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

Shelley A. Johns, PsyD, HSPP, ABPP[1], **Will L. Tarver, DrPH, MLIS**[2], **Ekin Secinti, MS**[3], **Catherine E. Mosher, PhD**[3], **Patrick V. Stutz, BA**[1], **Jennifer L. Carnahan, MD, MPH, MA**[1], **Tasneem L. Talib, PhD**[4], **Mackenzie L. Shanahan, MS**[3], **Micah T. Faidley, BA**[1], **Kelley M. Kidwell, PhD**[5], **Kevin L. Rand, PhD**[3]

[1]Indiana University School of Medicine, Regenstrief Institute, Indianapolis, IN, USA

[2]Division of Cancer Prevention and Control, College of Medicine, The Ohio State University, Columbus, OH, USA

[3]Department of Psychology, Indiana University-Purdue University Indianapolis, Indianapolis, IN, USA

[4]Indiana University School of Nursing, Indianapolis, IN, USA

[5]Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, MI, USA

Abstract

This systematic review and meta-analysis was designed to determine the efficacy of mindfulness-based 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

Corresponding author: Shelley A. Johns, PsyD, HSPP, ABPP, Regenstrief Institute, Inc., 1101 W 10th St, RF-226, Indianapolis, IN 46202, USA. Phone: 1-317-274-9127. sheljohn@iu.edu.

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
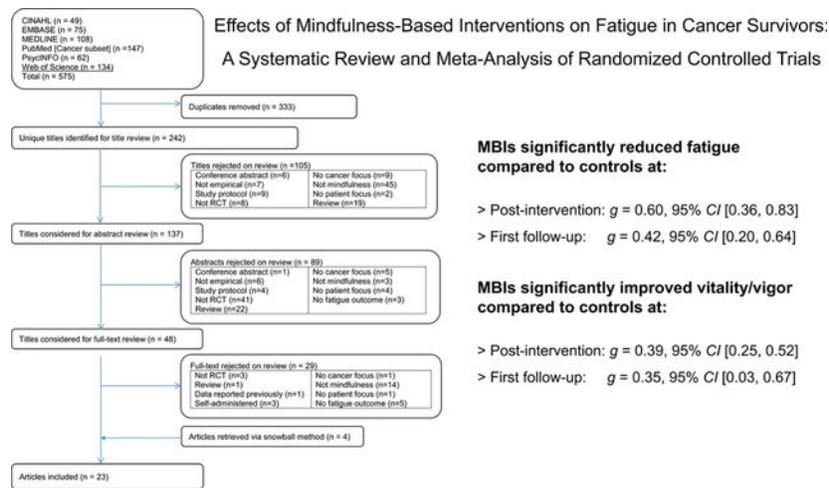
Keywords

mindfulness; cancer; fatigue; vitality; vigor; randomized controlled trial; systematic review; meta-analysis

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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 the senior author (KLR) when needed.

2.6. Quality of Evidence Assessment

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 $d = (\bar{x}_T - \bar{x}_C)/SD_P$), where $\bar{x}_T$ and $\bar{x}_C$ 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 post-intervention 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.

Acknowledgments

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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.
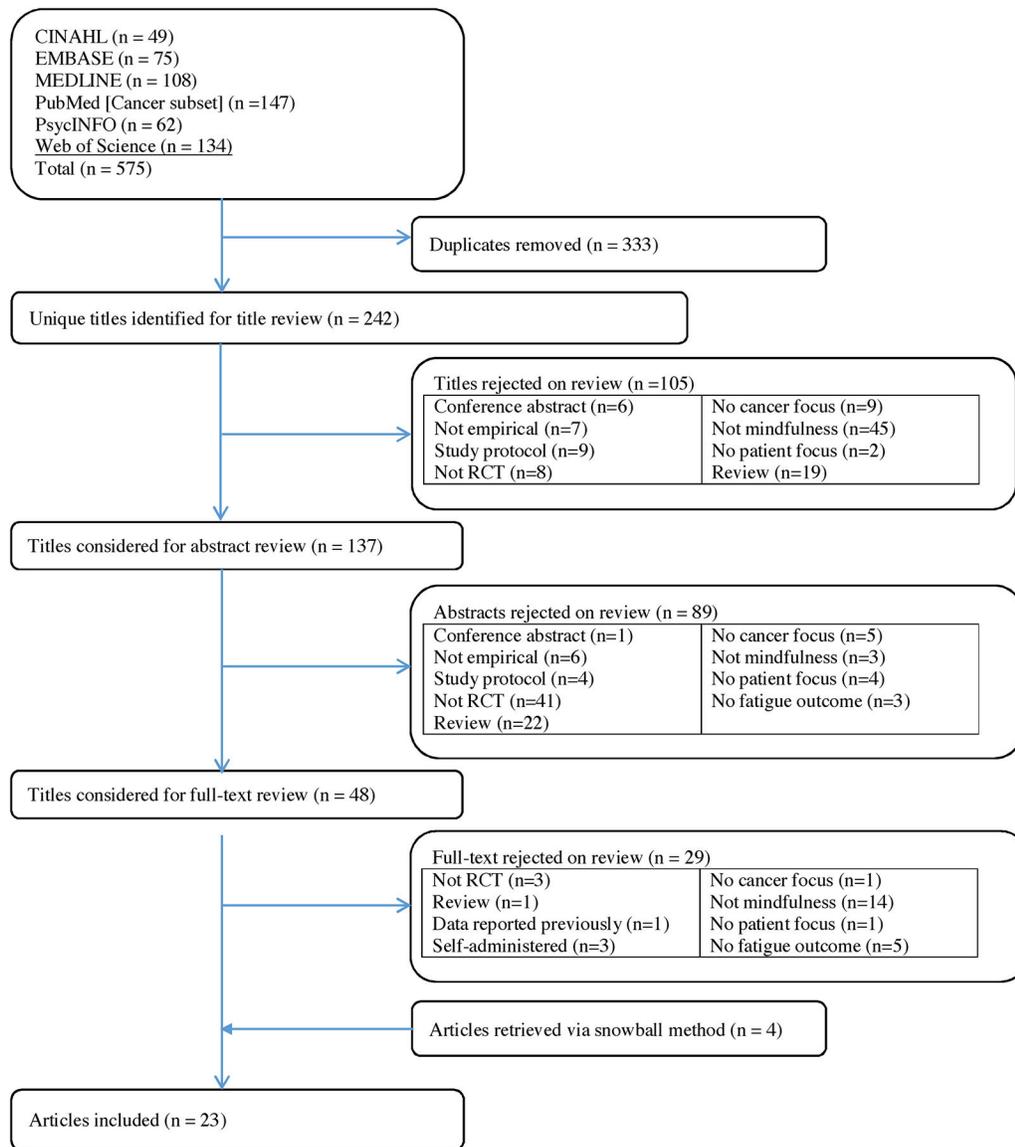
Figure 1.
Systematic review flowchart.
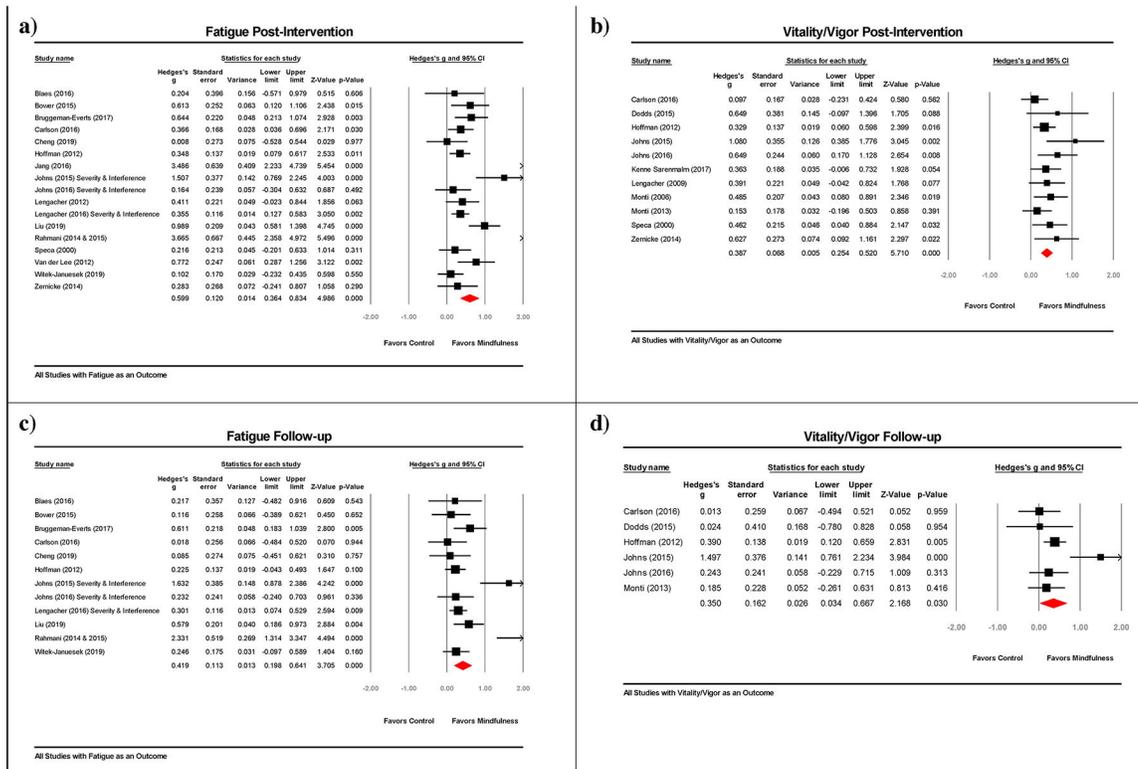
Figure 2.
Forest plots for the intervention effect on (a) fatigue at post-intervention, (b) vitality/vigor at post-intervention, (c) fatigue at follow-up, and (d) vitality/vigor at follow-up.
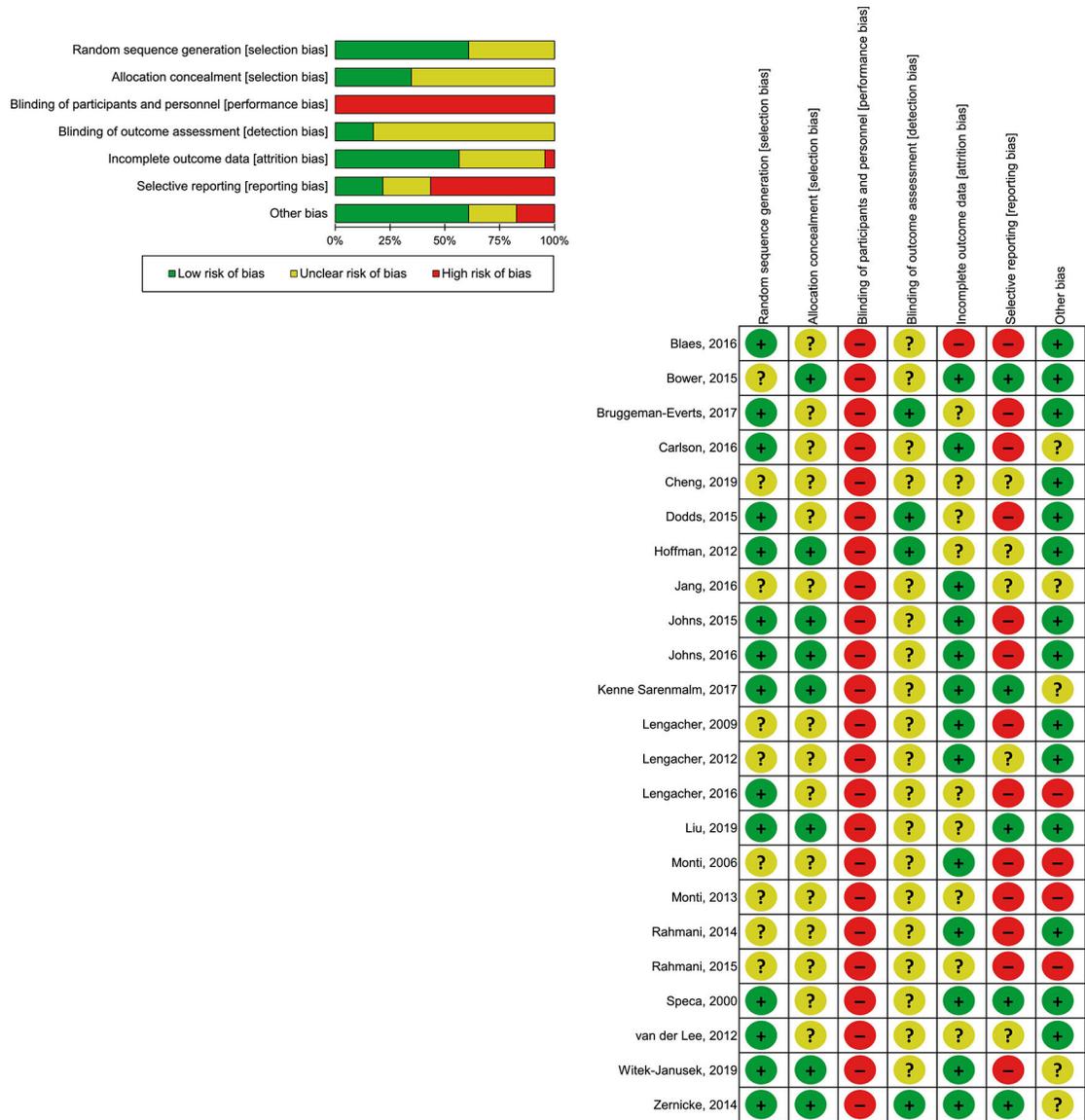
Figure 3.
Risk of bias summary of authors' judgments for each included study and risk of bias graph of authors' judgments as percentages across all included studies.

Table 1.

Operationalization of the search terms by topic.

Topic	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.

Table 2.

Characteristics of the included studies

Author, year	Sample	Fatigue eligibility criterion	Sample size		Mean age		Gender distribution [N (%) female]		Race/Ethnicity [N (%)]		Origin	Intervention		Outcome assessment	
			MBI	Control(s)	MBI	Control(s)	MBI	Control(s)	MBI	Control(s)		MBI	Control(s)	Follow-up time point(s)	Fatigue outcome (Measure)
Blaes, 2016	Any cancer type (69.0% breast), stage I-III, 6 mos. post-curative tx	NA	28	14	55	57	26 (92.9%)	12 (85.7%)	NR	NR	United States	MBCR; 8 weekly 2.5-hour sessions + 8-hour retreat	Waitlist	Post-interv. 2 mos. post-interv.	Fatigue (FACT-F)[b]
Bower, 2015	Breast cancer, stage 0-III dx at age 50, 3 mos. to 10 years post-tx (excl. hormone therapy)	NA	39	32	46.1	47.7	39 (100.0%)	32 (100.0%)	White: 29 (74.4%) Black: 1 (2.6%) Asian: 3 (7.7%) Other: 6 (15.4%)	White: 25 (78.1%) Black: 1 (3.1%) Asian: 5 (15.6%) Other: 1 (3.1%)	United States	MAPs; 6 weekly 2-hour sessions	Waitlist	Post-interv. 3 mos. post-interv.	Fatigue (FSI)
Bruggeman-Everts, 2017	Any cancer type (47.3% breast), 3 mos. post-curative tx (excl. hormone therapy), score 4 Distress Thermometer	35 CIS-FS	55	62 (AAF); 50 (PE)	51.36	56.45 (AAF); 56.54 (PE)	39 (70.9%)	44 (80.0%; AAF); 40 (80.0%; PE)	NR	NR	The Netherlands	Web-based eMBCT; 4 hours/week for 9 weeks	Home-based AAF; 3 hours/week for 9 weeks PE emails; 10 min./week for 9 weeks	Post-interv. 4 mos. post-interv.	Fatigue severity (CIS-FS)[a,b]
Carlson, 2016	Breast cancer, stage 0-IV, 3 mos. post-tx (excl. hormone therapy)	NA	134	118	55.12	54.14	134 (100.0%)	118 (100.0%)	NR	NR	Canada	MBCR; 8 weekly 1.5-hour sessions + 6-hour retreat	SET; 12 weekly 1.5-hour sessions SMS;** 1-day minimal attention waitlist	Post-interv. 6 mos. post-interv. 12 mos. post-interv.	Fatigue (POMS)[b] Vigor (POMS)[b]
Cheng, 2019	Any cancer type (65.4% breast), stage I-III, 1 mo. post-curative tx	NA	25	27	54.04[b]	53.74[b]	23 (92.0%)	24 (88.9%)	NR	NR	Taiwan	Unspecified Mindfulness interv. 12 weekly 2-hour sessions	Qigong; 12 weekly 2-hour sessions	Post-interv. 3 mos. post-interv.	Cancer Related Fatigue (CRF scale)

Author, year	Sample	Fatigue eligibility criterion	Sample size MBI	Sample size Control(s)	Mean age MBI	Mean age Control(s)	Gender distribution [N (%) female] MBI	Gender distribution [N (%) female] Control(s)	Race/Ethnicity [N (%)] MBI	Race/Ethnicity [N (%)] Control(s)	Origin	Intervention MBI	Intervention Control(s)	Follow-up time point(s)	Fatigue outcome (Measure)
Dodds, 2015	Breast cancer, stage I-IV, 10 years post-adj. systemic chemo	NA	12*	16*	54.7	55.8	12 (100.0%)	16 (100.0%)	White: 11 (91.7%) Other: 1 (8.3%)	White: 12 (75.0%) Other: 4 (25.0%)	United States	CBCT; 8 weekly 2-hour sessions + booster 1 mo. post-interv.	Waitlist	Post-interv. 1 mo. post-interv.	Vitality (SF-12)
Hoffman, 2012	Breast cancer, stage 0-III, 2 mos. to 2 years post-tx (excl. hormone therapy)	NA	103*	111*	49.0	50.1	103 (100.0%)	111 (100.0%)	NR	NR	United Kingdom	Original MBSR; 8 weekly 2-hour sessions (session 1 and 8 were 2.25 hours) + 6-hour retreat	Waitlist	Post-interv. 1 mo. post-interv.	Fatigue (POMS) Vigor (POMS)
Jang, 2016	Breast cancer, stage 0-III, <2 years post-curative tx	NA	12	12	51.75	51.42	12 (100.0%)	12 (100.0%)	NR	NR	South Korea	Adapted MBAT; 12 weekly 45-minute sessions	Waitlist	Post-interv.	Fatigue (QLQ-C30)
Johns, 2015	Any cancer type (86% breast), stage I-IV, 3 mos. post-tx (excl. hormone therapy)	4 FSI-SC	18	17	58.8	55.7	17 (94.4%)	16 (94.1%)	White: 15 (83.3%) Other: 3 (16.7%)	White: 13 (76.5%) Other: 4 (23.5%)	United States	Adapted MBSR; 7 weekly 2-hour sessions	Waitlist	Post-interv. 1 mo. post-interv.	Fatigue (FSI)[a,b] Vitality (SF-36)[b]
Johns, 2016	Breast or colorectal cancer (85% breast), stage 0-III, 3 mos. to 5 years post-tx (excl. hormone therapy)	4 FSI-SC	35	36	56.9	56.4	33 (94.3%)	31 (86.1%)	White: 27 (77.1%) Other: 8 (22.9%)	White: 23 (63.9%) Other: 13 (36.1%)	United States	Adapted MBSR; 8 weekly 2-hour sessions	PES; 8 weekly 2-hour sessions	Post-interv. 6 mos. post-interv.	Fatigue (FSI)[a] Vitality (SF-36)
Kenne Sarenmalm, 2017	Breast cancer, post-adj. chemo and/or radiation	NA	62	52 (S-MBSR); 52 (UC)	57.2	57.2 (S-MBSR); 57.2 (UC)	62 (100.0%)	52 (100.0%; S-MBSR); 52 (100.0%; UC)	NR	NR	Sweden	Adapted MBSR; 8 weekly 2-hour sessions	Self-guided MBSR; 2 hours/week for 8 weeks UC	Post-interv.	Vitality (SF-36)

Author, year	Sample	Fatigue eligibility criterion	Sample size		Mean age		Gender distribution [N (% female)]		Race/ Ethnicity [N (%)]		Origin	Intervention		Outcome assessment	
			MBI	Control(s)	MBI	Control(s)	MBI	Control(s)	MBI	Control(s)		MBI	Control(s)	Follow-up time point(s)	Fatigue outcome (Measure)
Lengacher, 2009	Breast cancer, stage 0-III, 18 mos. post-curative tx (surgery + adj. radiation or chemo)	NA	40*	42*	57.1	58.0	40 (100.0%)	42 (100.0%)	White: 36 (87.8%) Black: 2 (4.9%) Hispanic: 6 (14.6%) Other: 3 (7.3%)	White: 34 (79.1%) Black: 8 (18.6%) Hispanic: 3 (7.0%) Other: 1 (2.3%)	United States	Adapted MBSR(BC); 6 weekly 2-hour sessions	Waitlist	Post-interv.	Vitality (SF-36)[b]
Lengacher, 2012	Breast cancer, stage 0-III, 18 mos. post-curative tx (surgery + adj. radiation or chemo)	NA	40*	42*	57.1	58.0	40 (100.0%)	42 (100.0%)	White: 36 (87.8%) Black: 2 (4.9%) Hispanic: 6 (14.6%) Other: 3 (7.3%)	White: 34 (79.1%) Black: 8 (18.6%) Hispanic: 3 (7.0%) Other: 1 (2.3%)	United States	Adapted MBSR(BC); 6 weekly 2-hour sessions	Waitlist	Post-interv.	Fatigue symptom cluster (MDASI)
Lengacher, 2016	Breast cancer, stage 0-III, 2 weeks to 2 years post-tx	NA	167	155	56.5	57.6	167 (100.0%)	155 (100.0%)	White: 112 (67.1%) Black: 21 (12.6%) Hispanic: 19 (11.4%) Other: 15 (9.0%) NR: 0 (0.0%)	White: 110 (71.0%) Black: 16 (10.3%) Hispanic: 14 (9.0%) Other: 13 (8.4%) NR: 2 (1.3%)	United States	Adapted MBSR(BC); 6 weekly 2-hour sessions	Waitlist	Post-interv. 1.5 mos. post-interv.	Fatigue (FSI)
Liu, 2019	Differentiated thyroid cancer (DTC), stage I-IV (excl. metastasis to other organ), first upcoming radioactive iodine tx scheduled	NA	49*	53*	43.32	42.38	34 (69.4%)	38 (71.7%)	NR	NR	China	Adapted MBSR; 8 weekly 2.5-hour sessions	UC	Post-interv. 3 mos. post-interv.	Fatigue (QLQ-C30)

Author, year	Sample	Fatigue eligibility criterion	Sample size MBI	Sample size Control(s)	Mean age MBI	Mean age Control(s)	Gender distribution [N (%) female] MBI	Gender distribution [N (%) female] Control(s)	Race/Ethnicity [N (%)] MBI	Race/Ethnicity [N (%)] Control(s)	Origin	Intervention MBI	Intervention Control(s)	Outcome assessment Follow-up time point(s)	Outcome assessment Fatigue outcome (Measure)
Monti, 2006	Any female cancer type (46% breast), stage 0-IV, 4 mos. to 2 years post-dx	NA	56	55	53.1	54.1	56 (100.0%)	55 (100.0%)	White: 45 (80.4%) Black: 10 (17.9%) Asian: 1 (1.8%) Hispanic: 0 (0.0%) Other: 0 (0.0%)	White: 38 (69.1%) Black: 13 (23.6%) Asian: 1 (1.8%) Hispanic: 2 (3.6%) Other: 1 (1.8%)	United States	Original MBAT; 8 weekly 2.5-hour sessions	Waitlist	Post-interv.	Vitality (SF-36)[b]
Monti, 2013	Breast cancer, stage 0-IV, 6 mos. to 3 years post-dx or post-recurrence	NA	98	93	56.9	56.4	98 (100.0%)	93 (100.0%)	White: 59 (60.2%) Black: 35 (35.7%) Other: 4 (4.1%)	White: 54 (58.1%) Black: 37 (38.8%) Other: 2 (2.2%)	United States	Original MBAT; 8 weekly 2.5-hour sessions	BCSG; 8 weekly 2.5-hour sessions	Post-interv. 6 mos. post-interv.	Vitality (SF-36)[b]
Rahmani, 2014	Breast cancer, stage I-III, 1 mo. post-dx	NA	12	12 (MCT); 12 (UC)	43.25	44.92 (MCT); 44.08 (UC)	12 (100.0%)	12 (100.0%; MCT); 12 (100.0%; UC)	NR	NR	Iran	Adapted MBSR; 8 weekly 2-hour sessions	MCT; 8 weekly sessions UC	Post-interv. 2 mos. post-interv.	Fatigue (QLQ-C30)
Rahmani, 2015	Breast cancer, stage I-III, 1 mo. post-dx	>4 FSS-P	12	12	43.25	44.08	12 (100.0%)	12 (100.0%)	NR	NR	Iran	Adapted MBSR; 8 weekly 2-hour sessions	UC	Post-interv. 2 mos. post-interv.	Fatigue severity (FSS-P)[a]
Speca, 2000	Any cancer type (43% breast), stage I-IV	NA	53*	37*	54.9	48.9	46 (86.8%)	27 (73.0%)	NR	NR	Canada	Adapted MBSR; 7 weekly 1.5-hour sessions	Waitlist	Post-interv.	Fatigue (POMS) Vigor (POMS)
van der Lee, 2012	Any cancer type (60% breast), 1 year post-curative tx	35 CIS-FS	59*	24*	53.1	49.4	51 (86.4%)	19 (79.2%)	NR	NR	The Netherlands	Adapted MBCT; 8 weekly 2.5-hour sessions + 6-hour retreat + 2.5-hour booster 2	Waitlist	Post-interv. 6 mos. post-interv.	Fatigue severity (CIS-FS)[a]

Author, year	Sample	Fatigue eligibility criterion	Sample size		Mean age		Gender distribution [N (%) female]		Race/ Ethnicity [N (%)]		Origin	Intervention		Outcome assessment	Fatigue outcome (Measure)
			MBI	Control(s)	MBI	Control(s)	MBI	Control(s)	MBI	Control(s)		MBI	Control(s)	Follow-up time point(s)	
Witek-Janusek, 2019	Breast cancer, stage 0-III, post-surgery	NA	84 *	80 *	55	55.2	84 (100.0%)	80 (100.0%)	White: 68 (81.0%) Black: 10 (11.9%) Asian: 1 (1.2%) Hispanic: 2 (2.4%) Other: 1 (1.2%) NR: 2 (2.4%)	White: 58 (72.5%) Black: 13 (16.3%) Asian: 1 (1.3%) Hispanic: 5 (6.3%) Other: 2 (2.5%) NR: 1 (1.3%)	United States	Original MBSR; 8 weekly 2.5-hour sessions + 6-hour retreat (after week 5)	ACC 8 weekly 2.5-hour sessions of education	Interv. midpoint Post-interv. 1 mo. post-interv. 6 mos. post-interv. mos. post-interv.	Fatigue (MFSI-SF)
Zernicke, 2014	Any cancer type (33.9% breast), 3 years post-tx	NA	30	32	58	58	22 (73.3%)	23 (71.9%)	NR	NR	Canada	Online MBCR 8 weekly 2-hour sessions + 6-hour retreat (after week 6)	Waitlist	Post-interv.	Fatigue (POMS) [b] Vigor (POMS) [b]

Note. AAF: Ambulant Activity Feedback; ACC: Active Control Condition; adj.: adjuvant; BC: breast cancer; BCSG: Breast Cancer Support Group; BL: baseline; CBCT: Cognitively-Based Compassion Training; chemo: chemotherapy; CIS-FS: Checklist Individual Strength-Fatigue Severity subscale; CRF scale: Cancer Related Fatigue scale; dx: diagnosis; eMBCT: web-based MBCT; excl.: excluding; FACT-F: Functional Assessment in Cancer Therapy-Fatigue; FSI: Fatigue Symptom Inventory; FSI-SC: Fatigue Symptom Inventory-Severity Composite; FSS-P: Fatigue Severity Scale - Persian; interv.: intervention; MAPs: Mindful Awareness Practices; MBAT: Mindfulness-Based Art Therapy; MBCR: Mindfulness-Based Cancer Recovery; MBCT: Mindfulness-Based Cognitive Therapy; MBI: Mindfulness-based intervention; MBSR: Mindfulness-Based Stress Reduction; MCT: Metacognitive Therapy; MDASI: MD Anderson Symptom Inventory; MFSI-SF: Multidimensional Fatigue Scale Inventory-Short Form; min.: minutes; mo.: month; NA: not applicable; NR: not reported; PE: Psycho-educational; PES: Psycho-Educational Support; POMS: Profile of Mood States; QLQ-C30: Quality of Life Questionnaire-Core 30; SET: Supportive Expressive Therapy; SF-12: Medical Outcome Study-Short Form 12-Item Health Survey; SF-36: Medical Outcomes Study-Short Form 36-Item General Health Survey; SMS: Stress Management Seminar; tx: treatment; UC: Usual Care.

*
Number analyzed in outcome sample; full randomized sample *N* differs slightly.

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

[a]
Primary outcome(s) of the respective study.

[b]
Some of the data were not reported in study publications but were provided by the authors upon request.

Table 3.

Characteristics of mindfulness-based interventions

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	9	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%

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 neurodevelopmental 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%

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	No	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

Note: ACC: Active Control Condition; BC: breast cancer; CBCT: Cognitively-Based Compassion Training; eMBCT: web-based MBCT; interv.: intervention; MAPs: Mindful Awareness Practices; MBAT: Mindfulness-Based Art Therapy; MBCR: Mindfulness-Based Cancer Recovery; MBCT: Mindfulness-Based Cognitive Therapy; MBSR: Mindfulness-Based Stress Reduction; min.: minutes; mo.: month; NA: not applicable; NR: not reported; PES: Psycho-Educational Support.

Table 4.

Overall effect sizes for fatigue and vitality/vigor outcomes

Post-intervention Outcome	Sample Size		Effect Size Estimate			Heterogeneity				Publication Bias		
	K	n	Hedges's g	95% CI	p	Q	p	I²	Fail-safe N	Criterion N	Egger's test	p
Fatigue	17	1,592	0.60	[0.36, 0.83]	<0.001	74.99	<0.001	78.66	436	95	t(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	t(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	t(10) = 1.85	0.047
Vitality/Vigor	6	474	0.35	[0.03, 0.67]	0.030	12.42	0.029	59.75	14	40	t(4) = 0.30	0.391

Note: K = number of studies. n = total number of participants included in the analysis. Q = Cochran's (1954) Q-statistic of heterogeneity. I^2 = percentage of between-study variability. Fail-safe N = Rosenthal's Fail-safe N. Criterion N. Criterion N = 5K+10.

Table 5.

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

Moderator	Outcome	Sample Size		Moderator Effect Size Estimate			Heterogeneity		
		K	n	B	95% CI	p	$Q_{(w)}$	df	p
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	9	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	6	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	9	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	6	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	9	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	6	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	11	1,050	−0.22	[−0.48, 0.04]	0.096	8.69	9	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	6	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	9	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	6	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	9	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	6	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	8	751	0.01	[−0.00, 0.02]	0.075	7.76	6	0.256
	Fatigue Follow-up	8	1,045	−0.00	[−0.01, 0.01]	0.978	16.19	6	0.013

Moderator	Outcome	Sample Size		Moderator Effect Size Estimate			Heterogeneity		
		K	n	B	95% CI	p	$Q_{(w)}$	df	p
	Vitality/Vigor Follow-up	6	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	6	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 = non-active 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 post-intervention and follow-up assessment in months.