**The questionable efficacy of manualized psychological treatments for distressed breast cancer patients: An individual patient data meta-analysis**

**Authors:** James Templea,b (PhD), Peter Salmona,b (DPhil), Catrin Tudur-Smithc (PhD), Christopher D Huntleya (MSc), Angela Byrnea,b (DClinPsy), and Peter L Fishera,b (PhD)

a Department of Psychological Sciences, University of Liverpool, Whelan Building, Liverpool, UK,

b Royal Liverpool and Broadgreen University Hospitals NHS Trust, Liverpool, UK**,**

c Department of Biostatistics, Waterhouse Building, University of Liverpool, Liverpool, UK

**Corresponding author:** James Temple; School of Psychological Sciences, University of Liverpool, Whelan Building, Brownlow Hill, Liverpool, L69 3GB, UK. Email: James.Temple@liv.ac.uk; Tel: +44(0)151 7958394; Fax: +44(0)151 7945537

**Acknowledgments of research support for the study:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Disclaimer:** The authors acknowledge no financial interest or benefit arising from the direct applications of their research

**Declarations of interest:** None

**ABSTRACT**

Previous meta-analyses conclude that psychological treatments are efficacious for emotional distress in breast cancer (BCa). However, the practical relevance of these meta-analyses is questionable; none focused specifically on clinically distressed patients or whether treatment effects were clinically significant. In a two-stage individual patient data (IPD) meta-analysis of 17 randomized controlled trials of manualized psychological treatments in BCa, we evaluated treatment efficacy in distressed BCa patients (n=1,591) using clinical significance and effect size analyses. Outcomes were anxiety, depression, and general distress, evaluated at post-treatment and follow-up. Moderators examined were treatment type, treatment format, therapists’ profession, control condition, age, outcome measure, and trial quality. Treated patients were more likely than controls to recover from anxiety and general distress at post-treatment (14-15% more treated patients recovered), but not at mean 8-months follow-up. Overall recovery rates were low: across outcomes, at post-treatment, only 30-32% of treated patients and 15-25% of controls recovered; at follow-up, only 21-30% of treated patients and 18-35% of controls recovered. Small between-group effect sizes in favour of treatment were found across outcomes at post-treatment (g=0.32-0.34) but not at follow-up. Across the different analysis methods, few moderator effects were found. More efficacious psychological treatments are needed for distressed BCa patients.

**Key words**

Individual patient data meta-analysis, clinical significance, psychological treatments, breast cancer, emotional distress, recovery

One in eight women in the United States and one in seven women in the United Kingdom are diagnosed with breast cancer (BCa) in their life-time (Cancer Research UK, 2018; Siegel, Miller, & Jemal, 2018). Approximately 50% of BCa patients report clinical levels of anxiety and/or depression shortly after diagnosis, and 25% of patients do so in each of the second, third and fourth years after diagnosis (Bouchard et al., 2016; Burgess et al., 2005). Emotional distress associated with BCa reduces quality of life, intensifies pain and fatigue, increases health care costs, and reduces adherence to treatment (Badger, Braden, Mishel, & Longman, 2004; Bultz & Carlson, 2006; Carlson & Bultz, 2004; Colleoni et al., 2000). Emotional distress also increases risk of suicide (Reddy, 2010), the incidence being 1.6 times higher in BCa patients who are within the first five years post diagnosis than in the general population (Misono, Weiss, Fann, Redman, & Yueh, 2008).

Two Cochrane reviews (Jassim, Whitford, Hickey, & Carter, 2015; Mustafa, Carson‐Stevens, Gillespie, & Edwards, 2013) and nine additional meta-analyses (Cobeanu & David, 2018; Coutiño-Escamilla, Piña-Pozas, Garces, Gamboa-Loira, & López-Carrillo, 2019; Duijts, Faber, Oldenburg, van Beurden, & Aaronson, 2011; Naaman, Radwan, Fergusson, & Johnson, 2009; Tatrow & Montgomery, 2006; Xiao et al., 2017; Ye et al., 2018; Zhang, Xu, Wang, & Wang, 2016; Zimmermann, Heinrichs, & Baucom, 2007) of randomized control trials (RCTs) have concluded that efficacious psychological treatments for emotional distress in BCa exist. Therefore, health care policies and clinical practice guidelines internationally specify that psychological treatment should be available to BCa patients as part of their routine care throughout the disease trajectory (Dauchy et al., 2012; National Institute of Health and Care Excellence, 2004; Holland, Watson, & Dunn, 2011; Howell et al., 2009; Li et al., 2016; National Comprehensive Cancer Network, 2003; Page & Adler, 2008; Reese, Weis, Schmucker, & Mittag, 2017; Tit et al., 2017; National Breast Cancer Centre, 2003).

However, a recent review of the methodology of RCTs of psychological treatments for emotional distress in BCa cast doubt on the conclusion that efficacious psychological treatments exist (Temple, Salmon, Tudur-Smith, Huntley, & Fisher, 2018). Specifically, Temple et al. (2018) identified two respects in which conclusions of previous meta-analyses are based on RCTs that are not relevant to clinical practice. First, whereas clinical practice guidelines recommend psychological treatment only for BCa patients who are clinically distressed (National Comprehensive Cancer Network, 2003), only 15% of relevant RCTs screened patients for distress (Temple et al., 2018), and no meta-analysis excluded non-distressed patients or provided separate analyses specifically for those with distress. Second, for a psychological treatment to be reproducible it must follow clear steps specified in a treatment manual (Westen, Novotny, & Thompson-Brenner, 2004). Therefore, the standards by which a treatment is considered ‘evidence-based’ in the United States require that it is based on replicable manualized approaches (APA, 2006; Chambless & Hollon, 1998; Öst, 2008). Comparable standards apply in the UK where recommended treatments are underpinned by evidence largely derived from RCTs of which manualized treatments, integral to trial quality, are typically used (NICE, 2009). However, only 51% of RCTs of psychological treatments for emotional distress in BCa used a manual (Temple et al., 2018), and no meta-analysis excluded non-manualized treatments or examined whether manualization influenced treatment outcome.

Temple et al. (2018) also warned that conclusions of previous meta-analyses have been based solely on effect sizes. While effect sizes indicate differences between conditions at the group level, they provide no information about individual variability in treatment response (Loerinc et al., 2015), making it difficult for researchers, clinicians, service providers and policy-makers to interpret the practical value of the treatments. To indicate the proportion of patients who benefit from treatment, and therefore its relevance to clinicians and services, an evaluation of clinical significance is needed. The main criterion for clinical significance is ‘recovery’ (Keller, 2003; Patten, Grigoriadis, & Beaulieu, 2011), which refers to patients returning to normal functioning. A more lenient criterion is improvement, which refers to patients improving to a significant degree. Unfortunately, in BCa, only 11% of RCTs (Temple et al., 2018) and no meta-analyses have evaluated the clinical significance of treatments. When evaluating clinical significance, it is also important to assess deterioration, i.e. clinically significant worsening of symptoms. In mental health settings, around 5-15% of patients deteriorate in psychotherapy RCTs irrespective of condition (Rozental, Magnusson, Boettcher, Andersson, & Carlbring, 2017).

Moreover, clinicians and policy-makers need additional information that previous meta-analyses have not made clear. First, they need to know the long-term efficacy of psychological treatment, ideally a year or more after completion of psychological treatment. Four previous meta-analyses included long-term effects (Cobeanu & David, 2018; Duijts et al., 2011; Jassim et al., 2015; Tatrow & Montgomery, 2006). However, three of these aggregated effects 0-12 months post-treatment (Duijts et al., 2011; Jassim et al., 2015; Tatrow & Montgomery, 2006), and the fourth aggregated effects 3-12 months post-treatment (Cobeanu & David, 2018). Therefore, the durability of treatment gains in BCa remains unknown. Second, clinicians and policy-makers need to know whether treatment efficacy is influenced by the type of psychological treatment, its format (i.e. group or individual), its timing within the disease trajectory (i.e. soon after diagnosis and/or surgery, during acute medical treatment, or in survivorship), or the profession of the therapist. Only three meta-analyses examined which types of psychological treatment are most efficacious, each reaching a different conclusion; Jassim et al. (2015), Zimmermann et al. (2007), and Naaman et al. (2009) reported that cognitive behavioural therapy, psychoeducation and supportive therapy were the most efficacious treatments, respectively, relative to control conditions. Treatment format does not consistently influence outcomes; Zimmermann et al. (2007) reported that individual treatments were more effective than treatments delivered in a group, while Cobeanu & David (2018) reported no difference in outcomes by treatment format. Two meta-analyses examined if timing of treatment delivery had an influence on outcome; Zimmermann et al. (2007) found that treatments delivered directly after diagnosis or surgery achieved better psychological outcomes than those delivered during or after medical treatment (i.e. chemotherapy and radiotherapy); while Duijts et al. (2011) found no difference between interventions delivered during BCa treatment (type of medical treatment was not specified) compared to those delivered after BCa treatment. Finally, two meta-analyses in BCa examined if therapists’ profession influenced treatment outcome. One meta-analysis found treatments delivered by psychologists achieved better clinical outcomes compared to other allied health professionals (Zimmermann et al., 2007); whereas Cobeanu & David (2018) found therapists’ profession did not impact treatment outcome.

There are further methodological limitations of previous meta-analyses that may have biased their results. First, although poor quality RCTs often overestimate treatment outcome (Barth et al., 2013; Bohlmeijer, Prenger, Taal, & Cuijpers, 2010; Bolier et al., 2013; Cuijpers, van Straten, Bohlmeijer, Hollon, & Andersson, 2010; Huhn et al., 2014), only one meta-analysis in BCa examined whether treatment outcome was influenced by RCT quality; Naaman et al. (2009) reported that higher quality RCTs were associated with better treatment outcomes than lower quality RCTs. Second, although the nature of the control condition with which a psychological treatment is being compared can influence treatment outcome (Cuijpers, Van Straten, Warmerdam, & Smits, 2008; Gould, Coulson, & Howard, 2012), only one meta-analysis in BCa examined whether treatment outcome was related to the type of control condition; Zimmermann et al. (2007) found that psychological treatments were associated with better outcomes when being compared to treatment as usual (TAU) or wait-list controls (WLCs) than when compared to active controls. Third, although a meta-analysis in a mixed cancer population found that patient age influenced treatment efficacy, with better treatment outcomes in patients with older age (Heron-Speirs, Harvey, & Baken, 2013), no meta-analysis in BCa alone has examined age as a moderator of treatment outcome. Finally, as not all outcome measures are equal in their psychometric properties, including responsiveness to change, treatment outcome may depend on the outcome measure used. However, no meta-analysis in BCa has examined if outcome measure moderates treatment outcome.

An individual patient data meta-analysis (IPD-MA) can overcome some of the limitations of previous meta-analyses and provide the additional information that clinicians and policy-makers require. IPD-MAs are considered the ‘gold standard’ in meta-analysis techniques (Stewart & Parmar, 1993; Stewart & Tierney, 2002). Instead of using summary statistics from published RCTs, IPD-MA combines participant-level data from each relevant RCT into a common dataset. In the present context, IPD-MA has two specific advantages over traditional meta-analysis. First, IPD-MA allows analyses which have not been reported in the included RCTs (Cooper & Patall, 2009). Crucially, this would allow non-distressed patients to be excluded from analyses, enabling the evaluation of treatment effects specifically for patients who meet criteria for being clinically distressed. Second, IPD-MA can evaluate the clinical significance of treatments. Different methods for determining clinical significance exist (Hageman & Arrindell, 1999; Hsu, 1996; Jacobson, Follette, & Revenstorf, 1984; Jacobson & Truax, 1991; Nunnally & Kotsch, 1983; Speer, 1992), all of which class patients as ‘recovered’, ‘improved’, ‘unchanged’, or ‘deteriorated’. In mental health settings, these different methods agree highly (Bauer, Lambert, & Nielsen, 2004; McGlinchey, Atkins, & Jacobson, 2002). The method developed by Jacobson and colleagues (Jacobson et al., 1984; Jacobson & Truax, 1991) has become the most widely used (Ogles, Lunnen, & Bonesteel, 2001) and has good construct validity (Lunnen & Ogles, 1998; Newnham, Harwood, & Page, 2007; Ronk, Hooke, & Page, 2016) but, to our knowledge, has never been applied in BCa patients.

The Jacobson method uses two criteria. The first requires calculation of a cut-off point on a well-validated outcome measure to determine whether an individual’s post-treatment score has a greater probability of being drawn from a functional *vs* a dysfunctional population. The second requires calculation of a ‘reliable change index’ (RCI), which determines whether the extent of change from pre- to post-treatment is statistically reliable (i.e. beyond that which can be accounted for by measurement error). Applying these two criteria, patients in RCTs can be allocated to four categories: a) ‘recovered’, if they make statistically reliable change and move from a dysfunctional to a functional population; b) ‘improved’, if they make statistically reliable change but do not move from a dysfunctional to a functional population; c) ‘unchanged’, if they do not make statistically reliable change; and d) ‘deteriorated’, if they make statistically reliable change for the worse.

**Aims of the present study**

To overcome limitations of previous meta-analyses and provide findings of more practical relevance, we conducted an IPD-MA to evaluate the efficacy of manualized psychological treatments for emotional distress specifically in clinically distressed BCa patients using Jacobson’s clinical significance analysis. The primary outcome was recovery, the optimal treatment outcome in mental health settings; secondary outcomes were improvement and deterioration. So that we could detect whether different methods of analysis suggested different conclusions, we also evaluated efficacy using IPD effect size analysis. We evaluated treatment efficacy at post-treatment and follow-up, and aimed to examine the influence of several potential study level moderators of treatment outcome: treatment type, treatment format (i.e. group or individual), treatment timing (i.e. before, during, or after completion of primary medical treatment), therapists’ profession, nature of the control condition, age, outcome measure, and methodological quality of the RCT.

**METHOD**

This IPD-MA broadly followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Individual Participant Data (PRISMA-IPD) statement (Stewart et al., 2015).

**Eligibility criteria**

Eligibility criteria for the IPD-MA follow the PICOS framework (Liberati et al., 2009).

***Participants***

RCTs exclusively comprising females aged 18 years or older with a histologically confirmed diagnosis of BCa were included. Participants across all tumour stages (i.e. stage 0-IV) and all phases of the BCa disease trajectory (i.e. soon after diagnosis, during acute medical treatment, or post-acute medical treatment) were included irrespective of time since diagnosis or the type (e.g. chemotherapy and/or radiotherapy) and intent (i.e. curative and/or palliative) of medical treatment received.

***Interventions***

Psychological interventions were defined as manualized treatments using psychological techniques. Manualized treatments were liberally operationalized as those in published reports that: referred to use of a “manual” or “manualized treatment”; referenced a published manual when describing the treatment; or reported that the treatment had been described elsewhere and the referenced source indicated a manual. If a published report was ambiguous about whether a manual was followed, for example reporting that treatment was *“based on”* a specific manual, the authors were contacted for clarification. Evaluations of complementary or ‘alternative’ treatments (i.e. yoga, hypnosis, reiki, logotherapy, art therapy, dance therapy) were excluded. We also excluded treatments that involved no interaction between therapist and patient (i.e. exclusively relied on written or visual material) or were targeted at surgical distress.

***Controls***

RCTs using TAU, WLC, assessment only or active control (i.e. some form of intervention to control for nonspecific factors) conditions were included. RCTs comparing two or more specific psychological treatments without a control were excluded.

***Outcomes***

The primary outcome was emotional distress defined as anxiety, depression or general distress (i.e. general mood disturbance, global emotional distress, or a combination of anxiety and depression). Identification of patients experiencing clinical levels of emotional distress requires an outcome measure with an established clinical cut-off score. Therefore, only RCTs using a validated outcome measure with an established cut-off for clinical levels of distress were included. We received IPD for RCTs using the following outcome measures: Hospital Anxiety and Depression scale (HADS; Zigmond & Snaith, 1983), Profile of Mood States (POMS; McNair, 1971), Centre for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977), and the State-Trait Anxiety Inventory (STAI; Spielberger & Gorsuch, 1983). These measures are among the most widely used (Temple et al., 2018) and well-validated (Han et al., 2015; Johnston, Pollard, & Hennessey, 2000; Metzger, 1976; Nyenhuis, Yamamoto, Luchetta, Terrien, & Parmentier, 1999) outcome measures in BCa RCTs.

***Studies***

Only RCTs published in English in a peer-reviewed journal were included.

**Search strategy & study selection**

PubMed, PsycINFO, Web of Science, Scopus, PsycARTICLE, and AMED were searched from their inception until 15th April 2019 using a combination of Medical Subject Headings (MeSH) terms and keywords to identify psychological treatment trials for emotional distress in BCa. The final search strategy developed for PubMed (see appendix A in the online supplementary material) was adapted for each database. Reference lists of both eligible RCTs and previous meta-analyses in BCa were hand-searched for additional studies.

Initially, titles and abstracts of all papers were screened by one reviewer (JT) to remove duplicates and clearly irrelevant studies. To check for consistency in selection, a random 50% of abstracts and titles were independently assessed by a second reviewer (AB). At this stage, agreement between reviewers was high (81%). Most disagreements were due to one reviewer adopting an overly liberal approach. Next, full text articles of potentially relevant papers were independently assessed for inclusion by both reviewers (JT & AB). At this stage, agreement between reviewers was also high (92%). Following assessment of inter-rater agreement, discrepancies were resolved through discussion with a third reviewer (PF).

**Data extraction**

The authors of eligible RCTs were contacted, and anonymized raw data on relevant outcome measures at pre-treatment, post-treatment and follow-up, plus the treatment condition of each patient was requested. Two reviewers (JT & CH) extracted group level data from published reports of eligible RCTs, including: year of publication; country of origin; age; tumour stage; time since diagnosis; type of medical treatment received; timing of treatment within the BCa trajectory (i.e. soon after diagnosis, during acute medical treatment, or post-acute medical treatment); type and format of each treatment and control condition; profession of the therapists delivering each treatment and control condition; and duration and number of sessions of each treatment and control condition.

**Identifying the distressed sample**

We included patients who scored above established cut-offs for clinical levels of emotional distress pre-treatment on the relevant outcome measures: STAI trait (STAI-T; ≥39; Knight, Waal‐Manning, & Spears, 1983; Therrien & Hunsley, 2012), HADS anxiety (HADS-A; ≥8; Singer et al., 2009; Hinz & Brähler, 2011); CES-D (≥16; Radloff, 1977); HADS depression (HADS-D; ≥8; Singer et al., 2009; Hinz & Brähler, 2011); HADS total (HADS-T; ≥13; Singer et al., 2009); or POMS total mood disturbance (POMS-TMD; ≥37; Cella et al., 1989; Classen et al., 2008).

The cut-off scores for the HADS-A, D & T are established in cancer patients. A cut-off score of ≥13 on the HADS-T provides the best balance between sensitivity and specificity (Singer et al., 2009). Hinz & Brähler (2011) found that cut-off scores of ≥8 or ≥11 should be used to indicate severity of anxiety or depression on the respective subscale. As the cut-off score of ≥8 provides a better balance between sensitivity and specificity (Singer et al., 2009), this was chosen for both subscales. The POMS-TMD clinically meaningful cut off score for emotional distress in cancer patients of ≥37 was used as recommended by Classen et al. (2008). Clinically meaningful cut-off scores have yet to be established in cancer on the CES-D or STAI-T. Therefore, the widely used cut-off scores of ≥16 and ≥39 for clinical levels of emotional distress in the general population were used, respectively (Radloff, 1997; Knight, Waal‐Manning, & Spears, 1983; Therrien & Hunsley, 2012).

**Coding and scoring of potential moderators**

***Treatment type***

Treatments were coded into six broad categories: ‘cognitive-behavioural-based’ treatments’ (CBT: treatments primarily targeting specific thoughts or behaviours using cognitive behavioural techniques); ‘mindfulness-based treatments’ (MBT: treatments primarily focusing on meditation, visualisation, and present-moment awareness); ‘psycho-education’ (treatments primarily providing psychological education); ‘support’ (treatments primarily emphasizing a supportive environment by providing emotional or social support); ‘psychodynamic’ (treatments primarily based on theories or principles of psychoanalysis); or ‘other’ (treatments that either did not fit a defined category or combined different approaches without emphasizing any one). The categorisation of treatments was discussed by two reviewers (JT & PF) until consensus was reached.

***Treatment format***

Treatments were coded as ‘individual’ (delivered to patients individually) or ‘group’ (delivered to more than one patient simultaneously).

***Treatment Timing***

There was too much variability within most of the included RCTs to examine the moderating effect of treatment timing. Inclusion criteria used by many RCTs were often broad and included patients across multiple stages of the cancer treatment trajectory; this prevented the aggregation of data at the study level. Furthermore, it was often unclear when patients received psychological treatment i.e. before, during, or after completion of acute medical treatment within the RCT.

***Therapists’ profession***

Treatments were coded as being delivered by ‘clinical psychologists’ or ‘other professionals’ (delivered to patients by healthcare professionals other than clinical psychologists). Treatments delivered by a mixture of clinical psychologists and other professionals (e.g. a clinical psychologist and a medical social worker) were excluded from the analysis.

***Nature of the control condition***

Control conditions were coded into four broad categories: active (participants received an intervention to control for nonspecific factors, which the authors designated a control condition); TAU (participants received standard care); WLC or assessment only (participants received no treatment); or educational material (participants received written information about health care after cancer).

***Age***

The mean age of the total sample for each RCT was used to investigate whether treatment outcome was moderated by age.

***Outcome measure***

We received IPD for the followingoutcome measures: HADS-A or STAI-T for anxiety, CES-D or HADS-D for depression, and HADS-T or POMS-TMD for general distress.

***Methodological quality***

Methodological quality was assessed by two reviewers (JT & CH) using a modified version (Temple et al., 2018) of the Psychotherapy Outcome Study Methodology Rating Form (POMRF; Öst, 2008). This comprises 19 items, each scored on a three-point Likert scale: 0 (poor), 1 (fair), or 2 (good), producing a total score from 0 to 38, with higher scores indicating better quality. Interrater reliability, assessed using the intra-class correlation coefficient (ICC), indicated good inter-rater reliability (0.88; 95% CI, 0.65–0.96). Following calculation of the ICC, discrepancies were resolved by discussion with a third reviewer (PF).

**General analysis strategy**

We examined each outcome variable (anxiety, depression, and general distress) separately. All outcomes were assessed by self-report questionnaires (i.e. STAI-T & HADS-A for anxiety; HADS-D & CES-D for depression; and HADS-T & POMS-TMD for general distress) in the same analysis. We analysed outcomes at two time periods: post-treatment, defined as the earliest assessment point ≤8 weeks after treatment ended; and follow-up, defined as the earliest assessment point ≥6 months after treatment ended (we had planned to evaluate treatment effects ≥12 months after treatment ended but only three RCTs provided such data). The Jacobson’s clinical significance analysis and IPD effect size analysis were conducted using a standard two-stage IPD approach (Riley, Lambert, & Abo-Zaid, 2010). Each analysis comprised two main elements:

***Clinical significance analysis***

1. Calculation of recovery, improvement and deterioration rates using Jacobson’s first and second criteria.
2. Evaluation of whether recovery, improvement or deterioration rates were moderated by treatment type, treatment format, therapists’ profession, nature of the control condition, age, outcome measure or methodological quality.

***Effect size analysis***

1. Calculation of standardized mean difference (SMD) effect sizes.
2. Evaluation of whether SMD effect sizes were moderated by treatment type, treatment format, therapists’ profession, nature of the control condition, age, outcome measure or methodological quality.

**Statistical analysis**

***Preliminary analysis***

Not all eligible RCTs provided IPD. Therefore, we compared pooled SMD between-group effect sizes of RCTs providing IPD with those not providing IPD at post-treatment to assess whether effects differed across samples (in the absence of IPD, we could not select distressed patients from the RCTs not providing IPD. Therefore, all effect sizes in this analysis were calculated based on total samples i.e. distressed and non-distressed participants). For the RCTs not providing IPD, effect sizes and 95% confidence intervals (CIs) were calculated using the data available from published reports. We also explored differences between RCTs providing IPD and those not providing IPD in baseline sample characteristics (age sand sample size) and psychological treatment characteristics (type, format, and duration). Chi-square tests were used to compare treatment type and format, and *t*-tests were used to compare age, sample size, and treatment duration.

***Clinical significance analysis***

*Recovery, improvement, and deterioration rates.* A cut-off point to determine whether a patient was more likely to be drawn from a functional or dysfunctional population was calculated separately for each outcome measure (Jacobson’s first criterion). To determine this cut-off, three methods exist (Jacobson et al., 1984): a) patients’ post-treatment score falls outside the range of dysfunctionality, defined as falling at least two standard deviations (SDs) beyond the mean of the dysfunctional population, in the direction of functionality; b) patients’ post-treatment score falls within the range of functionality, defined as falling within two SDs of the mean of the functional population; and c) patients’ post-treatment score has a greater probability of being drawn from the functional than the dysfunctional population (Jacobson et al., 1984). Unfortunately, for the STAI-T, CES-D, POMS-TMD, and HADS-A, D, & T, appropriate normative data for functional BCa populations has not been published. Thus, only cut-off a) could be used. Table 1 shows, for each outcome measure, the cut-off score for being within the range of the functional population. Using the formula reported in Noble, Reilly, Temple, and Fisher (2018) and data in Table 1, the RCI (Jacobson’s second criterion) was calculated separately for each outcome measure to determine the change in score that would be statistically reliable at p<0.05 (Table 1).

The proportions of patients classed as ‘recovered’, ‘improved’, or ‘deteriorated’ following treatment, and 95% CIs, were calculated for each treatment and control condition. Proportions were pooled across trials using a random effects proportion meta-analysis (DerSimonian & Laird, 1986). Overall proportions were pooled at post-treatment and follow-up but proportions for potential moderator variables were only pooled at post-treatment because too few data were available at follow-up. The Stuart-Ord (inverse double arcsine square root) method (Stuart & Ord, 1994) was used to stabilize variance among studies.

Risk differences (RDs) with 95% CIs were then calculated to estimate the difference in recovery, improvement, and deterioration rates between treated and control patients. RDs were calculated by subtracting the proportion of patients who ‘recovered’, ‘improved’, or ‘deteriorated’ in the control group from the respective proportion in the treatment group. RDs were pooled across trials using the Mantel-Haenszel random effects model (Mantel & Haenszel, 1959). All RDs were scaled so that positive values represented effects in favour of treatment. In cases where RCTs had multiple treatment or control groups, each comparison was evaluated separately. However, as multiple comparisons from the same RCT are not mutually independent, the number of patients in the relevant treatment or control group was divided equally between each comparison. Heterogeneity between studies was tested using Cochrane’s Q-test and the proportion of total variation that was due to heterogeneity was expressed as the I2 statistic, with values greater than 50% indicating at least moderate heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003). Proportion and RD analyses were conducted on a per-protocol rather than intent-to-treat (ITT) basis because, at post-treatment and follow-up, we only received IPD for patients who completed post-treatment and/or follow-up assessments.

*Sensitivity analyses.* Sensitivity analyses excluding RD outliers were conducted. A RD was considered an outlier when its 95% CI was outside the 95% CI of the overall mean RD. Two RCTs included multimodal treatment designed to alleviate insomnia and associated distress (CBT for insomnia; Dirksen & Epstein, 2008; Savard, Simard, Ivers, & Morin, 2005). Given that primary outcomes in these RCTs included emotional distress, they were included to allow greater inclusivity. However, sensitivity analyses excluding RDs for these two RCTs were conducted.

*Influence of potential moderators.* Potential moderators could only be explored at post-treatment because too few data were available at follow-up. We conducted sub-group analyses using Cochrane’s Q test to explore whether treatment type, treatment format, therapists’ profession, nature of the control condition or outcome measure moderated RDs, and weighted meta-regression analyses to explore whether age or methodological quality moderated RDs (as meta-regression could not be run with Mantel-Haenszel weights, inverse variance random effects models were used). A minimum of two studies was required for a sub-group to be included in the sub-group analysis; and a minimum of ten studies was required to conduct weighted meta-regression (Fu et al., 2011).

***Effect size analysis***

*SMD effect sizes.* SMD between-group effect sizes with 95% CIs were calculated using IPD by dividing the difference in mean value between treated and control patients by the pooled SD (Cohen, 1988). SMDs were adjusted for small-sample bias using Hedges’ g (Hedges, 1989) and were pooled across RCTs using the inverse variance random effects model (DerSimonian & Laird, 1986). All SMDs were scaled so that positive values represented effects in favour of treatment. Effect sizes of 0.2, 0.5 and 0.8 are considered small, medium, and large, respectively (Cohen, 1988). An effect size of <0.2 can be statistically significant but is considered trivial (Cohen, 1988). While these benchmarks were developed for Cohens’ d, they are also widely applied to Hedges’ g (Santoft et al., 2019). We tested for heterogeneity and evaluated RCTs that had multiple treatment or control groups using the same techniques as in the RD analysis. All effect size analyses were conducted on a per-protocol basis as explained above.

*Sensitivity analyses.* We identified effect size outliers and explored whether the two RCTs that included multimodal treatment designed to alleviate insomnia and associated distress impacted effect sizes using the same techniques as in the RD analysis.

*Influence of potential moderators.* The same techniques as in the RD analysis were used to explore whether effect sizes were moderated by treatment type, treatment format, therapists’ profession, nature of the control condition, age, outcome measure or methodological quality.

**Statistical software**

RD and effect size analyses were conducted using Comprehensive Meta-Analysis, version 3.3.07; while the proportion meta-analysis was conducted using StatsDirect version 3.0.171.

**RESULTS**

**Study selection**

The database search retrieved 2,502 citations; 10 more were identified through hand searching. After removal of duplicates, 1,717 remained for screening based on title and abstract. Of these, 1,408 clearly did not meet inclusion criteria. Full text articles of the remaining 309 citations were retrieved and assessed. In total, 38 articles corresponding to 36 RCTs published between January 1980 and April 2019 were eligible. Seventeen (total participants=3,156) of the 36 (total participants=6,162) eligible RCTs provided IPD and were included. Figure 1 shows the study selection. A complete list of references of the included RCTs can be found in Appendix B in the online supplementary material.

Of the 3,156 patients for whom IPD was obtained, 1,591 (50%) scored above the cut-offs scores for one or more outcome measures, indicating clinical levels of emotional distress pre-treatment, and were therefore included in analyses for which they exceeded the relevant cut-off (e.g. STAI-T or HADS-A cut-off for anxiety). Of these patients, 950 (treatment=490; control=466), 730 (treatment=390; control=340) and 1,093 (treatment=636; control=457), respectively, scored above the established cut-offs for anxiety, depression, and general distress. For anxiety, 770 patients (treatment=399; control=371) and 166 patients (treatment=91; control=95), respectively, scored above the establish cut-offs on the HADS-A and STAI-T. For depression, 461 patients (treatment=245; control=216) and 269 patients (treatment=145; control=124, respectively, scored above the establish cut-offs on the HADS-D and CES-D. For general distress, 601 patients (treatment=325; control=276) and 492 patients (treatment=311; control=181), respectively, scored above the establish cut-offs on the HADS-T and POMS-TMD.

**Study and patient characteristics**

Table 2 describes the patient characteristics for each included RCT. Patients had a mean age of 53 (median 53; range 48-58). The time since patients were diagnosed with BCa was only reported in 10 RCTs. Of these, the mean was 26 months (median 21 months; range 0-74 months). Most RCTs included patients across a range of BCa disease stages - fourteen exclusively included non-metastatic BCa patients, one exclusively included metastatic BCa patients, and two included BCa patients irrespective of metastases. In one RCT, patients received psychological treatment prior to the beginning of primary medical treatment; in eight, patients received psychological treatment after completion of primary and adjuvant therapy (i.e. radiotherapy and chemotherapy); in one, patients were receiving lifetime medical treatment for metastatic BCa and in seven, patients either received psychological treatment at different phases of the disease trajectory or it was unclear at what point in the disease trajectory patients received psychological treatment (i.e. before, during, or after completion of acute medical treatment.

Table 3 describes characteristics of each RCT. In total, 20 treatment and 17 control conditions were included in our analyses. Nine treatments were categorised as CBT, three as support, three as psychoeducation, three as ‘other’ (described as *‘emotional expression’*, a *‘body mind spirit intervention’*, and a *‘multicomponent biobehavioral intervention’*), one as MBT, and one as psychodynamic. The mean duration of treatment was reported in 16 RCTs. Of these, the mean duration was 14 hours (median 15; range 2-30) over nine sessions (median 8; range 2-18). Fourteen treatments were delivered in a group format and six were individual. Six treatments were delivered by clinical psychologists; ten were delivered by other allied health professionals; two were delivered by a mixture of professionals (i.e. clinical psychologists and other professionals); and two did not report who delivered treatment.

Of the 17 control conditions, five were categorised as TAU (which included support and advice from BCa nurses, written information on local cancer counselling centres, and an unstructured therapist-led peer support group), five as active controls (which included condensed versions of the active treatment with the purportedly ‘active’ ingredients removed, a stress management seminar, a non-directive peer support group, and a BCa wellness and education program), five as WLC or assessment only, and two as educational material (which included a videotape on breast self-examination and booklets on health care after cancer, managing emotions, financial issues, helping children understand BCa and sexuality). In both RCTs providing controls with educational material, the same material was given to the treatment group. The duration and number of sessions of control conditions was only reported in 12 RCTs. Of these, the mean duration was seven hours (median 6; range 0-30) over four sessions (median 1; range 0-15). Four of the control conditions were delivered by nurses, one by clinical psychologists, one by graduate level interventionists, one by social workers, and one by a mixture of therapists. Seven more did not require a therapist (e.g. WLC or assessment only) and two studies did not report who delivered the treatment.

The mean post-treatment assessment took place one week after treatment ended (median 0; range 0-8). Of the nine RCTs reporting follow-up data (i.e. the earliest assessment point ≥6 months after treatment ended), the mean follow-up assessment took place eight months after treatment ended (median 8; range 6-12). The mean total quality score on the POMRF was 16.8 out of 38, with median 16, and range 9-29 (i.e. mean 44% of the maximum possible score, median 41%, range 24-76%).

For patients providing outcome data for anxiety, the weighted mean proportion of missing data in the treatment group was 10% (95% CI, 5-17) at post-treatment and 11% (95% CI, 3-22) at follow-up. This compared to 9% (95% CI, 4-16) and 12% (95% CI, 8-16), respectively, in the control group. For patients providing outcome data for depression, the weighted mean proportion of missing data in the treatment group was 13% (95% CI, 7-20) at post-treatment and 15% (95% CI, 9-22) at follow-up. This compared to 13% (95% CI, 6-22) and 17% (95% CI, 7-29), respectively, in the control group. For patients providing outcome data for general distress, the weighted mean proportion of missing data in the treatment group was 13% (95% CI, 7-21) at post-treatment and 15% (95% CI, 9-22) at follow-up. This compared to 13% (95% CI, 6-22) and 17% (95% CI, 7-29), respectively, in the control group.

**Preliminary analysis**

Effect sizes of RCTs that provided IPD (n=17) and those that did not provide IPD (n=19) did not differ for anxiety or general distress at post-treatment but they did differ for depression; RCTs that did not provide IPD had larger effects than those that did (see Figure C3 in the online supplementary material). RCTs that provided IPD and those that did not provide IPD did not differ on sample characteristics (i.e. age and sample size) or psychological treatment characteristics (i.e. type, format or duration; see appendix C in the online supplementary material).

**Clinical significance analysis**

***Recovery*** ***rates***

At post-treatment, the weighted recovery rate for anxiety was 30% (95% CI, 22-38) for treated patients and 15% (95% CI, 9-22) for controls, corresponding to a significant RD of 0.15. The weighted recovery rate for general distress was 30% (95% CI, 25-34) for treated patients and 15% (95% CI, 10-21) for controls, corresponding to a significant RD of 0.14. These RDs indicate that, on average, 15% and 14% more treated patients than controls recovered from anxiety and general distress, respectively. The weighted recovery rate for depression was 32% (95% CI, 20-45) for treated patients and 25% (95% CI, 15-38) for controls, which corresponded to a non-significant RD of 0.04.

At follow-up, weighted recovery rates for anxiety, depression, and general distress were 30% (95% CI, 15-47), 29% (95% CI, 9-55), and 21% (95% CI, 8-38) for treated patients and 35% (95% CI, 21-49), 28% (95% CI, 6-57), and 21% (95% CI, 8-38) for controls, which corresponded to non-significant RDs of -0.03, -0.01, and 0.03, respectively. Moderate heterogeneity was indicated for depression (I2=62%; see Table 5; see appendix D2 in the online supplementary material for individual RDs for recovery for each RCT).

***Influence of potential moderators on recovery rates***

Methodological quality moderated recovery rates for general distress; in comparison to controls, treated patients had a higher probability of recovering in higher quality trials (β=0.01, 95% CI 0-0.03, p=0.04), Methodological quality did not moderate recovery rates for anxiety or depression. Treatment type, treatment format, therapists’ profession, nature of the control condition, age, and the outcome measure used did not moderate recovery rates (see Table 4; see appendix E in the online supplementary material for weighted meta-regression analysis).

***Improvement and deterioration rates***

*Improvement rates.* At post-treatment, the weighted improvement rate for anxiety was 49% (95% CI, 40-57%) for treated patients and 29% (95% CI, 22-37%) for controls, which corresponded to a significant RD of 0.21. The weighted improvement rate for depression was 50% (95% CI, 38-62%) for treated patients and 38% (95% CI, 32-44%) for controls, which corresponded to a significant RD of 0.10. The weighted improvement rate for general distress was 55% (95% CI, 48-63) for treated patients and 38% (95% CI, 30-46) for controls, which corresponded to a significant RD of 0.17. These RDs indicate that, on average, 21%, 10%, and 17% more treated patients than controls improved for anxiety, depression, and general distress, respectively. Moderate heterogeneity was indicated for anxiety (I2=61%) and general distress (I2=55%; see Table 6; see appendix D3 in the online supplementary material for individual RDs for improvement for each RCT).

At follow-up, weighted improvement rates for anxiety, depression, and general distress were 47% (95% CI, 28-66), 47% (95% CI, 31-63), and 45% (95% CI, 30-60) for treated patients and 50% (95% CI, 36-64), 49% (95% CI, 29-68), and 46% (95% CI, 29-63) for controls, corresponding to non-significant RDs of 0.03, -0.03, and -0.01, respectively (see Table 7; see appendix D4 in the online supplementary material for individual RDs for improvement for each RCT).

*Deterioration rates.* At post-treatment, weighted deterioration rates for anxiety, depression and general distress were 7% (95% CI, 4-11), 6% (95% CI, 3-8), and 8% (95% CI, 6-11) for treated patients and 11% (95% CI, 8-15), 8% (95% CI, 4-12), and 13% (95% CI, 10-16) for controls, corresponding to non-significant RDs of -0.03, -0.02, and -0.03, respectively (see Table 8; see appendix D5 in the online supplementary material for individual RDs for deterioration for each RCT ).

At follow-up, weighted deterioration rates for anxiety, depression and general distress were 12% (95% CI, 6-19), 4% (95% CI, 2-7), and 8% (95% CI, 4-13) for treated patients and 9% (95% CI, 5-16), 8% (95% CI, 5-13), and 15% (95% CI, 8-23) for controls, corresponding to non-significant RDs of 0.01, -0.02, and -0.04, respectively (see Table 9; see appendix D6 in the online supplementary material for individual RDs for deterioration for each RCT).

***Influence of potential moderators on improvement and deterioration rates***

*Improvement rates.* Treatment type moderated improvement rates for general distress; in comparison to controls, the probability of improving was higher for CBT (RD=0.35) than psychoeducation (RD=0.04), support (RD=0.01), and ‘other’ treatments (RD=0.00). Treatment type did not moderate improvement rates for anxiety or depression. The outcome measure used moderated improvement rates for depression; in comparison to controls, treated patients had a higher probability of improving in trials using the HADS-D (RD=0.16) than the CES-D (RD=-0.02). Outcome measures did not moderate improvement rates for anxiety or general distress.

Methodological quality moderated improvement rates for general distress; in comparison to controls, treated patients had a higher probability of improving in higher quality trials (β=0.03, 95% CI 0.01-0.05, p=0.01) but not for anxiety or depression. Therapists’ profession moderated improvement rates for anxiety; in comparison to controls, treated patients had a higher probability of improving if treatment was delivered by a clinical psychologist (RD=0.33) than other professionals (RD=0.10) but not for depression or general distress. Treatment format, control condition, and age were not moderators of improvement rates on any outcome (see Table 6; see appendix E in the online supplementary material for weighted meta-regression analysis).

*Deterioration rates.* Treatment type moderated deterioration rates for general distress; in comparison to controls, the probability of deteriorating was lower in CBT (RD=-0.09) and psychoeducation (RD=-0.04) but higher in ‘other’ treatments (RD=0.02) and support (RD=0.09). Treatment type did not moderate deterioration rates for anxiety or depression (see Table 8). Treatment format, therapists’ profession, nature of the control condition, age, outcome measure, and methodological quality did not moderate deterioration rates on any outcome (see Table 8; see appendix E in the online supplementary material for weighted meta-regression analysis).

**Sensitivity analysis**

In the RD analysis for recovery, one outlier was identified for anxiety at post-treatment. After its removal, the overall RD remained significant. No other outliers were identified.

The exclusion of the two RCT including multimodal treatment designed to alleviate insomnia and associated distress did not impact RDs for recovery or deterioration on any outcome. However, after their removal, the overall RD for depression was no longer significant (p=0.07; see Table 4; see appendix D1 in the online supplementary material for individual RDs for recovery, improvement and deterioration for each RCT).

**Effect size analysis**

At post-treatment, there were small but significant effect sizes in favour of treated patients for anxiety (g=0.34), depression (g=0.32) and general distress (g=0.33). At follow-up, the difference between treated patients and controls, as measured by the pooled SMD effect size, was trivial and no longer significant for anxiety (g=-0.07), depression (g=0.03), or general distress (g=0.11; see Table 11; see appendix D8 in the online supplementary material for individual effect sizes for each RCT).

***Influence of potential moderators on effect sizes***

Treatment type moderated between-group effect sizes for anxiety and general distress. For anxiety, there was a medium effect in favour of CBT (g=0.56) but a trivial effect for support (g=-0.05). There were insufficient studies (n<2) to evaluate the remaining treatment types. For general distress, there was a medium effect in favour of CBT (g=0.68) but trivial effects for ‘other’ treatments, (g=0.15), psychoeducation (g=0.11), and support (g=-0.11). Treatment type did not moderate effect sizes for depression (see Table 10).

Methodological quality moderated effect sizes for general distress with higher quality trials having larger treatment effects (β=0.06, 95% CI 0.01-0.10, p=0.01). Methodological quality did not moderate effect sizes for anxiety or depression. Age moderated effect sizes for anxiety with larger effects for participants of older age (β=0.08, 95% CI 0.00-0.16, p=0.04). Age did not moderate effect sizes for depression or general distress. Treatment format, therapists’ profession, nature of the control condition, and type of outcome measure used did not moderate effect sizes on any outcome (see Table 10; see appendix E in the online supplementary material for weighted meta-regression analysis).

***Sensitivity analysis***

One outlier was identified for general distress. After its removal, the overall effect size remained significant. No other outliers were identified.

The exclusion of the two RCTs including multimodal treatment designed to alleviate insomnia and associated distress did not impact effect sizes on any outcome (see Table 10; see appendix D7 in the online supplementary material for individual effect sizes for each RCT).

**DISCUSSION**

We used an IPD-MA to evaluate the efficacy of manualized psychological treatments for clinically distressed BCa patients on three outcomes: anxiety, depression, and general distress. By using Jacobson’s clinical significance analysis, we were able to investigate recovery rates and report improvement and deterioration rates. At post-treatment, treated patients were more likely than controls to recover from anxiety and general distress but not from depression. Treated patients also had a greater probability of improving than controls in anxiety, depression and general distress. However, treated patients were no more likely than controls to recover or improve on any outcome after a mean of 8 months follow-up. The probability of deteriorating did not differ between treated and control patients on any outcome at post-treatment or follow-up.

To detect whether different methods of analysis suggested different conclusions, we also evaluated treatment efficacy using IPD effect size analysis. The two methods largely converged. However, findings from the clinical significance analysis added a realistic indication of the *practical* significance of *statistically* significant findings. Despite statistically significant evidence of benefits for treated patients relative to controls at post-treatment for anxiety and general distress, the clinical significance analysis revealed that these benefits were small; only 15% and 14% more treated than control patients recovered from anxiety and general distress, respectively. Moreover, regardless of whether patients received treatment or control conditions, the proportion recovering was low; across outcomes, only 30-32% of treated patients recovered compared to 15-25% of controls. At follow-up, the proportion recovering remained low: only 21-30% of treated patients and 18-35% of controls recovered. The proportion of patients deteriorating was small, at around 10%.

Across the different methods of analysis, few moderator effects of treatment were found. The format of treatment (i.e. individual or group) and the nature of control condition did not moderate recovery, improvement or deterioration rates, nor did it moderate effect sizes, on any of the three outcomes (anxiety, depression, general distress).

Age moderated effect sizes for anxiety, with the magnitude of treatment effects greater the older the participants; the type of outcome measure moderated improvement rates for depression with patients more likely to be categorised as improved in trials measuring depression using the HADS-D than in trials using the CES-D relative to patients in control conditions; and therapists profession moderated improvement rates for anxiety, with clinical psychologists achieving higher improvement rates than other professionals. However, further exploration of whether specific allied health professional’s moderate treatment outcome, and whether this differs across the type of psychological treatment being delivered may help to determine training needs.

CBT seemed to be more efficacious than other treatments for some outcomes. For general distress, higher improvement rates, lower deterioration rates and larger effect sizes were found for patients receiving CBT than other therapeutic modalities; and for anxiety, CBT produced larger effect sizes than support. Treatment type did not moderate any form of clinical or statistical outcome for depression. Thus, CBT seems to lead to larger improvement rates and lower dextrorotation rates for general distress than other types of treatments but is no more advantageous than other treatments in terms of recovery. However, as there were more trials examining CBT (n=9) than other therapeutic modalities, the generalisability of these results may be limited.

Finally, methodological quality did moderate recovery and improvement rates for general distress; in comparison to controls, treated patients were more likely to recover and improve in higher quality trials. This finding was supported by the effect size analysis with higher quality trials having larger treatment effects. This diverges from previous meta-analyses that have shown that higher quality trials are associated with smaller treatment effects (Barth et al., 2013; Bohlmeijer, Prenger, Taal, & Cuijpers, 2010; Bolier et al., 2013; Cuijpers, van Straten, Bohlmeijer, Hollon, & Andersson, 2010; Huhn et al., 2014). The exclusion of the two RCTs testing the efficacy of multimodal treatment designed to alleviate insomnia and associated distress did not impact recovery, improvement or deterioration rates, or effect sizes for anxiety or general distress. However, treatment outcome for depression was affected, after their removal, patients in the multimodal treatment arm were no more likely to improve than those patients in the control condition. This may be attributable to decreased power due to the lower sample size.

There is no clear agreement about what proportion of distressed BCa patients, and how many more treated patients than controls, need to recover for a psychological treatment to be considered efficacious. However, recovery from psychological treatment in mental health populations provides a possible benchmark. When the same methodology as in the present study (i.e. the Jacobson method) has been used to define recovery in reviews in mental health populations (Fisher & Durham, 1999; Fisher & Wells, 2005; Ogles, Lambert, & Sawyer, 1995; Springer, Levy, & Tolin, 2018), psychological treatments have produced higher recovery rates (40-70%) than those we found (~30%). However, none of the reviews using the Jacobson method in mental health settings have assessed recovery in controls, so we do not know to what extent psychological treatment improves recovery rates beyond those achieved through receiving a control condition in those populations. However, in reviews in mental health populations that have used clinical significance methodology other than the Jacobson method (Cartwright‐Hatton, Roberts, Chitsabesan, Fothergill, & Harrington, 2004; Cuijpers et al., 2014; Ekers, Richards, & Gilbody, 2008; Öst & Ollendick, 2017; Öst, Riise, Wergeland, Hansen, & Kvale, 2016; Warwick et al., 2017; Zhou et al., 2015) differences in recovery rates between treated and control patients generally exceed those we found in BCa both at post-treatment (differences of 19-50%) and follow-up (differences of 28-55%) .

Our findings are also less encouraging than those of previous meta-analyses of the effects of psychological treatments on emotional distress in BCa. We can use our effect size analysis to make a direct comparison with the results of those analyses. The previous meta-analyses found small between-group effect sizes for general distress (0.26-0.31), and small to large between-group effect sizes for anxiety (0.28-1.1) and depression (0.21-1.13) at post-treatment (Cobeanu & David, 2018; Duijts et al., 2011; Jassim et al., 2015; Mustafa et al., 2013; Naaman et al., 2009; Tatrow & Montgomery, 2006; Xiao et al., 2017; Ye et al., 2018; Zhang et al., 2016; Zimmermann et al., 2007). By comparison, the post-treatment between-group effect sizes in our analysis were all small (0.32-0.34). In addition, unlike the previous meta-analyses, we reported a mean 8-month follow-up, finding no significant between-group effects whatsoever at this time. Moreover, as explained above, the clinical significance analysis indicated that there were no significant differences in recovery or improvement rates between treated and control patients at follow-up, with only around one third of all patients recovering. Thus, based on the effect size comparisons with previous meta-analyses in BCa and based on recovery rate comparisons in mental health populations, we can conclude only that psychological treatments for distressed BCa patients provide short-term benefit. Importantly, psychological treatment appears to increase the rate with which improvement and recovery is achieved for some patients, which is clinically meaningful for the patient, their families and significant others. However,these treatments seem less efficacious than those in mental health populations.

To some extent, our disappointing findings by comparison with those of previous meta-analyses might reflect our different methodology, whereby we sought evidence that would be more relevant to clinical practice than that arising from previous meta-analyses. We included only trials that used manualized treatments, and only analysed data for patients who were distressed. Moreover, by examining follow-up and by using clinical significance analysis, we were able to assess whether treatment benefits persisted and to what extent their effects were clinically significant. Therefore, our findings suggest that, for practitioners and policy-makers to be able to identify efficacious psychological treatment for distressed BCa patients, more convincing evidence is required than is presently available.

One possible reason why current evidence is disappointing might be that treatments have been inadequately implemented in trials. Although we only included trials that used manualized treatment, trials did not assess therapists’ adherence or competence to treatment, and most trials were delivered by professionals other than clinical psychologists (e.g. nurses, students or social workers). However, while therapists’ profession moderated improvement rates for anxiety, it did not moderate recovery rates, deterioration rates or effect sizes, suggesting that the profession of therapist had little impact on outcome. Another important possibility is that current therapeutic approaches are insufficient to meet the needs of distressed BCa patients. Most treatments were based on CBT, support or psychoeducation. In CBT, the central premise is that unrealistic appraisals of events initiate and maintain emotional distress. CBT therefore commonly seeks to reduce distress by testing the reality of unrealistic negative automatic thoughts (NATS; Rouf, 2004). However, NATs troubling BCa patients are often realistic (e.g. ‘my cancer may return’ or ‘my cancer is putting a financial strain on my family’). Thus, challenging such thoughts might be ineffective in BCa (Greer, Park, Prigerson, & Safren, 2010). Likewise, supportive interventions and psychoeducation often focus on fears of cancer recurrence or changes in body-image but, as with CBT, realistic appraisals of events can be resistant to change. Psychotherapeutic approaches that challenge, not the content of specific negative thoughts but, instead, the processes which lead individuals to respond negatively to such thoughts might therefore be more suitable in BCa. An additional advantage of focusing on psychological processes is that it offers the potential to address comorbid emotional problems. This could benefit BCa patients who often present with mixed symptoms of anxiety and depression. Examples of such approaches include MBT, acceptance and commitment therapy (ACT), and metacognitive therapy (MCT), all of which are manualized treatments for which preliminary evidence of efficacy in cancer is growing (e.g. Rost, Wilson, Buchanan, Hildebrandt, & Mutch, 2012; Fisher et al., 2019; Würtzen et al., 2013). In this meta-analysis, only one treatment was based on MBT and none on MCT or ACT. Thus, we could not evaluate their efficacy.

In addition to being unable to examine the treatment effects of emerging interventions for BCa patients with clinical levels of distress; several factors potentially limited the robustness of our conclusions. First, only 50%, (17 of 36) of eligible RCTs provided IPD which could compromise generalisability. However, there were no significant differences in the between-group effect sizes for included versus non-included RCTs for two of our three primary outcomes; anxiety or general distress; there was a significantly larger effect size for depression in favour of the treatment conditions compared to treatment as usual. However, the comparisons of between-group effects sizes between included and non-included trials were based on the total sample of all trials, most of which included non-distressed participants.

Second, the evaluation of the efficacy of psychological treatment specifically for clinically distressed BCa patients necessitated the sole inclusion of RCTs using an outcome measure with an established cut-off for clinical levels of distress. However, using established measures with sound psychometric properties could enhance both the internal and external validity of our results

Third, it is possible the current study overestimated the efficacy of psychological treatments because analyses were only based on patients who completed post-treatment and/or follow-up assessments. Notably larger effects have been found for trials conducted on a per-protocol basis compared to an ITT basis (Cuijpers et al., 2010).

Fourth, several sociodemographic factors (e.g. income and education level) and clinical factors (e.g. type of medical treatment patients received and the point in the disease trajectory patients received psychological treatment) known to be clinically relevant were not included as potential moderators in this IPD-MA as the data was not requested and could not extracted from published reports. Testing the moderating impact of additional sociodemographic and clinical variables not included in this IPD-MA is clinically relevant and should be examined in subsequent RCTs of psychological treatment for BCa patients with clinical levels of emotional distress. Testing the moderating effect of age was examined at the study level (i.e. mean age was used for each RCT) rather than the participant level. Examining age at the study level increases the likelihood of bias as it does not account for within-study variation; the mean age for each RCT does not properly reflect the actual age of participants within the sample (Riley, Lambert, & Abo-Zaid, 2010; Riley & Steyerberg, 2010).

Our findings point to important challenges for future research. Health care policies specify that psychological treatment should be available to BCa patients as part of their routine care (Holland et al., 2011; Page & Adler, 2008; Tit et al., 2017). However, current evidence does not indicate that psychological treatment can yet adequately meet the needs of distressed BCa patients. Clearly, research is urgently required so that practitioners can direct patients to efficacious treatments, and policy-makers can ensure that efficacious treatments are made available. Researchers need to confront four specific challenges. First, treatments should in future be assessed according to their clinical significance and the persistence of their benefits (only three RCTs in this study examined long-term treatment effects i.e. ≥12 months after completion of psychological treatment). Short-term benefits for a small minority of distressed patients should not be the end-point of treatment development in this area, and researchers will need to seek benefits at least as good as those that psychological treatment achieves in mental health populations. Second, researchers will need to ensure that treatments are administered accurately. Thus, as well as using treatment manuals, they will need to ensure that treatments are delivered by certified trained therapists, and to confirm therapist adherence and competence. Third, determining if psychological treatments reduce other forms of distress e.g. fear of cancer recurrence, traumatic stress symptoms, and body image concerns is required to enable assessment of the breadth of impact of psychological interventions. Finally, since existing treatments have not yet been shown to deliver the level or persistence of benefits that are needed, researchers should be open to new therapeutic modalities that may be more efficacious in the context of physical health conditions such as BCa.

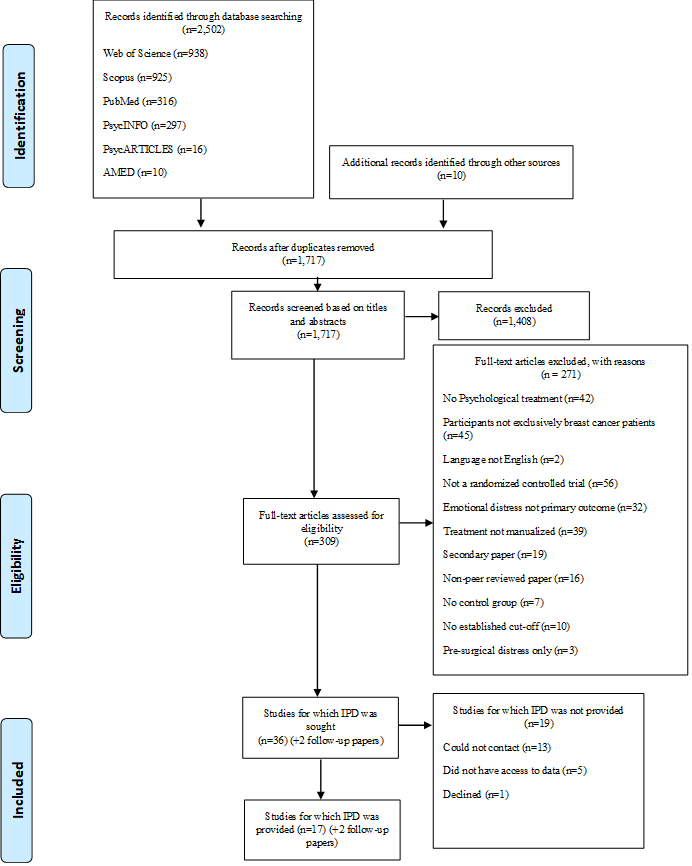
**Conclusion**

Based on the RCTs included in this IPD-MA, we conclude that approximately 70% of distressed BCa patients remain distressed following psychological treatment. Patients receiving psychological treatment are slightly more likely to recover from anxiety and general distress than those receiving a control condition immediately after treatment ends. However, patients receiving psychological treatment are no more likely than controls to recover from depression and, after around 8 months, they are no more likely to have recovered from anxiety, depression or general distress. More efficacious psychological treatments are needed for BCa patients with emotional distress.

FIGURES

Figure 1

*PRISMA flow chart showing trial identification and selection*



TABLES

Table 1.

*Data used to determine the Reliable Change Index (RCI) and cut off point a) on each outcome measure*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome measure** | **n1** | **M1** | **SD1** | **Sdiff** | **Rxx** | **RCI** | **Cut-off point a)a** |
| CES-D | 351b | 27.95 | 10.98 | 5.15 | 0.89 | 10 | 6 |
| HADS-D | 511c | 10.57 | 2.58 | 1.67 | 0.79 | 3 | 5 |
| POMS-TMD | 492 | 67.9 | 25.03 | 11.29 | 0.9 | 22 | 18 |
| HADS-T | 807c | 20.03 | 5.27 | 2.79 | 0.86 | 5 | 9 |
| HADS-A | 866c | 11.51 | 2.93 | 1.75 | 0.82 | 3 | 6 |
| STAI-T | 186 | 49.64 | 7.96 | 4.06 | 0.87 | 8 | 38 |
| *Note.* n1= number of individuals scoring above established cut-offs for clinical levels of emotional distress pre-treatment; M1= pre-treatment mean; SD1 = pre-treatment standard deviation; Sdiff = pre-treatment standard error of difference; Rxx = internal consistency; RCI = reliable change index at p<0.05; a Score required post-treatment to be classed as part of the normal population; b we included pre-treatment scores on the CES-D (n=39) from one additional trial (Badger et al., 2013) for which we received IPD but excluded from the IPD-MA because there was no control condition, and one additional treatment group from Stanton et al. (2005) for which we received IPD (n=43) but excluded from the IPD-MA because it involved no interaction between therapist and patient (i.e. it was based exclusively on visual material); c we included pre-treatment scores (n=68 for HADS-T, n=31 for HADS-D; n=76 for HADS-A) fromone additional trial (Rissanen, Nordin, Ahlgren, & Arving, 2015) for which we received IPD but excluded from the IPD-MA because there was no control condition, and one additional treatment group (n=25 for HADS-T; n=19 for HADS-D; n=20 for HADS-A) from Desautels et al. (2018) because it involved no interaction between therapist and patient (i.e. it was based exclusively on visual material) | | | | | | | |

Table 2.

*Characteristics of patients included in the IPD-MA*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Mean age** | **BCa metastases** | **Mean time since diagnosis (months)** | **Total sample size** | **Distressed sample size** | **Distressed sample size by measure** |
| Andersen et al. (2004; 2007) | 51 | Non-metastatic | NR | 227 | 95 | POMS-TMD = 95 |
| Antoni et al. (2001) | 50 | Non-metastatic | NR | 136 | 44 | CES-D = 44 |
| Beutel et al. (2014) | 52 | Non-metastatic | NR | 156 | 156 | HADS-A = 141 HADS-D = 156 HADS-T = 155 |
| Bredal et al. (2014) | 55 | Non-metastatic | 0 | 367 | 219 | HADS-A = 207 HADS-D = 108 HADS-T = 178 |
| Carlson et al. (2013) | 55 | Non-metastatic | 25 | 271 | 108 | POMS-TMD = 108 |
| Classen et al. (2008) | 50 | Non-metastatic | 7 | 353 | 169 | HADS-A = 131 HADS-D = 54 POMS-TMD = 113 |
| Desautels et al. (2018) | 57 | Non-metastatic | 14 | 51 | 34 | HADS-D = 28 HADS-A = 26 HADS-T = 33 |
| Dirksen et al. (2007) | 58 | Non-metastatic | 74 | 81 | 37 | STAI-T = 33 CES-D = 19 |
| Dolbeault et al. (2009) | 53 | Non-metastatic | NR | 203 | 153 | STAI-T = 153 POMS-TMD = 100 |
| Groarke et al. (2012) | 54 | All stages | NR | 179 | 71 | HADS-A = 63 HADS-D = 24 HADS-T = 53 |
| Ho et al. (2016) | 48 | Non-metastatic | 24 | 157 | 74 | HADS-A = 64 HADS-D =23 HADS-T:60 |
| Lechner et al. (2014) | 51 | All stages | 14 | 114 | 114 | CES-D = 114 |
| Merckaert et al. (2016) | 51 | Non-metastatic | NR | 159 | 91 | HADS-A = 83 HADS-D = 36 HADS-T = 71 |
| Sandgren et al. (2003;2007) | 55 | Non-metastatic | 2 | 237 | 76 | POMS-TMD = 76 |
| Savard et al. (2005) | 54 | Non-metastatic | 21 | 57 | 25 | HADS-A = 24 HADS-D = 6 HADS-T = 18 |
| Savard et al. (2006) | 52 | Metastatic | 71 | 37 | 33 | HADS-A = 31 HADS-D = 26 HADS-T = 33 |
| Stanton et al. (2005) | 58 | Non-metastatic | NR | 371 | 92 | CES-D = 92 |
| NR = not reported | | | | | | |

Table 3.

*Characteristics of trials included in the IPD-MA*

| **Author** | **Treatment** | | | |  | **Control** | | | | **Outcome measures** | **Quality score** | **Country** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Type of treatment** | **Mode of delivery** | **Total length (hrs)** | **Therapists** |  | **Type of control** | **Total length (hrs)** | **Mode of delivery** | **Therapists** |
| Andersen et al. (2004; 2007) | Other | Group | 27 | Clinical psychologists |  | Assessment only | 0 | - | - | POMS | 15 | USA |
| Antoni et al. (2001) | CBT | Group | 20 | Post-doctoral fellows & advanced graduate students in clinical psychology |  | Condensed version of active treatmenta | 5-6 | Group | Post-doctoral fellows & advanced graduate students in clinical psychology | CES-D | 14 | USA |
| Beutel et al. (2014) | PsyDy | Individual | NRb | Certified psychodynamic therapists & advanced post-graduate trainees |  | Offered referral to GP for psychological/ pharmacological treatmentc | NRd | - | NR | HADS | 20 | Germany |
| Bredal et al. (2014) | Psychoedu | Group | 10 | Nurses |  | Nurse-led supportc | 6 | Group | Nurses | HADS | 12 | Norway |
| Carlson et al. (2013) | MBT | Group | 21 | NR |  | Stress management seminara | 6 | Group | NR | POMS | 19 | Canada |
|  | Supportive therapy | Group | 18 | NR |  |  |  |  |  |  |  |  |
| Classen et al. (2008) | Support + education material | Group | 18 | Nurses, social workers & psychologists |  | Education material | - | - | - | HADS, POMSe | 16 | USA |
| Desautels et al. (2018) | CBT | Individual | 8 | Doctoral level student in clinical psychology |  | Wait-list control | 0 | - | - | HADS | 29 | Canada |
| Dirksen et al. (2007) | CBT | Group | 5.5f | Master’s level Registered Nurse therapist |  | Educational components of active treatmenta | 5.5f | Group | Master’s level Registered Nurse therapist | CES-D, STAI | 16 | USA |
| Dolbeault et al. (2009) | CBT | Group | 16 | Clinical psychologists |  | WLC | 0 | - | - | POMS, STAI | 15 | France |
| Groarke et al. (2012) | CBT | Group | 15 | Clinical psychologists |  | Support from oncology nursesc | NR | NR | Oncology nurses | HADS | 15 | Ireland |
| Ho et al. (2016) | Other | Group | 16 | Clinical psychologist & medical social worker |  | Self-help support groupa | 16 | Group | Social workers | HADS | 18 | Hong Kong |
|  | Supportive therapy | Group | 16 | Social workers |  |  |  |  | - |  |  |  |
| Lechner et al. (2014) | CBT | Group | 15 | Clinical psychologists |  | Educational information delivered by therapista | 15 | Group | Graduate-level interventionist | CES-D | 19 | USA |
| Merckaert et al. (2016) | CBT | Group | 30 | Clinical psychologists |  | Peer supportc | 16 | Group | Clinical psychologists | HADS | 15 | Belgium |
| Sandgren et al. (2003;2007) | Psychoedu | Individualg | 3 | Nurses |  | Nurse help line was availablec | NR | Individualg | Nurses | POMS | 9 | USA |
|  | Other | Individualg | 3 | Nurses |  | - | - | - | - | - |  |  |
| Savard et al. (2005) | CBT | Group | 13.5 | Masters level psychologist |  | Wait-list control | 0 | - | - | HADS | 19 | Canada |
| Savard et al. (2006) | CBT | Individual | 11 | Clinical psychologists |  | Wait-list control | 0 | - | - | HADS | 20 | Canada |
| Stanton et al. (2005) | Psychoedu + education material | Individual | 1.8 | Trained cancer educators at masters- or doctoral-level |  | Education material | - | - | - | CES-D | 15 | USA |
| *Note.* Hyphen indicates not applicable; PsyDy = Psychodynamic; CBT = cognitive behavioural therapy; MBT = mindfulness-based therapy; Psychoedu = psychoeducation; USA = United States; NR = not reported; hrs = hours; a active control; b number of sessions varied (mean 18, range 0-31); c treatment as usual; d number of sessions varied (mean 2.4, range 0-24); e Classen et al. (2008) provided IPD for general distress on both the HADS-T and POMS-TMD. We chose to use IPD for general distress on the POMS-TMD as this was their primary outcome measure; f session 1 = 2 hours, sessions 2-4 = ≤1 hour, sessions 5-6 = 15 minutes; g session delivered individually via the telephone | | | | | | | | | | | | |

Table 4.

*Weighted recovery rates and risk differences for recovery at post-treatment (≤8 weeks after treatment)*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | **Weighted recovery rates** | | **Risk differences for recovery rates** | | | | |
| **Component** |  | **k** | **n** | **Treatment %  [95% CI]** | **Control % [95% CI]** | **RDa [95% CI]** | **p** | **I2** | **Q(df)** | **p** |
| **Anxiety** | | | | | | | | | | |
| Overall effect |  | 12 | 865 | 30% [22-38%] | 15% [9-22%] | 0.15 [0.07-0.22] | <0.01\* | 0.38 |  |  |
| Outlier(s) removed |  | 11 | 802 |  |  | 0.11 [0.06-0.16] | <0.01\* | 0 |  |  |
| Insomnia Tx removed |  | 10 | 815 | 28% [21-37%] | 15% [8-22%] | 0.14 [0.06-0.21] | <0.01\* | 0.45 |  |  |
| Treatment format |  |  |  |  |  |  |  |  | 0.66(1) | 0.42 |
| *Individual* |  | 3 | 152 | 28% [14-44%] | 9% [3-17%] | 0.19 [0.08-0.30] | <0.01 | 0 |  |  |
| *Group* |  | 9 | 713 | 30% [21-40%] | 17% [10-25%] | 0.13 [0.05-0.21] | <0.01 | 0.44 |  |  |
| Treatment type |  |  |  |  |  |  |  |  | 2.73(1) | 0.1 |
| *CBT* |  | 7 | 391 | 33% [19-49%] | 11% [5-18%] | 0.22 [0.09-0.35] | <0.01 | 0.61 |  |  |
| *Psychodynamic* |  | 1 | - |  |  | - | - | - |  |  |
| *Psychoeducation* |  | 1 | - |  |  | - | - | - |  |  |
| *Support* |  | 2 | 147 | 25% [16-35%] | 19% [11-29%] | 0.07 [-0.07-0.20] | 0.34 | 0 |  |  |
| *Other* |  | 1 | - |  |  | - | - | - |  |  |
| Control type |  |  |  |  |  |  |  |  | 0.47(2) | 0.79 |
| *Active* |  | 3 | 90 | 28% [17-41%] | 20% [9-33%] | 0.1 [-0.07-0.28] | 0.25 | 0 |  |  |
| *TAU* |  | 4 | 446 | 34% [24-46%] | 17% [9-28%] | 0.18 [0.02-0.33] | 0.02\* | 0.72 |  |  |
| *WLC/ no treatment* |  | 4 | 216 | 27% [10-48%] | 7% [2-15%] | 0.17 [0.02-0.32] | 0.02\* | 0.41 |  |  |
| *Edu material* |  | 1 | - |  |  | - | - | - |  |  |
| Therapists' profession |  |  |  |  |  |  |  |  | 2.64(1) | 0.1 |
| *Clin Psychologist* |  | 5 | 337 | 36% [17-57%] | 11% [4-21%] | 0.24 [0.06-0.41] | 0.01\* | 0.73 |  |  |
| *Other professional* |  | 5 | 397 | 28% [22-35%] | 21% [14-29%] | 0.08 [-0.01-0.16] | 0.07 | 0 |  |  |
| Outcome measure |  |  |  |  |  |  |  |  | 0.25(1) | 0.62 |
| *HADS-A* |  | 10 | 689 | 32% [25-39%] | 18% [13-23%] | 0.16 [0.07-0.24] | <0.01\* | 0.43 |  |  |
| *STAI-T* |  | 2 | 176 | 22% [3-52%] | 7% [0-19%] | 0.11 [-0.03-0.26] | 0.11 | 0.25 |  |  |
| **Depression** | | | | | | | | | | |
| Overall effect |  | 14 | 624 | 32% [20-45%] | 25% [15-38%] | 0.04 [-0.03,0.11] | 0.23 | 0.19 |  |  |
| Outlier(s) remover |  |  |  |  |  |  |  |  |  |  |
| Insomnia Tx removed |  | 12 | 601 | 30% [18-43%] | 23% [12-35%] | 0.04 [-0.03-0.12] | 0.24 | 0.29 |  |  |
| Treatment format |  |  |  |  |  |  |  |  | 1.59(1) | 0.21 |
| *Individual* |  | 4 | 227 | 35% [20-52%] | 24% [16-33%] | 0.08 [-0.03,0.20] | 0.16 | 0.07 |  |  |
| *Group* |  | 10 | 397 | 31% [15-48%] | 25% [10-43%] | 0.01 [-0.03,0.04] | 0.75 | 0 |  |  |
| Treatment type |  |  |  |  |  |  |  |  | 0.27(2) | 0.87 |
| *CBT* |  | 8 | 229 | 36% [15-61%] | 30% [11-53%] | 0.03 [-0.06,0.12] | 0.51 | 0.15 |  |  |
| *Psychodynamic* |  | 1 | - |  |  | - | - | - |  |  |
| *Psychoeducation* |  | 2 | 163 | 22% [11-35%] | 24% [15-35%] | -0.01 [-0.14,0.12] | 0.87 | 0 |  |  |
| *Support* |  | 2 | 57 | 32% [18-48%] | 26% [0-71%] | 0.04 [-0.29,0.36] | 0.83 | 0.45 |  |  |
| *Other* |  | 1 | - |  |  | - | - | - |  |  |
| Control type |  |  |  |  |  |  |  |  | 3.65(3) | 0.3 |
| *Active* |  | 5 | 189 | 21% [3-47%] | 10% [0-30%] | 0.09 [-0.10,0.28] | 0.36 | 0.57 |  |  |
| *TAU* |  | 4 | 276 | 35% [27-43%] | 27% [19-36%] | 0.08 [-0.03,0.18] | 0.15 | 0 |  |  |
| *WLC/ no Treatment* |  | 3 | 51 | 55% [32-77%] | 41% [21-62%] | 0.19 [-0.07,0.45] | 0.15 | 0 |  |  |
| *Edu material* |  | 2 | 108 | 24% [8-45%] | 32% [13-56%] | -0.07 [-0.23,0.09] | 0.4 | 0 |  |  |
| Therapists’ profession |  |  |  |  |  |  |  |  | 0.52(1) | 0.47 |
| *Clin Psychologist* |  | 4 | 189 | 30% [2-71%] | 26% [2-66%] | 0.00 [-0.03-0.04] | 0.95 | 0 |  |  |
| *Other professional* |  | 7 | 266 | 30% [20-40%] | 25% [17-33%] | 0.04 [-0.06-0.14] | 0.43 | 0 |  |  |
| Outcome measure |  |  |  |  |  |  |  |  | 3.66(1) | 0.06 |
| *HADS-D* |  | 10 | 392 | 37% [31-44%] | 30% [22-39%] | 0.09 [0.00,0.18] | 0.04 | 0 |  |  |
| *CES-D* |  | 4 | 232 | 15% [2-37%] | 15% [1-39% | 0 [-0.03,0.03] | 0.97 | 0 |  |  |
| **General distress** | | | | | | | | | | |
| Overall effect |  | 16 | 937 | 30% [25-34%] | 15% [10-21%] | 0.14 [0.08,0.20] | <0.01\* | 0.18 |  |  |
| Outlier(s) removed |  |  |  |  |  |  |  |  |  |  |
| Insomnia Tx removed |  | 15 | 922 | 30% [25-35%] | 16% [11-22%] | 0.14 [0.08-0.20] | <0.01\* | 0.21 |  |  |
| Treatment format |  |  |  |  |  |  |  |  | 1.68(1) | 0.2 |
| *Individual* |  | 5 | 245 | 34% [23-45%] | 12% [5-21%] | 0.20 [0.09,0.32] | <0.01\* | 0.18 |  |  |
| *Group* |  | 11 | 692 | 29% [24-33%] | 16% [10-23%] | 0.12 [0.05,0.18] | <0.01\* | 0.14 |  |  |
| Treatment type |  |  |  |  |  |  |  |  | 7.06(3) | 0.07 |
| *CBT* |  | 6 | 290 | 33% [26-40%] | 9% [5-15%] | 0.24 [0.16,0.33] | <0.01\* | 0 |  |  |
| *Psychodynamic* |  | 1 | - |  |  | - | - |  |  |  |
| *MBT* |  | 1 | - |  |  | - | - |  |  |  |
| *Psychoeducation* |  | 2 | 192 | 37% [17-59%] | 28% [19-38%] | 0.08 [-0.17,0.34] | 0.52 | 0.55 |  |  |
| *Support* |  | 3 | 163 | 26% [18-35%] | 24% [11-40%] | 0.06 [-0.08,0.20] | 0.43 | 0.12 |  |  |
| *Other* |  | 3 | 143 | 23% [15-33%] | 13% [6-24%] | 0.10 [-0.02,0.22] | 0.11 | 0 |  |  |
| Control type |  |  |  |  |  |  |  |  | 3.31(2) | 0.19 |
| *Active* |  | 4 | 128 | 28% [14-44%] | 19% [6-38%] | 0.10 [-0.04,0.23] | 0.16 | 0 |  |  |
| *TAU* |  | 6 | 472 | 30% [23-37%] | 17% [9-27%] | 0.12 [0.03,0.21] | 0.01\* | 0.24 |  |  |
| *WLC/ no treatment* |  | 5 | 244 | 30% [23-38%] | 9% [4-15%] | 0.22 [0.13,0.32] | <0.01\* | 0.05 |  |  |
| *Edu material* |  | 1 | - |  |  | - | - |  |  |  |
| Therapists’ profession |  |  |  |  |  |  |  |  | 0.31(1) | 0.58 |
| *Clin Psychologist* |  | 5 | 321 | 29% [23-36%] | 11% [6-16%] | 0.19 [0.11-0.27] | <0.01\* | 0 |  |  |
| *Other professional* |  | 7 | 429 | 29% [23-37%] | 14% [16-25%] | 0.15 [0.04-0.26] | 0.01\* | 0.42 |  |  |
| Outcome measure |  |  |  |  |  |  |  |  | 0.33(1) | 0.57 |
| *HADS-T* |  | 9 | 528 | 27% [22-32%] | 11% [6-19%] | 0.16 [0.08,0.24] | <0.01\* | 0.35 |  |  |
| *POMS-TMD* |  | 7 | 409 | 33% [25-41%] | 20% [12-30%] | 0.13 [0.04,0.21] | <0.01\* | 0 |  |  |
| Note. k = number of treatment/control group comparisons; n = number of patients; RD = risk difference; CI = confidence interval; I2 = measure of heterogeneity; Q = ratio of variation to within-study error; DF = degrees of freedom; CBT = cognitive behavioural therapy; MBT= mindfulness-based therapy; support = supportive therapy; edu = education; a risk differences were scaled so that positive values represented effects in favour of treatment; \* = p<0.05 | | | | | | | | | | |

Table 5.

*Weighted recovery rates and risk differences for recovery at follow-up (≥6 months after treatment)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | **Weighted recovery rates** | | **Risk differences for recovery rates** | | |
| **Outcome** |  | **k** | **n** | **Treatment %  [95% CI]** | **Control %  [95% CI]** | **RDa [95% CI]** | **p** | **I2** |
| Anxiety |  | 5 | 417 | 30% [15-47%] | 35% [21-49%] | -0.03 [-0.12-0.06] | 0.48 | 0 |
| Depression |  | 8 | 389 | 29% [9-55%] | 28% [6-57%] | -0.01 [-0.14-0.12] | 0.86 | 0.62 |
| General distress |  | 8 | 497 | 21% [8-38%] | 18% [7-34%] | 0.03 [-0.03-0.09] | 0.31 | 0 |
| *Note.* k = number of treatment/control group comparisons; n = number of patients; RD = risk difference; CI = confidence interval; I2 = measure of heterogeneity; a were scaled so that positive values represented effects in favour of treatment | | | | | | | | |

Table 6.

*Weighted improvement rates and risk differences for improvement at post-treatment (≤8 weeks after treatment)*

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Weighted improvement rates** | | | | | | **Risk differences for improvement rates** | | | | |
| **Component** |  | **k** | | **n** | **Treatment % [95% CI]** | **Control % [95% CI]** | **RDa [95% CI]** | **p** | **I2** | **Q(df)** | **p** |
| **Anxiety** | | | | | | | | | | | |
| Overall effect |  | 12 | | 865 | 49% [40-57%] | 29% [22-37%] | 0.21 [0.10-0.32] | <0.01\* | 0.61 |  |  |
| Outlier(s) removed |  |  | |  |  |  |  |  |  |  |  |
| Insomnia Tx removed |  | 10 | |  | 47% [38-56%] | 30% [22-39%] | 0.18 [0.07-0.29] | <0.01\* | 0.62 |  |  |
| Treatment format |  |  | |  |  |  |  |  |  |  |  |
| *Individual* |  | 3 | | 169 | 58% [29-84%] | 36% [25-48%] | 0.21 [-0.14-0.55] | 0.24 | 0.73 | 0.00(1) | 1 |
| *Group* |  | 9 | | 713 | 46% [38-54%] | 27% [18-36%] | 0.21 [0.09-0.33] | <0.01\* | 0.62 |  |  |
| Treatment type |  |  | |  |  |  |  |  |  | 3.75(1) | 0.05 |
| *CBT* |  | 7 | | 408 | 55% [41-69] | 23% [14-34%] | 0.32 [0.17-0.47] | <0.01\* | 0.58 |  |  |
| *Psychodynamic* |  | 1 | | - |  |  |  |  |  |  |  |
| *Psychoeducation* |  | 1 | | - |  |  |  |  |  |  |  |
| *Support* |  | 2 | | 147 | 35% [17-57%] | 33% [22-44%] | 0.04 [-0.19-0.28] | 0.71 | 0.43 |  |  |
| *Other* |  | 1 | | - |  |  |  |  |  |  |  |
| Control type |  |  | |  |  |  |  |  |  | 0.48(2) | 0.79 |
| *Active* |  | 3 | | 117 | 42% [19-67%] | 29% [17-44%] | 0.14 [-0.24-0.53] | 0.47 | 0.75 |  |  |
| *TAU* |  | 4 | | 446 | 51% [44-59%] | 33% [25-42%] | 0.21 [0.04-0.37] | 0.02\* | 0.70 |  |  |
| *WLC/ no treatment* |  | 4 | | 207 | 53% [29-76%] | 24% [9-43%] | 0.29 [0.05-0.52] | 0.02\* | 0.58 |  |  |
| *Edu material* |  | 1 | | - |  |  |  |  |  |  |  |
| Therapists' profession |  | | |  |  |  |  |  |  | 3.93(1) | 0.04\* |
| *Clin Psychologist* |  | | 5 | 337 | 57%[40-74%] | 22%[12-33%] | 0.33 [0.19-0.48] | <0.01\* | 0.51 |  |  |
| *Other professional* |  | | 5 | 397 | 43%[32-54%] | 36%[29-43%] | 0.10 [-0.07-0.28] | 0.24 | 0.59 |  |  |
| Outcome measure |  |  | |  |  |  |  |  |  | 1.7(1) | 0.19 |
| *HADS-A* |  | 10 | | 706 | 49% [40-58%] | 34% [29-39%] | 0.18 [0.05-0.30] | 0.01\* | 0.61 |  |  |
| *STAI-T* |  | 2 | | 176 | 50% [22-78] | 13% [7-20%] | 0.34 [0.13-0.56] | <0.01\* | 0.46 |  |  |
| **Depression** | | | | | | | | | | | |
| Overall effect |  | 14 | | 624 | 50% [38-62%] | 38% [32-44%] | 0.1 [0.00-0.20] | 0.04\* | 0.34 |  |  |
| Outlier(s) remover |  |  | |  |  |  |  |  |  |  |  |
| Insomnia Tx removed |  | 12 | | 601 | 49% [36-62%] | 38% [31-44%] | 0.1 [-0.00-0.21] | 0.07 | 0.43 |  |  |
| Treatment format |  |  | |  |  |  |  |  |  | 3.57(1) | 0.06 |
| *Individual* |  | 4 | | 242 | 64% [43-82%] | 42% [32-51%] | 0.23 [0.03-0.43] | 0.03\* | 0.51 |  |  |
| *Group* |  | 10 | | 397 | 43% [30-56%] | 37% [28-47%] | 0.02 [-0.07-0.11] | 0.69 | 0 |  |  |
| Treatment type |  |  | |  |  |  |  |  |  | 1.06(2) | 0.59 |
| *CBT* |  | 8 | | 294 | 53% [33-72%] | 36% [27-46%] | 0.09 [-0.04-0.22] | 0.18 | 0.18 |  |  |
| *Psychodynamic* |  | 1 | | - |  |  |  |  |  |  |  |
| *Psychoeducation* |  | 2 | | 163 | 37% [27-47%] | 36% [26-47%] | 0 [-0.15-0.15] | 0.97 | 0 |  |  |
| *Support* |  | 2 | | 57 | 42% [16-70%] | 46% [12-82%] | -0.03 [-0.28-0.22] | 0.83 | 0 |  |  |
| *Other* |  | 1 | | - |  |  |  |  |  |  |  |
| Control type |  |  | |  |  |  |  |  |  | 7.08(3) | 0.07 |
| *Active* |  | 5 | | 214 | 35% [19-52%] | 27% [19-36%] | 0.01 [-0.11-0.13] | 0.90 | 0 |  |  |
| *TAU* |  | 4 | | 276 | 53% [31-74%] | 39% [31-47%] | 0.13 [-0.05-0.32] | 0.16 | 0.58 |  |  |
| *WLC/ no treatment* |  | 3 | | 42 | 75% [49-94%] | 45% [25-66%] | 0.34 [0.09-0.59] | 0.01\* | 0 |  |  |
| *Edu material* |  | 2 | | 108 | 46% [33-59%] | 50% [33-68%] | -0.04 [-0.23-0.15] | 0.68 | 0 |  |  |
| Therapists' profession |  | | |  |  |  |  |  |  | 0.23(1) | 0.63 |
| *Clin Psychologist* | 4 | | | 189 | 50%[18-82%] | 35%[21-51%] | 0.11 [-0.12-0.33] | 0.36 | 0.59 |  |  |
| *Other professional* | 7 | | | 266 | 42%[33-52%] | 38%[29-46%] | 0.04 [-0.07-0.16] | 0.46 | 0 |  |  |
| Outcome measure |  |  | |  |  |  |  |  |  | 4.5(1) | 0.03\* |
| *HADS-D* |  | 10 | | 407 | 57% [43-70%] | 41% [34-48%] | 0.16 [0.04-0.29] | 0.01\* | 0.33 |  |  |
| *CES-D* |  | 4 | | 232 | 35% [20-51%] | 33% [21-47%] | -0.02 [-0.13-0.09] | 0.73 | 0 |  |  |
| **General distress** | | | | | | | | | | | |
| Overall effect |  | 16 | | 937 | 55% [48-63%] | 38% [30-46%] | 0.17 [0.07-0.27] | <0.01\* | 0.55 |  |  |
| Outlier(s) removed |  |  | |  |  |  |  |  |  |  |  |
| Insomnia Tx removed |  | 15 | | 922 | 56% [48-63%] | 39% [31-47%] | 0.17 [0.07-0.27] | <0.01\* | 0.58 |  |  |
| Treatment format |  |  | |  |  |  |  |  |  | 0.45(1) | 0.5 |
| *Individual* |  | 5 | | 266 | 70% [56-82%] | 46% [34-58%] | 0.24 [-0.02-0.49] | 0.07 | 0.74 |  |  |
| *Group* |  | 11 | | 692 | 49% [42-56%] | 35% [26-44%] | 0.14 [0.05-0.23] | <0.01\* | 0.32 |  |  |
| Treatment type |  |  | |  |  |  |  |  |  | 23.12(3) | <0.01\* |
| *CBT* |  | 6 | | 311 | 63% [49-76%] | 26% [18-34%] | 0.35 [0.25-0.45] | <0.01\* | 0 |  |  |
| *Psychodynamic* |  | 1 | | - |  |  |  |  |  |  |  |
| *MBT* |  | 1 | | - |  |  |  |  |  |  |  |
| *Psychoeducation* |  | 2 | | 192 | 48% [33-63%] | 47% [21-75%] | 0.04 [-0.10-0.18] | 0.58 | 0 |  |  |
| *Support* |  | 3 | | 163 | 43% [28-58%] | 44% [26-62%] | 0.01 [-0.15-0.16] | 0.94 | 0 |  |  |
| *Other* |  | 3 | | 143 | 49% [34-65%] | 49% [26-72%] | 0.00 [-0.16-0.16] | 1 | 0 |  |  |
| Control type |  |  | |  |  |  |  |  |  | 4.31(2) | 0.12 |
| *Active* |  | 4 | | 161 | 43% [25-62%] | 37% [19-56%] | 0.04 [-0.14-0.22] | 0.64 | 0 |  |  |
| *TAU* |  | 6 | | 472 | 54% [44-64%] | 38% [27-51%] | 0.15 [-0.01-0.31] | 0.06 | 0.65 |  |  |
| *WLC/ no treatment* |  | 5 | | 233 | 67% [52-81%] | 35% [20-51%] | 0.32 [0.13-0.51] | <0.01\* | 0.57 |  |  |
| *Edu material* |  | 1 | | - |  |  |  |  |  |  |  |
| Therapists' profession |  | | |  |  |  |  |  |  | 1.78(1) | 0.18 |
| *Clin Psychologist* | 5 | | | 321 | 31% [3-72%] | 12% [1-32%] | 0.29 [0.13-0.45] | <0.01\* | 0.57 |  |  |
| *Other professional* | 7 | | | 429 | 32% [10-61%] | 22% [10-36%] | 0.14 [-0.02-0.30] | 0.09 | 0.59 |  |  |
| Outcome measure |  |  | |  |  |  |  |  |  | 3.13(1) | 0.08 |
| *HADS-T* |  | 10 | | 549 | 55% [41-58%] | 32% [25-38%] | 0.25 [0.13-0.37] | <0.01\* | 0.51 |  |  |
| *POMS-TMD* |  | 7 | | 409 | 56% [50-62% | 51% [36-65%] | 0.06 [-0.13-0.24] | 0.49 | 0.55 |  |  |
| *Note.* k = number of treatment/control group comparisons; n = number of patients; RD = risk difference; CI = confidence interval; I2 = measure of heterogeneity; Q = ratio of variation to within-study error; DF = degrees of freedom; CBT = cognitive behavioural therapy; MBT= mindfulness-based therapy; support = supportive therapy; edu = education; a risk differences were scaled so that positive values represented effects in favour of treatment; \* = p<0.05 | | | | | | | | | | | |

Table 7.

*Weighted improvement rates and risk differences for improvement at follow-up (≥6 months after treatment)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | | **Weighted improvement rates** | | **Risk differences for improvement rates** | | |
| **Outcome** |  | **k** | **n** | **Treatment % [95% CI]** | **Control % [95% CI]** | **RDa [95% CI]** | **p** | **I2** |
| Anxiety |  | 5 | 417 | 47% [28-66%] | 50% [36-64%] | 0.03 [-0.06-0.13] | 0.47 | 0 |
| Depression |  | 8 | 389 | 47% [31-63%] | 49% [29-68%] | -0.03 [-0.15-0.08] | 0.58 | 0.29 |
| General distress |  | 8 | 497 | 45% [30-60%] | 46% [29-63%] | -0.01 [-0.09-0.07] | 0.83 | 0 |
| *Note.* k = number of treatment/control group comparisons; n = number of patients; RD = risk difference; CI = confidence interval; I2 = measure of heterogeneity; a risk differences were scaled so that positive values represented effects in favour of treatment | | | | | | | | |

Table 8.

*Weighted deterioration rates and risk differences for deterioration at post-treatment (≤8 weeks after treatment)*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | | | | **Weighted deterioration rates** | | | | **Risk differences for deterioration rates** | | | | | | | |
| **Component** |  | **k** | | **n** | | **Treatment % [95% CI]** | | **Control % [95% CI]** | **RDa [95% CI]** | | **p** | **I2** | | | **Q(df)** | **p** | |
| **Anxiety** | | | | | | | | | | | | | | | | | |
| Overall effect |  | 12 | | 865 | | 7% [4-11%] | | 11% [8-15%] | -0.03 [-0.07-0.01] | | 0.15 | 0.12 | | |  |  | |
| Outlier(s) removed |  |  | |  | |  | |  |  | |  |  | | |  |  | |
| Insomnia Tx removed |  | 10 | | 815 | | 7% [4-12%] | | 11% [8-15%] | -0.03 [-0.07-0.01] | | 0.18 | 0 | | |  |  | |
| Treatment format |  |  | |  | |  | |  |  | |  |  | | | 0.13(1) | 0.72 | |
| *Individual* |  | 3 | | 152 | | 5% [0-13%] | | 10% [4-18%] | -0.01 [-0.10-0.08] | | 0.76 | 0 | | |  |  | |
| *Group* |  | 9 | | 713 | | 7% [4-12%] | | 11% [8-16%] | -0.03 [-0.08-0.02] | | 0.18 | 0.24 | | |  |  | |
| Treatment type |  |  | |  | |  | |  |  | |  |  | | | 3.04(1) | 0.08 | |
| *CBT* |  | 7 | | 391 | | 3% [1-6%] | | 11% [5-18%] | -0.06 [-0.13-0.00] | | 0.06 | 0.34 | | |  |  | |
| *Psychodynamic* |  | 1 | | - | |  | |  |  | |  |  | | |  |  | |
| *Psychoeducation* |  | 1 | | - | |  | |  |  | |  |  | | |  |  | |
| *Support* |  | 2 | | 147 | | 16% 8-27%] | | 10% [4-19%] | 0.05 [-0.06-0.15] | | 0.38 | 0 | | |  |  | |
| *Other* |  | 1 | | - | |  | |  |  | |  |  | | |  |  | |
| Control type |  |  | |  | |  | |  |  | |  |  | | | 3.73(2) | 0.16 | |
| *Active* |  | 3 | | 90 | | 10% [1-27%] | | 9% [1-23%] | 0.00 [-0.10-0.10] | | 0.98 | 0 | | |  |  | |
| *TAU* |  | 4 | | 446 | | 7% [2-14%] | | 10% [7-14%] | -0.01 [-0.06-0.04] | | 0.58 | 0 | | |  |  | |
| *WLC/ no* |  | 4 | | 216 | | 3% [0-8%] | | 17% [9-28%] | -0.12 [-0.22—0.02] | | 0.02\* | 0.22 | | |  |  | |
| *Edu material* |  | 1 | | - | |  | |  |  | |  |  | | |  |  | |
| Therapists' profession |  | |  | |  | |  |  |  | |  | |  | 3.6(1) | | | 0.06 |
| *Clin Psychologist* |  | | 5 | | 337 | | 13% [7-22%] | 13% [7-22%] | -0.09 [-0.17-0.00] | | 0.04\* | |  |  | | |  |
| *Other professional* |  | | 5 | | 397 | | 10% [4-18%] | 10% [6-16%] | 0.01 [-0.05-0.07] | | 0.72 | |  |  | | |  |
| Outcome measure |  |  | |  | |  | |  |  | |  |  | | | 0.52(1) | 0.47 | |
| *HADS-A* |  | 10 | | 689 | | 8% [4-12%] | | 11% [8-15%] | -0.02 [-0.06-0.03] | | 0.44 | 0.05 | | |  |  | |
| *STAI-T* |  | 2 | | 176 | | 4% [1-9%] | | 8% [0-27%] | -0.06 [-0.17-0.05] | | 0.28 | 0.5 | | |  |  | |
| **Depression** | | | | | | | | | | | | | | | | | |
| Overall effect |  | 14 | | 624 | | 6% [3-8%] | | 8% [4-12%] | -0.02 [-0.06-0.02] | | 0.35 | 0 | | |  |  | |
| Outlier(s) remover |  |  | |  | |  | |  |  | |  |  | | |  |  | |
| Insomnia Tx removed |  | 12 | | 601 | | 6% [3-8%] | | 7% [4-12%] | -0.02 [-0.05-0.02] | | 0.41 | 0 | | |  |  | |
| Treatment format |  |  | |  | |  | |  |  | |  |  | | | 0.26(1) | 0.61 | |
| *Individual* |  | 4 | | 227 | | 5% [2-9%] | | 9% [2-19%] | -0.03 [-0.13-0.06] | | 0.48 | 0.48 | | |  |  | |
| *Group* |  | 10 | | 397 | | 6% [3-10%] | | 7% [3-12%] | -0.01 [-0.05-0.04] | | 0.78 | 0 | | |  |  | |
| Treatment type |  |  | |  | |  | |  |  | |  |  | | | 0.30(1) | 0.86 | |
| *CBT* |  | 8 | | 279 | | 5% [2-9%] | | 5% [2-122%] | 0 [-0.06-0.05] | | 0.9 | 0 | | |  |  | |
| *Psychodynamic* |  | 1 | | - | |  | |  |  | |  |  | | |  |  | |
| *Psychoeducation* |  | 2 | | 163 | | 7% [2-13%] | | 5% [1-11%] | 0.01 [-0.05-0.08] | | 0.68 | 0 | | |  |  | |
| *Support* |  | 2 | | 57 | | 16% [0-51%] | | 14% [3-31%] | -0.03 [-0.22-0.16] | | 0.73 | 0.11 | | |  |  | |
| *Other* |  | 1 | | - | |  | |  |  | |  |  | | |  |  | |
| Control type |  |  | |  | |  | |  |  | |  |  | | | 0.36(3) | 0.95 | |
| *Active* |  | 5 | | 189 | | 10% [3-19%] | | 10% [3-22%] | -0.00 [-0.11-0.10] | | 0.14 | 0 | | |  |  | |
| *TAU* |  | 4 | | 276 | | 4% [1-7%] | | 6% [0-16%] | -0.03 [-0.11-0.04] | | 0.4 | 0.52 | | |  |  | |
| *WLC/ no treatment* |  | 3 | | 51 | | 2% [0-9%] | | 3% [0-15%] | 0 [-0.12-0.12] | | 1 | 0 | | |  |  | |
| *Edu material* |  | 2 | | 108 | | 7% [2-15%] | | 9% [2-19%] | 0 [-0.10-0.10] | | 0.94 | 0.11 | | |  |  | |
| Therapists' profession | | |  | |  | |  |  |  | |  | |  | 0.69(1) | | | 0.41 |
| *Clin Psychologist* | | | 4 | | 189 | | 5% [1-10%] | 6% [0-14%] | -0.02 [-0.05-0.05] | | 0.63 | | 0 |  | | |  |
| *Other professional* | | | 7 | | 266 | | 7%[3-14%] | 5%[2-9%] | 0.05 [-0.03-0.08] | | 0.47 | | 0 |  | | |  |
| *Outcome measure* |  |  | |  | |  | |  |  | |  |  | | | 0.50(1) | 0.48 | |
| *HADS-D* |  | 10 | | 392 | | 4% [2-7%] | | 8% [4-13%] | -0.03 [-0.07-0.02] | | 0.22 | 0 | | |  |  | |
| *CES-D* |  | 4 | | 232 | | 8% [4-13%] | | 8% [2-17%] | 0.01 [-0.08-0.09] | | 0.87 | 0.27 | | |  |  | |
| **General distress** | | | | | | | | | | | | | | | | | |
| Overall effect |  | 16 | | 937 | | 8% [6-11%] | | 13% [10-16%] | -0.03 [-0.07-0.02] | | 0.20 | 0.21 | | |  |  | |
| Outlier(s) removed |  |  | |  | |  | |  |  | |  |  | | |  |  | |
| Insomnia Tx removed |  | 15 | | 922 | | 8% [6-11%] | | 13% [9-16%] | -0.03 [-0.07-0.02] | | 0.25 | 0.24 | | |  |  | |
| Treatment format |  |  | |  | |  | |  |  | |  |  | | | 0.01(1) | 0.95 | |
| *Individual* |  | 5 | | 245 | | 6% [3-10%] | | 11% [6-18%] | -0.03 [-0.09-0.04] | | 0.44 | 0 | | |  |  | |
| *Group* |  | 11 | | 692 | | 9% [6-13%] | | 13% [9-18%] | -0.03 [-0.09-0.03] | | 0.34 | 0.39 | | |  |  | |
| Treatment type |  |  | |  | |  | |  |  | |  |  | | | 10.58(3) | 0.01\* | |
| *CBT* |  | 6 | | 290 | | 4% [2-8%] | | 15% [7-24%] | -0.09 [-0.15—0.02] | | 0.01\* | 0.03 | | |  |  | |
| *Psychodynamic* |  | 1 | | - | |  | |  |  | |  |  | | |  |  | |
| *MBT* |  | 1 | | - | |  | |  |  | |  |  | | |  |  | |
| *Psychoeducation* |  | 2 | | 192 | | 9% [4-15%] | | 14% [7-22%] | -0.04 [-0.13-0.06] | | 0.46 | 0.17 | | |  |  | |
| *Support* |  | 3 | | 163 | | 16% [10-24%] | | 7% [2-15%] | 0.09 [0.00-0.18] | | 0.06 | 0 | | |  |  | |
| *Other* |  | 3 | | 143 | | 9% [3-17%] | | 8% [2-17%] | 0.02 [-0.07-0.14] | | 0.61 | 0 | | |  |  | |
| Control type |  |  | |  | |  | |  |  | |  |  | | | 1.43(2) | 0.49 | |
| *Active* |  | 4 | | 128 | | 12% [5-23%] | | 12% [4-25%] | 0.02 [-0.09-0.14] | | 0.71 | 0 | | |  |  | |
| *TAU* |  | 6 | | 472 | | 7% [4-10%] | | 13% [9-18%] | -0.05 [-0.10-0.00] | | 0.06 | 0 | | |  |  | |
| *WLC/ no treatment* |  | 5 | | 244 | | 6% [2-12%] | | 14% [5-26%] | -0.07 [-0.19-0.05] | | 0.26 | 0.56 | | |  |  | |
| *Edu material* |  | 1 | | - | |  | |  |  | |  |  | | |  |  | |
| Therapists' profession | | |  | |  | |  |  |  | |  | |  | 0.14(1) | | | 0.71 |
| *Clin Psychologist* | | | 5 | | 321 | | 6% [2-12%] | 12% [5-27%] | -0.05 [-0.14-0.03] | | 0.23 | | 0.52 |  | | |  |
| *Other professional* | | | 7 | | 429 | | 8% [4-12%] | 14% [9-19% | -0.03 [-0.09-0.02] | | 0.26 | | 0.05 |  | | |  |
| Outcome measure |  |  | |  | |  | |  |  | |  |  | | | 0.94(1) | 0.33 | |
| *HADS-T* |  | 9 | | 528 | | 6% [3-10%] | | 13% [9-17%] | -0.05 [-0.10-0.00] | | 0.04\* | 0 | | |  |  | |
| *POMS-TMD* |  | 7 | | 409 | | 11% [8-15%] | | 12% [6-21%] | 0 [-0.09-0.09] | | 0.96 | 0.49 | | |  |  | |
| *Note.* k = number of treatment/control group comparisons; n = number of patients; RD = risk difference; CI = confidence interval; I2 = measure of heterogeneity; Q = ratio of variation to within-study error; DF = degrees of freedom; CBT = cognitive behavioural therapy; MBT= mindfulness-based therapy; support = supportive therapy; edu = education; a risk differences were scaled so that positive values represented effects in favour of treatment; \* = p<0.05 | | | | | | | | | | | | | | | | | |

Table 9.

*Weighted deterioration rates and risk differences for deterioration at follow-up (≥6 months after treatment)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | **Weighted deterioration rates** | | **Risk differences for deterioration** | | |
| **Outcome** |  | **k** | **n** | **Treatment % [95% CI]** | **Control %  [95% CI]** | **RDa [95% CI]** | **p** | **I2** |
| Anxiety |  | 5 | 417 | 12% [6-19%] | 9% [5-16%] | 0.01 [-0.04-0.06] | 0.68 | 0 |
| Depression |  | 8 | 389 | 4% [2-7%] | 8% [5-12%] | -0.02 [-0.06-0.02] | 0.28 | 0 |
| General distress |  | 8 | 497 | 8% [4-13%] | 15% [8-23%] | -0.04 [-0.09-0.01] | 0.09 | 0.15 |
| *Note.* k = number of treatment/control group comparisons; n = number of patients; RD = risk difference; CI = confidence interval; I2 = measure of heterogeneity; a risk differences were scaled so that positive values represented effects in favour of treatment | | | | | | | | |

Table 10.

*Effect sizes at post-treatment (≤8 weeks after treatment)*

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Effect sizes (g)** | | | | | | | |
| **Component** |  | **k** | **n** | **ga** | **p** | **i2** | **Q(df)** | **p** | |
| **Anxiety** | | | | | | | | | |
| Overall effect |  | 12 | 865 | 0.34 [0.13-0.54] | <0.01\* | 0.49 |  |  |  |
| Outlier(s) removed |  | - | - | - | - | - |  |  | |
| Insomnia Tx removed |  | 10 | 815 | 0.32 [0.09-0.56] | 0.01\* | 0.57 |  |  | |
| Treatment format |  |  |  |  |  |  | 2.26(1) | 0.13 | |
| *Individual* |  | 3 | 152 | 0.78 [0.12-1.44] | 0.02\* | 0.61 |  |  | |
| *Group* |  | 9 | 713 | 0.25 [0.04-0.46] | 0.02\* | 0.42 |  |  | |
| Treatment type |  |  |  |  |  |  | 7.43(1) | 0.01\* | |
| *CBT* |  | 7 | 391 | 0.56 [-.26-0.87] | <0.01\* | 0.45 |  |  | |
| *Psychodynamic* |  | 1 | - | - | - | - |  |  | |
| *Psychoeducation* |  | 1 |  | - | - | - |  |  | |
| *Support* |  | 2 | 147 | -0.05 [-0.37-0.27] | 0.76 | 0 |  |  | |
| *Other* |  | 1 | - | - | - | - |  |  | |
| Control Type |  |  |  |  |  |  | 4.21(2) | 0.12 | |
| *Active* |  | 3 | 90 | 0.18 [-0.28-0.64] | 0.45 | 0.2 |  |  | |
| *TAU* |  | 4 | 446 | 0.27 [-0.02-0.55] | 0.07 | 0.53 |  |  | |
| *WLC/ no treatment* |  | 4 | 216 | 0.68 [0.33-1.03] | <0.01\* | 0.17 |  |  | |
| *Edu material* |  | 1 | - | - | - | - |  |  | |
| Therapists' profession |  |  |  |  |  |  | 1.07(1) | 0.3 | |
| *Clin Psychologist* |  | 5 | 337 | 0.48 [0.16-0.80] | <0.01\* | 0.45 |  |  | |
| *Other professional* |  | 5 | 397 | 0.23 [-0.14-0.59] | 0.22 | 0.58 |  |  | |
| Outcome measure |  |  |  |  |  |  | 1.57(1) | 0.21 | |
| *HADS-A* |  | 10 | 689 | 0.30 [0.06-0.53] | 0.01\* | 0.51 |  |  | |
| *STAI-T* |  | 2 | 176 | 0.54 [0.24-0.84] | <0.01\* | 0 |  |  | |
| **Depression** | | | | | | | | | |
| Overall effect |  | 14 | 624 | 0.32 [0.11-0.53] | <0.01\* | 0.33 |  |  | |
| Outlier(s) remover |  | **-** | - | - | - | - |  |  | |
| Insomnia Tx removed |  | 12 | 587 | 0.28 [0.07-0.48] | 0.01\* | 0.29 |  |  | |
| Treatment format |  |  |  |  |  |  | 0.12(1) | 0.74 | |
| *Individual* |  | 4 | 227 | 0.37 [-0.11-0.84] | 0.13 | 0.61 |  |  | |
| *Group* |  | 10 | 397 | 0.28 [0.04-0.51] | 0.02\* | 0.18 |  |  | |
| Treatment type |  |  |  |  |  |  | 2.91(2) | 0.23 | |
| *CBT* |  | 8 | 279 | 0.33 [0.09-0.57] | 0.01\* | 0.03 |  |  | |
| *Psychodynamic* |  | 1 | - | - | - |  |  |  | |
| *Psychoeducation* |  | 2 | 163 | -0.01 [-0.32-0.30] | 0.94 | 0 |  |  | |
| *Support* |  | 2 | 57 | 0.17 [-0.36-0.69] | 0.53 | 0 |  |  | |
| *Other* |  | 1 | - | - | - | - |  |  | |
| Control type |  |  |  |  |  |  | 5.12(3) | 0.16 | |
| *Active* |  | 5 | 189 | 0.61 [0.04-1.17] | 0.03\* | 0.59 |  |  | |
| *TAU* |  | 4 | 276 | 0.31 [0.03-0.58] | 0.03\* | 0.21 |  |  | |
| *WLC/ no treatment* |  | 3 | 51 | 0.57 [0.02-1.12] | 0.04\* | 0 |  |  | |
| *Edu material* |  | 2 | 108 | -0.04 [-0.43-0.34] | 0.83 | 0 |  |  | |
| Therapists' profession |  |  |  |  |  |  | 0.66(1) | 0.42 | |
| *Clin Psychologist* |  | 4 | 189 | 0.15 [-0.14-0.43] | 0.31 | 0 |  |  | |
| *Other professional* |  | 7 | 266 | 0.33 [-0.03-0.69] | 0.07 | 0.42 |  |  | |
| Outcome measure |  |  |  |  |  |  | 0.08(1) | 0.78 | |
| *HADS-D* |  | 10 | 392 | 0.36 [0.14-0.58] | <0.01 | 0.10 |  |  | |
| *CES-D* |  | 4 | 232 | 0.29 [-0.19-0.76] | 0.24 | 0.63 |  |  | |
| **General distress** | | | | | | | | | |
| Overall effect |  | 16 | 937 | 0.33 [0.13-0.52] | <0.01\* | 0.49 |  |  | |
| Outlier(s) removed |  | 15 | 905 | 0.28 [0.10-0.40] | <0.01\* | 0.34 |  |  | |
| Insomnia Tx removed |  | 15 | 922 | 0.33 [0.12-0.53] | <0.01\* | 0.52 |  |  | |
| Treatment format |  |  |  |  |  |  | 0.90(1) | 0.34 | |
| *Individual* |  | 5 | 245 | 0.51 [0.04-0.98] | 0.03\* | 0.61 |  |  | |
| *Group* |  | 11 | 692 | 0.26 [0.05-0.57] | 0.02\* | 0.39 |  |  | |
| Treatment type |  |  |  |  |  |  | 12.5(3) | 0.01\* | |
| CBT |  | 6 | 290 | 0.68 [0.36-1.00] | <0.01\* | 0.39 |  |  | |
| Psychodynamic |  | 1 | - | - | - | - |  |  | |
| MBT |  | 1 | - | - | - | - |  |  | |
| Psychoeducation |  | 2 | 192 | 0.11 [-0.18-0.39] | 0.46 | 0 |  |  | |
| Support |  | 3 | 163 | -0.11 [-0.43-0.21] | 0.5 | 0 |  |  | |
| Other |  | 3 | 143 | 0.15 [-0.24-0.53] | 0.46 | 0.16 |  |  | |
| Control type |  |  |  |  |  |  | 2.2(2) | 0.33 | |
| *Active* |  | 4 | 128 | 0.22 [-0.20-0.63] | 0.31 | 0.10 |  |  | |
| *TAU* |  | 6 | 472 | 0.28 [0.06-0.50] | 0.01\* | 0.25 |  |  | |
| *WLC/ no treatment* |  | 5 | 244 | 0.65 [0.17-1.12] | 0.01\* | 0.63 |  |  | |
| *Edu material* |  | 1 | - | - | - |  |  |  | |
| Therapists' profession |  |  |  |  |  |  | 0.49(1) | 0.48 | |
| *Clin Psychologist* |  | 5 | 321 | 0.47 [0.15-0.80] | <0.01\* |  |  |  | |
| *Other professional* |  | 7 | 429 | 0.31 [-0.00-0.62] | 0.05 |  |  |  | |
| Outcome measure |  |  |  |  |  |  | 2.82(1) | 0.09 | |
| *HADS-T* |  | 9 | 528 | 0.47 [0.22-0.73] | <0.01\* | 0.45 |  |  | |
| *POMS-TMD* |  | 7 | 409 | 0.14 [-0.16-0.44] | 0.37 | 0.48 |  |  | |
| *Note.* k = number of treatment/control group comparisons; n = number of patients; g = hedges’ g; CI = confidence interval; I2 = measure of heterogeneity; Q = ratio of variation to within-study error; DF = degrees of freedom; CBT = cognitive behavioural therapy; MBT= mindfulness-based therapy; support = supportive therapy; edu = education; a effect sizes were scaled so that positive values represented effects in favour of treatment; \* = p<0.05 | | | | | | | | | |

Table 11.

*Effect sizes at follow-up (≥6 months after treatment)*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Effect sizes (g)** | | | | |
| **Outcome** |  | **k** | **n** | **g   [95% CI]** | **p** | **I2** |
| Anxiety |  | 5 | 417 | -0.07 [-0.27-0.12] | 0.45 | 0 |
| Depression |  | 8 | 389 | 0.03 [-0.28-0.33] | 0.86 | 0.50 |
| General distress |  | 8 | 497 | 0.11 [-0.07-0.28] | 0.25 | 0 |
| *Note.* k = number of treatment/control group comparisons; n = number of patients; g = hedges’ g; CI = confidence interval; I2 = measure of heterogeneity; a effect sizes were scaled so that positive values represented effects in favour of treatment | | | | | | |

**REFERENCES**

APA Presidential Task Force on Evidence‐Based Practice (2006). Evidence‐based practice in psychology. American Psychologist, 61, 271–285.

Badger, T. A., Braden, C. J., Mishel, M. H., & Longman, A. (2004). Depression burden, psychological adjustment, and quality of life in women with breast cancer: Patterns over time. *Research in Nursing & Health, 27*(1), 19-28.

Barth, J., Munder, T., Gerger, H., Nüesch, E., Trelle, S., Znoj, H., . . . Cuijpers, P. (2013). Comparative efficacy of seven psychotherapeutic interventions for patients with depression: A network meta-analysis. *PLoS Medicine, 10*(5), e1001454.

Bauer, S., Lambert, M. J., & Nielsen, S. L. (2004). Clinical significance methods: A comparison of statistical techniques. *Journal of Personality Assessment, 82*(1), 60-70.

Bohlmeijer, E., Prenger, R., Taal, E., & Cuijpers, P. (2010). The effects of mindfulness-based stress reduction therapy on mental health of adults with a chronic medical disease: A meta-analysis. *Journal of Psychosomatic Research, 68*(6), 539-544.

Bolier, L., Haverman, M., Westerhof, G. J., Riper, H., Smit, F., & Bohlmeijer, E. (2013). Positive psychology interventions: A meta-analysis of randomized controlled studies. *BMC Public Health, 13*(1), 119.

Bouchard, L. C., Antoni, M. H., Blomberg, B. B., Stagl, J. M., Gudenkauf, L. M., Jutagir, D. R., . . . Derhagopian, R. P. (2016). Postsurgical depressive Symptoms and proinflammatory cytokine elevations in women undergoing primary treatment for breast cancer. *Psychosomatic Medicine, 78*(1), 26-37.

Bultz, B. D., & Carlson, L. E. (2006). Emotional distress: The sixth vital sign-future directions in cancer care. *Psycho-Oncology, 15*(2), 93-95.

Burgess, C., Cornelius, V., Love, S., Graham, J., Richards, M., & Ramirez, A. (2005). Depression and anxiety in women with early breast cancer: Five year observational cohort study. *BMJ, 330*(7493), 702.

Cancer Research UK. (2018). *Breast cancer statistics.* Retrieved 2nd June 2019, from https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer#heading-Four

Carlson, L. E., & Bultz, B. D. (2004). Efficacy and medical cost offset of psychosocial interventions in cancer care: Making the case for economic analyses. *Psycho‐Oncology, 13*(12), 837-849.

Cartwright‐Hatton, S., Roberts, C., Chitsabesan, P., Fothergill, C., & Harrington, R. (2004). Systematic review of the efficacy of cognitive behaviour therapies for childhood and adolescent anxiety disorders. *British Journal of Clinical Psychology, 43*(4), 421-436.

Cella, D. F., Tross, S., Orav, E. J., Holland, J. C., Silberfarb, P. M., & Rafla, S. (1989). Mood states of patients after the diagnosis of cancer. *Journal of Psychosocial Oncology, 7*(1-2), 45-54.

Chambless, D. L., & Hollon, S. D. (1998). Defining empirically supported therapies. *Journal of Consulting and Clinical Psychology, 66*(1), 7-18.

Classen, C. C., Kraemer, H. C., Blasey, C., Giese‐Davis, J., Koopman, C., Palesh, O. G., . . . Westendorp, J. (2008). Supportive–expressive group therapy for primary breast cancer patients: A randomized prospective multicenter trial. *Psycho‐Oncology, 17*(5), 438-447.

Cobeanu, O., & David, D. (2018). Alleviation of side effects and distress in breast cancer patients by cognitive-behavioral interventions: A systematic review and meta-analysis. *Journal of Clinical Psychology in Medical Settings*, 1-21.

Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd ed.): Erlbaum Associates, Hillsdale.

Colleoni, M., Mandala, M., Peruzzotti, G., Robertson, C., Bredart, A., & Goldhirsch, A. (2000). Depression and degree of acceptance of adjuvant cytotoxic drugs. *The Lancet, 356*(9238), 1326-1327.

Cooper, H., & Patall, E. A. (2009). The relative benefits of meta-analysis conducted with individual participant data versus aggregated data. *Psychological Methods, 14*(2), 165-176.

Coutiño-Escamilla, L., Piña-Pozas, M., Garces, A. T., Gamboa-Loira, B., & López-Carrillo, L. (2019). Non-pharmacological therapies for depressive symptoms in breast cancer patients: Systematic review and meta-analysis of randomized clinical trials. *The Breast,* 44, 135-143

Cuijpers, P., Karyotaki, E., Weitz, E., Andersson, G., Hollon, S. D., & van Straten, A. (2014). The effects of psychotherapies for major depression in adults on remission, recovery and improvement: A meta-analysis. *Journal of Affective Disorders, 159*, 118-126.

Cuijpers, P., van Straten, A., Bohlmeijer, E., Hollon, S., & Andersson, G. (2010). The effects of psychotherapy for adult depression are overestimated: A meta-analysis of study quality and effect size. *Psychological Medicine, 40*(2), 211-223.

Cuijpers, P., Van Straten, A., Warmerdam, L., & Smits, N. (2008). Characteristics of effective psychological treatments of depression: A metaregression analysis. *Psychotherapy Research, 18*(2), 225-236.

Dauchy, S., Léger, I., des Guetz, G., Ellien, F., Tidjani, L., Zelek, L., . . . Spano, J.-P. (2012). Quelle prise en charge psychologique pour les patients âgés atteints de cancer? *Psycho-Oncologie, 6*(1), 43-49.

DerSimonian, R., & Laird, N. (1986). Meta-analysis in clinical trials. *Controlled Clinical Trials, 7*(3), 177-1

Dirksen, S. R., & Epstein, D. R. (2008). Efficacy of an insomnia intervention on fatigue, mood and quality of life in breast cancer survivors. *Journal of Advanced Nursing, 61*(6), 664-675. 88.

Duijts, S. F., Faber, M. M., Oldenburg, H. S., van Beurden, M., & Aaronson, N. K. (2011). Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health‐related quality of life in breast cancer patients and survivors—a meta‐analysis. *Psycho‐Oncology, 20*(2), 115-126.

Ekers, D., Richards, D., & Gilbody, S. (2008). A meta-analysis of randomized trials of behavioural treatment of depression. *Psychological Medicine, 38*(5), 611-623.

Fisher, P. L., Byrne, A., Fairburn, L., Ullmer, H., Abbey, G., & Salmon, P. (2019). Brief metacognitive therapy for emotional distress in adult cancer survivors. *Frontiers in Psychology, 10*. 162.

Fisher, P. L., & Durham, R. C. (1999). Recovery rates in generalized anxiety disorder following psychological therapy: an analysis of clinically significant change in the STAI-T across outcome studies since 1990. *Psychological medicine, 29*(6), 1425-1434.

Fisher, P. L., & Wells, A. (2005). How effective are cognitive and behavioral treatments for obsessive–compulsive disorder? A clinical significance analysis. *Behaviour Research and Therapy, 43*(12), 1543-1558.

Fu, R., Gartlehner, G., Grant, M., Shamliyan, T., Sedrakyan, A., Wilt, T. J., . . . Ismaila, A. (2011). Conducting quantitative synthesis when comparing medical interventions: AHRQ and the Effective Health Care Program. *Journal of Clinical Epidemiology, 64*(11), 1187-1197.

Gould, R. L., Coulson, M. C., & Howard, R. J. (2012). Cognitive behavioral therapy for depression in older people: A meta‐analysis and meta‐regression of randomized controlled trials. *Journal of the American Geriatrics Society, 60*(10), 1817-1830.

Greer, J. A., Park, E. R., Prigerson, H. G., & Safren, S. A. (2010). Tailoring cognitive-behavioral therapy to treat anxiety comorbid with advanced cancer. *Journal of Cognitive Psychotherapy, 24*(4), 294-313.

Hageman, W., & Arrindell, W. A. (1999). Establishing clinically significant change: Increment of precision and the distinction between individual and group level of analysis. *Behaviour Research and Therapy, 37*(12), 1169-1193.

Han, X., Lin, C. C., Li, C., Moor, J. S., Rodriguez, J. L., Kent, E. E., & Forsythe, L. P. (2015). Association between serious psychological distress and health care use and expenditures by cancer history. *Cancer, 121*(4), 614-622.

Hedges, L. V. (1989). An unbiased correction for sampling error in validity generalization studies. *Journal of Applied Psychology, 74*(3), 469-477.

Heron-Speirs, H. A., Harvey, S. T., & Baken, D. M. (2013). Moderators of psycho-oncology therapy effectiveness: meta-analysis of therapy characteristics. *Journal of psychosocial Oncology*, 31(6), 617-641.

Higgins, Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *BMJ: British Medical Journal, 327*(7414), 557-560.

Hinz, A., & Brähler, E. (2011). Normative values for the hospital anxiety and depression scale (HADS) in the general German population. *Journal of Psychosomatic Research, 71*(2), 74-78.

Holland, Watson, M., & Dunn, J. (2011). The IPOS new International Standard of Quality Cancer Care: Integrating the psychosocial domain into routine care. *Psycho‐Oncology, 20*(7), 677-680.

Howell, D., Currie, S., Mayo, S., Jones, G., Boyle, M., Hack, T., . . . Collacutt, V. (2009). A Pan-Canadian clinical practice guideline: Assessment of psychosocial health care needs of the adult cancer patient. *Toronto: Canadian Partnership Against Cancer (Cancer Journey Action Group) and the Canadian Association of Psychosocial Oncology*.

Hsu, L. M. (1996). On the identification of clinically significant client changes: Reinterpretation of Jacobson's cut scores. *Journal of Psychopathology and Behavioral Assessment, 18*(4), 371-385.

Huhn, M., Tardy, M., Spineli, L. M., Kissling, W., Förstl, H., Pitschel-Walz, G., . . . Davis, J. M. (2014). Efficacy of pharmacotherapy and psychotherapy for adult psychiatric disorders: A systematic overview of meta-analyses. *JAMA Psychiatry, 71*(6), 706-715.

Jacobson, N. S., Follette, W. C., & Revenstorf, D. (1984). Psychotherapy outcome research: Methods for reporting variability and evaluating clinical significance. *Behavior Therapy, 15*(4), 336-352.

Jacobson, N. S., & Truax, P. (1991). Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology, 59*(1), 12-19.

Jassim, G. A., Whitford, D. L., Hickey, A., and Carter, B. (2015). Psychological interventions for women with non-metastatic breast cancer. *Cochrane Database of Systematic Reviews.*28:CD008729.doi:10.1002/14651858.cd008729.pub214651858.CD008729.pub2

Johnston, M., Pollard, B., & Hennessey, P. (2000). Construct validation of the hospital anxiety and depression scale with clinical populations. *Journal of Psychosomatic Research, 48*(6), 579-584.

Keller, M. B. (2003). Past, present, and future directions for defining optimal treatment outcome in depression: Remission and beyond. *Jama Network, 289*(23), 3152-3160.

Knight, R. G., Waal‐Manning, H. J., & Spears, G. F. (1983). Some norms and reliability data for the State‐Trait Anxiety Inventory and the Zung Self‐Rating Depression scale. *British Journal of Clinical Psychology,* 22(4), 245-249.

Li, M., Kennedy, E. B., Byrne, N., Gérin-Lajoie, C., Katz, M. R., Keshavarz, H., . . . Green, E. (2016). Management of depression in patients with cancer: A clinical practice guideline. *Journal of Oncology Practice, 12*(8), 747-756.

Loerinc, A. G., Meuret, A. E., Twohig, M. P., Rosenfield, D., Bluett, E. J., & Craske, M. G. (2015). Response rates for CBT for anxiety disorders: Need for standardized criteria. *Clinical Psychology Review, 42*, 72-82.

Lunnen, K. M., & Ogles, B. M. (1998). A multiperspective, multivariable evaluation of reliable change. *Journal of Consulting and Cinical Psychology, 66*(2), 400-410.

Mantel, N., & Haenszel, W. (1959). Statistical aspects of the analysis of data from retrospective studies of disease. *Journal of the National Cancer Institute, 22*(4), 719-748.

McGlinchey, J. B., Atkins, D. C., & Jacobson, N. S. (2002). Clinical significance methods: Which one to use and how useful are they? *Behavior Therapy, 33*(4), 529-550.

McNair, D. M. (1971). *Manual profile of mood states*: Educational & Industrial testing service.

Metzger, R. L. (1976). A reliability and validity study of the state‐trait anxiety inventory. *Journal of Clinical Psychology, 32*(2), 276-278.

Misono, S., Weiss, N. S., Fann, J. R., Redman, M., & Yueh, B. (2008). Incidence of suicide in persons with cancer. *Journal of Clinical Oncology, 26*(29), 4731-4738.

Mustafa, M., Carson‐Stevens, A., Gillespie, D., & Edwards, A. G. (2013). Psychological interventions for women with metastatic breast cancer. *Cochrane Database of Systematic Review* (6).

Naaman, S. C., Radwan, K., Fergusson, D., & Johnson, S. (2009). Status of psychological trials in breast cancer patients: A report of three meta-analyses. *Psychiatry: Interpersonal and Biological Processes, 72*(1), 50-69

National Comprehensive Cancer Network. (2003). Distress management. Clinical practice guidelines. *Journal of the National Comprehensive Cancer Network: JNCCN, 1*(3), 344-374.

National Institute for Clinical Excellence. (2004). Guidance on cancer services: Improving supportive and palliative care for adults with cancer: the manual. National Institute for Clinical Excellence.

Newnham, E. A., Harwood, K. E., & Page, A. C. (2007). Evaluating the clinical significance of responses by psychiatric inpatients to the mental health subscales of the SF-36. *Journal of Affective Disorders, 98*(1-2), 91-97.

NICE. (2009). *Depression in adults: recognition and management.* Retrieved from <https://www.nice.org.uk/guidance/CG90/chapter/Key‐priorities‐for‐implementation>

Noble, A. J., Reilly, J., Temple, J., & Fisher, P. L. (2018). Cognitive-behavioural therapy does not meaningfully reduce depression in most people with epilepsy: A systematic review of clinically reliable improvement. *Journal of Neurology, Neurosurgery, and Psychiatry*, jnnp-2018-317997; DOI: 10.1136/jnnp-2018-317997.

Nunnally, J. C., & Kotsch, W. E. (1983). Studies of individual subjects: Logic and methods of analysis. *British Journal of Clinical Psychology, 22*(2), 83-93.

Nyenhuis, D. L., Yamamoto, C., Luchetta, T., Terrien, A., & Parmentier, A. (1999). Adult and geriatric normative data and validation of the profile of mood states. *Journal of Clinical Psychology, 55*(1), 79-86.

Ogles, B. M., Lambert, M. J., & Sawyer, J. D. (1995). Clinical significance of the National Institute of Mental Health Treatment of Depression Collaborative Research Program data. *Journal of Consulting and Clinical Psychology, 63*(2), 321-326.

Ogles, B. M., Lunnen, K. M., & Bonesteel, K. (2001). Clinical significance: History, application, and current practice. *Clinical Psychology Review, 21*(3), 421-446.

Öst, L.-G. (2008). Efficacy of the third wave of behavioral therapies: A systematic review and meta-analysis. *Behaviour Research and Therapy, 46*(3), 296-321.

Öst, L.-G., & Ollendick, T. H. (2017). Brief, intensive and concentrated cognitive behavioral treatments for anxiety disorders in children: A systematic review and meta-analysis. *Behaviour Research and Therapy, 97*, 134-145.

Öst, L.-G., Riise, E. N., Wergeland, G. J., Hansen, B., & Kvale, G. (2016). Cognitive behavioral and pharmacological treatments of OCD in children: A systematic review and meta-analysis. *Journal of Anxiety Disorders, 43*, 58-69.

Page, A. E., & Adler, N. E. (2008). *Cancer care for the whole patient: Meeting psychosocial health needs.* Washington, DC: National Academic Press

Patten, S., Grigoriadis, S., & Beaulieu, S. (2011). Clinical effectiveness, construct and assessment. *Journal of Affective Disorders, 132*, S3-S8.

Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement, 1*(3), 385-401.

Reddy, M. (2010). Suicide incidence and epidemiology. *Indian Journal of Psychological Medicine, 32*(2), 77-82.

Reese, C., Weis, J., Schmucker, D., & Mittag, O. (2017). Development of practice guidelines for psychological interventions in the rehabilitation of patients with oncological disease (breast, prostate, or colorectal cancer): Methods and results. *Psycho‐Oncology, 26*(10), 1513-1518.

Riley, R. D., Lambert, P. C., & Abo-Zaid, G. (2010). Meta-analysis of individual participant data: rationale, conduct, and reporting. *BMJ, 340*, c221.

Riley, R. D., & Steyerberg, E. W. (2010). Meta‐analysis of a binary outcome using individual participant data and aggregate data. *Research Synthesis Methods, 1*(1), 2-19.

Rissanen, R., Nordin, K., Ahlgren, J., & Arving, C. (2015). A stepped care stress management intervention on cancer‐related traumatic stress symptoms among breast cancer patients—a randomized study in group vs. individual setting. *Psycho‐Oncology, 24*(9), 1028-1035.

Ronk, F. R., Hooke, G. R., & Page, A. C. (2016). Validity of clinically significant change classifications yielded by Jacobson-Truax and Hageman-Arrindell methods. *BMC Psychiatry, 16*(1), 187.

Rost, A. D., Wilson, K., Buchanan, E., Hildebrandt, M. J., & Mutch, D. (2012). Improving psychological adjustment among late-stage ovarian cancer patients: Examining the role of avoidance in treatment. *Cognitive and Behavioral Practice, 19*(4), 508-517.

Rouf, K. (2004). *Oxford guide to behavioural experiments in cognitive therapy*: Oxford University Press, Oxford.

Rozental, A., Magnusson, K., Boettcher, J., Andersson, G., & Carlbring, P. (2017). For better or worse: An individual patient data meta-analysis of deterioration among participants receiving Internet-based cognitive behavior therapy. *Journal of Consulting and Clinical Psychology, 85*(2), 160-177.

Santoft, F., Axelsson, E., Öst, L.-G., Hedman-Lagerlöf, M., Fust, J., & Hedman-Lagerlöf, E. (2019). Cognitive behaviour therapy for depression in primary care: Systematic review and meta-analysis. *Psychological Medicine*, 1-9.

Savard, J., Simard, S., Ivers, H., & Morin, C. M. (2005). Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects. *Journal of Clinical Oncology, 23*(25), 6083-6096.

Siegel, R. L., Miller, K. D., & Jemal, A. (2018). Cancer statistics, 2018. *CA: A Cancer Journal for Clinicians, 68*(1), 7-30. doi: doi:10.3322/caac.21442

Singer, S., Kuhnt, S., Götze, H., Hauss, J., Hinz, A., Liebmann, A., . . . Schwarz, R. (2009). Hospital anxiety and depression scale cutoff scores for cancer patients in acute care. *British journal of cancer*, 100(6), 908-912.

Speer, D. C. (1992). Clinically significant change: Jacobson and Truax (1991) revisited. *Journal of Consulting and Clinical Psychology, 60*(3), 402-408.

Spielberger, C. D., & Gorsuch, R. L. (1983). *State-trait anxiety inventory for adults: Manual and sample: Manual, instrument and scoring guide*: Consulting Psychologists Press.

Springer, K. S., Levy, H. C., & Tolin, D. F. (2018). Remission in CBT for adult anxiety disorders: A meta-analysis. *Clinical Psychology Review, 61*, 1-8.

Stanton, A. L., Ganz, P. A., Kwan, L., Meyerowitz, B. E., Bower, J. E., Krupnick, J. L., . . . Belin, T. R. (2005). Outcomes from the Moving Beyond Cancer psychoeducational, randomized, controlled trial with breast cancer patients. *Journal of Clinical Oncology, 23*(25), 6009-6018.

Stewart, L. A., & Parmar, M. K. (1993). Meta-analysis of the literature or of individual patient data: is there a difference? *The Lancet, 341*(8842), 418-422.

Stewart, L. A., & Tierney, J. F. (2002). To IPD or not to IPD? Advantages and disadvantages of systematic reviews using individual patient data. *Evaluation & the Health Professions, 25*(1), 76-97.

Stewart, L. A., Clarke, M., Rovers, M., Riley, R. D., Simmonds, M., Stewart, G., & Tierney, J. F. (2015). Preferred reporting items for a systematic review and meta-analysis of individual participant data: the PRISMA-IPD statement. *JAMA*, 313(16), 1657-1665.

Stuart, A., & Ord, J. (1994). *JK Kendall's Advanced Theory of Statistics.* (6th ed.). London, England: Arnold Publishers.

Tatrow, K., & Montgomery, G. H. (2006). Cognitive behavioral therapy techniques for distress and pain in breast cancer patients: A meta-analysis. *Journal of Behavioral Medicine, 29*(1), 17-27.

Temple, J., Salmon, P., Tudur-Smith, C., Huntley, C. D., & Fisher, P. L. (2018). A systematic review of the quality of randomized controlled trials of psychological treatments for emotional distress in breast cancer. *Journal of Psychosomatic Research*, 108, 22–31. https://doi.org/10.1016/j.jpsychores.2018.02.013.

Tit, A., Camilla, A., Angela, A., Marco, A., Gianni, A., Barceló, A. M., . . . Keith, C. (2017). *European guide on quality improvement in comprehensive cancer control*: National Institute of Public Health.

Therrien, Z., & Hunsley, J. (2012). Assessment of anxiety in older adults: a systematic review of commonly used measures. *Aging & mental health*, 16(1), 1-16.

Turner, J., Zapart, S., Pedersen, K., Rankin, N., Luxford, K., & Fletcher, J. (2003). *Clinical practice guidelines for the psychosocial care of adults with cancer*: National Breast Cancer Centre, National Cancer Control Initiative.

Warwick, H., Reardon, T., Cooper, P., Murayama, K., Reynolds, S., Wilson, C., & Creswell, C. (2017). Complete recovery from anxiety disorders following Cognitive Behavior Therapy in children and adolescents: A meta-analysis. *Clinical Psychology Review, 52*, 77-91.

Westen, D., Novotny, C. M., & Thompson-Brenner, H. (2004). The empirical status of empirically supported psychotherapies: Assumptions, findings, and reporting in controlled clinical trials. *Psychological Bulletin, 130*(4), 631-663.

Würtzen, H., Dalton, S. O., Elsass, P., Sumbundu, A. D., Steding-Jensen, M., Karlsen, R. V., . . . Johansen, C. (2013). Mindfulness significantly reduces self-reported levels of anxiety and depression: results of a randomised controlled trial among 336 Danish women treated for stage I–III breast cancer. *European Journal of Cancer, 49*(6), 1365-1373.

Xiao, F., Song, X., Chen, Q., Dai, Y., Xu, R., Qiu, C., & Guo, Q. (2017). Effectiveness of psychological interventions on depression in patients after breast cancer surgery: A meta-analysis of randomized controlled trials. *Clinical Breast Cancer, 17*(3), 171-179.

Ye, M., Du, K., Zhou, J., Zhou, Q., Shou, M., Hu, B., . . . Liang, S. (2018). A meta‐analysis of the efficacy of cognitive behavior therapy on quality of life and psychological health of breast cancer survivors and patients. *Psycho‐Oncology*. *27*(7), 1695-1703.

Zhang, J., Xu, R., Wang, B., & Wang, J. (2016). Effects of mindfulness-based therapy for patients with breast cancer: A systematic review and meta-analysis. *Complementary Therapies in Medicine, 26*, 1-10.

Zhou, X., Hetrick, S. E., Cuijpers, P., Qin, B., Barth, J., Whittington, C. J., . . . Michael, K. D. (2015). Comparative efficacy and acceptability of psychotherapies for depression in children and adolescents: A systematic review and network meta‐analysis. *World Psychiatry, 14*(2), 207-222.

Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica, 67*(6), 361-370.

Zimmermann, T., Heinrichs, N., & Baucom, D. H. (2007). “Does one size fit all?” Moderators in psychosocial interventions for breast cancer patients: a meta-analysis. *Annals of Behavioral Medicine, 34*(3), 225-239.

**Supplementary Materials**

**The questionable efficacy of manualized psychological treatments for distressed breast cancer patients: An individual patient data meta-analysis**

**APPENDIX A**

***PubMed search strategy***

|  |  |
| --- | --- |
| **1** | Randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] NOT (animals [mh] NOT humans [mh] |
| **2** | “Psychotherapy”[Mesh] OR “psychotherapy” OR “psychological therapy” OR “counselling” OR “counselling” OR “psychological intervention” OR “cognitive behavioural therapy” OR “group therapy” OR “psychosocial therapy” |
| **3** | “Breast Neoplasms”[mesh] OR “breast neoplasms” OR “breast cancer” |
| **4** | “Depression”[Mesh] OR “depressive disorder”[Mesh] OR “depressive disorder” OR “anxiety”[Mesh] Or “anxiety disorders”[Mesh] OR “anxiety disorders” OR “anxiety” OR “depression” OR “emotional distress” OR “psychological distress” |
| **5** | “gene therapy” OR “genetic\*” |
| **6** | 1 AND 2 AND 3 AND 4 NOT 5 |
| *Note.* Filters: English Language only; MeSH, Medical Subject Headings; mh, Mesh Heading; Tiab, Title or Abstract; SH, Subject Heading | |

**APPENDIX B**

***References of Included RCTs***

Andersen, B. L., Farrar, W. B., Golden-Kreutz, D., Emery, C. F., Glaser, R., Crespin, T., & Carson III, W. E. (2007). Distress reduction from a psychological intervention contributes to improved health for cancer patients. *Brain, Behavior, and Immunity*, 21(7), 953-961.

Andersen, B. L., Farrar, W. B., Golden-Kreutz, D. M., Glaser, R., Emery, C. F., Crespin, T. R., . . . Carson, W. E. (2004). Psychological, behavioral, and immune changes after a psychological intervention: A clinical trial. *Journal of Clinical Oncology,* 22(17), 3570-3580.

Antoni, M. H., Lehman, J. M., Kilbourn, K. M., Boyers, A. E., Culver, J. L., Alferi, S. M., . . . Harris, S. D. (2001). Cognitive-behavioral stress management intervention decreases the prevalence of depression and enhances benefit finding among women under treatment for early-stage breast cancer. *Health Psychology*, 20(1), 20-32.

Beutel, M. E., Weissflog, G., Leuteritz, K., Wiltink, J., Haselbacher, A., Ruckes, C., . . . Braehler, E. (2014). Efficacy of short-term psychodynamic psychotherapy (STPP) with depressed breast cancer patients: results of a randomized controlled multicenter trial. *Annals of Oncology*, 25(2), 378-384.

Bredal, I. S., Karesen, R., Smeby, N. A., Espe, R., Sorensen, E. M., Amundsen, M., . . . Ekeberg, O. (2014). Effects of a psychoeducational versus a support group intervention in patients with early-stage breast cancer: Results of a randomized controlled trial. *Cancer Nursing,* 37(3), 198-207.

Carlson, L. E., Doll, R., Stephen, J., Faris, P., Tamagawa, R., Drysdale, E., & Speca, M. (2013). Randomized controlled trial of mindfulness-based cancer recovery versus supportive expressive group therapy for distressed survivors of breast cancer. *Journal of Clinical Oncology*, 31(25), 3119-3126.

Classen, C. C., Kraemer, H. C., Blasey, C., Giese-Davis, J., Koopman, C., Palesh, O. G., . . . Spiegel, D. (2008). Supportive-expressive group therapy for primary breast cancer patients: a randomized prospective multicenter trial. *Psycho-Oncology*, 17(5), 438-447.

Desautels, C., Savard, J., Ivers, H., Savard, M.-H., & Caplette-Gingras, A. (2018). Treatment of depressive symptoms in patients with breast cancer: A randomized controlled trial comparing cognitive therapy and bright light therapy. *Health Psychology*, 37(1), 1-13.

Dirksen, S. R., & Epstein, D. R. (2008). Efficacy of an insomnia intervention on fatigue, mood and quality of life in breast cancer survivors. *Journal of Advanced Nursing,* 61(6), 664-675.

Dolbeault, S., Cayrou, S., Bredart, A., Viala, A. L., Desclaux, B., Saltel, P., ... & Dickes, P. (2009). The effectiveness of a psycho‐educational group after early‐stage breast cancer treatment: results of a randomized French study. *Psycho‐Oncology*, 18(6), 647-656.

Groarke, A., Curtis, R., & Kerin, M. (2013). Cognitive‐behavioural stress management enhances adjustment in women with breast cancer*. British Journal of Health Psychology*, 18(3), 623-641.

Ho, R. T., Fong, T. C., Lo, P. H., Ho, S. M., Lee, P. W., Leung, P. P., . . . Chan, C. L. (2016). Randomized controlled trial of supportive-expressive group therapy and body-mind-spirit intervention for Chinese non-metastatic breast cancer patients. *Support Care Cancer*, 24(12), 4929-4937.

Lechner, S. C., Whitehead, N. E., Vargas, S., Annane, D. W., Robertson, B. R., Carver, C. S., . . . Antoni, M. H. (2014). Does a community-based stress management intervention affect psychological adaptation among underserved black breast cancer survivors? *Journal of the National Cancer Institute Monographs*, 2014 (50), 315-322.

Merckaert, I., Lewis, F., Delevallez, F., Herman, S., Caillier, M., Delvaux, N., . . . Razavi, D. (2017). Improving anxiety regulation in patients with breast cancer at the beginning of the survivorship period: a randomized clinical trial comparing the benefits of single-component and multiple-component group interventions. *Psycho-Oncology,* 26(8), 1147-1154.

Sandgren, A. K., & McCaul, K. D. (2003). Short-term effects of telephone therapy for breast cancer patients. *Health Psychology*, 22(3), 310-315.

Sandgren, A. K., & McCaul, K. D. (2007). Long‐term telephone therapy outcomes for breast cancer patients. *Psycho‐Oncology* 16(1), 38-47.

Savard, J., Simard, S., Giguere, I., Ivers, H., Morin, C. M., Maunsell, E., . . . Marceau, D. (2006). Randomized clinical trial on cognitive therapy for depression in women with metastatic breast cancer: psychological and immunological effects. *Palliative Support Care*, 4(3), 219-237.

Savard, J., Simard, S., Ivers, H., & Morin, C. M. (2005). Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects. *Journal of Clinical Oncology*, 23(25), 6083-6096.

Stanton, A. L., Ganz, P. A., Kwan, L., Meyerowitz, B. E., Bower, J. E., Krupnick, J. L., . . . Belin, T. R. (2005). Outcomes from the moving beyond cancer psychoeducational, randomized, controlled trial with breast cancer patients. *Journal of Clinical Oncology*, 23(25), 6009-6018.

**APPENDIX C.**

*Table C1.* Comparison of sample characteristics, psychological treatment characteristics and methodological quality of trials providing IPD and those not providing IPD

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **IPD provided (n=17)** | **IPD not provided (n=19)** | **IPD provided vs IPD not provided** | |
|  |  |  | statistical test | p value |
| **Sample characteristics** |  |  |  |  |
| Mean sample size | 198 | 165 | t(33)=0.81 | 0.43 |
| Mean age, years | 53 | 51 | t(30)=1.7 | 0.1 |
| **Psychological treatment characteristics** |  |  |  |  |
| Mean duration (hours) | 14.1 | 14 | t(36)=0.51 | 0.96 |
| Treatment type |  |  | x2(5)=4.24 | 0.52 |
| CBT | 9 | 7 |  |  |
| Psychodynamic | 1 | 0 |  |  |
| Other | 3 | 4 |  |  |
| Psychoeducation | 3 | 2 |  |  |
| MBT | 1 | 5 |  |  |
| Supportive therapy | 3 | 3 |  |  |
| Intervention Format |  |  | x2(2)=1.10 | 0.58 |
| Individual | 6 | 5 |  |  |
| Group | 14 | 15 |  |  |
| Couple | 0 | 1 |  |  |
| CBT = cognitive behavioural therapy; MBT = mindfulness-based therapy | | | | |

*Figure C2.* Comparison of effect sizes for trials providing IPD and those not providing IPD for anxiety at post-treatment

**Test for subgroup differences: Q = 2.09, df = 1 (p = 0.15)**

*Note*. WLC = waitlist control; BMS = body mind spirit; SEGT = supportive expressive group therapy; TAU = treatment as usual; SCM = self-care management

*Figure C3.* Comparison of effect sizes for trials providing IPD and those not providing IPD for depression at post-treatment

**Test for subgroup differences: Q = 6.23, df = 1 (p = 0.01\*)**

*Note*. WLC = waitlist control; BMS = body mind spirit; SEGT = supportive expressive group therapy; TAU = treatment as usual; SCM = self-care management

*Figure C4.* Comparison of effect sizes for trials providing IPD and those not providing IPD for general distress at post-treatment

**Test for subgroup differences: Q = 0.98, df = 1 (p = 0.32)**

*Note*. WLC = waitlist control; BMS = body mind spirit; SEGT = supportive expressive group therapy; EE = emotional expression; HE = breast cancer health education; MBSR = mindfulness-based stress reduction

**APPENDIX D.**

*Table D1. Weighted recovery rates and risk differences for recovery at post-treatment (≤8 weeks after treatment)*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | **Weighted recovery rates** | | | | **Risk differences for recovery rates** | | |
| **Trial** |  | **Tx n** | **Ctrl n** | **Tx %** | **Tx  [95% CI]** | **Ctrl %** | **Ctrl  [95% CI]** | **RDa** | **95% CI** | **p** |
| **Anxiety** | | | | | | | | | | |
| Beutel 2014 |  | 54 | 50 | 24% | [13-38%] | 8% | [2-19%] | 0.16 | [0.02-0.30] | 0.02 |
| Bredal 2014 |  | 90 | 106 | 32% | [23-43%] | 28% | [20-38%] | 0.04 | [-0.09-0.17] | 0.55 |
| Classen 2008 |  | 56 | 57 | 27% | [16-40%] | 18% | [9-30%] | 0.09 | [-0.06-0.24] | 0.23 |
| Desautels 2018 |  | 19 | 6 | 16% | [3-40%] | 0% | [0-46%] | 0.16 | [-0.10-0.41] | 0.22 |
| Dirksen 2008 |  | 13 | 16 | 38% | [14-68%] | 13% | [2-38%] | 0.26 | [-0.05-0.57] | 0.10 |
| Dolbeault 2009 |  | 72 | 75 | 11% | [5-21%] | 3% | [0=9%] | 0.08 | [0.00-0.17] | 0.04 |
| Groarke 2013 |  | 35 | 28 | 54% | [37-71%] | 11% | [2-28%] | 0.44 | [0.23-0.64] | 0.00 |
| Ho BMS |  | 16 | 11.5 | 31% | [11-59%] | 22% | [4-55%] | 0.10 | [-0.23-0.42] | 0.57 |
| Ho SEGT |  | 22 | 11.5 | 18% | [5-40%] | 22% | [4-55%] | -0.04 | [-0.32-0.25] | 0.81 |
| Merckeart 2016 |  | 40 | 43 | 30% | [17-47%] | 19% | [8-33%] | 0.11 | [-0.07-0.30] | 0.22 |
| Savard 2005 |  | 9 | 12 | 44% | [14-79%] | 17% | [2-49%] | 0.28 | [-0.11-0.66] | 0.16 |
| Savard 2006 |  | 12 | 11 | 50% | [21-79%] | 9% | [0-41%] | 0.41 | [0.08-0.74] | 0.02 |
| **Depression** | | | | | | | | | | |
| Antoni 2001 |  | 18 | 22 | 28% | [10%-53%] | 18% | [5-40%] | 0.10 | [-0.17-0.36] | 0.47 |
| Beutel 2014 |  | 59 | 58 | 36% | [24-49%] | 21% | [11-33%] | 0.15 | [-0.01-0.31] | 0.07 |
| Bredal 2014 |  | 47 | 52 | 28% | [16-43%] | 25% | [14-39%] | 0.03 | [-0.15-0.20] | 0.76 |
| Classen 2008 |  | 26 | 18 | 35% | [17-56%] | 44% | [22-69%] | -0.10 | [-0.39-0.20] | 0.51 |
| Desautels 2018 |  | 19 | 8 | 42% | [20-67%] | 25% | 3-65%] | 0.17 | [-0.20-0.54] | 0.37 |
| Dirksen 2008 |  | 13 | 5 | 31% | [9-61%] | 40% | [5-85%] | -0.09 | [-0.59-0.41] | 0.72 |
| Groarke 2013 |  | 12 | 12 | 33% | [10-65%] | 42% | [15-72%] | -0.08 | [-0.47-0.30] | 0.67 |
| Ho BMS |  | 5 | 3.5 | 40% | [5-85%] | 0% | [0-65%] | 0.40 | [-0.09-0.89] | 0.11 |
| Ho SEGT |  | 9 | 3.5 | 22% | [3-60%] | 0% | [0-65%] | 0.22 | [-0.17-0.62] | 0.27 |
| Lechner 2014 |  | 53 | 57 | 0% | [0-7%] | 0% | [0-6%] | 0.00 | [-0.03-0.03] | 1.00 |
| Merckeart 2016 |  | 21 | 15 | 48% | [26-70%] | 40% | [16-68%] | 0.08 | [-0.25-0.40] | 0.65 |
| Savard 2005 |  | 2 | 3 | 100% | [16-100%] | 67% | [9-99%] | 0.33 | [-0.30-0.97] | 0.30 |
| Savard 2006 |  | 10 | 9 | 60% | [26-88%] | 44% | [14-79%] | 0.16 | [-0.29-0.60] | 0.49 |
| Stanton 2005 |  | 40 | 24 | 15% | [6-30%] | 21% | [7-42%] | -0.06 | [-0.25-0.14] | 0.56 |
| **General distress** | | | | | | | | | | |
| Andersen 2004 |  | 48 | 30 | 21% | [10-35%] | 10% | [2-27%] | 0.11 | [-0.05-0.27] | 0.18 |
| Beutel 2014 |  | 59 | 57 | 20% | [11-33%] | 7% | [2-17%] | 0.13 | [0.01-0.26] | 0.03 |
| Bredal 2014 |  | 81 | 78 | 27% | [18-38%] | 28% | [19-40%] | -0.01 | [-0.15-0.13] | 0.88 |
| Carlson 2013 MBSR |  | 27 | 7 | 52% | [32-71%] | 36% | [6-77%] | 0.16 | [-0.24-0.56] | 0.43 |
| Carlson 2013 SEGT |  | 29 | 7 | 21% | [8-40%] | 36% | [6-77%] | -0.15 | [-0.53-0.23] | 0.44 |
| Classen 2008 |  | 49 | 44 | 31% | [18-45%] | 27% | [15-43%] | 0.03 | [-0.15-0.22] | 0.72 |
| Desautels 2018 |  | 23 | 9 | 39% | [20-61%] | 0% | [0-34%] | 0.39 | [0.15-0.63] | 0.00 |
| Dolbeault 2009 |  | 47 | 48 | 32% | [19-47%] | 8% | [2-20%] | 0.24 | [0.08-0.39] | 0.00 |
| Groarke 2013 |  | 28 | 25 | 36% | [19-56%] | 8% | [0-26%] | 0.28 | [0.07-0.48] | 0.01 |
| Ho BMS |  | 14 | 10 | 14% | [2-43%] | 5% | [0-38%] | 0.09 | [-0.13-0.32] | 0.42 |
| Ho SEGT |  | 24 | 10 | 21% | [7-42%] | 5% | [0-38%] | 0.16 | [-0.05-0.37] | 0.14 |
| Merckeart 2016 |  | 39 | 32 | 26% | [13-42%] | 13% | [4-29%] | 0.13 | [-0.05-0.31] | 0.15 |
| Sandgren 2003 EE |  | 30 | 10.5 | 30% | [15-49%] | 24% | [4-58%] | 0.06 | [-0.24-0.37] | 0.69 |
| Sandgren 2003 HE |  | 22 | 10.5 | 50% | [28-72%] | 24% | [4-58%] | 0.26 | [-0.07-0.59] | 0.12 |
| Savard 2005 |  | 8 | 7 | 25% | [3-65%] | 0% | [0-41%] | 0.25 | [-0.09-0.59] | 0.15 |
| Savard 2006 |  | 13 | 11 | 38% | [14-68%] | 9% | [0-41%] | 0.29 | [-0.02-0.61] | 0.07 |
| Tx = treatment; ctrl = control; n = number of patients; RD = risk difference; CI = confidence interval; BMS = body mind spirit; SEGT = supportive expressive group therapy; MBSR = mindfulness-based stress reduction; EE = emotional expression; HE = breast cancer health education; a risk differences were scaled so that positive values represented effects in favour of treatment | | | | | | | | | | |

*Table D2. Weighted recovery rates and risk differences for recovery at follow-up (≥6 months after treatment)*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | **Weighted recovery rates** | | | | **Risk differences for recovery rates** | | |
| **Trial** |  | **Tx n** | **Ctrl n** | **Tx %** | **Tx  [95% CI]** | **Ctrl %** | **Ctrl  [95% CI]** | **RDa** | **95% CI** | **p** |
| **Anxiety** | | | | | | | | | | |
| Bredal 2014 |  | 90 | 101 | 52% | [41-63%] | 53% | [43-63%] | -0.01 | [-0.15-0.13] | 0.86 |
| Classen 2008 |  | 49 | 55 | 18% | [9-32%] | 25% | [15-39%] | -0.07 | [-0.23-0.09] | 0.38 |
| Groarke 2012 |  | 35 | 28 | 40% | [24-58%] | 36% | [19-56%] | 0.04 | [-0.20-0.28] | 0.73 |
| Ho 2016 BMS |  | 15 | 11 | 20% | [4-48%] | 23% | [4-57%] | -0.03 | [-0.35-0.29] | 0.87 |
| Ho 2016 SEGT |  | 22 | 11 | 14% | [3-35%] | 23% | [4-57%] | -0.09 | [-0.38-0.20] | 0.53 |
| **Depression** | | | | | | | | | | |
| Antoni 2001 |  | 17 | 18 | 35% | [14-62%] | 11% | [1-35%] | 0.24 | [-0.03-0.51] | 0.08 |
| Bredal 2014 |  | 45 | 47 | 71% | [56-84%] | 77% | [62-88%] | -0.05 | [-0.23-0.12] | 0.55 |
| Classen 2008 |  | 28 | 19 | 32% | [16-52%] | 37% | [16-62%] | -0.05 | [-0.32-0.23] | 0.74 |
| Groarke 2012 |  | 12 | 12 | 33% | [10-65%] | 33% | [10-65%] | 0.00 | [-0.38-0.38] | 1.00 |
| Ho 2016 BMS |  | 5 | 3.5 | 60% | [15-95%] | 14% | [0-77%] | 0.46 | [-0.11-1.02] | 0.11 |
| Ho 2016 SEGT |  | 9 | 3.5 | 22% | [3-60%] | 14% | [0-77%] | 0.08 | [-0.38-0.54] | 0.73 |
| Lechner 2014 |  | 52 | 56 | 0% | [0-7%] | 0% | [0-6%] | 0.00 | [-0.04-0.04] | 1.00 |
| Stanton 2005 |  | 38 | 24 | 5% | [0-18%] | 38% | [19-59%] | -0.32 | [-0.14-0.12] | 0.86 |
| **General distress** | | | | | | | | | | |
| Andersen 2004 |  | 44 | 29 | 34% | [20-50%] | 24% | [10-44%] | 0.10 | [-0.11-0.31] | 0.35 |
| Bredal 2014 |  | 81 | 76 | 53% | [42-64%] | 54% | [42-65%] | -0.01 | [-0.16-0.15] | 0.91 |
| Classen 2008 |  | 45 | 42 | 29% | [16-44%] | 36% | [22-52%] | -0.07 | [-0.26-0.13] | 0.50 |
| Groarke 2012 |  | 28 | 25 | 36% | [19-56%] | 16% | [5-36%] | 0.20 | [-0.03-0.43] | 0.09 |
| Ho 2016 BMS |  | 13 | 9.5 | 8% | [0-36%] | 5% | [0-40%] | 0.02 | [0.18-0.23] | 0.81 |
| Ho 2016 SEGT |  | 24 | 9.5 | 25% | [10-47%] | 5% | [0-40%] | 0.20 | [-0.03-0.42] | 0.08 |
| Sandgren 2003 EE |  | 30 | 10 | 0% | [0-16%] | 0% | [0-31%] | 0.00 | [-0.13-0.13] | 1.00 |
| Sandgren 2003 HE |  | 21 | 10 | 0% | [0-12%] | 0% | [0-31%] | 0.00 | [-0.14-0.14] | 1.00 |
| n = number of patients; RD = risk difference; CI = confidence interval; BMS = body mind spirit; SEGT = supportive expressive group therapy; MBSR = mindfulness-based stress reduction; EE = emotional expression; HE = breast cancer health education; a risk differences were scaled so that positive values represented effects in favour of treatment | | | | | | | | | | |

*Table D3. Weighted improvement rates and risk differences for improvement at post-treatment (≤8 weeks after treatment)*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | **Weighted improvement rates** | | | | **Risk differences for improvement rates** | | |
| **Trial** |  | **Tx n** | **Ctrl n** | **Tx %** | **Tx  [95% CI]** | **Ctrl %** | **Ctrl  [95% CI]** | **RDa** | **95% CI** | **p** |
|  | | | | | | | | | | |
| **Anxiety** | | | | | | | | | | |
| Beutel 2014 |  | 54 | 50 | 52% | [38-66%] | 34% | [21-49%] | 0.18 | [-0.01-0.37] | 0.06 |
| Bredal 2014 |  | 90 | 106 | 48% | [37-59%] | 40% | [30-50%] | 0.08 | [-0.06-0.22] | 0.25 |
| Classen 2008 |  | 56 | 57 | 45% | [31-59%] | 32% | [20-45%] | 0.13 | [-0.05-0.31] | 0.15 |
| Desautels 2018 |  | 19 | 6 | 32% | [13-57%] | 50% | [12-88%] | -0.18 | [-0.64-0.27] | 0.42 |
| Dirksen 2008 |  | 13 | 16 | 69% | [39-91%] | 19% | [4-46%] | 0.50 | [0.19-0.82] | 0.00 |
| Dolbeault 2009 |  | 72 | 75 | 38% | [26-50%] | 11% | [5-20%] | 0.27 | [0.14-0.40] | 0.00 |
| Groarke 2013 |  | 35 | 28 | 66% | [48-81%] | 18% | [6-37%] | 0.48 | [0.27-0.69] | 0.00 |
| Ho BMS |  | 16 | 11.5 | 38% | [15-65%] | 35% | [10-67%] | 0.03 | [-0.34-0.39 | 0.88 |
| Ho SEGT |  | 22 | 11.5 | 23% | [8-45%] | 35% | [10-67%] | -0.12 | [-0.45-0.21] | 0.47 |
| Merckeart 2016 |  | 40 | 43 | 45% | [29-62%] | 33% | [19-49%] | 0.12 | [-0.08-0.33] | 0.24 |
| Savard 2005 |  | 9 | 12 | 56% | [21-86%] | 17% | [2-48%] | 0.39 | [0.00-0.78] | 0.05 |
| Savard 2006 |  | 12 | 11 | 92% | [62-100%] | 36% | [11-69%] | 0.55 | [0.23-0.88] | 0.00 |
| **Depression** | | | | | | | | | | |
| Antoni 2001 |  | 18 | 22 | 44% | [25-57%] | 41% | [21-64%] | 0.04 | [-0.27-0.34] | 0.82 |
| Beutel 2014 |  | 59 | 58 | 73% | [60-84%] | 41% | [29-55%] | 0.32 | [0.14-0.49] | 0.00 |
| Bredal 2014 |  | 47 | 52 | 34% | [21-49%] | 33% | [20-47%] | 0.01 | [-0.17-0.20] | 0.89 |
| Classen 2008 |  | 26 | 18 | 54% | [33-73%] | 61% | [36-83%] | -0.07 | [-0.37-0.22] | 0.63 |
| Desautels 2018 |  | 19 | 8 | 58% | [33-80%] | 38% | [9-76%] | 0.20 | [-0.20-0.61] | 0.32 |
| Dirksen 2008 |  | 13 | 5 | 46% | [19-75%] | 40% | [5-85%] | 0.06 | [-0.45-0.57] | 0.81 |
| Groarke 2013 |  | 12 | 12 | 33% | [10-65%] | 42% | [15-72%] | -0.08 | [-0.47-0.30] | 0.67 |
| Ho BMS |  | 5 | 3.5 | 60% | [15-95%] | 14% | [0-77%] | 0.46 | [-0.11-1.02] | 0.11 |
| Ho SEGT |  | 9 | 3.5 | 22% | [3-60%] | 14% | [0-77%] | 0.08 | [-0.38-0.54] | 0.73 |
| Lechner 2014 |  | 53 | 57 | 17% | [8-30%] | 21% | [11-34%] | -0.04 | [-0.19-0.11] | 0.59 |
| Merckeart 2016 |  | 21 | 15 | 67% | [43-85%] | 47% | [21-73%] | 0.20 | [-0.12-0.52] | 0.23 |
| Savard 2005 |  | 2 | 3 | 100% | [16-100%] | 67% | [9-99%] | 0.33 | [-0.30-0.97] | 0.30 |
| Savard 2006 |  | 10 | 9 | 90% | [55-100%] | 44% | [14-79%] | 0.46 | [0.08-0.83] | 0.02 |
| Stanton 2005 |  | 40 | 24 | 40% | [25-47%] | 42% | [22-63%] | -0.02 | [-0.27-0.23] | 0.90 |
| **General distress** | | | | | | | | | | |
| Andersen 2004 |  | 48 | 30 | 60% | [45-74%] | 57% | 37-75% | 0.01 | [-0.19-0.26] | 0.74 |
| Beutel 2014 |  | 59 | 57 | 71% | [58-82%] | 39% | [26-52%] | 0.33 | [0.15-0.50] | 0.00 |
| Bredal 2014 |  | 81 | 78 | 42% | [31-53%] | 36% | [25-48%] | 0.06 | [0.09-0.21] | 0.43 |
| Carlson 2013 MBSR |  | 27 | 7 | 67% | [46-83%] | 57% | [18-90%] | 0.10 | [-0.31-0.50] | 0.65 |
| Carlson 2013 SET |  | 29 | 7 | 48% | [29-67%] | 57% | [18-90%] | -0.09 | [-0.50-0.32] | 0.67 |
| Classen 2008 |  | 49 | 44 | 51% | [36-66%] | 50% | [35-65%] | 0.01 | [-0.19-0.21] | 0.92 |
| Desautels 2018 |  | 23 | 9 | 83% | [61-95%] | 33% | [7-70%] | 0.49 | [0.15-0.84] | 0.01 |
| Dolbeault 2009 |  | 47 | 48 | 57% | [42-72%] | 23% | [12-37%] | 0.35 | [0.16-0.53] | 0.00 |
| Groarke 2013 |  | 28 | 25 | 50% | [31-69%] | 12% | [3-31%] | 0.38 | [0.16-0.60] | 0.00 |
| Ho BMS |  | 14 | 10 | 29% | [8-58%] | 20% | [3-56%] | 0.09 | [-0.26-0.43] | 0.62 |
| Ho SEGT |  | 24 | 10 | 25% | [10-47%] | 20% | [3-56%] | 0.05 | [-0.25-0.35] | 0.75 |
| Merckeart 2016 |  | 39 | 32 | 54% | [37-70%] | 34% | [19-53%] | 0.19 | [-0.03-0.42] | 0.09 |
| Sandgren 2003 EE |  | 30 | 10.5 | 50% | [31-69%] | 67% | [33-91%] | -0.17 | [-0.50-0.17] | 0.33 |
| Sandgren 2003 HE |  | 22 | 10.5 | 59% | [36-79%] | 67% | [33-91%] | -0.08 | [-0.43-0.28] | 0.67 |
| Savard 2005 |  | 8 | 7 | 38% | [9-76%] | 14% | [0-58%] | 0.23 | [-0.19-0.66] | 0.28 |
| Savard 2006 |  | 13 | 11 | 92% | [64-100%] | 36% | [11-69%] | 0.56 | [0.24-0.88] | 0.00 |
| Tx = treatment; ctrl = control; n = number of patients; RD = risk difference; CI = confidence interval; BMS = body mind spirit; SEGT = supportive expressive group therapy; MBSR = mindfulness-based stress reduction; EE = emotional expression; HE = breast cancer health education; a risk differences were scaled so that positive values represented effects in favour of treatment | | | | | | | | | | |

*Table D4. Weighted improvement rates and risk differences for improvement at follow-up (≥6 months after treatment)*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | **Weighted improvement rates** | | | | **Risk differences for improvement rates** | | |
| **Trial** |  | **Tx n** | **Ctrl n** | **Tx %** | **Tx  [95% CI]** | **Ctrl %** | **Ctrl  [95% CI]** | **RDa** | **95% CI** | **p** |
| **Anxiety** | | | | | | | | | | |
| Bredal 2014 |  | 90 | 101 | 73% | [63-82%] | 67% | [57-76%] | 0.06 | [-0.07-0.19] | 0.360.36 |
| Classen 2008 |  | 49 | 55 | 45% | [31-60%] | 42% | [29-56%] | 0.03 | [-0.16-0.22] | 0.75 |
| Groarke 2012 |  | 35 | 28 | 60% | [42-76%] | 46% | [28-66%] | 0.14 | [-0.11-0.38] | 0.28 |
| Ho 2016 BMS |  | 15 | 11 | 27% | [8-55%] | 41% | [14-73%] | -0.14 | [-0.51-0.22] | 0.45 |
| Ho 2016 SEGT |  | 22 | 11 | 23% | [8-45%] | 41% | [14-73%] | -0.18 | [-0.52-0.16] | 0.29 |
| **Depression** | | | | | | | | | | |
| Antoni 2001 |  | 17 | 18 | 65% | [38-86%] | 44% | [26-67%] | 0.20 | [-0.12-0.53] | 0.22 |
| Bredal 2014 |  | 45 | 47 | 71% | [56-84%] | 85% | [72-94%] | -0.14 | [-0.31-0.03] | 0.10 |
| Classen 2008 |  | 28 | 19 | 54% | [34-72%] | 42% | [20-67%] | 0.11 | [-0.17-0.40] | 0.44 |
| Groarke 2012 |  | 12 | 12 | 42% | [15-72%] | 67% | [35-90%] | -0.25 | [-0.64-0.14] | 0.20 |
| Ho 2016 BMS |  | 5 | 3.5 | 80% | [28-99%] | 29% | [0-86%] | 0.51 | [-0.07-1.10] | 0.09 |
| Ho 2016 SEGT |  | 9 | 3.5 | 22% | [3-60%] | 29% | [0-86%] | -0.06 | [-0.61-0.48] | 0.82 |
| Lechner 2014 |  | 52 | 56 | 21% | [11-35%] | 25% | [14-38%] | -0.04 | [-0.20-0.12] | 0.63 |
| Stanton 2005 |  | 38 | 24 | 32% | [18-49%] | 46% | [26-67%] | -0.14 | [-0.39-0.11] | 0.26 |
| **General distress** | | | | | | | | | | |
| Andersen 2004 |  | 44 | 29 | 57% | [41-72%] | 62% | [42-79%] | -0.05 | [-0.28-0.18] | 0.65 |
| Bredal 2014 |  | 81 | 76 | 74% | [63-83%] | 80% | [70-89%] | -0.06 | [-0.19-0.07] | 0.35 |
| Classen 2008 |  | 45 | 42 | 62% | [47-76%] | 57% | [41-72%] | 0.05 | [-0.16-0.26] | 0.63 |
| Groarke 2012 |  | 28 | 25 | 46% | [28-66%] | 40% | [21-61%] | 0.06 | [-0.20-0.33] | 0.64 |
| Ho 2016 BMS |  | 13 | 9.5 | 31% | [9-61%] | 37% | [10-72%] | -0.06 | [-0.46-0.34] | 0.76 |
| Ho 2016 SEGT |  | 24 | 9.5 | 33% | [16-55%] | 37% | [10-72%] | -0.04 | [-0.40-0.32] | 0.85 |
| Sandgren 2003 EE |  | 30 | 10 | 17% | [6-35%] | 15% | [1-50%] | 0.02 | [-0.24-0.28] | 0.90 |
| Sandgren 2003 HE |  | 21 | 10 | 29% | [11-52%] | 15% | [1-50%] | 0.14 | [-0.09-0.07] | 0.83 |
| n = number of patients; RD = risk difference; CI = confidence interval; BMS = body mind spirit; SEGT = supportive expressive group therapy; MBSR = mindfulness-based stress reduction; EE = emotional expression; HE = breast cancer health education; a risk differences were scaled so that positive values represented effects in favour of treatment | | | | | | | | | | |

*Table D5. Weighted deterioration rates and risk differences for deterioration at post-treatment (≤8 weeks after treatment)*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | **Weighted deterioration rates** | | | | **Risk differences for detrioration rates** | | |
| **Trial** |  | **Tx n** | **Ctrl n** | **Tx %** | **Tx  [95% CI]** | **Ctrl %** | **Ctrl  [95% CI]** | **RDa** | **95% CI** | **p** |
| **Anxiety** | | | | | | | | | | |
| Beutel 2014 |  | 54 | 50 | 9% | [3-20%] | 8% | [2-19%] | 0.01 | [-0.01-0.12] | 0.82 |
| Bredal 2014 |  | 90 | 106 | 12% | [6-21%] | 13% | [7-21%] | -0.01 | [-0.10-0.08] | 0.84 |
| Classen 2008 |  | 56 | 57 | 13% | [5-24%] | 9% | [3-19%] | 0.04 | [-0.08-0.15] | 0.52 |
| Desautels 2018 |  | 19 | 6 | 0% | [0-18%] | 0% | [0-46%] | 0.00 | [-0.20-0.20] | 1.00 |
| Dirksen 2008 |  | 13 | 16 | 0% | [0-25%] | 0% | [0-21%] | 0.00 | [-0.13-0.13] | 1.00 |
| Dolbeault 2009 |  | 72 | 75 | 4% | [0-12%] | 15% | [8-25%] | -0.11 | [-0.20—0.01] | 0.03 |
| Groarke 2013 |  | 35 | 28 | 0% | [0-10%] | 7% | [0-24%] | -0.07 | [[-0.18-0.04] | 0.20 |
| Ho BMS |  | 16 | 11.5 | 6% | [0-30%] | 13% | [0-45%] | -0.07 | [-0.30-0.16] | 0.56 |
| Ho SEGT |  | 22 | 11.5 | 23% | [8-45%] | 13% | [0-45%] | 0.10 | [-0.16-0.36] | 0.47 |
| Merckeart 2016 |  | 40 | 43 | 5% | [0-17%] | 5% | [0-16%] | 0.00 | -0.09-0.10] | 0.94 |
| Savard 2005 |  | 9 | 12 | 0% | [0-34%] | 33% | [10-65%] | -0.33 | [-0.63—0.04] | 0.03 |
| Savard 2006 |  | 12 | 11 | 0% | [0-26%] | 18% | [2-52%] | -0.18 | [-0.43-0.07] | 0.15 |
| **Depression** | | | | | | | | | | |
| Antoni 2001 |  | 18 | 22 | 11% | [1-35%] | 0% | [0-15%] | 0.11 | [-0.05-0.27] | 0.18 |
| Beutel 2014 |  | 59 | 58 | 3% | [0-12%] | 17% | [9-29%] | -0.14 | [-0.25—0.03] | 0.01 |
| Bredal 2014 |  | 47 | 52 | 4% | [0-15%] | 4% | [0-13%] | 0.00 | [-0.07-0.08] | 0.92 |
| Classen 2008 |  | 26 | 18 | 4% | [0-20%] | 11% | [1-35%] | -0.07 | [-0.24-0.09] | 0.38 |
| Desautels 2018 |  | 19 | 8 | 0% | [0-18%] | 0% | [0-37%] | 0.00 | [-0.16-0.16] | 1.00 |
| Dirksen 2008 |  | 13 | 5 | 0% | [0-25%] | 20% | [0-72%] | -0.20 | [-0.56-0.16] | 0.28 |
| Groarke 2013 |  | 12 | 12 | 0% | [0-26%] | 0% | [0-26%] | 0.00 | [-0.15-0.15] | 1.00 |
| Ho BMS |  | 5 | 3.5 | 0% | [0-52%] | 14% | [0-77%] | -0.14 | [-0.59-0.30] | 0.53 |
| Ho SEGT |  | 9 | 3.5 | 33% | [7-70%] | 14% | [0-77%] | 0.19 | [-0.29-0.67] | 0.44 |
| Lechner 2014 |  | 53 | 57 | 8% | [2-18%] | 12% | [5-24%] | -0.05 | [-0.16-0.06] | 0.40 |
| Merckeart 2016 |  | 21 | 15 | 0% | [0-16%] | 0% | [0-22%] | 0.00 | [-0.11-0.11] | 1.00 |
| Savard 2005 |  | 2 | 3 | 0% | [0-84%] | 0% | [0-71%] | 0.00 | [-0.53-0.53] | 1.00 |
| Savard 2006 |  | 10 | 9 | 0% | [0-31%] | 0% | [0-34%] | 0.00 | [-0.18-0.18] | 1.00 |
| Stanton 2005 |  | 40 | 24 | 8% | [2-20%] | 4% | [0-21%] | 0.03 | [-0.08-0.15] | 0.57 |
| **General distress** | | | | | | | | | | |
| Andersen 2004 |  | 48 | 30 | 13% | [5-25%] | 7% | [0-22%] | 0.06 | [-0.07-0.19] | 0.38 |
| Beutel 2014 |  | 59 | 57 | 7% | [2-16%] | 14% | [6-26%] | -0.07 | [-0.18-0.04] | 0.20 |
| Bredal 2014 |  | 81 | 78 | 7% | [3-15%] | 14% | [7-24%] | -0.07 | [-0.16-0.03] | 0.17 |
| Carlson 2013 MBSR |  | 27 | 7 | 7% | [0-24%] | 14% | [0-37%] | -0.07 | [-0.35-0.21] | 0.63 |
| Carlson 2013 SET |  | 29 | 7 | 17% | [6-36%] | 14% | [0-37%] | 0.03 | [-0.26-0.32] | 0.84 |
| Classen 2008 |  | 49 | 44 | 12% | [5-25%] | 5% | [0-15%] | 0.08 | [-0.03-0.19] | 0.17 |
| Desautels 2018 |  | 23 | 9 | 0% | [0-15%] | 11% | [0-48%] | -0.11 | [-0.34-0.12] | 0.34 |
| Dolbeault 2009 |  | 47 | 48 | 6% | [1-18%] | 27% | [15-42%] | -0.21 | [-0.35—0.06] | 0.00 |
| Groarke 2013 |  | 28 | 25 | 0% | [0-12%] | 8% | [0-26%] | -0.08 | [-0.20-0.04] | 0.20 |
| Ho BMS |  | 14 | 10 | 0% | [0-23%] | 5% | [0-38%] | -0.05 | [-0.24-0.14] | 0.61 |
| Ho SEGT |  | 24 | 10 | 21% | [7-42%] | 5% | [0-38%] | 0.16 | [-0.05-0.37] | 0.14 |
| Merckeart 2016 |  | 39 | 32 | 8% | [2-21%] | 13% | [4-29%] | -0.05 | [-0.19-0.09] | 0.51 |
| Sandgren 2003 EE |  | 30 | 10.5 | 7% | [0-22%] | 5% | [0-37%] | 0.02 | [-0.14-0.18] | 0.81 |
| Sandgren 2003 HE |  | 22 | 10.5 | 9% | [1-29%] | 5% | [0-37%] | 0.04 | [-0.13-0.22] | 0.63 |
| Savard 2005 |  | 8 | 7 | 0% | [0-37%] | 14% | [0-58%] | -0.14 | [-0.45-0.17] | 0.37 |
| Savard 2006 |  | 13 | 11 | 0% | [0-25%] | 0% | [0-28%] | 0.00 | [-0.15-0.15] | 1.00 |
| Tx = treatment; ctrl = control; n = number of patients; RD = risk difference; CI = confidence interval; BMS = body mind spirit; SEGT = supportive expressive group therapy; MBSR = mindfulness-based stress reduction; EE = emotional expression; HE = breast cancer health education; a risk differences were scaled so that positive values represented effects in favour of treatment | | | | | | | | | | |

*Table D6. Weighted deterioration rates and risk differences for deterioration at follow-up (≥6 months after treatment)*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | **Weighted deterioration rates** | | | | **Risk differences for deterioration rates** | | |
| **Trial** |  | **Tx n** | **Ctrl n** | **Tx %** | **Tx  [95% CI]** | **Ctrl %** | **Ctrl  [95% CI]** | **RDa** | **95% CI** | **p** |
| **Anxiety** | | | | | | | | | | |
| Bredal 2014 |  | 90 | 101 | 4% | [1-11%] | 5% | [2-11%] | -0.01 | [-0.07-0.05] | 0.87 |
| Classen 2008 |  | 49 | 55 | 12% | [5-25%] | 7% | [2-18%] | 0.05 | [-0.06-0.16] | 0.40 |
| Groarke 2012 |  | 35 | 28 | 17% | [7-34%] | 7% | [0-24%] | 0.10 | [-0.06-0.26] | 0.21 |
| Ho 2016 BMS |  | 15 | 11 | 20% | [4-48%] | 23% | [4-57%] | -0.03 | [-0.35-0.29] | 0.87 |
| Ho 2016 SEGT |  | 22 | 11 | 9% | [1-29%] | 9% | [5-16%] | -0.14 | [-0.41-0.14] | 0.33 |
| **Depression** | | | | | | | | | | |
| Antoni 2001 |  | 17 | 18 | 0% | [0-20%] | 6% | [0-27%] | -0.06 | [-0.20-0.09] | 0.45 |
| Bredal 2014 |  | 45 | 47 | 2% | [0-12%] | 2% | [0-11%] | 0.00 | [-0.06-0.06] | 0.98 |
| Classen 2008 |  | 28 | 19 | 0% | [0-12%] | 11% | [1-33%] | -0.11 | [-0.26-0.05] | 0.18 |
| Groarke 2012 |  | 12 | 12 | 17% | [2-48%] | 8% | [0-38%] | 0.08 | [-0.18-0.35] | 0.53 |
| Ho 2016 BMS |  | 5 | 3.5 | 0% | [0-52%] | 29% | [0-86%] | -0.29 | [-0.77-0.20] | 0.25 |
| Ho 2016 SEGT |  | 9 | 3.5 | 0% | [0-20%] | 29% | [0-86%] | -0.29 | [-0.74-0.17] | 0.22 |
| Lechner 2014 |  | 52 | 56 | 4% | [0-13%] | 9% | [3-20%] | -0.05 | [-0.14-0.04] | 0.27 |
| Stanton 2005 |  | 38 | 24 | 5% | [0-18%] | 4% | [0-21%] | 0.01 | [-0.10-0.12] | 0.84 |
| **General distress** | | | | | | | | | | |
| Andersen 2004 |  | 44 | 29 | 2% | [0-12%] | 3% | [0-18%] | -0.01 | [-0.09-0.07] | 0.77 |
| Bredal 2014 |  | 81 | 76 | 4% | [0-10%] | 4% | [0-11%] | -0.00 | [-0.06-0.06] | 0.94 |
| Classen 2008 |  | 45 | 42 | 4% | [0-15%] | 17% | [7-31%] | -0.12 | [-0.25-0.01] | 0.06 |
| Groarke 2012 |  | 28 | 25 | 4% | [0-18%] | 12% | [3-31%] | -0.08 | [-0.23-0.06] | 0.25 |
| Ho 2016 BMS |  | 13 | 9.5 | 0% | [0-25%] | 26% | [5-63%] | -0.26 | [-0.55-0.03] | 0.08 |
| Ho 2016 SEGT |  | 24 | 9.5 | 13% | [3-32%] | 26% | [5-63%] | -0.14 | [-0.45-0.17] | 0.38 |
| Sandgren 2003 EE |  | 30 | 10 | 20% | [8-39%] | 25% | [4-61%] | -0.05 | [-0.35-0.25] | 0.75 |
| Sandgren 2003 HE |  | 21 | 10 | 19% | [5-42%] | 25% | [4-61%] | -0.06 | [-0.38-0.26] | 0.71 |
| n = number of patients; RD = risk difference; CI = confidence interval; BMS = body mind spirit; SEGT = supportive expressive group therapy; MBSR = mindfulness-based stress reduction; EE = emotional expression; HE = breast cancer health education; a risk differences were scaled so that positive values represented effects in favour of treatment | | | | | | | | | | |

*Table D7. Effect sizes at post-treatment (≤8 weeks after treatment)*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Effect sizes (g)** | | |
| **Trial** |  | **Tx n** | **Ctrl n** | **ga** | **95% CI** | **p** |
| **Anxiety** | | | | | | |
| Beutel 2014 |  | 54 | 50 | 0.33 | [-0.05-0.72] | 0.09 |
| Bredal 2014 |  | 90 | 106 | 0.11 | [-0.17-0.39] | 0.45 |
| Classen 2008 |  | 56 | 57 | 0.00 | [-0.36-0.37] | 0.99 |
| Desautels 2018 |  | 19 | 6 | 1.42 | [0.45-2.39] | 0.00 |
| Dirksen 2008 |  | 13 | 16 | 0.56 | [-0.16-1.29] | 0.13 |
| Dolbeault 2009 |  | 72 | 75 | 0.53 | [0.21-0.86] | 0.00 |
| Groarke 2013 |  | 35 | 28 | 0.77 | [0.26-1.28] | 0.00 |
| Ho BMS |  | 16 | 11.5 | 0.25 | [-0.49-0.99] | 0.51 |
| Ho SEGT |  | 22 | 11.5 | -0.24 | [-0.94-0.46] | 0.50 |
| Merckeart 2016 |  | 40 | 43 | 0.00 | [-0.42-0.43] | 0.98 |
| Savard 2005 |  | 9 | 12 | 0.42 | [-0.42-1.26] | 0.32 |
| Savard 2006 |  | 12 | 11 | 0.94 | [0.10-1.77] | 0.03 |
| **Depression** | | | | | | |
| Antoni 2001 |  | 18 | 22 | 0.53 | [-0.10-1.15] | 0.10 |
| Beutel 2014 |  | 59 | 58 | 0.60 | [0.23-0.97] | 0.00 |
| Bredal 2014 |  | 47 | 52 | 0.10 | [-0.29-0.49] | 0.61 |
| Classen 2008 |  | 26 | 18 | 0.17 | [-0.42-0.77] | 0.56 |
| Desautels 2018 |  | 19 | 8 | 0.85 | [0.02-1.68] | 0.05 |
| Dirksen 2008 |  | 13 | 5 | 1.35 | [0.27-2.42] | 0.01 |
| Groarke 2013 |  | 12 | 12 | 0.18 | [-0.59-0.96] | 0.64 |
| Ho BMS |  | 5 | 3.5 | 1.95 | [0.44-3.45] | 0.01 |
| Ho SEGT |  | 9 | 3.5 | 0.15 | [-0.99-1.29] | 0.80 |
| Lechner 2014 |  | 53 | 57 | 0.10 | [-0.27-0.47] | 0.59 |
| Merckeart 2016 |  | 21 | 15 | 0.15 | [-0.50-0.80] | 0.66 |
| Savard 2005 |  | 2 | 3 | 0.41 | [-0.91-1.74] | 0.54 |
| Savard 2006 |  | 10 | 9 | 0.33 | [0.53-1.20] | 0.45 |
| Stanton 2005 |  | 40 | 24 | -0.20 | [-0.70-0.30] | 0.44 |
| **General distress** | | | | | | |
| Andersen 2004 |  | 48 | 30 | 0.04 | [-0.14-0.49] | 0.86 |
| Beutel 2014 |  | 59 | 57 | 0.48 | [0.12-0.85] | 0.01 |
| Bredal 2014 |  | 81 | 78 | 0.13 | [-0.18-0.44] | 0.43 |
| Carlson 2013 MBSR |  | 27 | 7 | 0.44 | [-0.38-1.26] | 0.29 |
| Carlson 2013 SET |  | 29 | 7 | -0.28 | [-1.08-0.53] | 0.50 |
| Classen 2008 |  | 49 | 44 | -0.12 | [-0.52-0.29] | 0.57 |
| Desautels 2018 |  | 23 | 9 | 1.48 | [0.65-2.32] | 0.00 |
| Dolbeault 2009 |  | 47 | 48 | 0.73 | [0.32-1.14] | 0.00 |
| Groarke 2013 |  | 28 | 25 | 0.76 | [0.21-1.31] | 0.01 |
| Ho BMS |  | 14 | 10 | 0.70 | [-0.11-1.51] | 0.09 |
| Ho SEGT |  | 24 | 10 | 0.04 | [-0.68-0.76] | 0.92 |
| Merckeart 2016 |  | 39 | 32 | 0.20 | [-0.26-0.66] | 0.40 |
| Sandgren 2003 EE |  | 30 | 10.5 | -0.07 | [-0.76-0.62] | 0.84 |
| Sandgren 2003 HE |  | 22 | 10.5 | 0.01 | [-0.71-0.73] | 0.98 |
| Savard 2005 |  | 8 | 7 | 0.39 | [-0.57-1.36] | 0.43 |
| Savard 2006 |  | 13 | 11 | 0.83 | [0.02-1.64] | 0.05 |
| Tx = treatment; ctrl = control; n = number of patients; RD = risk difference; CI = confidence interval; BMS = body mind spirit; SEGT = supportive expressive group therapy; MBSR = mindfulness-based stress reduction; EE = emotional expression; HE = breast cancer health education; a effect sizes were scaled so that positive values represented effects in favour of treatment | | | | | | |

*Table D8. Effect sizes at follow-up (≥6 months after treatment)*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Effect sizes (g)** | | |
| **Trial** |  | **Tx n** | **Ctrl n** | **ga** | **95% CI** | **p** |
| **Anxiety** | | | | | | |
| Bredal 2014 |  | 90 | 101 | -0.02 | [-0.30-0.27] | 0.90 |
| Classen 2008 |  | 49 | 55 | -0.21 | [-0.59-0.17] | 0.28 |
| Groarke 2012 |  | 35 | 28 | -0.08 | [-0.57-0.41] | 0.74 |
| Ho 2016 BMS |  | 15 | 11 | 0.05 | [-0.70-0.80] | 0.90 |
| Ho 2016 SEGT |  | 22 | 11 | -0.05 | [-0.75-0.66] | 0.90 |
| **Depression** | | | | | | |
| Antoni 2001 |  | 17 | 18 | 0.66 | [-0.01-1.33] | 0.05 |
| Bredal 2014 |  | 45 | 47 | -0.15 | [-0.55-0.26] | 0.48 |
| Classen 2008 |  | 28 | 19 | 0.12 | [-0.45-0.69] | 0.68 |
| Groarke 2012 |  | 12 | 12 | -0.27 | [-1.05-0.50] | 0.49 |
| Ho 2016 BMS |  | 5 | 3.5 | 1.12 | [-0.16-2.39] | 0.09 |
| Ho 2016 SEGT |  | 9 | 3.5 | 0.32 | [-0.78-1.42] | 0.57 |
| Lechner |  | 52 | 56 | 0.07 | [-0.31-0.44] | 0.72 |
| Stanton 2005 |  | 38 | 24 | -0.63 | [-1.15—0.11] | 0.02 |
| **General distress** | | | | | | |
| Andersen 2004 |  | 44 | 29 | 0.18 | [-0.28-0.65] | 0.44 |
| Bredal 2014 |  | 81 | 76 | -0.09 | [-0.40-0.23] | 0.59 |
| Classen 2008 |  | 45 | 42 | 0.23 | [-0.19-0.64] | 0.29 |
| Groarke 2012 |  | 28 | 25 | 0.21 | [-0.32-0.74] | 0.44 |
| Ho 2016 BMS |  | 13 | 9.5 | 0.48 | [-0.33-1.28] | 0.25 |
| Ho 2016 SEGT |  | 24 | 9.5 | 0.33 | [-0.39-1.06] | 0.37 |
| Sandgren 2003 EE |  | 30 | 10 | 0.15 | [-0.55-0.85] | 0.68 |
| Sandgren 2003 HE |  | 21 | 10 | -0.17 | [-0.91-0.56] | 0.65 |
| Tx = treatment; ctrl = control; n = number of patients; RD = risk difference; CI = confidence interval; BMS = body mind spirit; SEGT = supportive expressive group therapy; MBSR = mindfulness-based stress reduction; EE = emotional expression; HE = breast cancer health education; a effect sizes were scaled so that positive values represented effects in favour of treatment | | | | | | |

**APPENDIX E.**

*Table E1. The influence of methodological quality and age on risk differences for recovery, improvement, and deterioration at post-treatment (≤8 weeks after treatment)*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Risk differences for recovery rates** | | | |  | **Risk differences for improvement rates** | | | | **Risk differences for deterioration rates** | | | | |
| **Moderator variable** |  | **k** | **β** | **95% CI** | **p** |  | **k** | **β** | **95% CI** | **p** | **k** | **β** | **95% CI** | **p** |
| **Anxiety** | | | | | | | | | | | | | | | |
| Age |  | 12 | 0.01 | [-0.01,0.04] | 0.31 |  | 12 | 0.03 | [-0.01, 0.07] | 0.14 | 12 | -0.00 | [-0.02-0.01] | 0.61 |
| Methodological quality |  | 12 | 0.00 | [-0.01,0.02] | 0.49 |  | 12 | -0.01 | [-0.04,0.02] | 0.47 | 12 | 0.00 | [-0.01,0.13] | 0.96 |
| **Depression** | | | | | | | | | | | | | | | |
| Age |  | 14 | -0.00 | [-0.02,0.02] | 0.72 |  | 14 | -0.01 | [-0.04, 0.03] | 0.61 | 14 | 0.01 | [-0.01-0.02] | 0.49 |
| Methodological quality |  | 14 | 0.01 | [-0.01,0.02] | 0.56 |  | 14 | 0.02 | [-0.00,0.05] | 0.10 | 14 | -0.01 | [-0.02,0.00] | 0.22 |
| **General distress** | | | | | | | | | | | | | | | |
| Age |  | 16 | 0.01 | [-0.01, 0.03] | 0.44 |  | 16 | 0.01 | [-0.03, 0.05] | 0.68 | 16 | -0.02 | [-0.03-0.00] | 0.06 |
| Methodological quality |  | 16 | 0.01 | [0.00,0.03] | 0.04\* |  | 16 | 0.03 | [0.01,0.05] | 0.01\* | 16 | -0.00 | -0.01,0.01 | 0.55 |
| *Note.*  k = number of treatment/control group comparisons; RD = risk difference; CI = confidence interval; β = beta value; \* = p<0.05 | | | | | | | | | | | | | | | |

*Table E2. The influence of methodological quality and age on effect sizes at post-treatment (≤8 weeks after treatment)*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Effect sizes (g)** | | | |
| **Moderator variable** |  | **k** | **β** | **95% CI** | **p** |
| **Anxiety** | | | | | |
| Age |  | 12 | 0.08 | [0.00-0.15] | 0.04\* |
| Methodological quality |  | 12 | 0.05 | [-0.00,0.11] | 0.06 |
| **Depression** | | | | | |
| Age |  | 14 | -0.02 | [-0.09-0.06] | 0.68 |
| Methodological quality |  | 14 | 0.04 | [-0.01,0.09] | 0.1 |
| **General distress** | | | | | |
| Age |  | 16 | 0.04 | [-0.05-0.12] | 041 |
| Methodological quality |  | 16 | 0.06 | [0.01,0.10] | 0.01\* |
| *Note.*  k = number of treatment/control group comparisons; g = hedges’ g; CI = confidence interval; β = beta value; \* = p<0.05 | | | | | |