A Randomized Controlled Pilot Study on Mindfulness-Based Cognitive Therapy for Unipolar Depression in Patients With Chronic Pain

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ABSTRACT

Objective: Chronic pain is a disabling illness, often comorbid with depression. We performed a randomized controlled pilot study on mindfulness-based cognitive therapy (MBCT) targeting depression in a chronic pain population.

Method: Participants with chronic pain lasting ≥ 3 months; *DSM-IV* major depressive disorder (MDD), dysthymic disorder, or depressive disorder not otherwise specified; and a 16-item Quick Inventory of Depressive Symptomatology-Clinician Rated (QIDS-C_{16}) score ≥ 6 were randomly assigned to MBCT (n = 26) or waitlist (n = 14). We adapted the original MBCT intervention for depression relapse prevention by modifying the psychoeducation and cognitive-behavioral therapy elements to an actively depressed chronic pain population. We analyzed an intent-to-treat (ITT) and a per-protocol sample; the per-protocol sample included participants in the MBCT group who completed at least 4 of 8 sessions. Changes in scores on the QIDS-C_{16} and 17-item Hamilton Depression Rating Sale ($HDRS_{17}$) were the primary outcome measures. Pain, quality of life, and anxiety were secondary outcome measures. Data collection took place between January 2012 and July 2013.

Results: Nineteen participants (73%) completed the MBCT program. No significant adverse events were reported in either treatment group. ITT analysis (n = 40) revealed no significant differences. Repeated-measures analyses of variance for the per-protocol sample (n = 33) revealed a significant treatment × time interaction ($F_{1,31} = 4.67$, $P = .039$, $\eta^2_p = 0.13$) for QIDS-C_{16} score, driven by a significant decrease in the MBCT group ($t_{18} = 5.15$, $P < .001$, $d = 1.6$), but not in the control group ($t_{13} = 2.01$, $P = .066$). The $HDRS_{17}$ scores did not differ significantly between groups. The study ended before the projected sample size was obtained, which might have prevented effect detection in some outcome measures.

Conclusions: MBCT shows potential as a treatment for depression in individuals with chronic pain, but larger controlled trials are needed.

Trial Registration: ClinicalTrials.gov identifier: NCT01473615

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Chronic pain is a highly prevalent, costly condition that poses a substantial burden on patients, their significant others, and society. In an internet-based survey,[1] the prevalence of chronic pain in the United States was calculated to be 30.7%, meaning that approximately 1 in 3 Americans lives with chronic pain.

Chronic pain has high comorbidity with psychiatric disorders.[2] Depression is the most common of these, with a mean prevalence rate of comorbid major depressive disorder (MDD) in patients with chronic pain ranging from 18% in population-based settings up to 85% in specialized pain clinics.[3] Patients with chronic pain and comorbid depression experience greater pain intensity, greater interference due to pain, and more pain behaviors, specifically including affective distress and facial/audible expressions as measured by the Pain Behavior Check List.[4,5] In addition, depression is associated with poorer occupational[6] and social function,[7] increased health care utilization,[8] and increased risk of attempted and completed suicide.[9] Treatment of depression in people with chronic pain is therefore a major public health imperative.

Recently, there has been an increasing interest in mindfulness-based therapies, such as mindfulness-based stress reduction (MBSR)[10] and the adapted program for depression relapse prevention, mindfulness-based cognitive therapy (MBCT).[11] Mindfulness-based interventions teach participants meditation techniques that increase awareness of current moment experience and promote an accepting attitude toward oneself.[12] These techniques are believed to help participants disengage from dysfunctional automatic thinking patterns and create a more accepting stance toward physical and emotional pain.[13] MBSR was originally developed for stress reduction in a chronic medically ill population, and it does not specifically target depression. MBCT integrates aspects of cognitive-behavioral therapy (CBT) and MBSR; it focuses more explicitly on "decentering," which refers to the process of disengagement of negative automatic thoughts and is associated with

a significant reduction in depressive symptoms.[14] MBCT has been proved effective for depression relapse prevention,[15–20] and there is increasing evidence that it also can be effective for active depression.[21–23] Research in mindfulness-based interventions for chronic pain show promising results,[24] but there is a lack of well-designed studies.[25] To our knowledge, there are no studies that specifically address the effectiveness of a mindfulness-based intervention for depression in a chronic pain population.

Given what the literature has shown, there is a good chance that integrating aspects of mindfulness and CBT might create synergistic effects in the treatment of depression in patients with chronic pain.[25,26] We therefore developed an MBCT program that specifically targets active depression in individuals with chronic pain and carried out a randomized controlled pilot trial of this intervention. We predicted that MBCT would be a feasible and effective intervention in our sample, with minimal side effects and a retention rate of 70% to 80%. We hypothesized that participants who completed a predetermined "minimum effective dose" of at least 4 of 8 MBCT sessions as proposed by Teasdale et al[15] would demonstrate a significant decrease in depressive symptoms as measured on the 16-item Quick Inventory of Depressive Symptomatology-Clinician Rated (QIDS-C_{16}) and the 17-item Hamilton Depression Rating Scale ($HDRS_{17}$) compared to the control condition.

Clinical Points

- Depressive symptoms are highly prevalent in patients suffering from chronic pain and are related to a greater disease burden.
- Research focusing on psychotherapeutic treatment modalities targeting depression in a chronic pain population is mostly lacking.
- Mindfulness-based cognitive therapy may be a promising treatment targeting depression in a chronic pain population.

METHODS

Patient Recruitment and Inclusion/Exclusion Criteria

The study was carried out at the Depression Clinical and Research Program of the Massachusetts General Hospital (MGH). Participants were recruited by clinician referral from outpatient clinics that manage chronic pain and by web-based advertisements. At the screening visit, participants signed an informed consent approved by our Institutional Review Board and were administered the Structured Clinical Interview for *DSM-IV* (SCID).[27]

Inclusion criteria included (*a*) age ≥ 18 years; (*b*) the presence of chronic pain, which has persisted for at least 3 months; (*c*) meeting criteria for MDD, dysthymic disorder, or depressive disorder not otherwise specified (NOS) as defined by *DSM-IV* criteria; and (*d*) a score ≥ 10 on the QIDS-C_{16}. After initiation of the study, the cutoff was reduced to a QIDS-C_{16} score ≥ 6 (indicative of at least mild depressive symptoms) to allow more ample recruitment. Concurrent psychotherapy, psychopharmacotherapy, and chronic pain treatments were allowed, though subjects were asked to make as few changes as possible in their psychotherapy treatment and stay on a stable dose of psychotropics/analgesics as much as possible for the duration of the study and for 8 weeks prior to the study.

Exclusion criteria included (*a*) a primary diagnosis other than MDD, dysthymic disorder, or depressive disorder NOS or any history of psychosis or mania; (*b*) substance abuse or dependence within the last 3 months; (*c*) serious medical conditions (eg, poorly controlled diabetes, severe congestive heart failure) that had not been stable for at least 3 months; (*d*) current active suicidal or self-injurious potential necessitating immediate treatment; (*e*) general conditions that would impede participation in a group intervention, as assessed by the evaluating clinician (eg, severe personality disorders, cognitive impairment, tendencies toward physical aggression); and (*f*) significant current meditation practice (specifically, more than 3 hours of insight/mindfulness/Vipassana meditation per week).

A total of 71 participants were screened, of whom 40 were ultimately randomized, as described in the Results section (Figure 1). Participants were reimbursed $40 for their participation. The MBCT program was provided free of charge. The study was approved by the Partners Human Research Committee, Massachusetts General Hospital (protocol 2011-P-001699/1).

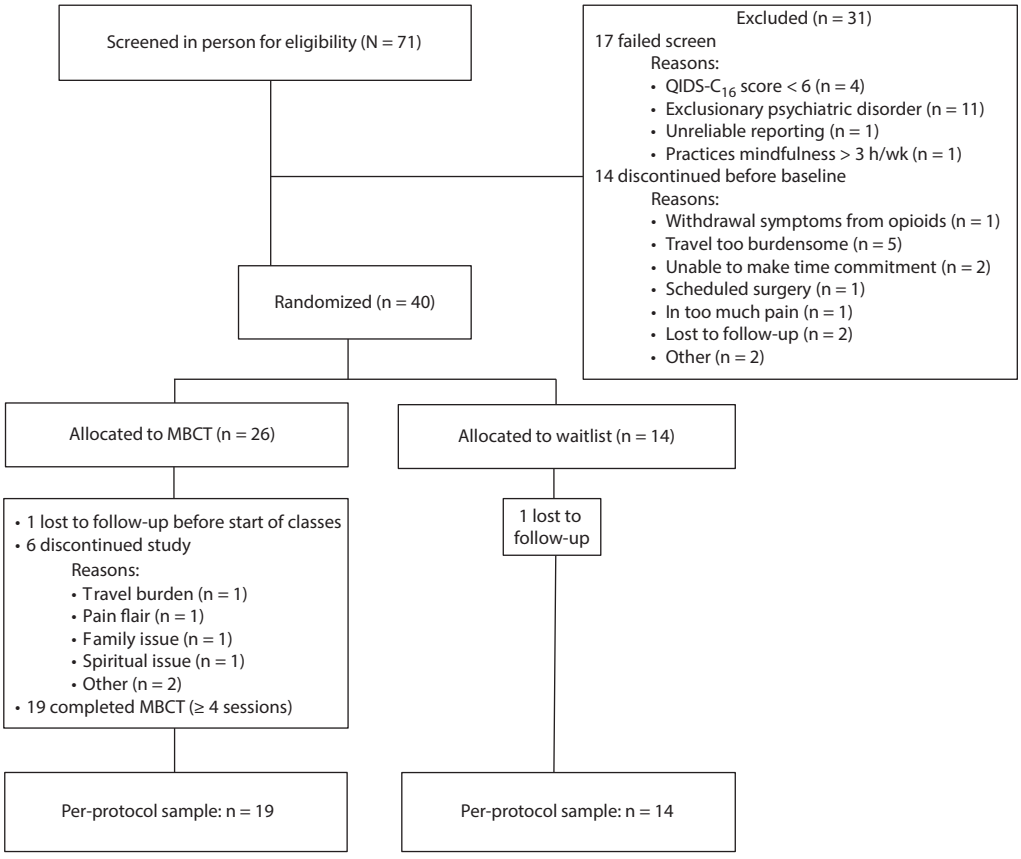
Treatment Assignment

Participants who fulfilled the inclusion criteria were randomly allocated to MBCT in addition to their treatment as usual (TAU) or else to continue with their TAU, if any (waitlist control condition). The randomization ratio for waitlist control to MBCT was 1:2, which allowed us to fill the MBCT groups with participants more quickly. In order to assure equal gender distribution in both groups, we stratified for gender.

Intervention

The intervention was based on the MBCT program developed by Segal et al.[11,28] The program combines elements of CBT with a "mindful" approach to thoughts and feelings, characterized by non-judgmental awareness of internal experience, including a significant meditation component. MBCT comprises a manualized 8-week group skills program with sessions that each last 2 hours. The program includes daily homework exercises, which mainly consist of guided or unguided mindfulness techniques. We adapted the original program to our specific population by modifying the psychoeducation and CBT elements to a depressed chronic pain population. This adaptation included psychoeducation linking chronic pain, negative thoughts, negative emotions, and depressive behaviors such as withdrawal; identifying automatic thoughts related to chronic pain; and paying attention to behavioral elements such as pacing of activities. We also included meditations that specifically focused on cultivating mindfulness in relationship to chronic pain.

Figure 1. CONSORT Chart



Abbreviations: MBCT = mindfulness-based cognitive therapy, QIDS-C_{16} = 16-item Quick Inventory of Depressive Symptoms-Clinician Rated.

The MBCT intervention was delivered at MGH in classes of 7 to 12 persons and was co-taught by an experienced licensed independent clinical social worker with advanced clinical training in therapeutic mindfulness and a fellow in psychology.

Waitlist

Participants who were randomly assigned to the waitlist control were offered the MBCT treatment at no costs after completion of the study.

Treatment as Usual

Treatment as usual for MBCT and control subjects included all regular visits with the pain physician, psychiatrist and psychotherapist and prescribed pain and/or antidepressant medications.

Efficacy, Safety, and Feasibility Measures

The change in the QIDS-C_{16}[29] and $HDRS_{17}$[30] scores were the primary outcome measures. Secondary outcome measures were based on the core outcome measures recommended by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT),[31] including pain, as measured by the Brief Pain Inventory short form (BPI)[32] and visual analog scale (VAS) ratings for average last week's pain intensity[33]; quality of life, as measured by the Short-Form Health Survey (SF-36)[34]; and anxiety, as measured by the Beck Anxiety Inventory (BAI).[35] Within 2 weeks after the last treatment session, participants rated their subjective impression of improvement by the standardized Patient Global Impression of Change questionnaire (PGIC).[36] All secondary outcome measures were collected using research electronic data capture (REDCap) tools.[37]

For safety reasons, all subjects completed a phone assessment every 2 weeks with a study clinician or a clinical fellow, at which time the QIDS-C_{16} and $HDRS_{17}$ were administered. Documentation of any side effect or adverse event was completed at every assessment by having the study physician inquire about and record any adverse events experienced by the participants.

Feasibility was assessed descriptively by calculating overall retention rates based on number of classes completed.

Statistical Analysis

Sample size calculation. Meta-analyses of mindfulness-based therapy in populations with mood disorders show relatively large effect sizes (Hedges *g* of 0.59) for improving depressive symptoms.[38] Assuming an estimate of a medium effect size (Cohen $d = 0.5$), a total sample size of 46 subjects

Table 1. Demographic and Clinical Characteristics of the Intent-To-Treat Sample

Characteristic[a]	All Evaluable Subjects (N = 40)	Baseline MBCT (n = 26)	Baseline Waitlist (n = 14)	*P* Value (t/χ^2 test)
Sex				.28
Male	10 (25.0)	5 (19.2)	5 (35.7)	
Female	30 (75.0)	21 (80.8)	9 (64.3)	
Race				.60
White	36 (90.0)	24 (92.3)	12(85.7)	
African American	4 (10.0)	2 (7.7)	2 (14.3)	
Ethnicity				.29
Hispanic	2 (5.0)	1 (3.8)	1 (7.1)	
Non-Hispanic	34 (85.0)	21 (80.8)	13 (92.9)	
Not reported	4 (10.0)	4 (15.4)	0 (0)	
Marital status[b]				.91
Married/live together	15 (48.4)	9 (50.0)	6 (46.2)	
Separated/widowed/divorced	6 (19.4)	3 (16.7)	3 (23.1)	
Never married	10 (32.3)	6 (33.3)	4 (30.8)	
Employment status[c]				.75
Employed	11 (30.6)	8 (34.8)	3 (23.1)	
Disabled	13 (36.1)	8 (34.8)	5 (38.5)	
Other	12 (33.3)	7 (30.4)	5 (38.5)	
Depression diagnosis				1.0
Major depressive disorder	34 (85.0)	22 (84.6)	12 (85.7)	
Not otherwise specified	6 (15.0)	4 (15.4)	2 (14.3)	
Antidepressant medication use[b]	18 (48.6)	11 (44.0)	7 (58.3)	.32
Age, mean (SD), y	50.7 (11.4)	51.3 (11.9)	49.9 (11.1)	.75
Years of education, mean (SD)[b]	16.5 (2.5)	16.4 (2.6)	16.6 (2.5)	.82

[a]Values shown as n (%) unless otherwise specified.
[b]Based on n = 37 due to 3 missing values.
[c]Based on n = 36 due to 4 missing values.
Abbreviation: MBCT = mindfulness-based cognitive therapy.

would provide 90% power to detect a difference between treatments. Assuming an attrition rate of approximately 20%, we originally sought to include 60 subjects.

Outcomes. Outcome measures were evaluated separately for an intent-to-treat (ITT) sample (n = 40) and a per-protocol sample (n = 33). The per-protocol sample comprised all waitlist control participants and all MBCT participants who completed a predetermined "minimum effective dose" of at least 4 MBCT sessions as proposed by Teasdale et al.[15] Because not all per-protocol subjects would necessarily be "completers" (ie, attend all study assessments conducted every 2 weeks), last observation carried forward (LOCF) was used for both per-protocol and ITT analyses. Baseline characteristics were compared between groups by the independent-samples *t* test for continuous variables and by the χ^2 test and Fisher exact test for categorical variables. The paired-samples *t* test was used to compare outcome variables from baseline to end. Repeated-measures analysis of variance (ANOVA) was used to compare changes in depression, pain, anxiety, and quality of life. The independent-samples *t* test was used to compare the PGIC ratings. For all analyses, significance was set as $\alpha = .05$ (2-tailed). Statistical procedures were performed with SPSS software, version 22. Data collection took place between January 2012 and July 2013. The study is registered in ClinicalTrials.gov under identifier NCT01473615.

RESULTS

Of the 71 subjects screened, 17 failed to meet inclusion criteria and 14 withdrew before the baseline visit. Figure 1 shows the patient flow from screening to completion of the study, including reasons for screen fail and for early discontinuation.

Demographic and clinical characteristics of the ITT sample are shown in Table 1. All 40 participants randomized (26 in the intervention arm and 14 in the control group) were evaluable by ITT for the primary outcome measures.

Of the 26 participants who started the MBCT classes, 19 (73%) completed the "minimum effective dose" of 4 MBCT sessions: mean attendance was 7 of 8 classes). In total, 33 participants (including the aforementioned 19 subjects in the intervention arm and 14 in the control group) were evaluable by per-protocol analysis for the primary outcome measures (6 of these had baseline QIDS-C_{16} scores between 6 and 9 per the modified entry criteria). Due to both technical and compliance problems with the REDCap surveys, fewer participants were evaluable for the secondary outcome measures (Tables 2 and 3).

There were no significant adverse events in either treatment arm except for 1 participant in the intervention group who discontinued because she had spiritual issues, possibly related to the treatment. Other adverse events reported included bronchitis, nausea, and urinary burning, which were not related to the intervention.

Independent-samples *t* test, χ^2 test, and Fisher exact test yielded no statistically significant differences in baseline demographic and clinical characteristics between the groups (Table 1). The SF-36 subscales, except for Vitality (lower in the intervention group), showed no statistically significant differences between the groups (Table 2). The study population suffered from a wide variety of pain conditions, including chronic back pain, migraines, neuropathic pain, osteoarthritis, and fibromyalgia. Eighty-five percent of the participants suffered from MDD and 15% from minor depressive disorder (within the broader category of depressive disorder NOS). None of the participants suffered from dysthymic disorder. Forty-nine percent of the participants were taking antidepressant medication, including monotherapy with serotonin-norepinephrine reuptake inhibitors (SNRIs) (18.9%), tricyclic antidepressants (5.4%), selective serotonin reuptake inhibitors (SSRIs) (2.7%), and other antidepressants (including bupropion and trazodone) (8.1%) or combined pharmacotherapy (13.5%).

Primary Outcome Measures for ITT Sample

Clinical improvement measured by both the QIDS-C_{16} and the $HDRS_{17}$ was greater for the MBCT group than for the control group, but the difference between groups did not reach statistical significance (Figure 2A).

Table 2. Baseline and End Point Data on Outcome Measures for the Intent-To-Treat Sample[a]

Outcome Measure	All Evaluable Subjects (N = 40)	Baseline		End Point		Significance of Time-by- Treatment Interaction, *F (df)*	*P*
		MBCT (n = 26)	Waitlist (n = 14)	MBCT	Waitlist		
QIDS-C_{16}	12.6 (3.5)	13.1 (3.4)	11.5 (3.7)	9.4 (6.1)	9.5 (3.7)	1.31 (1,38)	.26
$HDRS_{17}$	18.6 (4.9)	18.9 (4.6)	18.1 (5.6)	14.9 (8.1)	15.6 (4.9)	0.50 (1,38)	.48
VAS Average Pain Intensity	6.1 (1.5)	6.1 (1.6)	5.9 (1.4)	5.6 (1.7)	5.6 (2.3)	0.09 (1,38)	.77
BPI Pain Interference[b]	6.7 (2.2)	6.7 (2.1)	6.9 (2.4)	6.0 (2.0)	6.4 (2.4)	0.11 (1,32)	.74
BAI[c]	35.5 (10.1)	36.8 (11.3)	33.0 (7.1)	33.2 (8.8)	33.2 (6.6)	2.32 (1,33)	.14
SF-36							
Physical Functioning[c]	46.9 (24.3)	48.0 (24.9)	44.6 (24.1)	52.4 (26.0)	44.2 (24.6)	1.36 (1,33)	.25
Role Limitations Physical[c]	10.7 (24.5)	14.1 (29.0)	4.1 (9.7)	17.4 (33.2)	12.5 (29.2)	0.24 (1,33)	.63
Role Limitations Emotional[c]	21.0 (32.4)	21.7 (29.5)	19.4 (38.8)	33.3 (41.4)	22.2 (29.6)	0.43 (1,33)	.52
Vitality[c]	18.7 (17.5)	13.7 (11.0)	28.3 (23.6)†	21.7 (20.3)	22.1 (18.0)	8.45 (1,33)	.01*
Mental Health[c]	41.4 (17.8)	37.7 (18.1)	48.3 (15.4)	48.9 (21.0)	47.7 (19.9)	5.10 (1,33)	.03*
Social Functioning[c]	36.4 (22.9)	33.6 (19.6)	41.7 (28.4)	42.7 (25.4)	40.0 (25.7)	1.80 (1,33)	.19
Pain[c]	29.3 (16.7)	29.1 (16.8)	29.6 (17.2)	31.0 (20.1)	39.8 (24.4)	4.34 (1,33)	.05
General Health[c]	38.4 (18.1)	36.1 (18.6)	42.9 (16.8)	40.0 (23.2)	47.1 (18.9)	0.00 (1,33)	.96
PGIC[d]	…	…	…	2.7 (1.0)	4.0 (0.9)	…	…

[a]Values shown as mean (SD).
[b]Based on n = 34 due to 6 missing values.
[c]Based on n = 35 due to 5 missing values.
[d]Based on n = 27 due to 13 missing values.
*Statistically significant time × treatment interaction.
†$P < .05$ vs MBCT group at baseline.
Abbreviations: BAI = Beck Anxiety Inventory, BPI = Brief Pain Inventory, $HDRS_{17}$ = 17-item Hamilton Depression Rating Scale, MBCT = mindfulness-based cognitive therapy, PGIC = Patient Global Impression of Change questionnaire, QIDS-C_{16} = 16-item Quick Inventory of Depressive Symptoms-Clinician Rated, SF-36 = 36-item Short-Form Health Survey, VAS = visual analog scale.
Symbol: … = not applicable.

Table 3. Baseline and End Point Data on Outcome Measures for the Per-Protocol Sample[a]

Outcome Measure	All Evaluable Subjects (N = 33)	Baseline		End Point		Significance of Time-by-Treatment Interaction, *F (df)*	*P*
		MBCT (n = 19)	Waitlist (n = 14)	MBCT	Waitlist		
QIDS-C_{16}	11.9 (3.2)	12.3 (2.9)	11.5 (3.7)	7.2 (3.5)	9.5 (3.7)	4.67 (1,31)	.04*
$HDRS_{17}$	18.0 (5.1)	18.0(4.8)	18.1 (5.6)	12.8 (6.7)	15.6 (4.5)	1.53 (1,31)	.23
VAS Average Pain Intensity	5.9 (1.6)	6.0 (1.7)	5.9 (1.4)	5.5 (1.7)	5.6 (2.3)	0.05 (1,31)	.83
BPI Pain Interference[b]	6.7 (2.2)	6.6 (2.2)	6.9 (2.4)	5.7 (2.0)	6.3 (2.4)	0.55 (1,27)	.47
BAI[c]	34.4 (9.5)	35.4 (10.9)	33.0 (7.1)	30.7 (5.9)	33.2 (6.6)	3.03 (1,28)	.10
SF-36							
Physical Functioning[c]	46.2 (24.4)	47.2 (25.2)	44.6 (24.1)	52.8 (26.6)	44.1 (24.6)	1.71 (1,28)	.20
Role Limitations Physical[c]	12.5 (26.1)	18.1 (31.9)	4.1 (9.7)	22.2 (36.3)	12.5 (29.2)	0.12 (1,28)	.73
Role Limitations Emotional[c]	22.2 (34.3)	24.1 (32.0)	19.4 (38.8)	38.9 (44.6)	22.2 (29.6)	0.64 (1,28)	.43
Vitality[c]	21.7 (17.2)	17.2 (9.7)	28.3 (23.5)	27.5 (19.3)	22.1 (18.0)	9.37 (1,28)	.01*
Mental Health[c]	44.3 (16.6)	41.5 (17.3)	48.3 (15.4)	55.8 (16.8)	47.7 (19.9)	7.09 (1,28)	.01*
Social Functioning[c]	38.9 (23.1)	37.1 (19.5)	41.6 (28.4)	48.8 (24.5)	40.0 (25.7)	2.20 (1,28)	.15
Pain[c]	29.0 (16.7)	28.6 (16.7)	29.6 (17.2)	30.1 (21.1)	39.8 (24.4)	3.00 (1,28)	.10
General Health[c]	39.3 (17.5)	36.9 (18.0)	42.9 (16.8)	41.9 (23.5)	47.1 (18.9)	0.02 (1,28)	.89
PGIC[d]	…	…	…	2.7 (1.0)	4.0 (0.9)	…	…

[a]Values shown as mean (SD).
[b]Based on n = 29 due to 4 missing values.
[c]Based on n = 30 due to 3 missing values.
[d]Based on n = 27 due to 6 missing values.
*Statistically significant time × treatment interaction.
Abbreviations: BAI = Beck Anxiety Inventory, BPI = Brief Pain Inventory, $HDRS_{17}$ = 17-item Hamilton Depression Rating Scale, MBCT = mindfulness-based cognitive therapy, PGIC = Patient Global Impression of Change questionnaire, QIDS-C_{16} = 16-item Quick Inventory of Depressive Symptoms-Clinician Rated, SF-36 = 36-item Short-Form Health Survey, VAS = visual analog scale.
Symbol: … = not applicable.

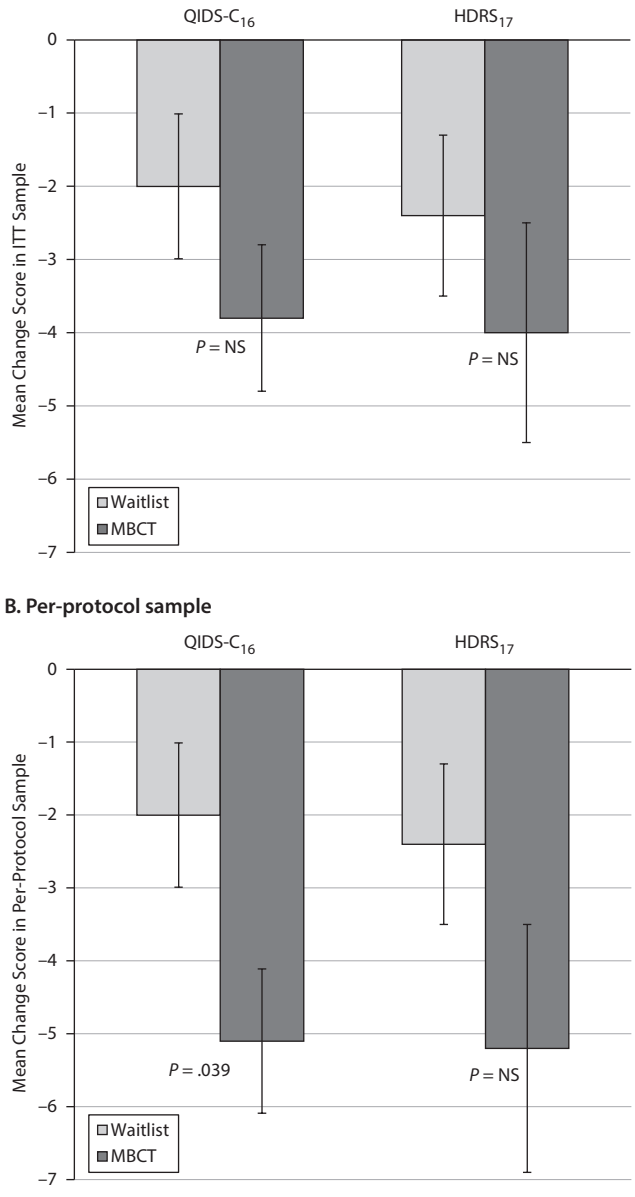
Primary Outcome Measures for Per-Protocol Sample

In the per protocol sample, repeated-measures ANOVA with time (baseline and end point) as the repeated measure, treatment arm as the between-subjects factor, and the QIDS-C_{16} score as the dependent variable revealed a significant time × treatment interaction ($F_{1,31} = 4.67$, $P = .039$, $\eta^2_p = 0.13$) for the QIDS-C_{16}, driven by a significant decrease in the MBCT ($t_{18} = 5.15$, $P < .001$, $d = 1.6$), but not in the control group ($t_{13} = 2.01$, $P = .066$) (Figure 2B). The Cohen *d* effect size of the improvement on the QIDS-C_{16} over time for MBCT relative to waitlist control was 0.77. Clinical improvement as measured by the $HDRS_{17}$ was also greater for the MBCT group than for the control group, but the difference between groups did not reach statistical significance (Figure 2B).

Secondary Outcome Measures for ITT Sample

The secondary outcome measures revealed no significant findings on time × treatment interaction for pain (VAS ratings of pain intensity and BPI pain interference) and

Figure 2. Depression Rating Scale Score Changes in the ITT Sample and Per-Protocol Sample[a]



[a]Error bars are ± 1 SEM; *P* values refer to group-by-time interaction effects as revealed by repeated-measures analyses of variance.
Abbreviations: $HDRS_{17}$ = 17-item Hamilton Depression Rating Scale, ITT = intent to treat, MBCT = mindfulness-based cognitive therapy, NS = nonsignificant, $QIDS\text{-}C_{16}$ = 16-item Quick Inventory of Depressive Symptoms-Clinician Rated.

anxiety (BAI). For quality of life, as measured by the SF-36, two health dimensions showed a significant time × group interaction: Mental Health ($F_{1,33} = 5.10$, $P = .031$, $\eta^2_p = 0.13$), driven by a significant increase in the MBCT group ($t_{22} = 3.40$, $P = .003$, $d = 0.57$), but not in the control group ($t_{11} = -0.19$, $P = .854$); and Vitality ($F_{1,33} = 8.45$, $P = .006$, $\eta^2_p = 0.20$), driven by a significant increase in the MBCT group ($t_{22} = 2.59$, $P = .017$, $d = 0.50$), but not in the control group ($t_{11} = -1.92$, $P = .082$). However, because the MBCT group had a significantly lower Vitality score at baseline, this positive interaction might be due to regression to the mean. All other measured health dimensions revealed no significant differences between groups. Participants who had received MBCT treatment reported a significantly higher subjective impression of clinical improvement (mean = 2.7 or "minimally improved" to "much improved") compared to control subjects (mean = 4.0 or "no change") ($t_{25} = 3.47$, $P = .002$).

Secondary Outcome Measures for Per-Protocol Sample

The secondary outcome measures revealed no significant findings on time × treatment interaction for pain (VAS ratings of pain intensity and BPI pain interference) and anxiety (BAI). For quality of life, as measured by the SF-36, two health dimensions showed a significant time × group interaction; Mental Health ($F_{1,28} = 7.09$, $P = .013$, $\eta^2_p = 0.20$), driven by a significant increase in the MBCT group ($t_{17} = -3.650$, $P = .002$, $d = 0.83$), but not in the control group (t_{11}, $P = .854$); and Vitality ($F_{1,28} = 9.37$, $P = .005$, $\eta^2_p = 0.25$), driven by a significant increase in the MBCT group ($t_{17} = -2.69$, $P = .016$, $d = 0.68$), but not in the control group ($t_{11} = 1.92$, $P = .082$). All other measured health dimensions revealed no significant differences between groups. Participants who had received MBCT treatment reported a significantly higher subjective impression of clinical improvement (mean = 2.5 or "minimally improved" to "much improved") compared to controls (mean = 4.0 or "no change") ($t_{23} = 3.696$, $P = .001$).

DISCUSSION

This pilot study shows positive outcomes for MBCT for depression (in the per-protocol sample) and mental health (both in the ITT and the per-protocol sample), but not for pain intensity. This finding is in line with the treatment goal of our MBCT program and psychotherapeutic interventions of chronic pain in general, which is not to remove or reduce the pain itself, but rather to find ways of managing the pain and the adverse consequences on mental health and quality of life. Interestingly, a recent randomized controlled trial from van Ravesteijn et al[39] focusing on MBCT for patients with medically unexplained symptoms, including chronic pain, also found significant improvement on mental health functioning, in particular with regard to vitality, but no significant findings on physical health and bodily pain.

While pain has both physical and psychological components, MBCT may address primarily the psychological components, by minimizing reactions to physical pain, such as worrying, catastrophizing, avoidance, and self-blaming. That this study shows no effects at all on pain intensity was somewhat unexpected, given that meta-analyses of psychological therapies typically do show small to moderate effects on pain intensity.[25,40] However, the most recent Cochrane meta-analysis on psychological therapies for chronic pain found the strongest effects on mood and the weakest effects on pain.[40]

Because this pilot study had only a small sample size, we might have had just enough power to detect effects on mood in the per-protocol sample but may have been underpowered to detect the smaller effects on pain intensity. Larger studies should help to answer this question.

The measurement of depression in a chronic pain population is particularly challenging because chronic pain can cause many symptoms that are also common in depression.[41] In this study, the decrease of depression severity in the MBCT completers was significant only in the per-protocol sample as measured by the QIDS-C_{16}. Interestingly, $HDRS_{17}$ scores did not decrease significantly. This finding might be explained by the fact that the $HDRS_{17}$, as opposed to the QIDS-C_{16}, has a larger emphasis on somatic symptoms, such as insomnia, which are less likely to change in a chronic pain population. Despite the limited research on the application of depression rating scales in chronic pain populations, there is some evidence that a substantial number of $HDRS_{17}$ items do not seem to track changes in depression in chronic pain populations.[42] To our knowledge, no study has been carried out to validate the QIDS-C_{16} in a medically ill population. Because the QIDS-C_{16} has less emphasis on somatic symptoms, it might be less prone to confounding by nonspecific symptoms in a chronic pain population. As a post hoc analysis, we examined a sub-portion of the $HDRS_{17}$ including only psychological symptoms (mood, guilt, suicide, psychic anxiety, and insight). Improvement in these selective symptoms was greater for the intervention group than for the control group but did not reach significance (data not shown). With respect to anxiety, a similar explanation might have played a role in the nonsignificant findings, because the BAI also emphasizes somatic items.[43] Hoge et al[44] reported similar concerns regarding the Hamilton Anxiety Scale.

As expected, tolerability and acceptability were good, with almost no adverse effects and a retention rate of 73%, which can be considered high in a population suffering from chronic pain.[45]

This pilot study had several limitations. Due to various challenges in recruitment, we were unable to obtain the full complement of participants that we hoped for, resulting in underpowering. Also, this study was initially powered according to a 1:1 randomization ratio, but due to recruitment challenges we switched to a randomization ratio of 2 MBCT subjects for every control subject, which resulted in a greater loss of statistical power. In addition, design sensitivity was reduced by lowering the symptom threshold to a level of mild depressive symptoms (QIDS-C_{16} score ≥ 6). However, despite the fact that there might be less room for improvement (floor effect), the inclusion of less severely depressed individuals adds to the generalizability of our results to chronic pain populations in general with varying levels of depression severity. Moreover, the lower symptom threshold is more consistent with our inclusion diagnoses (MDD and depressive disorder NOS [including minor depression]). These methodological shortcomings might have prevented detection of relevant effects on some clinical outcome measures. For example, the SF-36 yielded mixed results, with benefits primarily in psychological measures, such as mental health and vitality, but less impact on physical domains such as pain and physical functioning. Nonetheless, this result is consistent with the rest of the findings, which favor impact on depression rather than pain.

The second major limitation is the heterogeneity of the population regarding chronic pain conditions and depressive disorders, as well as treatments and prescribed medications, which may confound the results. In addition, some participants did change their medications and other concurrent treatments during the course of the study, and this, too, may have impacted the findings. Because of our small sample size and variability in treatment changes, we did not attempt to correct for concomitant medications and treatments. Future larger investigations should incorporate more rigorous detailing and controlling for concomitant medications and other therapies. Because data were missing on some of the secondary outcome measures, this, too, may have prevented more robust findings of effect.

Finally, because of the pilot nature of this study, we did not include an active comparison group but used a waitlist control group, which does not adequately control for placebo effects induced by nonspecific factors such as attention in patient-provider interactions.[46] We did try to control for attention as much as possible by keeping all office and phone visits with the clinician equal in both the MBCT group and the control group.

It is nonetheless promising that, despite these limitations, we found a significant decrease of depressive symptoms as noted with the QIDS-C_{16} in the per-protocol analysis, with a large effect size. Also, patients in the MBCT group reported a significantly higher subjective impression of clinical improvement compared to controls, indicating a subjective improvement in all components of their health experience. These findings support our hypothesis that integrating CBT and mindfulness might create a synergistic effect and result in improved outcomes, at least with regard to depression.

In summary, we have obtained preliminary evidence that MBCT may be a feasible and potentially effective intervention for treating depression in patients with chronic pain, based on positive findings in 1 of 2 primary outcomes in the per-protocol analysis, though not in the ITT analysis. While these findings should be interpreted with caution, they support follow-up investigation, particularly because depression is a highly debilitating and difficult-to-treat condition that, when present in a chronic pain population, complicates the treatment and outcome of chronic pain. Adding MBCT to the available treatments may widen the therapeutic scope of potential interventions. Finally, because MBCT is delivered in a group setting, it may also represent a potentially cost-efficient treatment modality. Future larger randomized controlled trials comparing MBCT to attention control and comparative effectiveness studies of MBCT and CBT in this population are warranted.

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