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ORIGINAL REPORT

Randomized Controlled Trial of Mindfulness-Based Cancer Recovery Versus Supportive Expressive Group Therapy for Distressed Survivors of Breast Cancer (MINDSET)

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ABSTRACT

Purpose
To compare the efficacy of the following two empirically supported group interventions to help distressed survivors of breast cancer cope: mindfulness-based cancer recovery (MBCR) and supportive-expressive group therapy (SET).

Patients and Methods
This multisite, randomized controlled trial assigned 271 distressed survivors of stage I to III breast cancer to MBCR, SET, or a 1-day stress management control condition. MBCR focused on training in mindfulness meditation and gentle yoga, whereas SET focused on emotional expression and group support. Both intervention groups included 18 hours of professional contact. Measures were collected at baseline and after intervention by assessors blind to study condition. Primary outcome measures were mood and diurnal salivary cortisol slopes. Secondary outcomes were stress symptoms, quality of life, and social support.

Results
Using linear mixed-effects models, in intent-to-treat analyses, cortisol slopes were maintained over time in both SET ($P = .002$) and MBCR ($P = .011$) groups relative to the control group, whose cortisol slopes became flatter. Women in MBCR improved more over time on stress symptoms compared with women in both the SET ($P = .009$) and control ($P = .024$) groups. Per-protocol analyses showed greater improvements in the MBCR group in quality of life compared with the control group ($P = .005$) and in social support compared with the SET group ($P = .012$).

Conclusion
In the largest trial to date, MBCR was superior for improving stress levels, quality of life, and social support for distressed survivors of breast cancer. Both SET and MBCR also resulted in more normative diurnal cortisol profiles than the control condition. The clinical implications of this finding require further investigation.

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INTRODUCTION

Approximately 70% of North American women currently diagnosed with breast cancer survive active treatment, resulting in a growing cohort of long-term survivors,[1] many of whom continue to have high levels of distress, often requiring psychosocial care.[2,3] Two of the most closely studied, manualized, and well-validated group interventions for cancer support are mindfulness-based stress reduction (MBSR)[4] and supportive-expressive therapy (SET),[5] but the two have never been directly compared. MBSR for patients with cancer, adapted by us and called mindfulness-based cancer recovery (MBCR),[6] has been shown to be effective across a range of outcomes including stress symptoms, mood, fatigue, quality of life, sleep disturbance, and several biomarkers.[7] The literature on MBSR/MBCR for patients with cancer has been reviewed extensively, and level 1 evidence supports its efficacy.[8-10] SET has also been empirically validated as psychologically effective for both patients with early-stage and metastatic breast cancer[11-14] across outcomes such as depression, trauma symptoms, pain, and social support.

Similarities between interventions are the group format, size, structure, and contact hours. However, the two treatment modalities are distinct in their content, focus, and theoretical underpinnings, with the focus of SET on group support and emotional expression and the focus of MBCR on mindfulness meditation, yoga practice, and sustaining mindful awareness in day-to-day life. Hence, it is likely that outcomes from the two interventions

may differ across specific dimensions of psychosocial well-being and stress-related biomarkers.

Markers of the integrity of the hypothalamic-pituitary-adrenal axis are often aberrant, reflecting dysregulated hypothalamic-pituitary-adrenal functioning, in some patients with breast cancer. Such cortisol dysregulations have been associated with poorer survival in metastatic breast cancer,[15-17] suggesting that this marker may be biologically informative, but there is little research investigating its clinical relevance in early-stage cancer. MBSR/MBCR can modify cortisol rhythms,[18-22] and steeper cortisol slopes have been associated with greater emotional expressiveness in SET.[23] By measuring salivary cortisol, we can assess the effects of each intervention on this biomarker, providing a glimpse into the integrity of the body's regulatory systems.

The purpose of this study was to compare the efficacy of MBCR, SET, and a minimal-treatment control condition on outcomes in distressed survivors of breast cancer. The primary research question was as follows: What are the comparative magnitude and direction of changes before versus after intervention among the three groups on psychological symptomatology and diurnal salivary cortisol profiles? We hypothesized that both MBCR and SET would be superior to control on all outcomes and that MBCR would be superior to SET and control for reducing stress symptoms, whereas SET would be superior for improving social support.

PATIENTS AND METHODS

Study Design

The trial used a multicenter, longitudinal, randomized controlled design with three groups (MBCR, SET, and a minimal-treatment control group; 2:2:1 allocation ratio); assessments occurred at baseline before random assignment and after intervention. Patients were randomly assigned in cohorts of up to 30 women at two sites, Calgary and Vancouver. The protocol was approved by the institutional review board at each center.

Inclusion and Exclusion Criteria

Inclusion criteria included the following: women diagnosed with stage I, II, or III breast cancer; completion of all treatments with the exception of hormonal or trastuzumab therapy at least 3 months previously; age greater than 18 years; and score of 4 or higher on the Distress Thermometer[24] to ensure a sample of patients who were experiencing clinically meaningful distress.[25] Exclusion criteria included the following: concurrent *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Axis I diagnosis of either psychosis, substance abuse, bipolar disorder, or active suicidality (depression, anxiety disorders, and adjustment disorders were not excluded; current use of psychotropic medications (eg, antipsychotics, anxiolytics; use of antidepressants was recorded but not an exclusionary factor because of their high prevalence of use); concurrent autoimmune disorder; and past participation in an MBCR or SET group.

Recruitment

Strategies included recruitment from breast cancer clinics, media publicity, brochures and posters, community outreach, and identification of patients through cancer registries in both sites, followed by direct mailing of personalized study invitation letters. Research assistants (RAs) recorded the number of patients who contacted them through all methods and subsequent accrual rates.

Procedures

When interested participants contacted the RA, they were phone screened and, if interested, scheduled for an interview to further explain the study, confirm eligibility, and provide informed consent. They then completed the assessment battery (1 hour). Participants collected saliva samples four times a day for 3 days before random assignment (30 minutes after waking and at 12:00 PM, 5:00 PM, and bedtime) using cotton saliva swabs (Sali-Savers; ALPCO Diagnostics, Windham, NH). They recorded the actual time of sampling. After intervention completion, participants again collected 3 days of salivary cortisol samples. Samples were sent to the Kirschbaum Laboratory (Dresden, Germany) for analysis.[26]

Random Assignment and Blinding

Once each cohort (ranging in size from 11 to 39 participants; mean, 27 participants) was assembled and baseline data collected, participants were randomly assigned using the Research Randomizer Web site (http://www.randomizer.org/) 2:2:1 by the biostatistician to one of the MBCR, SET, or control programs. The intervention began within 2 weeks of random assignment. At the time of initial assessment, participants and RAs were blind to condition.

Interventions

MBCR. MBCR has its roots in contemplative spiritual traditions, in which mindfulness, conscious awareness in the present moment in an open and nonjudgmental manner, is actively practiced.[4] The intervention was modeled on the MBSR program developed at the Massachusetts Medical Center,[4] modified by Carlson and Speca[6] as MBCR, and validated in a series of previous studies.[18,27-34] Sessions were led by trained staff that have facilitated previous MBCR trials. The program consisted of 8 weekly group sessions of 90 minutes each plus a 6-hour workshop between weeks 6 and 7 for a total of 18 contact hours. The average study group size was six people across both sites, but participants were integrated into ongoing clinical groups of up to 20 participants with a variety of cancer types.

SET. The SET group was based on a manualized treatment developed by the Psychosocial Treatment Laboratory's Breast Cancer Intervention Program at Stanford University.[5] The goals of the therapy include facilitating mutual support and family support, enhancing openness and emotional expressiveness, integrating a changed self and body image into the view of self, improving coping skills and doctor-patient relationships, and detoxifying feelings around death and dying. The program consisted of 12 weekly group sessions of 90 minutes each. The therapists in the current study were also therapists in other multisite trials and were well trained in SET. The average group size was six people across both study sites, and as with MBSR, participants were integrated into ongoing clinical groups of up to 12 participants.

Control condition. The minimal-treatment control condition was a 1-day (6-hour) didactic stress management seminar (SMS), based on the work of the University of Miami Center for Psycho-Oncology Research.[35] Although this group did not control for contact time, it was meant as an approximation of usual care, without denying patients some form of intervention, minimizing the likelihood of demoralization for those randomly assigned to the control condition and hence maximizing accrual.

Measures

Background measures. Demographics (age, sex, and socioeconomic status), medical history, psychiatric history, current medications, and previous experience with yoga or meditation were assessed.

Disease parameters. Chart reviews were conducted to determine stage of disease and date of diagnosis at the time of study enrollment.

Primary Outcome Measures

Mood. The Profile of Mood States (POMS)[36] yields scores on six dimensions (anxiety, depression, anger, vigor, fatigue, and confusion), which were summed to form a Total Mood Disturbance score, used in the primary analysis. The POMS has been widely used in psychiatric and medical populations, including patients with cancer.[37]

Cortisol. Cortisol was measured in saliva at four time periods (awakening peak, noon, 5:00 PM, and bedtime) over 3 days to account for the large variation of levels throughout the day.[26]

Secondary Outcome Measures

Stress. The short form of the Symptoms of Stress Inventory (SOSI),[38] the Calgary SOSI (C-SOSI),[39] measures physical, psychological, and behavioral responses to stressful situations. The questionnaire consists of 56 items and eight subscales. The total score was used.

Quality of life. The Functional Assessment of Cancer Therapy–Breast (FACT-B)[40] is a self-report questionnaire designed to measure multidimensional quality of life in patients with breast cancer. The FACT-B consists of the

Functional Assessment of Cancer Therapy–General,[41] a general cancer quality-of-life measure, plus the Breast Cancer Subscale with items specific to quality of life in patients with breast cancer.

Social support. Medical Outcomes Study Social Support Survey (MOS-SSS).[42] This 19-item questionnaire covers the following four dimensions of functional social support: tangible support, affectionate support, positive social interaction, and emotional or informational support. The total score was used.

Data Analysis

Assuming an intraclass coefficient (ICC) of 0.05, inflation factor of 1.55, two-tailed α of .05, 80% power, and 10% drop-out rate using a cluster randomized design, our accrual target was 300 participants. Baseline characteristics were summarized using descriptive statistics. Potential baseline differences in demographic and medical variables between the two sites were assessed. Cortisol values were excluded from the analyses if they were either greater or lower than four standard deviations from the mean or the sample collection time deviated more than four standard deviations from the mean collection time. The cortisol data were positively skewed. To correct this, base-10 logarithm transformations were applied. For each participant, a slope of all 12 cortisol log-transformed values was estimated using standard linear regression. A more negative slope value represents steeply declining profiles, whereas a slope value close to zero or a positive value suggests morning peaks accompanying later afternoon elevation of cortisol, unusually timed peaks, or aberrant profiles. Analyses for cortisol included the primary outcome of cortisol slope, as well as cortisol concentrations at each collection time point. Correlations were examined among the cortisol measures and potential confounding variables, including age, cancer severity, time since diagnosis, alcohol and nicotine intake, quality of sleep, and diet.

Intent-to-treat (ITT) and per-protocol analyses (including those who attended half or more of the intervention sessions and completed both pre- and postintervention assessments) were both used for all data analysis. We used mixed-effects methods with a random intercept model, which accounts for the variances both between participants and within participants. For each dependent measure, a 3 (group) $\times$ 2 (time) linear mixed model

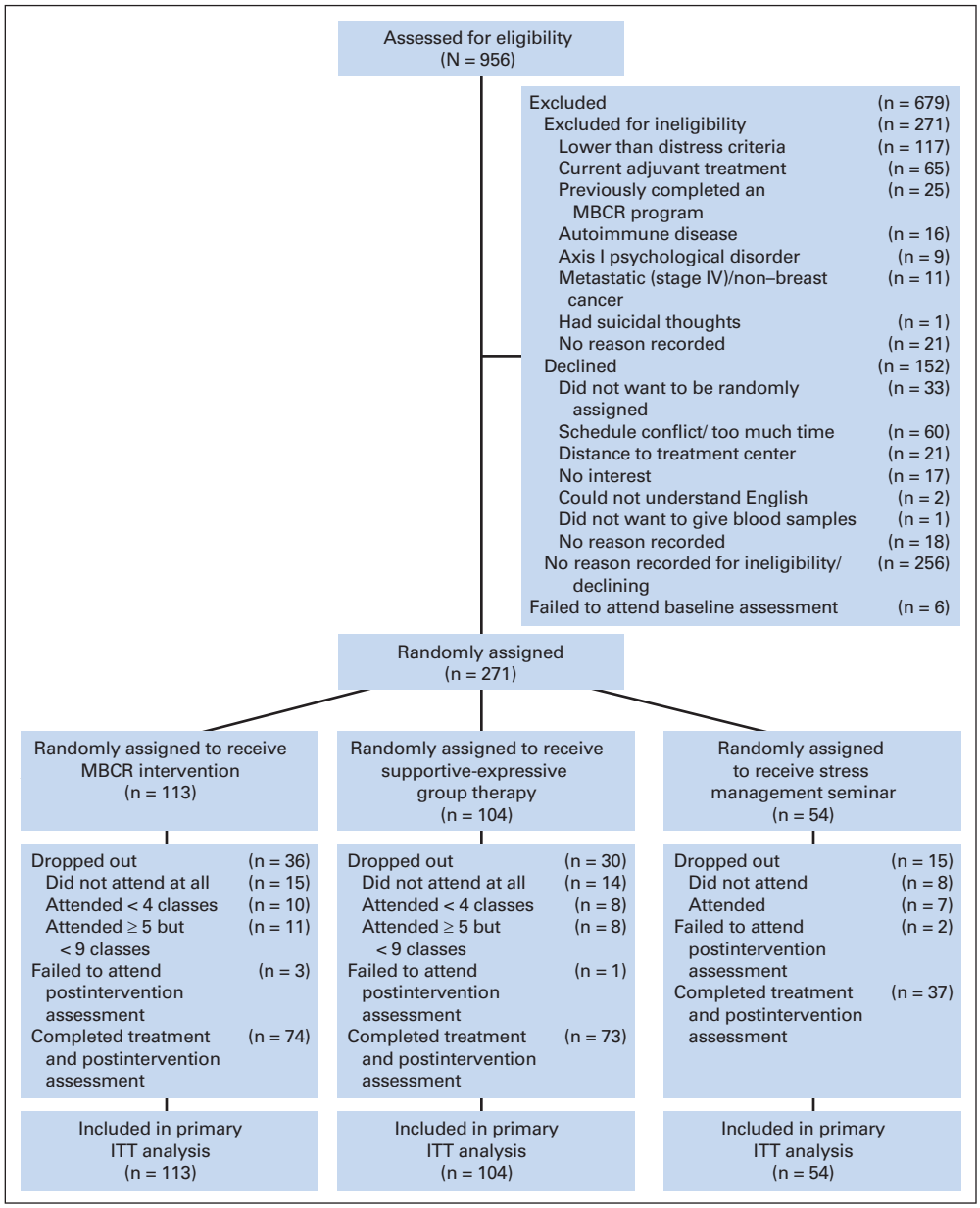

Fig 1. CONSORT flowchart. ITT, intent to treat; MBCR, mindfulness-based cancer recovery.

for repeated measures with maximum likelihood estimation of parameters was conducted followed by pair-wise contrasts for the three groups. Because the multiple tests used increased the likelihood of identifying chance effects, we used a false discovery rate procedure, the Hochberg correction,[43] to restrict the number of false positives for each pair-wise comparison for the primary outcomes (POMS and cortisol slopes) but not for the secondary outcomes. This is a less restrictive approach than family-wise approaches to dealing with multiple tests.[44] ICC and effect sizes (η^2) were calculated for all the outcome measures.

RESULTS

The flow of participants is depicted in Figure 1.

Participants

Two hundred seventy-one women were randomly assigned in eight cohorts in Vancouver and 10 cohorts in Calgary, and groups ran between October 2007 and December 2010. Table 1 lists demographic

Table 1. Baseline Demographic and Clinical Characteristics of Participants Across Conditions

Characteristic	MBCR (n = 113)		SET (n = 104)		SMS (n = 54)	
	No. of Participants	%	No. of Participants	%	No. of Participants	%
Age, years[a]						
Mean	54.66		53.62		56.27	
SD	9.71		10.11		10.89	
Education, years[b]						
Mean	15.37		15.58		14.82	
SD	2.99		2.88		2.75	
Time since diagnosis, months[a]						
Mean	25.56		27.74		22.75	
SD	24.33		35.94		14.67	
Marital status[c]						
Single	18	15.9	17	16.3	6	11.1
Cohabiting/married	67	59.3	64	61.5	33	61.1
Divorced/separated/widowed	24	21.3	15	14.4	13	24.1
Employment[d]						
Unemployed/retired/disabled	41	36.3	42	40.4	24	44.4
Part time	25	22.1	26	25.0	8	14.8
Full time	45	39.8	31	29.8	20	37.0
Cancer stage[e]						
0	4	3.5	1	1.0	2	3.7
I	41	36.3	44	42.3	22	40.7
II	42	37.2	37	35.6	18	33.3
III	12	10.6	14	13.5	10	18.5
IV	1	0.9	2	1.9	0	0
POMS TMD score[f]						
Mean	35.27		40.34		32.61	
SD	32.75		38.44		29.14	
C-SOSI score[g]						
Mean	66.95		73.29		66.10	
SD	28.49		32.92		29.09	
FACT-B score[h]						
Mean	96.40		93.37		97.86	
SD	22.28		24.39		21.43	
MOS-SSS score[i]						
Mean	66.10		68.86		69.03	
SD	22.32		21.45		21.25	
Cortisol slope[j]						
Mean	−0.05		−0.05		−0.06	
SD	0.02		0.02		0.02	

Abbreviations: C-SOSI, Calgary Symptoms of Stress Inventory; FACT-B, Functional Assessment of Cancer Therapy–Breast; MBCR, mindfulness-based cancer recovery; MOS-SSS, Medical Outcomes Study Social Support Survey; POMS TMD, Profile of Mood States Total Mood Disturbance; SD, standard deviation; SET, supportive-expressive therapy; SMS, stress management seminar.

[a]Data missing for five participants.
[b]Data missing for 11 participants.
[c]Data missing for 14 participants.
[d]Data missing for nine participants.
[e]Data missing for 21 participants.
[f]Data missing for nine participants. Higher scores indicate more severe mood disturbance.
[g]Data missing for five participants. High scores indicate more severe stress symptoms.
[h]Data missing for four participants. High scores indicate greater quality of life.
[i]Data missing for eight participants. High scores indicate greater social support.
[j]Data missing for 29 participants. More positive slopes indicate aberrant diurnal cortisol profile. The data are in log-transformed values.

Table 2. Primary Outcomes: Intent-to-Treat Analyses of Mood and Cortisol Slope (log-transformed values) Before and After the Intervention

Outcome	MBCR			SET			SMS			*P*			Effect Size η^{2*}
	No. of Participants	Mean	95% CI	No. of Participants	Mean	95% CI	No. of Participants	Mean	95% CI	Group	Time	Group × Time	
POMS TMD													
Baseline	110	35.15	28.74 to 41.56	100	40.67	33.96 to 47.39	52	33.33	24.04 to 42.62	.053	< .001	.042	0.020
After intervention	69	15.48	8.07 to 22.89	73	31.53	24.15 to 38.91	37	24.77	14.46 to 35.08				
Cortisol slope													
Baseline	87	−.050	−.055 to −.046	87	−.045	−.049 to −.040	44	−.059	−.066 to −.053	.160	.615	.009	0.022
After intervention	60	−.055	−.061 to −.050	63	−.053	−.058 to −.047	32	−.050	−.057 to −.042				

Abbreviations: MBCR, mindfulness-based cancer recovery; POMS TMD, profiles of mood states total mood score; SET, supportive-expressive group therapy; SMS, stress management seminar.
*η^2 is the effect size for the Group by Time interaction. Convention for size interpretation 0.01 (small), 0.06 (medium), 0.14 (large) effects.

and medical characteristics and baseline scores. Data were missing from variable numbers of women across outcomes on questionnaires as a result of noncompletion (Table 1). Missing cortisol values across assessment times were a result of not enough saliva volume (n = 4) or failure to provide saliva samples (n = 25). The groups were well balanced on their demographics and medical characteristics. Despite the inclusion criterion of stage I to III cancers, seven women with stage 0 cancer and three women with stage IV cancer participated; the diagnostic stage was only later verified as outside the criterion by chart review. Given that these women all met the other inclusion criteria, most notably being distressed, we chose to retain them in the analyses. Participants at the two sites were significantly different in the proportions of cancer stage (Vancouver: stage 0, 0%; I, 40.3%; II, 41.7%; III, 16.0%; IV, 2.1%; and Calgary: stage 0, 5.6%; I, 46.8%; II, 34.7%; III, 12.9%; IV, 0%; $P < .001$), marital status (Vancouver: single, 22.4%; married/cohabitating, 47.6%; divorced/widowed, 20.4%; and Calgary: single, 6.9%; married/cohabitating, 73.1%; divorced/widowed, 16.9%; $P < .001$), and total education years (mean, 15.9 years for Vancouver *v* 14.6 years for Calgary; $P < .001$); therefore, site was added as a covariate for all the analyses.

Attrition

There were no significant differences in the proportion of patients who dropped out of the study between the three treatment groups (MBCR, n = 39, 34.5%; SET, n = 31, 29.8%; SMS, n = 17, 31.5%; $P = .755$).

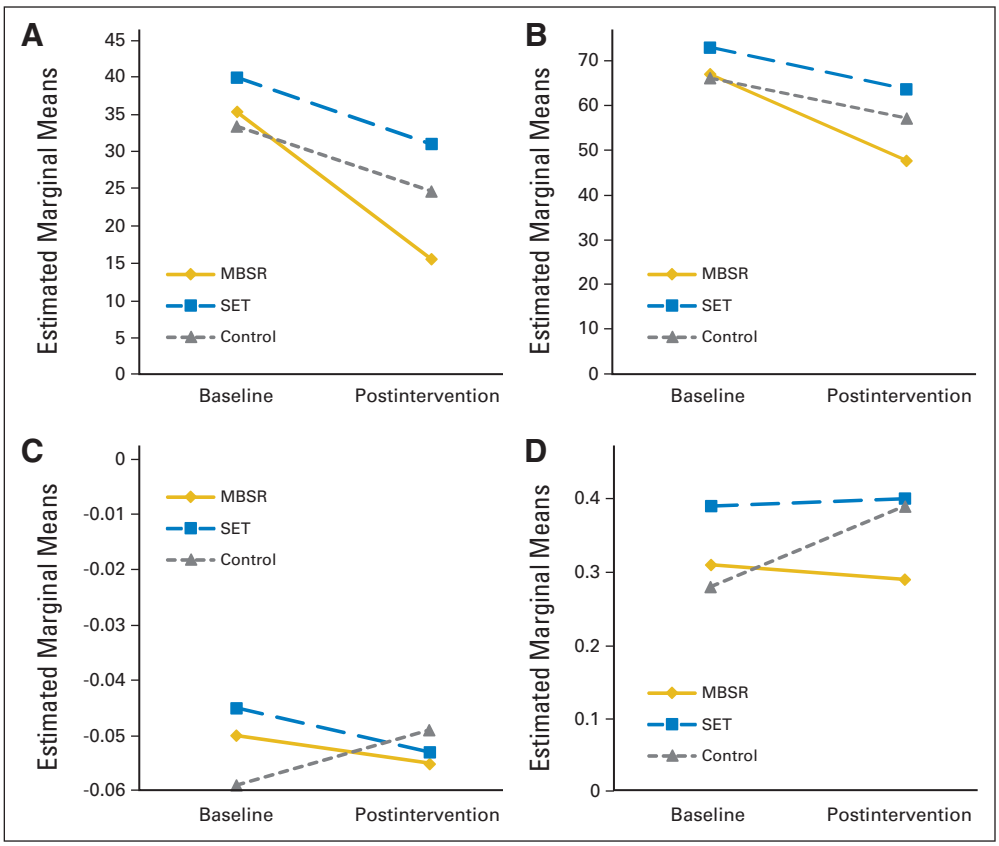

Fig 2. Estimated marginal means (intent to treat) for (A) Profile of Mood States Total Mood Disturbance; (B) Calgary Symptoms of Stress Inventory; (C) Ln diurnal cortisol slopes; and (D) Ln bedtime cortisol. MBSR, mindfulness-based stress reduction; SET, supportive-expressive therapy.

Table 3. Secondary Outcomes: ITT Analyses of Stress Symptoms, Quality of Life, Social Support, and Cortisol Time Points and Per-Protocol Analyses of All Outcomes Before and After the Intervention

Outcome	MBCR			SET			SMS			*P*			Effect size η^{2*}
	No. of Participants	Mean	95% CI	No. of Participants	Mean	95% CI	No. of Participants	Mean	95% CI	Group	Time	Group × Time	
ITT													
C-SOSI													
Baseline	111	66.84	61.12 to 72.55	101	73.24	67.26 to 79.23	54	66.07	57.88 to 74.25	.020	< .001	.015	0.040
After intervention	70	47.57	41.12 to 54.03	73	63.78	57.27 to 70.29	37	57.20	48.16 to 66.24				
FACT-B													
Baseline	111	96.58	92.45 to 100.72	102	93.49	89.18 to 97.80	54	97.91	91.99 to 103.83	.275	< .001	.051	0.031
After intervention	69	107.89	103.19 to 112.60	71	101.67	96.92 to 106.41	37	101.02	94.47 to 107.57				
MOS-SSS													
Baseline	111	66.23	62.17 to 70.29	100	69.14	64.88 to 73.41	52	68.19	62.29 to 74.08	.997	.324	.062	0.026
After intervention	70	70.56	66.06 to 75.06	72	67.94	63.36 to 72.51	37	68.39	62.04 to 74.74				
Wakening cortisol													
Baseline	100	1.09	1.04 to 1.13	92	1.08	1.03 to 1.13	47	1.15	1.08 to 1.22	.374	.656	.134	0.008
After intervention	70	1.08	1.03 to 1.14	69	1.14	1.09 to 1.20	34	1.12	1.04 to 1.20				
Noon cortisol													
Baseline	101	0.72	0.68 to 0.76	93	0.79	0.74 to 0.83	48	0.77	0.71 to 0.83	.205	.171	.638	−0.008
After intervention	66	0.71	0.66 to 0.76	69	0.74	0.69 to 0.79	35	0.75	0.68 to 0.82				
5:00 PM cortisol													
Baseline	100	0.50	0.45 to 0.55	93	0.55	0.50 to 0.61	48	0.51	0.44 to 0.59	.193	.014	.617	−0.004
After intervention	71	0.53	0.47 to 0.59	68	0.60	0.54 to 0.66	34	0.59	0.51 to 0.67				
Bedtime cortisol													
Baseline	100	0.31	0.26 to 0.37	91	0.40	0.34 to 0.45	46	0.28	0.20 to 0.36	.019	.187	.141	0.004
After intervention	69	0.30	0.23 to 0.36	68	0.41	0.34 to 0.47	33	0.38	0.29 to .047				
Per protocol													
POMS TMD													
Baseline	73	33.74	25.86 to 41.62	72	38.10	30.20 to 46.01	36	34.18	23.01 to 45.35	.166	<.001	.052	0.020
After intervention	69	14.56	6.56 to 22.57	73	29.83	22.00 to 37.70	37	25.15	14.07 to 36.23				
C-SOSI													
Baseline	73	67.42	60.36 to 74.47	73	70.40	63.35 to 77.45	37	63.00	53.06 to 72.90	.178	<.001	.009	0.043
After intervention	70	48.00	40.88 to 55.13	73	61.72	54.67 to 68.77	37	54.84	44.92 to 64.76				
FACT-B													
Baseline	73	96.08	91.00 to 101.15	73	95.88	90.81 to 100.95	37	102.66	95.52 to 109.79	.607	<.001	.020	0.032
After intervention	69	107.55	102.41 to 112.70	71	103.41	98.30 to 108.51	37	104.53	97.40 to 111.67				
MOS-SSS													
Baseline	73	65.10	60.17 to 70.03	72	70.67	65.73 to 75.61	36	66.60	59.62 to 73.57	.673	.284	.041	0.026
After intervention	70	69.69	64.72 to 74.66	72	69.14	64.20 to 74.08	37	67.19	60.26 to 74.13				
Cortisol slope													
Baseline	61	−.052	−.057 to −.046	66	−.044	−.049 to −.039	32	−.054	−.061 to −.046	.196	.327	.070	0.020
After intervention	60	−.055	−.061 to −.050	63	−.052	−.058 to −.047	32	−.049	−.056 to −.041				
Wakening cortisol													
Baseline	70	1.09	1.04 to 1.15	71	1.06	1.00 to 1.11	34	1.10	1.02 to 1.18	.964	.267	.125	0.007
After intervention	70	1.09	1.03 to 1.14	69	1.13	1.08 to 1.19	34	1.10	1.02 to 1.18				
Noon cortisol													
Baseline	71	0.73	0.68 to 0.78	72	0.77	0.72 to 0.82	35	0.73	0.66 to 0.80	.701	.409	.772	−0.008
After intervention	66	0.72	0.67 to 0.77	69	0.74	0.69 to 0.79	35	0.73	0.66 to 0.80				
5:00 PM cortisol													
Baseline	70	0.52	0.46 to 0.58	71	0.52	0.47 to 0.88	35	0.49	0.41 to 0.58	.814	.007	.436	−0.002
After intervention	71	0.54	0.48 to 0.60	68	0.58	0.52 to 0.64	34	0.58	0.50 to 0.67				
Bedtime cortisol													
Baseline	71	0.31	0.25 to 0.37	70	0.37	0.31 to 0.43	33	0.30	0.21 to 0.39	.102	.172	.260	0.005
After intervention	69	0.29	0.23 to 0.36	68	0.39	0.33 to 0.46	33	0.39	0.30 to .048				

Abbreviations: C-SOSI, Calgary symptoms of stress inventory; FACT-B, functional assessment of cancer therapy-breast; ITT, intention to treat; MBCR, mindfulness-based cancer recovery; MOS-SSS, medical outcomes study social support survey; POMS TMD, profiles of mood states total mood score; SET, supportive-expressive group therapy; SMS, stress management seminar.

*η^2 is the effect size for the Group by Time interaction. Convention for size interpretation 0.01 (small), 0.06 (medium), 0.14 (large) effects.

ICC Calculation

We used random intercepts to model an error structure that accounted for overall differences among participants, as well as variability among the blocks to which participants were randomly assigned. The ICCs for treatment blocks were small, ranging from 0 to 0.078.

Primary Outcomes: Mood and Cortisol Slopes

Table 2 lists the ITT analyses of scores of mood and cortisol slopes before and after the intervention. Linear mixed-effects modeling showed a significant group × time interaction for the POMS Total Mood Disturbance score ($P = .042$; Table 2; Fig 2A). However,

corrected follow-up pair-wise comparisons indicated no significant differences between MBCR and SET ($P = .024$) and SMS ($P = .051$).

Primary analyses of cortisol slopes included cancer severity, nicotine intake (per day), and quality of sleep as covariates because these were significantly correlated with baseline cortisol slopes. Baseline slopes were available from 242 patients. Of the 242 patients, 172 also had data for postintervention cortisol slopes. ITT analyses showed a significant group × time interaction ($P = .009$; Table 2; Fig 2C). Diurnal cortisol slopes were significantly more negative after SET (mean change, −0.008; $P = .003$) and MBCR (mean change, −0.005; $P = .014$) compared with SMS (mean change, 0.10). Within-group analyses showed a significant increase in the cortisol slope from baseline to postintervention in SMS ($P = .014$). No significant changes were found within SET ($P = .058$) or MBCR ($P = .124$). There were no significant group × time interaction effects for cortisol concentrations at any single collection point, but a time × group contrast between MBCR and SMS was significant for bedtime cortisol concentrations ($P = .044$; Table 3), which were elevated after SMS (mean change, 0.11) but slightly decreased after MBCR (mean change, −0.02; Fig 2D).

Secondary Outcomes: Stress Symptoms, Quality of Life, and Social Support

ITT analyses (Table 2) showed a significant group × time interaction on the C-SOSI ($P = .015$; Fig 2B), such that there was a greater reduction in stress symptoms after MBCR (mean change, −19.3) compared with both SET (mean change, −9.46; $P = .009$) and SMS (mean change, −8.87; $P = .023$; Fig 2B), with a small to medium effect size. There were no significant group × time interaction effects for the FACT-B ($P = .065$) or MOS-SSS ($P = .063$).

Per-Protocol Analyses

Per-protocol analyses (Table 3) showed a significant group × time interaction for C-SOSI ($P = .009$), FACT-B ($P = .020$), and MOS-SSS ($P = .040$). Follow-up pair-wise comparisons indicated greater reduction of stress symptoms after MBCR (mean change, −19.4) compared with both SET (mean change, −8.68; $P = .006$) and SMS (mean change, −8.14; $P = .016$) and greater improvement in quality of life after MBCR compared with SMS (mean change, 11.35 *v* 3.62, respectively; $P = .005$). There was also greater improvement in overall social support after MBCR compared with SET (mean change, 4.33 *v* −1.19, respectively; $P = .012$).

DISCUSSION

This study is the first to directly compare an MBSR-based intervention (MBCR) with SET, two active, empirically supported psychosocial treatments for distressed survivors of breast cancer. As predicted, MBCR emerged as superior for decreasing symptoms of stress and also for improving overall quality of life and social support in these women, even though we hypothesized that SET might be superior on social support. Improvements were small to medium in size and generally smaller than those reported in our previous work with mixed groups of patients with cancer, perhaps due to the direct comparison with another active intervention. The clinical importance of these small differential improvements is uncertain and will require further evaluation.[27,28]

Cortisol profiles were significantly altered after program completion. Participants in both MBCR and SET maintained the initial steepness of cortisol slopes, whereas SMS participants evidenced increasingly flatter diurnal cortisol slopes, with a small between-group effect size. Hence, the two interventions buffered unfavorable biologic changes that may occur without active psychosocial intervention. Because abnormal or flattened cortisol profiles have been related to both poorer psychological functioning and shorter survival time in breast,[16,17,45,46] lung,[47] and renal cell[48] carcinoma, this finding may point to the potential for these psychosocial interventions to improve biologic processes related to both patient-reported outcomes and more objective indices. More work is needed to fully understand the clinical meaning of these parameters in primary breast cancer.

The value of mindfulness-based interventions for survivors of cancer is potentially multifaceted. The emphasis is not on changing the situation; rather, skills taught through mindfulness practice help participants change their way of relating to given life situations. MBCR helps facilitate development of positive emotional regulation strategies such as acceptance and gently extinguishes unhelpful strategies including worry, rumination, and experiential avoidance.[49,50] As participants allow graduated exposure to feared thoughts and feelings during meditation practice, cultivated in an accepting and nonjudgmental environment, feared stimuli lose much of their power. The result is often a sense of heightened control, calm, peace, and serenity, even in the face of the many uncontrollable elements of cancer.[31]

This study has several strengths, including the large sample size and the inclusion of women who were suffering from significant distress at baseline. Some limitations are the inclusion of only patients with breast cancer, which does not allow generalization to other types of cancers; the relatively high drop-out rates; lack of numerical ratings of treatment fidelity; and lack of long-term follow-up across groups. Although multiple tests were performed without correction for the secondary outcomes, these were exploratory in nature. Once corrected for multiple comparisons, the primary analysis of the POMS may have been slightly underpowered, because despite small effect sizes favoring MBCR, group differences were not statistically significant and the sample size was somewhat lower than our target. In sum, this study confirmed the benefits of MBCR for distressed survivors of breast cancer on measures of stress, quality of life, and social support, and the value of both MBCR and SET for maintaining healthy cortisol slopes in these women. Given this continually growing evidence of efficacy, cancer treatment centers should consider providing such interventions to needy patients as a routine part of comprehensive clinical care.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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

AUTHOR CONTRIBUTIONS

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