

# Outcomes of Online Mindfulness-Based Cognitive Therapy for Patients With Residual Depressive Symptoms

## A Randomized Clinical Trial

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**IMPORTANCE** Patients with residual depressive symptoms face a gap in care because few resources, to date, are available to manage the lingering effects of their illness.

**OBJECTIVE** To evaluate the effectiveness for treating residual depressive symptoms with Mindful Mood Balance (MMB), a web-based application that delivers mindfulness-based cognitive therapy, plus usual depression care compared with usual depression care only.

**DESIGN, SETTING, AND PARTICIPANTS** This randomized clinical trial was conducted in primary care and behavioral health clinics at Kaiser Permanente Colorado, Denver. Adults identified with residual depressive symptoms were recruited between March 2, 2015, and November 30, 2018. Outcomes were assessed for a 15-month period, comprising a 3-month intervention interval and a 12-month follow-up period.

**INTERVENTIONS** Patients were randomized to receive usual depression care (UDC; n = 230) or MMB plus UDC (n = 230), which included 8 sessions delivered online for a 3-month interval plus minimal phone or email coaching support.

**MAIN OUTCOMES AND MEASURES** Primary outcomes were reduction in residual depressive symptom severity, assessed using the Patient Health Questionnaire-9 (PHQ-9); rates of depressive relapse (PHQ-9 scores  $\geq 15$ ); and rates of remission (PHQ-9 scores  $< 5$ ). Secondary outcomes included depression-free days, anxiety symptoms (General Anxiety Disorder-7 Item Scale), and functional status (12-Item Short Form Survey).

**RESULTS** Among 460 randomized participants (mean [SD] age, 48.30 [14.89] years; 346 women [75.6%]), data were analyzed for the intent-to-treat sample, which included 362 participants (78.7%) at 3 months and 330 (71.7%) at 15 months. Participants who received MMB plus UDC had significantly greater reductions in residual depressive symptoms than did those receiving UDC only (mean [SE] PHQ-9 score, 0.95 [0.39],  $P < .02$ ). A significantly greater proportion of patients achieved remission in the MMB plus UDC group compared with the UDC only group (PHQ-9 score,  $< 5$ ;  $\beta$  [SE], 0.38 [0.14],  $P = .008$ ), and rates of depressive relapse were significantly lower in the MMB plus UDC group compared with the UDC only group (hazard ratio, 0.61; 95% CI, 0.39-0.95;  $P < .03$ ). Compared with the UDC only group, the MMB plus UDC group had decreased depression-free days (mean [SD], 281.14 [164.99] days vs 247.54 [158.32] days; difference, -33.60 [154.14] days;  $t = -2.33$ ;  $P = .02$ ), decreased anxiety (mean [SE] General Anxiety Disorder-7 Item Scale score, 1.21 [0.42],  $P = .004$ ), and improved mental functioning (mean [SE] 12-Item Short Form Survey score, -5.10 [1.37],  $P < .001$ ), but there was no statistically significant difference in physical functioning.

**CONCLUSIONS AND RELEVANCE** Use of MMB plus UDC resulted in significant improvement in depression and functional outcomes compared with UDC only. The MMB web-based treatment may offer a scalable approach for the management of residual depressive symptoms.

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Depression is the second leading cause of disability worldwide, with the frequently chronic and recurrent nature of the disorder contributing significantly to the global burden of disease.<sup>1</sup> Even low to moderate levels of residual depressive symptoms (RDS) are associated with significant impairment,<sup>2</sup> greater social role strain,<sup>3</sup> and risk of a negative prognosis.<sup>4</sup> Despite the availability of antidepressant medication, most patients with depression who achieve a clinical response to antidepressant medications experience RDS.<sup>5</sup> The public health risks of failing to address RDS are substantial, with the per capita costs of RDS (\$2144) approaching the costs associated with a major depressive episode (\$3133).<sup>6</sup> Patients with RDS often face a gap in care, whereby having achieved a marginal treatment response, they often are not provided resources for managing the lingering effects of the illness<sup>6,7</sup> or achieving remission.

The RDS are important treatment targets and often require tailored management strategies that can be sequenced with acute-phase treatment<sup>8,9</sup> and can be made widely accessible.<sup>10</sup> The Mindful Mood Balance (MMB) treatment, which provides digital delivery of the skills of mindfulness-based cognitive therapy, is an important option for achieving these aims.

Mindfulness-based cognitive therapy was designed specifically to be used sequentially after response to acute-phase treatment and has a strong evidence base, including for depression relapse prevention and management of RDS.<sup>11,12</sup> Studies of mindfulness-based cognitive therapy have reported moderate to large associations with reduction in RDS compared with antidepressant medications<sup>11</sup> or usual care.<sup>13</sup> The public health consequences of mindfulness-based cognitive therapy have been limited, however, because of dissemination challenges common to most in-person psychological interventions (eg, service costs, waiting lists, travel, and time training clinicians).<sup>14-17</sup>

Providing online therapies for patients who report RDS after routine care has been shown to be a promising approach to addressing these challenges and enhancing the dissemination of high-fidelity treatment of RDS.<sup>18,19</sup> Dimidjian et al<sup>20</sup> used a quasi-experimental design and tested MMB in patients who reported RDS after structured depression care at a large integrated health system (Kaiser Permanente Colorado) and reported that participants who received MMB showed a large effect size (Cohen  $d = 1.09$ ) for the reduction of RDS that was maintained for 6 months.

In the context of these pilot data, the aim of the current study was to conduct a definitive trial for treating RDS with MMB compared with usual depression care (UDC). We hypothesized that adding MMB to UDC compared with UDC alone would lead to significant reductions in RDS severity, lower rates of depressive relapse, and higher rates of remission based on the Patient Health Questionnaire-9 (PHQ-9) results. We also believed that MMB plus UDC compared with UDC alone would lead to significantly more depression-free days, lower anxiety (General Anxiety Disorder-7 Item Scale [GAD-7]), and higher functional status (12-Item Short Form survey [SF-12]). Outcomes were assessed during a 15-month period, including a 3-month intervention interval and a 12-month follow-up period.

## Key Points

**Question** Can web-based treatment of residual depressive symptoms lead to incremental benefits for adults when added to usual depression care?

**Finding** In this randomized clinical trial of 460 participants with residual depressive symptoms, those who received an online version of mindfulness-based cognitive therapy in addition to usual care had greater reductions in depressive and anxiety symptoms, higher rates of remission, and higher levels of quality of life compared with participants who received usual care only.

**Meaning** The findings support the value of online mindfulness-based cognitive therapy as an adjunctive, scalable approach for the management of residual depressive symptoms.

## Methods

### Trial Design

This 2-group, single-blind randomized clinical trial was approved by the institutional review boards of the University of Toronto, Kaiser Permanente Colorado, and the University of Colorado Boulder. All patients provided written informed consent before beginning study procedures. We compared the effectiveness of MMB plus UDC vs UDC alone (trial protocol in Supplement 1). Participants were randomized with an allocation ratio of 1:1 using the Research Electronic Data Capture randomization module with a file created by a random number generator in SAS, version 9.4 (SAS Institute Inc).<sup>21</sup> Study staff were blinded to the contents of the randomization file. **Figure 1** gives the study recruitment, randomization, and patient flow. This trial followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.

### Sample Recruitment

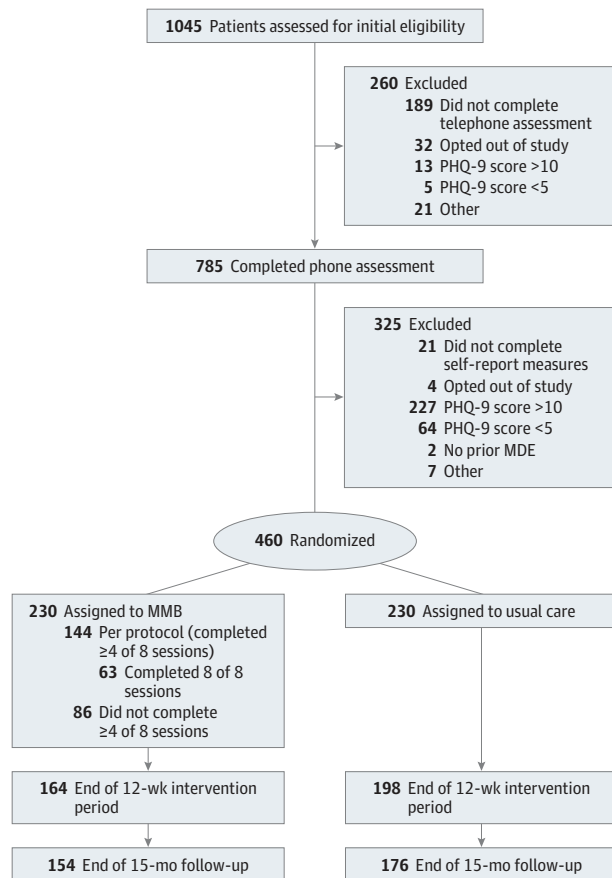
Study activities were completed online between March 2, 2015, and November 30, 2018, and consistent with a pragmatic trial, inclusion criteria were minimal. All participants were Kaiser Permanente Colorado members and were identified through either electronic medical records that indexed real-time PHQ-9 scores and depression diagnoses, electronic clinician referral, or medical office flyers. Participants were aged 18 years or older with at least 1 prior episode of major depressive disorder confirmed via telephone interview and had a current PHQ-9 score between 5 and 9.<sup>22</sup> Exclusion criteria included presence of schizophrenia, bipolar disorder, current psychosis, organic mental disorder, or pervasive developmental delay.

On the basis of effect sizes reported in Dimidjian et al,<sup>20</sup> we estimated 80% power for detecting an effect size of 0.36 or greater with  $\alpha = .05$  based on a 2-tailed test. A total of 1045 patients were screened, 785 completed telephone interviews, and 460 were randomized.

### Interventions

The MMB treatment was developed to provide the core components of the in-person mindfulness-based cognitive therapy

Figure 1. CONSORT Diagram



MDE indicates major depressive disorder; MMB, mindful mood balance; and PHQ-9, Patient Health Questionnaire -9.

program<sup>23</sup> in an online, 8-session, self-administered platform. The MMB treatment teaches participants how to disengage from habitual, automatic, dysfunctional cognitive patterns (ie, depression-related ruminative thought patterns), to reduce RDS and vulnerability to relapse. Each MMB session incorporates experiential practice, video-based vicarious learning, and didactic information.<sup>24,25</sup> During the intervention phase, participants were supported by a coach who provided motivational and technical support. Participants received a mean of 2.34 hours of coaching (sum of all hours spent coaching, divided by the number of coaches) during 12 weeks; this included a 45-minute orientation telephone call, 10-minute telephone check-ins for the first 2 weeks that tapered to weekly motivational emails, or telephone calls (eMethods 1 and 3 in Supplement 2).

Usual depression care followed the Kaiser Permanente Adult Depression National Guideline, an adaptation of STAR\*D (Sequenced Treatment Alternatives to Relieve Depression),<sup>26</sup> for antidepressant management. Patients also had access to individual or group psychotherapy through Kaiser Permanente's behavioral health clinics. Care pathways were determined by severity level and included treatment with

antidepressants, psychotherapy, or both (eMethods 2 in Supplement 2).

## Outcomes

Primary outcomes were reduction in RDS severity, rates of remission, and rates of depressive relapse. These were assessed via the PHQ-9, a 9-item self-report measure with a range of scores from 0 to 27 and higher scores indicating greater depression severity. Remission was defined as scores less than 5, and relapse was defined as scores of 15 or higher, a severity threshold consistent with a determination of clinical relapse.<sup>27</sup>

Secondary outcomes were reductions in anxiety symptoms, indexed by the Generalized Anxiety Disorder-7 (GAD-7),<sup>28</sup> a 7-item self-report measure with a range of scores from 0 to 21, with higher scores indicating greater anxiety severity. Functional status was assessed using the physical and mental functioning subscales of the Short Form 12 (SF-12) survey.<sup>29</sup> This measure comprises 12 questions and is scored on a range from 0 to 100, with 0 indicating lower levels of health. Depression-free days were calculated to characterize depression-related morbidity based on converting consecutive scores on the PHQ-9 into a scale from 0 to 1, with 1 corresponding to depression-free days (PHQ-9 score, <5) and 0 corresponding to continuing symptomatic status (PHQ-9 score, ≥15). Intermediate scores were assigned a linear prorated value between 0 and 1.<sup>30</sup>

## Statistical Analysis

All analyses were conducted with the intent-to-treat sample. We compared groups on baseline demographic and clinical characteristics using *t* tests for continuous variables and  $\chi^2$  tests for categorical variables. To test our primary hypotheses that participants receiving MMB would report a reduction in RDS during the 3-month intervention phase and that this reduction would be sustained across the 12-month follow-up period, we implemented hierarchical linear modeling.<sup>31-33</sup> To assess the best mathematical trajectory of change over time, every outcome was inspected visually through spaghetti plots and intervention-based mean profiles as well as quantitatively by comparison of the -2 (log-likelihood) Akaike information criterion and the Bayesian information criterion of various models, in which we compared linear change, log-linear change, polynomial change, and piecewise change with breakpoint at the 3-month time point corresponding to the end of the intervention phase (eTable 3 in Supplement 2). Consistently across outcomes, the piecewise linear change model with 2 phases provided the best fit. We also included a covariate-of-assessment time point to account for a systematic spike in PHQ-9 scores at assessment points at which participants completed an assessment battery comprised of all questionnaires compared with a briefer screening battery administered at other time points. Hierarchical linear models were replaced with hierarchical generalized linear models to accommodate binary outcomes, such as remission or nonremission, based on a PHQ-9 score of less than 5,<sup>31</sup> and analyses focusing on time-to (ie, first relapse) were compared using Cox proportional hazard regression models.<sup>34</sup> When fitting hierarchical linear models or hierarchical generalized linear models, an intent-to-

treat analysis was used with the intake score as the first outcome, instead of a covariate. Effect sizes for the respective within-intervention and between-intervention change measures for hierarchical linear models were derived as Cohen *d* per Feingold.<sup>35</sup> Percent differences were reported for hierarchical generalized linear models, and hazard ratios were reported for the time-to models.

As a sensitivity analysis for missing measures (eTable 4 in Supplement 2), we implemented a Markov Chain Monte Carlo imputation method through PROC MI of SAS, version 9.4 (SAS Institute).<sup>21,36</sup> Markov Chain Monte Carlo constructs a Markov chain long enough for the distribution of the elements to stabilize to a common, stationary distribution. Data augmentation is applied to bayesian inference with missing data by repeating a series of imputation and posterior steps. These 2 steps are iterated long enough for the results to be reliable for the imputed data set.<sup>37,38</sup>

## Results

Baseline demographic and clinical history variables for each group are presented in Table 1. Among 460 total participants (230 in each group), the mean (SD) age was 48.3 (14.9) years and 346 were women (75.6%). Of 456 total participants categorized by race, 419 (91.9%) were white and 8 (1.8%) were black; of 446 participants categorized by ethnicity, 39 (8.7%) were Hispanic, 8 (1.8%) were black, and 7 (1.5%) were Asian. Participants reported a mean (SD) of 7.5 (3.1) previous episodes of depression and at study intake; 78% of participants (355 of 455) reported receiving antidepressant medications, and 50% (219 of 435) reported receiving current psychotherapy.

### Intervention Exposure and Costs

Participants assigned to MMB plus UDC completed a mean (SD) of 4.8 (2.8) sessions of MMB of 8 total sessions, with 210 of 230 (91.3%) completing at least 1 treatment session, 144 (62.6%) completing at least 4 sessions, and 63 (27.4%) completing all 8 sessions. With respect to the use of therapy skills in the MMB sessions, participants practiced formal or informal mindfulness meditation for a mean (SD) of 46.1 (44.1) times during the 3-month intervention phase.

Pharmacy dispensing and psychotherapy data were available for 100% of the sample across the 15-month study period and indicated that 166 participants (72.2%) assigned to MMB plus UDC and 170 (73.9%) assigned to UDC only were dispensed psychotropic medication. With respect to psychotherapy, 111 (48.3%) assigned to MMB plus UDC and 114 (49.6%) assigned to UDC only had 2 or more psychotherapy visits. Differences between the groups were not significant for either utilization category.

The MMB treatment was designed as a stand-alone online intervention with minimal support. The cost of coaching support for 12 weeks, based on the average salary reported by the US Bureau of Labor Statistics (\$28.68 per hour, plus 31% benefit rate and 10% overhead rate [rent, information technology, and infrastructure] for a health educator in the United

States),<sup>39</sup> was \$96.67 for a mean of 2.34 hours per participant (sum of all hours spent coaching, divided by the number of coaches) and included orientation and follow-up telephone calls, emails, website tracking, and supervision.

### Serious Adverse Events

The number of serious adverse events reported was small and consistent with findings from previous trials<sup>12,20</sup>; 1 serious adverse event (overdose) was reported by a participant assigned to the MMB plus UDC group, with none reported by participants in the UDC group. With respect to clinical deterioration, we examined referrals to behavioral health for PHQ-9 scores of 13 or higher and crisis calls for PHQ-9, item 9 (suicide ideation endorsement). Our data indicated that clinical deterioration was more prevalent in the UDC group (eTable 1 in Supplement 2). Although the proportions did not differ between the groups ( $\chi^2 = 0.49$ ), on an absolute basis, the UDC group had more than twice as many alerts (127) as the MMB group (51).

### Intervention Effects on Primary Outcomes

Consistent with our hypothesis, patients assigned to MMB plus UDC had significantly greater reduction in RDS during the entire study period compared with patients assigned to UDC only (mean [SE] difference,  $-2.55 [0.29]$  vs  $-1.64 [0.27]$ ); the mean (SE) between-group difference in improvement in PHQ-9 score was  $0.91 (0.39)$ ;  $t = 2.34$ ,  $P = .02$ ). During the intervention phase, the mean (SE) estimated improvements in PHQ-9 score were  $-2.70 (0.23)$  for the MMB plus UDC group and  $-0.80 (0.20)$  for the UDC only group, with a significantly greater reduction in RDS for participants in the MMB plus UDC group compared with the UDC only group (mean [SE] between-group difference in reduction in PHQ-9 score,  $1.89 [0.33]$ ;  $t = 5.85$ ;  $P < .001$ ). During the 12-month follow-up period, patients in the MMB plus UDC group maintained their initial gains on the PHQ-9, with a mean (SE) increase of  $0.15 (0.26)$ , which was not statistically significant. Participants in the UDC group had continued improvement ( $-0.84 [0.24]$ ) that was significantly greater than that in participants in the MMB plus UDC group ( $0.98 [0.35]$ ;  $t = 2.81$ ;  $P = .003$ ).

Because a systematic increase in PHQ-9 scores occurred when data were acquired at assessment points when participants completed a comprehensive assessment battery compared with time points when participants completed only a brief screening battery and the PHQ-9 score increase at these time points was statistically significant ( $F_{1,430} = 132.68$ ,  $P < .001$ ), we ran these analyses again controlling for this effect. Patients assigned to MMB plus UDC had a significantly greater mean (SE) reduction in RDS on the PHQ-9 during the entire study period ( $-2.65 [0.29]$ ) compared with patients assigned to UDC only ( $-1.70 [0.27]$ ) (Figure 2), and the mean (SE) between-group difference in improvement in PHQ-9 score was  $0.95 (0.39)$ ;  $t = 2.43$ ,  $P < .02$ ). During the intervention phase, the mean (SE) estimated reductions in PHQ-9 score were  $-2.83 (0.24)$  for the MMB plus UDC group and  $-0.94 (0.22)$  for the UDC only group, with a significantly greater mean (SE) reduction in RDS for participants in the MMB plus UDC group compared with those in the UDC only group ( $1.89 [0.32]$ ;  $t = 5.84$ ;

Table 1. Participant Demographics and Clinical Characteristics

Characteristic	MMB Plus UDC Group (n = 230)	UDC Only Group (n = 230)	Total (N = 460)
Scores at intake, mean (SD)			
PHQ-9	7.20 (1.41)	7.29 (1.53)	7.24 (1.47)
GAD-7	6.51 (3.15)	6.20 (3.28)	6.35 (3.22)
SF-12 PCS	51.03 (9.88)	51.77 (9.61)	51.40 (9.74)
SF-12 MCS	34.27 (7.92)	34.22 (8.63)	34.25 (8.28)
Age, mean (SD), y	48.3 (15.1)	48.2 (14.7)	48.3 (14.9)
Sex, No. (%)			
Male	58 (25.3)	54 (23.6)	112 (24.4)
Female	171 (74.7)	175 (76.4)	346 (75.6)
Marital status, No. (%)			
Never married	55 (24.0)	48 (21.1)	103 (22.5)
Married, civil union, or common-law marriage	105 (45.8)	112 (49.1)	217 (47.5)
Divorced or separated	60 (26.2)	60 (26.3)	120 (26.3)
Widowed	9 (3.9)	8 (3.5)	17 (3.7)
Race/ethnicity, No. (%) <sup>a</sup>			
American Indian or Alaskan Native	1 (0.4)	2 (0.9)	3 (0.7)
Asian	3 (1.3)	4 (1.8)	7 (1.5)
Black or African American	4 (1.8)	4 (1.8)	8 (1.8)
Native Hawaiian or other Pacific Islander	0	1 (0.4)	1 (0.2)
White	212 (3.0)	207 (90.8)	419 (91.9)
Other	8 (3.5)	10 (4.4)	18 (4.0)
Hispanic or Latino, No. (%)	21 (9.4)	18 (8.1)	39 (8.7)
Educational level, No. (%) <sup>b</sup>			
Did not complete high school	3 (1.3)	3 (1.3)	6 (1.3)
Completed high school	33 (14.5)	24 (10.5)	57 (12.5)
Completed college or university (includes undergraduate, graduate, or professional degree)	191 (84.1)	202 (88.2)	393 (86.2)
Employment, No. (%)			
Full-time	131 (57.0)	124 (54.2)	255 (55.6)
Part-time	25 (10.9)	30 (13.1)	55 (12.0)
Student	5 (2.2)	7 (3.1)	12 (2.6)
Other	69 (30.0)	68 (29.7)	137 (29.8)
Income, US \$, No. (%)			
0-29 999	25 (11.0)	24 (10.5)	49 (10.8)
30 000-69 999	91 (40.1)	93 (40.8)	184 (40.4)
70 000-99 999	52 (22.9)	57 (25.0)	109 (24.0)
≥100 000	59 (26.0)	54 (23.7)	113 (24.8)
Age at onset of first episode of depression, mean (SD)	23.13 (13.29)	23.57 (13.28)	23.35 (13.27)
Weeks since last episode, mean (SD)	64.00 (150.86)	58.82 (114.16)	61.46 (134.00)
No. of previous episodes of depression, mean (SD)	7.44 (3.15)	7.48 (3.14)	7.46 (3.14)
Previous hospitalization for depression, No. (%)	36 (15.79)	36 (15.79)	72 (15.79)
Previous suicide attempt, No. (%)	39 (17.18)	43 (18.94)	82 (18.06)
Antidepressant at intake, No. (%)	178 (77.39)	177 (77.63)	355 (77.51)
Current psychotherapy, No. (%)	110 (50.69)	109 (50.00)	219 (50.34)
Current psychotherapy and antidepressant, No. (%)	84 (38.71)	85 (39.17)	169 (38.94)

Abbreviations: GAD-7 indicates Generalized Anxiety Disorder-7; MCS, mental component summary; MMB, Mindful Mood Balance; PCS, physical component summary; PHQ-9, Patient Health Questionnaire-9; SF-12, 12-item Short Form Survey; UDC, usual depression care.

<sup>a</sup> Race/ethnicity comparison is white vs nonwhite.

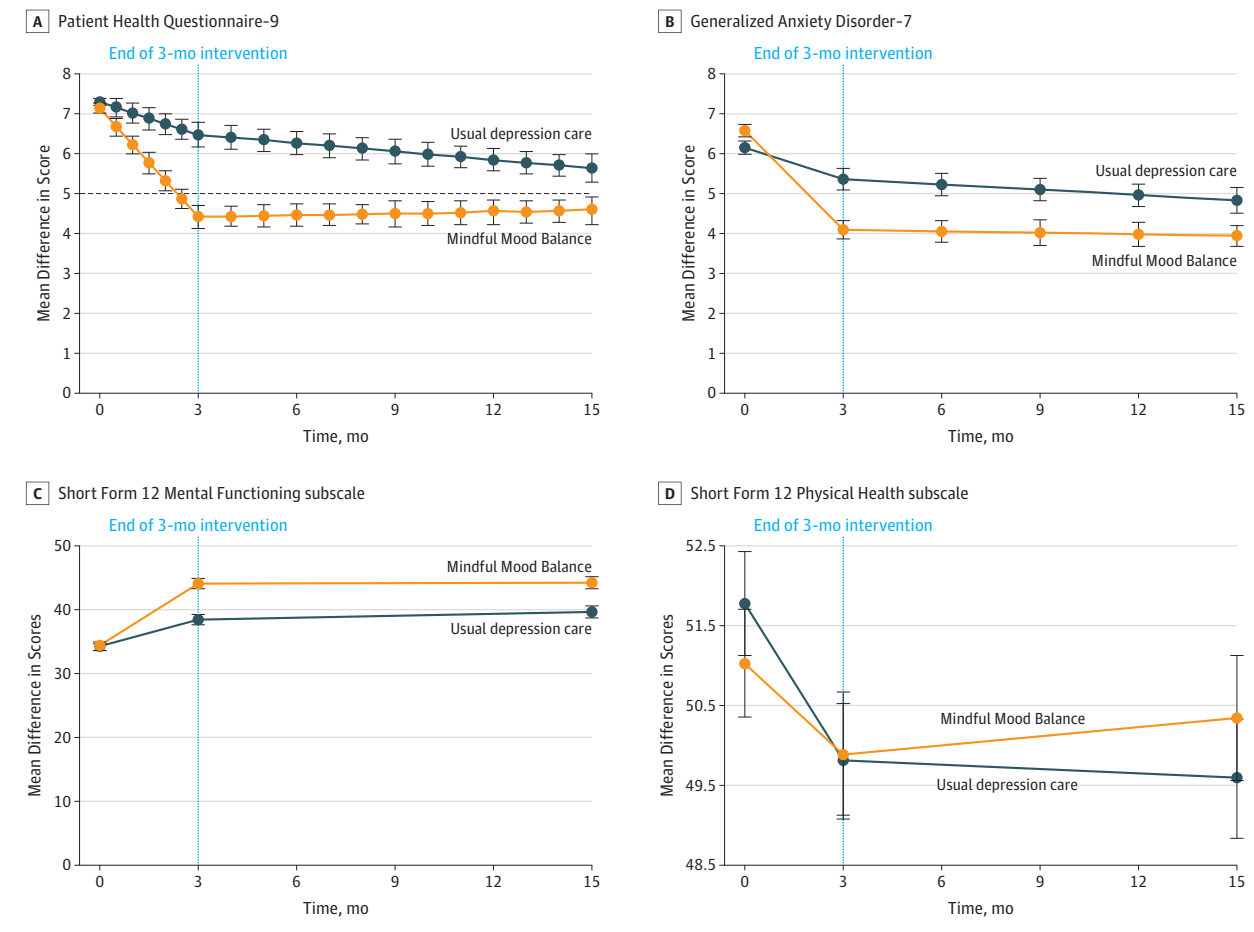
<sup>b</sup> Fisher exact test was used for educational level, part-time student, and unemployed comparison.

$P < .001$ ). During the 12-month follow-up period, patients in the MMB plus UDC group maintained their initial gains, an increase of 0.19 (0.26) that was not statistically significant. Par-

ticipants in the UDC only group showed continued improvement, (-0.76 [0.24]) that was significantly greater than that among participants in the MMB plus UDC group (0.95 [0.35])



**Figure 2. Differences Between the Mindful Mood Balance (MMB) Plus Usual Depression Care (UDC) Group and the UDC Only Group on Primary and Secondary Measures**



The vertical dotted line represents the end of the treatment interval; horizontal black dashed line, Patient Health Questionnaire-9 threshold of 5.

mean reduction in PHQ-9 scores in the follow-up for the UDC, analogous to reductions in RDS;  $t = 2.71$ ;  $P = .007$ ).

Consistent with our hypothesis that MMB would increase rates of remission (PHQ-9, <5) among participants, we found that a significantly greater mean (SE) proportion of participants during the entire study period in the MMB plus UDC group (59.4% [2.7%]) compared with the UDC alone group (47.0% [2.6%]) achieved remission. Mean (SE) between-group differences on the log-odds scale were 0.50 (0.15;  $t = 3.25$ ;  $P < .001$ ). During the intervention phase, both groups showed significant mean (SE) increases in the numbers of participants below the remission threshold (MMB plus UDC group: 57.2% [2.6%]; UDC only group: 35.7% [2.4%]), with a significantly greater number of participants achieving remission in the MMB plus UDC group compared with the UDC only group (mean [SE] between-group difference on log-odds scale, 0.88 [0.15];  $t = -5.89$ ;  $P < .001$ ). Similar to the 12-month outcomes reported above, gains were maintained in the MMB plus UDC group during the 12-month follow-up period, corresponding to a mean (SE) increase in the rate of remission of 2.2% (2.6%) that was not statistically significant. The UDC only group showed significantly greater mean (SE) rates of remission com-

pared with the MMB plus UDC group (11.3% [2.4%]; between-group differences in log-odds, 0.38 [0.14];  $t = 2.65$ ,  $P = .008$ ) (Table 2 and Table 3).

Treatment with MMB plus UDC also was associated with lower rates of relapse during the 12-month follow-up period, with 31 of 230 participants (13.5%) in this group crossing the relapse threshold (PHQ-9,  $\geq 15$ ) compared with 53 (23.0%) in the UDC only group (hazard ratio, 0.61; 95% CI, 0.39-0.95;  $\chi^2 = 4.83$ ;  $P < .03$ ). We additionally fit the time to first response, which yielded a significant intervention effect ( $\chi^2 = 11.89$ ,  $P < .001$ ) with a hazard ratio of 1.46 (95% CI, 1.18-1.80), indicating that the rate of response for MMB plus UDC was 45.6% greater than UDC alone.

### Intervention Effects on Anxiety and Quality of Life Outcomes

Consistent with our hypothesis, MMB plus UDC was significantly associated with greater improvement in anxiety symptom severity compared with UDC only, with participants in the MMB plus UDC group showing a mean (SE) decrease in GAD-7 score of 2.48 (0.31) points compared with 1.27 (0.29) points in the UDC group (mean [SE] between-group difference, 1.21

Table 2. Mean Group Differences and Effect Sizes for Primary and Secondary Outcomes

Measure	Within-Group Difference, Mean (SE)			Between-Group Effect Size, Cohen <i>d</i> (95% CI)
	MMB Plus UDC Group	UDC Group	Difference	
PHQ-9 score				
Total	-2.65 (0.29) <sup>a</sup>	-1.70 (0.27) <sup>a</sup>	0.95 (0.39) <sup>b</sup>	0.23 (0.04 to 0.41)
Intervention phase	-2.83 (0.24) <sup>a</sup>	-0.94 (0.22) <sup>a</sup>	1.89 (0.32) <sup>a</sup>	0.55 (0.36 to 0.73)
Follow-up phase	0.19 (0.26)	-0.76 (0.24) <sup>c</sup>	-0.95 (0.35) <sup>c</sup>	-0.25 (-0.44 to -0.07)
PHQ-9 remission (PHQ-9, <5)				
Total	1.23 (0.11) <sup>a</sup>	0.86 (0.10) <sup>a</sup>	-0.37 (0.12) <sup>c</sup>	-0.28 (-0.46 to -0.09)
Intervention phase	1.16 (0.12) <sup>a</sup>	0.37 (0.12) <sup>c</sup>	-0.79 (0.14) <sup>a</sup>	-0.55 (-0.73 to -0.36)
Follow-up phase	0.07 (0.10)	0.49 (0.10) <sup>a</sup>	0.42 (0.14) <sup>c</sup>	0.28 (0.10 to 0.47)
GAD-7 score				
Total	-2.48 (0.31) <sup>a</sup>	-1.27 (0.29) <sup>a</sup>	1.21 (0.42) <sup>c</sup>	0.27 (0.09 to 0.45)
Intervention phase	-2.34 (0.28) <sup>a</sup>	-0.75 (0.26) <sup>c</sup>	1.60 (0.37) <sup>a</sup>	0.40 (0.22 to 0.59)
Follow-up phase	-0.14 (0.30)	-0.53 (0.27)	-0.39 (0.40)	-0.09 (-0.27 to 0.09)
SF-12 score (PCS)				
Total	-1.86 (0.68) <sup>c</sup>	-2.39 (0.63) <sup>c</sup>	-0.53 (0.93)	-0.12 (-0.30 to 0.06)
Intervention phase	-1.64 (0.57) <sup>c</sup>	-2.38 (0.53) <sup>a</sup>	-0.74 (0.78)	-0.06 (-0.24 to 0.12)
Follow-up phase	-0.22 (0.69)	-0.003 (0.64)	0.22 (0.94)	-0.05 (-0.23 to 0.13)
SF-12 score (MCS)				
Total	10.27 (1.01) <sup>a</sup>	5.17 (0.93) <sup>a</sup>	-5.10 (1.37) <sup>c</sup>	0.45 (0.26 to 0.63)
Intervention phase	9.78 (0.81) <sup>a</sup>	4.11 (0.76) <sup>a</sup>	-5.67 (1.11) <sup>a</sup>	0.54 (0.35 to 0.73)
Follow-up phase	0.49 (0.98)	1.06 (0.90)	0.57 (1.33)	0.05 (-0.13 to 0.23)
Total depression-free days <sup>d</sup>	281.43 (164.99)	247.46 (158.32)	-33.97 (149.66) <sup>c</sup>	0.22 (0.04 to 0.40)

Abbreviations: GADS-7 indicates Generalized Anxiety Disorder-7; MCS, mental component summary; MMB, Mindful Mood Balance; PCS, physical component summary; PHQ-9, Patient Health Questionnaire-9; SF-12, 12-Item Short Form Survey; UDC, usual depression care.

<sup>a</sup>  $P < .001$ .

<sup>b</sup>  $P < .05$ .

<sup>c</sup>  $P < .01$ .

<sup>d</sup> Data are mean (SD) days.

[0.42];  $t = 2.90$ ,  $P = .004$ ).<sup>28</sup> With respect to quality of life outcomes, controlling for intake, MMB plus UDC was associated with more depression-free days during the entire study period compared with UDC alone (mean [SD], 281.14 [164.99] days vs 247.54 [158.32] days; difference: -33.60 [154.14] days;  $t = -2.33$ ;  $P = .02$ ).

Participation in MMB plus UDC was also associated with an increase in SF-12 mental functioning subscale score (mean [SD] increase, 10.27 [1.01] points vs 5.17 [0.93] points for UDC; mean [SD] difference, -5.10 [1.37];  $t = -3.72$ ;  $P = .001$ ). There was no statistically significant difference between groups on the physical health subscale of the SF-12 (mean [SE], -1.50 [1.44];  $t = 1.04$ ;  $P = .30$ ).

## Discussion

Treatment with MMB plus UDC for adults with partially remitted depression resulted in significant reductions in RDS compared with UDC only delivered by a large integrated health system. A greater percentage of MMB plus UDC participants achieved remission (PHQ-9 score, <5) and did not experience relapse (PHQ-9 score,  $\geq 15$ ). Benefits of MMB were evident within the 3-month intervention period and were maintained across the 12-month follow-up period.

Our findings align with prior evidence for the effects of mindfulness-based cognitive therapy on RDS<sup>11-13</sup> and showed that teaching affect-regulation skills to individuals with RDS can be extended through web-based delivery with MMB. In set-

tings that use routine monitoring of depressive symptoms, MMB can be integrated as an augmentation strategy or second care step for patients who achieve only partial remission after acute phase treatment.<sup>9,10</sup> Providing the right treatment at the right time can optimize depression outcomes by reducing undertreatment<sup>40</sup> and lowering patients' future risk profiles.<sup>4</sup> However, as Mohr and others<sup>41</sup> have cautioned, health system implementation must be engineered, rather than assumed. Our experience suggests that batch messaging through the Kaiser Permanente Colorado patient portal and clinician endorsement or recommendation were drivers of patient uptake and engagement.

Unlike most web-based interventions that address acute phase disorders, MMB targets psychological vulnerability after initial treatment and teaches skills to reverse symptom perpetuation and return.<sup>42,43</sup> This may be apparent in the differential effects reported on the SF-12, in which participants receiving MMB plus UDC showed improved mental functioning but no change in physical health.

The benefits of MMB plus UDC compared with UDC alone were evident on some of the secondary outcomes, including lower anxiety severity, more depression-free days, and improved functional outcomes. A focus on the overall illness burden in this population is vital because it can be rate limiting for the resumption of work and social roles.<sup>44,45</sup> For example, comorbid anxiety is associated with a diminished response to first-line treatments as well as poor long-term outcomes in patients with RDS,<sup>46,47</sup> and the presence of RDS has been associated with increased absenteeism and reduced productivity

Table 3. Descriptive Data for Primary and Secondary Outcomes Over Assessment Points

Month, Group	Score, Mean (SD)			
	PHQ-9	GAD-7	SF-12 MCS	SF-12 PCS
<b>Intervention Period</b>				
0				
UDC only (n = 230)	7.29 (1.53)	6.20 (3.28)	34.22 (8.63)	51.77 (9.61)
MMB plus UDC (n = 230)	7.20 (1.41)	6.51 (3.15)	34.27 (7.92)	51.03 (9.88)
0.5				
UDC only (n = 204)	7.45 (3.28)	NA	NA	NA
MMB plus UDC (n = 205)	6.44 (3.15)	NA	NA	NA
1.0				
UDC only (n = 202)	6.77 (3.58)	NA	NA	NA
MMB plus UDC (n = 190)	5.49 (2.99)	NA	NA	NA
1.5				
UDC only (n = 211)	7.68 (4.08)	NA	NA	NA
MMB plus UDC (n = 181)	5.90 (3.57)	NA	NA	NA
2.0				
UDC only (n = 194)	6.60 (3.59)	NA	NA	NA
MMB plus UDC (n = 172)	4.98 (3.37)	NA	NA	NA
2.5				
UDC only (n = 194)	6.09 (3.53)	NA	NA	NA
MMB plus UDC (n = 172)	4.48 (3.19)	NA	NA	NA
3.0				
UDC only (n = 198)	7.40 (4.27)	5.41 (3.75)	38.46 (10.34)	49.81 (9.55)
MMB plus UDC (n = 164)	5.19 (3.69)	3.71 (2.98)	44.10 (9.87)	49.87 (9.93)
<b>End of Active Treatment</b>				
4				
UDC only (n = 193)	6.48 (4.09)	NA	NA	NA
MMB plus UDC (n = 157)	4.39 (3.07)	4.43 (3.94) <sup>a</sup>	NA	NA
5				
UDC only (n = 191)	6.22 (3.84)	NA	NA	NA
MMB plus UDC (n = 160)	4.62 (3.59)	NA	NA	NA
6				
UDC only (n = 191)	6.16 (3.96)	5.25 (3.90)	NA	NA
MMB plus UDC (n = 158)	4.70 (3.55)	4.22 (3.48)	NA	NA
7				
UDC only (n = 189)	6.24 (4.13)	NA	NA	NA
MMB plus UDC (n = 158)	4.36 (3.42)	NA	NA	NA
8				
UDC only (n = 191)	5.89 (3.86)	NA	NA	NA
MMB plus UDC (n = 161)	3.90 (3.17)	NA	NA	NA
9				
UDC only (n = 191)	6.30 (4.23)	4.96 (3.85)	NA	NA
MMB plus UDC (n = 156)	4.65 (4.11)	3.89 (3.99)	NA	NA
10				
UDC only (n = 181)	5.95 (4.12)	NA	NA	NA
MMB plus UDC (n = 155)	4.15 (3.66)	NA	NA	NA
11				
UDC only (n = 182)	5.44 (3.56)	NA	NA	NA
MMB plus UDC (n = 154)	4.20 (3.71)	NA	NA	NA
12				
UDC only (n = 184)	5.57 (3.79)	4.74 (3.77)	NA	NA
MMB plus UDC (n = 151)	4.83 (3.74)	4.03 (3.80)	NA	NA

(continued)



Table 3. Descriptive Data for Primary and Secondary Outcomes Over Assessment Points (continued)

Month, Group	Score, Mean (SD)			
	PHQ-9	GAD-7	SF-12 MCS	SF-12 PCS
13				
UDC only (n = 184)	5.48 (3.82)	NA	NA	NA
MMB plus UDC (n = 157)	4.30 (3.47)	NA	NA	NA
14				
UDC only (n = 181)	5.16 (3.57)	NA	NA	NA
MMB plus UDC (n = 155)	4.01 (3.52)	NA	NA	NA
15				
UDC only (n = 176)	7.06 (4.76)	4.92 (4.23)	39.64 (11.93)	49.58 (9.82)
MMB plus UDC (n = 154)	5.10 (4.19)	3.49 (3.21)	44.37 (10.51)	50.34 (9.29)

Abbreviations: GAD-7 indicates Generalized Anxiety Disorder-7; MCS, mental component summary; MMB, Mindful Mood Balance; NA, not applicable; PCS, physical component summary; PHQ-9, Patient Health Questionnaire-9; SF-12, 12-Item Short Form Survey; UDC, usual depression care.

<sup>a</sup> Patients assigned MMB plus UDC (n = 58) were assessed using the GAD-7 at month 4.

at work.<sup>48</sup> In a sample of 771 workers, Beck et al<sup>49</sup> estimated that every 1-point increase in PHQ-9 score led to a mean productivity loss of 1.65%. This represents a significant labor cost to employers. Given its potentially lower costs, confidentiality, and increased accessibility offered by its online format, integrating MMB into occupational health or employee assistance programs may be a solution for addressing even minor depression in the workplace.

### Limitations

There are a number of limitations that deserve mention, including a lack of diversity in the sample that we studied. Consistent with a pragmatic trial, our assessment of patients with RDS relied on self-reported symptoms in the absence of a confirmatory diagnostic or clinical interview. This allowed us to detect RDS but not to fully characterize the prior duration of RDS, a variable that has been linked to illness course. Although the PHQ-9 has been subjected to considerable validation,<sup>27</sup> depressive relapse is often assessed via structured interview, and as such, the group difference in survival times favoring MMB plus UDC may reflect different rates of clinical deterioration rather than a discrete episode of major depressive disorder or full remission. Also, the spikes in PHQ-9 scores across both groups at the assessment points when a more comprehensive assessment battery was administered compared with scores at other time points with the brief symp-

tom screener are another possible limitation. We interpreted this pattern as a measurement artifact because of the order of the PHQ-9 (being placed last in the full assessment battery and first in the brief symptom screener) and controlled for these elevations in our statistical models; however, it is possible that the spikes reflect other, as yet unidentified processes. In addition, although MMB completion rates of 27% were lower than rates in recent reviews (eg, 63%),<sup>50</sup> the percentage of participants who received a minimum therapeutic exposure of 4 or more sessions was 62.6% (eTable 2 in Supplement 2). Future studies should explore methods for enhancing engagement, such as providing support tied to each individual MMB session or offering adherence-focused guidance.<sup>51</sup>

### Conclusions

Use of MMB plus UDC resulted in significant improvement in depression and functional outcomes compared with UDC only. The addition of MMB to UDC delivered by an integrated health system provides a pragmatic and accessible strategy to address the suboptimal treatment of patients with RDS in primary care and employment settings.<sup>52,53</sup> Further research on and design of effective implementation models is required to optimize the public health outcomes of MMB.<sup>41</sup>

#### ARTICLE INFORMATION

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**Correction:** This article was corrected on March 18, 2020, to fix the Conflict of Interest Disclosures and Additional Contributions sections.

**Author Contributions:** Dr Segal had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

**Concept and design:** Segal, Dimidjian, Beck, Boggs, Felder.

**Acquisition, analysis, or interpretation of data:** Dimidjian, Beck, Boggs, Vanderkruik, Metcalf, Gallop, Levy.

**Drafting of the manuscript:** Segal, Boggs, Vanderkruik, Gallop.

**Critical revision of the manuscript for important**

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**Statistical analysis:** Vanderkruik, Gallop, Levy.

**Obtained funding:** Segal, Dimidjian, Beck.

**Administrative, technical, or material support:** Beck, Boggs, Vanderkruik, Metcalf, Felder, Levy.

**Supervision:** Dimidjian, Beck.

**Conflict of Interest Disclosures:** Dr Segal reported being a codeveloper of Mindfulness Based Cognitive Therapy (MBCT) and receiving royalties from Guilford Press for the MBCT treatment manual and patient books; reported presenting keynote addresses at conferences, and MBCT clinical training workshops where he has received a fee, including from the Mind and Life Institute, the Omega Institute, and the University of California San Diego Center for Mindfulness; reported receiving revenue from online MBCT therapist training tools available on mindfulnoggin.com; and reported being a cofounder of Mindful Noggin, Inc,

which supports online dissemination of MBCT.

Dr Dimidjian reported receiving royalties from Guilford Press for a book based on MBCT for new and expectant mothers; reported presenting at conferences where she received a fee, including from the Mind and Life Institute and Becoming Jackson Whole; reported receiving revenue from online MBCT therapist training tools available on mindfulnoggin.com; and reported being a cofounder of Mindful Noggin, Inc, which supports online dissemination of MBCT. Dr Beck reported receiving grants from the National Institute of Mental Health during the conduct of the study. No other disclosures were reported.

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