI)	atigue (QLQ- C30)
Outcome as	Follow- up time point(s) (Post- interv. (Post- interv. s	Post- I interv. (1.5 mos. post- interv.	Post- I interv. 3 (mos. 6 post- interv.
tion	Control(s)	Waitlist	Waitlist	Waitlist	2
Interven	MBI	Adapted MBSR(BC); 6 weekly 2- hour sessions	Adapted MBSR(BC); 6 weekly 2- hour sessions	Adapted MBSR(BC); 6 weekly 2- hour sessions	Adapted MBSR; 8 weekly 2.5- hour sessions
	Origin	United States	United States	United States	China
micity [N 6)]	Control(s)	White: 34 (79.1%) Black: 8 (18.6%) Hispanic: 3 (7.0%) Other: 1 (2.3%)	White: 34 (79.1%) Black: 8 (18.6%) Hispanic: 3 (7.0%) Other: 1 (2.3%)	White: 110 (71.0%) Black: 16 (10.3%) Hispanic: 14 (9.0%) Other: 13 (8.4%) NR: 2 (1.3%)	Ж
Race/ Etl (%	MBI	White: 36 (87.8%) Black: 2 (4.9%) Hispanic: 6 (14.6%) Other: 3 (7.3%)	White: 36 36 (87.8%) Black: 2 (4.9%) Hispanic: 6 (14.6%) Other: 3 (7.3%)	White: 112 (67.1%) Black: 2 Black: 2 Black: 12.6%) Hispanic: 19 (11.4%) (11.4%) (11.4%) NR: 0 NR: 0 (0.0%)	X
istribution female]	Control(s)	42 (100.0%)	42 (100.0%)	155 (100.0%)	38 (71.7%)
Gender di [N (%)	MBI	40 (100.0%)	(100.0%)	167 (100.0%)	34 (69.4%)
an age	Control(s)	58.0	58.0	57.6	42.38
Me	MBI	57.1	57.1	56.5	43.32
aple size	Control(s)	42 *	42 *	155	53 *
San	MBI	40 *	40 *	167	49 *
	Fatigue eligibility criterion	NA	NA	NA	NA
	Sample	Breast cancer, stage 0-III, 18 mos, post- curative tx (surgery + adj, radiation or chemo)	Breast cancer, stage 0-III, 18 mos, post- curative tx (surgery + adj. radiation or chemo)	Breast cancer, stage 0-III, 2 weeks to 2 years post-tx	Differentiated thyroid cancer (DTC), stage F-IV (excl. metastasis to other organ), first there organ), first there is a stage there is a stagethere is
	Author, year	Fungacher, 2009 <i>Crit Rev Onc</i>	Lengacher, 2012 2013 2019 <i>Hematol.</i> Author manusc	1 1 1 1 1 1 1 1 1 1 1 1 1 1	- Liu, 2019

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assessment	Fatigue outcome (Measure)	Vitality (SF-36) ^b	Vitality (SF-36) ^b	Fatigue (QLQ- C30)	Fatigue severity (FSS-P) ^a	Fatigue (POMS) Vigor (POMS)	Fatigue severity (CIS-FS) ^a
Outcome	Follow- up time point(s)	Post- interv.	Post- interv. 6 mos. post- interv.	Post- interv. 2 mos. post- interv.	Post- interv. 2 mos. post- interv.	Post- interv.	Post- interv. 6 mos. post- interv.
ntion	Control(s)	Waitlist	BCSG; 8 weekly 2.5-hour sessions	MCT; 8 weekly sessions UC	UC	Waitlist	Waitlist
Interve	MBI	Original MBAT; 8 weekly 2:5- hour sessions	Original MBAT: 8 weekly 2.5- hour sessions	Adapted MBSR; 8 weekly 2- hour sessions	Adapted MBSR; 8 weekly 2- hour sessions	Adapted MBSR; 7 weekly 1.5- hour sessions	Adapted MBCT; 8 weekly 2.5- hour sessions + 6-hour retreat + 2.5-hour booster 2
	Origin	United States	United States	Iran	Iran	Canada	The Netherlands
thnicity [<i>N</i> %)]	Control(s)	White: 38 (69.1%) Black: 13 (23.6%) Asian: 1 (1.8%) Hispanic: 2 (3.6%) Other: 1 (1.8%)	White: 54 (58.1%) Black: 37 (38.8%) Other: 2 (2.2%)	NR	NR	NR	NR
Race/ E	MBI	White: 45 45 (80.4%) Black: 10 (17.9%) Asian: 1 (1.8%) Hispanic: 0 (0.0%) (0.0%)	White: 59 (60.2%) Black: 35 (35.7%) Other: 4 (4.1%)	NR	NR	NR	NR
listribution) female]	Control(s)	55 (100.0%)	93 (100.0%)	12 (100.0%; MCT); 12 (100.0%; UC)	12 (100.0%)	27 (73.0%)	19 (79.2%)
Gender d [N (%)	MBI	56 (100.0%)	98 (100.0%)	12 (100.0%)	12 (100.0%)	46 (86.8%)	51 (86.4%)
an age	Control(s)	54.1	56.4	44.92 (MCT); 44.08 (UC)	44.08	48.9	49.4
Me	MBI	53.1	56.9	43.25	43.25	54.9	53.1
nple size	Control(s)	55	93	12 (MCT); 12 (UC)	12	37 *	24 *
Sar	MBI	56	86	12	12	53 *	59 *
	Fatigue eligibility criterion	NA	NA	NA	>4 FSS-P	NA	35 CIS- FS
	Sample	Any female cancer type (46% breast), stage 0-IV, 4 mos. to 2 years post-dx	Breast cancer, stage 0-IV, 6 mos. to 3 years post-dx or post- recurrence	Breast cancer, stage I-III, 1 mo. post-dx	Breast cancer, stage I-III, 1 mo. post-dx	Any cancer type (43% breast), stage I-IV	Any cancer type (60% breast), 1 year post- curative tx
	Author, year	9002 [;] juuo <i>Crit Rev Oncol He</i>	E102, 5013 Would: Author manusc	2014 2014 altabilitati available	k 2505 ZMA ani, 2015 ZUI5 uni	Speca, 2000	van der Lee, 2012

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assessment	Fatigue outcome (Measure)		Fatigue (MFSI- SF)	Fatigue (POMS) ^b Vigor (POMS) ^b		
Outcome	Follow- up time point(s)		Interv. midpoint Post- interv. 1 mo. post- interv. 6 mos. post- interv.	Post- interv.	mpassion celuding; n; interv.: .I: · Scale · Scale · Quality of eneral Health	
ention	Control(s)		ACC 8 weekly 2.5-hour sessions of education	Waitlist	ely-Based Co BCT; excl.: e> Scale - Persia Therapy; MB sional Fatigue es; QLQ-C30 em 36-Item G	
Interv	MBI	mos. post- interv.	Original MBSR: 8 weekly 2.5- hour sessions + 6-hour retreat (after week 5)	Online MBCR 8 weekly 2- hour sessions + 6-hour retreat (after week 6)	:; CBCT: Cognitiv CT: web-based M : Fatigue Severity -Based Cognitive I-SF: Multidimen ofile of Mood Stat ss Study-Short Fo	
	Origin		United States	Canada	; BL: baseline agnosis; eMB posite; FSS-P : Mindfulness ventory; MFS vrt; POMS: Pre dical Outcome	
thnicity [N %)]	Control(s)		White: 58 (72.5%) Black: 13 (16.3%) Asian: 1 (1.3%) Hispanic: 5 (6.3%) Other: 2 (2.5%) NR: 1 (1.3%)	NR	Support Group e scale; dx: di Severity Com covery; MBCT overy; MBCT n Symptom In cational Suppo ey; SF-36: Me	
Race/ E	MBI		White: 68 68 (81.0%) 10 (11.9%) Asian: 1 (1.2%) Hispanic: 2 (2.4%) Other: 1 (1.2%) NR: 2 (2.4%) NR: 2 (2.4%)	NR	east Cancer elated Fatigu m Inventory. d Cancer Rei MD Anderso Psycho-Edu Health Surv	
listribution) female]	Control(s)		80 (100.0%)	23 (71.9%)	cer; BCSG: Bi cale: Cancer R atigue Symptc dfulness-Base apy; MDASI: cational; PES: Form 12-Item	
Gender d [N (%)	MBI		84 (100.0%)	22 (73.3%)	2: breast cano ccale; CRF so v; FSL-SC: F MBCR: Min MBCR: Min gnitive Therr Psycho-eduo Study-Short	
an age	Control(s)		55.2	58	: adjuvant; BC · Severity subs tom Inventor Art Therapy; MCT: Metaco reported; PE: real Outcome (cal Outcome	y.
Me	MBI		55	58	lition; adj ith-Fatigue iigue Symj ess-Based eduction; e; NR: not e; NR: not Care.	fers slight
nple size	Control(s)		80%	32	 Control Con- lividual Streng tigue; FSI: Fai AT: Mindfuln Sased Stress R not applicabl- ve Therapy; SI 	l sample <i>N</i> dif
San	MBI		84 *	30	C: Active scklist Ind nerapy-Fa tices; MB Ifulness-F Ifulness-F Expressive c: treatme	ndomized
	Fatigue eligibility criterion		۲Z	ΥN	Feedback; AC ; CIS-FS: Ché t in Cancer Th vareness Prac MBSR: Minc utes; mo.: mé T: Supportive nt Seminar; to	ample; full ra
	Sample		Breast cancer, stage 0-III, post- surgery	Any cancer type (33.9% breast), 3 years post-tx	unbulant Activity no: chemotherapy tional Assessment MAPs: Mindful Av ased intervention; rt Form; min mir naire-Core 30; SE Stress Manageme	lyzed in outcome s
	Author, year		Mitek- Januser 2016 2017 <i>Crit Rev Oncol Hematol</i> . Auti	é; 2015 75 75 75 75 76 76 76 76 76 76 76 76 76 76 76 76 76	and Backer, AAF: A Maraning; cher Adart-F: Func Adartervention; 1 Mindfulness-b Mindfulness-b Mindfulness-b Jiffe Question Survey; SMS:	* Number anal

** SMS outcomes not assessed; all participants offered re-randomization to MBCR or SET after 12-week waitlist period.

⁴Primary outcome(s) of the respective study.

 $b_{
m Some}$ of the data were not reported in study publications but were provided by the authors upon request.

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Characteristic	s of mindfulnes	s-based inter	ventions							
Author, year	Mindfulness- based intervention	Guided by theory?	Intervention dose (hours)	Retreat	Assigned home practice	Mindfulness interventionist	Fidelity monitoring	Refusal rate	Retention rate (post- intervention)	Retention rate (follow-up)
Blaes, 2016	MBCR	No	28	8-hour retreat	45 min./day, 7 days/week	MBSR-certified faculty with extensive MBCR training from Dr. Linda Carlson	NR	NR	82.93%	85.37%
Bower, 2015	MAPs	No	12	NA	5–20 min./ day, 7 days/ week	NR	NR	45.70%	92.86%	84.29%
Bruggeman- Everts, 2017	Web-based eMBCT	No	36	NA	NR	Psychologists (provided guidance remotely)	NR	26.39%	83.23%	84.43%
Carlson, 2016	MBCR	No	18	6-hour retreat	NR	NR	NR	15.90%	65.48%	51.59%
Cheng, 2019	Unspecified Mindfulness interv.	No	24	NA	NR	Rehabilitation counselor	NR	NR	100.00%	100.00%
Dodds, 2015	CBCT	No	16 + Booster 1 mo. post- interv.	NA	30 min./day, 3 days/week	CBCT-certified clinically-trained PhD social work researcher	50% of class videos reviewed by CBCT supervisor; fidelity outcomes NR	24.38%	100.00%	78.57%
Hoffman, 2012	Original MBSR	No	22.5	6-hour retreat	40–45 min./ day, 6–7 days/ week	MBSR-certified clinician/researcher	NR	17.29%	96.26%	92.06%
Jang, 2016	Adapted MBAT	No	6	NA	NR	Doctoral-level therapist with degree in expressive arts therapy and >10 year's experience in mental health medicine	NR	10.00%	95.83%	NA
Johns, 2015	Adapted MBSR	No	14	NA	20 min./day, 6 days/week	MBSR instructor with 6 years of MBSR teaching experience	NR	30.19%	100.00%	100.00%
Johns, 2016	Adapted MBSR	No	16	NA	NR	MBSR-trained physician and a doctoral-level clinical health psychologist with 9 and 3 years of MBSR teaching experience, respectively	25% of audio- recorded sessions randomly reviewed; fidelity ratings were 85.1% for MBSR and 95.8% for PES	33.04%	97.18%	95.77%

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Table 3.

Author, year	Mindfulness- based intervention	Guided by theory?	Intervention dose (hours)	Retreat	Assigned home practice	Mindfulness interventionist	Fidelity monitoring	Refusal rate	Retention rate (post- intervention)	Retention rate (follow-up)
Kenne Sarenmalm, 2017	Adapted MBSR	No	16	NA	20 min./day, 6 days/week	MBSR-certified instructor	NR	NR	93.79%	NA
Lengacher, 2009	Adapted MBSR(BC)	No	12	NA	15–45 min/ day, 6 days/ week	MBSR-certified psychologist	Independent assessor monitoring session consistency, quality, and timing of activities; fidelity outcomes NR	54.50%	97.62%	NA
Lengacher, 2012	Adapted MBSR(BC)	No	12	NA	NR	MBSR-trained licensed clinical psychologist	NR	54.50%	97.62%	NA
Lengacher, 2016	Adapted MBSR(BC)	No	12	NA	15–45 min/ day, 7 days/ week	MBSR-trained clinical psychologist	Adherence to protocol evaluated using structured observational method; fidelity outcomes NR	80.45%	92.86%	92.86%
Liu, 2019	Adapted MBSR	No	20	NA	NR	MBSR-qualified psychologist	NR	NR	90.83%	85.00%
Monti, 2006	Original MBAT	Yes; Self- regulation theory; Chapman's neurodeve- lopmental approach to art therapy	20	NA	30 min./day, 6 days/week	MBSR-certified, Master's-level registered art therapist	NR	NR	83.78%	NA
Monti, 2013	Original MBAT	No	20	NA	NR	MBSR-certified mental health therapists	Psychiatrist co- investigator randomly performed fidelity checks	3.46%	76.96%	NR
Rahmani, 2014	Adapted MBSR	No	16	NA	NR	MBSR-certified master clinical psychologists	NR	NR	100.00%	100.00%
Rahmani, 2015	Adapted MBSR	No	16	NA	NR	Master clinical psychologists	NR	NR	100.00%	100.00%
Speca, 2000	Adapted MBSR	No	10.5	NA	NR	NR	NR	NR	82.57%	NA
van der Lee, 2012	MBCT	No	26 + 2.5-hour booster 2 mos. post-interv.	6-hour retreat	45 min/day, 6 days/week	MBSR-trained therapists with 16 and 8 years of MBCT teaching experience, respectively	NR	23.66%	89.00%	81.00%

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Author, year	Mindfulness- based intervention	Guided by theory?	Intervention dose (hours)	Retreat	Assigned home practice	Mindfulness interventionist	Fidelity monitoring	Refusal rate	Retention rate (post- intervention)	Retention rate (follow-up)
Witek-Janusek, 2019	Original MBSR	Ŷ	26	6-hour retreat	NR	MBSR-certified licensed clinical psychologist	Principal investigator (a PhD nurse) reviewed audio-recorded sessions for fidelity until consistency established; research assistant attended each ACC session to monitor content consistency	20.19%	83.54%	79.27%
Zernicke, 2014	Online MBCR	No	22	6-hour retreat	45 min./day, 7 days/week	Masters-level licensed clinician specializing in behavioral medicine with 15 years of online MBSR teaching experience	Principal investigator monitored online classes for treatment fidelity throughout the trial according to adapted face-to- face MBCR manual	33.89%	91.94%	NA
<i>Note:</i> ACC: Active Mindfulness-Based NA: not applicable;	 Control Condition; Art Therapy; MBC NR: not reported; I 	BC: breast cance R: Mindfulness- PES: Psycho-Edu	er; CBCT: Cognitiw Based Cancer Reco 	ely-Based Coi very; MBCT:	mpassion Training Mindfulness-Base	;; eMBCT: web-based MBC :d Cognitive Therapy; MBS	T; interv.: intervention; ¹ R: Mindfulness-Based S	MAPs: Mind tress Reducti	ful Awareness Prac ion; min.: minutes;	ices; MBAT: mo.: month;

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outcomes
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Overall

	Samp	ole Size	Effec	tt Size Estimate	9	Η¢	sterogenei	ty		Publication	ı Bias	
Post-intervention Outcome	K	u	Hedges's g	95% CI	d	б	d	I^2	Fail-safe N	Criterion N	Egger's test	d
Fatigue	17	1,592	09.0	[0.36, 0.83]	<0.001	74.99	<0.001	78.66	436	95	l(15) = 3.22	0.003
Vitality/Vigor	11	1,050	0.39	[0.25, 0.52]	<0.001	11.46	0.323	12.74	112	65	(9) = 3.68	0.003
First Follow-up Outcome												
Fatigue	12	1,165	0.42	[0.20, 0.64]	<0.001	33.60	<0.001	67.27	120	70	h(10) = 1.85	0.047
Vitality/Vigor	9	474	0.35	[0.03, 0.67]	0.030	12.42	0.029	59.75	14	40	(4) = 0.30	0.391

ty. Fail-safe N =Rosenthal's Fail-safe N. Criterion N = 5K+10. Author Manuscript

Table 5.

Meta-regression analyses examining moderators of mindfulness intervention effects on fatigue and vitality/vigor outcomes

		Sam	ole Size	Modera	tor Effect Size E	stimate	Het	erogei	neity
Moderator	Outcome	Κ	и	В	95% CI	d	$arrho_{(w)}$	df	d
Gender	Fatigue Post-intervention	17	1,592	0.01	[-0.02, 0.05]	0.472	72.44	15	<0.001
	Vitality/Vigor Post-intervention	11	1,050	-0.01	[-0.03, 0.00]	0.107	8.87	6	0.450
	Fatigue Follow-up	12	1,165	-0.01	[-0.02, 0.00]	0.077	30.48	10	0.001
	Vitality/Vigor Follow-up	9	474	-0.04	[-0.14, 0.06]	0.418	11.78	4	0.019
Age	Fatigue Post-intervention	17	1,592	-0.08	[-0.16, -0.01]	0.035	63.66	15	<0.001
	Vitality/Vigor Post-intervention	11	1,050	0.01	[-0.04, 0.06]	0.607	11.22	6	0.261
	Fatigue Follow-up	12	1,165	-0.03	[-0.09, 0.03]	0.341	32.35	10	<0.001
	Vitality/Vigor Follow-up	9	474	0.03	[-0.13, 0.18]	0.727	12.40	4	0.015
Type of Mindfulness Intervention (MBSR vs. other)	Fatigue Post-intervention	17	1,592	-0.04	[-0.85, 0.77]	0.927	74.38	15	<0.001
	Vitality/Vigor Post-intervention	11	1,050	-0.15	[-0.39, 0.10]	0.242	10.09	6	0.343
	Fatigue Follow-up	12	1,165	-0.39	[-0.96, 0.18]	0.180	32.63	10	<0.001
	Vitality/Vigor Follow-up	9	474	-0.50	[-1.15, 0.16]	0.137	8.98	4	0.062
Type of Control Condition (Active vs. Non-active)	Fatigue Post-intervention	17	1,592	-0.63	[-1.41, 0.16]	0.116	69.46	15	<0.001
	Vitality/Vigor Post-intervention	Π	1,050	-0.22	[-0.48, 0.04]	0.096	8.69	6	0.466
	Fatigue Follow-up	12	1,165	-0.36	[-0.93, 0.20]	0.207	32.62	10	<0.001
	Vitality/Vigor Follow-up	9	474	-0.44	[-1.10, 0.22]	0.194	9.45	4	0.051
Intervention Dose	Fatigue Post-intervention	17	1,592	-0.04	[-0.09, 0.02]	0.193	74.70	15	<0.001
	Vitality/Vigor Post-intervention	11	1,050	-0.02	[-0.05, 0.02]	0.374	10.61	6	0.304
	Fatigue Follow-up	12	1,165	-0.01	[-0.05, 0.03]	0.624	33.57	10	<0.001
	Vitality/Vigor Follow-up	9	474	-0.06	[-0.20, 0.08]	0.383	12.07	4	0.017
Drop-out Rate	Fatigue Post-intervention	17	1,592	-0.03	[-0.07, 0.01]	0.169	73.56	15	<0.001
	Vitality/Vigor Post-intervention	11	1,050	-0.01	[-0.02, -0.00]	0.025	6.46	6	0.693
	Fatigue Follow-up	12	1,165	-0.02	[-0.04, 0.00]	0.110	31.00	10	0.001
	Vitality/Vigor Follow-up	9	474	-0.01	[-0.03, -0.00]	0.039	8.16	4	0.086
Refusal Rate	Fatigue Post-intervention	12	1,290	-0.01	[-0.03, 0.01]	0.320	40.30	10	<0.001
	Vitality/Vigor Post-intervention	×	751	0.01	[-0.00, 0.02]	0.075	7.76	9	0.256
	Fatigue Follow-up	8	1,045	-0.00	[-0.01, 0.01]	0.978	16.19	9	0.013

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		Samp	le Size	Modera	tor Effect Size E	stimate	Het	erogei	neity
Moderator	Outcome	K	u	В	95% CI	d	$arOmega_{(w)}$	df	d
	Vitality/Vigor Follow-up	9	474	0.02	[-0.02, 0.06]	0.353	11.01	4	0.026
Follow-up Time	Fatigue Follow-up	12	1,165	-0.09	[-0.25, 0.08]	0.312	33.34	10	<0.001
	Vitality/Vigor Follow-up	9	474	-0.08	[-0.21, 0.05]	0.205	9.53	4	0.049

Note: K = number of records included the analysis. n = total number of participants included in the analysis. Q(w) = the variance within group means. Age = the average age of the sample. Gender = percent female. *Type of Mindfulness Intervention* = MBSR vs other types of mindfulness interventions (reference = MBSR). *Type of Control Condition* = active vs. non-active control condition (reference = nonactive control condition). Intervention Dose = total intervention hours. Drop-out Rate = drop-out rate at post-intervention/follow-up. Refusal Rate = total refusal rate. Follow-up Time = time between postintervention and follow-up assessment in months.