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# Mindfulness-Based Stress Reduction Compared With Cognitive Behavioral Therapy for the Treatment of Insomnia Comorbid With Cancer: A Randomized, Partially Blinded, Noninferiority Trial

Sheila N. Garland, Linda E. Carlson, Alisa J. Stephens, Michael C. Antle, Charles Samuels, and Tavis S. Campbell

A B S T R A C T

# Purpose

Our study examined whether mindfulness-based stress reduction (MBSR) is noninferior to cognitive behavioral therapy for insomnia (CBT-I) for the treatment of insomnia in patients with cancer.

#### **Patients and Methods**

This was a randomized, partially blinded, noninferiority trial involving patients with cancer with insomnia recruited from a tertiary cancer center in Calgary, Alberta, Canada, from September 2008 to March 2011. Assessments were conducted at baseline, after the program, and after 3 months of follow-up. The noninferiority margin was 4 points measured by the Insomnia Severity Index. Sleep diaries and actigraphy measured sleep onset latency (SOL), wake after sleep onset (WASO), total sleep time (TST), and sleep efficiency. Secondary outcomes included sleep quality, sleep beliefs, mood, and stress.

#### Results

Of 327 patients screened, 111 were randomly assigned (CBT-I, n = 47; MBSR, n = 64). MBSR was inferior to CBT-I for improving insomnia severity immediately after the program (P = .35), but MBSR demonstrated noninferiority at follow-up (P = .02). Sleep diary-measured SOL was reduced by 22 minutes in the CBT-I group and by 14 minutes in the MBSR group at follow-up. Similar reductions in WASO were observed for both groups. TST increased by 0.60 hours for CBT-I and 0.75 hours for MBSR. CBT-I improved sleep quality (P < .001) and dysfunctional sleep beliefs (P < .001), whereas both groups experienced reduced stress (P < .001) and mood disturbance (P < .001).

#### Conclusion

Although MBSR produced a clinically significant change in sleep and psychological outcomes, CBT-I was associated with rapid and durable improvement and remains the best choice for the nonpharmacologic treatment of insomnia.

J Clin Oncol 32:449-457. © 2014 by American Society of Clinical Oncology

# INTRODUCTION

Estimates suggest that 36% to 59% of patients with cancer experience disturbed sleep and insomnia symptoms during and after the completion of cancer treatment, with 21% to 28% meeting a formal diagnosis of insomnia.<sup>1</sup> Cognitive behavioral therapy for insomnia (CBT-I) is considered the treatment of choice for insomnia by the American Academy of Sleep Medicine.<sup>2,3</sup> Sleep disturbance frequently co-occurs with distress, which can place patients with cancer at a further increased risk for sleep disturbances.<sup>4</sup> The relationship between distress and sleep disturbance is likely bidirectional,

suggesting that interventions to treat insomnia may be more beneficial if they are also effective at reducing cancer-related distress.

Mindfulness-based stress reduction (MBSR) has been shown to reduce distress and improve psychological well-being in patients with cancer.<sup>5-8</sup> Within the MBSR program, participants are guided in the development of mindfulness, defined as nonjudgmental awareness of the present moment, to modify appraisals of stressful situations and reduce overall levels of psychophysiologic arousal. Preliminary evidence suggests that MBSR may produce effects comparable to pharmacologic treatment for primary insomnia<sup>9</sup> and positively impact sleep

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Published online ahead of print at www.jco.org on January 3, 2014.

Supported in part by the Canadian Cancer Society Research Institute, the Alberta Cancer Board, and a Francisco J. Varela award from the Mind & Life Institute. L.E.C. holds the Enbridge Research Chair in Psychosocial Oncology, cofunded by the Canadian Cancer Society Alberta/Northwest Territories Division and the Alberta Cancer Foundation.

None of the funding sources participated in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the article. The corresponding author is independent of the commercial funders, has full access to all the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Clinical trial information: NCT01335776.

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0732-183X/14/3205w-449w/\$20.00

DOI: 10.1200/JCO.2012.47.7265

quality and quantity in patients with cancer.<sup>10-12</sup> Adequately powered and controlled trials are necessary before conclusive statements of efficacy are possible. The primary objective of the present study was to establish whether MBSR produces similar effects as CBT-I for reducing insomnia symptoms. We hypothesized that MBSR may be statistically noninferior to CBT-I for reducing insomnia severity immediately after the program (2 months) and at the 3-month follow-up (5 months), while also producing a greater reduction in cancer-related distress. The secondary objective was to compare MBSR with CBT-I on measures of subjective and objective sleep quality, stress symptomatology, mood disturbance, and dysfunctional sleep beliefs.

# **PATIENTS AND METHODS**

The initial trial design for this study was published previously.<sup>13</sup> Ethical approval was obtained from the Conjoint Health Research Ethics Board of the University of Calgary/Alberta Health Services. The reporting of this trial follows the extended CONSORT guidelines for reporting noninferiority and equivalence randomized controlled trials.<sup>14</sup>

#### Patients

Patients were recruited from a tertiary cancer center in Calgary, Alberta, Canada. Adults with a nonmetastatic cancer diagnosis were eligible for the trial if they had completed chemotherapy and radiation treatments at least 1 month before study entry. Participants were required to meet the diagnostic criteria of insomnia, defined as sleep latency or time awake after sleep onset greater than 30 minutes and sleep efficiency of less than 85%, with disturbances occurring 3 or more days per week for at least 1 month and producing significant impairment in functioning.<sup>15-17</sup> Patients using psychotropic medication were eligible as long they still met diagnostic criteria and if their dosage was stable in the previous 6 weeks. Patients were ineligible if they screened positive for the presence of another sleep or psychiatric disorder (eg, sleep apnea or alcohol dependency) or had previous treatment with MBSR or CBT-I. Participants completed questionnaires and tracked their sleep with a sleep diary and actigraph for 1 week at baseline and at 2 and 5 months of follow-up.

### Interventions

*CBT-I.* The CBT-I program was delivered to groups of six to 10 individuals over the course of eight, weekly, 90-minute sessions, for a total of 12 contact hours. The intervention followed the format of previously published CBT-I trials in patients with cancer.<sup>18,19</sup> CBT-I contains the following four individually validated strategies: stimulus control, sleep restriction, cognitive therapy, and relaxation training. Combined, this intervention targets and reduces sleep-related physiologic and cognitive arousal to re-establish restorative sleep function.

*MBSR.* The MBSR program is delivered to groups of 15 to 20 people over the course of eight, weekly, 90-minute sessions, plus one 6-hour weekend intensive silent retreat, for a total of 18 contact hours. A week-by-week description of the program has been previously published.<sup>20</sup> The program provides patients with psychoeducation on the relationship between stress and health, while meditation techniques and gentle yoga are practiced to support the development of mindful awareness and responding to stress.

This trial was designed to compare two interventions delivered in their standard forms. No modifications were made to the MBSR program, and the group sizes chosen were previously reported for that intervention.

#### **Treatment Fidelity**

Treatment integrity was primarily maintained by using program facilitators who were experienced and trained in one modality but not in the other. The facilitator of the MBSR program was a nurse trained in MBSR by the University of Massachusetts Medical School with more than 10 years of experience delivering this program to patients with cancer. The facilitator for the CBT-I program was a doctoral-level student in clinical psychology, with training in CBT-I from the University of Rochester Medical Center who was supervised by a PhD-level clinical health psychologist. Budget limitations prevented formal treatment integrity assessment.

#### Primary Outcome: Insomnia Severity

The Insomnia Severity Index (ISI) is a seven-item measure designed to measure severity of sleep onset and sleep maintenance difficulties, satisfaction with current sleep pattern, interference with daily functioning, impairment attributed to the sleep problem, and degree of distress elicited.<sup>21</sup>

## Secondary Outcomes

*Sleep quality: subjective.* A sleep diary was used to calculate subjective reports of sleep efficiency (SE), sleep onset latency (SOL), wake after sleep onset (WASO) including early morning awakenings, and total sleep time (TST).<sup>22</sup> The Pittsburgh Sleep Quality Index is a 19-item measure of subjective sleep quality over the previous month and is designed for clinical populations.<sup>23</sup>

*Sleep quality: objective.* The GT1M actigraph manufactured by Acti-Graph (Pensacola, FL) provides objective information on SE, SOL, TST, and WASO (including early morning awakenings). Data were analyzed using the software program provided by ActiGraph and the Sadeh algorithm for distinguishing sleep and wake activity.<sup>24</sup>

*Psychological outcomes.* The Calgary Symptoms of Stress Inventory is a 56-item measure of physical, psychological, and behavioral responses to stress-ful situations.<sup>25</sup> The Profile of Mood States–Short Form is a 37-item scale assessing overall mood disturbance.<sup>26,27</sup> The Dysfunctional Beliefs and Attitudes About Sleep Scale is designed to assess cognitions often associated with sleep disturbance.<sup>28</sup>

#### Sample Size

Sample size determination followed the recommendations outlined by Hwang and Morikawa.<sup>29</sup> The minimally important difference in insomnia severity is a reduction of 8 points on the ISI.<sup>30</sup> The noninferiority margin was established as 50% of the minimally important difference (or 4 points on the ISI). Sample size was calculated with a standard deviation of 6 points based on previous data.<sup>18,31</sup> Using a one-tailed test and a 5% significance level and accounting for 20% attrition, 35 participants in each group would provide adequate power (80%) to reject the null hypothesis that the ISI changes produced by MBSR are inferior to those produced by CBT-I.

#### Blinding and Random Assignment

The study was advertised generally as I-CAN SLEEP (A Research Program for Individuals with Insomnia and Cancer) so as to not reveal program content. Interested participants were told they would be assigned to one of two interventions, and the general content of both programs was described. After providing baseline data, participants were randomly assigned and informed via e-mail about their assigned program. Block random assignment was performed using a computer-based random assignment program with a 1:1 allocation ratio. Midpoint in the trial, the allocation ratio was adjusted to 2:1 to compensate for differential attrition in the MBSR group. The random allocation sequence was recorded on sequentially numbered, opaque, sealed, and stapled envelopes. The primary investigators were kept blind to allocation, and patients remained blind to the study hypotheses and the content of the other treatment group through the duration of their participation.

#### Statistical Methods

In noninferiority trials, intent-to-treat (ITT) analyses typically decrease the differences between groups and increase the chance of concluding that the two treatments are similar, whereas per-protocol (PP) analyses do not consider the impact that dropouts may have on outcome and downplay the possibility of patients remaining on the study being more likely to respond. As such, analyses were conducted on both the PP and ITT populations. The PP population included all randomly allocated patients who attended at least five of the eight classes. The ITT population included all randomly allocated participants regardless of attendance.

Independent-samples *t* test,  $\chi^2$  test, and Fisher's exact test were used to compare the groups regarding demographic and treatment variables. Linear mixed models (LMMs) for repeated measures were used to analyze the data. Effect sizes were calculated for both groups to quantify the impact of the treatment from baseline to the 2- and 5-month follow-ups.

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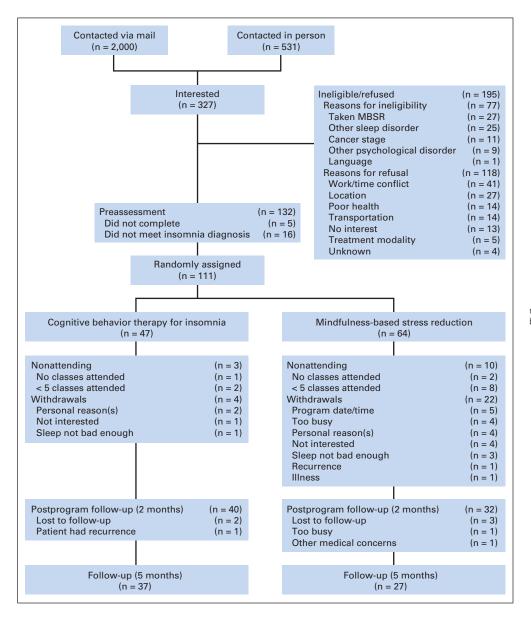


Fig 1. CONSORT diagram and recruitment flow chart. MBSR, mindfulnessbased stress reduction.

Noninferiority was assessed using an F test statistic generated from the LMM and CIs, as recommended by Mascha and Sessler.<sup>32</sup> The *P* value measures the probability that the MBSR mean is statistically smaller than the CBT-I mean plus the noninferiority margin of 4.0 and, when significant, provides evidence for noninferiority. The upper one-sided CI is the reference for whether the difference between the group means is less than the prespecified margin of noninferiority. Separate models were conducted for the primary outcome of insomnia severity and each of the secondary outcomes. An intraclass correlation coefficient was calculated to test whether the within-group effect of cohort accounted for significant variance in the primary outcome.

For each of the models, the random effect was participant, and the fixed effects were group (MBSR or CBT-I), time, baseline value, and the group-time interaction. Time was also set as a repeated measure. The restricted maximum likelihood estimate method was used to estimate the model parameters and SEs with a compound symmetry covariance structure to account for the correlation between measurements. We used type III fixed effects (F and *t*) and set the statistical significance of *P* values at P < .05. Pairwise comparisons were used to follow up any significant effects, and the least significant difference method was used to control for multiple

comparisons in the LMMs. IBM SPSS v. 20 (SPSS, Chicago, IL) was used for all analyses.

# RESULTS

Between September 2008 and March 2011, 327 patients were assessed and 111 were randomly assigned. Figure 1 shows reasons for ineligibility, refusal, and withdrawal. The participants who withdrew from the MBSR program typically did so within the first three classes. Across treatment groups, individuals who withdrew from the study were less educated and had higher levels of insomnia severity at baseline than completers. For those remaining individuals, there were no significant differences in attendance and adherence between the groups. Table 1 lists the baseline demographic, treatment, and insomnia characteristics. Random assignment successfully produced group equivalence. There were no significant differences in attrition or treatment effect by sex.

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Demographic or Clinical	All Pat Rando Assig (N =	omly Ined	Total P Who Co Program	mpleted	Patients to CBT-I		Patients , to M (n =	IBSR	
Characteristic	No	%	No.	%	No.	%	No.	%	F
Sex									.09
Male	31	28	20	28	8	21	12	38	
Female	80	72	52	72	32	79	20	62	
Age, years									.5
Mean	58.5		59.		58		60.		
SD	11.0		11.			.46	12.		
Range	35-	88	36-	88	36	-88	36-	-87	
Education, years									.9
Mean	15.		15.			.75	15.		
SD	3.5	3	3.5	56	4.	02	2.9	91	
Range	6-3	3	11-	33	11-	-33	11-	-25	
Employment									.4
Homemaker	11	10	5	7	3	8	2	6	
Full time	31	28	24	33	13	33	11	34	
Part time	22	20	13	18	10	25	3	9	
Retired	35	32	25	35	12	30	13	41	
Disabled	12	11	5	7	2	5	3	9	
Ethnicity									.0
White/European	100	90	67	93	38	96	29	91	
Native/Aboriginal	3	3	1	1	1	2			
Asian	7	7	1	1			3	9	
Black	1	1	3	4	1	2			
Insomnia duration, years									.9
Mean	6.8	18	6.7	71	6.	74	6.0	67	
SD	6.6		6.5		6.		6.		
Range	0.10-2		0.22-2		0.39-3		0.22-2		
Disease duration, years	0.102	.0.00	0.22 /	20.00	0.00	21.02	0.22 1	20.00	.9
Mean	3.1	9	3.2	21	3.:	23	3.1	19	.0
SD	4.0		4.3		4.8		3.8		
Range	0.17-2		0.17-2			29.76	0.17-		
Cancer location	0.17-2	.9.70	0.17-2	29.70	0.22-	29.70	0.17-	19.90	.4
	53	48	35	40	22	FO	10	20	.4
Breast				49	23	58	12	38	
Prostate Blood/lumanh	12	11	8	11	3	8	5	16 15	
Blood/lymph	11	10	8	11	3	8	5	15	
Female genitourinary	10	10	6	8	4	10	2	6	
Colon/Gl	7	6	5	7	2	5	3	9	
Head and neck	9	8	5	7	2	5	3	9	
Lung	7	6	4	6	3	8	1	3	
Skin	2	2	1	1			1	3	
Previous treatments									.9
Surgery	91	82	59	82	35	88	24	75	
Chemotherapy	58	52	35	49	20	50	15	47	
Radiation	51	46	30	42	17	43	13	41	
Hormonal	12	11	10	14	6	15	4	13	
Current treatments									.4
Hormonal	24	22	15	21	9	23	6	19	
Sedatives/hypnotics	29	26	22	31	12	30	10	31	
Anxiolytics	14	13	11	15	9	23	2	6	
Antidepressants	23	21	15	21	11	28	4	13	

NOTE. Percentages may not equal 100% because of rounding.

Abbreviations: CBT-I, cognitive-behavioral therapy for insomnia; MBSR, mindfulness-based stress reduction; SD, standard deviation.

# Noninferiority Analysis of Insomnia Severity

The intraclass correlation coefficient for cohort and baseline insomnia severity equaled 0.017 (P = .56), indicating that approximately 2% of the proportion of total variance was attributable to

between-cohort differences, leaving 98% attributable to differences within individuals. As such, cohort was not included as a random effect in the model. In both the PP and ITT analyses, the post-treatment ISI scores in the MBSR group were higher than the

Measure	MBSR		CBT-
	IVIDSH		CBI-
er-protocol population			
No. of patients	32		40
Before program (baseline)			
Mean score	16.34		18.25
SE	0.75		0.67
Difference in score*		-1.91	
95% CI	-0	.09 to -3.	90
Р		.06	
After program (2 months)			
EMM score	11.86		8.20
SE	0.65		0.58
Difference in score*		3.65	
Upper 95% Cl		5.11	
P		.35	
Follow-up (5 months)			
EMM score	10.73		8.6
SE	0.71		0.6
Difference in score*		2.07	
Upper 95% Cl		3.62	
Р		.02	
ntent-to-treat population			
No. of patients	64		47
Before program (baseline)			
Mean score	18.23		17.8
SE	0.53		0.6
Difference in score*		0.36	
95% CI	-1	.26 to 1.98	3
Р		.66	
After program (2 months)			
EMM score	12.06		8.28
SE	0.61		0.54
Difference in score*		3.78	
Upper 95% Cl		5.12	
P		.39	
Follow-up (5 months)			
EMM score	11.07		9.0
SE	0.67		0.56
Difference in score*		2.02	
Upper 95% Cl		3.47	
Р		.01	

NOTE. Baseline values were compared using two-sample *t* test, and actual means are presented. After program and follow-up values were compared using linear mixed models adjusting for baseline, and marginal means are presented. Noninferiority is concluded if the upper 95% Cl is less than a margin of 4 and the *P* value for the test of noninferiority is P < .05. Abbreviations: CBT-I, cognitive-behavioral therapy for insomnia; EMM, esti-

mate marginal mean; MBSR, mindfulness-based stress reduction.

\*Difference = mean MBSR minus mean CBT-I.

CBT-I group; however, at the 5-month follow-up, the one-sided CI was within the noninferiority margin of 4 and P < 0.05, demonstrating noninferiority of MBSR to CBT-I. Table 2 lists the exact values.

# Sleep and Psychological Outcomes

Results of the LMM analysis for sleep and psychological outcomes for the PP sample are listed in Table 3. The ITT analysis produced similar results to the PP analysis, and the results are listed in Table 4. The pairwise comparisons are reported for the PP analyses.

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# **Sleep Dairies**

There were significant interactions on sleep diary measures of SOL and SE, with the change produced by the CBT-I group exceeding that produced by MBSR. With regard to SOL, for the CBT-I group, the greatest change was observed between baseline and immediately after the program at 2 months ( $\Delta = 20.74$ , P < .001). The MBSR group reported significant improvements occurring between after the program and follow-up ( $\Delta = 11.28$ , P = .007). At follow-up, the CBT-I group demonstrated a 22-minute decrease in SOL, whereas the MBSR group reported a 14-minute decrease. For SE, CBT-I was significantly better than MBSR after the program (difference = -7.53, P < .001) and at follow-up (difference = -4.14, P = .030). The greatest amount of change occurred between baseline and after the program (at 2 months) for both groups (MBSR:  $\Delta = -4.70$ , P < .006; CBT-I:  $\Delta = -11.90$ , P < .001).

There were significant group and time effects demonstrated for WASO and TST. The greatest amount of change in WASO occurred between baseline and after the program (at 2 months) for both groups (MBSR:  $\Delta = 29.51$ , P < .001; CBT-I:  $\Delta = 36.23$ , P < .001). The reduction in WASO from baseline to follow-up was 35.84 minutes for the CBT-I group and 36.46 minutes for the MBSR group. For TST, both groups reported significant improvement from after the program to follow-up (MBSR:  $\Delta = -0.65$ , P < .001; CBT-I:  $\Delta = -0.38$ , P = .017) but not from baseline to after the program. The increase in TST from baseline to follow-up was 0.60 hours for the CBT-I group and 0.75 hours for the MBSR group.

# Actigraphy

There were no significant interactions observed for the actigraphic sleep parameters. The CBT-I group recorded significant improvements in SOL from baseline to follow-up (difference = 5.55, P = .031). The MBSR group demonstrated significant improvement in WASO from baseline to follow-up (difference = 16.52, P = .040), whereas the CBT-I group demonstrated the greatest improvement from baseline to after the program (difference = 24.72, P < .001). The increase in TST detected by actigraphy from baseline to follow-up was 6 minutes for the CBT-I group and 18 minutes for the MBSR group. The largest improvements in TST for both groups were demonstrated between after the program and follow-up (MBSR: difference = -33.14, P < .001; CBT-I: difference = -28.95, P < .001). Actigraphic SE improved from baseline to after the program (difference = -3.44, P = .006) for the CBT-I group only.

# Sleep Quality, Sleep Beliefs, Symptoms of Stress, and Mood Disturbance

There were significant interactions between the MBSR and CBT-I groups on measures of sleep quality (Pittsburgh Sleep Quality Index) and dysfunctional sleep beliefs (Dysfunctional Beliefs and Attitudes About Sleep Scale), with the change produced by the CBT-I group exceeding that produced by MBSR at both time points. There was a main effect of time for mood disturbance (Profile of Mood States–Short Form) and symptoms of stress (Calgary Symptoms of Stress Inventory), indicating that both groups experienced significant improvements over time.

Baseline     After Progenu IZ montrol     Follow/Up (E montrel)     Effect Size (Chic dimensione)     Effect Size (Chic dimensione)	Baseline     Baseline       Estimated Marginal     SE       Group Mean     SE       43.49     2.44       41.29     2.73       74.82     4.61       80.08     4.51       6.37     0.12       6.37     0.12       6.37     0.13       73.19     1.16       73.19     1.16       73.19     1.16       73.19     1.16       73.19     1.16       73.19     1.16       73.19     1.16       73.19     1.16       73.19     1.16       73.19     1.16       73.19     1.16       73.19     1.16       73.19     1.16       106.33     5.21       106.33     5.92       413.57     6.63       79.19     1.00       79.19     1.00		http	Effect Siz									
Enrone Manya	Estimated Marginal Group Mean     SE       Source Mean     SC       Same     43.49     2.44       41.29     2.44       41.29     2.44       Source Mean     SC       Same     43.49     2.44       Same     41.29     2.44       Same     74.82     4.61       Source Same     5.31     1.16       Same     73.19     1.16       72.87     73.19     1.16       Same     73.19     1.53       Same     12.28     1.37       Same     12.39     1.53       Same     1.235     5.21       Same     1.66.33     5.21       Same     1.06.33     5.21       Same     79.19     1.00       Same     79.13     1.00			Raseline to	e (Cohen's d)		LMN	Statistic	al Tests* (type I	ll tests of	fixed effe	cts)	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	43.49   2.44     41.29   2.73     74.82   4.04     80.08   4.51     6.32   0.12     6.32   0.13     6.32   0.13     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     72.87   0.13     12.98   1.53     12.98   1.53     12.98   1.53     403.59   5.92     79.19   1.00     79.19   1.00						oup Effect Af	٩			Grou	o-Time Intera	ction
	43.49   2.44     41.29   2.73     41.29   2.73     74.82   4.04     80.08   4.51     80.08   4.51     80.08   4.51     80.08   4.51     80.08   4.51     80.08   4.51     6.37   0.12     6.37   0.12     6.37   0.13     73.19   1.16     72.87   1.16     72.87   1.30     12.98   1.53     12.98   1.53     12.98   1.53     12.98   1.53     12.98   1.53     12.98   1.53     12.98   1.53     12.98   1.53     106.33   5.21     403.59   5.21     79.19   1.00     79.19   1.00					-	5	-		-	-	5	-
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	43.49   2.44     41.29   2.73     74.82   4.51     80.08   4.51     80.08   4.51     74.82   4.04     80.08   4.51     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     72.87   1.30     12.29   1.37     12.29   1.53     12.98   1.53     12.98   1.53     12.98   1.53     12.98   1.53     12.89   1.53     12.89   1.53     12.98   1.53     12.98   1.53     12.98   1.53     12.88   0.89     73.89   0.89     73.91   1.00     79.19   1.00						1,67.70					2,134.72	.004
128     273     363     273     373     273     373 <td>41.29   2.73     74.82   4.04     80.08   4.51     80.08   4.51     6.37   0.13     6.37   0.13     6.37   0.13     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     72.87   1.30     12.29   1.37     12.29   1.37     12.29   1.53     12.29   1.53     12.39   1.53     12.38   0.137     12.28   0.592     106.33   5.92     403.59   5.92     73.19   1.00     79.19   1.00</td> <td></td> <td></td> <td></td> <td>1.24</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	41.29   2.73     74.82   4.04     80.08   4.51     80.08   4.51     6.37   0.13     6.37   0.13     6.37   0.13     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     73.19   1.16     72.87   1.30     12.29   1.37     12.29   1.37     12.29   1.53     12.29   1.53     12.39   1.53     12.38   0.137     12.28   0.592     106.33   5.92     403.59   5.92     73.19   1.00     79.19   1.00				1.24								
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	74.82 4.04   80.08 4.51   80.22 0.12   6.37 0.12   6.37 0.12   6.37 0.13   73.19 1.16   73.19 1.16   73.19 1.16   72.87 1.30   12.29 1.37   12.29 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   13.57 6.63   705.9 5.92   79.19 1.00				0.86								
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	74.82 4.04   80.08 4.51   80.08 4.51   6.32 0.12   6.37 0.13   73.19 1.16   72.87 1.16   72.89 1.37   12.29 1.37   12.29 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   13.79 5.21   403.59 5.92   79.19 0.89   79.19 1.00						1,72.72					2,137.93	.670
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	80.08 4.51 6.32 0.12 6.37 0.13 73.19 1.16 72.87 1.30 12.29 1.37 12.29 1.37 12.29 1.37 12.29 1.37 12.29 5.21 403.59 5.21 403.59 5.92 413.57 6.63 79.19 1.00				1.57								
	6.32 0.12 6.37 0.13 72.87 1.16 72.87 1.30 12.29 1.37 12.29 1.37 106.33 5.21 403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00				1.34								
	6.32 0.12 6.37 0.13 7.3.19 1.16 72.87 1.30 12.29 1.37 12.29 1.37 106.33 5.21 403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00						1,69.13					2,134.38	.553
	6.37 0.13 7.3.19 1.16 72.87 1.30 12.29 1.37 12.29 1.37 12.29 1.37 106.33 5.21 403.59 5.92 413.57 6.63 79.19 1.00				-0.81								
7319     116     50.0     139     60.0     118     10.11 <td>73.19 1.16   72.87 1.30   12.29 1.37   12.29 1.53   12.98 1.53   12.99 5.21   106.33 5.21   403.59 5.92   413.57 6.63   79.19 1.00</td> <td></td> <td></td> <td></td> <td>-0.98</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	73.19 1.16   72.87 1.30   12.29 1.37   12.29 1.53   12.98 1.53   12.99 5.21   106.33 5.21   403.59 5.92   413.57 6.63   79.19 1.00				-0.98								
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	73.19 1.16   72.87 1.30   72.87 1.37   12.29 1.37   12.29 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 1.53   12.98 0.633   403.59 5.92   403.59 5.92   70.19 0.89   79.19 1.00						1,71.17					2,135.70	.008
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	72.87 1.30 12.29 1.37 12.98 1.53 12.98 1.53 106.33 5.21 403.59 5.92 413.57 6.63 79.19 1.00				-1.58								
1229     137     734     144     0.55     0.51     0.71     1,130     0.33     2,1130     0.33     2,1290     0.33     2,130     0.33     2,131     0.33     2,133     0.33     2,133     0.33     2,133     0.33     2,134     0.33     2,134     0.33     2,134     0.33     2,134     0.33     2,134     0.33     2,134     0.33     2,136,17     0.33     2,136,17     0.33     2,136,17     0.33     2,136,17     0.33     2,136,17     0.33     2,136,17     0.33     2,136,17     0.34     2,136,17     0.34     2,136,17     0.34     2,136,17     0.34     2,136,17     0.34     2,136,17     0.34     2,136,17     0.34     2,136,17     0.34     2,136,14     0.34     2,136,14     0.34     2,136,14     0.34     2,136,14     0.34     2,136,14     0.34     2,136,14     0.34     2,136,14     0.34     0.34     3,136     3,136     3,136     3,136     3,136     3,136     3,136     3,136     3,136     3,1	12.29 1.37 12.98 1.53 106.33 5.21 403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00				-1.03								
1228     137     7x     144     153     10     141     2129     721     103     211     211 <td>12.29 1.37 12.98 1.53 108.79 4.66 106.33 5.21 403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00</td> <td></td>	12.29 1.37 12.98 1.53 108.79 4.66 106.33 5.21 403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00												
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	12.29 1.37 12.98 1.53 106.33 5.21 403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00					93	1,61.00	.003				2,129.06	.119
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1.2.98 1.53 108.79 4.66 106.33 5.21 403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00				0.51								
10873     466     840     466     840     603     601     034     17221     105     213643     01     17364     01     17364     01     103     213643     01     11365     213643     01     11365     213643     01     11365     213643     01     11365     213631     01     11365     213631     01     11365     213631     01     11365     213631     01     11365     213631     01     11365     213631     01     11365     213631     01     11365     213631     01     11365     213631     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01     11365     01	108.79 4.66 106.33 5.21 403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00			1	0.27								
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	108.79 4.66 106.33 5.21 403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00						1,72.21					2,138.42	.255
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	106.33 5.21 403.59 5.92 3 413.57 6.63 3 78.28 0.89 79.19 1.00				0.94								
41357     52     380.07     5.32     409.01     6.23     0.03     -0.14     7.86     0.01     1,71.35     0.04     1185     2.136.31     0.01     0.186     2.136.31     0.01     0.186     2.136.31     0.01     0.186       7332     0.89     81.71     0.89     81.71     0.89     81.71     0.89     9.01     1,7154     233     7.09     2,136.31     0.01     1,756       7323     0.65     81.30     0.10     1,15     -0.01     1,47     233     7.09     2,136.49     0.01     1,75       7324     0.65     11.86     0.65     10.73     0.71     1.36     1,41     2,33     7.09     2,136.49     0.01     1,75       11270     0.35     11.86     0.65     1,136     0.71     1.36     1,41     2,134     0.01     1,126     2,134.49     0.01     1,136       11270     0.35     1,136     1,41     1,36     1,41     1,41     1,41     1,41     1,41	403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00				0.52								
403.59     532     380.07     532     4001     6.24     0.63     -0.14       7328     089     81.71     089     81.71     089     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     81.71     0.89     1.71.54     7.70     2.135.91     0.70     1.76       17.75     0.58     8.20     0.56     0.71     1.36     1.41.30     0.20     1.12.81     0.01     81.94     0.01     81.94     0.01     81.94     0.01     81.94     0.01     81.94     0.01     81.94     0.01     81.94     0.01     81.94     0.01     81.94     0.01     81.94     0.01     81.94     0.0	403.59 5.92 413.57 6.63 78.28 0.89 79.19 1.00						1,71.35					2,136.31	.621
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	413.57 6.63 78.28 0.89 79.19 1.00				-0.14								
78.2     0.89     81.71     0.89     83.14     0.94     -0.61     -0.84     1.15     2.03     2.136.31     0.01     1.15       79.19     1.00     79.23     1.00     81.69     81.60     1.15     -0.01     -1.41     9.64     2.136.31     0.01     8.09     0.01     1.05     1.03     9.14     9.14     9.65     10.73     0.01     1.36     0.01     8.09<	78.28 0.89 79.19 1.00				-0.44								
73.26     0.69     81.71     0.89     85.14     0.94     -0.61     -1.41       73.19     1.00     79.32     1.00     79.32     1.00     7.32     0.81.71     0.88     0.01     -1.41     0.04     -0.01     -1.41     0.01     8.19     0.01     8.09     11.128     0.01     8.09     10.0     8.09     10.0     8.09     10.11128     0.01     8.09     10.14     1.41     1.4	78.28 0.89 79.19 1.00						1,71.54	.233				2,136.91	.176
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	79.19 1.00				-0.84								
17.75     0.58     8.20     0.58     8.66     0.61     2.59     2.41     7.42     1,67.87     0.08     111.28     0.01     8.00       16.89     0.65     11.86     0.65     10.73     0.71     1.36     1,60     111.28     2,135.40     0.01     8.09       12.70     0.35     7.18     0.35     7.19     0.36     2.52     2.47     9.00     18.94     0.01     18.94       12.70     0.35     7.18     0.35     0.71     1.36     2.605     1,68.53     0.01     80.02     2,135.40     0.01     18.94       12.72     0.39     10.72     0.36     0.42     0.36     0.365     2,135.40     0.01     10.36       6657     2.21     47.04     2.29     1.25     1.37     0.20     1,69.72     .657     35.55     2,135.99     .001     1.03       6657     2.21     47.04     2.29     1.25     1.37     .657     .657     35.55     2,135.99     .001	eep and psychological outcomes ISI total score				-1.41								
17.75   0.58   8.20   0.58   8.66   0.61   2.59   2.41   1.6787   0.08   111.28   2.135.40   0.01   8.00     re   16.89   0.65   11.86   0.65   10.73   0.71   1.36   1.60   8.00   18.94   0.01   8.00   9.00   18.04   9.01   18.04   9.01   18.04   9.01   18.04   9.01   18.04   9.01   18.04   9.01   18.04   9.01   18.04   9.01   18.04   9.01   10.01   10.02   18.04   9.01   10.01	ISI total score												
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$							1,67.87				00	2,134.44	.001
	17.75 0.58				2.41								
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	16.89 0.65				1.60								
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$							1,68.53				18.	2,135.45	.001
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	12.70 0.35				2.47								
66.57   2.21   49.04   2.21   47.04   2.29   1.25   1.37   66.57   35.55   2.135.99   001   1.03     66.57   2.21   49.04   2.21   47.04   2.29   1.25   1.37   55.55   2.135.99   001   1.03     66.57   2.15   51.99   2.47   49.69   2.69   0.86   0.98   0.98   0.64   1.67.55   .425   18.26   2.134.18   .001   0.86     27.62   2.31   11.70   2.04   12.16   2.46   1.09   1.02   0.64   1.67.55   .425   18.26   2.134.18   .001   0.86     27.62   2.62   12.73   2.81   0.70   0.84   1.67.55   .425   18.26   2.134.18   .001   0.86     5.41   0.18   2.01   1.02   0.70   0.84   1.70.577   .001   48.94   2.136.523   .001   15.16     5.41   0.18   2.01   2.01   2.01   2.15   1.89   .001   15.16   .16   .01   .01   .01 </td <td>12.72 0.39</td> <td></td> <td></td> <td></td> <td>1.38</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	12.72 0.39				1.38								
66.57   2.21   49.04   2.21   47.04   2.29   1.25   1.37     63.39   2.47   51.99   2.47   49.69   2.69   0.86   0.98     63.39   2.47   51.99   2.47   49.69   2.69   0.86   0.98     27.62   2.31   11.70   2.04   12.16   2.46   1.09   1.02     27.62   2.62   12.73   2.81   0.70   0.84   1,67.55   .425   18.26   2,134.18   .001   0.86     27.62   2.62   12.73   2.81   0.70   0.84   1,67.55   .425   18.26   2,134.18   .001   0.86     26.58   2.62   12.73   2.81   0.70   0.84	C-SOSI total score					20	1,69.72					2,136.00	.361
63.39 2.47 51.99 2.47 49.69 2.69 0.86 0.98   27.62 2.31 11.70 2.04 12.16 2.46 1.09 1.02   25.58 2.62 15.26 2.62 12.73 2.81 0.70 0.84 1,67.55 .425 18.26 2,134.18 .001 0.86   25.58 2.62 12.73 2.81 0.70 0.84 1,67.55 .425 18.26 2,134.58 .001 0.86   5.41 0.18 2.62 12.73 2.81 0.70 0.84 2,156.523 .001 15.16   5.41 0.18 2.06 0.18 3.21 0.19 2.15 1.89   5.77 1,70.577 .001 48.94 2,136.523 .001 15.16	66.57 2.21				1.37								
27.62 2.31 11.70 2.04 12.16 2.46 1.09 1.02   25.58 2.62 15.26 2.02 12.73 2.81 0.70 0.84   55.11 0.18 0.10 1.02 1.02 1.02 1.02   25.58 2.62 12.73 2.81 0.70 0.84   5.41 0.18 2.01 189 2.15.56   5.41 0.18 2.16 0.19 2.15 15.16   5.41 0.18 2.96 0.19 2.15 1.89	63.99 2.47				0.98								
27.62 2.31 11.70 2.04 12.16 2.46 1.09 1.02   25.58 2.62 12.73 2.81 0.70 0.84   25.54 16.26 2.62 12.73 2.81 0.70 0.84   5.41 0.18 2.96 0.18 2.15 1.89   5.41 0.18 2.15 1.89   5.41 0.18 0.00 0.00 0.00	POMS-SF total score						1,67.55					2,134.19	.425
25.58 2.62 15.26 2.62 12.73 2.81 0.70 0.84 25.77 1,70.577 .001 48.94 2,136.523 .001 15.16 5.41 0.18 2.96 0.18 3.21 0.19 2.15 1.89 7.00 7.00 7.00 7.00 7.00 7.00 7.00 7.00	27.62 2.31				1.02								
5.41 0.18 2.96 0.18 3.21 0.19 2.15 1.89 5.41 0.18 2.96 0.18 3.21 0.19 2.15 1.89 5.00 5.00 5.00 5.00 5.00 5.00 5.00 5.00	25.58 2.62		2		0.84								
5.41 0.18 2.96 0.18 3.21 0.19 2.15 For one are one and one one one							1,70.577					2,136.522	.001
	5.41 0.18				1.89								
0.20 0.22 0.00	MBSR 5.25 0.20 4.56	0.20	4.60 0.22		0.55								
	Abbreviations: CBT-I, cognitive-behavioral therapy for insomnia; C-SO: MM linear mixed model: MRSB mindfulness-based strass reduction.	SI, Calgary Syr	nptoms of Stress Inve	intory; DBAS-	16, Dysfunction	Sleen Ou	efs and Att	itudes /	bout Sleep S	cale; ISI,	Insomni	a Severity	
bbreviations: CBT-I, cognitive-behavioral therapy for insomnia; C-SOSI, Calgary Symptoms of Stress Inventory; DBAS-16, Dysfunctional Beliefs and Attitudes About Sleep Scale; ISI, Insomnia Severity II	VIIV, linear mixed model; IVIBSR, mindfulness-based stress reduction; ake after sleep onset.	PUINIS-SF, Pro	IIE OT IVIOOD STATES-SI	ort Form; PSC	u, Pittspurgn	sleep Uu	ality Index	SUL, SI	eep onset late	ncy; ISI	, total sid	ep time; v	₹ >
Abbreviations: CBT-I, cognitive-behavioral therapy for insomnia; C-SOSI, Calgary Symptoms of Stress Inventory; DBAS-16, Dysfunctional Beliefs and Attitudes About Sleep Scale; ISI, Insomnia Severity Index; LMM, linear mixed model; MBSR, mindfulness-based stress reduction; POMS-SF, Profile of Mood States-Short Form; PSQI, Pittsburgh Sleep Quality Index; SOL, sleep onset latency; TST, total sleep time; WASO,	wake after sleep onset. *Effects evaluated at 5 months												

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	Baseline		After Program (2 mo	months)	Follow-Up (5 mor	months)	Effect Size	(Cohen's d)		LMP	A Statis	ical Tests	LMM Statistical Tests* (type III tests of fixed effects)	ests of	fixed eff	ects)	
	Estimated Marginal		Estimated Marginal		Estimated Marginal		Baseline to	Baseline to		Group Effect			Time Effect		Grot	Group-Time Interaction	raction
Outcome	Group Mean	SE	Group Mean	SE	Group Mean	SE	2 Months	5 Months	ш	đť	Ρ	ш	đf	μ	ш	đf	Ρ
Sleep diary SOL, minutes									15.42	1,96.46	.001	35.74	2,171.04	.001	5.82	2,171.40	.004
CBT-I	44.79	2.25	23.96	2.41	22.58	2.47	1.30	1.37									
MBSR	46.05	1.937	40.67	2.68	30.00	3.09	0.29	0.78									
WASO, minutes									3.29	1,105.70	.073	56.77	2,178.74	.001	0.93	2,179.09	.395
CBT-I	72.50	3.62	36.23 40.40	3.86	36.41 40 FF	3.95	1.41	1.39									
	/0.03	3.09	48.40	4.30	40.D4	4.40	0.89	1.04	000	× 0 0 0 7 7	000	L CC		500	10		
ISI, hours		0	0		L			0	0.00	1,108.64	999.	23.54	2,179.63	100.	1.07	2,179.44	1 .346
MESE	0.27 R 10	01.0	0.40 6.37	0.12	0.65	0.13	-0.30	-0.05									
Sloom officional 20	0.10	0.0	10.0	0.12	1.01	2.0	77.0	0.00	1010	1 110 00	100	60 1E	7 170 67	100	5 07	7 170 60	000
oleep eniclency, 70 CBT-I	72.95	1.01	84.97	1.08	84.86	1.11	-1.67	-1.63	13.12	1, 1 10.00	- nn.	CI.20	2,11,0.07	- 00.	0.97	2,170.0	
MBSR	71.85	0.87	77.06	1.20	80.53	1.38	-0.62	-0.94									
Actigraphy									00 01	10 1	500	00	00 02 0	0	50 0	0 0 0 0 0	
		0	C C T	L	C T T	00	L C	L	12.03	01.10,1	100.	4.03	2,11/2.00	010	CD.7	2,11/2.03	C/U. 6
MRCR	12.3/	1.18	1.1.16	07.1	10.12	1.32 1.45	111	0.04 7.07									
	0.01	70.1	D	t.	0t.0-	<u>}</u>		17:0	CC V	1 103 80	610	1 E GE	0 187 08	100	1 60	7 187 07	1 28
CBT-I	107.94	4.06	83.64	4.30	79.05	4.52	0.85	0.98	77.4		2	0000	2, 102.00	- 00.	<u>-</u>	2,102.0	
MBSR	107.05	3.51	97.09	4.85	89.51	5.68	0.29	0.46									
TST, minutes									7.22	1,109.41	.008	13.61	2,180.20	.001	1.56	2,180.20	.212
CBT-I	401.70	5.17	376.63	5.46	405.20	5.74	0.67	-0.09									
MBSR	404.47	4.45	393.03	6.17	426.04	7.25	0.26	-0.44									
Sleep efficiency, %									3.24	1,106.25	.075	10.62	2,181.55	.001	1.76	2,181.54	t .175
CBT-I	78.40	0.77	81.69	0.81	83.24	0.85	-0.61	-0.87									
MBSR	78.74	0.66	79.29	0.92	81.41	1.03	-0.09	-0.38									
Sleep and psychological outcomes	St																
ISI total score	r r	L	000	L	L	C L	LOO		15.78	1,111.92	.001	163.14	2,180.26	.001	6.57	2,180.51	.002
CBI-I	11.11	19.0	8.28	0.54	9.05	0.56	2.65	2.37									
IVIDOR PSOI total score	17.34	0.44	00.21	10.0	10.11	0.0/	-33 -	70.1	21 73	1 113 10	100	111 12	0 181 08	100	22 E1	0 1 8 1 1 0	100
CBT-I	12.57	030	7 19	0.32	7 19	0.33	2 53	2 48	r.		-	1	0.101,4		- 0.1		
MESE	12.37	0.26	10.93	0.36	02.6	0.00	0.62	1 04									
C-SOSI total score									2.20	1.113.10	.141	51.51	2.179.19	.001	0.64	2.179.07	, 527
CBT-I	66.48	1.95	49.04	2.05	47.78	2.13	1.27	1.34									
MBSR	67.02	1.67	53.54	2.31	51.48	2.55	0.84	0.90									
POMS-SF total score									1.56	1,103.90	.214	26.73	2,180.18	.001	0.53	2,180.38	3 .589
CBT-I	27.74	2.06	12.22	2.17	13.85	2.31	1.07	0.93									
MBSR	27.86	1.76	16.52	2.45	16.66	2.71	0.66	0.61									
DBAS-16 total score									43.61	1,116.13	.001	76.21	2,181.98	.001	20.71	2,182.01	.001
CBT-I	5.45	0.15	2.96	0.16	3.18	0.17	2.30	2.05									
MBSR	5.39	0.13	4.61	0.19	4.68	0.20	0.61	0.52									

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#### DISCUSSION

The goal of this study was to compare MBSR with CBT-I for the treatment of insomnia in patients with cancer. Our data provide some evidence in support of our hypothesis that MBSR may be statistically noninferior to CBT-I for reducing insomnia severity. The change observed in the MBSR group at 5 months was within the noninferiority margin; however, CBT-I produced greater improvement in insomnia severity immediately after the program, and this was maintained at follow-up. Contrary to our hypothesis that MBSR would have additional psychological benefit, both interventions were similarly effective for improving mood and stress symptoms.

When examined individually, the CBT-I group maintained greater overall improvement in subjective SOL, SE, sleep quality, and dysfunctional sleep beliefs than the MBSR group. Progressive improvement over time was demonstrated in both groups on subjectively measured WASO and TST, as well as symptoms of stress and mood disturbance. When effects were broken down across outcomes by assessment time, the CBT-I group frequently demonstrated the largest change between baseline and after the program (at 2 months), whereas the MBSR produced ongoing or delayed effects.

This study is characterized by several strengths, including an active comparison group, random assignment, manualized interventions, and a defined eligibility criterion. To our knowledge, this is the first study of CBT-I or MBSR to use a modified blind-to-treatment protocol, intended to reduce the selection bias that is frequently associated with trials of behavioral interventions. In the future, a measurement of preference or credibility should be included to examine the potential influence of treatment acceptability on study withdrawal and outcomes.

Although the innovative aspects of this study make it clinically and theoretically valuable, the most notable limitation is the differential attrition observed between groups. Although the exact reasons are unknown, we believe that patient preference may have contributed to the significant attrition observed in the MBSR group. Compared with CBT-I, it may be less obvious to participants not already inclined to choose MBSR how learning meditation and yoga could contribute to sleep improvements. Additionally, 27 potential participants were excluded because they had already taken the MBSR program; hence, those with a clear interest in mindfulness were not enrolled. As such, the observed improvement likely underestimates the efficacy of MBSR in a general cancer population with insomnia who would voluntarily choose this type of therapy. Furthermore, the statistical approach used in this study has limitations. LMM is intended to protect against bias when data are missing at random, but this is compromised when there are unobserved factors associated with dropout, such as patient preference. Future studies with missing data should consider incorporating the use of sensitivity analyses.<sup>33</sup>

A second limitation is the absence of a no-treatment control group, which prevents an exploration of alternate explanations for change over time; however, longitudinal research has demonstrated that insomnia remains relatively stable once developed.<sup>1</sup> Third, the additional 6 hours of contact time received by participants in the MBSR group raises the possibility of even greater relative improvement for the CBT-I group if it had been matched for time. Research demonstrating that CBT-I participants receive maximum dosing after 4 weeks reduces this likelihood.<sup>34</sup> Finally, we were unable to formally assess treatment integrity; however, the research was designed to minimize risk of treatment contamination, and measures were taken throughout the study to promote fidelity.

Noninferiority trials typically assess a new treatment to determine whether it produces results that are not significantly worse than an already established treatment while delivering additional benefits, such as reducing cost or adverse effects. In this case, noninferiority was only demonstrated at the 5-month follow-up, suggesting that although MBSR may produce clinically significant improvements with time, the treatment effects of CBT-I are both rapid and durable. As such, CBT-I remains the treatment of choice for patients with cancer with insomnia.

# AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

# **AUTHOR CONTRIBUTIONS**

Conception and design: Sheila N. Garland, Linda E. Carlson, Michael C. Antle, Charles Samuels, Tavis S. Campbell Collection and assembly of data: Sheila N. Garland Data analysis and interpretation: Sheila N. Garland, Linda E. Carlson, Alisa J. Stephens, Michael C. Antle, Tavis S. Campbell Manuscript writing: All authors Final approval of manuscript: All authors

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