

The Effect of Mindfulness-Based Therapy on Symptoms of Anxiety and Depression in Adult Cancer Patients and Survivors: A Systematic Review and Meta-Analysis

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Objective: The use of mindfulness-based therapy (MBT) in oncology settings has become increasingly popular, and research in the field has rapidly expanded. The objective was by means of a systematic review and meta-analysis to evaluate the current evidence for the effect of MBT on symptoms of anxiety and depression in adult cancer patients and survivors. **Method:** Electronic databases were searched, and researchers were contacted for further relevant studies. Twenty-two independent studies with a total of 1,403 participants were included. Studies were coded for quality (range: 0–4), and overall effect size analyses were performed separately for nonrandomized studies ($K = 13$, $n = 448$) and randomized controlled trials (RCTs; $K = 9$, $n = 955$). Effect sizes were combined using the random-effects model. **Results:** In the aggregated sample of nonrandomized studies (average quality score: 0.5), MBT was associated with significantly reduced symptoms of anxiety and depression from pre- to posttreatment corresponding to moderate effect sizes (Hedges's g) of 0.60 and 0.42, respectively. The pooled controlled effect sizes (Hedges's g) of RCTs (average quality score: 2.9) were 0.37 for anxiety symptoms ($p < .001$) and 0.44 for symptoms of depression ($p < .001$). These effect sizes appeared robust. Furthermore, in RCTs, MBT significantly improved mindfulness skills (Hedges's $g = 0.39$). **Conclusion:** While the overall quality of existing clinical trials varies considerably, there appears to be some positive evidence from relatively high-quality RCTs to support the use of MBT for cancer patients and survivors with symptoms of anxiety and depression.

Keywords: mindfulness, cancer, anxiety, depression, meta-analysis

Anxiety and depression are common and debilitating problems associated with diagnosis and treatment of cancer. Compared to the general population, depression is more prevalent in cancer patients (e.g., Christensen et al., 2009; Honda & Goodwin, 2004), and depression has been associated with prolonged hospitalization (Prieto et al., 2002), higher mortality (Pinquart & Duberstein, 2010), and reduced quality of life (Reich, Lesur, & Perdrizet-Chevallier, 2008). The deteriorating effect of depression on health may be larger when depression is comorbid with a medical disease (Moussavi et al., 2007). Apparently, there is a bidirectional relationship between cancer and depression. The prevalence of depression increases with severity of cancer, and there is some evidence

to suggest that depression predicts cancer progression (Spiegel & Giese-Davis, 2003). Recent research indicates that depression is associated with various biological markers of inflammation, including so-called pro-inflammatory cytokines (e.g., Howren, Lamkin, & Suls, 2009). Following an infection, the physiological concentrations of pro-inflammatory cytokines have been found to induce symptoms of sickness, including fatigue, sleepiness, loss of appetite, and social withdrawal (Dantzer & Kelley, 2007). From these observations, it has been hypothesized that pro-inflammatory cytokines, due to prolonged activation of the peripheral immune system in some medically ill people, including cancer patients, may act on the brain in ways that lead to the development of symptoms of depression (Dantzer, O'Connor, Freund, Johnson, & Kelly, 2008).

Moreover, depression is often further complicated by comorbid anxiety, which may lead to more severe psychological symptoms and greater psychosocial disability, compared to patients with only one of these disorders (Hirschfeld, 2001). Of those who meet the criteria for major depression, approximately 50% in the general population and 65% in primary care settings also suffer from an anxiety disorder (Kessler et al., 1996; Olfson et al., 1997). Large-scale studies using self-report methods have found that clinically significant emotional distress, including symptoms of anxiety and depression, is prevalent in about 35% of all cancer patients (e.g., Carlson et al., 2004; Zabora, Brintzenhofesoc, Curbow, Hooker,

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& Piantadosi, 2001). In many cases these symptoms persist for months or even years after cancer treatment completion (e.g., Bleiker, Pouwer, van der Ploeg, Leer, & Ader, 2000). According to a meta-analysis of studies using standardized diagnostic interviews, the prevalence of major depression and anxiety disorders in patients with cancer is approximately 15% and 10%, respectively, and 38% for any mood disorder (Mitchell et al., 2011). Meanwhile, the prevalence of depression seems to vary as a function of cancer type, with the highest rates found among patients with pancreatic, oropharyngeal, lung, and breast cancer (Massie, 2004). It is also important to note that the risk of developing anxiety or depression is particularly high during the first year following cancer diagnosis (e.g., Burgess et al., 2005; Rowland, 1999). In a 5-year observational cohort study, Burgess et al. (2005) found that almost 50% of women with early breast cancer fulfilled the criteria for disorders of anxiety or depression in the first year after cancer diagnosis. Thus, in general, symptoms of anxiety and depression among cancer patients appear to be well documented, and early identification and effective treatment should be considered essential for comprehensive cancer care.

Recently, mindfulness-based therapy (MBT) has become an increasingly popular psychological intervention for cancer patients, and in the past 10 years, several studies of MBT for cancer patients have emerged in the research literature. MBT was derived from ancient eastern meditation and yoga traditions, particularly Buddhism, and has been secularized and adapted to meet the needs of the Western population. Mindfulness is generally defined as intentional nonjudgmental awareness of present-moment experiences (e.g., Baer, 2003; Kabat-Zinn, 2003). MBT includes mindfulness-based stress reduction (MBSR; Kabat-Zinn, 1990) and mindfulness-based cognitive therapy (MBCT; Segal, Williams, & Teasdale, 2002). Both are clinical group intervention programs used for acute reduction of distress symptoms as well as for relapse prevention by means of systematic training in mindfulness meditation combined with didactic and experiential learning methods. The aim of MBT is to teach participants to deal more effectively with experience as it arises in the present moment, including nonjudgmental awareness of feelings, thoughts, and bodily sensations. Aiming at counteracting experiential avoidance and developing greater emotional tolerance, participants are gradually taught to turn toward and accept intense bodily sensations and emotional discomfort as they engage in different mindfulness practices, such as the body scan, simple yoga exercises, walking meditation, and prolonged periods of sitting meditation. Through the practice of mindfulness, patients are provided with attentional skills that allow them to recognize the automatic activation of dysfunctional thought processes, including depression-related rumination, and to disengage from these by redirecting attention to experience as it unfolds and changes moment by moment (Kabat-Zinn, 1990; Segal et al., 2002). At the core of MBT is the ability to step back from analytic thought and verbal problem solving to simply allow experience to be as it is.

Paying attention to present-moment reality, cultivated by the practice of mindfulness, may be of particular importance to cancer patients. One could speculate that some sources of stress, anxiety, and depression for cancer patients may be related to concerns about the past (e.g., rumination about the causes of cancer or regrets about former life priorities) and future-related worries (e.g., fear of increased pain, psychological suffering, or the loss of life

itself). Hence, it is possible that formal periods of mindfulness practice can serve as a restorative refuge into the present moment, free from the inexorable demands and worries of life as a cancer patient (Specia, Carlson, Mackenzie, & Angen, 2006).

Results from meta-analyses suggest that MBT is effective for reduction of psychological distress, including symptoms of anxiety and depression, in nonclinical populations (Chiesa & Serretti, 2009), chronic medical diseases (Bohlmeijer, Prenger, Taal, & Cuijpers, 2010), cancer patients (Ledesma & Kumano, 2009), and across various clinical samples (e.g., anxiety and mood disorders, eating disorders, heart disease, cancer, pain disorders, and diabetes; Baer, 2003; Grossman, Niemann, Schmidt, & Walach, 2004; Hofmann, Sawyer, Witt, & Oh, 2010). Furthermore, results from a recent meta-analysis of six large randomized controlled trials (RCTs) indicate that MBCT effectively reduces the risk of relapse for patients with recurrent major depressive disorder (Piet & Hougaard, 2011).

As more studies have been published, the efficacy of MBT for cancer patients has been evaluated in a number of narrative reviews (Matchim & Armer, 2007; Ott, Norris, & Bauer-Wu, 2006; Shennan, Payne, & Fenlon, 2011; Smith, Richardson, Hoffman, & Pilkington, 2005). These reviews generally conclude that MBT leads to improvements in mood and stress symptoms, suggesting that MBT is a promising intervention for oncology patients. However, none of these studies have attempted to quantify the results from the included studies. Two more recent systematic reviews have included quantitative, that is, meta-analytic, methods to evaluate the effect of MBT. In the first meta-analysis, Ledesma and Kumano (2009) included 10 studies (seven nonrandomized studies, three RCTs) of mindfulness treatment programs for cancer patients published between 2000 and 2007 and reported moderate to small pooled effect sizes (ESs) for combinations of various measures of mental (Cohen's $d = 0.48$) and physical health ($d = 0.18$). It could be argued, however, that the included studies were less suitable for meta-analysis, as the types and durations of mindfulness training differed considerably between studies. For example, one study included in the review combined mindfulness training and art therapy, and treatment duration varied from 6 to 15 weeks between studies. Furthermore, as the outcome measures were lumped together in two broad categories, the interpretability of results may be limited. In the second and more recent meta-analysis of 39 studies, Hofmann et al. (2010) analyzed the efficacy of MBT on symptoms of anxiety and depression in a broad range of psychological and medical disorders. For the nine studies (seven nonrandomized studies, two RCTs) that had included cancer patients, they found a pooled uncontrolled ES (Hedges's g) of 0.63 ($p < .01$) for symptoms of anxiety (eight studies) and 0.45 ($p < .01$) for symptoms of depression (seven studies). Since the publication of this meta-analysis, several RCTs have been conducted, and the overall empirical literature of MBT for cancer patients has more than doubled. However, at this point in time, there has been no meta-analysis investigating the controlled effect of RCTs of MBT on symptoms of anxiety and depression in cancer patients and survivors. In addition, change in mindfulness skills associated with MBT has not been quantitatively evaluated across studies.

The present article reports the first formally adequate meta-analytic evaluation, conducted according to the Meta-Analysis Reporting Standards (MARS) established by the American Psychological Association (APA; APA Publications and Communica-

tions Board Working Group on Journal Article Reporting Standards, 2008), of MBT for symptoms of anxiety and depression in cancer patients. To avoid excluding a substantial portion of the existing outcome research, we chose a comprehensive approach, including all available studies. However, taking the quality of the trials into consideration, meta-analyses were conducted separately for nonrandomized studies and RCTs. Our objective was by means of meta-analysis of the currently available results to test the hypothesis that MBT is an effective treatment for reduction of symptoms of anxiety and depression in adult cancer patients and survivors. Furthermore, we expected MBT to be associated with improved mindfulness skills.

Method

Inclusion Criteria

Studies were included in the meta-analysis using the following eligibility criteria:

Type of studies: Studies of MBSR or MBCT for cancer patients or cancer survivors, reported in the English language.

Type of participants: Participants aged 18 years or above with a current or former diagnosis of cancer.

Type of interventions: MBSR or MBCT conducted according to Kabat-Zinn (1990) or Segal et al. (2002), respectively.

Type of outcome measures: Validated continuous measures of anxiety or depression symptom severity, included at both pre- and postintervention, with reported data sufficient for estimating ESs.

Search Strategies

Several electronic databases (EMBASE, PubMed, PsycINFO, Web of Science, Scopus, and the Cochrane Controlled Trials Register) were searched to identify eligible studies from first available year to March 5, 2012, using the search terms ((mindfulness*) OR (MBSR) OR (MBCT)) AND cancer). Reference lists of selected articles and other reviews were inspected, relevant studies registered at ClinicalTrials.gov were identified, and researchers in the field of MBT for cancer were contacted for relevant unpublished studies. First, duplicates were removed from the total sample of identified records. Abstracts from the remaining records were then screened, and relevant articles were retrieved for eligibility assessment. Studies fulfilling the inclusion criteria were then selected for evaluation by means of meta-analysis. The search was conducted independently by the first author (Jacob Piet), and the retrieval process was double-checked by the second author (Hanne Würtzen). Disagreement was resolved by discussion.

Coding Procedures

A coding sheet for extraction of data from the included studies was developed by the last author (Robert Zachariae), and the following information was collected independently by the first (Jacob Piet) and second authors (Hanne Würtzen): (a) participant characteristics (including age, sex, disease characteristics [cancer

type and stage], treatment [radiation and/or chemotherapy], and time since diagnosis), (b) group characteristics (including type of MBT, comparison condition, number of participants in each group, number of MBT sessions, and adherence to MBT), (c) type of outcome measures (including severity of anxiety and depression symptoms, and measures of mindfulness), and (d) methodological quality of studies using the Jadad scale (Jadad et al., 1996) by assigning one point for each of the following criteria modified to account for difficulties in blinding participants to MBT: (1) The study was randomized; (2) the randomization procedure was described and appropriate, that is, allocation was randomly conducted independent of the investigators, using methods that allowed each participant equal chance of being assigned to either the intervention or control condition; (3) blind outcome assessment was reported (blinding of both therapists and participants, as required by the original Jadad criteria, is not possible); and (4) number and reasons of withdrawals and dropouts were collected and reported for each group. One point was given for each Jadad criterion met, yielding a maximum total score ranging from 0 to 4. The results of the data extraction of the two authors were compared, and any disagreements were resolved by discussion. In addition, for study quality scoring, the interrater reliability was assessed.

Statistical Methods

Computed ES statistics were standardized weighted mean differences based on Hedges's g for continuous measures of anxiety, depression, and mindfulness. ESs were weighted by the inverse standard error (i.e., taking the precision of each study into account) and presented with 95% confidence intervals (CIs). Hedges's g is a variation of Cohen's d (Cohen, 1988), correcting for potential bias due to small sample sizes (Hedges & Olkin, 1985). According to Cohen's (1988) ES conventions, the magnitude of Hedges's g can be expressed as small (0.2), medium (0.5), and large (0.8).

Quantitative data syntheses were carried out separately for (a) nonrandomized studies and (b) RCTs. ESs derived from nonrandomized studies were based on pre–post within-group differences. To estimate pre–post within-group ESs (i.e., the magnitude of pre–post changes in the treatment group alone), the standard deviation of the difference between means is used, and the correlation between respective time point measures is required.¹ The information needed to calculate this correlation is rarely available from study reports, and when it was unavailable, we therefore, as recommended by Rosenthal (1993), assumed a conservative estimation of $r = .7$ for each included study. ESs derived from RCTs were based on mean pre- to posttreatment change scores (using the standard deviation of posttreatment scores) for both MBT and

¹ Within-group pre–post ESs were calculated using the following formula: $d = \left(\frac{Y_1 - Y_2}{S_{\text{diff}}} \right) \sqrt{2(1 - r)}$, where Y_1 and Y_2 are the pre- and posttreatment sample means, S_{diff} is the standard deviation of the difference, and r is the correlation between pre- and posttreatment scores. Cohen's d was converted to Hedges's g using a correction factor: $J = 1 - \frac{3}{4df - 1}$, where df is the degrees of freedom used to estimate the within-group standard deviation. For within-group ESs, the degrees of freedom for calculating J are $n - 1$, where n is the treatment group sample size. Then, $g = J \times d$.

control conditions.² To investigate the longer term effects associated with MBT, we analyzed change in symptoms of anxiety and depression from pretreatment to the last available follow-up period.

To obtain a summary statistic, ESs were pooled across studies using the inverse variance random-effects model (DerSimonian & Laird, 1986). In this model, ES parameters for individual studies are treated as if they are a random sample from a larger population, thus allowing for generalization beyond the observed studies (Hedges & Vevea, 1998). Independence of results was ensured for all analyses. Thus, if a study reported results for more than one type of outcome measure of either anxiety or depressive symptom severity, an average ES across respective measures was calculated, so that only one result per study was used for each quantitative data synthesis.

Funnel plots of study ESs and fail-safe N statistics were applied to detect potential bias in the publication of study results. A funnel plot is a graphic illustration of ESs from individual studies in relation to a measure of study size or precision. In general, estimates of effect have more precision the larger the study, and therefore, ESs derived from smaller studies are likely to scatter more widely at the bottom of the graph. In the absence of bias, the plot should resemble an inverted funnel, with ESs symmetrically distributed in relation to the overall mean ES (Sterne, Egger, & Moher, 2008). We included a formal test of funnel-plot asymmetry provided by Egger, Smith, Schneider, and Minder (1997) to examine whether the association between ESs and a measure of study size, such as the standard error of the effects, was significantly greater than what could be expected by chance alone. The funnel-plot trim and fill method by Duval and Tweedie (2000) was used to test and (if needed) adjust for possible bias in the pooled ES by taking into account ESs from the estimated number of missing studies. The fail-safe N statistic was included to provide an estimate of the number of unpublished or unretrieved equal-sample-size studies with an ES of zero needed to reduce the overall effect to a nonsignificant level ($p > .05$; Rosenthal & Rubin, 1988). Rosenthal (1991) has suggested that a fail-safe number exceeding $5K + 10$, with K being the number of studies included in the meta-analysis, is a robust indicator of no publication bias due to the file drawer problem.

To establish whether the results of studies were consistent, tests of heterogeneity were conducted using Q and I^2 statistics. Q calculates the probability value for heterogeneity of studies. The I^2 quantity provides a measure of the degree of inconsistency in studies by estimating the amount of variance in a pooled ES that can be accounted for by heterogeneity in the sample of studies (Higgins, Thompson, Deeks, & Altman, 2003). An I^2 value of 0% indicates no observed heterogeneity, while values of 25%, 50%, and 75% are considered low, moderate, and high, respectively.

Prior to the literature search, a statistical power analysis was carried out following the procedure suggested by Hedges and Pigott (2001). The two RCs of the effects of MBT on symptoms of anxiety and/or depression in cancer patients or survivors available to Hofmann and colleagues (2010) had a mean sample size of 86. Under the assumption that subsequently published RCTs would have used sample sizes of at least the same magnitude, it was estimated that we would be able to detect a small to moderate pooled ES (Cohen's $d = 0.3$) with a total of seven RCTs with an

alpha of 5% and a statistical power of 80%, using a random-effects model.

Statistical analyses were conducted manually and with the computer software program Comprehensive Meta-Analysis, Version 2 (Borenstein, Hedges, Higgins, & Rothstein, 2005). Overall, the study followed the APA MARS, which provide detailed information recommended for inclusion in manuscripts reporting meta-analyses (APA Publications and Communications Board Working Group on Journal Article Reporting Standards, 2008).

Results

Study Selection

The study selection process is illustrated in Figure 1 using the PRISMA flow diagram (Moher, Liberati, Tetzlaff, Altman, & the PRISMA Group, 2009) with reasons for exclusion. Our search strategy identified a total of 670 records, of which 22 independent studies, fulfilling the inclusion criteria, were selected for meta-analytic evaluation.

Study Characteristics

Characteristics of the 22 included studies are summarized in Table 1. All studies investigated the effect of MBSR ($K = 18$) or MBCT ($K = 4$) for symptoms of anxiety or depression in cancer patients or survivors (in this article, K refers to number of included studies, n to number of participants). Sample sizes varied from 12 to 267, with a total of 1,403 participants. Participants included in the studies were patients with breast cancer ($K = 8$), prostate cancer ($K = 1$), or mixed cancers ($K = 13$). As patient characteristics for each study were generally reported for the initial sample, the following summary of information for participants included in the meta-analysis (mainly completers) is merely an approximation. The majority of participants (approximately 77%) were breast cancer patients. In the total sample, the mean age was approximately 55 years (range: 48–67), and approximately 85% were women (range: 0%–100%). In studies reporting adherence to MBT ($K = 10$), an average of 81% (range: 63%–96%) attended at least 75% of all MBT sessions. Fifteen studies reported data on time since diagnosis using either the mean, median, or intervals. The average mean time since diagnosis was 34.4 months (range: 24–69) for nonrandomized studies ($K = 5$) and 24.3 months (range: 8–46) for RCTs ($K = 4$). Within RCTs, there were no differences in time since diagnosis between MBT and controls. Among 14

² Controlled pre–post ESs were calculated using the following formula:

$$d = \frac{\Delta_1 - \Delta_2}{\sqrt{\frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{n_1 + n_2 - 2}}}$$

where Δ_1 and Δ_2 are the mean pre–post change scores for the treatment group and control condition, respectively; n_1 and n_2 are the sample sizes of each group; and S_1 and S_2 are the standard deviations of the posttreatment scores for each group. Cohen's d was then converted to Hedges's g using correction factor J . For controlled ESs, $J = 1 - \frac{3}{4df - 1}$, where df is the degrees of freedom used to estimate the within-groups standard deviation, pooled across groups. The degrees of freedom for calculating J for two independent groups are $n_1 + n_2 - 2$. Then, $g = J \times d$.

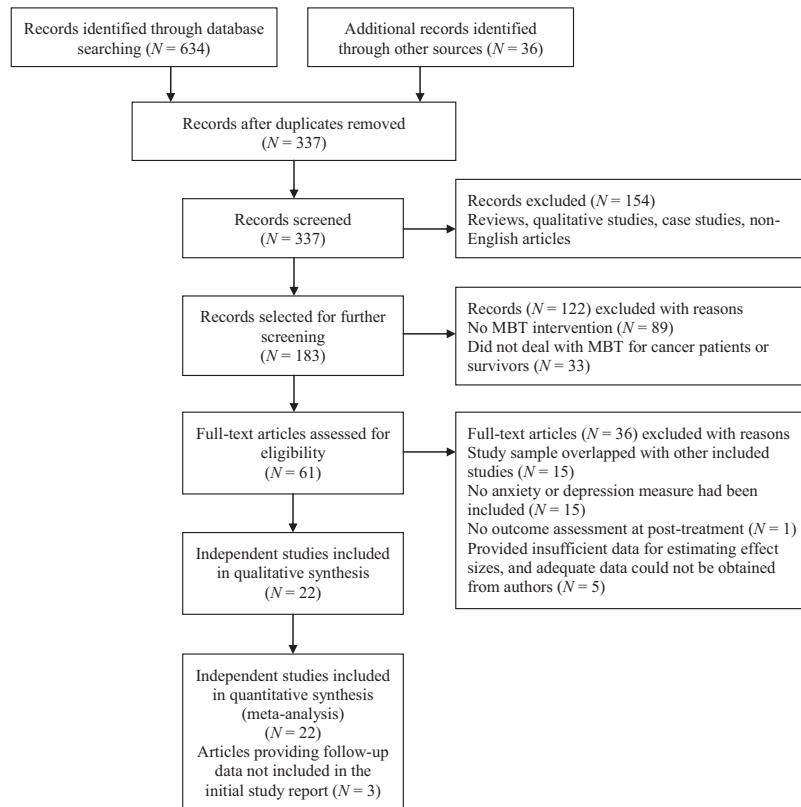


Figure 1. Flow of information from identification to inclusion of studies. MBT = mindfulness-based therapy.

studies with available data, seven studies (three nonrandomized studies and four RCTs) reported active radiation and/or chemotherapy at baseline for a subset of participants (range: 11%–80%). In the four RCTs (Hoffman, Ersser, Hopkinson, Nicholls, & Harrington, 2012; Kingston et al., 2012; Lengacher et al., 2009; Würtzen et al., 2012), there were no significant differences between groups for this variable. In general, all RCTs reported successful randomization, that is, no significant baseline differences between MBT and controls on a number of patient characteristics, such as age, employment status, educational status, relationship status, income, cancer type and stage, time since diagnosis, comorbidities, use of medication, and current cancer treatments. However, not all of these variables were assessed in all RCTs.

In all, data from 13 nonrandomized studies and nine RCTs were available to us. Two nonrandomized studies included a control group, comparing MBT to either a healing arts program or a wait-list control condition (Garland, Carlson, Cook, Lansdell, & Specia, 2007; Labelle, Campbell, & Carlson, 2010). The nine RCTs compared MBT to wait-list controls ($K = 6$) or treatment as usual ($K = 3$). Five RCTs reported data on intention-to-treat (ITT) participants with last observation carried forward (LOCF) as the most common method for substitution of missing values.³ Of the 22 included studies, three were unpublished, that is, study manuscripts were either in progress (Johns, Brown, Beck-Coon, Monahan, & Kroenke, 2012) or submitted for publication (Kingston et al., 2012; Würtzen et al., 2012). On average, the number of MBT

sessions was 7.8 (range: 6–8). Eight studies (four nonrandomized studies, four RCTs) obtained follow-up data sufficient for estimating ESs, with a mean posttreatment follow-up period of 6.6 months (range: 1–12).

The measures of anxiety and depression symptom severity from which ESs were derived are shown in Table 1. Altogether, 11 studies included a measure of mindfulness, using either the Mindfulness Attention Awareness Scale (Brown & Ryan, 2003), the Five Facet Mindfulness Questionnaire (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006), the Freiburg Mindfulness Inventory (Walach, Buchheld, Buttenmüller, Kleinknecht, & Schmidt, 2006), or the Kentucky Inventory of Mindfulness Skills (Baer, Smith, & Allen, 2004). These were all scored using a total score, with higher scores indicating higher levels of mindfulness.

The methodological quality of the included studies using the modified Jadad criteria ranged from 0 to 4 ($M = 1.48$, $SD = 1.41$). The average quality score was 0.5 for nonrandomized studies ($K = 13$) and 2.9 for RCTs ($K = 9$). The interrater reliability for quality scoring of all included studies using kappa statistics was 0.82 ($p < .001$). For nonrandomized studies and RCTs, kappa was 0.69 ($p = .01$) and 0.84 ($p < .001$), respectively, indicating overall good agreement between the two raters.

³ The reader should note that LOCF is no longer the preferred method for substitution of missing values (see Allison, 2002; Schafer & Graham, 2002).

Table 1
Description of Included Studies

Study	Sample	% female	Mean age (years)	Groups (n)	Total sample used	Number of MBT sessions	Anxiety measures	Hedges's g	95% CI	Depression measures	Hedges's g	95% CI	Jadad score
Category 1: Nonrandomized studies													
Birmie, Garland, & Carlson (2010)	Mix of cancer site and stage; BC = 19%	52	63	MBSR (21)	21	8 + 3-hr retreat	POMS anx	0.36	[0.03, 0.69]	POMS dep; C-SOSI dep	0.16	[-0.17, 0.49]	0
Carlson & Garland (2005)	Mix of cancer site and stage; BC = 59%	78	54	MBSR (63)	63	8 + 3-hr retreat	POMS anx; SOSI anx	0.51	[0.31, 0.71]	POMS dep; SOSI dep	0.44	[0.24, 0.64]	0
Carlson, Speca, Patel, & Goodey (2003); Carlson, Speca, Farris, & Patel (2007) ^a	Breast and prostate cancer; BC = 83%	NR	55	MBSR (42)	42	8 + 3-hr retreat	POMS anx; SOSI anx	0.21	[-0.03, 0.44]	POMS dep; SOSI dep	0.15	[-0.09, 0.38]	1
S. K. Chambers, Foley, Galt, Ferguson, & Clutton (2011)	Prostate cancer	0	67	MBCT (12)	12	8 + 4-hr retreat	HADS anx	0.31	[-0.11, 0.73]	HADS dep	0.12	[-0.29, 0.53]	1
Dobkin (2008)	BC	100	54	MBSR (13)	13	8				CES-D	0.58	[0.15, 1.01]	0
Garland, Carlson, Cook, Lansdell, & Speca (2007)	Mix of cancer site and stage; BC = 56%	91	53	MBSR (60); HA (44)	60	8 + 3-hr retreat	POMS anx; SOSI anx	0.50	[0.29, 0.70]	POMS dep; SOSI dep	0.45	[0.24, 0.65]	0
Kieviet-Stijnen, Visser, Gaussen, & Hudig (2008)	Mix of cancer site and stage; BC = 40%	72	48	MBSR (47)	47	8 + 8-hr retreat	POMS anx	0.36	[0.13, 0.58]	POMS dep	0.30	[0.08, 0.52]	1
Labelle, Campbell, & Carlson (2010)	Mix of cancer site and stage; BC = 77%	100	53	MBSR (46); WL (31)	46	8 + 6-hr retreat				CESD-10	0.54	[0.30, 0.77]	1
Lengacher et al. (2011)	BC Stage 0-I	100	57	MBSR (17)	17	8	STAI	0.49	[0.12, 0.86]	CES-D	0.57	[0.19, 0.95]	1
Matousek & Dobkin (2010)	BC Stage 0-IV	100	56	MBSR (57)	57	8 + 6-hr retreat				CES-D	0.65	[0.43, 0.87]	1
Sharplin et al. (2010)	Mix of cancer site and stage; BC = 50%	86	52	MBCT (13)	13	8	STAI	1.11	[0.60, 1.62]	BDI-II	0.67	[0.23, 1.11]	0
Tacon, Caldera, & Ronaghan (2004)	BC	100	53	MBSR (27)	27	8	STAI State anxiety	1.25	[0.87, 1.64]				0
Tacon, Caldera, & Ronaghan (2005)	BC	100	52	MBSR (30)	30	8	STAI State anxiety	1.20	[0.84, 1.55]				0

Table 1 (continued)

Study	Sample	% female	Mean age (years)	Groups (n)	Total sample used	Number of MBT sessions	Anxiety measures	Hedges's g	95% CI	Depression measures	Hedges's g	95% CI	Jadad score
Category 2: Randomized controlled trials													
Brånström, Kvillemo, Brandberg, & Moskowitz (2010); Brånström, Kvillemo, & Moskowitz (2011) ^a	Mix of cancer site and stage; BC = 76%	99	52	MBSR (32); WL (39)	71	8	HADS anx	0.26	[-0.20, 0.73]	HADS dep	0.28	[-0.19, 0.74]	2
Foley, Baillie, Huxter, Price, & Sinclair (2010)	Mix of cancer site and stage; BC = 42%	77	55	MBCT (55); WL (60)	115	8 + 5-hr retreat	HAM-A	0.64	[0.27, 1.01]	HAM-D	0.90	[0.52, 1.28]	4
Hoffman, Ersser, Hopkinson, Nicholls, & Harrington (2012)	BC Stage 0-III	100	49	MBSR (103); WL (111)	214	8 + 6-hr retreat	POMS anx	0.39	[0.12, 0.66]	POMS dep	0.17	[-0.09, 0.44]	4
Johns, Brown, Beck-Coon, Monahan, & Kroenke (2012)	Mix of cancer site and stage; BC = 77%	94	57	MBSR (18); WL (17)	35	7	GAD-7	0.30	[-0.35, 0.95]	PHQ-8	1.15	[0.45, 1.85]	4
Kingston et al. (2012)	Mix of cancer site and stage; BC = 38%	63	50	MBCT (7); TAU (6)	13	8	POMS anx; HADS anx	0.89	[-0.20, 1.97]	POMS dep; HADS dep	0.37	[-0.65, 1.40]	2
Lengacher et al. (2009)	BC Stage 0-III	100	58	MBSR (40); UC (42)	82	6	STAI	0.57	[0.13, 1.00]	CES-D	0.48	[0.05, 0.92]	3
Lerman, Jarski, Rea, Gellish, & Vicini (2011)	Mix of cancer site and stage; BC = 71%	100	57	MBSR (48); WL (20)	68	8 + 4-hr retreat	SCL-90-R anx	0.20	[-0.32, 0.72]	C-SOSI dep; SCL-90-R dep	0.47	[-0.06, 0.99]	1
Speca, Carlson, Goodey, & Angen (2000); Ursuliak, Goodey, Angen, & Speca (2001) ^a	Mix of cancer site and stage; BC = 42%	81	51	MBSR (53); WL (37)	90	7	POMS anx; SOSI anx	0.42	[0.00, 0.85]	POMS dep; SOSI dep	0.42	[0.00, 0.84]	3
Würzten et al. (2012)	BC Stage I-III	100	54	MBSR (130); TAU (137)	267	8 + 5-hr retreat	SCL-90-R anx	0.22	[-0.02, 0.46]	SCL-90-R dep; MDI; CED-D	0.22	[-0.02, 0.46]	3

Note. anx = anxiety subscale; BC = breast cancer; BDI-II = Beck Depression Inventory-II (Beck, Steer, & Brown, 1996); CES-D = Center for Epidemiologic Studies-Depression Scale (Radloff, 1977); CES-D-10 = Center for Epidemiologic Studies Depression Inventory-10 (Andresen, Malmgren, Carter, & Patrick, 1994); CI = confidence interval; C-SOSI = Calgary Symptoms of Stress Inventory (Carlson & Thomas, 2007); dep = depression subscale; GAD-7 = Generalized Anxiety Disorder 7 (Spitzer, Kroenke, Williams, & Lowe, 2006); HA = healing through the creative arts; HADS = Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983); HAM-A = Hamilton Anxiety Rating Scale (Hamilton, 1959); HAM-D = Hamilton Depression Rating Scale (Hamilton, 1960); MBCT = mindfulness-based cognitive therapy; MBSR = mindfulness-based stress reduction; MBT = mindfulness-based therapy; MDI = Major Depression Inventory (Bech, Rasmussen, Olsen, Noerholm, & Abildgaard, 2001); NR = not reported; PHQ-8 = Patient Health Questionnaire depression scale (Kroenke et al., 2009); POMS = Profile of Mood States (McNair, Lorr, & Droppleman, 1971); SCL-90-R = Hopkins Symptom Checklist-Revised (Derogatis, 1992); SOSI = Symptoms of Stress Inventory (Leckie & Thompson, 1979); STAI = State Trait Anxiety Inventory (Spielberger, Gorsuch, & Lushene, 1983); TAU = treatment as usual; UC = usual care; WL = wait list.

^a Articles providing follow-up data not included in the initial study report.

Individual-study ESs with 95% CIs for measures of symptoms of anxiety and depression are shown in Table 1.

Quantitative Data Synthesis of Nonrandomized Studies

Pre-post effect sizes. As shown in Table 2, pooled pre-post within-group ESs were significant for reduction in symptoms of anxiety (Hedges's $g = 0.60$, range: 0.21–1.25) and depression (Hedges's $g = 0.42$, range: 0.12–0.67), respectively. In studies that investigated pre-post changes in measures of mindfulness ($K = 6$), MBT was associated with improved mindfulness skills, corresponding to a small to moderate ES (Hedges's $g = 0.44$; see Table 2 for details).

Publication bias. As seen in Table 2, the fail-safe number exceeded the criterion considerably for pre-post change in measures of anxiety and depression symptoms. Using Egger's regression test, we found no evidence of asymmetry in the funnel plot of ESs for reduction in symptoms of anxiety, $t(8) = 1.78$, $p = .11$, or depression, $t(9) = 0.04$, $p = .97$.

Heterogeneity of studies. High and moderate between-study heterogeneity was detected for pre-post analyses of anxiety and depression symptoms, respectively (see Table 2 for details).

Effects at follow-up. Four nonrandomized studies reported follow-up data for measures of anxiety and depression symptom severity. The average follow-up period was 7.5 months (range: 3–12). Pooled ESs (Hedges's g) for pre- to follow-up changes were 0.55 (95% CI [0.39, 0.70], $p < .001$) for reduction in anxiety symptoms ($K = 4$, $n = 108$) and 0.38 (95% CI [0.15, 0.61], $p = .001$) for reduction in depression symptoms ($K = 4$, $n = 108$). There was no evidence of between-study heterogeneity for within-group effects at follow-up for either anxiety symptoms ($Q = 2.79$, $p = .43$, $I^2 = 0\%$) or depression symptoms ($Q = 6.26$, $p = .10$, $I^2 = 52\%$). The fail-safe N for effects at follow-up was 48 for reduction of anxiety symptoms and 21 for reduction of depression symptoms, suggesting that only ESs at follow-up for reduction of anxiety symptoms should be considered robust (fail-safe N criterion = 30). The difference in effect between ESs at posttreatment

and follow-up was $g = 0.05$ for reduction of symptoms of anxiety and $g = 0.04$ for reduction of symptoms of depression, indicating that MBT-associated effects were largely maintained over the average follow-up period.

Quantitative Data Synthesis of Randomized Controlled Trials

Controlled effect sizes. Pooled controlled ESs of RCTs for reduction in symptom severity were significant, in favor of MBT, for both symptoms of anxiety (Hedges's $g = 0.37$) and symptoms of depression (Hedges's $g = 0.44$; see Table 2 for details). Using the binomial ES display, which has been suggested as a more intuitive and practical measure (Rosenthal & Rubin, 1982), the controlled ES of 0.37 for reduction of anxiety symptoms corresponded to approximately 59% improvement in the MBT group compared to 41% improvement in the control group. For the controlled ES of 0.44 for reduction in symptoms of depression, the corresponding figures for improvement were 61% in MBT compared to 39% in controls.

The pooled controlled ES for change in measures of mindfulness was statistically significant (Hedges's $g = 0.39$, $K = 5$), but less robust, as indicated by the fail-safe number below the criterion (see Table 2).

Publication bias. For the controlled analyses of RCTs of change in both anxiety and depression symptoms, the fail-safe number exceeded the criterion for robustness of results. Egger's regression test showed no evidence of asymmetry in the funnel plot of controlled ESs for reduction in symptoms of either anxiety, $t(7) = 1.15$, $p = .29$, or depression, $t(7) = 1.77$, $p = .12$. However, using the trim and fill method, one missing study was located in the funnel plot of ESs for reduction in anxiety symptoms. Imputing the ES for the missing study yielded an adjusted pooled ES of 0.36 (95% CI [0.24, 0.49], $p < .001$).

Heterogeneity of studies. As seen in Table 2, there was evidence of moderate between-study heterogeneity among con-

Table 2
Overall Effect Sizes for Anxiety, Depression, and Mindfulness, Including Effect Size Statistics

Outcome measure	Sample size		Overall effect size estimate			Heterogeneity			Fail-safe N^a	Criterion ^b
	K	n	Hedges's g	95% CI	p	Q	p	I^2 (%)		
Nonrandomized studies										
Anxiety	10	332	0.60	[0.39, 0.80]	<.001	43.6	<.001	79	364	60
Depression	11	390	0.42	[0.30, 0.53]	<.001	18.54	.05	46	271	65
Mindfulness	6	156	0.44	[0.32, 0.57]	<.001	5.08	.41	2	57	40
Randomized controlled trials										
Anxiety	9	959	0.37	[0.24, 0.50]	<.001	6.0	.65	0	66	55
Depression	9	955	0.44	[0.24, 0.64]	<.001	16.3	.04	51	82	55
Mindfulness	5	513	0.39	[0.20, 0.58]	<.001	4.38	.36	9	21	35

Note. The table shows overall effect size estimates for change in measures of anxiety, depression, and mindfulness, presented with 95% CIs, p values for the test of significance, and statistics for tests of heterogeneity and publication bias. Effect sizes for nonrandomized studies were based on pre-post within-group differences, while effect sizes derived from randomized controlled trials were based on mean pre- to posttreatment change scores for both mindfulness-based therapy and control conditions. K = number of studies; n = number of participants; CI = confidence interval.

^a Fail-safe N is the estimated number of unpublished studies with an effect size of zero needed to reduce the overall result to a nonsignificant level ($p > .05$). ^b A fail-safe N exceeding the criterion ($5 \times K + 10$) indicates a robust result, that is, no evidence of publication bias.

trolled ESs for change in symptoms of depression, while no heterogeneity was detected for change in symptoms of anxiety.

ITT analyses. Five RCTs reported data on ITT participants. Mean controlled ESs for reduction in symptoms of anxiety ($K = 5$, $n = 517$) and depression ($K = 5$, $n = 517$) in the pooled ITT sample were 0.45 (95% CI [0.27, 0.62], $p < .001$) and 0.55 (95% CI [0.20, 0.89], $p = .002$), respectively, both favoring MBT.

Controlled effects at follow-up. Four RCTs reported follow-up data for MBT and controls, with an average follow-up period of 5.75 months (range: 1–12). Pooled pre-follow-up ESs of RCT were 0.26 (95% CI [0.10, 0.42], $p = .002$) for anxiety symptoms ($K = 4$, $n = 581$) and 0.19 (95% CI [0.03, 0.36], $p = .02$) for depression symptoms ($K = 4$, $n = 576$), both favoring MBT. There was no evidence of between-study heterogeneity for controlled effects at follow-up for reduction of either anxiety symptoms ($Q = 0.75$, $p = .86$, $I^2 = 0\%$) or depression symptoms ($Q = 1.58$, $p = .66$, $I^2 = 0\%$). These ESs, however, were not robust, as indicated by the fail-safe numbers of 4 and 1, respectively, both below the criterion of 30.

The overall results from the main quantitative data syntheses are summarized in Table 2.

Discussion

MBT has become an increasingly popular intervention, but little is still known about its efficacy among cancer patients and survivors. Neither of the two previous meta-analyses, which included data on effects of MBT in cancer patients, focused exclusively on MBT as a means to reduce symptoms of anxiety and depression in cancer patients but did include different clinical populations (Hofmann et al., 2010) or different effects for a wide range of mental and physical health problems (Ledesma & Kumano, 2009). Furthermore, in the brief period of time since these meta-analyses were published, the number of studies, including several RCTs, of MBT for cancer patients has more than doubled. This has allowed for a more comprehensive meta-analysis to investigate the effects of MBT separately for nonrandomized studies and RCTs.

Our literature search identified a total of 22 independent studies, including nine RCTs. The overall results for nonrandomized studies ($K = 13$) were significant, with uncontrolled pre-post ESs in the moderate range for reduction in symptoms of anxiety (Hedges's $g = 0.60$) and depression (Hedges's $g = 0.42$). Although the results appeared to be unbiased, moderate to high levels of heterogeneity was observed for these analyses, indicating that individual-study ESs differed more than could be expected by chance alone. Between-study heterogeneity of these effects could be due to variation in a number of factors, for example, severity of cancer, cancer treatment status, comorbid anxiety and/or depressive disorders, use of antidepressant medication, level of rumination, and degree of motivation for participating in MBT. It is also possible that differences in the skills of MBT teachers could contribute to increased heterogeneity between study ESs. Unfortunately, these potentially predictive factors of MBT outcomes were not systematically reported and therefore could not be evaluated. The quality of nonrandomized studies was generally very low (average quality score: 0.5).

In the overall analysis of RCTs ($K = 9$, $n = 955$), results showed controlled ESs in the small to moderate range for reduction in symptoms of anxiety (Hedges's $g = 0.37$) and depression

(Hedges's $g = 0.44$). These effects were significant and robust, and heterogeneity was low to moderate (0% for reduction of anxiety symptoms, 51% for reduction of depression symptoms). The average quality score for RCTs was 2.9, altogether suggesting that these results are considerably more reliable compared to the results of nonrandomized studies.

Effects at follow-up were significant for reduction in symptoms of anxiety and depression, corresponding to small to moderate ESs for nonrandomized studies ($K = 4$) and small ESs for RCTs ($K = 4$). These results are based on very few studies. Although no heterogeneity was found for any effects at follow-up, only the pooled pre-follow-up ES, derived from nonrandomized studies, for reduction in symptoms of anxiety (Hedges's $g = 0.55$) was robust according to fail-safe N statistics. Therefore, results for MBT-associated effects at follow-up should be considered preliminary.

Hofmann et al. (2010) represents the only previous systematic review of MBT that allows for adequate comparison with findings from the present study. Although Hofmann and colleagues included a wide range of psychological and medical disorders in their meta-analysis of MBT, they also conducted a number of subgroup analyses. For studies of cancer patients, they found an overall uncontrolled pre-post ES (Hedges's g) of 0.63 for anxiety symptoms and 0.45 for depression symptoms. These ESs were based on relatively few studies (eight and seven, respectively), but their findings match our results of nonrandomized studies showing pooled pre-post ESs in the moderate range for reduction in severity of symptoms of anxiety and depression. However, in the present study, controlled ESs derived from RCTs were somewhat lower for reduction of anxiety symptoms (Hedges's $g = 0.37$).

Several systematic reviews have investigated the effect of other psychosocial approaches to treating symptoms of anxiety and/or depression in cancer patients (e.g., Devine & Westlake, 1995; Fann et al., 2008; Newell, Sanson-Fisher, & Savolainen, 2002; Sheard & Maguire, 1999; Williams & Dale, 2006). Overall, these reports provide conflicting findings. While there are some data to support the use of group therapy, psychoeducation, communication skills training, self-esteem building, structured counseling, and cognitive behavioral therapy, recent reviews underscore the strong need for more rigorous research before recommendations can be made for or against the use of specific psychological interventions for cancer patients (Fann et al., 2008; Newell et al., 2002; Williams & Dale, 2006). A meta-analysis of 19 controlled studies of different group and individual psychological interventions for cancer patients found small to moderate pooled ESs (Cohen's d) of 0.36 and 0.19 for reducing symptoms of anxiety and depression, respectively (Sheard & Maguire, 1999). Compared to these summarized ESs, MBT appears to be equally or more effective for reducing symptoms of anxiety and depression. It should, however, be emphasized that large ESs for reducing anxiety or depression in cancer patients have been reported in recent randomized studies of cognitive-behavioral therapy, including behavioral activation and/or problem solving therapy (Hopko et al., 2011; Nezu, Nezu, Felgoise, McClure, & Houts, 2003).

Compared to other effective forms of psychological treatment, MBT may represent a more general approach to dealing with psychological distress by teaching participants to relate more skillfully to their experience. MBT has been shown to be effective for reducing symptoms of anxiety and depression across a wide range

of problems and disorders, presumably by targeting rumination and emotional avoidance, both considered to be maintaining processes across mood and anxiety disorders (e.g., Barlow, Allen, & Choate, 2004; Harvey, Watkins, Mansell, & Shafran, 2004). MBT is also a low-cost treatment (one therapist can lead a rather large group), specifically aimed at improving emotion regulation through greater acceptance and better control of attention. As such, MBT may provide a useful alternative or supplement to other effective interventions that mainly focus on change through behavioral activation or active problem solving.

To our knowledge, the present study is the first using a meta-analytic approach to investigate change in mindfulness skills associated with MBT. Results of both nonrandomized studies and RCTs showed significant improvement in mindfulness skills at posttreatment, corresponding to small to moderate ESs. Staying present to the unfolding of experience by paying attention non-judgmentally to thoughts, feelings, and bodily sensations has been described as an important faculty for healthy regulation of emotions (e.g., R. Chambers, Gullone, & Allen, 2009), and it may be incompatible with transdiagnostic processes such as emotional avoidance, worry, and rumination. One could speculate that increased capacity to be mindful could be an important mechanism by which MBT exerts its beneficial effects. Indeed, a number of studies have found that change in mindfulness mediates symptom reduction by MBT (e.g., Carmody & Baer, 2008; Kuyken et al., 2010).

The present study has several strengths. It is the first formal meta-analysis investigating the effect of MBT on symptoms of anxiety and depression in cancer patients and survivors, as well as the first study using meta-analyses to investigate MBT-associated change in measures of mindfulness. To not exclude a substantial portion of the research of MBT for cancer patients, we included data from all available studies. Study aims, inclusion criteria, and methods of analysis were prespecified and generally highly focused. Pooled ES estimates were computed separately for nonrandomized studies and RCTs, and risk of publication bias and heterogeneity between studies was carefully assessed. As described earlier, we used the random-effects model as recommended by Hedges and Vevea (1998) and generally strove to be conservative in our statistical approach for estimating ESs and investigating potential publication biases. To limit reporting bias, we followed the APA MARS (APA Publications and Communications Board Working Group on Journal Article Reporting Standards, 2008).

A number of limitations should also be noted. As with any meta-analysis, the study was limited by its inclusion criteria and basic statistical assumptions. All participants were diagnosed with cancer, mostly breast cancer, but cancer stage and time since diagnosis varied both within and between studies. Therefore, conclusions cannot be drawn about the differential effects of MBT for different patients with regard to these characteristics. Furthermore, the majority of participants were women with breast cancer, and results should not be generalized to male cancer populations. Although study outcomes were restricted to continuous and validated measures of symptoms of anxiety and depression, specific measures applied varied across studies. A major shortcoming of the currently available literature on MBT for reducing symptoms of anxiety and depression among cancer patients is the lack of samples systematically diagnosed with mood or anxiety disorders and the poor methodological quality of many study reports. Using

the modified Jadad criteria, we found considerable variation in the quality of included studies. The average quality score for the 13 nonrandomized studies ($n = 448$) was 0.5, compared to an average quality score of 2.9 for the nine included RCTs ($n = 955$).

On the basis of the results from RCTs in this meta-analysis and the criteria recommended by Chambless and Hollon (1998), including independent replication of efficacy for a specific problem or population in randomized clinical trials, MBT might be considered an empirically supported psychological intervention efficacious for reduction of symptoms of anxiety and depression in cancer patients and survivors. However, MBT cannot be said to be efficacious and specific, as no studies included an active comparison group to control for effects of nonspecific processes, for example, expectation of change, participating in a group, and/or receiving attention from an interested person. Furthermore, although anxiety and depression are prevalent among cancer patients and all studies included valid and reliable measures of anxiety or depression symptom severity, no study included participants based on standardized diagnostic criteria for mood or anxiety disorders. Therefore, results may not generalize to cancer patients with such psychiatric disorders. Furthermore, the mean study quality score of 2.9 for RCTs leaves considerable room for improvement. As mentioned, none of the included RCTs included an active comparison group, and only five RCTs reported data on the ITT sample.

Importantly, MBT appears to be feasible to be delivered in oncology settings. Adding to the external validity of findings from this meta-analysis, several RCTs were conducted in clinical oncology settings (e.g., Foley, Baillie, Huxter, Price, & Sinclair, 2010; Hoffman et al., 2012; Lerman, Jarski, Rea, Gellish, & Vicini, 2011; Specca, Carlson, Goodey, & Angen, 2000; Würtzen et al., 2012), and high adherence to MBT was reported. Also, MBT has been shown to be feasible in primary care settings, where most patients with mood and anxiety disorders are treated (e.g., Kuyken et al., 2008; Finucane & Mercer, 2006). However, although MBT is a low-cost treatment, it is time consuming for participants due to extensive daily homework and requires well-trained MBT teachers.

In conclusion, while the overall quality of existing clinical trials varies considerably, there appears to be some positive evidence from a number of relatively high-quality RCTs to support the use of MBT for cancer patients and survivors with symptoms of anxiety and depression.

It is strongly recommended that future research apply more stringent designs (e.g., randomization with active control as comparison), follow recent established standards for reporting of clinical trials such as the Journal Article Reporting Standards (APA Publications and Communications Board Working Group on Journal Article Reporting Standards, 2008) or the Consolidated Standards of Reporting Trials (Schulz, Altman, & Moher, 2010), investigate MBT in cancer patients with well-diagnosed depression or anxiety disorders, and explore critical patient variables, for example, physical and mental symptom severity, levels of rumination, and use of antidepressant medication, that may moderate the effect of MBT for cancer patients. In general, MBT research should consider more rigorous designs (e.g., componential control designs) to investigate specific effects and potential mechanisms of change.

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