#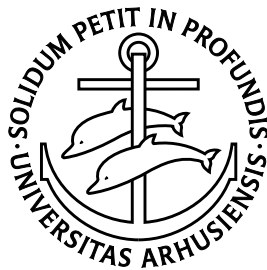 Mindfulness-based therapy for social phobia, recurrent depression, and psychological symptoms in cancer patients and survivors

PhD dissertation

Jacob Piet

Department of Psychology

Aarhus University

Denmark

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List of papers

Paper 1

Piet, J., Hougaard, E., Hecksher, M. S., & Rosenberg, N. K. (2010). A randomized pilot study of mindfulness-based cognitive therapy and group cognitive-behavioral therapy for young adults with social phobia. *Scandinavian Journal of Psychology, 51*, 403-410.

Paper 2

Piet, J., & Hougaard, E. (2011). The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: A systematic review and meta-analysis. *Clinical Psychology Review, 31*, 1032-1040.

Paper 3

Piet, J., Würtzen, H., & Zachariae, R. (2012). The effect of mindfulness-based therapy on symptoms of anxiety and depression in adult cancer patients and survivors: A systematic review and meta-analysis. *Journal of Consulting and Clinical Psychology*. Advance online publication. doi: 10.1037/a0028329

Summary

Background: Mindfulness originates from ancient eastern meditation and yoga traditions. Generally defined as paying attention on purpose in a non-judgmental way to present moment experiences (physical sensations, affective states, thoughts, mental imagery, and stimuli from the external environment), mindfulness is believed to cultivate a stable, non-reactive, and compassionate awareness beneficial for general psychological health and well-being. In this thesis, mindfulness-based therapy (MBT) is used as a generic term for two clinical intervention programs based on systematic training in mindfulness meditation, namely mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy (MBCT). Although recently developed, MBT has been extensively researched and applied for treatment of distress among various psychological and medical disorders. MBT may be considered a unified treatment for negative affectivity.

Objective: The overall thesis aim was to investigate the effect of MBT on negative affectivity (anxiety and depression) in three different clinical populations, including social phobia (SP), recurrent major depressive disorder (MDD) in remission, and cancer patients and survivors.

Method: The study in paper 1 was a randomized pilot study, while studies described in papers 2 and 3 were systematic reviews and meta-analyses. In the first study (paper 1), a cross-over design was used to pilot test MBCT alone and in combination with group cognitive-behavioral therapy (GCBT) for young adults with a primary diagnosis of SP. In the second study (paper 2), we collected and evaluated the evidence for the effect of MBCT for prevention of relapse in recurrent MDD based on randomized controlled trials (RCTs). In the third study (paper 3), we searched and retrieved relevant studies to evaluate the effect of MBT on symptoms of anxiety and depression in adult cancer patients and survivors, including both non-randomized studies and RCTs. *Results:* Findings from the study described in paper 1 showed that MBCT was effective for reducing symptoms of SP corresponding to a pre-post effect size (Cohens *d*) of 0.78. The effect of MBCT was numerically lower but not significantly different from the effect of GCBT. Having received both forms of

treatment participants showed further improvement at 6-months follow-up. In the study described in paper 2, results were based on relapse data from 6 RCTs totaling 593 participants with recurrent MDD in remission. Overall, compared to treatment as usual (TAU) or pill placebo, MBCT effectively reduced the risk of relapse by 34%. In a subgroup analysis of participants with three or more previous episodes of depression, the relative risk reduction was 43% in favor of MBCT. Data from two studies showed no risk reduction by MBCT among a small subgroup sample of 50 participants with only two previous episodes. In head-to-head comparisons in two studies, MBCT was at least as effective as maintenance antidepressant medication. Finally, the results from study 3 showed significant reductions in symptoms of anxiety and depression among cancer patients and survivors. In 13 non-randomized studies with a total of 448 participants, the magnitude of the overall effects associated with MBT corresponded to moderate pre-post effect sizes (Hedges's g) of 0.60 for reduction of anxiety symptoms and 0.42 for reduction of depression symptoms. In 9 RCTs with a total of 955 participants, MBT significantly reduced symptoms of anxiety (Hedges's $g = 0.37$) and depression (Hedges's $g = 0.44$), compared to TAU or wait list controls. Furthermore, across studies, MBT significantly improved mindfulness skills (Hedges's $g = 0.39$). ***Conclusion:*** Results presented in paper 1 provide preliminary evidence for the efficacy of MBT for young adults with SP, while the evidence derived from RCTs in papers 2 and 3, support the use of MBCT/MBT as an effective intervention for a) relapse prevention in people with recurrent MDD in remission, and b) cancer patients and survivors with symptoms of anxiety and depression.

Dansk resume

Baggrund: Mindfulness stammer fra østerlandske yoga og meditative traditioner. Mindfulness defineres generelt som det at være bevidst opmærksom på en ikke-dømmende måde over for nuværende oplevelser (kropslige fornemmelser, følelsesmæssige tilstande, tanker, forestillings-billeder, og stimuli fra omgivelserne), og antages at kultivere en stabil, ikke-reaktiv og medfølende bevidsthed gavnlig for almen psykologisk sundhed og velvære. I nærværende afhandling benyttes mindfulness-baseret terapi (MBT) som fællesbetegnelse for to interventionsprogrammer baseret på systematisk mindfulness meditationstræning, nemlig mindfulness-baseret stress reduction (MBSR) og mindfulness-baseret kognitiv terapi (MBKT). MBT er relativt nyudviklet, men har allerede været genstand for omfattende forskning, og er blevet anvendt til behandling af psykologiske symptomer blandt diverse medicinske og psykologiske lidelser. MBT kan tilsyneladende betragtes som en transdiagnostisk behandling af negativ affekt. ***Formål:*** Det overordnede formål med afhandlingen, var at undersøge effekten af MBT over for negativ affekt (angst og depression) blandt tre forskellige kliniske populationer, herunder unge voksne med socialfobi, personer i bedring efter tilbagevendende svær depression, samt kræftpatienter of kræftoverlevere. ***Metode:*** Undersøgelsen i artikel 1 var en randomiseret pilotundersøgelse, mens undersøgelserne i artikel 2 og 3 blev udført på baggrund af en systematisk gennemgang og meta-analyse af den relevante forskningslitteratur. I den første undersøgelse (artikel 1) blev der anvendt et cross-over design til at teste virkningen af MBKT alene og i kombination med gruppe-baseret kognitiv adfærdsterapi (KAT) over for unge voksne med socialfobi. I den anden undersøgelse (artikel 2) samlede vi den nuværende evidens fra randomiserede kontrollerede studier med henblik på at evaluere effekten af MBKT som tilbagefaldsforebyggelse ved tilbagevendende svær depression. I den sidste undersøgelse (artikel 3), foretog vi en systematisk litteratursøgning med det formål at evaluere effekten af MBT over for angst- og depressive symptomer hos voksne med en nuværende eller tidligere kræftdiagnose. ***Resultater:*** Resultater for undersøgelsen i artikel 1 viste, at MBKT var effektivt til håndtering af

socialfobiske symptomer svarende til en før-efter effektstørrelse (Cohens *d*) på 0.78. Effekten af MBKT var numerisk lavere, omend ikke signifikant forskellig fra KAT. Deltagerne viste yderligere forbedringer ved 6-måneders opfølgning, efter at have modtaget begge former for behandling. Resultater for undersøgelsen i artikel 2 var baseret på tilbagefaldsdata fra 6 randomiserede kliniske studier med i alt 593 deltagere i bedring efter tilbagevendende svær depression. Den overordnede analyse viste, at MBKT effektivt reducerede risikoen for tilbagefald med 34% sammenlignet med sædvanlig behandling eller medicinsk placebo. I en undergruppeanalyse af patienter med tre eller flere tidligere depressive episoder, var risikoreduktionen 43% til fordel for MBKT. For personer med kun to tidligere episoder (*n* = 50)*, blev der ikke fundet tilbagefaldsforebyggende effekt af MBKT. Resultater fra to studier viste, at MBKT var mindst lige så effektivt som vedligeholdende antidepressiv medicinsk behandling. I meta-analysen af MBT i artikel 3 blev der overordnet fundet signifikante reduktioner i angst- og depressive symptomer blandt kræftpatienter og kræftoverlevere. De samlede resultater for 13 ikke-randomiserede studier (*n* = 448) viste moderate før-efter effektstørrelser (Hedges's *g*) på 0.60 for angstsymptomer og 0.42 for depressive symptomer. For 9 randomiserede kontrollerede studier (*n* = 955) viste de samlede resultater, at MBT signifikant reducerede symptomer på angst (Hedges's *g* = 0.37) og depression (Hedges's *g* = 0.44), sammenlignet med sædvanlig behandling eller venteliste kontrol. Resultater for meta-analysen viste desuden, at MBT førte til signifikant forbedrede mindfulness-færdigheder (Hedges's *g* = 0.37).

Konklusion: Resultater for undersøgelsen i artikel 1 bidrager med foreløbig evidens for virkningen af MBKT over for unge voksne med sociafobi, mens evidensen fra randomiserede kliniske forsøg i artikel 2 og 3 bringer empirisk støtte til anvendelse af MBCT/MBT som en effektiv intervention over for a) forebyggelse af tilbagefald hos personer i bedring efter tilbagevendende svær depression, og b) kræftpatienter og kræftoverlevere med symptomer på angst og depression.

Abbreviations

ADIS-IV = Anxiety Disorders Interview Schedule for DSM-IV

ACT = Acceptance and Commitment Therapy

APA = American Psychological Association

CBT = Cognitive-Behavioral Therapy

CONSORT = Consolidated Standards of Reporting Trials

DBT = Dialectical Behavior Therapy

DSM-IV = Diagnostic and Statistical Manual of Mental Disorders – 4th edition

FFMQ = Five Facet Mindfulness Questionnaire

GAD = Generalized anxiety disorder

GCBT = Group Cognitive-Behavioral Therapy

JARS = Journal Article Reporting Standards

m-ADM = Maintenance Antidepressant Medication

MARS = Meta-Analysis Reporting Standards MASS = Mindfulness Attention Awareness Scale

MBCT = Mindfulness-Based Cognitive Therapy

MBSR = Mindfulness-Based Stress Reduction

MBT = Mindfulness-based therapy

MDD = Major depressive disorder

PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses

PD = Panic disorder

RCT = Randomized controlled trial

SCID-II = Structured Clinical Interview for DSM-IV Axis II personality disorders

SP = Social phobia

TAU = Treatment as usual

Introduction

Ancient meditative traditions have long claimed that mindfulness meditation can be practiced to alleviate psychological suffering and improve well-being. It is, however, only recently that traditional mindfulness practices have been secularized and integrated into the mainstream of society, including fields of medicine, healthcare, and psychology.

The field of clinical psychology has become increasingly commitment to evidence-based clinical practice, and, in recent years, mindfulness-based clinical interventions have been investigated using rigorous methodology of modern empirical science. In the tradition of cognitive-behavioral therapy (CBT), treatment approaches that emphasize mindfulness and acceptance, have been called the third wave, following classical behavior therapy and traditional cognitive therapy. Research on the clinical application of mindfulness has emerged from a number of important basic scientific questions, including: What is mindfulness? Can it be reliably measured? How is it related to other psychological constructs? Are mindfulness-based interventions effective? If so, how effective are they? Which clinical populations might benefit from such interventions? Furthermore, are improved mindfulness skills responsible for the outcome of mindfulness-based interventions? What other mechanisms might explain therapeutic change?

In general, mindfulness has become very popular, and research in the field has increased almost exponentially during the last ten years. To illustrate the recent year-by-year increase in peer-reviewed publications on mindfulness, a systematic search on the term *mindfulness* was carried out. Results shown in Figure 1 were obtained by searching abstracts recorded in psycINFO, a database established by the American Psychological Association. The search was carried out on February 5, 2012, and limited to peer-reviewed publications in the English language. On average, for the time period 1970 to 1990, there were less than 2 publications per year compared to more than 180 publications per year for the period 2005-2011 (PsycINFO, February 2012).

Figure 1. Peer-reviewed publications on mindfulness by year of publication
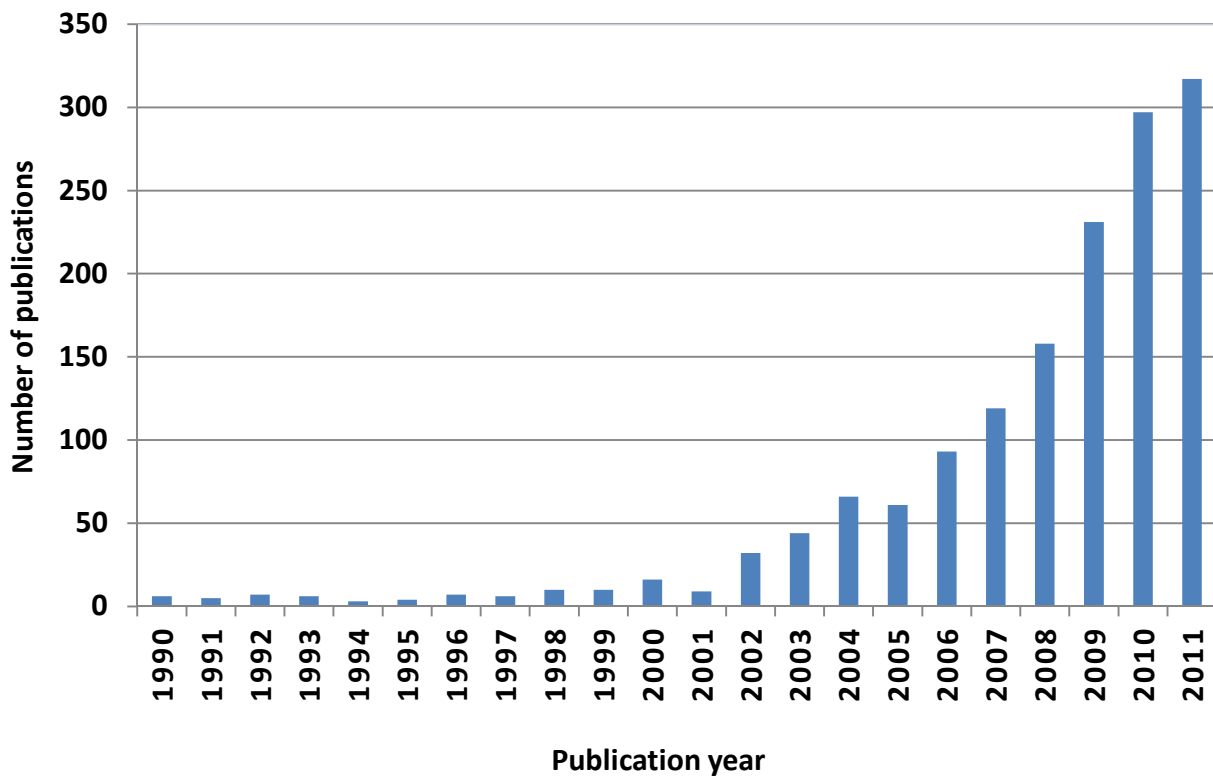
This thesis is comprised of three published research papers on the efficacy of mindfulness-based therapy (MBT). In this thesis, the term MBT is used as a generic term for two psychological intervention programs based on systematic training in mindfulness, namely mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy (MBCT). Prior to presenting the studies, described in each of the three papers, an introduction is given to the field of mindfulness. Initially, the concept of mindfulness is defined and described, followed by a section on measuring mindfulness. Next, the main predominant treatment approaches that emphasize mindfulness and acceptance are described and their evidence base is highlighted. Then, it is briefly argued that MBT may be considered a unified or transdiagnostic approach for the treatment of negative affectivity. Although research on the processes responsible for change in psychotherapy in general is relatively sparse, proposed theory and empirical studies on mechanisms and mediators of change specific to MBT are accounted for. Finally, for each study, the background, objective, method, results, and

conclusion are summarized, and an overall discussion is provided before each full-text article is presented.

Describing and defining mindfulness

Mindfulness is a particular way of directing attention that originates from ancient meditative traditions, particularly Buddhism. Practiced within Buddhist monasteries and hermitages for more 2500 years, mindfulness meditation has been applied to cultivate emotional balance and stability of attention, as well as greater compassion towards oneself and others (Goldstein, 2002; Williams & Kabat-Zinn, 2011).

The word *mindfulness* is the English translation of the Pali word *sati* or the equivalent Sanskrit word *smrti*. *Sati* has connotations to awareness, attention, and remembering. While remembering, as part of the original etymology of *sati*, is somewhat misleading, a closer examination of the foundational Buddhist texts suggests that "direct knowing", "bare attention", or "lucid awareness" of phenomena in the present, may better capture the essence of the meaning of the word, as it was used by the historical Buddha, Siddhartha Guatama, to describe the heart of meditative practices (Bodhi, 2011; Engler, 1986; Nyanaponika, 1973).

Meditation has been defined as "a family of techniques which have in common a conscious attempt to focus attention in a non-analytical way, and an attempt not to dwell on discursive, ruminating thought" (Shapiro, 1980, p. 14). The scientific literature on meditation frequently includes a distinction between contemplative approaches based on concentration versus approaches based on mindfulness. In concentration-based forms of meditation, the focus of attention is restricted to a single stimulus, such as the breath (internal stimulus) or a candle (external stimulus). In contrast, mindfulness meditation may involve observation of both internal and external stimuli as they spontaneously arise in field of awareness on a moment to moment basis. This particular form of mindfulness meditation is often spoken of as *choiceless awareness*. Concentration practices may

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produce states of peace and tranquility, while the practice of mindfulness is said to facilitate insight into the nature of conscious experience, through heightened awareness of the ongoing stream of perceptual phenomena (Brown & Ryan, 2004).

The principal instruction in the practice of both concentration and mindfulness is to notice when attention wanders, and then simply, gently but firmly, redirect it to the intended focus of attention. In mindfulness, instructions may include noticing the nature of the distraction (e.g. worrying or planning), before returning to the intended object of attention. Concentrative forms of meditation are presumed to strengthen the capacity for sustained attention over time and they are often considered preliminary to the practice of mindfulness (Bogart, 1991; Sharpiro, 1980). In mindfulness-based interventions, however, aspects of concentration are incorporated into the systematic training of mindfulness. Initially, as participants are introduced to the practice of sitting meditation, attention is focused on the physical sensations of the breath, and then later on, as they become more experienced, a period of practice may include paying attention to the broader field of awareness, including sensations of the body, feelings, sounds, and thoughts.

The essential feature of mindfulness may be described as heightened or sustained attention to and awareness of current events and experiences (Brown & Ryan, 2003). As such, mindfulness has been contrasted a) mind states where attention is characterized by absorption in the past or the future, including being preoccupied with memories, regrets, plans, worries, and fantasies, and b) compulsive and automatic behaviors characterized by a lack of awareness of one's actions. In the terminology used in the recent clinical literature, this mode of functioning without much awareness has been called *automatic pilot* (e.g. Segal, Williams, & Teasdale, 2002). Furthermore, mindfulness has been differentiated from various forms of self-focused attention and awareness which have in common a central cognitive component characterized by self-reflectiveness, evaluation, and judgment. In a recent meta-analysis, self-focused attention has been associated with negative affect in both clinical and non-clinical populations (Mor & Winquist, 2002), and it has been proposed to

be a maintaining factor across several psychological disorders (Harvey, Watkins, Mansell, & Shafran, 2004). Despite similarities, the concept of mindfulness and self-focused attention should be clearly distinguished. Mindfulness is based on direct perception (i.e. relating to experience without elaborating on it via discursive thinking), and Baer (2007) has argued that mindfulness training may have a direct impact on self-focused attention, as the ability to simply observe experience increases while reactivity to observed stimuli decreases.

Fundamentally, mindfulness is a quality of consciousness rooted in awareness and attention. Awareness can be defined as the conscious registration of both internal stimuli (e.g. feelings, bodily sensations, thoughts, mental imagery) and external stimuli (e.g. sights, sounds, smells), while the faculty of attention involves the ability to select and bring into focus one particular source of information, while ignoring or excluding other sources available from the broader field of awareness (e.g. Brown, Ryan, & Creswell, 2007; Williams, 2008). In general, sensory information, when it becomes the object of attention, is held in awareness only for a brief period of time, before being processed and colored by cognition, including concepts, ideas, beliefs, opinions, and expectations. The critical point seems to be that the contents of awareness, including thoughts, feelings, and bodily sensations, are rapidly evaluated and often automatically judged to be either good or bad based on prior experience and conditioning. The capacity of the mind to make judgments and attribute specific meaning to things and events can be useful and adaptive in guiding behavior towards goal attainment. On the other hand, it may work to distort the view of reality and prevent the person perceiving from seeing things more objectively, as they really are.

On a theoretical level, the term "doing mode" has been used to refer to the goal oriented conceptual mode of information processing (e.g. Segal, Teasdale, & Williams, 2004; Williams, 2008). Doing mode is described as a mental problem solving strategy in which the individual seeks to reduce the discrepancy between current states and more desirable states. Applied to solve concrete external problems, mental operations carried out within the doing mode are often adaptive,

as they can lead to productive actions capable of dissolving the perceived discrepancy. However, the doing mode of mind can be dysfunctional and counterproductive for dealing with emotional states such as sadness or anxiety. In such situations, attention may be constantly monitoring the discrepancy between the current situation of feeling sad and the more desired situation of being happy. This continuous comparison between "how I feel" and "how I would like to feel" can increase distress. If the problem is not solved, negative representations of the current situation (to be avoided or fixed) are repeatedly activated in the doing mode, and may lead to more severe psychopathological processes such as excessive avoidance, worry, and rumination. Consistently shown to predict depression, rumination is a passive mode of responding to distress that involves repetitive thinking about the possible causes and consequences of one's negative feelings and problems (Nolen-Hoeksama, Wisco, & Lyumbomirsky, 2008). Depressive rumination augments sad mood, however, paradoxically, individuals who ruminate often express the belief that rumination will bring insight, and ultimately solve their problems (Nolen-Hoeksema, 1991; Lyumbomirsky & Nolen-Hoeksema, 1995).

Being mode on the other hand is a mindful and receptive mode of information processing. It is non-conceptual, experiential, and facilitates a more direct perception of moment-by-moment experience. Mindfulness as such involves a stance of observation or watchfulness, in which the unfolding of experience is both felt and known, but without absorption and without automatically reacting to it (e.g. by means of negative thinking, suppression, or avoidance). In particular, it is a way of directly knowing and relating to experience without the usual habitual overlay of analytic thought and verbal problem solving.

Mindfulness meditation practice is fundamentally concerned with actively cultivating conscious awareness and attention of moment-by-moment experience. It brings awareness of the current mode of mind, and allows the individual to intentionally disengage from operating within the discrepancy-based doing mode, in favor of greater acceptance of the way things are. In short,

mindfulness training may cultivate the ability to recognize and stabilize the state of being fully present to reality (non-conceptual, direct, and experiential processing) versus distracted and caught up in discursive thinking (conceptual, language-based, and analytic processing). In mindfulness practice, according to Segal, Williams, & Teasdale (2002), "the focus of a person's attention is opened to admit whatever enters experience, while at the same time, a stance of kindly curiosity allows the person to investigate whatever appears, without falling prey to automatic judgment or reactivity" (p. 322-323).

Recently, as mindfulness have been secularized, researched, and integrated into clinical intervention programs, a number of contemporary definitions have been proposed (see Table 1). While definitive consensus has not been obtained, researchers and clinicians do appear to agree that mindfulness essentially refers to the capacity for paying attention on purpose to moment-by-moment experience without judgment. To facilitate this faculty of attention, mindfulness practice involves intentional allocation and regulation of attention towards moment-by-moment experience together with an attitude of non-judgment and acceptance. Despite overlap between the proposed definitions of mindfulness, there is also a lack of consensus, apparently because different researchers have emphasized different aspects of the concept, for example by defining mindfulness either as an intention, a process, a state, a set of skills, etc. This may be problematic to the extent that different measures for assessing mindfulness have been developed based on different criteria and definitions. From a research perspective, it is particularly critical if the results derived from different measures of mindfulness cannot be meaningfully compared across studies.

Although mindfulness may appear deceptively simple, it is often described as a complex phenomena with subtle meanings that are not easily captivated by a single definition (e.g. Block-Lerner, Salters-Pednault, & Tull, 2005; Bodhi, 2011; Brown & Ryan, 2004; Brown, Ryan, & Creswell, 2007). Dreyfus (2011) has argued that the standard definition of mindfulness as a non-elaborative and non-judgmental present-centered awareness, does reflect the practical instructions

given during mindfulness training, but fails to include the most central feature, namely the ability to

hold the object of mindfulness in sustained attention, regardless of whether the object is present or

not.

Table 1. Contemporary definitions of mindfulness

- Mindfulness means paying attention in a particular way: on purpose, in the present moment, and nonjudgmentally (Kabat-Zinn, 1994, p. 4).

- Mindfulness meditation can be defined as the effort to intentionally pay attention, nonjudgmentally, to present-moment experience and sustain this attention over time (Miller et al., 1995, p. 193).

- Mindfulness… is bringing one´s complete attention to the present experience on a moment to moment basis (Marlatt & Kristeller, 1999, p. 68).

- Mindfulness is the nonjudgmental observation of the ongoing stream of internal and external stimuli as they arise (Baer, 2003, p. 125).

- Mindfulness is… the state of being attentive to and aware of what is taking place in the present (Brown & Ryan, 2003, p. 822).

- An operational working definition of mindfulness is: the awareness that emerges through paying attention on purpose, in the present moment, and nonjudgmentally to the unfolding of experience moment by moment (Kabat-Zinn, 2003, p. 145).

- Mindfulness… is a process of regulating attention in order to bring a quality of nonelaborative awareness to current experience and a quality of relating to one´s experience within an orientation of curiosity, experiential openness and acceptance (Bishop et al., 2004, p. 234).

- Mindfulness is a process that involves moving toward a state in which one is fully observant of external and internal stimuli in the present moment, and open to accepting (rather than attempting to change or judge) the current situation (Orsillo et al, 2004, p. 77).

- As a set of skills, mindfulness practice is the intentional process of observing, describing, and participating in reality nonjudgmentally, in the moment, and with effectiveness (i.e., using skilful means) (Robins, Schmidt & Linehan, 2004, p. 37).

- Mindfulness… is awareness of present experience with acceptance (Germer, 2005, p. 7).

Measuring mindfulness

Research on the clinical application of mindfulness may be advanced by operationalising and

quantifying the concept of mindfulness. Carefully developed and validated tools for assessing

mindfulness can provide the ground for investigating fundamental research questions such as: Does

the practice of mindfulness lead to improvement in the ability to respond mindfully (with greater awareness and less cognitive-behavioral reactivity) to experience in everyday life? Furthermore, if so, are improvements in mindfulness skills responsible for the therapeutic outcome of mindfulness-based interventions?

More than half a dozen self-report questionnaires for measures of mindfulness have been developed and published (see Table 2). Two of the most commonly used measures are the Mindfulness Awareness Attention Scale (MASS; Brown & Ryan, 2003) and the Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006). Both the MAAS and the FFMQ have been translated into Danish language using a back translation procedure with final back translations approved by the first author of each inventory, Kirk Warren Brown and Ruth Baer, respectively (see appendix A and B).

The MAAS is a 15-item instrument designed to measure individual differences in attention to and awareness of experience in daily life, including different activities, thoughts, emotions, and physical sensations. Respondents are instructed to rate the frequency of their experience, described in each statement, using a 6-point Likert-type scale ranging from 1 (almost always) to 6 (almost never). The MAAS yields a single total score with higher scores indicating greater levels of mindfulness. The MAAS was constructed as an indirect measure of mindfulness (i.e. each statement describes an experience which is inconsistent with being mindful), as experiences of mindlessness according to the authors are more accessible and much more common compared to being fully aware in the present moment. The MAAS has shown adequate internal consistency and good test-retest reliability. Additionally, correlational studies of the MASS has demonstrated a) convergent validity with clarity of emotional states, ability to repair mood, openness to experience, positive affectivity, self-esteem, optimism, vitality, and life satisfaction, and b) discriminant validity with neuroticism, anxiety, depression, health complains, somatization, and negative affectivity (Brown & Ryan, 2003).

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The FFMQ is a 39-item instrument based on exploratory factor analysis of the combined pool of items from five previously published mindfulness questionnaires (Baer et al., 2006). The authors reported results suggesting a five-factor solution for measuring mindfulness, and items with the highest loadings on each of the five factors were selected for inclusion in the questionnaire. The FFMQ uses a 5-point Likert-type scale (1 = *never or very rarely true* to 5 = *very often or always true*) in assessing five elements of mindfulness, including *observing, describing, acting with awareness, nonjudging of inner experience* and *non-reactivity to inner experience.* Baer et al. (2006) found good internal consistency for each the five subscales, as well as significant correlations in the expected direction with several variables related to mindfulness, including a) self-compassion (i.e. the ability to relate kindly towards oneself during periods of emotional distress), openness to experience, and emotional intelligence (positive correlations) and b) dissociation, absent mindedness, psychological symptoms, neuroticism, thought suppression, and experiential avoidance (negative correlations).

Despite sound evidence for the usefulness of published measures of mindfulness, Grossman (2008) have critiqued the many attempts to quantify the construct of mindfulness, arguing that most researchers, who have developed instruments for assessing mindfulness, a) possess only limited personal experience of Buddhist meditation, and b) have not adequately studied the traditional Buddhist sources from which the concept of mindfulness was originally derived. Moreover, he points out the risk of discrepancy between individuals self-rated (subjective) understanding of how mindful they are versus how mindful they actually are. Furthermore, personal meditation experience may influence the semantic understanding of questionnaire items. One could speculate that mindfulness practice over time, despite true improvement in the ability to stay present, may cause some respondents to rate themselves as less mindful as their understanding of mindfulness becomes refined and rooted in direct experience.

For more elaborate accounts on the topic of defining and measuring mindfulness, see Baer (2011), Block-Lerner et al. (2005), Brown & Ryan (2004), Grossman (2008), as well as references given in Table 2.

Table 2. Published self-report questionnaires for measuring mindfulness

Mindfulness questionnaires	Item examples
Mindfulness Attention Awareness Scale (MAAS; Brown & Ryan, 2003)	• I tend not to notice feelings of physical tension or discomfort until they really grab my attention. (R) • I find myself preoccupied with the future or the past. (R)
Kentucky Inventory of Mindfulness Skills (KIMS; Baer, Smith & Allen, 2004)	• I pay attention to how my emotions affect my thoughts and behavior. • When I do things, my mind wanders off and I'm easily distracted. (R)
Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006)	• When I am walking, I deliberately notice the sensations of my body moving. • I tell myself I shouldn't be feeling the way I am feeling. (R)
Toronto Mindfulness Scale (TMS; Lau et al., 2006)	• I experienced my thoughts more as event in my mind than as necessarily accurate reflections of the way things 'really' are. • I was curious about each of the thoughts and feelings that I was having.
Freiburg Mindfulness Inventory (FMI; Walach et al., 2006)	• I am open to the experience of the present moment. • In difficult situations, I can pause without immediately reacting
Cognitive and Affective mindfulness Scale-revised (CAMS-R; Feldman et al., 2007)	• It is easy for me to concentrate on what I am doing. • I can accept things I cannot change.
Philedalphia Mindfulness Scale (PHLMS; Cardaciotto et al., 2008)	• I am aware of what thoughts are passing through my mind. • I try to distract myself when I feel unpleasant emotions. (R)
Southampton Mindfulness Questionnaire (SMQ; Chadwick et al. (2008)	• Usually when I experience distressing thoughts and images, I am able just to notice them without reacting. • Usually when I experience distressing thoughts and images, I find it so unpleasant I have to distract myself and not notice them. (R)

Note. R = reverse scoring of item.

The clinical application of mindfulness

Eastern spiritual traditions have long claimed that mindfulness as a capacity of awareness can be developed and refined through the practice of meditation, which will eventually lead to reduced psychological suffering, and positive qualities such as greater concentration, acceptance, insight,

and compassion (Goldstein, 2002). It is, however, only recently that clinicians and researchers in the West have begun to argue that mindfulness training may be helpful to people suffering from diverse mental health and physical problems. Accordingly, during the last three decades, the practice of mindfulness meditation has been secularized and implemented into different clinical intervention programs that are now being investigated using the rigorous procedures and statistical methods of modern science.

Mindfulness strategies are used in several therapeutic systems. In the clinical literature, a distinction is often made between interventions based on training in mindfulness meditation and interventions that incorporate mindfulness strategies into multifaceted treatment programs. Intervention programs incorporating mindfulness include dialectical behaviour therapy (DBT) (Linehan, 1993), and acceptance and commitment therapy (ACT) (Hayes, Strosahl & Wilson, 1999), while interventions based on mindfulness meditation training include mindfulness-based stress reduction (MBSR) (Kabat-Zinn, 1982; 1990) and mindfulness-based cognitive therapy (MBCT) (Segal, Williams & Teasdale, 2002), as well as variations of these programs. Recently, MBSR and MBCT have collectively been called mindfulness-based therapy (MBT) (Hofmann et al., 2010).

Dialectical Behavior Therapy

DBT is a distinguished and multifaceted approach to the treatment of borderline personality disorder. DBT combines individual therapy with group-based skills training, and is primarily conducted within a cognitive-behavioral framework, although elements of psycho-dynamic therapy, systemic therapy, and mindfulness from the Buddhist Zen tradition are included. DBT emphasizes the therapeutic relation and validation of the client's experience, as well as training in different skills, including emotion regulation. According to this model of treatment, the dialectic between acceptance and change is a central therapeutic issue. Mindfulness in DBT is conceptualized and

taught as a number of core skills including the ability to observe, describe and participate, while maintaining a focused attention and a nonjudgmental attitude. The goal is to facilitate a) greater attentional control to prevent negative thoughts about the past and/or the future and b) improved affect tolerance by applying acceptance-based strategies to situations in which behavior oriented solutions are inadequate or directly harmful (Linehan, 1993; Lynch, Chapman, Rosenthal, Kuo, & Linehan, 2006). Randomized clinical trials have provided substantial evidence for the effectiveness of DBT (Linehan, Armstrong, Suarez. Allmen & Heard, 1991; Linehan, Heard & Armstrong, 1993; Linehan, Tutek, Heard & Armstrong, 1994; Koons et al., 2001; Verheul et al., 2003). In fact, according to Linehan & Dexter-Mazza (2008), DBT has proven effective in six RCT's by three independent research groups, and can as such be classified as an effective evidence-based treatment for borderline personality disorder.

Acceptance and Commitment Therapy

Acceptance and commitment therapy (ACT) is theoretically founded in contemporary behavior analysis, in particular the so-called relational frame theory, which gives an account of the impact of language and cognition on human behavior (Hayes, 2004; Hayes & Wilson, 1993). Applied both as individual therapy and group-based therapy, ACT represents a general treatment paradigm from which specific treatment protocols have been developed. According to Hayes, Masuda, Bissett, Luoma, & Guerro (2004) different forms of psychopathology may be viewed as a) ineffective attempts to control private experience, including thoughts and emotions, b) tendencies to be dominated by cognitive processes, such as rumination and worry, which reduces the ability to be in direct contact with the surroundings and one's own immediate experience, and c) lack of clarity about personal core values, and an inability to act in accordance with them. ACT aims to reduce verbal problem solving strategies, such as rumination, while improving participants' willingness to remain in contact with present moment experiences. In ACT, acceptance-based strategies are

intended to strengthen a decentered and observing perspective on cognitions, emotions and bodily sensations. This strategy is opposed to experiential avoidance which according to Hayes (2004) is a central transdiagnostic characteristic. ACT focuses on personal goals and core values as a foundation for facilitating behavioral change. A recent meta-analytic review by Powers, Vörding, & Emmelkamp (2009) evaluated the overall effect of ACT for different mental and physical problems in 18 randomized controlled trials (RCT's) with a total of 917 participants. Results showed that ACT was effective, corresponding to pooled effect sizes (Hedges' *g*) of 0.42 compared to TAU and 0.68 compared to wait list or psychological placebo controls, for reducing primary target symptoms among a variety of psychological and physical health related problems.

Apparently, several RCT's provide support for the use of DBT and ACT. However, a recent systematic review and meta-analysis, in which the methodological quality of these studies were critically evaluated (Öst, 2008), concludes that DBT and ACT do not yet fulfil the criteria for "empirically supported" treatments provided by the working group of the Society of Clinical Psychology of the American Psychological Association (e.g. Chambless and Hollon, 1998).

In addition to established treatment programs like DBT and ACT, researchers have provided theoretical rationales for integrating mindfulness approaches into existing protocols in the treatment of depression (Martell, Dimidjian, & Herman-Dunn, 2010), generalized anxiety disorder (Roemer & Orzillo, 2002; Wells, 2002), post traumatic stress disorder (Wolfsdorf & Zlotnick, 2001), substance abuse (Marlat, 2002), and eating disorder (Kristeller & Hallett, 1999).

Mindfulness-Based Stress Reduction

Mindfulness-based stress reduction (MBSR) is the pioneering work by Kabat-Zinn (1982; 1990) who first introduced mindfulness into the field healthcare and medicine. MBSR was originally developed in a setting of behavioral medicine at Massachusetts University as a method for stress reduction in the treatment chronic pain and other stress-related disorders. Constituting an 8-week

intervention program, MBSR is based on intensive training in mindfulness meditation, and conducted as a group format including up to 30 participants who meet for weekly sessions of 2½ hour. In addition, MBSR includes an all-day intensive mindfulness session incorporated into the sixth week of the program. To deepen the experience of mindfulness, participants are invited to remain in silence during the entire day, while being guided in a series of different mindfulness practices. During sessions, poetry is often used as a source of inspiration to convey the nature of mindfulness and put participants' experiences of practicing mindfulness in a wider perspective.

Overall, MBSR includes a number of distinct formal mindfulness practices, which are introduced in group sessions and assigned as homework using CD's with guided instructions. The formal practices for cultivating mindfulness in MBSR include the following:

1) The *body-scan*, which is most often practiced in a lying down position. In this practice, participants are guided to pay attention with curiosity and openness in sequence to sensations in different parts of the body. Instructions are given to notice when attention has wandered, and then to gently escort it back to the physical sensations in the body. The body scan is the first formal mindfulness practice introduced to participants. Practiced in session 1, 2 and 8, and as homework for the first four weeks of the program, the body scan provides a means of grounding awareness in the body, and it offers the possibility of learning to be present with bodily sensations, as they are. Even sensations related to difficult experiences that could otherwise lead to rumination or attempts to suppress, change, or avoid, are embraced in mindfulness as part the territory of human experience. Accordingly, when practicing the body scan, participants are sometimes challenged by exposure to a variety of physical and emotional states, including restlessness, boredom, sleepiness, irritation, and pain.

2) *Sitting meditation*, in which participants are instructed to sit in a relaxed, upright, dignified, and wakeful posture, provides a foundational basis from which attention is directed to experience in the present moment. Sitting meditation is included in session 2-7, and the lengths of practice

periods vary from 10 to 45 minutes. During periods of sitting meditation, the eyes can be either closed or open. For some participants who may prefer to have their eyes open, instructions are often given to maintain a soft downward gaze to minimize visual impressions that may otherwise, in the beginning, easily distract the focus of attention. Sitting meditation starts by using the physical sensations of breathing to anchor attention in the present. Participants are oftentimes guided to intentionally pay attention to the full duration of the in breath, as it enters the body, and the full duration of the out breath, as it leaves the body, by means of facilitating the ability to remain concentrated in an unbroken and stable manner. However, when the mind wanders away from the breath, as the focal point of attention, participants are asked to notice it, and then gently redirect attention back to the sensations of breathing. The program proceeds and the focus of attention during a period of sitting meditation shifts as participants are taught to pay attention non-judgmentally not only to the breath, but also to bodily sensations, sounds from the environment, thoughts, and emotions. As in the body scan, the unpleasant sensations that will inevitable occur during long periods of sitting are consciously experienced with curiosity, openness, and acceptance, to the best degree possible. If thoughts arise in relation to difficult sensations or emotions, attention is gently guided back to the concrete physical sensation in the body. If bodily sensations or emotions are overly intense, attention may be focused on the breath, simply by breathing consciously while allowing the experience to be as it is. When focusing on sounds, participants are guided to notice the quality, tone and volume of sounds, allowing them to be consciously perceived while coming and going, without categorizing or analyzing them. A similar approach is taken towards thoughts. Instead of being absorbed in thoughts and automatically elaborating on their content, in a way where one thought leads to another, participants are encouraged to simply observe them as events that enters and leaves the field of awareness. Over time, this practice presumable allows participants to recognize, in the moment, that thoughts are relative, that is, not necessarily a valid expression of what is true and real in relation to oneself, others, and the world. Later in the

program the practice of choiceless awareness is introduced to cultivate participants' ability to attend mindfully to whatever is spontaneously arising in the field of awareness, that is, doing so without getting caught up in discursive thinking.

3) *Hatha yoga exercises* may be characterized as meditation in movement. They are included in session 3 and as homework in week 3-6, to cultivate non-judgmental awareness during simple stretching postures. Participants are invited to notice the tendency to sometimes be competitive with one-self or others, and striving to become better. Rather than struggling to make progress, participants are asked to simply pay attention to sensations in the body while stretching and breathing, and taking an attitude of kindness and acceptance with responsibility not to stretch beyond the natural limitation of the body. Essentially, yoga exercises provide a ground for exploring the body with awareness, kindness and acceptance.

4) *Walking meditation* provides another opportunity to establish awareness in the present moment by paying attention to the concrete physical sensations of walking. Walking meditation is usually practiced in a slow tempo. Instructions include deliberately attending to the lifting of each foot, the movement of the legs, the contact with the surface, and the sense of shifts and balance. Whenever participants become aware that they have been distracted from this practice, they are simply instructed to redirect attention back to the conscious experience of walking. Meditation based on walking can be particular helpful at times when sitting meditation is too intense or anxiety provoking. It can help to slow down the frequency of thoughts, and bring forth a feeling of presence, simplicity and joy, simple by walking with awareness without an agenda or a specific destination, other than gradually, step by step, arriving more fully in the present moment.

In addition to the systematic practice of mindfulness, MBSR includes a psycho-educative component with didactic information on stress, including its causes, and implications.

Finally, mindfulness in MBSR is applied to ordinary activities in daily life, such as showering, tooth brushing, eating a meal, or doing the dishes. The extensive homework in MBSR

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requires participants to practice mindfulness for at least 45 min a day, six days a week. A more detailed description of the MBSR-program can be found in Kabat-Zinn (1982; 1990) and Baer & Kritemeyer (2006).

Mindfulness-Based Cognitive Therapy

Mindfulness-based cognitive therapy (MBCT) is a manualized program largely based on the MBSR curriculum, but specifically modified and designed to prevent relapse in formerly depressed people. As such, MBCT integrates elements of cognitive-behavioral therapy (CBT) for depression (Beck, Rush, Shaw, & Emery (1979) with systematic training in mindfulness meditation (Kabat-Zinn, 1990). It is conducted as an 8 week group-based intervention of up to 12 participants, with weekly sessions of approximately 2 hours. In addition to the central features of the MBSR-program (i.e. body scan, sitting meditations, simple yoga exercises, and walking meditation) MBCT includes a three minutes breathing space meditation intended to a) help participants to step out of the automatic pilot mode during daily activities, and b) assist them in coping more effectively with difficult experiences that may arise at any time during the day (Segal et al., 2002; Coffman, Dimidjian & Baer, 2006). In the second half of the program, difficult issues or situations are deliberately introduced during longer period of meditation to allow participants to practice mindfulness in relation to the specific thoughts, emotions, and bodily sensations that may follow as a consequence bringing a difficult situation to mind. Already in the being mode while practicing meditation, participants may have the experience of actually being able to tolerate or simply be with physical or emotional states that they would otherwise have avoided.

In an information processing theory Teasdale, Segal & Williams (1995) suggested that previously depressed individuals have developed associations between feelings of sadness and negative patterns of thinking. Compared to never-depressed individuals they are more likely to (re)encounter an episode of depression, as even mild states of low mood may reactivate patterns of

negative thinking similar to those that were active during previous episodes. The assumption of differential cognitive reactivity between depressed and never-depressed individuals has been confirmed in several experimental mood-induction studies, showing that previously depressed people react to the induced low-mood-state with significantly greater negative assumptions about themselves and the world (Ingram, Miranda, & Segal, 1998).

According to the cognitive model underlying MBCT, the act of intentionally directing attention in an undivided manner towards present moment-to-moment experience, uses much of the available attentional resources, thereby leaving little room for processing configurations related to depressive relapse. Accordingly, the practice of mindfulness is presumed to interfere with ruminative processing. Rumination is believed to be central characteristic among depressive individuals, and as mentioned empirical data suggest that ruminative thinking perpetuates depressed mood (Nolen-Hoeksema, 1991). During mindfulness-training negative thoughts that arise in the field of awareness are non-judgmentally noticed whereupon attention is redirected to the present moment. This continuous regulation of attention prevents further negative associations that might otherwise escalate into ruminative depressogenic patterns of thinking (Teasdale 1999; Segal et al., 2002; Segal, Teasdale & Williams, 2004).

Mindfulness as a unified treatment approach

Emerging evidence suggest that emotional disorders may be more similar than previously perceived in terms of etiology, diathesis, and latent emotional structure. According to Barlow, Allen, & Choate (2004), the notion of considerable overlap among these disorders is strongly supported by high rates of current and lifetime comorbidity, and by the observation that psychological treatment for a specific disorder often has an effect on comorbid conditions. Also, there is evidence from research using confirmatory factor analysis that negative affectivity in anxiety and mood disorders is a higher-order factor to symptoms-specific disorder factors (Brown, Chorpita, & Barlow, 1998).

Accordingly, Barlow and colleagues have argued that a unified treatment approach targeting underlying psychological vulnerabilities common among disorders may prove to be a more efficient and effective strategy compared to disorder specific treatment protocols.

MBSR and MBCT are very similar intervention programs that have collectively been termed mindfulness-based therapy (MBT). In line with the unified approach to treatment, it is noteworthy that MBT appears to be effective for reducing negative affectivity across a wide range of medical and psychological disorders, especially given that symptoms reduction by no means is an explicit aim of MBT. Rather, the goal of MBT is to teach participants to relate differently to present moment experiences, including greater awareness and acceptance of distressing thoughts, feelings, and bodily sensations. As pointed out by Baer (2007), one speculation is that MBT may be a generic form of treatment that is broadly beneficial by targeting dysfunctional processes such as rumination, worry, self-focused attention, and emotional avoidance, all of which are characteristic of a number of psychological disorders (Barlow et al., 2004; Harvey et al., 2004; Hayes, Wilson, Gifford, Follette, & Strosahl 1996). Acknowledging that MBT has shown generic efficacy and applicability, Teasdale, Segal, & Williams (2003) have argued, however, that tailoring MBT to specific formulations of particular conditions or disorders, as done with MBCT for depression, is likely to improve therapy outcome. Enhanced understanding of how mindfulness training may address the nature and maintaining processes of specific disorders, is, according to these authors, likely to facilitate a more focused and effective intervention, while reducing the risk of enfeebled applications of mindfulness.

Efficacy of mindfulness-based therapy

The growing popularity of mindfulness among clinicians and clients has imposed a strong need for science to investigate the efficacy of MBT. Although this field of research is relatively new, a large number of studies have provided preliminary results. Overall, the evidence suggest that MBT may

have significant health related benefits for individuals suffering from depression (Barnhofer et al., 2009; Eisendrath et al., 2008; Finucane & Mercer, 2006; Kenny & Williams, 2007; Mathew, Hayley, Kenny, & Denson, 2010), recurrent depression (Bondolfi et al., 2010; Godfrin and van Heeringen, 2010; Kuyken et al., 2008; Ma & Teasdale, 2004; Segal et al., 2010; Teasdale et al., 2000), bipolar disorder (Miklowitz et al., 2009; Weber et al., 2010), generalized anxiety disorder (GAD) (Cragie, Rees, Marsh, & Nathan, 2008; Evans et al., 2008), panic disorder (PD) (Kim et al., 2010), GAD and/or PD (Kabat-Zinn et al., 1992; Kim et al., 2009; Lee et al., 2007), social phobia (SP) (Koszycki, Benger, Shlik, & Bradwejn, 2007; Piet, Hougaard, Hecksher, & Rosenberg, 2010; included in the Thesis), heterogeneous anxiety disorders (Vøllestad, Sivertsen, & Nielsen, 2011), attention-deficit/hyperactivity disorder (Zylowska et al., 2008), psychosis (Chadwick, Taylor & Abba, 2005; Chadwick, Hughes, Russell, Russell, & Dagnan, 2009), binge eating disorder (Kristeller & Hallet, 1999), substance abuse (Bowen et al., 2006) chronic fatigue syndrome (Surawy, Roberts, & Silver, 2005), chronic pain (Kabat-Zinn, 1982; Rosenzweig et al., 2010; Sagula & Rice, 2004), Psoriasis (Kabat-Zinn et al. 1998), fibromyalgia (Kaplan, Goldenberg, & Galvin-Nadeau, 1993; Goldenberg et al., 1994; Grossman, Tiefenthaler-Gilmer, Raysz, & Kesper, 2007; Lush et al., 2009; Sephton et al., 2007), coronary artery disease (Tacon, McComb, Caldera, & Randolph, 2003) and cancer (e.g. Bränström, Kvillemo, Brandberg, & Moskowitz, 2010; Fooley, Baillie, Huxter, Price, & Sinclair, 2010; Speca, Carlson, Goodey, & Angen, 2000). Results from many of these studies have been combined using meta-analytic procedures.

Baer (2003) made the first extensive review of the empirical literature on mindfulness-based interventions. Since then, as research on mindfulness has continued to expand, a number of meta-analytic reviews have appeared. Overall, results from these meta-analyses indicate that MBT is a promising intervention likely to be effective for reduction of psychological distress, including symptoms of anxiety and depression, in non-clinical populations (Chiesa & Serretti, 2009), chronic medical diseases (Bohlmeijer, Prenger, Taal, & Cuijpers, 2010), cancer patients (Ledesma &

Kumano, 2009; Piet, Würtzen, & Zachariae, 2012; included in the thesis), and across various clinical samples, including anxiety and mood disorders, eating disorders, heart disease, cancer, pain disorders, and diabetes (Baer, 2003; Grossman, Niemann, Schmidt, & Walach, 2004; Hofmann et al., 2010).

The meta-analysis by Hofmann et al. (2010) investigated the effect of MBT on symptoms of anxiety and depression in a broad range of psychological and medical disorders. They included 39 controlled and uncontrolled studies, totaling 1140 participants, and reported overall pre-post effect sizes of 0.63 (Hedges *g*) for reduction in symptoms of anxiety, and 0.59 for reduction in symptoms of depression. For patients diagnosed with anxiety or mood disorders, MBT was related to large effect sizes of 0.97 and 0.95 for reduction in symptoms of anxiety and depression, respectively.

Furthermore, results based on 6 large RCT's with a total of 593 participants in the meta-analysis by Piet & Hougaard (2011; included in the Thesis), indicated that MBCT is an effective intervention for relapse prevention in remitted patients with recurrent major depressive disorder (MDD).

Mechanisms of change in mindfulness-based therapy

Investigating the effects and proposed mechanisms of change of psychological interventions are important scientific aims, especially given that clinical psychology has become increasingly committed to evidence-based clinical practice. Although research in the field has primarily focused on assessing treatment outcome, for instance, based on symptoms of anxiety and depression, many are now increasingly concerned with the specific processes underlying therapeutic change. Scientific insight into the mechanisms by which effective treatment programs work can prove helpful in optimizing treatment efficacy, e.g. by prioritizing active components of treatment, while excluding elements that are not associated with therapeutic change. There is growing evidence to support the use of MBT, but how does it work to produce change in symptoms and behaviors?

Carmody (2009) has proposed a general theoretical model inspired by Damasio (2003) to explain how MBT may be effective by targeting automatic attentional processes believed to maintain psychological distress. The model specifies that effortful direction and regulation of attention towards affect neutral present moment stimuli, such as the breath, is likely to interrupt dysfunctional automatic associations between negative thoughts, distressing feelings, and unpleasant bodily sensations. However, if attention is undirected, automatic associations may constitute a vicious self-maintaining cycle in which attention remains preoccupied with distress-related thoughts, feelings, and bodily sensations. Training in mindfulness involves repeated and deliberate disengagement from habitual attention processes, and may over time facilitate greater attentional control as well as increased awareness of the focus of attention at any given moment.

It is a basic view in MBT that difficult experience, including anxious/depressive thoughts and feelings, are not in and of themselves a problem. Rather, it is the way people relate to these sometimes inevitable states that matters, and makes the situation seem either workable or uncontrollable. Therapeutic benefits are assumed to take place due to change in the way of relating to experience, and MBT is specifically concerned with teaching people to decenter from their thoughts and emotions without suppressing, avoiding, or denying them (Segal et al., 2002; 2004). Thus, the process of "decentering", also called "disidentification" or "reperceiving", has been described as a meta-mechanism of mindfulness, involving a shift in perception from identifying personally with the content of negative thoughts and feelings to relating to negative experiences as mental objects or events that arise in the mind. (Moore, 1996; Shapiro, Carlson, Astin, & Freedman, 2006; Teasdale et al., 1995). For example, the thought "I am useless" is likely to have significant negative impact if it is perceived as an absolute truth, as opposed to becoming aware of the fact that I am having the thought "I am useless", and seeing it merely as a passing mental phenomena of relative truth. This decentered perspective on negative thoughts and feelings, presumable facilitated by training in mindfulness, has been termed meta-cognitive awareness (e.g. Teasdale et al., 2002).

In addition, several reviews have emphasized a number of change-related processes relevant to MBT, including exposure, insight, relaxation, acceptance, self-compassion, self-regulation and self-management (see Baer, 2003; Brown et al., 2007; Shapiro et al., 2006). For example, exposure is known to be an effective component in the treatment of several psychological disorders. Akin to the strategy of interoceptive exposure, where clients are instructed to self-induce symptoms of panic and anxiety by means of hyperventilation or aerobic activity (see Barlow & Craske, 2000), participants in MBT are guided to mindfully explore the difficult sensations and feelings that naturally arise during yoga exercises and prolonged periods of sitting meditation. Indeed, although very gentle, yoga exercises in MBT may provoke intense bodily sensations. Presumably, this mindfulness-based approach to exposure cultivates greater willingness to experience and tolerate difficult emotional states, including intense physical sensations, without becoming preoccupied with judgmental negative thinking or attempts to avoid or escape. Instead, the experience may be allowed to change naturally over time.

While theory can be useful, proposed mechanisms of change should ideally be investigated using adequate methods of empirical research. In psychotherapy research, according to Kazdin (2007), the term *mechanism* is used to refer to the processes or events that are responsible for the change produced by an intervention, while the related, but less specific, term *mediator* describes an intervening variable that accounts statistically for the relationship between an intervention and the outcome. There are a number of statistical procedures for investigating the mediating effect of variables proposed to facilitate change over time (e.g. Baron & Kenny, 1986; Kazdin, 2007; Kraemer et al., 2002; Preacher & Hayes, 2004; 2008). In short, the initial requirements for establishing mediation are significant associations between a) the intervention and the proposed mediator of change, and b) the proposed mediator and the therapeutic outcome. Furthermore, a timeline is required, although often overlooked in studies claiming to demonstrate mediation, to establish a causal relationship between the mediator and therapy outcome, that is, demonstrating

change in the mediator variable prior to change in the outcome variable. In the absence of time lack between mediator and outcome, no inferences of causality can be made.

Empirical research investigating the underlying mechanisms by which MBT exerts its beneficial effects is currently in its infancy. Mindfulness is a fundamental capacity of human consciousness, and MBT was designed to systematically refine and improve this basic faculty of non-judgmental present moment awareness, assuming it would be beneficial in dealing with difficult emotions, bodily sensations, and dysfunctional thought patterns. One important research question has been: Does training in mindfulness meditation lead to improved mindfulness skills? A number of recent studies, all including a validated measure of mindfulness, have provided positive answers to this question, showing that MBT or prolonged mindfulness meditation practice significantly improves the ability to be mindful in everyday life (e.g. Baer et al. 2008; Carmody & Baer 2008; Cormody, Reed, Kristeller & Merriam 2008; Cohen-Katz et al. 2005; Michalak, Heidenreich, Meibert, & Schulte, 2008; Lau et al. 2006; Shapiro, Brown & Biegel, 2007; Shapiro et al. 2008). Although mindfulness improves after MBT, and has been positively correlated with several measures of psychological health, these findings do not prove that mindfulness per se is an active ingredient in MBT, as no evidence was provided that improvement in the capacity to be mindful is directly responsible for therapeutic change. A few studies have approached this question using mediation analyses. For example, Carmody & Baer (2008) investigated MBSR among 174 adults participants with stress-related problems, and found that improvement in mindfulness skills, as measured by the FFMQ, mediated the relationship between time spent on formal mindfulness practice and observed reductions in psychological symptoms. Similarly, in a randomized wait list controlled trial by Shapiro et al. (2008), improvement in mindfulness after participation in MBSR significantly mediated reductions in stress and rumination. Additionally, in this study, the amount of time spent on daily mindfulness practice significantly predicted a more favorable outcome of MBSR.

In a study of MBCT for people with recurrent depression in remission, Kuyken et al. (2010) found that increased mindfulness and self-compassion at post-treatment, mediated the effect of MBCT on symptoms of depression at 15-months follow-up. Similarly another study, although less rigorously conducted, provided preliminary evidence that increased mindfulness and reduced brooding (an aspect of rumination) may mediate the effect of MBCT on symptoms of depression in partially remitted MDD patients (Shahar, Britton, Sbarra, Figueredo, & Bootzin, 2010).

A general criticism of studies that claim to investigate mediation, including Carmody & Baer (2008) and Shapiro et al. (2008), is that data on the proposed mediator and treatment outcome are collected at the same point in time, while the applied model of mediation is assumed to be sequential. This issue is critical because evidence of true mediation exists only when the treatment under investigation produces change in the proposed mediator prior to change in therapeutic outcome. However, investigating true mediation is likely to be a rather complicated quest. For instance, at what point in time during the course of a specific intervention should one expect change in the mediator to occur prior to change in the intervention outcome? If several time points are included, ideally the magnitude of change in the mediator would predict the degree to which symptoms are subsequently reduced.

Results from two uncontrolled studies of predictors of relapse after MBCT for previously depressed patients are in line with findings from the study of mediation by Kuyken et al. (2010). Michalak et al. (2008) found increased mindfulness during MBCT, and showed that post treatment levels of mindfulness significantly predicted MDD relapse over a 12 month follow-up period, that is, lower mindfulness scores were associated with greater risk of relapse, even after controlling for residual depressive symptoms and number of previous episodes. Correspondingly, Michalak, Hölz & Teismann (2010) used a similar design and found that rumination decreased during MBCT, while post treatment levels of rumination predicted relapse over 12 months, with higher scores on

rumination associated with greater risk of relapse, after controlling for residual symptoms and number of prior episodes.

There is some evidence that meta-awareness (i.e. the ability to experience negative thoughts and feelings as mental events rather than as inherent aspects of the self) may be central to change produced by MBT. Teasdale et al. (2002) found that meta-awareness increased in recovered or residually depressed patients for whom risk of relapse was reduced by either MBCT or cognitive therapy. The authors proposed that MBCT and cognitive therapy may share a common therapeutic mechanism for relapse prevention in depression by changing the way participants relate to negative thoughts and feelings, rather than by changing their belief in thought content. The finding of improved meta-awareness by MBCT has been replicated in a subsequent trial comparing MBCT to TAU (Hargus, Crane, Barnhofer, & Williams, 2010).

As described earlier, MBCT specifically targets cognitive reactivity (i.e. the tendency to respond to states of low mood with patterns of negative thinking) by teaching attentional skills that allow participants to disengage from ruminative processes and relate to present moment pleasant and unpleasant experiences with greater awareness, tolerance and kindness. In support of the treatment rationale, MBCT has been found to reduce self-reported cognitive reactivity (Raes, Dewulf, Van Heeringen, & Williams, 2009). This finding is in line with a recent waitlist controlled study, in which participants who had undergone 8 weeks of mindfulness training, overall demonstrated less neural reactivity to a sadness provocation (Farb et al., 2010). The authors suggested that mindfulness may represent a specific neural path for reducing affective reactivity, and the accompanying psychopathological vulnerability, by balancing regulatory responses with attentional monitoring of less valenced and more sensory visceral information. Somewhat related, Barnhofer et al. (2007) found that MBCT helped individuals with previously suicidal depression to retain a more balanced pattern of emotion related brain activation, as evidenced by balanced

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prefrontal asymmetry, compared to controls that showed significant deterioration towards stronger right-sided activation, associated with a more avoidant affective style.

Investigating participants' experiences of MBT may complement findings from empirical research and provide important hints to potential mechanisms of change underlying the effect of MBT. Qualitative research has identified a number of overarching themes of participants' experiences of MBT, including the following: Living in the present moment, cultivating mindfulness skills, and, in particular, developing an attitude of acceptance (Mason & Hargreaves (2001); group participation as a validating experience, and ongoing support beyond the end of the program (Finucane and Mercer, 2006); a sense of control over depression, acceptance of depression-related thoughts and feelings, expressing and meeting personal needs in relationships, as well as different struggles related to participating in MBT (Allen, Bromley, Kuyken, & Sonnenberg, 2009).

In sum, MBT may achieve its beneficial effects by reducing rumination and cognitive reactivity, while providing a supportive group environment, and improving the ability to be mindful and self-compassionate.

Aims of the project

The overall aim of this thesis was to investigate the efficacy of MBT on negative affectivity (anxiety and depression) in three different clinical populations. In study 1, using a randomized cross-over design, we pilot tested the effect and feasibility of MBCT alone and in combination with group cognitive-behavioral therapy (GCBT) for young adults with social phobia (SP). It was hypothesized 1) that MBCT would achieve moderate to large effect sizes somewhat smaller than the large effect sizes we expected to find for GCBT, and 2) that adding MBCT to GCBT would increase the magnitude of the effect compared to the effect achieved immediately after GCBT alone. Hypotheses were expressed in terms of effect sizes due to insufficient power for detecting

significant between-group differences. The aim of study 2 was by means of a systematic review and meta-analysis to evaluated the effect of MBCT for prevention of relapse in people with recurrent major depressive disorder (MDD) in remission; both for different control conditions, and for subgroups of patients due to the number of prior episodes of depression. In study 3, the aim was to conduct a systematic review and meta-analysis of the currently available results to test the hypothesis that MBT is an effective intervention for reduction of symptoms of anxiety and depression in cancer patients and survivors. In addition, in study 3, we expected mindfulness skills to be improved after MBT.

Summary of paper 1

Background: Social phobia (SP) is a prevalent anxiety disorder characterized by marked and persistent fear of social or performance situations. In feared situations, individuals with SP are concerned about embarrassment and that others will judge them negatively. The lifetime prevalence rate of the disorder is approximately 7-13%, and time of onset usually occurs in adolescence. In the absence of intervention, the course of the disorder is likely to be chronic with a high degree of comorbidity and impairments in social and occupational functioning. *Objective:* The objective of this study was to pilot test MBCT alone and in combination with group cognitive-behavioral therapy (GCBT) for young adults with SP. *Method:* The study included 26 participants aged 18-25 with a primary diagnosis of SP. Participants were diagnosed using the Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV) and the Structured Clinical Interview for DSM-IV Axis II personality disorders (SCID-II), and randomly allocated to either eight 2-hour sessions of MBCT or twelve 2-hour sessions of GCBT. The study used a cross-over design in which participants eventually received both forms of treatment, i.e. half of the participants (group 1) first received MBCT then GCBT, while the other half first received GCBT then MBCT. Outcome, including a SP composite measure, was assessed at post-treatment, and at 6- and 12-month follow-up. Statistical

analyses included a) comparing baseline demographics characteristics and clinical characteristics between groups, b) estimating the magnitude of within-group changes for both groups across all time points, c) calculating the number of participants with reliable and clinically significant change on SP symptom scales, and d) comparing MBCT and GCBT after the first treatment period using a one-way between-group analysis of covariance (ANCOVA) with pre-treatment scores as covariates. *Results:* Results showed moderate-high pre-post effect sizes for MBCT (Cohens $d = 0.78$ on the composite SP measure, $p < 0.05$). These were not significantly different, although generally numerically lower, compared to pre-post effect sizes for GCBT (Cohens $d = 1.15$ on the composite SP measure, $p < 0.05$). Having received both forms of treatment participants in both groups further improved over time with pre-follow-up effect sizes of 1.42 and 1.62, respectively, at 6-month after the entire treatment period. *Conclusion:* Results from this study provide preliminary support for MBCT as a useful, low cost treatment for patients with SP, although MBCT is probably less efficacious than CBT.

Summary of paper 2

Background: Major depressive disorder (MDD) is a common mental disorder characterized by one or more episodes of major depression (i.e. depressed mood or loss of interest or pleasure in almost all activities, together with four or more additional symptoms of depression, lasting for a period of at least 2 weeks). The life time prevalence rate of MDD is about 20%, and it is associated with a high degree subjective distress and psychosocial disability. MDD is often considered a recurrent disorder due to very high relapse rates (50-90%). The risk of relapse increases with each new episode of depression. Among people meeting the criteria for MDD about 20% develop a chronic condition with symptoms lasting more than two years. MDD is the leading cause of disease burden in many western countries, and effective prevention interventions are a high priority enterprise within the field of mental health. *Objective:* The study objective was to evaluate the effect of

MBCT for prevention of relapse or recurrence among people with recurrent MDD in remission.

Method: The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). Eligible studies were found by searching several electronic databases, including EMBASE, PubMed, PsycINFO, Web of Science, Scopus, and the Cochrane Controlled Trials Register, and MBCT researchers were contacted for further relevant studies. Inclusion criteria were a randomized controlled design to investigate MBCT for MDD relapse prevention among adult participants diagnosed with recurrent MDD in remission. The outcome measures used in combining studies were the number of participants meeting the diagnostic criteria for a new MDD episode over the follow-up period. The methodological quality of study reports was assessed using nine criteria. Statistical analyses included estimating effect sizes in the form relative risk ratios (*RRs*) for relapse/recurrence between groups over the total follow-up period. Effect sizes were calculated using the following formula: $RR = \frac{MBCTrelapse/\ MBCTtotal}{Controlrelapse/\ Controltotal}$. Effect sizes were weighted by the inverse standard error and combined using the random effects model. Between-study heterogeneity was assessed and analyses were carried out to detect potential publication biases. Meta-analyses were performed separately for a) MBCT versus controls, including TAU, and placebo + clinical management (PLA); and b) MBCT versus maintenance antidepressant medication (m-ADM). Furthermore, pre-specified subgroup analyses of participants with < or ≥ 3 MDD episodes were carried out. *Results:* Six RCT's with a total of 593 participants were included. Based on relapse data from five studies with a total of 408 participants, MBCT significantly reduced the risk of relapse/recurrence with a risk ratio of 0.66 for MBCT compared to TAU or pill placebo, corresponding to a relative risk reduction of 34% in favor of MBCT. In a pre-planned subgroup analysis of participants with three or more previous episodes, the relative risk reduction was 43% in favor of MBCT. However, no risk reduction was found in a small sample of participants with only two episodes (*n* = 50). In two studies, comparing MBCT to m-ADM, the

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combined risk ratio was 0.80 (*n* = 177), corresponding to a non-significant relative risk reduction of 20% in favor of MBCT. No heterogeneity was found for any of the above overall analyses.

Conclusion: The results of this meta-analysis indicate that MBCT is an effective intervention for relapse prevention in patients with recurrent MDD in remission, at least in case of three or more previous MDD episodes.

Summary of paper 3

Background: Severe symptoms of anxiety and depression are common and debilitating problems associated with cancer diagnosis and treatment. Depression among cancer patients has been associated with prolonged hospitalization, higher mortality, and reduced quality of life. Clinically significant emotional distress, including symptoms of anxiety and depression, is prevalent in approximately 35% of all cancer patients. The risk of developing anxiety and/or depression appears to be particularly high during the first year after cancer diagnosis. Thus, a recent five year observational study by Burgess and colleagues (2005) found that almost 50% of women with early breast cancer fulfilled the diagnostic criteria for disorders of anxiety or depression in the first year following cancer diagnosis. In general, symptoms of anxiety and depression among cancer patients appear to be well-documented and therefore effective treatment should be considered important for comprehensive cancer care. *Objective:* The study objective was by means of a systematic review and meta-analysis to evaluate the current evidence for the effect of mindfulness-based therapy (MBT) on symptoms of anxiety and depression in adult cancer patients and survivors. *Method:* The study was carried out according to the Meta-Analysis Reporting Standards (MARS) established by the American Psychological Association (APA). We searched several electronic databases to retrieve studies eligible for inclusion in the meta-analysis. Inclusion criteria were studies of MBSR or MBCT for adult cancer patients and survivors, with validated continuous outcome measures of anxiety or depression symptom severity. The methodological quality of studies were assessed using the Jadad scale (range: 0-4) with modified criteria to account for difficulties in blinding participants

to MBT. Overall effect size analyses were performed separately for non-randomized studies and RCT's. Effect size statistics were standardized weighted mean differences based on Hedges' *g*. Effect sizes derived from non-randomized studies were estimated based on pre-post within-group differences (i.e. the magnitude of change at post-treatment for MBT alone). In RCT's, effect sizes were estimated based mean pre- to post-treatment change scores (using the standard deviation of post-treatment scores) for both MBT and control conditions. In both study categories, effect sizes were combined using the inverse variance random effects model. Additionally, heterogeneity between studies was assessed, and tests were included to detect potential bias in the publication of study results. ***Results:*** The overall results of non-randomized studies (average quality score: 0.5) indicated that MBT was associated with significantly reduced symptoms of anxiety and depression from pre- to post-treatment, corresponding to pooled effect sizes of 0.60 and 0.42, respectively. Pre-post changes in measures of mindfulness was moderate in effect (Hedges *g* = 0.44). In RCT's (average quality score: 2.9), polled controlled effect sizes were 0.37 for symptoms of anxiety and 0.44 for symptoms of depression, both favoring MBT compared to TAU or wait list controls. Furthermore, in RCT's MBT significantly improved mindfulness skills compared to controls (Hedges *g* = 0.39). ***Conclusion:*** While the overall quality of existing clinical trials varies considerably, there appears to be some positive evidence from a number of relatively high quality RCT's to support the use of MBT for cancer patients and survivors with symptoms of anxiety and depression.

Discussion

Summary of findings

Main results from the three studies included in this thesis, suggest that MBT may be effective for reduction of negative affectivity in three different clinical populations, namely young adults with SP, people with recurrent MDD in remission, and adult cancer patients and survivors.

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In the first study, MBCT effectively reduced primary symptoms in young adults with SP corresponding to moderate-large pre-post effect sizes. We found no significant difference in effect between MBCT and GCBT, although the magnitude of the effect of MBCT was generally somewhat lower compared to GCBT. Participants showed further improvements at 6-months follow-up after having received both forms of treatment. Adherence to both MBCT and GCBT was high, and participants were generally highly satisfied with both treatments. The results of this study are similar to findings from two recent studies of MBSR for people with SP, showing significant pre-post reductions in symptoms of anxiety and depression (Koszycki et al., 2007; Goldin & Gross, 2010).

In the second study, meta-analytic findings based on data from RCTs showed that MBCT effectively reduced the risk of relapse by 34% compared to TAU or pill placebo. For patients with three or more previous episodes of depression, the relative risk of relapse was 43% in favor of MBCT. However, no risk reduction by MBCT was found among a small subgroup sample of patients with only two prior episodes of depression. In two studies with head-to-head comparisons, the pooled relapse data showed that MBCT was at least as effective as m-ADM.

In the third study, investigating the effect of MBT on symptoms of anxiety and depression in adult cancer patients and survivors, effect analyses were performed separately for non-randomized studies and RCTs. For non-randomized studies, overall results showed significant MBT-associated effect sizes in the moderate range for pre-post reduction in symptoms of anxiety and depression. Meta-analytic findings derived from RCTs indicated that MBT significantly reduced symptoms of anxiety and depression corresponding to small-moderate effect sizes. Another interesting result, derived from RCT's, is that MBT significantly improved mindfulness skills from pre- to post-treatment. This finding provides some ground for the speculation that improved capacity for non-judgmental present moment awareness may be a central mechanism by which MBT exerts its health related benefits. The study by Kuyken et al. (2010) provides empirical support for this assumption.

By taking into account the temporal precedence of the proposed mediator variables, the authors reported results showing that increased mindfulness and self compassion across treatment mediated the effect of MBCT on symptoms of depression at 15 months follow-up. However, to my knowledge, this is the only study of true mediation of change by MBT, and therefore replication is highly warranted.

Methodological considerations

Being the first investigation of MBCT for SP, study 1 makes a significant contribution to the clinical research literature. However, important methodological issues should be noted. First, the study is a small pilot study ($n = 26$) with insufficient power to test the primary hypothesis. Indeed, to achieve 80% power for detecting a significant difference in effect between MBCT and GCBT, corresponding to a small-moderate between-group effect size (Cohens $d = 0.30$), we would have needed a total sample of 356 participants. Moreover, due to the cross-over design, MBCT and GCBT could not be compared beyond the first treatment period. Ideally, a more useful design would have included a large sample randomized three arm trial comparing MBCT, GCBT, and a waitlist control group (with no crossing over) at post treatment and follow-up periods.

Paper 2 reports the first formally adequate meta-analytic evaluation of the effect of MBCT for relapse prevention among patients with recurrent MDD in remission. In this study, findings were based on RCTs of high methodological quality, and no evidence of between-study heterogeneity or publication bias was found. However, the study is limited by the relative small number of RCTs that were available to us when the study was carried out. Particularly, only two studies compared MBCT with m-ADM, and only one study estimated the cost-effectiveness of MBCT. Furthermore, the subgroup analysis of participants with only two prior MDD episodes was based on small subgroup sample of 50 participants in two studies. Also, we were unable to draw any conclusions

about the specific effects of MBCT, as no RCTs included a psychological placebo or componential control condition.

Conducted according to the Meta-Analysis Reporting Standards (MARS) established by the American Psychological Association, the study presented in paper 3 is the first formal meta-analysis to evaluate the effect of MBT on symptoms of anxiety and depression in cancer patients and survivors. Also, to our knowledge this study is the first using meta-analyses to investigate MBT-associated change in measures of mindfulness. This study accounted for the variation in study quality by separately analyzing data from non-randomized studies and RCTs. Although overall findings from non-randomized studies showed significant improvement in mindfulness skills and reductions in symptoms of depression in MBT participants, with no evidence of publication bias, the overall study quality of this category was very low. As most studies did not include a control condition, one main critique is that the positive findings cannot be directly attributed to MBCT. However, results derived from this category of studies closely match the overall findings of RCTs that were generally of much higher methodological quality. There were some limitations to the study. It was not possible to draw any conclusions about the differential effect of MBT with regard to cancer stage and time since diagnosis, as these potentially predictive variables varied both within and between studies. Also, results should not be generalized to male cancer populations as the majority of participants were women. Another important shortcoming is the lack of study samples systematically diagnosed with mood and anxiety disorders, known to be prevalent among cancer patients.

Clinical implications

Findings from the three studies included in the thesis may have important clinical implications. While results presented in paper 1 suggest that MBCT is a promising intervention for SP patients, meta-analytic findings derived from RCT's in papers 2 and 3 allow for more firm conclusions, as

the evidence appear to be strong enough to support the use of a) MBCT for relapse prevention of MDD in remission, at least in case of three or more previous episodes, and b) MBT for reduction of symptoms of anxiety and depression among cancer patients and survivors. For these specific problems, MBT might be established as an empirically supported psychological intervention according to the guidelines of the Society for Clinical Psychology from the American Psychological Association (see Chambless & Hollon, 1998). Therefore, findings from papers 2 and 3 may have substantial practical implications.

For patients with SP, cognitive behavioral therapy (CBT) is currently considered the psychological intervention of first choice. However, up to 40-50% patients show little or no improvement after CBT. We found preliminary evidence that MBCT may be a useful and effective treatment for SP patients. Generally, adherence to MBCT and satisfaction among participants were high. As such, MBCT may prove to be a useful alternative to CBT; perhaps especially for those SP patients who prefer a more general intervention for negative affectivity, rather than treatment for a psychiatric disorder. Also, as noted in paper 1, MBCT is a low cost treatment that is easy to implement in various clinical settings. Results from a recent study using functional magnetic resonance imaging (fMRI) suggest that mindfulness training for SP patients may reduce emotional reactivity while improving emotion regulation, changes that are likely to facilitate reduction in clinical symptoms (Goldin & Gross, 2010).

In study 2, based on relapse data from RCTs, MBCT was found to effectively reduce the risk of relapse compared to TAU or pill placebo. Furthermore, pooled data from two studies suggest that MBCT as a relapse prevention intervention is at least comparable to m-ADM for MDD patients with three or more previous episodes. Clearly, further replication is needed. However, if tenable, this finding is of high practical importance, since m-ADM is currently the standard treatment for depressive prophylaxis, and for patients with more than two prior episodes a maintenance dose of ADM is generally recommended for lifetime. Indeed, as an alternative, many patients will prefer a

psychological intervention with no medical side effects. Worth noting is that one study (Kuyken et al., 2008) found that MBCT was superior to m-ADM for reducing residual depressive symptoms and improving quality of life. Based on the current evidence, the UK National Institute for Health and Clinical Excellence now recommends MBCT for MDD patients in remission after three or more previous episodes (NICE, 2009).

The evidence derived from RCTs in study 3 appears to be strong enough to support the use of MBT for cancer patients and survivors with symptoms of anxiety and depression. Indeed, effective treatment is clearly needed in comprehensive cancer care, as symptoms of anxiety and depression are well-documented among cancer patients. The emphasis in MBT on living life in the present moment, may be particularly important to people diagnosed with a life threatening disease such as cancer. Not only may they need to deal effectively with rumination and worry, they may also be especially motivated to live the rest of their lives more fully with awareness, as if it really mattered. It is important to note that MBT appears to be feasible to be delivered in clinical oncology settings. Several of the RCTs included in the meta-analysis in paper 3 were conducted in oncology settings, and adherence to MBT was generally high with an average 81% attending at least 75% of all MBT sessions. It is possible, if not likely, that meta-analytic findings from RCT's in paper 3, may contribute to recommendations provided in future National Health Service guidelines for effective psychological treatment of symptoms of anxiety and depression among cancer patients and survivors.

There may be some general advantages of MBT relative to other effective psychological interventions. MBT is a low-cost intervention (one therapist can lead a rather large group of people) that appears to be easy to implement in different clinical settings. For some individuals the acceptance-based approach of MBT may be more suitable and lead to higher treatment adherence compared to interventions that are primarily concerned with directly changing thoughts, emotions, symptoms, and behaviors. As mentioned in paper 1, it is also possible that some people despite

specific diagnoses may prefer a general stress reduction course based on training in mindfulness, instead of a treatment for a psychiatric disorder. However, as pointed out in paper 3, although MBT has some obvious advantages, it is still a time consuming intervention due to extensive daily homework, and it requires well-trained MBT teachers.

Conclusion/future directions

The main findings from the three studies included in this thesis, add to the growing body of evidence for MBT. In the study presented in paper 1, we conclude that the findings provide preliminary support for MBCT as a useful, low-cost treatment for patients with SP, although MBCT is probably less efficacious compared to CBT. In paper 2, the conclusion is that meta-analytic findings support the use of MBCT as a low cost intervention for relapse prevention in patients with recurrent MDD in remission, at least in case of three or more previous episodes. Finally, in paper 3, we conclude that while there is considerable variation in the methodological quality of existing clinical trials, there appears to be some positive evidence from relatively high quality RCTs to support the use of MBT for cancer patients and survivors with symptoms of anxiety and depression.

Although the evidence in general suggest that MBT is a promising intervention for reduction of negative affectivity, several reviews (e.g. Baer, 2003; Piet et al., 2012; included in the Thesis) have emphasized the fact that many studies in the research literature suffer from a number of methodological limitations. The observation underscores the need for applying more stringent designs in future studies of MBT. This includes RCTs conducted in accordance with established guidelines for reporting of clinical trials, such as the Journal Article Reporting Standards (JARS; APA Publications and Communications Board Working Group on Journal Article Reporting Standards, 2008) or the Consolidated Standards of Reporting Trials (CONSORT; Schultz, Altman, & Moher, 2010). Among important trial standards, a power analysis should be performed, the randomization procedure should be described, data on the intention-to-treat sample should be

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reported, primary and secondary outcomes should be clearly defined and pre-specified, applied statistical methods should be adequate and well described, effect sizes should be calculated and presented with 95% confidence intervals for each outcome variable, and reasons for withdrawals and dropouts should be reported. The study should be registered at ClinicalTrials.gov, and ideally, to optimize transparency and credibility of findings, a study protocol should be published before the trial is carried out.

RCT's have high priority as the golden standard of intervention studies. If possible and appropriate, RCT's investigating the effect of MBT should include an active comparison group in the form of medical or psychological placebo to control for non-specific therapeutic factors including expectations of change, receiving attention from an interested person, and support by intervention group members. To designate MBT as efficacious and specific in its mechanisms of action, future studies need to demonstrate that MBT is superior to conditions controlling for such non-specific processes (see Chambless & Hollon, 1998). A step further in investigating specific effects of MBT would be the use of a dismantling design in which the active comparison condition follow the same group format as MBT, but without intensive meditation training. If no difference is found between a componential control intervention and MBT, and both prove to be more effective than usual care or wait list controls, it is likely that meditation training is an unnecessary treatment component (see Williams, Russell, & Russell, 2008; Williams et al., 2010).

As is the case for research on other forms of psychotherapy, it may be important to begin to explore differential treatment effects. Even though the evidence-base for MBT is growing, and mechanisms of change are being investigated, research has not yet provided answers to the question: For whom, within a specific clinical population, is MBT most effective? For example, as pointed out in paper 2, there appears to be a need for investigating the differential effect of MBCT for MDD patients with low versus high risk of relapse, as MBCT may be particularly helpful for those most vulnerable to depression, regardless of the number of prior episodes. It may also be that

individual differences, including personality traits, severity of symptoms, levels of rumination and worry, use of antidepressant medication, degree of motivation for participating in MBT, etc., may prove to be important predictors/moderators of treatment outcome. Indeed, in the field of mindfulness-based clinical intervention, there are still many unresolved important questions to be explored by future research.

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Appendix A

Danish translation of the Mindfulness Attention Awareness Scale (MAAS)

Skema vedrørende opmærksomhed i hverdagen

Herunder finder du en række udsagn om oplevelser i din hverdag. Ved at benytte skalaen fra 1–6 bedes du angive, hvor ofte eller sjældent du for tiden har hver oplevelse. Svar venligst i overensstemmelse med det, som virkelig svarer til din oplevelse, frem for hvordan du mener, din oplevelse bør være. Husk også at skrive navn og dato på arket.

Fulde navn: _____

Dato: _____

1 = **Næsten altid**	
2 = **Meget ofte**	
3 = **Ganske ofte**	
4 = **Ganske sjældent**	
5 = **Meget sjældent**	
6 = **Næsten aldrig**	

1.	Jeg kan have en følelse uden at være bevidst om den før nogen tid senere.	
2.	Jeg ødelægger eller vælter ting, fordi jeg ikke passer på, er uopmærksom eller tænker på noget andet.	
3.	Jeg har svært ved at holde fokus på det, der sker i nuet.	
4.	Jeg har en tendens til at gå hurtigt for at nå frem, uden at lægge mærke til hvad jeg oplever undervejs.	
5.	Jeg har en tendens til ikke at bemærke følelser af fysisk anspændthed eller ubehag, før de virkelig kræver min opmærksomhed.	
6.	Jeg glemmer en persons navn, næsten lige efter jeg har fået det at vide for første gang.	
7.	Det virker som om, jeg "kører på autopilot" uden at være ret bevidst om det, jeg laver.	
8.	Jeg skynder mig gennem aktiviteter uden rigtigt at være opmærksom på dem.	
9.	Jeg bliver så fokuseret på det mål, jeg ønsker at opnå, at jeg mister følingen med det, jeg laver lige nu.	
10.	Jeg udfører arbejde eller opgaver automatisk, uden at være opmærksom på det jeg laver.	
11.	Jeg oplever, at jeg lytter til nogen med et halvt øre, samtidig med at jeg laver noget andet.	
12.	Jeg kører et sted hen "på autopilot" og undrer mig bagefter over, hvorfor jeg tog derhen.	
13.	Jeg oplever, at jeg hovedsageligt tænker på fremtiden eller fortiden.	
14.	Jeg gør ting uden at være opmærksom på det.	
15.	Jeg småspiser, uden at være bevidst om at jeg spiser.	

Appendix B

Danish translation of the Five Facet Mindfulness Questionnaire (FFMQ)

Navn _____   Dato_____

5-FACET MINDFULNESS SPØRGESKEMA

Vurdér venligst hvert enkelt af de følgende udsagn ved brug af nedenstående skala. Ud for hvert udsagn bedes du skrive det tal, som bedst beskriver <u>din egen opfattelse</u> af det, som <u>generelt gælder for dig.</u>

1	2	3	4	5
Aldrig eller meget sjældent sandt	**Sjældent sandt**	**Nogle gange sandt**	**Ofte sandt**	**Meget ofte eller altid sandt**

_____ 1. Når jeg går, lægger jeg bevidst mærke til de fysiske fornemmelser af min krop, der bevæger sig.

_____ 2. Jeg er god til at finde ord, som beskriver mine følelser.

_____ 3. Jeg kritiserer mig selv for at have irrationelle eller upassende følelser.

_____ 4. Jeg lægger mærke til mine fornemmelser og følelser uden at behøve at reagere på dem.

_____ 5. Når jeg foretager mig noget, så vandrer mine tanker, og jeg bliver let distraheret.

_____ 6. Når jeg tager et bad, er jeg opmærksom på fornemmelserne af vandet på min krop.

_____ 7. Jeg har let ved at sætte ord på mine overbevisninger, meninger og forventninger.

_____ 8. Jeg er ikke opmærksom på det, jeg foretager mig, fordi jeg dagdrømmer, bekymrer mig eller fordi jeg på anden vis bliver distraheret.

_____ 9. Jeg iagttager mine følelser uden at fortabe mig i dem.

_____ 10. Jeg siger til mig selv, at jeg ikke burde føle, sådan som jeg føler.

_____ 11. Jeg lægger mærke til, hvordan mad og drikke påvirker mine tanker, kropslige fornemmelser og følelser.

_____ 12. Det er svært for mig at finde ord, som beskriver, hvad jeg tænker.

_____ 13. Jeg bliver let distraheret.

_____ 14. Jeg synes, nogle af mine tanker er unormale eller dårlige, og jeg burde ikke tænke sådanne tanker.

_____ 15. Jeg lægger mærke til fysiske fornemmelser, såsom vinden i mit hår eller solstråler på mit ansigt.

_____ 16. Det er vanskeligt for mig at finde de rette ord til at udtrykke, hvordan jeg har det med forskellige ting.

_____ 17. Jeg vurderer, om mine tanker er gode eller dårlige.

_____ 18. Jeg har svært ved at holde fokus på det, der sker i nuet.

_____ 19. Når jeg har ubehagelige tanker eller billeder i hovedet, træder jeg et skridt tilbage og er opmærksom på tanken eller billedet uden at blive overvældet af det.

GÅ VENLIGST TIL NÆSTE SIDE ÷

1	2	3	4	5
Aldrig eller meget sjældent sandt	Sjældent sandt	Nogle gange sandt	Ofte sandt	Meget ofte eller altid sandt

_____ 20. Jeg er opmærksom på lyde, såsom ure der tikker, fugle der kvidrer, eller biler der kører forbi.

_____ 21. I vanskelige situationer kan jeg stoppe op uden at reagere med det samme.

_____ 22. Når jeg har en fornemmelse i min krop, er det vanskeligt for mig at beskrive den, fordi jeg ikke kan finde de rette ord.

_____ 23. Det virker som om, jeg "kører på autopilot" uden at være ret bevidst om det, jeg laver.

_____ 24. Når jeg har ubehagelige tanker eller billeder i hovedet, føler jeg mig rolig kort tid efter.

_____ 25. Jeg siger til mig selv, at jeg ikke burde tænke, sådan som jeg gør.

_____ 26. Jeg lægger mærke til, hvordan ting lugter eller smager.

_____ 27. Selv når jeg føler mig stærkt oprevet, kan jeg sætte ord på det, som sker.

_____ 28. Jeg skynder mig gennem aktiviteter uden rigtigt at lægge mærke til dem.

_____ 29. Når jeg har ubehagelige tanker eller billeder i hovedet, er jeg i stand til blot at bemærke dem uden at reagere.

_____ 30. Jeg synes, nogle af mine følelser er dårlige eller upassende, og jeg burde ikke føle dem.

_____ 31. Jeg lægger mærke til synsindtryk i kunst eller i naturen, såsom farver, former, struktur eller mønstre af lys og skygge.

_____ 32. Jeg har en naturlig evne til at sætte ord på mine oplevelser.

_____ 33. Når jeg har ubehagelige tanker eller billeder i hovedet, bemærker jeg dem blot og lader dem passere.

_____ 34. Jeg udfører opgaver automatisk, uden at være opmærksom på det jeg laver.

_____ 35. Når jeg har ubehagelige tanker eller billeder i hovedet, bedømmer jeg mig selv som god eller dårlig, afhængigt af hvad tanken/billedet handler om.

_____ 36. Jeg er opmærksom på, hvordan mine følelser påvirker mine tanker og handlinger.

_____ 37. Jeg kan som regel beskrive i detaljer, hvordan jeg har det for tiden.

_____ 38. Jeg gør ting uden at være opmærksom på det.

_____ 39. Jeg fordømmer mig selv, når jeg får ufornuftige ideer eller indfald.

Information om scoring

<u>Observere items:</u>
1, 6, 11, 15, 20, 26, 31, 36

<u>Beskrive items:</u>
2, 7, 12R, 16R, 22R, 27, 32, 37

<u>Handle med opmærksomhed items:</u>
5R, 8R, 13R, 18R, 23R, 28R, 34R, 38R

<u>Ikke-dømme items:</u>
3R, 10R, 14R, 17R, 25R, 30R, 35R, 39R

<u>Ikke-reagere items:</u>
4, 9, 19, 21, 24, 29, 33

Reference:

Baer, R. A., Smith, G. T., Hopkins, J., Krietemeyer, J., & Toney, L. (2006). Using self-report assessment methods to explore facets of mindfulness. *Assessment, 13*, 27-45.

Paper 1

Piet, J., Hougaard, E., Hecksher, M. S., & Rosenberg, N. K. (2010). A randomized pilot study of mindfulness-based cognitive therapy and group cognitive-behavioral therapy for young adults with social phobia. *Scandinavian Journal of Psychology, 51*, 403-410.

Personality and Social Sciences

A randomized pilot study of mindfulness-based cognitive therapy and group cognitive-behavioral therapy for young adults with social phobia

JACOB PIET,[1] ESBEN HOUGAARD,[1] MORTEN S. HECKSHER,[2] and NICOLE K. ROSENBERG[3]

[1]*Institute of Psychology, Aarhus University, Denmark*
[2]*KognitivGruppen, Denmark*
[3]*Clinic for Anxiety, Aarhus University Hospital, Denmark*

Piet, J., Hougaard, E., Hecksher, M. S., & Rosenberg, N. K. (2010). A randomized pilot study of mindfulness-based cognitive therapy and group cognitive-behavioral therapy for young adults with social phobia. *Scandinavian Journal of Psychology*, *51*, 403–410.

Twenty-six young participants, 18–25 years, with social phobia (SP) were randomly assigned to eight 2-hour sessions of group mindfulness-based cognitive therapy (MBCT) and twelve 2-hour sessions of group cognitive-behavioral therapy (CBT) in a crossover design with participants receiving treatments in reversed order. Outcome was assessed after treatments, and at 6- and 12-month follow-ups. MBCT achieved moderate-high pre-post effect sizes ($d = 0.78$ on a composite SP measure), not significantly different from, although numerical lower than those of CBT ($d = 1.15$). Participants in both groups further improved in the periods following their first and second treatment until 6-months follow-up (pre-follow-up ds = 1.42 and 1.62). Thus, MBCT might be a useful, low cost treatment for SP, although, probably, less efficacious than CBT.

Key words: Social phobia, social anxiety disorder, cognitive behavior therapy, group therapy, mindfulness, mindfulness-based cognitive therapy.

Jacob Piet, Institute of Psychology, Aarhus University, Nobelparken, Jens Chr. Skous Vej 4, 8000 Aarhus C, Denmark. Tel: +45 89424972; e-mail: jacobpj@psy.au.dk

INTRODUCTION

Background

Social phobia (SP), or social anxiety disorder is, according to the Diagnostic and Statistical Manual of Mental Disorders – 4th edition (DSM-IV), characterized by a marked and persistent fear of social or performance situations in which embarrassment may occur leading to marked distress for the person or significantly interfering with his or her work, education or social activities (American Psychiatric Association, 2000). The disorder might be specified as generalized SP if the anxiety includes most social situations.

According to a review by Furmark (2002) most epidemiological studies in Western countries based on DSM-III-R or DSM-IV have found lifetime prevalence rates of 7–13%. However, the figures vary considerably in different studies; probably mainly due to different cut-off lines for clinical caseness, since the required degree of distress or functional impairment is not specified in the DSM. A new, very large epidemiological study in six European countries found a lifetime prevalence estimate for SP of only 2.4% (Alonso, Angermeyer, Bernert *et al*., 2004). The onset of SP most often occurs in adolescence, and without intervention the disorder is likely to run a chronic course, characterized by a high degree of comorbidity and impairments in social and occupational functioning (Keller, 2003; Kessler, 2003). Only 5–10% of persons with SP receive treatment, and if treatment is sought, patients await on average more than 15 years after the onset of the disorder (Kessler, 2003; Wittchen & Fehm, 2003). The period from age 15 to 25 has been considered critical for the development of social impairments and comorbid disorders among persons with SP, thus implying the relevance of early interventions in the youth

and young adult periods of life (Kessler, 2003). There has, however, been little specific focus on the group of young adult persons with SP within the treatment literature (but see Tilfors, Carlbring, Furmark *et al*., 2008).

Cognitive behavioral therapy (CBT) has been shown to be efficacious for SP, and CBT is considered the psychological intervention of first choice for the disorder (Ponniah & Hollon, 2008; Rodebaugh, Holaway & Heimberg, 2004). Within-group, pre-post effect sizes (ES) in the form of Cohen's *d* vary between 0.84 and 1.16 in different meta-analyses (Federoff & Taylor, 2001; Norton & Price, 2007); and between-group, controlled ESs vary between 0.62 and 0.80 (Gould, Buckminster, Pollack, Otto & Yap, 1997; Hofmann & Smits, 2008). Clinical trials suggest, however, that up to 40–50% of patients with SP referred to CBT show little or no improvement (Hofmann & Bögels, 2006; Rodebaugh *et al*., 2004). It is therefore generally agreed upon that there is a need for further developments of treatments for SP.

Cognitive models of SP assume that attentional processes are important in the maintenance of SP (Clark and Wells, 1995; Hope, Gansler & Heimberg, 1989; Rapee & Heimberg, 1997). In a recent review, Bögels and Mansell (2004) outlined three types of such attentional processes supported by empirical evidence: hypervigilance, attentional avoidance, and heightened self-focus. The authors concluded that there is reasonable evidence to promote the use of attentional strategies in the treatment of SP.

Preliminary evidence from a few studies indicates that attentional training aimed at continuously redirecting the focus of attention from the self to the task at hand, or simply focusing attention outward, may be effective components in the treatment of SP (Bögels, 2006; Mulkens, Bögels, de Jong & Louwers, 2001; Wells & Papageorgiou, 1998).

Mindfulness is generally defined as non-judgmental awareness of present moment experiences (Baer & Krietemeyer, 2006), and mindfulness training is a type of attentional training intervention with increasing influence within CBT (Hayes, Folette & Linehan, 2004). Mindfulness-based stress reduction (MBSR) (Kabat-Zinn, 1982, 1990), and mindfulness-based cognitive therapy (MBCT) (Segal, Williams & Teasdale, 2002) are clinical intervention programs based on systematic training in mindfulness (there is a high degree of overlap between the two interventions). Clinical trials of MBSR and MBCT have reported significant reductions in symptoms of stress, anxiety and depression across a broad range of clinical and non-clinical populations (Baer, 2003; Brown, Ryan & Creswell, 2007). It is theoretically plausible that MBCT might have an effect on SP symptoms by training clients to gain attentional control and increased tolerance of negative affects, and thereby reducing worry, rumination and negative aspects of self-focused attention (Brown *et al.*, 2007; Segal *et al.*, 2002; Teasdale, 1999; Teasdale, Segal & Williams, 1995).

So far, only two studies have investigated mindfulness training in the treatment of SP, and none included MBCT. A pilot study conducted by Bögels, Sijbers & Voncken (2006) evaluated the effect of a 9-session individual treatment aimed at task concentration and mindfulness training in nine participants with severe SP. The treatment achieved a mean pre-post ES of 0.85 on self-reported symptoms of SP with results maintained at 2-month follow-up. Koszycki, Benger, Shlik and Bradwejn (2007) conducted a comparative randomized controlled trial of group CBT (GCBT) and MBSR including 53 participants with generalized SP. GCBT was significantly more effective than MBSR in reducing symptoms of SP, although treatments were equally effective in improving general functioning, mood and subjective well-being. The authors concluded that CBT remains the treatment of choice for SP, while MBSR may be a potentially useful alternative intervention for some individuals with SP that might be easier to deliver in some treatment settings. It is possible that a combination of mindfulness and CBT might lead to a better result than monotherapy with one of the methods, since the two methods focus on different aspects of SP maintenance mechanisms.

Aims of the present study

The aim of the study was to pilot test MBCT alone and in combination with GCBT for young adults with SP. It was hypothesized: (1) that MBCT alone would achieve a moderate pre-post ES ($d \geq 0.50$); somewhat smaller than the large ES ($d > 0.80$) expected for GCBT; and (2) that adding MBCT to GCBT would achieve a moderately higher ES than GCBT alone (immediately after GCBT treatment). The hypotheses are expressed in terms of ESs, since the study has insufficient power (0.23) to detect significant between-group differences for moderate ESs.

METHOD

Participants

The study was carried out at the Anxiety Specialty Clinic at the Educational and Research Clinic of the Department of Psychology, University of Aarhus, Denmark, and included 26 participants, aged 18–25 years

with a primary diagnosis of SP according to DSM-IV criteria (American Psychiatric Association, 2000). Exclusion criteria comprised: psychosis, severe depression, alcohol or drug dependence, bipolar disorder, cluster A and B personality disorders, and current (but not previous) psychopharmacological or psychotherapeutic treatment.

Participants were recruited by an announcement at the website of the Anxiety Clinic, a newspaper advertisement, a pamphlet with information on the study sent to general practitioners in the area, and by contacts to the Student Counselling Centre, and the Clinic for Anxiety and OCD at the Psychiatric Hospital. Potential participants were asked to send in a letter with a short description of their problems, and those judged to suffer from SP were invited to an assessment interview. Initially 43 patients were assessed, and 17 patients were excluded (see Fig. 1 for the flow of participants and reasons for exclusion).

Procedure

The participants were diagnosed by use of the Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV; Brown, DiNardo & Barlow, 1994), a reliable, structured interview for anxiety disorders and related conditions, and with the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II; First, Gibbon, Spitzer & Williams, 1997). Diagnostic interviews were carried out by trained research assistants. Diagnoses were assigned according to DSM-IV criteria. Information on demographic variables was collected during the first and second assessment interviews. Informed consent was obtained from all participants. The study was approved by the local county Ethical Committee, and by the Danish Data Protection Agency.

The participants were randomly allocated to one of the two treatment conditions in a crossover design, with both groups receiving both forms of treatment in reversed order, i.e., half of the participants first received MBCT (group 1) and the other half GCBT (group 2). Randomization was carried out in blocks of 14 or 12 (for group 1 and 2 respectively) by a secretary at the institute independent of the Anxiety Clinic. Outcome measures were collected at five data points: (1) prior to therapy; (2) after participants' first treatment (post 1), (3) after their second treatment (post 2); and at follow-ups (4) six months; and (5) 12 months after end of treatment. Since there was a 1–2-months' break between the two treatments, the study altogether covered a period of about 19 months (Fig. 1 illustrates the design of the study).

Treatments

GCBT was carried out according to a treatment program developed at the Clinic for Anxiety and OCD, Aarhus University Hospital. This program, described in a manual by Hougaard (2006) for both therapists and patients, combines elements from Heimberg's GCBT (Heimberg & Becker, 2002) and Clark & Wells' (1995) individual cognitive therapy for SP. The main components of treatment included: (a) psycho-education on SP and CBT, (b) analysis of patients' individualized case-formulations based on the Clark & Wells (1995) model, (c) cognitive restructuring (i.e., analysis and change of negative automatic thoughts), and (d) exposure to feared social situations via behavioral experiments. The participants borrowed a copy of the manual during the CBT treatment period. Homework assignments were given after each session of therapy. Treatment consisted of two weekly 2-hour sessions of individual therapy prior to 12 weekly 2-hour sessions of group therapy. Each group included up to six clients and two therapists. One therapist in each group had extensive training and experience (>10 years) in CBT for anxiety disorders.

MBCT was carried out according to a manual by Segal *et al.* (2002) developed for the treatment of chronic depression, with a few modifications for SP, mainly concerning the content of psycho-education. Main treatment components were mindfulness meditation techniques such as the body scan, gentle mindful yoga exercises, and sitting meditation. Participants were recommended to spend 30–40 minutes daily on homework practices of mindfulness. The intervention consisted of 8 weekly 2-hour sessions in groups with up to 14 participants. The therapist conducting MBCT was a highly experienced mindfulness instructor (trained by Mark Williams).
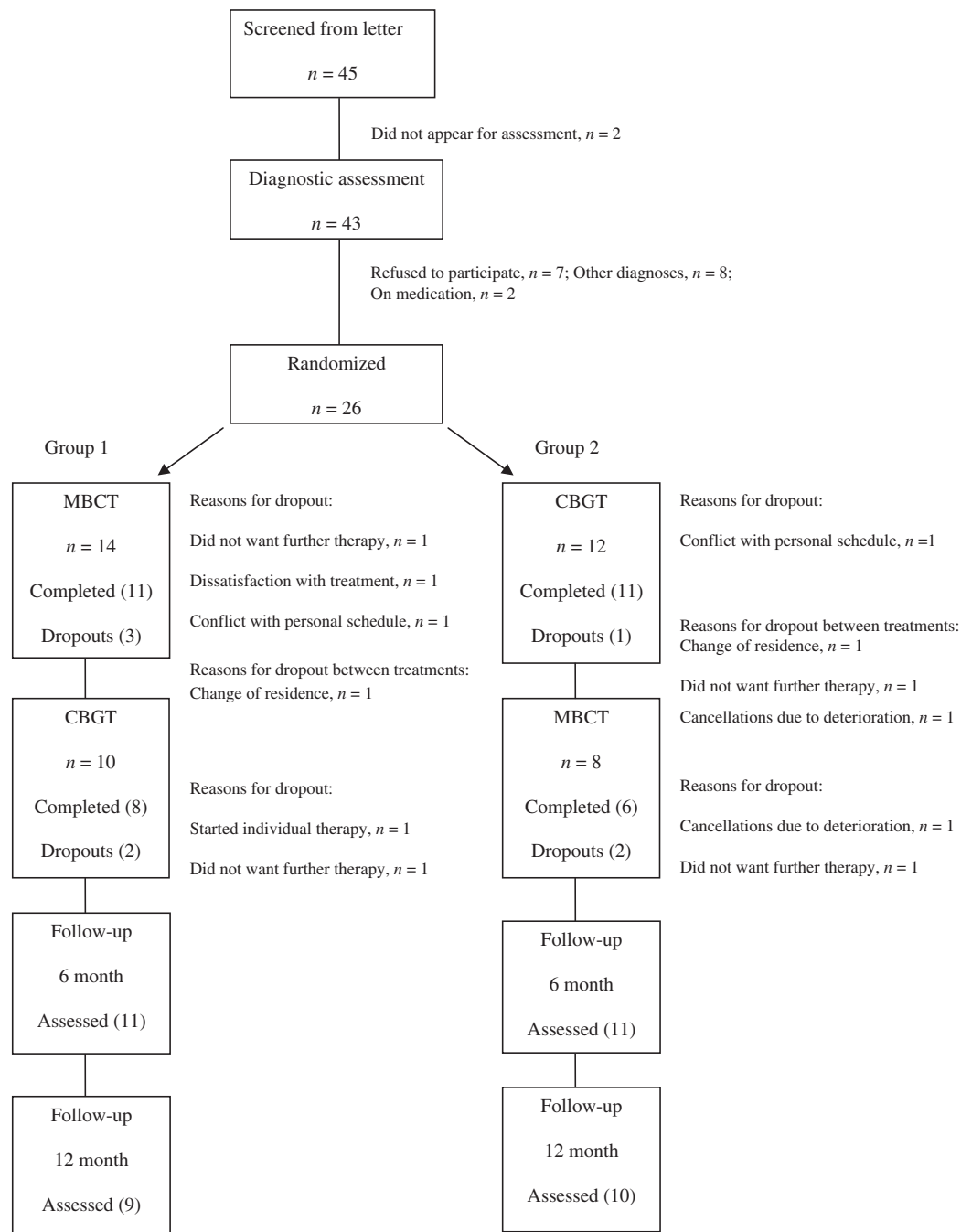
Fig. 1. Flow diagram.

Measures

Treatment outcome was evaluated by the following measures. The *Liebowitz Social Anxiety Scale* (*LSAS*; Liebowitz, 1987) is a widely used clinician administered 24-item scale assessing fear and avoidance of social interaction and performance situations. Fear and avoidance are separately assessed for each item on four-point scales from 0–3 (in the analyses we combined the two dimensions of the scale).

The *Social Phobia Scale* (*SPS*) and the *Social Interaction Scale (SIAS)* (Mattick & Clarke, 1998) are self-administered scales with 20 and 19 items, respectively, assessing fear of being scrutinized by others during social activities, and fear of social interaction in general. Items in SPS and SIAS are rated on five-point scales from 0–4.

The *Symptom Checklist-90-Revised* (*SCL-90-R*; Derogatis, 1977) is a 90-item self-report inventory designed to measure psychological symptoms common in psychiatric patients. Each item is rated on a five-point

scale from 0–4. The scale's global severity index (GSI), the mean score on all filled items, measures the overall level of psychological distress.

The *Beck Anxiety Inventory* (*BAI*; Beck & Steer, 1993) and the *Beck Depression Inventory* (*BDI-II*; Beck, Steer & Brown, 1996) are 21-item questionnaires assessing symptoms of anxiety and depression, respectively, with each item scored from 0–3.

The Inventory of Interpersonal Problems – Circumplex Version (*IIP-C*; Alden, Wiggins & Pincus, 1990) is a 64-item questionnaire assessing interpersonal problems with each item scored from 0–4.

The Fear of Negative Evaluation-Brief Version (*FNE-BV*; Leary, 1983) is a shortened version of the original 30-item version of FNE (Watson & Friend, 1969) that measures expectations and distress related to negative evaluation by others. The *FNE-BV* consists of 12 items each scored from 0–5.

Shehan Disability Scale (*SDS*; Shehan, 1983) is a simple scale of three items assessing current impairment in work, social life, and family life. Each

item is rated on a 0–10 point scale. SDS also assesses the number of days lost at work and the number of days of markedly reduced work productivity.

All of the above scales are widely used measures with acceptable psychometric properties (cf. references above), except for SDS, which has rather low internal consistency due to its very few items (e.g., Hambrick, Turk, Heimberg, Schneier & Liebowitz, 2004). LSAS, SPS and SIAS are generally recommended as measures of outcome in clinical studies of SP (Strupp, Horowitz & Lambert, 1997). SPS and SIAS measure different aspects of SP symptomatology that might be specifically relevant for specific and generalized SP, respectively.

A patient evaluation questionnaire was developed for measuring (1) satisfaction with treatment, and (2) experienced value of different treatment components. Each item was rated on scales from 1–5. (Only the satisfaction part of the questionnaire is dealt with in the present paper.)

All measures were administered at the first three data points. Follow-up assessment 6 months after treatment did not include IPP and FNE, and the follow-up 12 months after treatment only consisted of SIAS and SPS.

In line with general recommendations of focusing on disorder-specific symptoms in outcome research (Strupp *et al.*, 1997), measures of SP symptoms (LSAS, SPS and SIAS) are considered the primary measures of outcome in the study.

Statistical approach

Differences in baseline demographics and clinical characteristics as well as pre-treatment scores on outcome measures were compared between treatment groups using, as appropriate, Pearsons χ^2, Fisher's exact test or Student's *t*-test.

Within-group changes were analyzed by paired *t*-tests, and magnitude of change was estimated according to Cohen's formula: $d = (M_{before} - M_{after}) / SD_{(within)pooled}$ (Cohen, 1988; Rosenthal, 1984). This analysis was carried out for all outcome measures, as well as for a composite measure for the three specific SP measures (LSAS, SPS and SIAS). Following a procedure recommended by Rosenthal & Rosnov (2008) these measures were added and standardized $(M = 0, SD = 1)$ by converting scores *to* Z scores across all data points.

We also examined the number of participants with reliable and clinical change on the SP symptom scales according to the Jacobson & Truax (1991) criteria. In line with recommendations of Bauer, Lambert and Nielsen (2004) we used psychometric values from standardization studies with the scales in these calculations (cf. references to the scales above) (besides, there are no Danish norms for the scales).

A one-way between-group analysis of covariance (ANCOVA) with pre-treatment scores as covariates was used to compare treatments in the first treatment period. This method controls for baseline differences between groups, and it is useful when dealing with small sample sizes, as it reduces error variance and, thereby, increases the chance of detecting significant between-group differences. After crossover, groups were compared by means of unpaired *t*-tests.

All outcome analyses were conducted on both the intention-to-treat (ITT) sample and on treatment completers. Except for within-group ESs, only ITT data are presented, since results from the two analyses were almost identical for the first treatment period, and the high dropout rate in the second period made completer results difficult to interpret. In the ITT analyses, which included all randomized participants, missing values were substituted by means of last observation carried forward. All data were analyzed using SPSS Version 17, and all tests performed were two-tailed with α set at 0.05.

RESULTS

Baseline characteristics

Demographics and clinical characteristics for both groups are seen in Table 1, and baseline scores on outcome measures are seen in Table 2. There were no significant differences between the two groups on any of the baseline variables.

Table 1. *Demographic and clinical characteristics*

	Group 1 *n* = 14	Group 2 *n* = 12	*p*-values
Demographics			
Age, mean (*SD*)	21.6 (2.84)	22.1 (2.54)	0.68
Female gender, *n* (%)	11 (79)	7 (58)	0.40
Steady partnership, *n* (%)	5 (36)	4 (33)	1.00
In occupational or student role, *n* (%)	12 (86)	10 (83)	1.00
Clinical characteristics			
Age of onset, mean (*SD*)	13.1 (2.97)	15.3 (2.77)	0.06
Severity of SP (0–8), mean *(SD)*	5.6 (1.02)	5.4 (1.08)	0.71
Generalized SP, *n* (%)	12 (86)	12 (100)	0.48
Co-morbid axis-I disorders, *n* (%)	6 (43)	5 (42)	1.00
Co-morbid personality disorder, *n* (%)	1 (7)	3 (25)	0.30
Previous treatment			
Psychiatric hospitalization, *n* (%)	0	2 (17)	0.20
Antidepressants, *n* (%)	2 (14)	5 (42)	0.19
Psychotherapy, *n* (%)	9 (64)	7 (58)	1.00
Treatment in the follow-up period			
Antidepressants, *n* (%)	2 (14)	1 (8)	1.00
Psychotherapy, *n* (%)	3 (21)	3 (25)	1.00

Adherence to treatment

There was a high degree of adherence to treatments for both groups in the first treatment period, with 11 of 14 participants (78.6%) in group 1 (MBCT) and 11 of 12 (91.7%) in group 2 (GCBT) completing at least 75% of the sessions (difference not significant). Meanwhile, only 8 of 14 participants (57%) in group 1, and 6 of 12 (50%) in group 2 completed at least 75% of the second part of the treatment. Reasons for dropout are noted in Fig. 1.

Between group comparisons

A one-way analysis of covariance (ANCOVA) showed no significant differences between MBCT and GCBT after the first treatment period (post-1) on any of the included outcome variables (ITT data). However, as can be seen in Table 2, most outcome variables numerically favored the CBT group with a small between-group ES of 0.24 ($p = 0.54$) on the composite measure of SP.

There were also no differences between groups on any measure at the later data points (post-2, 6- and 12-months' follow-up) (unpaired *t*-tests).

Within-group changes

As can be seen in Table 2, both groups achieved moderate to large within-group ESs on most measures in the first treatment period (pre-post 1) with an ES on the SP composite measure for group 1 (MBCT) of 0.77 ($p = 0.03$), and for group 2 (GCBT) of 1.14 ($p < 0.01$) (ITT data). Both groups continued to improve until the 6-month follow-up. Pre-6-month follow-up ESs on the composite SP measure for the two groups were large, respectively 1.42 ($p < 0.01$) and 1.62 ($p < 0.01$). For the 17 participants that did not receive further treatment in the follow-up period (cf. Table 1)

the respective figures were 1.69 (p < 0.01) for group 1 (*n* = 9) and 1.55 (*p* < 0.01) for group 2 (*n* = 8).

Fig. 2 shows the development for the SP composite score up until 6-month follow-up (about one year after the start of the treatment). As can be seen, improvement in the two groups was rather similar. Only group 1 improved significantly during the second treatment period, where this group received GCBT, with a Post 1–Post 2 ES on the composite SP measure of 0.33 (*p* = 0.04). The corresponding ES for group 2 receiving MBCT in the period was 0.20 (*p* = 0.4). The changes from post 2–6-month follow-up were, however, as large as those from Post 1–Post 2 (ESs on the composite SP measure 0.40 [*p* = 0.06] and 0.31 [*p* = 0.11] for group 1 and 2).

Within-group ESs for completers of treatment from pre-post 1 on the composite SP measure were 0.78 (*p* = 0.07) for group 1 (MBCT, *n* = 11), and 1.26 (*p* < 0.01) for group 2 (GBCT, *n* = 11). The corresponding pre-post 2 and pre-6-month follow-up ESs were 0.81 (*p* = 0.02) and 1.34 (*p* = 0.02) for group 1 (*n* = 8), and 2.63 (*p* < 0.01) and 2.86 (*p* < 0.01) for group 2 (*n* = 6),
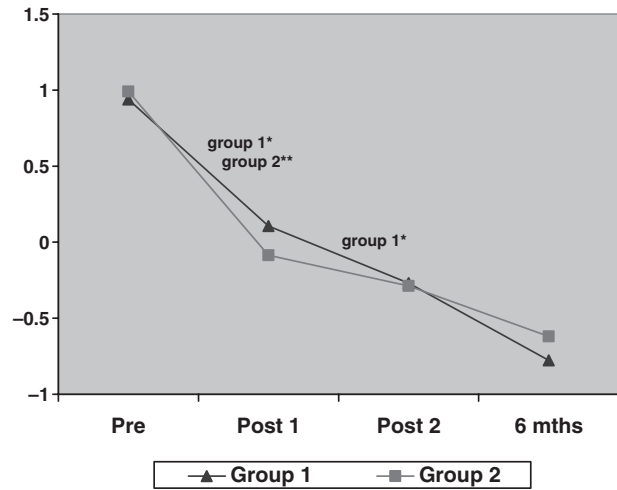
Fig. 2. Changes in mean social phobia composite over time for ITT. Within-group Significant Changes Between Data Points: * $P \leq 0.05$, ** $P < 0.01$.

Table 2. *Group means, standard deviations, and within-group effect sizes on dependent variables*

Measure	n	Pre M (SD) n = 26[a]	Post 1 M (SD) n = 23[a]	Post 2 M (SD) n = 19[a]	6 month follow-up n = 22[a]	12 month follow-up n = 19[a]	Pre-post 1 ES	Pre-post 2 ES	Pre-6 months ES	Pre-12 months ES
SPC										
Gr. 1	14	0.94 (1.11)	0.11 (1.05)	−0.27 (1.21)	−0.78 (1.31)	-	0.77*	1.04*	1.42*	-
Gr. 2	12	0.99 (1.04)	−0.08 (0.81)	−0.29 (1.18)	−0.62 (0.94)	-	1.15*	1.15*	1.62*	-
SPS										
Gr. 1	14	35.21 (13.22)	25.09 (12.25)	21.36 (12.74)	15.77 (13.79)	15.48 (12.56)	0.79*	1.07*	1.44*	1.53*
Gr. 2	12	35.06 (12.16)	23.90 (11.71)	21.21 (14.45)	19.48 (10.91)	21.33 (14.42)	0.93*	1.04*	1.35*	1.03*
SIAS										
Gr. 1	14	44.52 (13.87)	39.21 (13.90)	34.11 (14.48)	25.22 (18.17)	26.54 (15.51)	0.38	0.73*	1.19*	1.22*
Gr. 2	12	48.67 (15.79)	39.09 (13.27)	36.95 (15.00)	32.18 (14.45)	35.50 (15.34)	0.66*	0.76*	1.09*	0.85*
LSAS										
Gr. 1	14	59.29 (19.78)	41.64 (19.44)	36.21 (22.75)	32.72 (21.31)	-	0.90*	1.08*	1.29*	-
Gr. 2	11	71.37 (19.56)	49.56 (14.49)	46.76 (20.88)	39.79 (16.83)	-	1.27*	1.22*	1.73*	-
SCL-90-R										
Gr. 1	14	0.91 (0.51)	0.67 (0.40)	0.60 (0.41)	0.48 (0.51)	-	0.52*	0.67*	0.84*	-
Gr. 2	12	1.27 (0.49)	0.91 (0.36)	0.84 (0.45)	0.71 (0.48)	-	0.84*	0.91*	1.15*	-
BDI-II										
Gr. 1	14	13.06 (6.69)	9.00 (5.94)	7.57 (7.65)	6.57 (8.10)	-	0.64	0.76*	0.87*	-
Gr. 2	12	19.54 (8.99)	12.30 (7.90)	10.38 (9.39)	10.18 (8.90)	-	0.86*	1.00*	1.05*	-
BAI										
Gr. 1	14	12.31 (7.34)	11.24 (6.84)	10.19 (6.37)	7.29 (7.53)	-	0.15	0.31	0.68*	-
Gr. 2	12	17.93 (5.61)	13.58 (5.25)	10.92 (7.25)	10.92 (6.05)	-	0.80*	1.08*	1.20*	-
IPP										
Gr. 1	14	1.19 (0.52)	0.97 (0.52)	0.84 (0.55)	-	-	0.42	0.65*	-	-
Gr. 2	12	1.18 (0.38)	1.04 (0.45)	0.86 (0.41)	-	-	0.34	0.81*	-	-
FNE										
Gr. 1	14	46.05 (7.99)	41.93 (8.51)	38.75 (7.98)	-	-	0.50	0.91*	-	-
Gr. 2	12	49.32 (7.92)	47.09 (7.08)	43.24 (8.35)	-	-	0.30	0.75*	-	-
SDS										
Gr. 1	14	13.57 (6.00)	9.50 (7.38)	7.14 (4.96)	6.64 (6.86)	-	0.61*	1.17*	1.08*	-
Gr. 2	12	15.75 (6.06)	12.92 (6.99)	10.75 (7.10)	10.92 (6.42)	-	0.43	0.76*	0.77*	-

Notes: Data presented are ITT values. SPC: Social Phobia Composite, SPS: Social Phobia Scale, SIAS: Social Interaction Scale, LSAS: Liebowitz Social Anxiety Scale, SCL-90-R: Symptom Checklist-90-Revised, BDI-II: Beck Depression Inventory II, BAI: Beck Anxiety Inventory, IPP: Inventory of Interpersonal Problems, FNE: Fear of Negative Evaluation, SDS: Shehan Disability Scale. *N*: Number of participants, *M*: Mean, *SD*: Standard Deviation, ES: Effect Size.
[a] Number of observations at the data point.
* *p* < 0.05.

respectively. The larger ESs for group 2 at these later data points are related to differences in pre-treatment values for completers, i.e., 0.74 for group 1, compared to 2.10 for group 2 ($p = 0.07$).

Number of participants responding

There were no significant differences between groups on the number of participants with clinical and significant change on the SP symptom scales (LSAS, SPS and SIAS) at any data point based on different ways of calculation. Probably, the most reasonable criteria for a clinical significant response based on these measures are clinical and significant change on the observer-rated LSAS, and on one of the two self-report scales; i.e., from both an observer and a patient perspective (since SPS and SIAS measures different aspects of SP symptomatology relevant for different patients). Number of participants responding (ITT data) based on this criterion was: post 1: 1 (4%; 1 in group 1); post 2: 8 (31%; 4 in each group); and at 6-month follow-up: 15 (58%; 8 in group 1 and 7 in group 2). Number of participants with clinical and statistical change on at least one of the three scales was: post 1: 13 (50%; 6 in group 1 and 7 in group 2); post 2: 13 (50%; 7 in group 1 and 6 in group 2); and at 6-month follow-up: 19 (73%; 10 in group 1 and 9 in group 2). Number of participants with clinical and statistical significant changes on all three scales was: post 1: 1 (4%; 1 in group 1); post 2: 3 (12%; 1 in group 1 and 2 in group 2); and at 6-month follow-up: 9 (35%; 6 in group 1 and 3 in group 2).

Patient satisfaction

Participants were generally highly satisfied with treatment with no statistical differences between groups. Thus, after the first treatment period the mean satisfaction score on item 7 of the satisfaction scale, "How satisfied in general have you been with the treatment you received?" (scores from 1–5) was 3.67 for group 1 (MBCT) and 3.73 for group 2 (GCBT). After the end of the treatment period, when participants had received both treatments, it was 3.93. At that point the mean on item 3, "If a friend had problems like yours, would you recommend the form of treatment you received?" was 4.3.

DISCUSSION

The primary aim of the study was to pilot test MBCT alone and in combination with GCBT as a treatment for young adult patients with SP. MBCT produced significant pre-post improvements with moderate to high ESs (0.77 on the composite SP measure), not significantly different from, although numerically smaller than those achieved by group CBT (1.15 on the composite measure). Participants were generally highly satisfied with both treatments. The larger ESs achieved by completers in group 2 at post 2 and at 6-month follow-up are probably due to higher pre-treatment scores, which might be explained by a differential drop-out, with severe cases more likely to drop out after initial MBCT than after GBCT. Reasons for this differential dropout are, however, not obvious, and completer results are based on a small number of cases (8 and 6 for group 1 and 2, respectively).

The results of the study are similar to those of Koszycki *et al.* (2007) as to the ranking of results achieved by mindfulness and

GCBT, although they found a significant difference between GCBT and MBSR, possibly due to their larger sample ($n = 53$). Their pre-post ESs for both treatments were, however, larger than those of the present study, e.g., 1.49 for MBSR and 1.83 for GCBT on the LSAS (compared to 0.90 and 1.27 in the present study). The ESs achieved by GCBT in the present study are, however, in line with those generally reported in meta-analyses (Fedoroff and Taylor 2001; Norton & Price, 2007); as well as with ESs on SPS and SIAS in other recent studies (McEvoy, 2007), except for the studies by Clark and colleagues (Clark, Ehlers, Hackmann *et al.*, 2006; Mörtberg, Clark, Sundin & Åberg-Wistedt, 2007; Stangier, Heidenreich, Peitz, Lauterbach & Clark., 2003) that achieved very high ESs for individual CBT.

Even though mindfulness might not be as efficacious as traditional CBT, it could have some advantages in terms of low costs (one therapist can lead a rather large group), easiness to implement in many treatment settings, and acceptability for some SP patients preferring general stress-related courses to treatment for a psychiatric disorder.

The hypothesis that combined treatment with MBCT and GCBT would achieve moderately larger ESs than GCBT alone was not supported. Combining the two treatments only resulted in a significant, small increase in the within group composite ES of 0.33 when GCBT was added after MBCT, while the increase in ES of MBCT added to GCBT of 0.20 was insignificant. Besides, these changes were in line with those that took place in the no-treatment 6-month follow-up period. Generally, results from crossover studies are difficult to interpret, since changes after the crossover might be due to the new treatment introduced, or to late coming effects of the prior treatment – and, in the absence of a no-treatment control group, also to spontaneous recovery. The high degree of dropout in the second treatment period is, however, an argument against offering MBCT as a standard treatment after (or before) CBT. Some of the participants also complained of difficulties with the rather abrupt shift in treatment, since the two interventions require different home work, and some of their methods might not harmonize well (e.g., cognitive restructuring vs. mindful acceptance). A better strategy for combining the two methods probably would consist in assimilative integration of methods from MBCT into CBT, or vice versa. Thus, for instance, MBCT methods of training clients to gain attentional control and increased tolerance of negative affects might be useful supplements to CBT; while MBCT for SP might profit from CBT's disorder focused psychoeducation and scheduled exposure exercises.

An interesting result from the study, where we followed SP patients over a period of 19 months, is the gradual improvement that took place during the whole first year (see Fig. 2). This result is in line with meta-analytic findings of improvements for patients with SP in the follow-up period after treatment (Fedoroff and Taylor 2001; Norton & Price, 2007), although mean changes found have been small (mean $d < 0.20$). The rather impressive ESs at the 6-month follow-up in the study (composite ds of 1.42 and 1.62) is an argument for offering patients with SP treatment early in life, thereby counteracting their longstanding mental disorders and impediments of life documented in other studies (Keller, 2003; Kessler, 2003). However, in line with other studies we also found many non-responders, even at 6-month follow up (42%). Thus, the combined treatment of GCBT and MBCT did not

succeed in reducing the high number of patients with unsatisfactory outcomes found in prior studies of short-term CBT.

In the absence of a no treatment control condition it is, of course, not possible to rule out the possibility that improvement was due to natural history. Long-term, naturalistic studies have, however, found little spontaneous improvement among patients with SP (Bruce, Yonkers, Otto *et al.*, 2005), and SP patients on waitlists generally do not improve. One meta-analysis (Taylor, 1996) actually found a small, insignificant, *negative* pre-post ES of 0.15 for SP waitlist control groups. Further treatment in the follow-up period for nine participants might also have influenced follow-up data, even though there were no differences between participants with and without such treatment.

The study has several limitations. Thus, the study is a small pilot study with insufficient power to test the primary hypotheses. It has no wait-list or placebo control condition. The cross-over design limits any conclusion to be drawn from the follow-up data. The clinicians' rating on the LSAS was not blind as to treatment conditions, but the results on LSAS were in line with those based on patient self-report scales.

The main conclusion from the study is that it preliminarily supports MBCT as a useful, low cost treatment for patients with SP, although probably less efficacious than CBT.

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Paper 2

Piet, J., & Hougaard, E. (2011). The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: A systematic review and meta-analysis. *Clinical Psychology Review, 31*, 1032-1040.

The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: A systematic review and meta-analysis

Jacob Piet *, Esben Hougaard

University of Aarhus, Denmark

ABSTRACT

Background: Mindfulness-based cognitive therapy (MBCT) is a group-based clinical intervention program designed to reduce relapse or recurrence of major depressive disorder (MDD) by means of systematic training in mindfulness meditation combined with cognitive-behavioral methods.
Objective: By means of a meta-analysis to evaluate the effect of MBCT for prevention of relapse or recurrence among patients with recurrent MDD in remission.
Method: Electronic databases were searched and researchers were contacted for further relevant studies. Studies were coded for quality. Meta-analyses were performed by means of the Cochrane Collaboration Review Manager 5.1.
Results: Six randomized controlled trials with a total of 593 participants were included in the meta-analysis. MBCT significantly reduced the risk of relapse/recurrence with a risk ratio of 0.66 for MBCT compared to treatment as usual or placebo controls, corresponding to a relative risk reduction of 34%. In a pre-planned subgroup analysis the relative risk reduction was 43% for participants with three or more previous episodes, while no risk reduction was found for participants with only two episodes. In two studies, MBCT was at least as effective as maintenance antidepressant medication.
Conclusion: Results of this meta-analysis indicate that MBCT is an effective intervention for relapse prevention in patients with recurrent MDD in remission, at least in case of three or more previous MDD episodes.

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Contents

* Corresponding author at: University of Aarhus, Department of Psychology, Jens Chr. Skous Vej 4, 8000 Aarhus, Denmark. Tel.: +45 89424972.
  E-mail address: jacobpj@psy.au.dk (J. Piet).

1. Introduction

Originating from ancient eastern meditation and yoga traditions, mindfulness is generally described as a particular way of paying attention characterized by intentional and non-judgmental observation of present moment experiences, including bodily sensations, feelings, thoughts, and external stimuli from the environment (e.g. Baer, 2003; Grossman, Niemann, Schmidt, & Walach, 2004; Kabat-Zinn, 1994). Mindfulness-training, assumed to cultivate this capacity of awareness, has been adapted into clinical intervention programs including mindfulness-based stress reduction (MBSR) (Kabat-Zinn, 1990), and mindfulness-based cognitive therapy (MBCT) (Segal, Williams, & Teasdale, 2002). MBCT is an 8-session group intervention program with 8–15 participants designed for prevention of relapse or recurrence among patients with major depressive disorder (MDD) in remission.

MDD is a common mental disorder with a lifetime prevalence rate of about 20% (Kessler et al., 2005), and it is associated with a high degree of subjective distress and psychosocial disability (Judd et al., 2000). According to a recent report by the World Health Organization (WHO), MDD is currently the leading cause of disease burden, as measured by disability-adjusted life years (DALYs), in the United States of America and other middle- and high-income countries (WHO, 2008). Furthermore MDD is expected to be the leading cause of disease burden worldwide by the year 2030 (Ibid.). While the outlook for a first episode of MDD is rather good with spontaneous remission in most cases, the prognosis in the long run will often be poor with very high relapse or recurrence rates (50–90%); especially in case of prior depressive episodes (Judd, 1997; Mueller et al., 1999). With each new MDD episode the risk of worsening the course of the disease increases (Kessing, Hansen, Andersen, & Angst, 2004), and about 20% develops into chronic MDD with symptoms persisting for more than two years (Keller & Boland, 1998). Therefore, development of effective prevention interventions for MDD is a high priority enterprise within mental health.

The underlying model of MBCT specifies that previously depressed persons are characterized by greater cognitive vulnerability to states of low mood, as even mild dysphoric states may reactivate patterns of negative, ruminative thinking similar to those of previous episodes, causing the configuration of depression to be re-established (Segal, Williams, Teasdale, & Gemar, 1996; Teasdale, 1988; Teasdale, Segal, & Williams, 1995). MBCT may be assumed to work by targeting rumination and emotional avoidance, both considered to be maintaining processes across mood and anxiety disorders (e.g. Barlow, Allen, & Choate, 2004; Harvey, Watkins, Mansell, & Shafran, 2004; Hayes, Wilson, Gifford, Follette, & Strosahl, 1996).

It has been claimed (e.g., Teasdale, Segal, & Williams, 2003) that MBCT particularly benefits patients with three or more MDD episodes, since such patients are especially prone to engage in ruminative thinking. In fact, two randomized controlled trials (RCTs) (Ma & Teasdale, 2004; Teasdale et al., 2000), both of which stratified participants prior to randomization by number of episodes (2 versus 3 or more), found that MBCT only lowered risk of relapse in case of three or more MDD episodes.

MBCT integrates elements of cognitive behavioral therapy for depression (CBT) (Beck, Rush, Shaw, & Emery, 1979) with training in mindfulness meditation (Kabat-Zinn, 1990). The aim of MBCT is to teach patients to become more aware of and relate differently to their thoughts, feelings, and bodily sensations. Through the practice of mindfulness exercises, such as the body scan, simple yoga exercises, and prolonged periods of sitting meditation, patients are taught to 'turn towards' and accept intense bodily sensations and emotional discomfort, and they are provided with cognitive skills that allow them to recognize the automatic activation of habitual dysfunctional cognitive processes, such as depression-related rumination, to detach or "decentre" from the content of negative thoughts, and to disengage

from these processes by redirecting attention to experiences as they flux and change moment by moment.

Since the protocol release in 2002, MBCT has been adapted to different psychological disorders and conditions, and empirical research on the effectiveness of MBCT has expanded greatly. There is preliminary evidence of the effect of MBCT on pre-post symptoms of depression in people with fully or partially remitted depression (Britton, Haynes, Fridel, & Bootzin, 2010; Crane et al., 2008; Kingston, Dooley, Bates, Lawlor, & Malone, 2007); currently symptomatic depression (Barnhofer et al., 2009; Eisendrath et al., 2008; Kenny & Williams, 2007; Manicavasgar, Parker, & Perich, 2011; Mathew, Hayley, Kenny, & Denson, 2010); bipolar disorder (Miklowitz et al., 2009; Williams et al., 2008); social phobia (Piet, Hougaard, Hecksher, & Rosenberg, 2010); and generalized anxiety disorder (Craigie, Rees, Marsh, & Nathan, 2008; Evans et al., 2008). In a recent meta-analysis of mindfulness-based therapy, including MBSR and MBCT for different medical and psychological disorders, Hofmann, Sawyer, Witt, and Oh (2010) found a large pre-post effect size (Hedges's $g = 0.85$) of MBCT for symptoms of depression. Additionally, studies have found that MBCT reduces overgeneral autobiographical memory, which has been associated with depression and a number of detrimental effects on functioning (Heeren, Van Broeck, & Philippot, 2009; Williams, Teasdale, Segal, & Soulsby, 2000).

Research investigating potential mechanisms of action in MBCT is in its infancy. Recent studies suggest that the effect of MBCT may be facilitated or mediated by improved meta-awareness (Hargus, Crane, Barnhofer, & Williams, 2010; Teasdale et al., 2002); increased mindfulness and self-compassion (Kuyken et al., 2010); decreased rumination (Shahar, Britton, Sbarra, Figueredo, & Bootzin, 2010); reduced cognitive reactivity (Raes, Dewulf, Van Heeringen, & Williams, 2009); and a balanced pattern of emotion related brain activation (Barnhofer et al., 2007). Two studies on recovered recurrently depressed patients, respectively found increased mindfulness and reduced rumination during MBCT, and showed that post treatment levels of mindfulness and rumination significantly predicted MDD relapse over a 12 month follow-up period, even after controlling for residual depressive symptoms and number of previous episodes (Michalak, Heidenreich, Meibert, & Schulte, 2008; Michalak, Hölz, & Teismann, 2010).

Coelho, Canter, and Ernst (2007) conducted the first narrative review of controlled clinical trials of MBCT for participants with a history of depression. They identified two studies focussing on MBCT as a preventive treatment for recurrent MDD, and tentatively concluded that the program had an additive benefit to usual care for patients with three or more previous episodes of depression. Chiesa and Serretti (2011) recently reviewed 16 controlled studies of MBCT for different psychiatric disorders, including four studies on MBCT for MDD relapse prevention, thus further consolidating the tentative conclusions of Coelho et al. (2007).

While former research broadly has reviewed the effect of MBCT for different disorders, this article reports the first formally adequate meta-analytic evaluation, following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA); (Moher, Liberati, Tetzlaff, Altman, & The PRISMA Group, 2009), of the effectiveness of MBCT for relapse prevention among patients with recurrent MDD in remission.

The aim of this study was by means of a meta-analysis to evaluate the effect of MBCT for prevention of relapse or recurrence among patients with recurrent MDD in remission; both for different control conditions, and for subgroups of patients (< or ≥3 MDD episodes).

2. Method

The study was conducted in accordance with the PRISMA statement, which provides a detailed guideline of preferred reporting style for systematic reviews and meta-analyses (Liberati et al., 2009; Moher et al., 2009).

2.1. Inclusion criteria

Studies were included in the meta-analysis according to the following a priori criteria for eligibility:

Type of studies: RCTs of MBCT for prevention of relapse in recurrent MDD in remission, reported in English language, and published or accepted for publication in peer-reviewed journals. *Type of participants:* Participants aged 18 years or above, diagnosed with recurrent MDD in remission according to a formal diagnostic classification system.

Type of interventions: MBCT conducted according to the manual by Segal et al. (2002).

Type of outcome measures: Number of participants meeting the diagnostic criteria for a new MDD episode over the follow-up study period.

2.2. Identification of studies

Electronic databases (EMBASE, PubMed, PsycINFO, Web of Science, Scopus, and the Cochrane Controlled Trials Register) were searched to locate studies from the first available year to November 2010, using keywords ([(mindfulness-based cognitive therapy) OR (mindfulness based cognitive therapy) OR (MBCT)] AND depress*). In addition, reference lists of selected articles and other reviews were inspected, and leading researchers in the field of MBCT were contacted to identify further relevant studies. Initially, duplicates were removed from the total number of identified records. Abstracts from the remaining records were then screened to retrieve full-text articles for assessment of eligibility. Finally, studies fulfilling inclusion criteria were selected for meta-analytic evaluation. The retrieval process was checked by both authors.

2.3. Data collection

A data extraction sheet was developed, and the following data from included studies were extracted by the first author, and checked by the second: 1) participant characteristics (including age, sex, remission period, baseline depression score, number of prior episodes, age of first onset, history of antidepressant medication); 2) group characteristics (including intervention, comparison condition, number of group participants and dropouts, use of non-study treatments for depression within groups); and 3) MDD relapse/recurrence outcome (including number of relapse/recurrence between groups, diagnostic classification system, length of follow-up period).

2.3.1. Methodological quality of studies

The methodological quality of study reports was assessed by the two authors using a table adopted from Coelho et al. (2007) on nine criteria (see Table 2), including the following revised Jadad criteria (Jadad et al., 1996): a) the study was described as randomized, b) the randomization procedure was described and appropriate, i.e., study participants were randomly allocated independent of the investigators by methods "allowing each participant to have the same chance of receiving each intervention" (Jadad et al., 1996, p. 9), c) blind outcome assessments were reported (blindness of participants and therapists, as required by the original Jadad criteria, are not possible), d) number and reasons of withdrawals and dropouts were provided for each group. One point was assigned for each of the four fulfilled criteria, constituting a maximum Jadad score of 4 points. Disagreements between the two raters (in two cases) were resolved by discussion.

2.4. Statistical analysis

Computed effect sizes (ESs) were relative risk ratios (RRs) for relapse/recurrence between groups over total follow-up periods, presented with confidence intervals (CI). ESs were calculated from intention-to-treat (ITT) data, or from complete cases data, if appropriate ITT data were not available, using the following formula: $RR = \frac{MBCTrelapse / MBCTtotal}{Controlrelapse / Controlrelapse}$. ITT data was considered "appropriate" if adequate statistical methods, such as censoring, were used to handle drop out/missing data. ESs were weighted by the inverse standard error of the studies, thus taking precision or number of participants into account. The relative risk reduction was calculated as $100\% \times (1 - RR)$.

Statistical analyses were conducted using the computer software program *Review Manager 5.1* (RevMan), provided by The Cochrane Collaboration (Review Manager, 2011). Additional analyses, including meta-regression and tests of publication bias, which could not be performed within the RevMan program, were conducted by use of the software program Comprehensive Meta-analysis, Version 2 (CMA) (Borenstein, Hedges, Higgins, & Rothstein, 2005).

All analyses were performed within the inverse variance random effects model (DerSimonian & Laird, 1986). In this model ES parameters for individual studies are treated as if they were a random sample from a larger population, thus allowing for generalization beyond the observed studies (Hedges & Vevea, 1998). For the purpose of establishing whether the results of studies were consistent, tests of heterogeneity were included using Q and I^2 statistics. Q statistics calculates the probability value for heterogeneity of studies (significant heterogeneity is indicated by a p-value ≤ 0.05). The I^2 estimates the amount of variance in a pooled ES that can be accounted for by heterogeneity in the sample of studies (Higgins, Thompson, Deeks, & Altman, 2003). An I^2 value of 0% indicates no observed heterogeneity, while values of 25%, 50%, and 75% are considered low, moderate, and high.

Fail-Safe N statistics and a funnel plot of individual study ESs were used for detecting potential biases in the publication of study results. A funnel plot is a graphic illustration of ESs from individual studies in relation to a measure of study size or precision. In general, estimates of ESs have more precision the larger the study, and therefore ESs derived from smaller studies are likely to scatter more widely at the bottom of the graph. In the absence of bias, the plot should resemble an inverted funnel with ESs from individual studies symmetrically distributed in relation to the overall mean ES (Sterne, Egger, & Moher, 2008). If many small studies show large ESs (with individual risk ratios below the overall mean, and the funnel plot skewed to the left) it may indicate bias, since small studies with insignificant results are more likely not to be published (the file-drawer problem). In addition to the visual graph, we included a formal test of funnel plot asymmetry provided by Egger, Smith, Schneider, and Minder (1997), to examine whether the association between the overall estimated intervention effect and a measure of study size, such as the standard error of the intervention effect, was significantly greater than what could be expected by chance alone. The funnel plot Trim and Fill method by Duval and Tweedie (2000) was used to further test and (if needed) adjust for possible bias in the overall ES by taking into account ESs from the estimated number of missing studies. *Fail-Safe N* statistics was included to provide an estimate for the number of unpublished or unretrieved equal sample size studies with no intervention effect, needed to reduce the overall estimated ES to a non-significant level ($p > 0.05$) (Rosenthal & Rubin, 1988).

Separate meta-analyses were performed for: a) MBCT versus controls, including treatment as usual (TAU), and placebo + clinical management (PLA); and b) MBCT versus maintenance antidepressant medication (m-ADM). Pre-specified subgroup analyses of participants with < or ≥ 3 MDD episodes were carried out. Possible predictors of treatment outcome, publication year, sample size, and study quality, were explored by use of meta-regression analyses.

3. Results

3.1. Trial flow

The flow of information from identification to inclusion of studies is summarized in Fig. 1 using the PRISMA flow diagram (Moher et al., 2009). Our search strategy identified 666 publications. Duplicates were removed, and abstracts from the remaining 317 publications were screened. Initially reviews, qualitative studies, case studies, dissertation abstracts, study protocols, and non-English articles were excluded ($N = 171$) (in this article, N refers to number of studies; n to number of participants). The remaining 146 articles were selected for further screening, and exclusion was carried out for the following reasons: a) no MBCT intervention ($N = 98$) or b) did not deal with MBCT for prevention of relapse in recurrent major depressive disorder ($N = 40$). Eight full text articles on studies investigating the effect of MBCT on MDD relapse were retrieved and assessed for eligibility. Two full text articles (Michalak et al., 2008, 2010) were excluded because they did not use a randomized controlled design. Finally 6 studies, fulfilling the inclusion criteria, were selected for meta-analytic evaluation.

3.2. Characteristics of studies

Table 1 summarizes the characteristics of the six included studies investigating MBCT for prevention of relapse or recurrence in recurrent MDD. Study sample sizes ranged from 60 to 145 with a total of 593 randomized participants, 74% were women (range 63–81%), and the mean age was 46 (range of means 43–49). The mean baseline depression score was 4.9 for the Hamilton Depression Rating Scale, 17-item version (Hamilton, 1960), and 14.3 for the Beck Depression Inventory, 1st or 2nd version (Beck et al., 1996, 1961).

Participants in the studies had experienced either two or more ($N = 2$), or three or more ($N = 4$) previous episodes of MDD, with the mean/median number of prior episodes = 5.6 ($N = 2$)/3.4 ($N = 3$). The mean age of first onset of MDD was 28.3 years. Participants had a history of medical treatment for depression in 96% of all cases. In half of the studies ($N = 3$) participants were free of antidepressant medication (ADM) for at least 3 months prior to baseline assessment, one study allowed baseline use of ADM, and two studies included participants, who had been receiving m-ADM for at least the preceding 6 months. Four studies compared MBCT (+ TAU; henceforth just MBCT) to TAU, one compared MBCT to m-ADM, and one three-arm-trial compared MBCT, m-ADM, and PLA. Follow-up periods (from pre-treatment to final assessment) were 14 months ($N = 4$), 15 months ($N = 1$), and 18 months ($N = 1$). All studies reported relapse/recurrence in the form of a new MDD episode according to the *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edition revised (DSM-III-R), or 4th edition, (DSM-IV) (American Psychiatric Association, 1987, 1994).

The methodological quality of MBCT trial reports, including the revised Jadad criteria, is reported in Table 2. The studies achieved Jadad scores in the range of 2 to 4 points ($M = 3.00$, $SD = 0.63$).

3.3. Quantitative data synthesis

3.3.1. MBCT versus controls

Risk ratios for five studies comparing MBCT to controls (TAU or PLA) are shown in Fig. 2. The sample included relapse data on 408 participants. Risk ratios varied from 0.44 to 0.93 with an overall mean of 0.66 (95% CI [0.53, 0.82], $z = 3.81$, $p = 0.0001$), corresponding to a relative risk reduction of 34% in favor of MBCT. The relapse rate for MBCT participants ($n = 200$) was 38%, compared to 58% for controls ($n = 208$). There was no evidence of heterogeneity between the
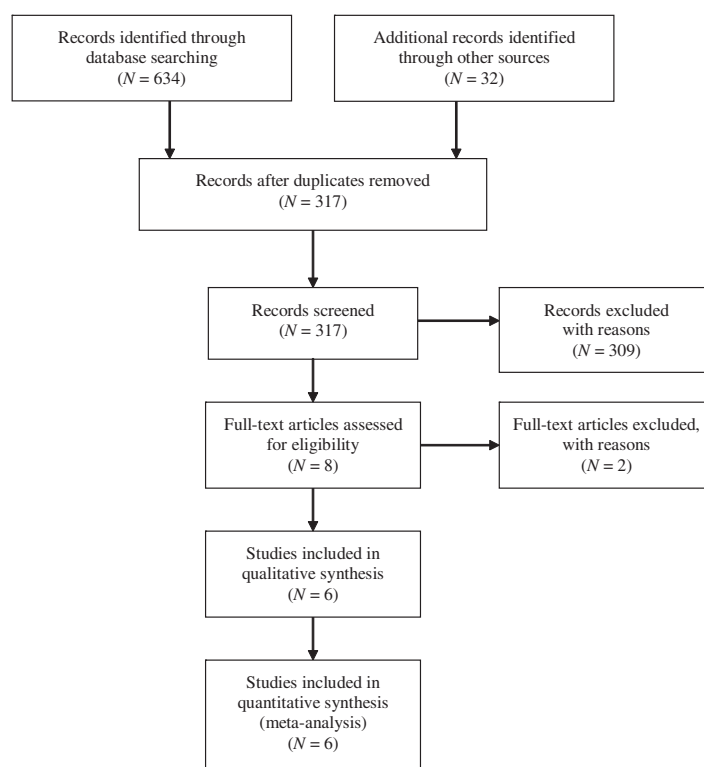

Fig. 1. Flow of information from identification to inclusion of studies.

Table 1
Characteristics of studies.

Study	n*	Participants	Percent women	Mean age	Mean baseline depression score	Previous Episodes; M or Mdn	Mean age of first onset	History of antidepressant medication (%)	Groups (n/protocol dropouts/included in meta-analysis)	Non-study medical/psychosocial treatments for depression during follow-up period (%)	Follow-up period
Bondolfi et al. (2010)	60	Recurrent MDD in remission for at least three months with three or more prior episodes; MADRS score ≤13 (≈ HAM-D≤10) at baseline; free of ADM for the preceding 3 months	72	47[a]	MADRS=3.5[a] / BDI-II=8.0[a]	4.0[a]	25[a]	100	MBCT (31/4/27) / TAU (29/1/28)	36/46[b] / 31/55[b]	14 months
Godfrin and van Heeringen (2010)	106	Recurrent MDD in remission for at least two months with three or more prior episodes; HAM-D score <14 at baseline; current ADM allowed	81	46	HAM-D=6.9 / BDI-II=20.0	NR	30	77	MBCT (52/18/40) / TAU (54/12/47)	73/27[c] / 64/28[d] / 61/13[c] / 62/13[d]	14 months
Kuyken et al. (2008)	123	Recurrent MDD in remission from recent episode with three or more prior episodes; on m-ADM for at least the preceding 6 months	77	49	HAM-D=5.7 / BDI-II=19.3	6.4	26	100	MBCT (61/9/61) / m-ADM (62/10/62)	25/NR[e] / NR/NR	15 months
Ma and Teasdale (2004)	75	Recurrent MDD in remission for at least three months with two or more prior episodes; HAM-D score <10 at baseline; free of ADM for the preceding 3 months	76	45	HAM-D=5.7 / BDI=14.3	3.0[a]	31	100	MBCT (37/6/36) / TAU (38/1/37)	19/19[b] / 35/22[b]	14 months
Segal et al. (2010)	84	Recurrent MDD in remission for at least seven months with three or more prior episodes; HAM-D score during remission ≤7 with occasional elevated scores between 8 and 14; on m-ADM for at least the preceding 7 months	63	44	HAM-D=2.8	4.7	31	100	MBCT (26/5/26) / m-ADM (28/7/28) / PLA (30/6/30)	NR/NR[f] / NR/NR[f] / NR/NR[f]	18 months
Teasdale et al. (2000)	145	Recurrent MDD in remission for at least 3 months with two or more episodes; HAM-D score <10 at baseline; free of ADM for the preceding 3 month	76	43	HAM-D=3.5 / BDI=10.0	3.3[a]	27	100	MBCT (76/14/71) / TAU (69/3/66)	45/49[b] / 40/34[b]	14 months

Note. ITT = intention-to-treat; MDD = major depressive disorder; MADRS = Montgomery–Asberg Depression Rating Scale (Montgomery & Asberg, 1979); HAM-D = Hamilton Depression Rating Scale (Hamilton, 1960); ADM = antidepressant medication; BDI-II = Beck Depression Inventory-II (Beck et al., 1996); MBCT = mindfulness-based cognitive therapy; TAU = treatment as usual; m-ADM = maintenance antidepressant medication; BDI = Beck Depression Inventory (Beck et al., 1961); and PLA = pill placebo + clinical management.
[a] Median.
[b] Once or more at any time during the follow-up period.
[c] Baseline assessment.
[d] Final follow-up assessment.
[e] 6-month follow-up assessment.
[f] Although numbers were not reported, patients who assessed non-study treatments for depression without a documented relapse were treated as censored observations in the data analysis.
* Number of randomized participants.

Table 2
Methodological quality of MBCT trial reports.

Authors (date)	Was the trial randomized?	Was the randomization procedure described and was it appropriate?	Was the treatment allocation concealed?	Were groups similar at baseline on prognostic indicators?	Were blind outcome assessments conducted?	Was the number of withdrawals/dropouts in each group mentioned?	In addition to stating the number of withdrawals/dropouts, were reasons given for each group?	Was an analysis conducted on the intention-to-treat sample?	Was a power calculation described?	Jadad score (revised, maximum score=4)
Bondolfi et al. (2010)	**Yes**	**Yes**	Yes	Yes	**Yes**	Yes	**No**	Yes[a]	Yes	3
Godfrin and van Heeringen (2010)	**Yes**	**Yes**	Yes	Yes	No	Yes	**No**	No	Yes	2
Kuyken et al. (2008)	**Yes**	**Yes**	Not clear	Yes	**Yes**	Yes	**Yes**	Yes	No	4
Ma and Teasdale (2004)	**Yes**	**Yes**	Yes	Yes	**Yes**	Yes	**No**	No[b]	No	3
Segal et al. (2010)	**Yes**	**Yes**	Yes	Yes	**Yes**	Yes	**No**	Yes	No	3
Teasdale et al. (2000)	**Yes**	**Yes**	Yes	Yes	**Yes**	Yes	**No**	No[b]	Yes	3

Note. Columns in bold constitute the revised Jadad Scale.
[a] ITT data was inappropriate, as patients with incomplete follow-up data were treated as survivors.
[b] Almost all cases (97%, 94%) included in the analyses.

Study or Subgroup	MBCT Events	MBCT Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 MBCT vs TAU						
Bondolfi 2010	9	27	10	28	8.6%	0.93 [0.45, 1.93]
Godfrin 2010	12	40	32	47	17.3%	0.44 [0.26, 0.74]
Ma 2004	14	36	23	37	19.7%	0.63 [0.39, 1.01]
Teasdale 2000	31	71	38	66	40.3%	0.76 [0.54, 1.06]
Subtotal (95% CI)		174		178	85.9%	0.66 [0.50, 0.87]
Total events	66		103			

Heterogeneity: Tau² = 0.02; Chi² = 3.96, df = 3 (P = 0.27); I² = 24%
Test for overall effect: Z = 2.99 (P = 0.003)

Study or Subgroup	MBCT Events	MBCT Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.2 MBCT vs PLA						
Segal 2010	10	26	18	30	14.1%	0.64 [0.36, 1.13]
Subtotal (95% CI)		26		30	14.1%	0.64 [0.36, 1.13]
Total events	10		18			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.54 (P = 0.12)

Study or Subgroup	MBCT Events	MBCT Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Total (95% CI)		200		208	100.0%	0.66 [0.53, 0.82]
Total events	76		121			

Heterogeneity: Tau² = 0.00; Chi² = 3.97, df = 4 (P = 0.41); I² = 0%
Test for overall effect: Z = 3.81 (P = 0.0001)
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.94), I² = 0%
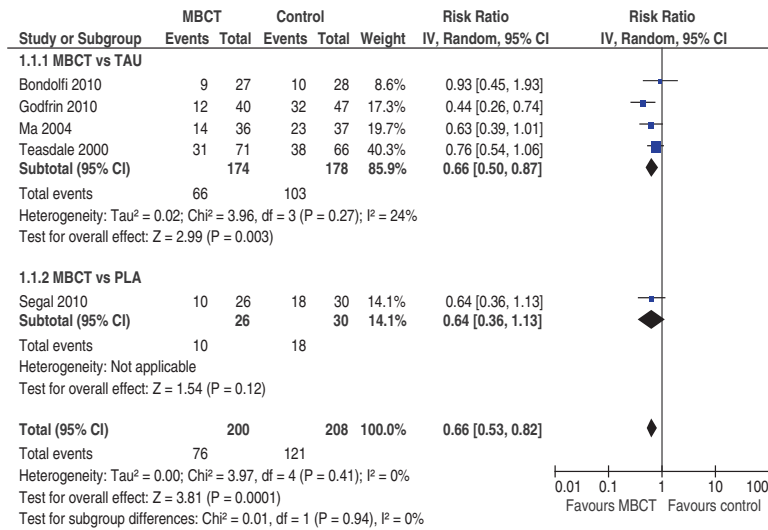
Favours MBCT   Favours control

Fig. 2. Comparison of risk of relapse between MBCT and controls, including ES statistics. Note. MBCT = mindfulness-based cognitive therapy; CI = confidence interval; TAU = treatment as usual; and PLA = placebo. Figure explanation: The first left-sided column shows included studies categorized into two subgroups according to use of different control conditions. The next columns indicate number of relapses (events) and total number of participants within MBCT and controls. The column "Weight" shows the weight ascribed to each individual study, taking into account the study sample size and precision of result (see text for an explanation). The column "Risk Ratio" shows the relative risk of relapse between MBCT and controls together with the confidence interval. A risk ratio below 1 favors MBCT, while a risk ratio above 1 favors the control group. The final column is a forest plot of the risk ratios. The length of the horizontal lines for each risk ratio within the forest plot indicates the interval of confidence, while the size of the squares indicates the size of the study sample. The bottom row of the figure shows the overall results.

studies ($I^2 = 0\%$, p = 0.41). The Fail Safe N analysis indicated that 14 missing equal sample size studies with no effect of MBCT compared to controls (i.e., a risk ratio of 1.0), would be needed to reduce the overall risk of relapse ES to a non-significant level (p > 0.05). Fig. 3 shows a plot of ESs in relation to the ES standard error. Eggers regression test showed no evidence of asymmetry in the ES funnel plot (t = 0.220, df = 3, p = 0.42), and the Trim and Fill method indicated that no missing studies (falling to the right of the overall mean ES) were needed to make the plot symmetric.

3.3.2. Number of prior episodes

Three studies comparing MBCT to controls in the form of TAU or PLA (Bondolfi et al., 2010; Godfrin & van Heeringen, 2010; Segal
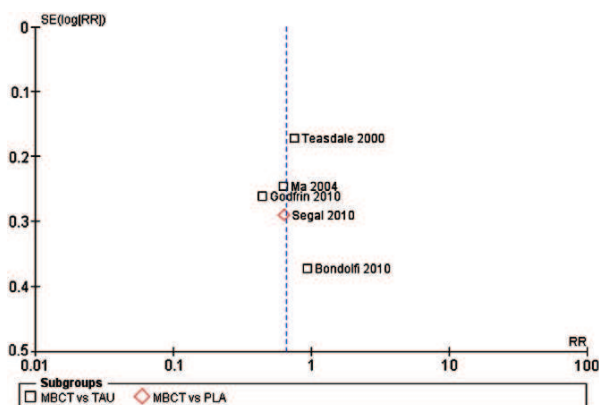

Fig. 3. Funnel plot of standard error by ESs for relative risk of relapse between MBCT and controls. Note. SE = standard error; RR = risk ratio; MBCT = mindfulness-based cognitive therapy; TAU = treatment as usual; and PLA = placebo. The funnel plot indicates absence of publication bias when individual study effect sizes (risk ratios) are relatively symmetrically distributed around the overall mean effect size, which is marked by the broken vertical line in the middle of the figure.

et al., 2010) only included participants with three or more previous MDD episodes, while two studies (Ma & Teasdale, 2004; Teasdale et al., 2000) had stratified prior to randomization on this variable, and separately analyzed relapse rates for this subgroup of patients. Risk ratios for MBCT and controls in these five studies reporting relapse data on participants with three or more prior episodes varied from 0.44 to 0.93 with an overall mean of 0.57 (95% CI [0.45, 0.72]), corresponding to a relative risk reduction of 43% in favor of MBCT (see Fig. 4). This overall mean ES was highly significant (z = 4.83, p < 0.00001), and there was no evidence of heterogeneity between the studies ($I^2 = 0\%$, p = 0.46). Relapse rates for this particular subgroup of patients were 36% and 63% for MBCT (n = 176) and controls (n = 182), respectively. The Fail Safe N for risk of relapse in participants with three or more previous episodes was 23, indicating that 23 missing studies with a risk ratio of 1.0 were needed to bring the observed mean ES to a non-significant level (p > 0.05). There was no evidence of funnel plot asymmetry using Eggers regression test (t = 0.59, df = 3, p = 0.30), or the Trim and Fill method.

Two studies (Ma & Teasdale, 2004; Teasdale et al., 2000) provided relapse data for a subgroup of participants with only two previous episodes of depression (n = 50). The overall risk ratio of 0.51 (95% CI [0.25, 1.05]) for relapse in this subgroup of patients showed a trend towards significance (z = 1.82; p = 0.07) favoring TAU compared to MBCT. Relapse rates were 27% for TAU participants, compared to 54% for MBCT participants.

3.3.3. MBCT versus m-ADM

Two studies compared MBCT to m-ADM. In the study by Kuyken et al. (2008), 123 participants in primary care with at least 3 MDD episodes on ADM for the previous 6 months in full or partial remission were randomized to either MBCT + ADM tapering, or m-ADM administered by the general practitioner in line with standard clinical practice and the British National Formulary. 75% of participants in the MBCT group had completely discontinued their ADM at 6 month follow-up. The three-arm-study by Segal et al. (2010) included arms of MBCT + ADM tapering (n = 26) and m-ADM (n = 30). Participants

Study or Subgroup	MBCT Events	MBCT Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
1.1.1 MBCT vs TAU							
Bondolfi 2010	9	27	10	28	9.8%	0.93 [0.45, 1.93]	
Godfrin 2010	12	40	32	47	19.8%	0.44 [0.26, 0.74]	
Ma 2004	10	28	21	27	18.1%	0.46 [0.27, 0.79]	
Teasdale 2000	22	55	33	50	36.1%	0.61 [0.41, 0.89]	
Subtotal (95% CI)		150		152	83.8%	0.56 [0.42, 0.73]	
Total events	53		96				
Heterogeneity: Tau² = 0.01; Chi² = 3.42, df = 3 (P = 0.33); I² = 12%							
Test for overall effect: Z = 4.25 (P < 0.0001)							
1.1.2 MBCT vs PLA							
Segal 2010	10	26	18	30	16.2%	0.64 [0.36, 1.13]	
Subtotal (95% CI)		26		30	16.2%	0.64 [0.36, 1.13]	
Total events	10		18				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.54 (P = 0.12)							
Total (95% CI)		176		182	100.0%	0.57 [0.45, 0.72]	
Total events	63		114				
Heterogeneity: Tau² = 0.00; Chi² = 3.62, df = 4 (P = 0.46); I² = 0%							
Test for overall effect: Z = 4.83 (P < 0.00001)							
Test for subgroup differences: Chi² = 0.19, df = 1 (P = 0.66), I² = 0%							

0.01   0.1   1   10   100
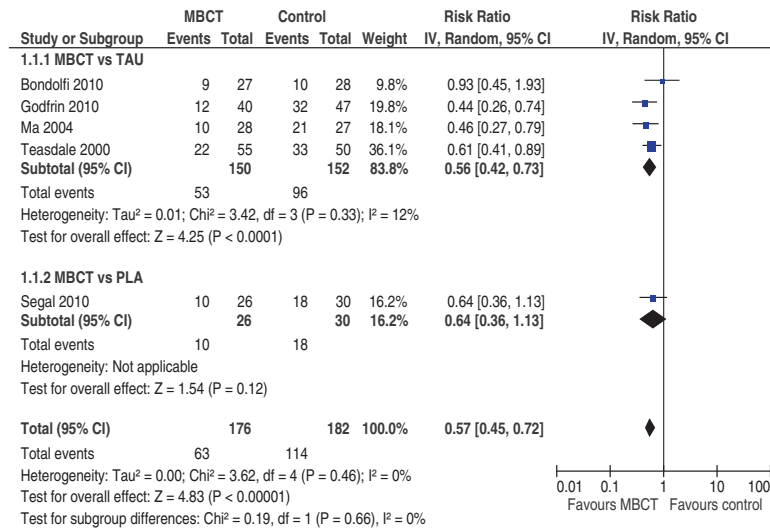Favours MBCT   Favours control

Fig. 4. Comparison of risk of relapse between MBCT and controls for participants with three or more previous episodes of major depression, including ES statistics. For figure explanation, see caption for Figure 2.

with at least 3 MDD episodes had been on ADM (primarily venlafaxine) with remission for at least seven months prior to randomization. ADM was administered according to a protocol by study psychiatrists with the same drug at the maximum tolerated effective dose in the study period. ADM in the MBCT condition was tapered gradually via reduced pill count during a 4-week period.

The combined relative risk ratio for MBCT versus m-ADM in the two studies was 0.80 (95% CI [0.60, 1.08], z = 1.45, p = 0.15), corresponding to a non-significant MBCT risk reduction of 20%, with no evidence of heterogeneity between the studies (I² = 0%, p = 0.91; see Fig. 5).

3.3.4. Regression analyses

Using risk of relapse ESs (the logarithm of risk ratios) as the dependent variable in meta-regression analyses of studies comparing MBCT to controls (shown in Fig. 2), no evidence of ES moderation was found by either publication year (B = −0.024, SE = 0.024, p = 0.31), sample size (B = 0.002, SE = 0.003, p = 0.57), or study quality (B = 0.144, SE = 0.260, p = 0.58). These analyses were underpowered and results should be interpreted with caution.

4. Discussion

The overall risk ratio for relapse or recurrence in MBCT versus control groups (TAU or PLA) of 0.66 in this meta-analysis is highly significant, indicating that MBCT (added to TAU) is an effective intervention for relapse prevention in recurrent MDD in remission. The ES corresponds to a relative risk reduction of 34%, with relapse rates of 38% and 58% for MBCT and controls, respectively. As can be seen from Table 2, the studies are generally of a high methodological

quality with a mean revised Jadad score of 3 out of max 4. There was no evidence of heterogeneity between individual studies, and no evidence of publication bias according to tests of funnel plot asymmetry. Fourteen missing studies of comparable sample size with an ES of zero would be needed to nullify the result. Therefore, the overall result of this meta-analysis should be considered credible.

A very substantial difference was found for the subgroup of participants with three or more previous episodes of MDD, in that the relapse rate for MBCT here was 36%, compared to 63% for control conditions (TAU or PLA), corresponding to a relative risk reduction of 43%.

On the other hand, it should be noted that the result for participants with only two episodes of MDD (n = 50) tendentially showed a lower risk of relapse for TAU compared to MBCT (relative risk reduction = 49%; p = 0.07). The tendentially higher relapse rate among MBCT treated patients with only two episodes is a rather paradoxical finding, since MBCT has been found generally to benefit depressed patients (Chiesa & Serretti, 2011; Hofmann et al., 2010), and since patients with three or more episodes formerly must have been patients with only two episodes. Teasdale et al. (2000) and Ma and Teasdale (2004) found that patients with two episodes reported later first episode onset, and Ma and Teasdale (2004) also found that such patients also reported less childhood adversity. They suggest that patients with only two episodes in their studies were derived from a less vulnerable population, less likely to suffer from dysphoria-activated depressive rumination that may be considered a primary target of MBCT. Indeed, Ma and Teasdale (2004) found that relapse was more often associated with significant life events in patients with only two prior episodes compared to patients with three or more episodes. They argue that MBCT may be ineffective for reducing relapse/recurrence provoked by stressful life events.
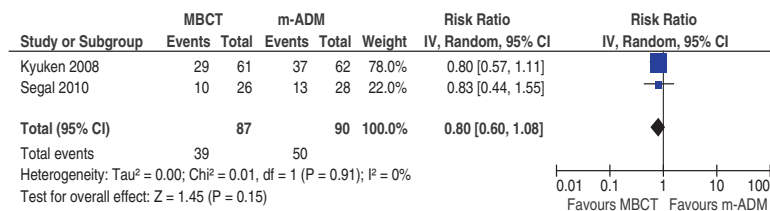

Study or Subgroup	MBCT Events	MBCT Total	m-ADM Events	m-ADM Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Kyuken 2008	29	61	37	62	78.0%	0.80 [0.57, 1.11]	
Segal 2010	10	26	13	28	22.0%	0.83 [0.44, 1.55]	
Total (95% CI)		87		90	100.0%	0.80 [0.60, 1.08]	
Total events	39		50				
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.91); I² = 0%							
Test for overall effect: Z = 1.45 (P = 0.15)							

0.01   0.1   1   10   100
Favours MBCT   Favours m-ADM

Fig. 5. Comparison of risk of relapse between MBCT and m-ADM, including ES statistics. Note. MBCT = Mindfulness-based cognitive therapy; and m-ADM = maintenance antidepressant medication. For further figure explanation, see caption for Fig. 2.

The non-significant higher relapse among MBCT participants with only two prior episodes could, of course, be a chance event. It should be noted, however that Segal et al. (2010) also found that MBCT did not reduce relapse risks compared to PLA for a subgroup of participants; namely those characterized by a stable remission period following three or more MDD episodes. Like number of depressive episodes, unstable remission has been found to be a negative prognostic variable in MDD (Nierenberg et al., 2010). Therefore, the possibility should be considered that MBCT may not be so helpful for remitted MDD patients with a lesser degree of risk of relapse.

Although more studies are needed for firm conclusions, results from the quantitative data synthesis of two studies suggest that MBCT is at least comparable to m-ADM for effective relapse prevention of recurrent MDD with three or more episodes. If tenable, this conclusion is of high practical importance, since m-ADM is generally recommended for such cases, and many patients will prefer a psychological alternative with no adverse medical side-effects. It is further worth noting that one of these studies found that MBCT was more effective than m-ADM for reducing residual depressive symptoms and improving quality of life (Kuyken et al., 2008).

MBCT is apparently a cost-efficient strategy for relapse prevention. Two studies (Ma & Teasdale, 2004; Teasdale et al., 2000) respectively reported that MBCT on average required less than 3 and 5 therapist contact hours per patient. The one study with actual cost-effectiveness calculations (Kuyken et al., 2008) found estimated annual per-patient total costs for the first 15 months of $2767 and $2340 for the MBCT and m-ADM conditions respectively (difference not significant). The incremental cost-effectiveness ratio for MBCT was estimated to be $962 per prevented relapse/recurrence, and $50 per depression-free day. MBCT was less expensive than m-ADM for the last three of the 15 months, perhaps indicating a more favorable cost-effectiveness of MBCT in the long run. Since MBCT can be delivered in groups with up to 15 participants, it is, anyhow, a low cost psychological intervention.

The present meta-analysis has several limitations. No formal protocol was developed before the review was carried out, although the study was highly focused, with pre-specified aims, inclusion criteria and methods of analysis. The search strategy only included studies published or accepted for publication. It is, however, unlikely that major accomplished studies are not published or close to publishing, due to the area's high degree of current interest. There is still a relatively small number of RCTs, thus limiting the value of sub-group analyses, and only two studies comparing MBCT with m-ADM. The studies do not allow for conclusions about the specific effects of MBCT, since there are no studies with psychological placebo or componential control. Only one study of the cost-effectiveness of MBCT was located.

In conclusion, this meta-analysis supports use of MBCT as a low cost intervention for relapse prevention in recurrent MDD in remission, at least in case of three or more previous episodes. Future research should investigate the differential effects of MBCT for patients with low and high risk of relapse; due to the few data on patients with only two prior episodes, it may be premature to exclude such patient, as has been done in most recent studies. More rigorous designs to investigate specific effects and change mechanisms of MBCT should also be considered.

Acknowledgments

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Paper 3

Piet, J., Würtzen, H., & Zachariae, R. (2012). The effect of mindfulness-based therapy on symptoms of anxiety and depression in adult cancer patients and survivors: A systematic review and meta-analysis. *Journal of Consulting and Clinical Psychology*. Advance online publication. doi: 10.1037/a0028329

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

Jacob Piet
Aarhus University

Hanne Würtzen
Danish Cancer Society Research Center

Robert Zachariae
Aarhus University Hospital and Aarhus University

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

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

Anxiety and depression are common and debilitating problems associated with diagnosis and treatment of cancer. Compared to the general population, depression is more prevalent in cancer patients (e.g., Christensen et al., 2009; Honda & Goodwin, 2004), and depression has been associated with prolonged hospitalization (Prieto et al., 2002), higher mortality (Pinquart & Duberstein, 2010), and reduced quality of life (Reich, Lesur, & Perdrizet-Chevallier, 2008). The deteriorating effect of depression on health may be larger when depression is comorbid with a medical disease (Moussavi et al., 2007). Apparently, there is a bidirectional relationship between cancer and depression. The prevalence of depression increases with severity of cancer, and there is some evidence to suggest that depression predicts cancer progression (Spiegel & Giese-Davis, 2003). Recent research indicates that depression is associated with various biological markers of inflammation, including so-called pro-inflammatory cytokines (e.g., Howren, Lamkin, & Suls, 2009). Following an infection, the physiological concentrations of pro-inflammatory cytokines have been found to induce symptoms of sickness, including fatigue, sleepiness, loss of appetite, and social withdrawal (Dantzer & Kelley, 2007). From these observations, it has been hypothesized that pro-inflammatory cytokines, due to prolonged activation of the peripheral immune system in some medically ill people, including cancer patients, may act on the brain in ways that lead to the development of symptoms of depression (Dantzer, O'Connor, Freund, Johnson, & Kelly, 2008).

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

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

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

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

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

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

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

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

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

Method

Inclusion Criteria

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

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

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

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

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

Search Strategies

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

Coding Procedures

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

Statistical Methods

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

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

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

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

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

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

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

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

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

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

Results

Study Selection

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

Study Characteristics

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

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

$$d = \frac{\Delta_1 - \Delta_2}{\sqrt{\dfrac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{n_1 + n_2 - 2}}},$$ where Δ_1 and Δ_2 are the mean pre–post

change scores for the treatment group and control condition, respectively; n_1 and n_2 are the sample sizes of each group; and S_1 and S_2 are the standard deviations of the posttreatment scores for each group. Cohen's d was then converted to Hedges's g using correction factor J. For controlled ESs, $J = 1 - \dfrac{3}{4df - 1}$, where df is the degrees of freedom used to estimate the within-groups standard deviation, pooled across groups. The degrees of freedom for calculating J for two independent groups are $n_1 + n_2 - 2$. Then, $g = J \times d$.
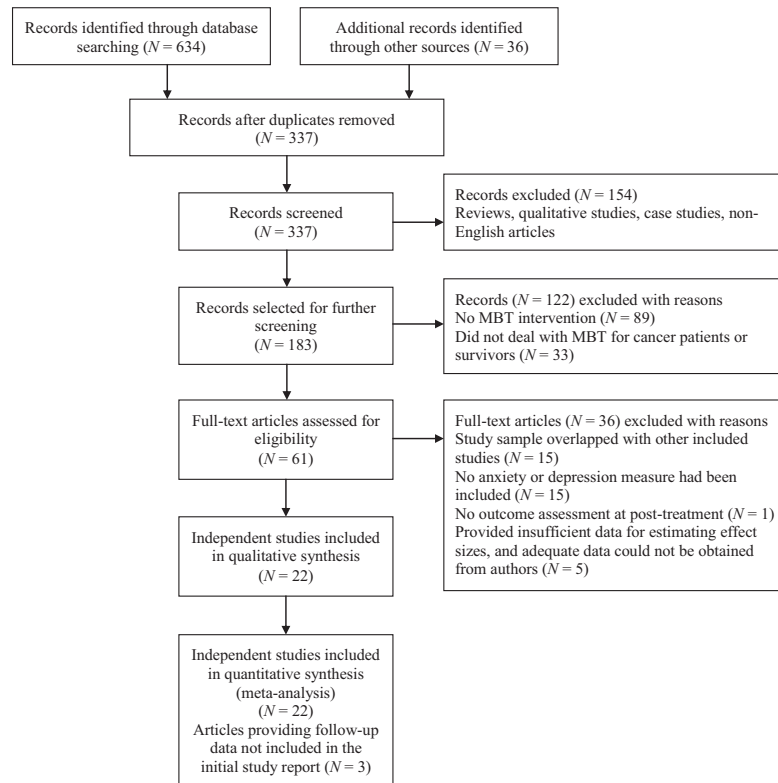
Figure 1. Flow of information from identification to inclusion of studies. MBT = mindfulness-based therapy.

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

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

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

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

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

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

Table 1
Description of Included Studies

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

(table continues)

Table 1 (*continued*)

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

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

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

Quantitative Data Synthesis of Nonrandomized Studies

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

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

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

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

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

Quantitative Data Synthesis of Randomized Controlled Trials

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

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

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

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

Table 2

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

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

Note.   The table shows overall effect size estimates for change in measures of anxiety, depression, and mindfulness, presented with 95% CIs, p values for the test of significance, and statistics for tests of heterogeneity and publication bias. Effect sizes for nonrandomized studies were based on pre–post within-group differences, while effect sizes derived from randomized controlled trials were based on mean pre- to posttreatment change scores for both mindfulness-based therapy and control conditions. K = number of studies; n = number of participants; CI = confidence interval.
[a] Fail-safe N is the estimated number of unpublished studies with an effect size of zero needed to reduce the overall result to a nonsignificant level ($p > .05$).   [b] A fail-safe N exceeding the criterion ($5 \times K + 10$) indicates a robust result, that is, no evidence of publication bias.

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

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

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

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

Discussion

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

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

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

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

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

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

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

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

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

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

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

A number of limitations should also be noted. As with any meta-analysis, the study was limited by its inclusion criteria and basic statistical assumptions. All participants were diagnosed with cancer, mostly breast cancer, but cancer stage and time since diagnosis varied both within and between studies. Therefore, conclusions cannot be drawn about the differential effects of MBT for different patients with regard to these characteristics. Furthermore, the majority of participants were women with breast cancer, and results should not be generalized to male cancer populations. Although study outcomes were restricted to continuous and validated measures of symptoms of anxiety and depression, specific measures applied varied across studies. A major shortcoming of the currently available literature on MBT for reducing symptoms of anxiety and depression among cancer patients is the lack of samples systematically diagnosed with mood or anxiety disorders and the poor methodological quality of many study reports. Using the modified Jadad criteria, we found considerable variation in the quality of included studies. The average quality score for the 13 nonrandomized studies ($n = 448$) was 0.5, compared to an average quality score of 2.9 for the nine included RCTs ($n = 955$).

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

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

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

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

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