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Review article

Mindfulness based cognitive therapy for psychiatric disorders: A systematic review and meta-analysis

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ABSTRACT

Mindfulness- based Cognitive Therapy (MBCT) is a meditation program based on an integration of Cognitive behavioural therapy and Mindfulness-based stress reduction. The aim of the present work is to review and conduct a meta-analysis of the current findings about the efficacy of MBCT for psychiatric patients. A literature search was undertaken using five electronic databases and references of retrieved articles. Main findings included the following: 1) MBCT in adjunct to usual care was significantly better than usual care alone for reducing major depression (MD) relapses in patients with three or more prior depressive episodes (4 studies), 2) MBCT plus gradual discontinuation of maintenance ADs was associated to similar relapse rates at 1 year as compared with continuation of maintenance antidepressants (1 study), 3) the augmentation of MBCT could be useful for reducing residual depressive symptoms in patients with MD (2 studies) and for reducing anxiety symptoms in patients with bipolar disorder in remission (1 study) and in patients with some anxiety disorders (2 studies). However, several methodological shortcomings including small sample sizes, non-randomized design of some studies and the absence of studies comparing MBCT to control groups designed to distinguish specific from non-specific effects of such practice underscore the necessity for further research.

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1. Introduction

In the last decade, interest in and research investigating mindfulness and mindfulness-based interventions has increased exponentially (Baer, 2003; Chiesa and Serretti, 2010). Mindfulness is currently defined in psychological terms as being characterized by paying total attention to the present moment with a non-judgmental awareness of inner and outer experiences (Kabat-Zinn, 1994). Increasing evidence suggests the potential usefulness of mindfulness-based interventions for the treatment of a large number of physical and mental disorders (Lynch et al., 2007; Pull, 2009; Chiesa and Serretti, 2010) as well as for the reduction of stress levels in healthy subjects (Chiesa and Serretti, 2009).

One of the most widely diffused mindfulness-based interventions is Mindfulness-based cognitive therapy (MBCT), a manualized 8-week skills-training group program (Segal et al., 2002) based upon the theoretical framework of information processing theories (Teasdale et al., 1995) and integrating aspects of Cognitive behavioural therapy for major depression (MD) (Beck et al., 1979) with components of the Mindfulness-based stress reduction program developed by Kabat-Zinn (Kabat-Zinn, 1990). MBCT was originally designed to teach patients in remission from recurrent MD to become more aware of, and to relate differently to, their thoughts, feelings, and bodily sensations. An example includes recognizing thoughts and feelings as passing events in the mind rather than necessarily accurate readouts of reality. The original program teaches skills that allow individuals to disengage from habitual, automatic dysfunctional cognitive routines as a way to reduce future risk of relapses and recurrences of MD (Segal et al., 2002).

More recently, however, MBCT has also been used for other clinical targets including, among the others, the reduction of inter-episodic depression and anxiety levels in patients suffering from bipolar disorder (BD) (e.g. Williams et al., 2008b) and the reduction of residual anxiety symptoms in patients suffering from anxiety disorders (e.g. (Kim et al., 2009)), finding preliminary support for the usefulness of MBCT for such conditions. Also, a number of uncontrolled studies have recently provided preliminary evidence for the usefulness of MBCT for patients with treatment-resistance MD (Kenny and Williams, 2007; Eisendrath et al., 2008) and for patients suffering from insomnia (Heidenreich et al., 2006; Ong et al., 2008; Yook et al., 2008), even though findings deriving from such studies should be considered with caution as very often initially positive findings derived from early uncontrolled studies are not supported when controlled studies are undertaken. Of note, while in some cases, such as for remitted BD and treatment-resistant MD patients, no adaptation of the original MBCT program was required (Kenny and Williams, 2007; Williams et al., 2008b), many adaptations including, as an example, the observation of the association between worried thoughts, mood and behaviours as well as psycho-education about cognitive distortions specific to panic disorder (PD) and generalized anxiety disorder (GAD) (Evans et al., 2008; Kim et al., 2009), were required in trials dealing with patients with non-affective psychiatric disorders such as anxiety disorders.

The importance of interventions such as MBCT that, in adjunct to standard treatments, could optimize standard care and enhance treatment outcomes can be best understood if one considers that psychiatric disorders are usually characterized by a chronic course, are related to a high social and economical burden (Mintz et al., 1992; Lish et al., 1994; Wyatt and Henter, 1995; Judd, 1997) and are only partially responsive to current treatments (Geddes et al., 2000; Scott, 2001; Goldberg et al., 2005; Scott et al., 2006; Paykel, 2007; Thuile et al., 2009). Taking as an example MD, note that it has a lifetime incidence in the United States of up to 12% in men and 20% in women (Kessler et al., 2003) and that it accounts for 4.4% of the global disease burden worldwide (World Health Organization, 2002). Unfortunately, however, according to recent findings, no more than 37% of patients suffering from MD achieve clinical remission after the first antidepressant (AD) treatment and the overall remission rate after several pharmacological treatments is about 67% (Rush et al., 2006). Additionally, despite receiving adequate psychological and/or pharmacological treatments such as cognitive psychotherapy or AD medications, patients who have experienced an MD episode carry a risk for relapse over the period of 1 year as high as 30-70% depending on prior and current therapeutic strategies (e.g (Ramana et al., 1995; Hollon et al., 2005). Taking into account such issues, the importance of interventions like MBCT, which could enhance current treatment options by reducing residual symptoms and preventing further relapses, becomes obvious, especially if one considers that MBCT also has the advantage of a group format that allows greater accessibility in clinical care.

Coelho et al. (2007) were the first authors to systematically review findings about the potential usefulness of MBCT for MD. In their review they concluded that available evidence suggested that for patients with three or more previous depressive episodes, MBCT could have an additive benefit to usual care. However, they also pointed out the notion that further research was needed to extend available findings and to clarify whether MBCT could have any specific effects (Coelho et al., 2007). More recently, Williams et al. (2008a) further pointed out the importance of authors other than the developers of the original MBCT program performing independent trials on the efficacy of such therapy for MD and for further disorders so as to provide evidence for the treatment transportability and generalizability.

Since the publication of the first reviews on this topic (Coelho et al., 2007; Williams et al., 2008a), a number of research groups have answered the call for independent trials focusing on the efficacy of MBCT for MD (e.g., Bondolfi et al., 2010; Godfrin and van Heeringen, 2010) as well as for further psychiatric disorders. Additionally Williams et al. (2008a) answered a number of critical questions raised by Coelho and colleagues regarding, as an example, the absence of randomization details and the lack of data about group effect on final outcomes in their early articles.

Overall, such observations suggest the need for a new update on this topic so as to summarize the continuously increasing amount of data about MBCT for psychiatric disorders as well as to give indications for further research. Note, in fact, that even though a meta-analysis focusing on the efficacy of mindfulness-based interventions, including MBCT and MBSR, for the reduction of anxiety and depressive symptoms has recently been published (Hofmann et al., 2010), that meta-analysis provided only an overall effect size for the combination of the effects of both MBSR and MBCT on depressive and anxiety symptoms. However such meta-analysis did not provide quantitative data about the effects of MBCT over a control condition as well as data about psychological changes and further measures (e.g. changes in the quality of life (QOF)) following MBCT. In addition, little attention has been paid so far to several key issues such as therapist's experience, adherence to practice, differences in prognostic factors at baseline and further issues which could represent undetected biases in mindfulness research (Orme-Johnson, 2008).

Accordingly, the aim of the present work is to review controlled studies focusing on the usefulness of MBCT for psychiatric disorders. In particular, building on the observations stated above, the primary hypotheses of this review are as follows: 1) MBCT in adjunct to usual care could be significantly better than usual care alone for reducing MD relapses in patients with three or more prior depressive episodes and not significantly different from an “active” control group on the same outcome measure, 2) the augmentation of MBCT could be useful for reducing residual depressive symptoms in patients with MD, 3) for reducing depressive and anxiety symptoms in patients with BD with residual symptoms and 4) for reducing anxiety symptoms in patients with anxiety disorders. Additionally, we have explored the relative effects of MBCT over other treatment strategies on further

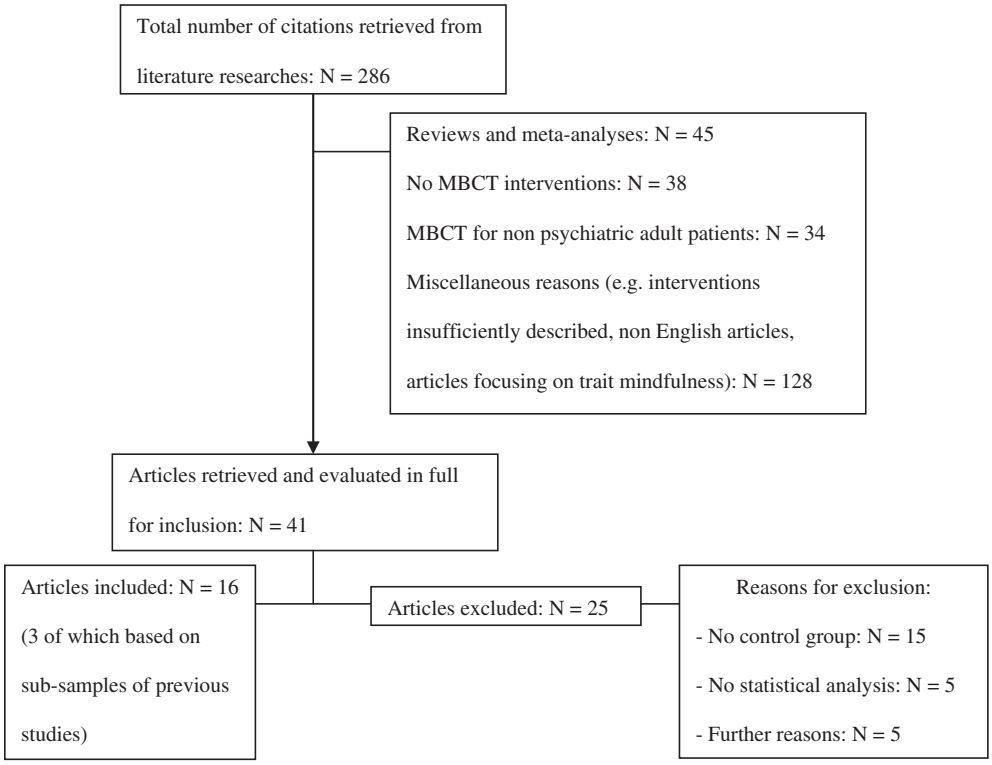

Fig. 1. Flow diagram of the review process.

measures including differences in psychological measures, QOF and cost/effectiveness of MBCT.

2. Methods

2.1. Literature research

A literature search was independently undertaken by the reviewers using MEDLINE, ISI web of science, the Cochrane database, EMBASE, PsychINFO and references of retrieved articles. The search included papers indexed by web based electronic databases mentioned above published up to July 2010. The search strategy considered only studies published in English. The main search terms were MBCT, "mindfulness meditation" and "mindfulness based cognitive therapy" in combination with the name of each major axis I psychiatric disorder (e.g. "major depression").

2.2. Selection of trials

Two reviewers searched independently for eligible articles for inclusion. Included studies had to: 1) investigate the efficacy of a MBCT intervention for patients suffering from psychiatric disorders, 2) provide quantitative data supported by statistical methodology, 3) include a control group procedure that was either inactive (for example a waiting list) or active (possibly oriented to control for nonspecific effects of MBCT such as group support, teacher's care and expectancy effect). Exclusion criteria were the following: 1) qualitative reports, 2) studies investigating non-psychiatric samples or mixed populations of patients (e.g. healthy subjects and MD patients joined together), 3) case reports and case series, 4) admixture of different techniques and 5) literature reviews.

2.3. Outcome measures

The main considered outcome measures were 1) differences in 1-year relapse and recurrence rates in patients suffering from MD assigned to MBCT or to a control group, 2) differences between post-intervention Beck Depression Inventory (BDI) (Beck et al., 1961) scores in partially remitted or non-remitted patients suffering from MD or BD assigned to MBCT or to a control group, (for studies focusing on patients in full remission it was assumed that the 8 weeks BDI scores were not significantly different from baseline scores, in accordance with data provided by the authors of such studies (e.g. (Teasdale et al., 2000; Ma and Teasdale, 2004)), 3) differences between post intervention Beck Anxiety Inventory (BAI) (Beck et al., 1988) scores in partially remitted or non remitted patients suffering from BD and anxiety disorders assigned to MBCT or to a control group. All such analyses were stratified for the disorder under investigation and for the type of control groups. Secondary outcome measures included 1) mean time to relapse in MD patients, 2) improvements gained after the MBCT program in psychological measures other than those mentioned above (e.g., Symptom Checklist 90 (SCL-90) (Derogatis et al., 1973)), 3) changes in QOF following MBCT and 4) cost/effectiveness of MBCT. For all primary outcome measures, a meta-analytic approach was used. Secondary outcome measures were reported in a narrative way.

Table 1
Excluded studies.

Study	Reason for exclusion
(Mason and Hargreaves, 2001)	No statistical analysis
(Watkins and Teasdale, 2004)	No control group
(Surawy et al., 2005)	No control group, admixture of different mindful techniques
(Finucane and Mercer, 2006)	No statistical analysis
(Kenny and Williams, 2007)	No control group
(Smith et al., 2007)	No statistical analysis
(Williams et al., 2007)	Case report
(Bertschy et al., 2008)	No statistical analysis
(Eisendrath et al., 2008)	No control group
(Kumar et al., 2008)	No control group
(Michalak et al., 2008)	No control group
(Williams et al., 2008a)	Article providing further details on past studies *
(Yook et al., 2008)	No control group
(Craigie et al., 2008)	No control group
(Evans et al., 2008)	No control group
(Raes et al., 2009)	Mixed population of patients
(Wilkinson-Tough et al., 2010)	Case series
(Allen et al., 2009)	No statistical analysis
(Baum et al., 2010)	No control group, admixture of different populations
(Miklowitz et al., 2009)	No control group
(Lovas and Barsky, 2010)	No control group
(Weber et al., 2010)	No control group
(Kim et al., 2010)	No control group
(Williams et al., 2010)	Non experimental article
(Miklowitz et al., 2009)	No control group

* Note that, although this study appears in the excluded studies, details reported in this article have been considered to improve the understanding of the methodological quality of two previous studies (Teasdale et al., 2000; Ma and Teasdale, 2004).

Table 2
Included studies and main details.

Study	Participants	Duration of trial (weeks)	MBCT/ Comparison group	ITT subjects	Primary outcome measures	Main findings
(Teasdale et al., 2000, 2002; Williams et al., 2000)	MD patients with 2 or more previous episodes in remission	60	MBCT + TAU TAU	76 69	Prevention of MD relapses and recurrences	Patients with 3 or more prior DE in the MBCT group showed significantly lower relapse rates at 1 year follow-up in comparison with the control group (22/55 vs. 33/50 respectively: $p<0.01$). No significant difference was observed in the subgroup of patients with only 2 prior DE at the same endpoint (9/16 vs. 5/16: $p>0.10$). Analyses in a sub-set of patients (MBCT + TAU group = 21; TAU group = 20) showed greater increases between pre-treatment and 8 weeks follow-up in the mean proportion of retrieved memories for specific and categoric events in the MBCT group as compared with the control group ($p<0.05$ and $p<0.01$ respectively)
Ma and Teasdale (2004)	MD patients with 2 or more previous DE in remission	60	MBCT + TAU TAU	37 38	Prevention of MD relapses and recurrences	Patients with 3 or more prior DE in the MBCT group showed significantly lower relapse rates at 1 year follow-up in comparison with the control group (10/28 vs. 21/27 respectively: $p=0.001$). No significant difference was observed in the subgroup of patients with only 2 prior DE at the same endpoint (4/8 vs. 2/10: $p>0.10$)
Kingston et al. (2007)	MD patients with 3 or more previous DE and residual depressive symptoms	8	MBCT + TAU TAU	8 11	Reduction of residual depressive symptoms (as measured with BDI)	Greater decreases in the BDI scores from pre-treatment to follow-up were observed in the MBCT group as compared with the control group ($p<0.05$)
Williams et al. (2008b)	Recurrently MD and BD patients with suicidal ideation in remission	8	*MD* MBCT + TAU TAU *BD* MBCT + TAU TAU	 21 20 7 7	Reduction of inter-episodic depression and anxiety symptoms (as measured with BDI and BAI respectively)	Significantly higher decreases in the BAI scores were observed in the MBCT group of BD patients as compared with the control group from pre-treatment to the endpoint ($p=0.009$). No significant difference was observed in the decrease of the BAI scores in the MBCT group of MD patients as compared with the control group as well as in the decreases of BDI scores in both MD and BD patients
Kuyken et al. (2008)	MD patients with 3 or more previous DE in full or partial remission	78	MBCT + discontinuation of ADM ADM	61 62	Prevention of MD relapses and recurrences	The MBCT group did not significantly differ from the control group in terms of relapse rates at 1 year (29/61 vs. 37/62 respectively ($p=0.21$). However the MBCT group reported significantly lower endpoint HAMD and BDI scores in comparison with the control group ($p=0.06$ and 0.04 respectively) as well as significantly higher improvements in several domains of the QOF (all p-values <0.05)
Crane et al. (2008)	MD and BD (with no manic episodes within the previous 6 months) patients with at least 1 DE and suicidal ideation with residual depressive symptoms	8	MBCT + TAU TAU	19 (6 BD) 23 (7 BD)	Reduction of residual depressive symptoms (as measured with BDI)	By the end of treatment the MBCT group had significantly smaller self discrepancies than the TAU group ($p=0.04$). Additionally, in the MBCT group the more the participants let go of unhelpful self guides, the more they shifted towards having smaller discrepancies between actual and ideal self at the end of treatment

Table 2 (*continued*)

Study	Participants	Duration of trial (weeks)	MBCT/ Comparison group	ITT subjects	Primary outcome measures	Main findings
Barnhofer et al. (2009)	Currently symptomatic patients with at least 3 previous DE and a history of suicidal ideation	8	MBCT + TAU TAU	16 15	Reduction of residual depressive symptoms (as measured with BDI)	A significantly higher decrease in BDI scores from baseline to endpoint was observed in the MBCT as compared with the control group ($p<0.001$). Six participants in the MBCT group achieved remission as compared with 1 participant only in the control group ($p=0.04$).
Hepburn et al. (2009)	MD patients in remission with 3 or more previous DE and a history of suicidality	8	MBCT + TAU TAU	33 35	-	By the end of treatment, BDI scores were significantly lower in the MBCT group than in the control group ($p<0.01$). Although any of the two groups showed significant reductions in thought suppression at endpoint, significantly reduced self-reported attempts to suppress thoughts were observed in the MBCT group ($p<0.01$)
Kim et al. (2009)	Non remitted PD and GAD patients after at least 6 months pharmacotherapy	8	DRUGS + MBCT DRUGS + ADEP	32 31	Reduction of residual anxiety symptoms (as measured with BAI)	Significantly superior decreases from baseline to endpoint were observed in the MBCT vs. ADEP group in the following measures: HAM-A, BAI , HAM-D, BDI, anxiety and depression subscales of the SCL-90 (all p-values <0.01). By the end of treatment, a significantly higher number of subjects in the MBCT achieved remission in comparison with the control group (16 vs. 0 respectively; $p<0.01$).
Bondolfi et al. (2010)	MD patients with 3 or more previous DE in remission	60	MBCT + TAU TAU	31 29	Prevention of MD relapses and recurrences	There were no significant differences in the relapse rates of the MBCT and the control group at the 1 year follow up (9/31 vs. 10/29; $p=0.78$). However relapses occurred earlier in the control group than in the MBCT group (median time to relapse = 61 vs. 204 days respectively; $p=0.006$)
Hargus et al. (2010)	Currently symptomatic patients with at least 3 previous DE and a history of suicidal ideation	8	MBCT + TAU TAU	14 13	-	Patients in the MBCT group displayed significant post treatment higher levels in meta-awareness and specificity in comparison with TAU group ($p=0.02$ and $p=0.001$ respectively)
Godfrin and van Heeringen (2010)	MD patients with 3 or more previous DE in remission	56	MBCT + TAU TAU	52 54	Prevention of MD relapses and recurrences	At the end of the study period relapse/recurrence rates were significantly reduced in the MBCT (12/52) vs. control (32/54) group ($p<0.0005$). Additionally, the time until first relapse increased in the MBCT as compared with the TAU groups and significant benefits were observed for several further psychological domains
Piet et al. (2010)	Social phobia	92	MBCT GCBT	14 12	Reduction of anxiety symptoms (as measured with BAI)	MBCT achieved moderate-high pre-post effect sizes ($d=0.78$ on a composite SP measure) not significantly different from than those of CBT ($d=1.15$). Participants to both groups further improved at the follow-up
Britton et al. (2010)	Partially remitted patients suffering from recurrent MD with residual sleep complaints	8	MBCT + TAU TAU	14 12	Reduction of residual depression symptoms (as measured with BDI)	Meditation practice was associated with several indices of increased cortical arousal, including more awakenings and stage 1 sleep and less slow-wave sleep relative to controls, increasing proportionally with the amount of practice. The MBCT group showed a larger decrease than controls over time on BDI scores ($p=0.005$)

MD: major depression; BD: bipolar disorder; ADM: antidepressant medications; MBCT: Mindfulness based cognitive therapy; TAU: treatment as usual; ADEP: Anxiety disorder education program; DE: depressive episodes; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; HAM-D: Hamilton Scale for Depression, HAM-A: Hamilton Scale for Anxiety; QOF: Quality of life; ITT = intent to treat; - = no primary outcome measure consistent with those of our review reported.

Table 3
Quality assessment of included studies.

Study	Randomization	Appropriate randomization	Drop outs and withdrawals	Single blinding for the main outcome measure	Treatment allocation concealment	Reported power calculation	Similarity in baseline prognostic factors	Therapist experience	Adherence to practice	Treatments allowed during the study period	Modified Jadad score
(Teasdale et al., 2000, 2002; Williams et al., 2000)	**Yes**	**Yes**	**Yes**	**Yes**	Yes	Yes	Yes	Three expert cognitive therapists with at least one prior experience of MBCT teaching	Not reported	Drug treatment, counselling, psychotherapy and other mental health contacts	4
Ma and Teasdale (2004)	**Yes**	**No**	**Yes**	**Yes**	Yes	No	Yes	Two expert cognitive therapists with at least 2 prior experiences of MBCT teaching	Not reported	Drug treatment, counselling, psychotherapy and other mental health contacts	2
Kingston et al. (2007)	**No**	**-**	**No**	**No**	No	No	Yes	Not reported	Not reported	Drug treatment. No details about psychological treatments	0
Williams et al. (2008b)	**Yes**	**Yes**	**Yes**	**Unclear**	Yes	No	Yes	Two expert cognitive and MBCT therapists (prior experience not reported)	Not reported	Drug treatment and psychotherapy	3
Kuyken et al. (2008)	**Yes**	**Yes**	**Yes**	**Yes**	Yes	No	Yes	Two expert MBCT therapists with at least two supervised prior MBCT teachings	85% in the MBCT group	Drug therapy only	4
Crane et al. (2008)	**Yes**	**Yes**	**Yes**	**Yes**	Yes	No	Yes	One of the founders of MBCT and an expert cognitive therapist trained in MBCT	Not reported	Drug therapy only	4
Barnhofer et al. (2009)	**Yes**	**Yes**	**Yes**	**Yes**	Yes	Yes	Yes	One expert CBT therapist with MBSR training supervised by one of the founders of MBCT	Homework records indicated that MBCT group practiced on an average of 4.98 days out of the six prescribed days	Drug therapy only	4

Bondolfi et al. (2010)	**Yes**	**Yes**	**Yes**	**Yes**	Yes	Yes	Yes	Expert therapists with at least 3 supervised MBCT teachings	Adherence to formal practice ranged from 65.4% to 91.7% in the first 8 weeks and from 11.5% to 60% in the 7th-12th months period	Drug therapy, counselling or psychotherapy	4
Hepburn et al. (2009)	**Yes**	**Yes**	**Yes**	**Yes**	Unclear	No	Yes	Expert CBT and MBCT therapists (prior experience not reported)	Not reported	Drug therapy and other medical sources	4
Kim et al. (2009)	**No**	**-**	**Yes**	**Yes**	No	No	Yes	Two psychiatrists with 3 years of MBCT experience	>80% in both groups	Drugs maintained at current dosages, psychotherapy not allowed	2
Hargus et al. (2010)	**Yes**	**Yes**	**Yes**	**Yes**	Yes	No	Yes	One expert CBT therapist with MBSR training supervised by one of the founders of MBCT	Homework records indicated that MBCT group practiced on an average of 4.98 days out of the six prescribed days	Drug therapy only	4
Godfrin and van Heeringen (2010)	**Yes**	**Yes**	**Yes**	**Unclear**	Yes	Yes	Yes	Medical practitioner with (unspecified) extensive experience of mindfulness meditation supervised by one of the founders of MBCT	Nor reported	Not clearly specified	3
Piet et al. (2010)	**Yes**	**Yes**	**Yes**	**No**	Unclear	No	Yes	Instructor with unspecified "high experience" trained by one of the founders of MBCT	High degree of adherence to treatments for both groups	None	3
Britton et al. (2010)	**Yes**	**Yes**	**Yes**	**Yes**	Yes	No	Yes	Instructor who received extensive training on MBCT and MBSR. Prior experience not specified	The mean adherence across all weeks was $78 \pm 22\%$	None	4

MBCT: Mindfulness based cognitive therapy. AD = antidepressants; * Only columns in bold were combined to determine the Jadad score.

2.4. Data extraction and synthesis

The data were independently extracted from the original articles by the reviewers using a comprehensive and pretested data extraction form (see appendix D1 and D2 in (Ospina et al., 2007)). Similarly to an early systematic review about MBCT (Coelho et al., 2007), quality of the studies was assessed using the Jadad Scale (Jadad et al., 1996). However such scale was modified by the authors to account for difficulties in blinding patients as to whether they received MBCT by allocating one point for single blinding of the outcome assessor (maximum Jadad score = 4). All disagreements were resolved through discussion. To supplement the Jadad score, we provided further methodological details of included trials that are not included in the original Jadad scale as well (Table 3). A score <3 was considered to be indicative of a low quality study.

2.5. Data analysis

Quantitative data that could be aggregated were entered into the Cochrane Collaboration Review Manager Software (RevMan version 5.0) and analyzed by RevMan analysis 1.01. For dichotomous outcomes, odds ratios (OR) and their 95% confidence intervals were calculated using a random effect model that takes into account possible differences in the implementation of interventions and characteristics of participants included. The analyses were performed on the intent to treat (ITT) population. For the main dichotomous outcome (relapse prevention in MD patients), we calculated the number needed to treat (NNT) as well (http://www.nntonline.net). For continuous outcomes, the standardized weighted mean differences (WMD) and their 95% confidence intervals were calculated using a random effect model (see above). The WMD is defined as the summation of the observed values multiplied with the allocated weights which is divided by the summation of the observed values and can be considered as a defence against giving undue weight to small studies with low variance. Continuous outcomes were analyzed on an endpoint basis, including only patients with a final assessment or with a last observation carried forward (in accordance with clinical data provided by the authors of original studies showing that treatment and control groups were not significantly different at baseline). Whether it was possible, sensitivity analysis were performed in higher quality studies separately. Data defined as secondary outcome measures were not meta-analyzed and were reviewed in a narrative way.

Heterogeneity across the studies was assessed by the Chi-squared and I-squared statistics and by visual inspection of the results. The Chi squared statistic P value <0.05 was taken to be suggestive of heterogeneity (Higgins et al., 2003). To explore the existence of a possible publication bias for the main outcome measures, whether a given outcome was investigated in more than two studies, we considered the funnel plot and calculated quantitatively the influence of the publication bias through Egger's analysis (Egger et al., 1997).

3. Results

3.1. Search results

The original search identified 286 particles. Two-hundred forty-five articles were excluded because they did not investigate the use of MBCT for patients suffering from psychiatric disorders. After the inclusion and exclusion criteria were applied to the remaining 41 studies, 16 trials, three of which (Williams et al., 2000; Teasdale et al., 2002; Hargus et al., 2010) were based on subsamples of early trials (Teasdale et al., 2000; Barnhofer et al., 2009), could be included in the present review and meta-analysis (Fig. 1). All apart from two studies (Kingston et al., 2007; Kim et al., 2009) employed a randomized controlled design. Thirteen trials focused on patients suffering from only (Teasdale et al., 2000; Williams et al., 2000; Teasdale et al., 2002; Ma and Teasdale, 2004; Kingston et al., 2007; Kuyken et al., 2008; Barnhofer et al., 2009; Hepburn et al., 2009; Bondolfi et al., 2010; Britton et al., 2010; Godfrin and van Heeringen, 2010; Hargus et al., 2010) or mainly (Crane et al., 2008) MD, one study analyzed MD and bipolar patients separately (Williams et al., 2008b), one study focused on patients with social phobia (Piet et al., 2010) and one study focused on patients with PD and GAD (Kim et al., 2009). Studies excluded after the initial screening and reasons for their exclusion are shown in Table 1. A summary of included studies is shown in Table 2. Quality of included studies is shown in Table 3.

3.2. Primary outcome measures

3.2.1. MBCT for relapse prevention in MD patients

Four randomized controlled studies investigated the efficacy of MBCT + treatment as usual (TAU) vs. TAU only (Teasdale et al., 2000; Ma and Teasdale, 2004; Bondolfi et al., 2010; Godfrin and van Heeringen, 2010) and one randomized controlled study compared MBCT + gradual discontinuation of maintenance ADs vs. continuation of ADs alone (Kuyken et al., 2008) for the prevention of MD recurrences and relapses over the period of 1 year. All such studies were performed in samples including only (Teasdale et al., 2000; Ma and Teasdale, 2004; Bondolfi et al., 2010; Godfrin and van Heeringen, 2010) or mainly (Kuyken et al., 2008) patients in remission. Earlier studies (Teasdale et al., 2000; Ma and Teasdale, 2004) provided data from patients with 2 and >2 prior depressive episodes separately. The choice of separating these sub-samples of patients was motivated by early observations suggesting that they could represent two distinct populations of patients (Post, 1992) and that MBCT showed efficacy only for the latter subsample (Teasdale et al., 2000; Ma and Teasdale, 2004). Accordingly, following studies (Kuyken et al., 2008; Bondolfi et al., 2010; Godfrin and van Heeringen, 2010) included only patients with ≥3 prior depressive episodes.

On the basis of the methodological design, data from four studies comparing MBCT + TAU vs. TAU only for the prevention of MD recurrences and relapses (Teasdale et al., 2000; Ma and Teasdale, 2004; Bondolfi et al., 2010; Godfrin and van Heeringen, 2010) could be aggregated. Taken together, data showed that 32% of patients with 3 or more past episodes of MD relapsed in the 12 months following MBCT as compared with 60% of patients in the control groups. Data analysis showed a significantly more favourable effect of MBCT + TAU (OR = 0.36 [95% CI = 0.19-0.48] $p<0.0003$, $I^2 = 39\%$) in comparison with TAU only (Fig. 2a). Additionally, results did not significantly change when higher quality studies were analyzed separately (Teasdale et al., 2000; Bondolfi et al., 2010; Godfrin and van Heeringen, 2010) (MBCT 32%, TAU 56%; OR = 0.36 [95% CI = 0.24;0.86] $p = 0.003$, $I^2 = 29\%$). The NTT needed to prevent a single relapse was 5 patients (CI 3-6).

A further study comparing MBCT + gradual discontinuation of maintenance ADs vs. continuation of ADs alone (Kuyken et al., 2008) found no significant difference in the number of relapses between the two treatment options (MBCT 47%, AD 60%; OR = 0.61 [95% CI = 0.30;1.25], $p = 0.18$). In such study 75% of patients who underwent the MBCT trial stopped maintenance ADs. Those with earlier onset and higher severity of the last episode were more likely to discontinue. Finally, two studies investigating the efficacy of MBCT + TAU vs. TAU only in the subsample of patients with only two prior MD episodes (Teasdale et al., 2000; Ma and Teasdale, 2004) did not find any significant difference between MBCT + TAU and TAU groups (MBCT 50%; TAU 27%; OR = 3.17 [95% CI = 0.97-10.37] $p = 0.16$, $I^2 = 0\%$).

In sum, current findings suggest that MBCT + TAU is better than TAU only for the prevention of MD relapses and that MBCT + gradual discontinuation of maintenance ADs is not significantly different from continuation of current antidepressant treatment.

3.2.2. MBCT for the short term reduction of depressive symptoms in patients with residual symptoms or with current MD

Three randomized controlled (Crane et al., 2008; Barnhofer et al., 2009; Britton et al., 2010) and one controlled (Kingston et al., 2007) studies investigated the efficacy of MBCT in adjunct to TAU vs. TAU only for the reduction of residual depressive symptoms, and one randomized controlled study compared MBCT + gradual discontinuation of maintenance ADs vs. continuation of ADs alone in a sample including subjects either in full or in partial remission (Kuyken et al., 2008). All studies assessed the reduction in depressive symptoms by means of the Beck Depression Inventory (BDI) (Beck et al., 1961) and provided data about short term changes following the 8-week MBCT program.

On the basis of the methodological design and of the similarity of the sample characteristics, data from two studies could be aggregated (Kingston et al., 2007; Barnhofer et al., 2009) (the data reported in the study of Crane et al. (2008) could not be aggregated because of the inclusion of both MD and BD patients joined together

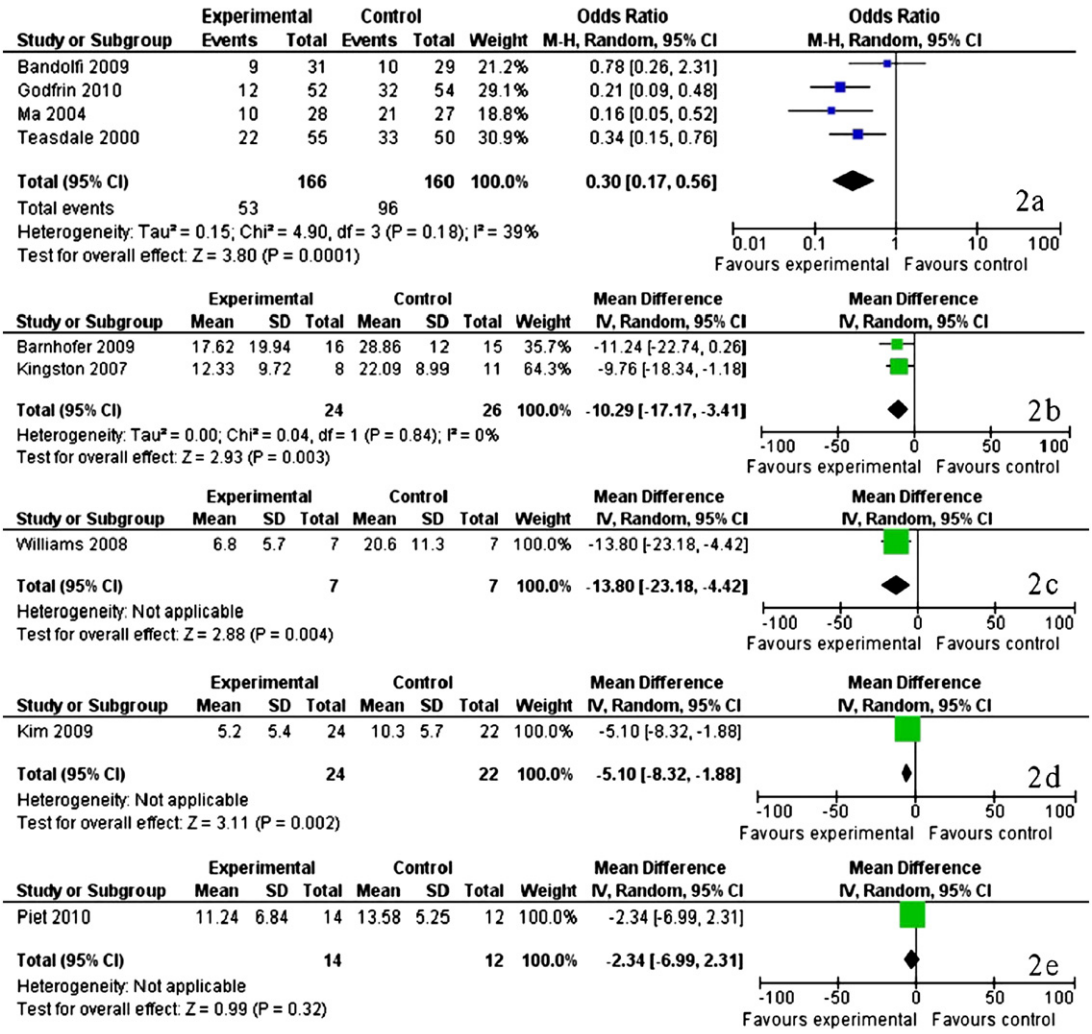

Fig. 2. a) Mindfulness based cognitive therapy (MBCT) + Treatment as usual (TAU) vs. TAU for relapse prevention of major depression (MD) at 1 year follow up; Numbers of relapsed patients for each group are shown; b) MBCT + TAU vs. TAU for the reduction of residual depressive symptoms in MD patients, c) MBCT + TAU vs. TAU for the reduction of residual anxiety symptoms in bipolar patients, d) MBCT + antidepressants vs. psycho-education + antidepressants for the reduction of residual anxiety symptoms in patients with panic disorder and generalized anxiety disorder, e) MBCT vs. group based cognitive therapy for the reduction of anxiety symptoms in patients with social phobia. For analyses d, e, and f, end-point means ± standard deviations Beck Depression Inventory (2b) or Beck Anxiety Inventory (2c, 2d and 2e) scores for each group are shown.

and those reported in the study of Britton et al. (2010) were excluded because more than half of the patients weres in remission at study entry and mean baseline BDI scores were extremely low (≤10); therefore, there could be insufficient room for improvement over the course of treatment). Data analysis of the short term effects of MBCT on BDI scores showed that MBCT + TAU was significantly better than TAU only for the reduction of residual depressive symptoms (WMD = -10.28 [95% CI = -17.18;-3.38], $p = 0.003$, $I^2 = 0\%$) (Fig. 2b). However only a marginally significant association was observed when data reported by the lower quality study (Kingston et al., 2007) were excluded (WMD = -11.24 [95% CI = -22.84;-0.36], $p = 0.06$), possibly because of the limited sample size of the study of Barnhofer et al. (2009).

Also, the only study comparing MBCT + gradual discontinuation of maintenance ADs vs. continuation of ADs alone (Kuyken et al., 2008) found a significantly higher reduction of BDI scores in the MBCT group in comparison with the control group (WMD = -4.35 [95% CI = -8.6; -0.10] $p = 0.04$). However, it should be pointed out that the study included both patients in full and in partial remission, thereby limiting the possibility to generalize such findings to patients in partial remission only. In sum, there is some evidence suggesting a positive additive effect of MBCT to TAU and of MBCT + gradual discontinuation of maintenance ADs vs. continuation of ADs alone for the reduction of residual depressive symptoms in patients suffering from MD.

3.2.3. MBCT for the short term reduction of BAI scores in patients with MD, BD and anxiety disorders

MD and BD: Williams et al. (2008b) investigated the effects of MBCT on BAI scores in patients suffering from MD and BD in remission with residual symptoms. The results showed that, while for MD patients no significant improvement was observed at the 8-week end-point in anxiety scores as measured by the BAI (WMD = 2.70, C.I = -3.38-8.78, $p = 0.38$), significantly higher decreases of BAI scores could be observed in the MBCT vs. the control group in bipolar patients (WMD = -13.80 [C.I = -23.18- -4.42] $p = 0.004$) (Fig. 2c). Unfortunately, however, the small sample size and the investigation of a sample of patients with concomitant suicidal ideation do not allow us to draw definitive conclusions, suggesting the necessity for further research on this topic.

Anxiety disorders: two studies, one non-randomized and one randomized controlled study, compared the effects of the adjunct of MBCT vs. psycho-education to current pharmacological treatment in 63 patients suffering from either GAD or PD who did not achieve

remission after at least 6 months of pharmacotherapy (Kim et al., 2009) and of MBCT vs. group based cognitive behavioural therapy (GCBT) for 26 patients with social phobia (Piet et al., 2010) respectively. Due to differences in target populations and type of comparators, results from such studies were analyzed separately.

A significant difference was observed at endpoint between BAI scores in patients with GAD or PD allocated to MBCT as compared to those allocated to psycho-education (WMD = -5.1 [C.I = -8.32- -1.88] $p = 0.002$) (Fig. 2d). Note, however, that the absence of randomization does not allow to rule out possible undetected differences between the two groups. On the other hand, no significant difference was observed on 8 weeks' BAI scores of patients with social phobia randomized to MBCT as compared to those randomized to GCBT (WMD = -2.34 [95% CI: -6.99-2.31] $p = 0.32$) (Fig. 2e). Note also that such study employed a crossover design, with both groups receiving both forms of treatment in reversed order, and follow up data indicated that combining the two treatments only resulted in a significant, small increase in the within group composite effect size of 0.33 when GCBT was added after MBCT, while the increase in effect size of MBCT added to GCBT (0.20) was not significant. It is worth mentioning, however, that the small sample size and the crossover design of this study complicate interpretation. The crossover design does not allow us to ascertain whether changes after the crossover might be due to the new treatment introduced or to late effects of the prior treatment. Therefore, these results should be considered with caution, and higher quality replications are needed.

3.2.4. Analysis of the publication bias

The funnel plot relative to the efficacy of MBCT for the prevention of depression relapses did not provide support for the existence of a publication bias (Fig. 3). Similarly, Egger's analysis did not reveal any significant bias ($p = 0.97$). Due to the paucity of studies, it was not possible to determine whether a publication bias existed with regard to further main outcome measures.

3.3. Secondary outcome measures

3.3.1. Time to relapse in MD patients

Four studies investigated differences existing between MBCT + TAU vs. TAU only in terms of time to relapse (Teasdale et al., 2000; Ma and Teasdale, 2004; Bondolfi et al., 2010; Godfrin and van Heeringen, 2010). In an early study, Teasdale et al. (2000) observed that the differences in relapse rates between TAU and MBCT became established within the first 10 weeks of the study period (28% vs. 8%), remained stable until 30 weeks, and then increased again. Similar findings were also reported in the following study performed by Ma and Teasdale (2004) and by Godfrin and van Heeringen (2010) who found that MBCT increased the average time to first relapse since study participation by nearly 15 weeks. Similarly, Bondolfi and colleagues (2010) observed that time to relapse was significantly longer with MBCT + TAU than TAU alone (median days to relapse were 204 (35-330) and 69 (15-91) days, respectively), although both groups relapsed at similar rates at the 1-year follow-up. The study also found that the amount of practice did not significantly differ between those who relapsed and those who did not.

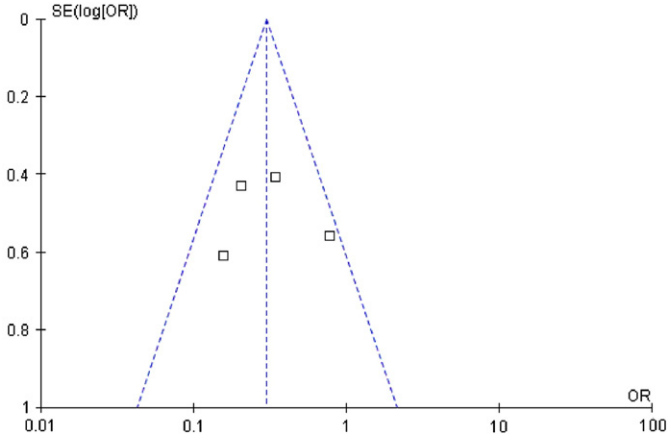

Fig. 3. funnel plot of the main primary outcome measures (MBCT + TAU vs. TAU for the prevention of MD relapses).

3.3.2. Changes in further psychological measures following MBCT

Major depression: In an attempt to clarify possible mechanisms of actions of MBCT interventions, several authors tried to investigate differences between psychological changes in MBCT compared with TAU groups. Crane et al. (2008) investigated the effects of MBCT on self discrepancy, one of the key psychological processes involved in the maintenance of depression (Strauman, 1989). The concept of self-discrepancy relies on the theory that people suffering from MD often believe themselves to be falling short of their own or other's goals or expectations. Although changes in self discrepancy were not associated with changes in residual depressive symptoms, a significant association between increases in ideal self similarity and the adoption of more adaptive ideal self-guides post treatment was observed in the MBCT group. The authors suggested that MBCT could protect against increases in self discrepancy and that it could also facilitate a shift in the goals of self-regulation, even though further research is needed to clarify why changes in self discrepancy were not directly related to improvements in depression scores in Crane et al. (2008)'s study.

Williams et al. (2000) also suggested that the positive effects of MBCT could be mediated by a reduction in overgeneral memory. Consonant with such hypothesis, the authors of this study observed in the MBCT group but not in the control group a significant shift from generic to specific memories, a pattern previously related to psychological health.

In a following study, Hepburn et al. (2009) tested the hypothesis that MBCT training could have an effect on thought suppression in formerly depressed patients with a history of suicidality. The authors observed that MBCT did not reduce thought suppression; however, it significantly reduced self-reported attempts to suppress thoughts in the previous week. The authors interpreted this finding as suggestive of an effect of MBCT on the reduction of ruminations which, in turn, could lead to a reduction of depression. In accordance with this finding, Kingston et al. (2007) observed a significant reduction of ruminative thinking in patients who practiced MBCT as compared with those who did not, even though the limited sample size and the absence of randomization suggest to consider such finding with caution. Additionally, Hargus et al. (2010) found that the adjunct of MBCT to TAU significantly improved levels of meta-awareness and specificity in currently depressed patients with an history of suicide. They interpreted these findings as suggestive of an effect of MBCT training on the ability to reflect on previous crises in a decentered way. This, in turn, could lead to an helpful way to relate differently to such experiences in order to prevent future suicidal relapses. Note, however, that none of these studies reported long-term data or a comparison with an active treatment. As a consequence, further studies are needed to determine the specific effects of MBCT and to assess whether results gained in the short term are maintained in the long term as well.

Anxiety disorders: The study performed by Kim et al. (2009) on patients with PD and GAD observed significantly higher decreases from baseline to endpoint in the MBCT as compared with the psycho-education group in the following measures: Hamilton rating scale for anxiety, HAM-D, BDI, anxiety and depression subscales of the SCL-90 (Derogatis et al., 1973) (all p-values <0.01). Additionally, by the end of treatment, a significantly higher number of subjects in the MBCT group achieved remission in comparison with the control group (16 vs. 0 respectively; $p < 0.01$). More recently, Piet et al. (2010) found

that patients with social phobia randomized to MBCT achieved moderate-high pre-post effect sizes ($d = 0.78$ on a composite measure of questionnaires under investigation) which did not significantly differ from, although they were numerically lower, than those of GCBT ($d = 1.15$). Note, however, that the absence of randomization of the first study as well as the limited sample size of the second one do not allow to draw definitive conclusions and suggest that such findings should be considered with caution.

3.3.3. Miscellaneous findings in MD patients

Results gained through MBCT programs seem to be independent form group effect. Both Williams et al. (2008a) and Kuyken et al. (2008) recently reported that no significant intra-group correlation was found in their studies, suggesting that MBCT had essentially the same effect in each cohort of patients. Furthermore reviewed studies reported high adherence, low attrition rates and no serious adverse events related to MBCT interventions, suggesting that MBCT could be a feasible and well tolerated intervention for most patients. MBCT was also found to have a significant effect on the quality of life of patients, as measured with standardized scales (World Health Organization, 2004) in patients suffering from MD (Kuyken et al., 2008) or GAD and PD (Kim et al., 2009). Also, MBCT was associated with several indices of increased cortical arousal, including more awakenings and stage 1 sleep and less slow-wave sleep, associated with simultaneous improvements in subjectively reported sleep quality as compared to a waiting list in a sample of partially remitted MD patients with residual sleep complaints (Britton et al., 2010). Of note, benefits on sleep measures increased proportionally with the amount of meditation practice.

Finally, Teasdale et al. (2000) calculated that the preventative effect of MBCT was achieved for an average investment of less than 5 hours of instructor time per patient, suggesting that offering a group skills-based training program to recovered depressed patients may be a cost-efficient strategy for prevention. Following this finding, Kuyken et al. (2008) investigated differences in terms of economical costs between MBCT and maintenance antidepressant treatment, finding no significant difference between these two treatment options.

4. Discussion

The present review and meta-analysis showed many important results. First of all, our findings suggest that the augmentation of MBCT to standard care could result in significantly lower relapse or recurrence rates in patients suffering from MD in comparison with standard care alone. In addition, we observed that MBCT + gradual discontinuation of maintenance ADs was not significantly different from antidepressants' continuation with respect to the number of relapse rates at 1 year.

Note, however, that despite the significance of these findings, the study performed by Kuyken et al. (2008) was the only one to suggest that MBCT could be comparable to an established treatment option for MD. On the other hand, on account of the methodological design of the remaining three studies, it is impossible to ascertain to what extent a further non specific intervention such as a social support group or mere attention could have yielded similar outcomes. Although Coelho et al. (2007) had already underscored this critical issue, in fact, the majority of newer studies have yet compared MBCT to a waiting list that does not allow to distinguish specific from non specific effects of MBCT. As a consequence, further studies aimed at comparing MBCT to similar interventions in terms of group support, teacher's care and expectancy effect are needed to determine the relative effect of the so-called "active ingredients" of MBCT such as sitting meditation practice. It is noteworthy, however, that since the publication of Coelho et al. (2007)'s review, two studies performed by groups other than the developers of MBCT have been published that suggest the superiority of the adjunct of MBCT to TAU over TAU alone, either in terms of relapse rates at the 1-year' follow-up (Godfrin and van Heeringen, 2010) or in terms of time to relapse (Bondolfi et al., 2010), providing preliminary evidence for treatment transportability and generalizability (Onken et al., 1997).

A second important finding of the present review regards the effects of MBCT on residual depressive symptoms. Reviewed studies suggest in fact an additive effect of MBCT to usual care for the reduction of residual depressive symptoms, even though such studies are affected by the same limitations of studies mentioned above. Note also that the use of self-assessment measures such as the BDI could raise concerns about the reliability of current data. Accordingly, future studies should rely on more rigorous external assessments.

Also, there is limited evidence to suggest a non specific effect of MBCT on the reduction of residual anxiety symptoms in BD patients, a specific effect on the reduction of residual anxiety symptoms in non remitted patients with GAD and PD as well as a not significantly different, even though numerically lower, effect on the reduction of anxiety symptoms in patients with social phobia as compared to classical GCBT. Note, however, that, on account of several limitations including limited sample size (Williams et al., 2008b; Piet et al., 2010), inadequate comparators (Williams et al., 2008b) as well as lack of randomization (Kim et al., 2009) in such studies, such findings should be considered with caution and no definitive conclusion can be drawn so far.

Finally, there is preliminary evidence suggesting possible changes related to MBCT interventions in MD patients such as a reduction in ruminations, overgeneral autobiographical memory and self-discrepancy between the real and the ideal self. However, this evidence falls short of replications and is affected by methodological shortcomings such as inappropriate or not reported methods of randomization and small sample sizes possibly related to false positive findings.

Additionally, it is noteworthy that the nature of the control (TAU) groups including pharmacotherapy and, in early studies, psychotherapy, raises concerns about the very effects of MBCT. However such concerns could be partially reduced by the comparable use of TAU between MBCT and control groups across all interventions. Also, on account of the admixture of different techniques (including Hatha yoga and psycho-educational information about MD and other disorders), it is not possible to determine whether mindfulness itself is the "active ingredient" of MBCT or not. Accordingly, future studies could use a dismantling design in order to help clinicians and researchers to distinguish the differential weight of specific components of MBCT on final outcome and to address critical questions including "who" could benefit from "what".

The present review and meta-analysis has some relevant limitations. First of all, similarly to an early systematic review on meditation (Ospina et al., 2007), we assessed the quality of reviewed studies using a standardized scale (Jadad et al., 1996) that was not specifically designed to assess the quality of meditation and psychotherapy studies. As Orme-Johnson (2008) recently pointed out, the development of a new quality scale which includes factors such as therapist's experience and adherence to practice in the global evaluation of study's quality in meditation studies is needed. Additionally, high quality meditation research should also insure proficient practice, ascertain whether participants correctly understand their practice, use state-of-the-art measurement methodology and make sure control subjects are not inadvertently practicing the same or another form of meditation. A second limitation regards the low quality of some of the included studies which reduces the significance of reviewed findings. As previously reported, the main methodological shortcomings were small sample size, lack of randomization details and the impossibility to conduct meditation studies using a double blind condition. It is encouraging, however, that most recent studies frequently reported and used appropriate randomization procedures. Also, taking into account the limited number and the heterogeneity of included studies, we could not perform an analysis of the moderator

effects of several key variables (e.g. age or disease condition) on clinical outcomes. Finally, a further limitation is represented by the decision to limit the research to articles published in English and by the exclusion of unpublished studies so that we could have missed a number of articles focusing on MBCT published in different languages or not indexed by electronic databases mentioned in the introduction.

In conclusion, current studies suggest an additive effect of MBCT to TAU in comparison with TAU only leading to a significant reduction of MD relapse or recurrence rates over the period of one year. They also suggest that MBCT could be similar to maintenance ADs in terms of prevention of MD relapses and recurrences, that the augmentation of MBCT could be useful for reducing residual depressive symptoms in patients with MD and for reducing anxiety symptoms in patients with BD in remission and in patients with some anxiety disorders. However, on account of the limitations stated above, further better designed studies are needed to determine the specific effects of MBCT for the majority of conditions mentioned above and to overcome such limitations as small sample size and lack of randomization that affect many of the included studies.

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