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Research Letter | Psychiatry

Symptom Worsening in Mindfulness-Based Cognitive Therapy

Simon B. Goldberg, PhD; Otto Simonsson, PhD; Fiona C. Warren, PhD; James E. Pustejovsky, PhD; Matthew J. Hirshberg, PhD; Shufang Sun, PhD; Françoise Jermann, PhD; Anne Speckens, MD, PhD; J. Mark G. Williams, PhD; Tim Dalgleish, PhD; Jesus Montero-Marin, PhD; Willem Kuyken, PhD

Introduction

The individual participant data (IPD) meta-analysis of mindfulness-based cognitive therapy (MBCT) for the prevention of depressive relapse or recurrence described by Kuyken et al[1] has supported the dissemination of MBCT as a frontline treatment for depression. MBCT is now recommended in multiple clinical guidelines including the National Institute for Health and Care Excellence in the UK and is widely implemented across health care systems. Since this meta-analysis was published, questions have been raised regarding the safety of mindfulness-based interventions. Two recent studies examined the occurrence of meditation-related harm in the context of MBCT.[2,3] Although definitions and rates of harm differed across these studies, both documented cases defined as reflecting patient-reported harm. Importantly, neither study included a control condition, making it impossible to evaluate the degree to which MBCT increased the likelihood of these experiences occurring. Establishing whether MBCT increases the likelihood of poor outcomes relative to a control condition is crucial for weighing the costs relative to benefits of this treatment. IPD allows evaluation of symptom worsening following treatment relative to controls, which is one indicator of treatment-related harm when examined within a randomized trial context in which causality can be inferred.[4,5] The present study is a preregistered secondary analysis of the Kuyken et al[1] IPD evaluating odds of symptom worsening for MBCT vs controls.

Methods

Deidentified IPD were gathered from 9 randomized clinical trials evaluating MBCT for the prevention of relapse and/or recurrence among adults (≥18 years) with recurrent major depressive disorder currently in remission or partial remission (eMethods 1 in Supplement 1). The sample included 1258 patients. Analyses were preregistered prior to analysis (eMethods 2 in Supplement 1). The original trials obtained ethics approval and participant informed consent; secondary analysis of deidentified data are not considered human participant research by the University of Wisconsin–Madison institutional review board. The report follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guideline. We conducted 2-stage (primary model) and 1-stage random-effects meta-analyses comparing the odds of increased depressive symptoms at posttreatment assessed via the Beck Depression Inventory defined as within-patient increases greater than or equal to 0.24 SDs[6] following MBCT vs control. A series of sensitivity analyses defined worsening differently.[7] Mirroring Kuyken et al,[1] we conducted analyses restricted to active controls (antidepressants or cognitive psychoeducation) and to controls taking antidepressants. Missingness was handled using multiple imputation for the 2-stage model and maximum likelihood for the 1-stage model. Tests were 2-sided with significance set at $P < .05$. Analysis code is available (eMethods 2 and 3 in Supplement 1). Analyses were conducted between July 17, 2025, and June 18, 2026.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Results

Among 1258 patients (596 MBCT, 662 control; mean (SD) age 47.1 [11.9] years; 75% female), completion of posttreatment assessment did not differ across conditions (odds ratio [OR], 0.91; 95% CI, 0.62-1.34). At posttreatment, of 534 MBCT patients and 597 control patients, 120 MBCT patients (22.5%) and 199 control patients (33.3%) reported worsened depressive symptoms. Relative to all controls, MBCT was not significantly associated with the odds of symptom worsening in the primary 2-stage model (OR, 0.60; 95% CI, 0.34-1.08), although the 1-stage model indicated MBCT decreased odds (OR, 0.57; 95% CI, 0.35-0.95) (**Figure**). There was moderate-to-substantial heterogeneity across studies ($I^{2,}$ = 72.7%; 95% CI, 34.9%-95.3%; τ = 0.72; Q[8] = 23.48; P = .003).

Relative to active controls, MBCT did not differ on odds of symptom worsening in the 2-stage (OR, 0.79; 95% CI, 0.48-1.30) or 1-stage model (OR, 0.72; 95% CI, 0.50-1.06). Heterogeneity was not significant (I^2 = 48.9%; 95% CI, 0.0%-96.4%; τ = 0.38; Q[4] = 8.41; P = .08).

Relative to antidepressants, MBCT did not differ on odds of symptom worsening in the 2-stage model (OR, 0.79; 95% CI, 0.39-1.59), although the 1-stage model indicated MBCT decreased odds (OR, 0.63; 95% CI. 0.43-0.92). Heterogeneity was moderate (I^2 = 57.1%; 95% CI, 0.0%-97.8%; τ = 0.53; Q[3] = 6.99; P = .07). Results for different definitions of worsenings had similar findings (**Table**).

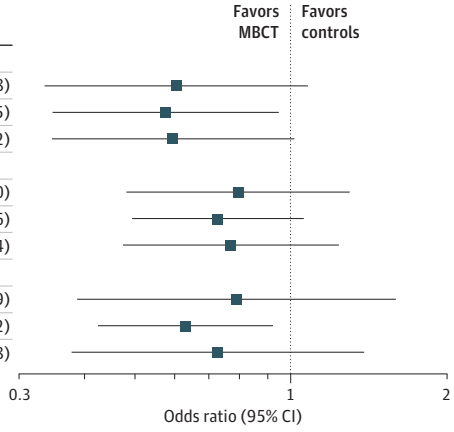
Discussion

Across models, we found no evidence that MBCT increased odds of depressive symptom worsening relative to controls. Consistent with recent large-scale mindfulness trials,[5,8] several models suggested MBCT was associated with lower odds of symptom worsening relative to controls, although this association did not emerge in our primary analyses (2-stage model) and was not significant relative to active controls. Differences across 1-stage and 2-stage approaches are known to occur, particularly in the presence of heterogeneity, as was present.[9]

Several limitations should be noted. The included trials focused on individuals in remission or partial remission from recurrent depression, so findings may not generalize to individuals with acute

Figure. Forest Plot of 1-Stage and 2-Stage Meta-Analyses Comparing Odds of Depression Symptom Worsening for MBCT vs Control Conditions

Comparison and method	I^2 (95% CI)	τ	Q	OR (95% CI)	P value	P value for Q statistic
MBCT vs all controls (k = 9)						
2-Stage (primary)	72.7 (34.9-95.3)	0.72	23.47	0.60 (0.34-1.08)	.09	.003
1-Stage	NA			0.57 (0.35-0.95)	.03	NA
2-Stage MI	68.3 (28.0-94.9)	0.64	22.52	0.59 (0.35-1.02)	.06	.01
MBCT vs active controls (k = 5)						
2-Stage (primary)	48.9 (0.0-96.4)	0.38	8.41	0.79 (0.48-1.30)	.36	.08
1-Stage	NA	0.08		0.72 (0.50-1.06)	.10	NA
2-Stage MI	42.4 (0.5-93.0)	0.34	7.32	0.77 (0.48-1.24)	.28	.24
MBCT vs antidepressants (k = 4)						
2-Stage (primary)	57.1 (0.0-97.8)	0.53	6.99	0.79 (0.39-1.59)	.51	.07
1-Stage	NA	0.00		0.63 (0.43-0.92)	.02	NA
2-Stage MI	41.7 (1.2-95.6)	0.42	5.75	0.72 (0.38-1.38)	.33	.29



Results are unadjusted. Multiple imputation (MI) was implemented in the mice package in R with 50 imputed datasets. Two-stage models were the preregistered primary models. Symptom worsening was defined as within-participant increase of greater than or equal to 0.24 SDs using baseline within-study SDs. One-stage models using multilevel logistic regression with likelihood of symptom worsening projected by group assignment, fixed intercept terms for each primary study, and random effects of group assignment for each primary study. To evaluate heterogeneity for the 1-stage models, likelihood ratio tests were conducted comparing models with and without random effects for group assignment, with boundary-corrected tests based on a mixture of χ^2_0 and χ^2_1distributions. No comparisons showed improved model fit with the addition of a random slope for mindfulness-based cognitive therapy (MBCT): all studies ($\chi^2_{[0:1]}$ = 2.40; P = .06), active controls ($\chi^2_{[0:1]}$ = 0.01; P = .47), and antidepressants ($\chi^2_{[0:1]}$ = 0.00; P > .99). NA indicates not applicable; OR indicates odds ratio.

Table. Meta-Analytic Results Across Sensitivity Analyses

Symptom worsening definition and model[a]	Odds ratio (95% CI)	*P* value	I^2 (95% CI)	τ	*Q*	*P* value for *Q*
Pooled SD[b]						
All studies						
2-Stage (primary)	0.58 (0.34-0.99)	.046	66.2 (20.8-94.7)	0.63	20.42	.009
1-Stage	0.55 (0.36-0.85)	.007	NA	0.45	NA	NA
2-Stage MI	0.58 (0.35-0.97)	.04	64.8 (20.9-94.6)	0.60	20.68	.02
Pooled SD[b]						
Active controls						
2-Stage (primary)	0.71 (0.47-1.08)	.11	30.1 (0-95)	0.26	6.09	.19
1-Stage	0.67 (0.49-0.92)	.02	NA	0	NA	NA
2-Stage MI	0.72 (0.46-1.12)	.14	31.6 (0.1-92.1)	0.28	6.08	.35
Pooled SD[b]						
Antidepressants						
2-Stage (primary)	0.71 (0.39-1.30)	.27	41.4 (0-97)	0.39	5.34	.15
1-Stage	0.61 (0.41-0.90)	.01	NA	0	NA	NA
2-Stage MI	0.71 (0.38-1.32)	.28	38.2 (0.6-95.3)	0.39	5.29	.31
≥17.5% Increase on BDI						
All studies						
2-Stage (primary)	0.61 (0.35-1.06)	.08	72.2 (34.3-95.3)	0.69	23.4	.003
1-Stage	0.59 (0.37-0.95)	.03	NA	0.54	NA	NA
2-Stage MI	0.61 (0.36-1.01)	.06	68.9 (28.1-94.7)	0.62	22.62	.009
≥17.5% increase on BDI						
Active controls						
2-Stage (primary)	0.82 (0.49-1.36)	.44	53.8 (0-97.6)	0.40	9.35	.05
1-Stage	0.81 (0.60-1.09)	.16	NA	0	NA	NA
2-Stage MI	0.80 (0.50-1.30)	.38	48.5 (1.1-96)	0.38	8.49	.14
≥17.5% Increase on BDI						
Antidepressants						
2-Stage (primary)	0.74 (0.37-1.47)	.39	57.7 (0-98.4)	0.53	6.74	.08
1-Stage	0.67 (0.46-0.98)	.04	NA	0	NA	NA
2-Stage MI	0.70 (0.39-1.27)	.25	31.8 (1.3-97.2)	0.41	5.66	.29
Within-study, within-arm SD[c]						
All studies						
2-Stage (primary)	0.56 (0.34-0.93)	.03	63.3 (16.3-94.3)	0.58	19.78	.01
1-Stage	0.54 (0.37-0.79)	.002	NA	0.34	NA	NA
2-Stage MI	0.58 (0.36-0.95)	.03	60.7 (16.6-94.2)	0.55	19.81	.03
Within-study, within-arm SD[c]						
Active controls						
2-Stage (primary)	0.67 (0.43-1.05)	.08	40.1 (0-96.8)	0.32	7.78	.10
1-Stage	0.64 (0.46-0.87)	.005	NA	0	NA	NA
2-Stage MI	0.7 (0.44-1.12)	.14	37.1 (0.2-93.8)	0.32	7.04	.28
Within-study, within-arm SD[c]						
Antidepressants						
2-Stage (primary)	0.65 (0.33-1.27)	.21	54.5 (0-98.1)	0.50	6.59	.09
1-Stage	0.56 (0.38-0.83)	.004	NA	0	NA	NA
2-Stage MI	0.68 (0.35-1.32)	.25	42.7 (1.2-96.3)	0.44	6.07	.24

Abbreviations: BDI, Beck Depression Inventory; MBCT, mindfulness-based cognitive therapy; MI, multiple imputation; NA, not applicable.

[a] Symptom worsening was defined as increased depressive symptoms of Cohen *d* greater than or equal to 0.24[6] calculated using baseline SDs pooled across studies, a 17.5% increase in symptoms on the Beck Depression Inventory relative to a given participant's baseline score,[10] or increased depressive symptoms of Cohen *d* greater than or equal to 0.24[6] calculated using posttreatment SD calculated separately by study and treatment group (ie, MBCT and control) within study.

[b] Indicates baseline.

[c] Indicates posttreatment.

depression or other clinical populations. While odds of symptom worsening on the Beck Depression Inventory is a useful indicator of potential harm, it does not capture the range of adverse experiences that may occur due to mindfulness training.[10] Future randomized trials should include a broader assessment of candidate adverse experiences.

Some individuals experience significant challenges over the course of mindfulness training.[10] However, randomized trials have not demonstrated a causal association with mindfulness interventions when harm is defined as symptom worsening. This supports continued dissemination of MBCT as an evidence-based treatment for recurrent depression.

ARTICLE INFORMATION

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Corresponding Authors: Simon B. Goldberg, PhD, Center for Healthy Minds and Department of Counseling Psychology, University of Wisconsin-Madison, 335 Education Building, 1000 Bascom Mall, Madison, WI 53703 (sbgoldberg@wisc.edu); Willem Kuyken, PhD, Department of Psychiatry, Warneford Hospital, Prince of Wales International Centre, University of Oxford, Oxford OX3 7JX, England (willem.kuyken@psych.ox.ac.uk).

Author Affiliations: Center for Healthy Minds, University of Wisconsin-Madison, Madison (Goldberg, Simonsson, Hirshberg); Department of Counseling Psychology, University of Wisconsin-Madison, Madison (Goldberg); Center for Social Sustainability, Department of Neurobiology, Care Sciences and Society, Karolinska Institute, Solna, Sweden (Simonsson); Institute of Health Research, Primary Care Research Group, Exeter Medical School, Exeter, England (Warren); Department of Educational Psychology, University of Wisconsin-Madison, Madison (Pustejovsky); Department of Behavioral and Social Sciences, Brown University School of Public Health, Providence, Rhode Island (Sun); Mindfulness Center, Brown University, Providence, Rhode Island (Sun); Center for Global Public Health, Brown University, Providence, Rhode Island (Sun); Department of Psychiatry, Geneva University Hospital, Geneva, Switzerland (Jermann); Department of Psychiatry, Radboudumc, Nijmegen, the Netherlands (Speckens); Department of Psychiatry, University of Oxford, Prince of Wales International Centre, Warneford Hospital, Oxford, England (Williams, Montero-Marin, Kuyken); Hong Kong Centre for Mindfulness, Hong Kong (Dalgleish); Medical Research Council Cognition and Brain Sciences Unit, University of Cambridge, Cambridge, England (Dalgleish); Department of Psychology, University of Cambridge, Cambridge, England (Dalgleish); Cambridgeshire and Peterborough NHS Foundation Trust, Cambridge, England (Dalgleish); Teaching, Research, & Innovation Unit, Parc Sanitari Sant Joan de Déu, Sant Boi de Llobregat, Barcelona, Spain (Montero-Marin); Consortium for Biomedical Research in Epidemiology and Public Health (CIBER Epidemiology and Public Health-CIBERESP), Madrid, Spain (Montero-Marin); Melbourne School of Psychological Sciences, University of Melbourne, Melbourne, Australia (Montero-Marin).

Author Contributions: Drs Goldberg and Pustejovsky had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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SUPPLEMENT 1.

eMethods 1. Inclusion/exclusion criteria
eMethods 2. Preregistered analysis plan and analysis code
eMethods 3. Additional analytic details
eReferences. References

SUPPLEMENT 2.

Data Sharing Statement