



## Mindfulness-Based Cognitive Therapy in Major depressive disorder - systematic review and metanalysis

### *Relação entre a Mindfulness-Based Cognitive Therapy e seu efeito no transtorno depressivo maior*

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#### Abstract

**Introduction:** MBCT practices increases the ability of concentration and attention, as well is particularly effective for people with current and treatment-resistant depression. **Objective:** To analyze the effects of the application of MBCT in symptoms of MDD. **Methods:** systematic review and meta-analysis. To find suitable studies, we searched PubMed/MEDLINE's database using the keywords mindfulness and major depressive disorder. Studies in English published between 2003 and 2015 were selected. The studies were evaluated according to their methodological quality by PEDro scale (score greater than 3), studies that showed empirical evidence, had an experimental study design (randomized and non-randomized), and whose full text was available. For the meta-analysis, we used a random-effects model with standardized mean differences and 95% confidence intervals. **Results:** Fourteen es were included, of which three were non-randomized, with only one group with intervention of MBCT, and 11 were randomized studies, divided into two-group samples and three-group samples. The non-randomized studies showed a PEDro score of 5, while the two-group and three-group randomized studies showed PEDro scores of 5-10 and 6-9, respectively. In the meta-analysis, the four randomized studies selected revealed a moderate effect of MBCT on the outcome of depression symptoms, with a mean difference of -0.52 (95% CI: -1.050 to -0.002;  $p = 0.04$ ). **Conclusion:** The MBCT presented as a promising alternative for the treatment of this disorder.

**Keywords:** Mindfulness. Depression. Behavior Therapy. Depressive Disorder Major.

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## Resumo

**Introdução:** MBCT práticas aumenta a capacidade de concentração e de atenção, assim é particularmente eficaz para as pessoas com depressão recorrente e resistentes ao tratamento. **Objetivo:** analisar os efeitos da aplicação da MBCT nos sintomas do Transtorno Depressivo Maior (TDM). **Metódos:** Revisão sistemática e metanálise. Utilizou-se para a busca dos estudos, a base de dados MEDLINE (PubMed), com os descritores *mindfulness* e *major depressive disorder*. Selecionaram-se artigos na língua inglesa entre os anos de 2003 a 2015. Os estudos foram avaliados quanto sua qualidade metodológica pela escala Pedro (pontuação maior que 3), que demonstrassem evidência empírica, com design de estudo experimental (randomizado e não randomizado) e estar disponível na íntegra. Para a metanálise utilizou-se modelo de efeitos aleatórios com diferenças médias padronizadas e intervalos de confiança de 95%. **Resultados:** Quatorze estudos foram incluídos, sendo 03 não randomizados, contendo apenas um grupo de intervenção da MBCT e 11 estudos randomizados, divididos em amostras de dois grupos e amostras de três grupos. Os estudos não randomizados apresentaram escala Pedro de 5 pontos, os randomizados de dois grupos (de 5 a 10 pontos) e de três grupos (de 6 a 9 pontos). Na metanálise os quatro 4 estudos randomizados selecionados, revelaram um efeito moderado da MBCT sobre o desfecho dos sintomas da depressão, com uma diferença média de -0.52 (IC 95%: -1.050 a -0.002;  $p = 0.04$ ). **Conclusão:** A MBCT apresenta-se como uma alternativa promissora para tratamento desse transtorno.

**Palavras-Chave:** Meditação. Depressão. Terapia Comportamental. Transtorno Depressivo Maior.

## Introduction

Major depressive disorder (MDD) is a complex disease with patterns of persistence, remission and relapse, which presents a likelihood of recurrence greater than 80% (1, 2). It has a global prevalence of 16% and it is estimated that it will be the second most prevalent illness by 2020, with an increase of 6.2% by 2030 (3, 4). It presents different prevalence rates among countries, 1.5% in Taiwan, 7.0% in South Korea, 19% in Lebanon, 9.2% in Germany, 9% in Chile (5), 3% to 54% in Africa (6), 6.4% to 16% in the USA (4, 7) and 2.7% in Thailand (8).

It is characterized by psychological, physical and behavioral symptoms, mainly including depressed mood, loss of energy, suicidal tendencies and decreases in interest, cognition, quality of life and academic or occupational functioning (9 - 11). Although psychological interventions are effective in the treatment of MDD, the prescription of antidepressant drugs is the mainstay of treatment to prevent relapse and recurrence (12), however, this may present some limitations, such as poor adherence and side effects (13).

Because of these limitations, some non-pharmacological alternatives have been implemented, including interventions in lifestyle, behavior modification, counseling and psychological therapies

(13, 14). One of these therapies is meditation, which is currently being integrated into the clinical practice for some medical conditions, such as hypertension, cancer, chronic pain, diabetes, etc. (15, 16) and psychiatric conditions, such as anxiety, suicidal tendencies, obsessive-compulsive disorder, personality disorders and especially for depression (17, 18).

Approximately 25 years ago, Jon Kabat-Zinn incorporated meditation (dating back more than 5,000 years) into medical practice, implementing the Mindfulness-Based Stress Reduction (MBSR) program, which is an adaptation of Buddhist techniques for stress reduction (19 - 21). Today, there is a range of therapeutic approaches based on mindfulness, such as Mindfulness-Based Eating Awareness Training, Mindfulness-Based Relationship Enhancement, Mindfulness-Based Relapse Prevention and Mindfulness-Based Cognitive Therapy (MBCT) (22).

Mindfulness-Based Cognitive Therapy (MBCT) is a group therapy with 10 to 15 participants held over 6 to 8 weeks, created specifically to help manage stress and depressive symptoms (23, 24). It is recommended by the National Institute for Health and Clinical Excellence, in the UK, as a medical treatment for people with recurrent depression (25, 26).

The benefits of this meditation can be associated with improvement in cognitive control, regulation of the emotions, positive mood and acceptance (27),

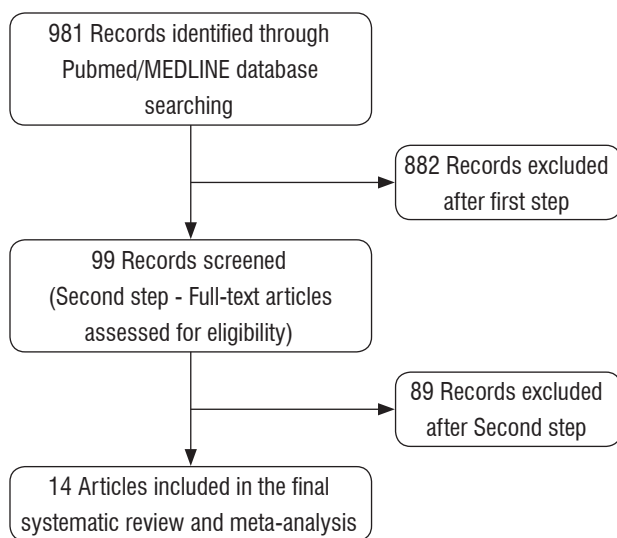
as it aims to teach patients to relate to unpleasant thoughts, feelings and bodily sensations. Therefore, it seems reasonable to assume that the practice can mitigate the symptoms of depression. Thus, the aim of this study was to analyze, through a systematic review and meta-analysis, the effects of the application of MBCT on symptoms of MDD.

## Methods

Studies were identified using the US National Library of Medicine - National Institutes of Health MEDLINE (PubMed/PMC) database. The procedures related to searching the database complied with the following steps:

First step - identification of descriptors controlled by the MeSH (Medical Subject Headings): 'Breast Cancer' and not controlled 'MBSR mindfulness-based stress reduction'.

The choice of articles for the construction of this study was based on the proposal of Cook and West (28) in which the process of inclusion/exclusion of studies typically has two phases: - In phase 1, only the title, abstract and keywords are examined. During this phase if the item is ineligible, based on the title and abstract, it is excluded. If there is any doubt, as in one case where the abstract contained insufficient information, the analysis of the article advances to phase 2; - In phase 2, the full text of each article is read to take the final inclusion/exclusion decision (Figure 1).



**Figure 1** -Flow diagram of search.

The methodological quality of all studies was assessed using the PEDro scale (29). The Physiotherapy Evidence Database (PEDro; <http://www.pedro.org.au>) is a free database of randomized controlled trials (RCTs), systematic reviews and clinical practice guidelines in physiotherapy. The PEDro scale is based on the Delphi list developed by Verhagen and colleagues at the Department of Epidemiology, University of Maastricht. The purpose of the PEDro scale is to help the users of the PEDro database rapidly identify which of the known or suspected randomized clinical trials (i.e. RCTs or CCTs) archived on the PEDro database are likely to be internally valid (criteria 2 - 9), and could have sufficient statistical information to make their results interpretable (criteria 10 - 11).

We excluded trials if interventions in the MDD contained other therapies, only accepted Mindfulness-Based Cognitive Therapy, as they did not match the scope of this study.

## Data Analysis

The Stata software (version 12.0; Stata Corp., College Station, USA) was used for data synthesis and analysis. A meta-analysis of four studies classified as randomized was conducted, as these presented depression scores in continuous data. Using the random effects and combined effects model the mean standardized differences with 95% confidence intervals were reported. All the studies had to compare the effect of MBCT with other intervention groups over a standard period of 8 weeks.

Heterogeneity between the results of the studies was assessed using the Cochran Q test and I<sup>2</sup> statistic, which defines 0% as absence of heterogeneity, 25% as low, 50% as moderate and  $\geq 75\%$  as high heterogeneity (30). P values  $\leq 0.05$  were considered statistically significant. The forest plot graph was used to detect any publication bias and the respective 95% CI of each study.

In order to investigate the effectiveness of the MBCT, the effect size of the difference in improvement and/or reduction of the depressive symptoms of the mean of the experimental and control groups was evaluated. Cohen's d was used for the calculation of the effect size, correcting the bias when the sample size was different using Hedges'g (31). According to the classification,  $0.20 \leq d < 0.50$  was considered an indicator of small,  $0.50 \leq d < 0.80$  medium and  $d \geq 0.80$  large effect size.

## Results

The search located 981 studies in the PubMed/ MEDLINE database, with the descriptors 'mindfulness-based cognitive therapy' AND 'major depressive disorder', of these, 14 studies were selected for analysis, due to fulfilling the inclusion criteria (Figure 1).

For a description of the studies in the tables, the following categories were considered: the year of publication, where the study was conducted, classification on the Pedro scale, scales used as measuring instruments, publishing journal, sample

(age group and gender), intervention (mindfulness and other psychological approaches), monitoring of the sample and results obtained (Table 1 and 2).

The countries where the studies were developed were mainly distributed between the USA and Europe, with one in Iran. The publication of the articles occurred between the years 2006 [1 (7.14%)], 2007 [1 (7.14%)], 2009 [1 (7.14%)], 2010 [2 (14.28%)], 2012 [1 (7.14%)], 2013 [3 (28.6%)], 2014 [2 (14.28%)], and 2015 [2 (14.28%)]. The scales used in the studies are shown in Table 1, with the BDI-II = Beck Depression Inventory-II being the scale most used [05 (41.66%)].

**Table 1** - Characteristics of the included studies

Studies	Years	Studies Local	Questionnaire	Journals
Finucane e Merce (32)	2006	Ayrshire, Scotland University of Glasgow (EUA)	BDI-II, BAI	BMC Psychiatry
Kenny e Willians (33)	2007	Queen Elizabeth Hospital (UK)	BDI	Behaviour Research and Therapy
Barnhofer et al. (34)	2009	Department of Psychiatry, Warneford Hospital (UK)	BDI-II; BSS	Behaviour Research and Therapy
Bondolfi et al. (35)	2010	Geneva e Lausanne University Hospitals (Suíça)	MADRS; HAM-D 17	Journal of Affective Disorders
Segal et al. (36)	2010	Centre for Addiction and Mental Health (CAMH), Toronto and St. Joseph's Healthcare, Hamilton	HAM-D 17	Arch Gen Psychiatry
Bieling et al. (42)	2012	Centre for Addiction and Mental Health (CAMH), Toronto and St. Joseph's Healthcare, Hamilton	HRSD	Journal of Consulting and Clinical Psychology
Van Vugt et al. (2)	2012	Department of Psychology in Tucson, University of Arizona. (EUA)	BDI; STAI-Y1, RSQ; TSST	Frontiers in Human Neuroscience
Batink et al. (43)	2013	Maastricht (Holanda)	HRSD; RSS	PLoS One
Munshi et al. (37)	2013	Langley Porter Psychiatric Hospital and Clinics (LPPH&C) at the University of California San Francisco (EUA)	BDI-II; RRS; STAI-Y1	Mindfulness
Omidí et al. (38)	2013	Social Welfare and Rehabilitation Sciences and Tehran University Counseling Centre (Irã)	BSI	Iran Red Crescent Med Jornal
Schoenberg e Speckens (39)	2014	Radboud University Medical Centre Nijmegen (Holanda)	IDS; RRS	Cogn Neurodyn
Williams et al. (40)	2014	Clinicas de saúde mental em Oxford, England, and Bangor, North Wales	BDI-II; Suicide Attempt and Self-Injury Interview	Jornal of Consuling and Clinical Psychology
Kuyken et al. (41)	2015	Quatro centros de UK: Bristol, Exeter and east Devon, north and mid Devon, and south Devon	BDI	Lancet
Shallcross et al. (13)	2015	Área urbana de Rocky Mountain West (EUA)	BDI-II	Jornal of Consuling and Clinical Psychology

Note: BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; BDI-II = Beck Depression Inventory-II; MADRS = Escala de Classificação da Depressão de Montgomery (Asber/Montgomery Asberg Depression Rating); HRSD = Hamilton Rating Scale for Depression; HAM-D 17 = Escala de Hamilton para Avaliação de Depressão; STAI-Y1 = Spielberger State-Trait Anxiety Inventory form Y; RSQ = Ruminative Responses Scale; TSST = Trier Social Stress Test; BSI = Brief Symptom Inventory; IDS-SR  $\geq$  21 = Inventory of Depressive Symptomatology- Self Report; RRS = Ruminative Response Scale; ICD-10 = criteria; DSM-IV-TR Axis I e II = Research Version of the Structured Clinical Interview; BSS = Beck Scale for Suicide Ideation; IDS = depressive symptom; RRS = response patterns towards feelings of sadness/depression.

Table 1 shows that, in the majority of studies [11 out of 14 studies in Table 2 (78.58%)] (2, 13, 32, 33, 34, 35, 36, 38, 39, 42, 43) the subjects were within the age group classified as adults (18 to 64 years old) and only [3 (21.42%)] (37, 40, 41) used samples with older adults (18 to 84 years old).

All the studies used MBCT as the intervention, based on the Manual derived from the work of Kabat-Zinn (19, 20). They performed this with people diagnosed with MDD according to the DSM-IV and were composed of mixed samples, totaling 1.416, predominantly [1.062 (75%)] female, and [354 (25%)] male participants.

The interventions of the studies presented different designs:

- Non-randomized studies [03 (21.42%)], containing only one MBCT group (32, 33, 37);
- Randomized studies [7 (50%)] with the samples divided into two groups, comparing MBCT: with a control [2 (2, 39)], with usual treatment and therapy [3 (34, 35, 43)], with medication [1 (41)] and with the focus on the four areas of nutrition, physical activity, functional movement and music therapy [1 (13)]; and samples divided into three groups, comparing MBCT: with medication and a placebo [2 (36, 42)], with cognitive therapy and the treatment as usual with therapy [2 (38, 40)].

The scores of the Pedro scale that measures the quality of the trials ranged from 5 to 10 points (total mean of all studies = 7.1 SD = 1.8). The non-randomized studies presented a Pedro score of 5 points (32, 33, 37), the randomized studies with two groups from 5 to 10 points (2, 13, 34, 35, 39, 41) and those with three groups from 6 to 9 points (36, 38, 40).

The three non-randomized studies, containing only an intervention group showed the result that

eight weeks of practice of MBCT led to decreases in the scores of depression (32, 33, 37), anxiety (32, 37), suicidal thoughts (33) and rumination (37).

Of the randomized studies with the samples divided into two groups, the results suggest that eight weeks of practice of MBCT presented better results in the scores of the rate and time of relapse, in the delay of the change of medication and in the demand for a therapist compared with TAU. Batink et al. (43) demonstrated improvement in rumination scores in a group with  $\geq 3$  depressive episodes (MBCT + TAU) and in a group with  $\geq 2$  depressive episodes (TAU). In the study of Van Vugt et al. (2) practicing MBCT decreased the scores of depression and anxiety, however, both groups (MCBT and Control) increased their tendency to sustain trains of positive words.

The randomized studies with samples divided into three groups demonstrated that eight weeks of practice of MBCT presented better results regarding time of relapse than the antidepressant medication (ADM) and placebo (PLA) groups (34) and than the cognitive psychological education (CPE) and treatment as usual (TAU) groups (40); being better than m-ADM and PLA (36) regarding the days to achieve remission. In the study by Bieling et al. (42) the MBCT, m-ADM and PLA groups did not show improvements in rumination, however the MBCT group improved the ability of the subjects to monitor and observe their thoughts and feelings. Conversely, in the study by Williams et al. (40) the CPE group showed better results related to more time before seeking a therapist and the use of new depressive medication than the MBCT and TAU groups. Omid et al. (38) showed similar results among the groups, with a decrease in depression and anxiety scores mainly in the MBCT group followed by the cognitive based therapy (CBT) and TAU groups.

**Table 2** - Characteristics of the studies Interventions

Author, year	Criteria Pedro scale	Subjects	Intervention	Findings
Finucane e Merce (32)	5/11	13 individuals with MDD (03 male, 10 female) (18 to 65 years old) (ICD-10)	GI - *MBCT	<b>Depression</b> BDII Mean (SD) Baseline to 8-week = 35.73(8.69) to 17.82(14.59) <b>Anxiety</b> BAI Mean (SD) Baseline to 8-week = 32.00(12.50) to 20.51(17.08) (To be continued)

**Table 2** - Characteristics of the studies Interventions

Author, year	Criteria Pedro scale	Subjects	Intervention	Findings
Kenny e Willians (33)	5/11	46 individuals with MDD (20 male, 59 female) (17 to 61 years old) (DSM-IV - SCID) (patients who were currently actively depressed, and who had not responded fully to standard treatments)	GI – *MBCT - moderate (n=26) (BDI ≤ 24) and, severe (n=29) (BDI ≥ 25) - With and Without thoughts of death and suicide  - Homework involved around 1 h per day of meditation or yoga, and other related formal and informal practices for the 8 weeks.	<b>BDI for suicidal Mean (SD)</b> - With thoughts of death and suicide = Baseline to 8-week = 27.2(10.6) to 14.8(10.6) - Without thoughts of death and suicide = Baseline to 8-week = 20.2(5.7) to 12.8(7.8) <b>Depression BDI Mean (SD) p</b> - moderate (BDI ≤ 24) = Baseline to 8-week = 17.2(4.3) to 11.5(7.8) - severe (BDI ≥ 25) = Baseline to 8-week = 33.2(6.4) to 17.1(11.2) Total = Baseline to 8-week = 24.39(9.8) to 13.9(9.7) p.00
Barnhofer et al. (34)	5/11	28 individuals with MDD (19 female, 9 male) (18 to 65 years old) (DSM-IV - SCID)	GI – (14) *MBCT  GII – (14) TAU	<b>Depression BDII Mean (SD) p</b> MBCT - Baseline to 8-week = 29.36(9.66) to 17.62(10.94) p.00 TAU - Baseline to 8-week = 31.32(10.79) to 28.86(12.97) ns <b>Suicide Ideation BSS Mean (SD)</b> MBCT - Baseline to 8-week = 2.21(2.45) to 1.14(1.79) TAU - Baseline to 8-week = 2.78(2.08) to 2.42(2.53) <b>Group did not meet criteria for a full episode of Major Depression at post-assessment</b> MBCT - 70% TAU - 18%
Bondolfi et al. (35)	8/11	55 individuals with MDD (43 female, 12 male) (18 to 65 years old) (DSM-IV - SCID)  (limited the inclusion to patients with 3 or more previous episodes; least three past depressive episodes (2 episodes in the past 5 years and at least one in the past 2 years); remission for at least 3 months at time of enrolment; history of treatment with antidepressants but to currently be off medication for at least 3 months before enrolment)	GI – (27) *MBCT + TAU  GII – (28) TAU  Follow-up = 14 months	<b>Antidepressant medication was reinstated in</b> MBCT+TAU - 36% TAU- 31% <b>Time to relapse</b> MBCT+TAU - 29 weeks TAU - 10 weeks <b>Delay until onset of antidepressant medication</b> MBCT+TAU - 204 day TAU - 111 day <b>One or more visit for counselling, psychotherapy or support from professional mental health staff was undertaken</b> MBCT+TAU - 46% TAU - 55%

(To be continued)

**Table 2** - Characteristics of the studies Interventions

Author, year	Criteria Pedro scale	Subjects	Intervention	Findings
Segal et al. (36)	9/11	84 individuals with MDD (48 female, 36 male) (18 to 65 years old) (DSM-IV - SCID) (disorder with a minimum of 2 past episodes and $\geq 16$ Hamilton Rating Scale for Depression)	<p>GI – (28) m-ADM (To maintenance antidepressant medication)</p> <p>GII – (26) *MBCT (To discontinuation antidepressant medication + MBCT)</p> <p>GIII – (30) PLA (To discontinuation antidepressant medication + placebo and clinical management)</p> <p>(Patients in both the placebo and MBCT conditions had their medication tapered gradually, during a 4-week period, via placebo substitution and reduced pill count, respectively, at the recommended rate for their specific medication to minimize the risk of discontinuation syndrome)</p> <p>Follow-up = 18 months</p>	<p><b>Rate of relapse</b></p> <p>M-ADM - 27%</p> <p>MBCT - 28%</p> <p>PLA - 71%</p> <p><b>Days to reach remission, mean (SD)</b></p> <p>M-ADM - 80.1(60.0)</p> <p>MBCT - 68.1(51.9)</p> <p>PLA - 90(57.8)</p>
Bieling et al. (42)	6/11	84 individuals with MDD (52 female, 32 male) (18 to 65 years old) (DSM-IV)	<p>GI – (28) ADM (To maintenance antidepressant medication)</p> <p>GII – (26) *MBCT (To discontinuation antidepressant medication + MBCT)</p> <p>GIII – (30) PLA (To discontinuation antidepressant medication + placebo)</p> <p>Follow-up = 6 months</p>	<p><b>Rumination Mean (SD)</b></p> <p><b>MBCT</b> - Baseline to 8-week = 17.40(4.10) to 17.73(3.91) ns</p> <p><b>ADM</b> - Baseline to 8-week = 19.12(2.20) to 19.33(2.66) ns</p> <p><b>PLA</b> - Baseline to 8-week = 19.12(2.83) to 19.05(3.36) ns</p>
Van Vugt et al. (2)	9/11	45 individuals with MDD (39 female, 06 male) (24 to 64 years old) (DSM-IV - SCID) To maintenance antidepressant medication	<p>GI – (19) control</p> <p>GII – (26) *MBCT</p>	<p><b>Depression BDI Mean p</b></p> <p>MBCT - Baseline to 8-week = 9.1 to 6.5 p.01</p> <p><b>Positive words (%)</b></p> <p>MBCT - Baseline to 8-week = 28.9 to 33.5</p> <p>Control - Baseline to 8-week = 27.3 to 30.5</p> <p><b>Negative words (%)</b></p> <p>MBCT - Baseline to 8-week = 27.2% to 27.4</p> <p>Control - Baseline to 8-week = 24.0 to 32.0</p> <p><b>Anxiety (STAI-Y1) Mean (SD)</b></p> <p>MBCT - Baseline to 8-week = 53.4(10.9) p/ 50.7 (11.12) p.05</p>
Batink et al. (43)	8/11	130 individuals with MDD (98 female, 32 male) (24 to 64 years old) (DSM-IV - SCID) To maintenance antidepressant medication	<p>GI – (64) *MBCT + TAU</p> <p>GII – (66) TAU</p> <p>Randomization was stratified according to number of depressive episodes (<math>\leq 2</math> MDE vs <math>\geq 3</math> MDE)</p>	<p><b>Rumination Mean (SD)</b></p> <p>MBCT + TAU- Baseline to 8-week = <math>\leq 2</math> - 7.8(8.5) to - 8.1(8.4) ns</p> <p>MBCT + TAU- Baseline to 8-week = <math>\leq 3</math> - 7.8(8.5) to - 7.5(8.8) ns</p> <p>TAU - Baseline to 8-week = <math>\leq 2</math> -2.7(7.7) to - 1.9(6.9) ns</p> <p>TAU - Baseline to 8-week = <math>\leq 3</math> -2.7(7.7) to - 3.7(8.6) ns</p>

(To be continued)

**Table 2** - Characteristics of the studies Interventions

Author, year	Criteria Pedro scale	Subjects	Intervention	Findings
Munshi et al. (37)	5/11	18 individuals with MDD (13 female, 05 male) (24 to 81 years old) (DSM-IV - SCID)	GI – *MBCT  Follow-up = 48.7 months	<b>Depression (BDI)</b> Mean p Baseline to 8-week to follow-up -18.78 to 5.33 to 5.89 p.00 <b>Rumination (RRS)</b> Mean Baseline to 8-week to follow-up - 49.28 to 44.41 to 40.11 p.00 <b>Anxiety (STAI-Y1)</b> Mean Baseline to 8-week to follow-up - 44.22 to 31.56 to 31.22 p.00
Omid et al. (38)	8/11	90 individuals with MDD (60 female, 30 male) (18 to 45 years old) (DSM-IV - SCID)	GI – (30) *MBCT  GII – (30) CBT (traditional Cognitive Behavior Therapy)  GIII – (30) TAU	<b>Depression (BSI)</b> Mean (SD) MBCT - Baseline to 8-week - 2.05(0.84) to 0.79(0.63) CBT - Baseline to 8-week - 2.18(0.57) to 0.79(0.51) TAU - Baseline to 8-week - 2.18(0.85) to 1.96(0.86) <b>Brief Symptom Inventory (BSI)</b> Mean (SD) MBCT - Baseline to 8-week - 1.62(0.56) to 0.72(0.46) CBT - Baseline to 8-week - 1.79(0.47) to 0.72(0.26) TAU - Baseline to 8-week - 1.79(0.50) to 1.59(0.52)
Schoenberg e Speckens (39)	7/11	51 individuals with MDD (60 female, 30 male) (21 to 65 years old) (DSM-IV-TR)	GI – (25) control  GII – (26) *MBCT	<b>Depression IDS</b> Mean (SD)p MBCT - Baseline to 8-week - 27.3(9.4) to 19.3(9.3) p.02 Control - Baseline to 8-week - 25.1(12.3) to 25.3(13.2) ns <b>Response patterns towards feelings of sadness/depression (RRS)</b> Mean (SD)p MBCT - Baseline to 8-week - 60.6(11.9) to 55.1(11.0) p.03 Control - Baseline to 8-week - 60.2(13.2) to 59.7(13.8) ns
Williams et al. (40)	6/11	255 individuals with MDD (198 female, 57 male) (18 to 70 years old) (DSM-IV - SCID and suicidal feelings and at least one other symptom of depression, which together were not attributable to bereavement, substances, or medical condition, but were impairing functioning)	GI – (99) *MBCT  GII – (103) **CPE (cognitive psychological education)  GIII – (53) TAU  Follow-up = 6 months	<b>Relapse to Major Depression (%)</b> MBCT - 46% CPE - 50% TAU - 53% <b>Antidepressant use (%)</b> MBCT - 18% CPE - 13% TAU - 21% <b>Looked for a psychiatrist (%)</b> MBCT - 10% CPE - 9% TAU - 11%

(To be continued)



(Conclusion)

**Table 2** - Characteristics of the studies Interventions

Author, year	Criteria Pedro scale	Subjects	Intervention	Findings
Kuyken et al. (41)	10/11	424 individuals with MDD (325 female, 99 male) (20 to 79 years old)	GI = (212) *MBCT-TS = mindfulness + support to taper or discontinue their maintenance antidepressant medication  GII = (212) m-ADM  Follow-up = 24 months	<b>Depression</b> BSII Mean (SD) <b>MBCT-TS</b> Baseline 13.8(12.4) to 1 month 9.9(9.7) to 9 months 11.0 (10.5) to 12 months 10.7(10.0) to 18 months 11.7(10.6) to 24 months 11.6(10.9) ns <b>m-ADM</b> Baseline 14.4(10.1) to 1 month 13.9(10.9) to 9 months 10.5(9.7) to 12 months 11.3(9.2) to 18 months 11.3(10.7) to 24 months 11.9(10.7) ns
Shallcross et al. (13)	8/11	51 individuals with MDD (38 female, 13 male) (18 to 65 years old) (DSM-IV - SCID)	GI – (29) *MBCT  GII – (22) **ACC active control condition  Follow-up = 12 months	<b>Depression</b> BDII Mean (SD) <b>MBCT</b> Baseline 12.1(7.5) to 1 month 11.9(7.2) to 6 months 8.2(6.9) to 12 months 7.0(6.1) <b>ACC</b> Baseline 11.9(6.6) to 1 month 7.1(6.4) to 6 months 6.2(5.7) to 12 months 7.2(6.0)  <b>Relapse to Major Depression</b> MBCT - 32.6% ACC - 30.4% <b>Antidepressant use</b> MBCT Baseline 30.4 to 1 month 28,1 ACC Baseline 26.1 to 1 month 22.2

Note: MBCT = Mindfulness-Based Cognitive Therapy; TAU = treatment-as-usual; MDD = Major depressive disorder; m-ADM or ADM = Maintenance Antidepressant Medication; PLA = placebo; CBT = Traditional Cognitive Behavior Therapy; DSM-IV (Diagnostic and Statistical Manual of Mental Disorders (SCID));

\*MBCT = Kabat-Zinn's (19) original 8-week program, weekly 2-hr sessions. Eight 2-h classes were held, up to an hour of which is spent in meditation practices. (body scan, sitting meditation, mindful movements, and 3-minute breathing space). MBCT sessions focus on cultivating mindfulness or nonjudgmental present-moment awareness of mental content and everyday activities. Exercises featuring: (1) guided (taped) awareness exercises directed at increasing moment-by-moment nonjudgmental awareness of bodily sensations, thoughts, and feelings; (2) accepting difficulties with a stance of self-compassion; (3) developing an "action plan" composed of strategies for responding to early warning signs of relapse/recurrence and (4) homework.

\*\*CPE (cognitive psychological education) Comprised all elements of the MBCT program except the experiential cultivation of mindfulness through meditation practice and followed the same format of eight weekly 2-hr classes (i.e., matched for time with MBCT), with follow-up classes at 6 weeks and 6 months. Thus, participants learned about the psychological processes of relapse and were encouraged to apply what they had learned outside the sessions, to help prevent relapse. They also learned how to recognize the warning signs of depression and the importance of disengaging from unhelpful processes such as rumination and experiential avoidance. CPE educated them about these processes through interactive practical exercises and group discussions.

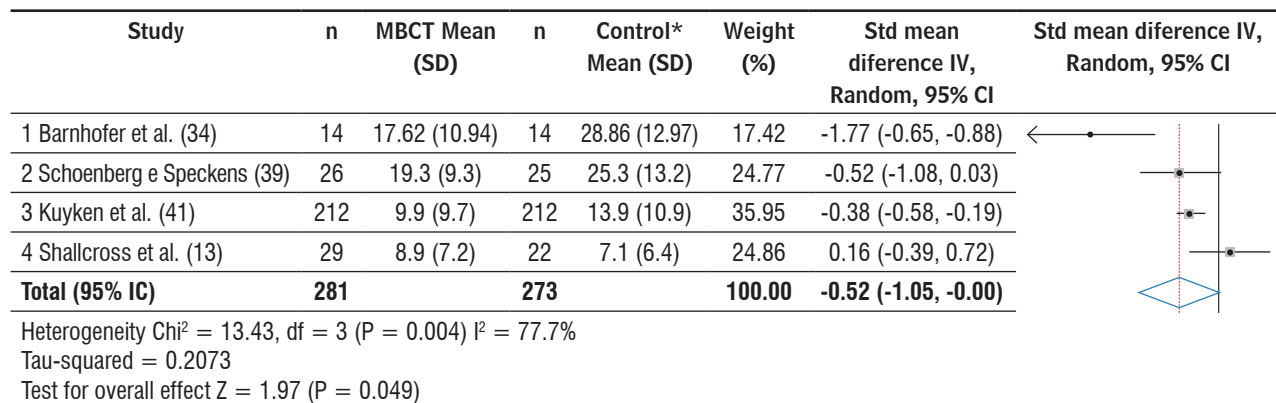
\*\*\*ACC (active control condition) Based on the validated and manualized Health Enhancement Program (HEP). It included classes in four therapeutic components including physical activity, functional movement, music therapy, and nutrition, each of which lacked a mindfulness element. In-class time (weekly classes lasted 2.5 hr for 8 weeks), group size (10–12 participants in each group), and time outside of class for homework (approximately 50 min per day).

Four studies presented continuous data (13, 34, 39, 41) and were classified for the performance of the meta-analysis (Figures 2 and 3). The meta-analysis showed a result that revealed a moderate effect of MBCT on the depression outcome with a significant effect estimation of -0.52 (95% CI: -1.050 to -0.002;  $p = 0.04$ ), revealing differences between the interventions.

It should be noted that the 95% CI of three articles and the diamond of the graph did not cross the statistically null line, indicating favorable results for MBCT regarding the depression scores, with only one

study showing favorable results for the intervention (ACC = active control condition). The analysis of heterogeneity showed a heterogeneous sample with  $p$  value of 0.04 for the  $Q$  test and  $I^2 = 77\%$ .

The result of effect size (ES) for the studies were: large effect size for the study of Barnhofer et al. (34) ( $d = 0.93$ , IC 95%: 0.15 a 1.71), followed by that of Schoenberg and Speckens (39), with a medium ES ( $d = 0.52$ , IC 95%: -0.03 a 1.08), and small ES for that of Kuyken et al. (41) ( $d = 0.38$ , IC 95%: -0.36 a 1.13) and Shallcross et al. (13) ( $d = -0.26$ , IC 95%: -0.81 a 0.29).

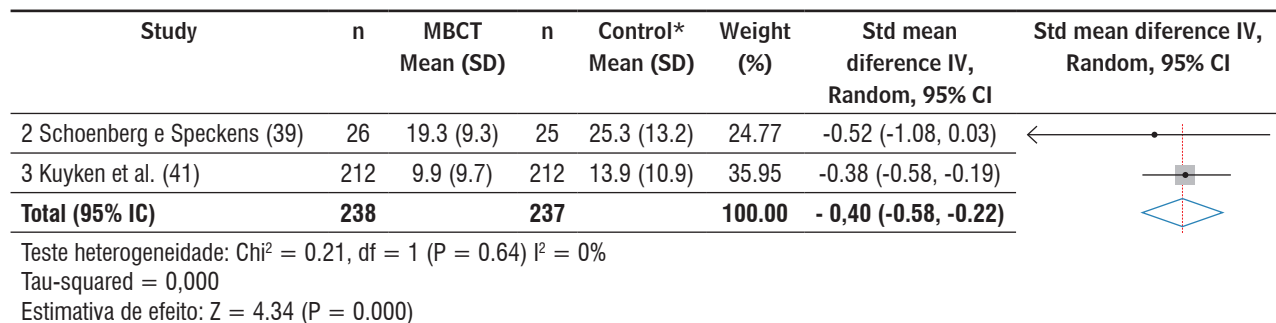


Note: \*Control: 1 TAU Treatment as Usual, 2 Control, 3 m-ADM = Maintenance Antidepressant Medication, 4 ACC = active control condition; CI= confidence intervals.

**Figure 2** - Meta-analysis of studies evaluating effects of MBCT on depression.

In analyzing the studies of Barnhofer et al. (34) and Shallcross et al. (13) (Figure 2) differences were observed that could generate bias (sample and publication) compared with the results of the other studies. Therefore an additional analysis of sensitivity was performed, replicating the

meta-analysis after excluding these two studies. The effect of MBCT on the depression scores remained, with a mean difference of -0.40 (95% CI: -0.58 to -0.03;  $p = 0.00$ ), with a lack of heterogeneity, according to the analysis using the  $Q$  test ( $p = 0.64$ ), with  $I^2 = 0\%$  (Figure 3).



Note: \*Control: 1 TAU Treatment as Usual, 2 Control, 3 m-ADM = Maintenance Antidepressant Medication, 4 ACC = active control condition; CI= confidence intervals.

**Figure 3** - Forest plot showing effects of MBCT on depression.

## Discussion

The results of a systematic review and meta-analysis (random effects model) and of the other studies (randomized and non-randomized studies) indicate that MBCT is likely to reduce depressive symptoms compared to the other treatments (control, TAU, ADM) and was shown to be equivalent to the ACC, in the improvement of scores of depression, anxiety, rumination and positive thoughts and words, among others.

It is assumed that, with the improvement of a symptom of depression, there is a tendency for improvement of various other symptoms together. In this review it was chosen to highlight some of these symptoms and their relationships with others, which could provide subsidies for understanding the treatment of individuals with MDD.

Firstly, the reduction of rumination and negative thoughts and the increase in sustaining trains of positive words were shown in two studies, with the effect in both the MBCT and the Control groups (2, 33). Both associated results are important in the treatment of MDD, as rumination is a persistent symptom and, although the content of rumination is typically negative, it is the persistent style (not content) of thought which is the central key to rumination, causing the person to have difficulties in attention and cognition (44, 45).

Desire is considered a component of human existence and desire and attachment are seen as the root of human suffering in Buddhist philosophy (46). From the cognitive perspective, desire reflects information processing and is rooted in cognitive processes (e.g. memory, expectations) (47).

Thus the practice of MBCT is beneficial to these symptoms, as it combines cognitive therapy with intensive training in meditation (48), focusing on observation and working on cognitive and affective processes. It teaches individuals to become more aware and to relate to themselves (49), helping to eliminate the patterns of rumination and negative thoughts that can contribute to relapse, bringing awareness to the experience of desire, teaching the subjects to observe without reacting or judging, and to avoid suffering (50).

The regular practice of MBCT increases the thickness of the cortex in the areas of the somatosensory system, which is positively correlated with increased awareness of the body (51). It also leads individuals to accept experience as impermanent, recognizing that neither the positive state nor the negative state

are long lasting and allowing them to realize that the effort exerted to achieve or hold on to a certain state of being is not only useless, but can cause suffering (52).

The positive relationship between the practice of MBCT and improvement in depressive symptoms is consistent with several other studies. Petrocchis and Ottaviani (53) showed decreased rumination and increased positive thoughts mediated by the impact of non-judgment, with 41 subjects, in a longitudinal study of up to 2 years of practice. Schroevers and Brandsma (54) found improvements in positive attitudes (feeling enthusiastic and active) and decreases in negative attitudes (negative mood, anger, sadness and nervousness), with 64 individuals, in eight weeks of practice. Sephton et al. (55) reported decreased use of antidepressants, pain, improvements in the symptoms of depression and in sleep, with 91 women with fibromyalgia, after 8 weeks of practice.

Secondly, another result that should be mentioned is the higher number of women in the samples compared to men. It is assumed that some risk factors may be triggering MDD, such as biological aspects, hormonal fluctuations during the reproductive period, menopause and psychosocial aspects (social and family roles) in women and sexual abuse in childhood, behavior disorder, drug abuse and stressful life events (mainly financial and professional problems) in men (56, 57).

Women with MDD are more prone to anxiety disorder and suicide ideation while men show more agitation, substance abuse and if prone to suicide tend to be successful (58). In the present review, two studies showed decreased suicidal tendencies, with MBCT proving better than TAU in both. Hargus et al. (59) studied 27 depressed individuals with suicidal crises or warning signs for their last crisis and observed that the MCBT group obtained better results than the TAU group, as it caused individuals to reflect on the previous crises in a detailed and decentralized way, allowing them to relate to these experiences.

Thirdly, many of the selected studies made comparisons between MBCT and other therapeutic interventions. What may differentiate MBCT from other therapies is that, despite perception and attention being constant features of normal body functioning, MBCT aims to raise awareness by improving the perception and attention in the current reality (60).

In this review, MBCT was shown to be better when compared with TAU for various depressive symptoms, for rate and time of relapse and for the time of seeking a psychotherapist. In only one study MBCT and ADM

were found to be equivalent. Kuykem et al. (41) showed similar results between the two regarding relapse rate and days of remission. Greater improvements in depressive symptoms compared with TAU has also been observed in other studies, such as that of Godfrin and Van Heeringen (61) with 106 depressed individuals, after 56 weeks, where they observed reductions in the time and rate of relapse and in the depressive mood and improvements in the quality life in the MBCT + TAU group, compared to the TAU only group.

Two interventions (ACC e CPE) showed a trend of better results than the practice of MBCT, in the use of antidepressants, in seeking a psychotherapist and in the relapse rate in patients with MDD. It should be highlighted that both therapeutic interventions resembled MBCT, because ACC uses the elements of MBCT with increased physical exercise, functional movements, music therapy and nutrition. Cognitive psychological education, as in MBCT, uses interactive practical exercises and group discussions to teach individuals about the psychological processes of relapses, monitoring of the mood, the importance of recognizing the various elements of the experience (thoughts, emotions, feelings and behavior) and to switch off negative aspects, such as rumination (62).

In this review, one study showed that CBT presented results similar to MBCT, with the improvement of the general symptoms of depression. The study of Manicavasgar, Parker and Perich (63), which compared MCBT to CBT, also showed the same results regarding the symptoms of depression. This can be explained because CBT incorporates aspects of meditation added to the monitoring of thought, identification of cognitive distortions, self-esteem, goal setting and the identification of problems and supports (64). Cladder-Micus et al. (65) highlighted that this union is important because MBCT develops self-compassion and focuses on the process of thinking, while CBT focuses on the content of the thoughts.

Some limitations of this meta-analysis should be considered. The first is the quality of the studies (Table 1), not always achieving top marks in the Pedro scale. The second is that some studies did not report basic data of the descriptive and inferential statistics, presenting only frequency values. Thirdly, non-randomized clinical trials were included and the meta-analysis of these studies was not performed. This choice was due to the need observed in the literature for an article that also presented innovative

results even though not carried out randomly. Fourthly, choosing the articles from just one database may have led to the absence of intervention studies with excellent quality accepted in other databases. This choice was made because this database is freely accessible and has quality in its publications.

## Conclusion

This systematic review and meta-analysis suggests that MBCT can be considered a promising alternative for the treatment of MDD. The results show that MBCT alone is effective for the main symptoms of MDD, however, when integrated with other cognitive interventions (TAU ACC, CPE, CBT) and with the use of medications (ADM) it is shown to be more effective. These findings demonstrate the need for greater provision of alternative treatments for MDD, which would reduce intervention costs and could increase the coverage.

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