VOLUME 31 · NUMBER 25 · SEPTEMBER 1 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

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

Linda E. Carlson, Richard Doll, Joanne Stephen, Peter Faris, Rie Tamagawa, Elaine Drysdale, and Michael Speca

Linda E. Carlson, Rie Tamagawa, and Michael Speca, University of Calgary; Peter Faris, Alberta Health Services, Calgary, Alberta; Richard Doll, Joanne Stephen, and Elaine Drysdale, BC Cancer Agency; Elaine Drysdale, University of British Columbia, Vancouver, British Columbia, Canada.

Published online ahead of print at www.jco.org on August 5, 2013.

Supported by a grant from the Canadian Breast Cancer Research Alliance. 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.

The sponsors played no role in study design, execution, analysis, interpretation, or article preparation.

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

Clinical trial information: NCT00390169.

Corresponding author: Linda E. Carlson, PhD, Department of Psychosocial Resources, Holy Cross Site, 2202 2nd St SW, Calgary, Alberta, Canada T2S 3C1; e-mail: l.carlson@ucalgary.ca.

© 2013 by American Society of Clinical Oncology

0732-183X/13/3125w-3119w/$20.00

DOI: 10.1200/JCO.2012.47.5210

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.

J Clin Oncol 31:3119-3126. © 2013 by American Society of Clinical Oncology

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

Information downloaded from jco.ascopubs.org and provided by at MEMORIAL SLOAN KETTERING on February 24, 2016
Copyright © 2013 American Society of Clinical Oncology. All rights reserved.

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

Information downloaded from jco.ascopubs.org and provided by at MEMORIAL SLOAN KETTERING on February 24, 2016
Copyright © 2013 American Society of Clinical Oncology. All rights reserved.

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

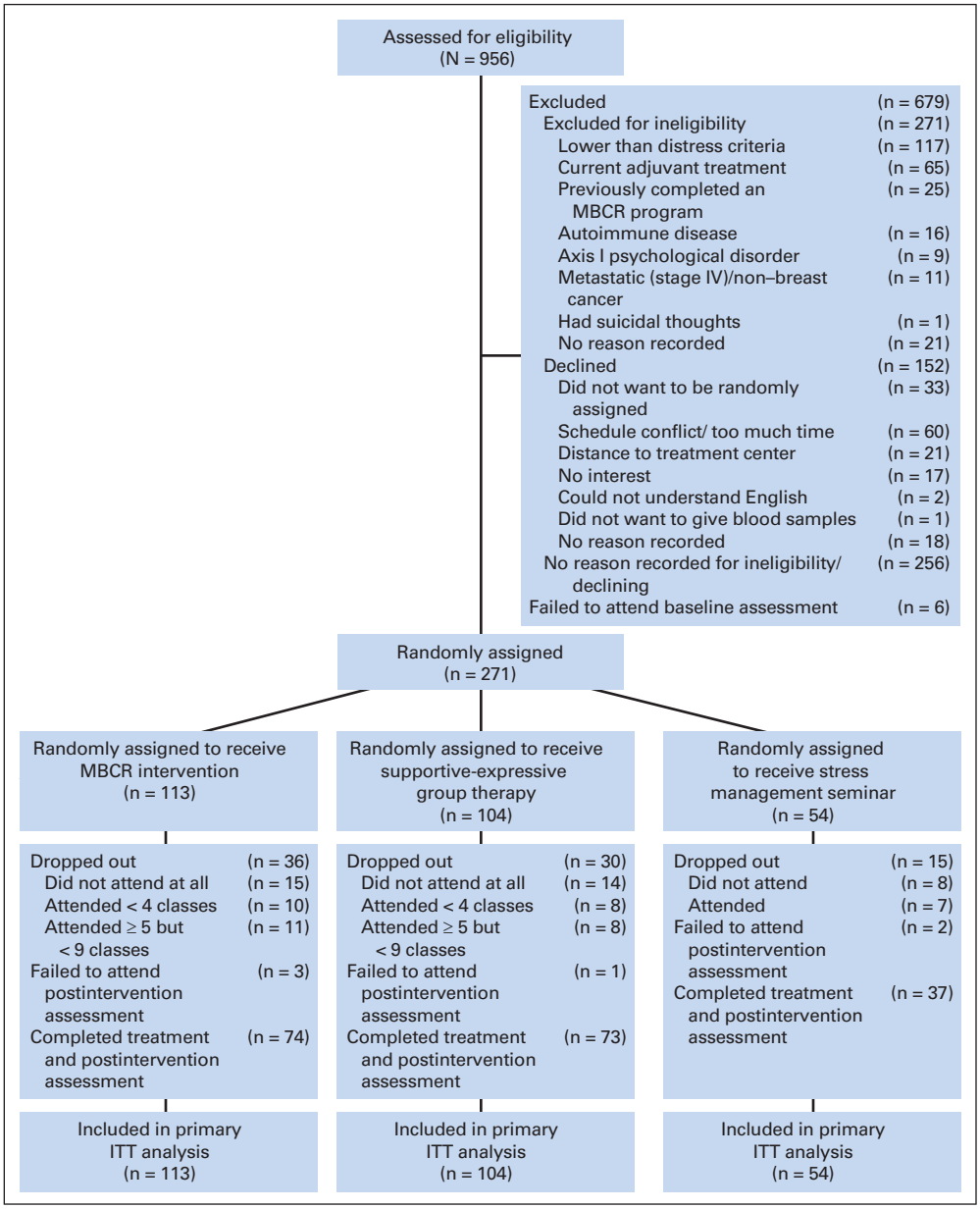

Fig 1. CONSORT flowchart. ITT, intent to treat; MBCR, mindfulness-based cancer recovery.

© 2013 by American Society of Clinical Oncology

Information downloaded from jco.ascopubs.org and provided by at MEMORIAL SLOAN KETTERING on February 24, 2016
Copyright © 2013 American Society of Clinical Oncology. All rights reserved.

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.

 © 2013 by American Society of Clinical Oncology

Information downloaded from jco.ascopubs.org and provided by at MEMORIAL SLOAN KETTERING on February 24, 2016
Copyright © 2013 American Society of Clinical Oncology. All rights reserved.

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%; $P = .755$).

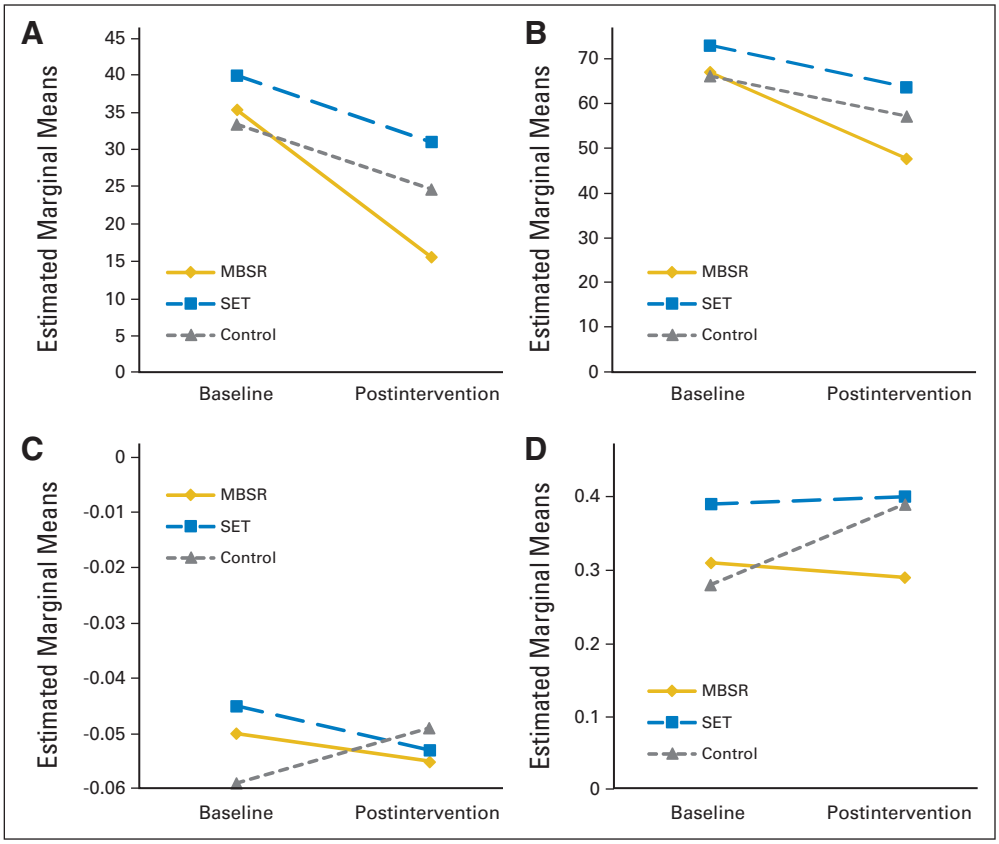

Fig 2. Estimated marginal means (intent to treat) for (A) Profile of Mood States Total Mood Disturbance; (B) Calgary Symptoms of Stress Inventory; (C) Ln diurnal cortisol slopes; and (D) Ln bedtime cortisol. MBSR, mindfulness-based stress reduction; SET, supportive-expressive therapy.

© 2013 by American Society of Clinical Oncology

Information downloaded from jco.ascopubs.org and provided by at MEMORIAL SLOAN KETTERING on February 24, 2016
Copyright © 2013 American Society of Clinical Oncology. All rights reserved.

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,

 © 2013 by American Society of Clinical Oncology

Information downloaded from jco.ascopubs.org and provided by at MEMORIAL SLOAN KETTERING on February 24, 2016
Copyright © 2013 American Society of Clinical Oncology. All rights reserved.

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

Conception and design: Linda E. Carlson, Richard Doll, Joanne Stephen, Peter Faris, Elaine Drysdale, Michael Speca
Collection and assembly of data: Linda E. Carlson, Richard Doll, Joanne Stephen, Rie Tamagawa, Elaine Drysdale
Data analysis and interpretation: Linda E. Carlson, Peter Faris, Rie Tamagawa
Manuscript writing: All authors
Final approval of manuscript: All authors

© 2013 by American Society of Clinical Oncology

Information downloaded from jco.ascopubs.org and provided by at MEMORIAL SLOAN KETTERING on February 24, 2016
Copyright © 2013 American Society of Clinical Oncology. All rights reserved.

REFERENCES

1. Ellison LF, Wilkins K: Canadian trends in cancer prevalence. Health Rep 23:7-16, 2012
2. Ganz PA: Survivorship: Adult cancer survivors. Prim Care 36:721-741, 2009
3. Mitchell AJ, Chan M, Bhatti H, et al: Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: A meta-analysis of 94 interview-based studies. Lancet Oncol 12:160-174, 2011
4. Kabat-Zinn J: Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain and Illness. New York, NY, Delacourt, 1990
5. Classen C, Diamond S, Soleman A, et al: Brief Supportive-Expressive Group Therapy for Women With Primary Breast Cancer: A Treatment Manual. Stanford, CA, Stanford University School of Medicine, 1993
6. Carlson LE, Speca M: Mindfulness-Based Cancer Recovery: A Step-by-Step MBSR Approach to Help You Cope With Treatment and Reclaim Your Life. Oakville, CA, New Harbinger, 2010
7. Carlson LE, Labelle LE, Garland SN, et al: Mindfulness-based interventions in oncology, in Didonna F (ed): Clinical Handbook of Mindfulness. New York, NY, Springer, 2009, pp 383-404
8. Ledesma D, Kumano H: Mindfulness-based stress reduction and cancer: A meta-analysis. Psychooncology 18:571-579, 2009
9. Matchim Y, Armer JM, Stewart BR: Mindfulness-based stress reduction among breast cancer survivors: A literature review and discussion. Oncol Nurs Forum 38:E61–E71, 2011
10. Musial F, Büssing A, Heusser P, et al: Mindfulness-based stress reduction for integrative cancer care: A summary of evidence. Forsch Komplementmed 18:192-202, 2011
11. Butler LD, Koopman C, Neri E, et al: Effects of supportive-expressive group therapy on pain in women with metastatic breast cancer. Health Psychol 28:579-587, 2009
12. Classen CC, Kraemer HC, Blasey C, et al: Supportive-expressive group therapy for primary breast cancer patients: A randomized prospective multicenter trial. Psychooncology 17:438-447, 2008
13. Grassi L, Sabato S, Rossi E, et al: Effects of supportive-expressive group therapy in breast cancer patients with affective disorders: A pilot study. Psychother Psychosom 79:39-47, 2010
14. Kissane DW, Grabsch B, Clarke DM, et al: Supportive-expressive group therapy for women with metastatic breast cancer: Survival and psychosocial outcome from a randomized controlled trial. Psychooncology 16:277-286, 2007
15. Sephton S, Spiegel D: Circadian disruption in cancer: A neuroendocrine-immune pathway from stress to disease? Brain Behav Immun 17:321-328, 2003
16. Sephton SE, Sapolsky RM, Kraemer HC, et al: Diurnal cortisol rhythm as a predictor of breast cancer survival. J Natl Cancer Inst 92:994-1000, 2000
17. Abercrombie HC, Giese-Davis J, Sephton S, et al: Flattened cortisol rhythms in metastatic breast cancer patients. Psychoneuroendocrinology 29: 1082-1092, 2004
18. Carlson LE, Speca M, Patel KD, et al: Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients. Psychoneuroendocrinology 29:448-474, 2004
19. Lengacher CA, Kip KE, Barta M, et al: A pilot study evaluating the effect of mindfulness-based stress reduction on psychological status, physical status, salivary cortisol, and interleukin-6 among advanced-stage cancer patients and their caregivers. J Holist Nurs 30:170-185, 2012
20. Brand S, Holsboer-Trachsler E, Naranjo JR, et al: Influence of mindfulness practice on cortisol and sleep in long-term and short-term meditators. Neuropsychobiology 65:109-118, 2012
21. Matousek RH, Pruessner JC, Dobkin PL: Changes in the cortisol awakening response (CAR) following participation in mindfulness-based stress reduction in women who completed treatment for breast cancer. Complement Ther Clin Pract 17:65-70, 2011
22. Witek-Janusek L, Albuquerque K, Chroniak KR, et al: Effect of mindfulness based stress reduction on immune function, quality of life and coping in women newly diagnosed with early stage breast cancer. Brain Behav Immun 22:969-981, 2008
23. Giese-Davis J, DiMiceli S, Sephton S, et al: Emotional expression and diurnal cortisol slope in women with metastatic breast cancer in supportive-expressive group therapy: A preliminary study. Biol Psychol 73:190-198, 2006
24. National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology: NCCN Practice Guidelines for the Management of Psychosocial Distress. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp
25. Mitchell AJ: Short screening tools for cancer-related distress: A review and diagnostic validity meta-analysis. J Natl Compr Canc Netw 8:487-494, 2010
26. Kirschbaum C, Hellhammer DH: Salivary cortisol in psychoneuroendocrine research: Recent developments and applications. Psychoneuroendocrinology 19: 313-333, 1994
27. Speca M, Carlson LE, Goodey E, et al: A randomized, wait-list controlled clinical trial: The effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. Psychosom Med 62: 613-622, 2000
28. Carlson LE, Ursuliak Z, Goodey E, et al The effects of a mindfulness meditation based stress reduction program on mood and symptoms of stress in cancer outpatients: Six month follow-up. Support Care Cancer 9:112-123, 2001
29. Carlson LE, Speca M, Patel KD, et al: Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress, and immune parameters in breast and prostate cancer outpatients. Psychosom Med 65:571-581, 2003
30. Carlson LE, Garland SN: Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients. Int J Behav Med 12:278-285, 2005
31. Mackenzie MJ, Carlson LE, Munoz M, et al: A qualitative study of self-perceived effects of mindfulness-based stress reduction (MBSR) in a psychosocial oncology setting. Stress Health 23:59-69, 2007
32. Carlson LE, Brown KW: Validation of the Mindful Attention Awareness Scale in a cancer population. J Psychosom Res 58:29-33, 2005
33. Birnie K, Garland SN, Carlson LE: Psychological benefits for cancer patients and their partners participating in mindfulness-based stress reduction (MBSR). Psychooncology 19:1004-1009, 2010
34. Carlson LE, Speca M, Faris P, et al: One year pre-post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. Brain Behav Immun 21:1038-1049, 2007
35. Antoni MH, Lechner S, Diaz A, et al: Cognitive behavioral stress management effects on psychosocial and physiological adaptation in women undergoing treatment for breast cancer. Brain Behav Immun 23:580-591, 2009
36. McNair DA, Lorr M, Droppelman LF: Profile of Mood States. San Diego, CA, Educational and Industrial Testing Service, 1971
37. Cassileth BR, Lusk EJ, Brown LL, et al: Psychosocial status of cancer patients and next of kin: Normative data from the profile of mood states. J Psychosoc Oncol 3:99-105, 1985
38. Leckie MS, Thompson E: Symptoms of Stress Inventory. Seattle, WA, University of Washington, 1979
39. Carlson LE, Thomas BC: Development of the Calgary Symptoms of Stress Inventory (C-SOSI). Int J Behav Med 14:249-256, 2007
40. Brady MJ, Cella DF, Mo F, et al: Reliability and validity of the Functional Assessment of Cancer Therapy-Breast (FACT-B) quality-of-life instrument. J Clin Oncol 15:974-986, 1997
41. Cella DF: Manual of the Functional Assessment of Cancer Therapy (FACT) Scales. Chicago, IL, Rush Presbyterian-St. Luke's Medical Center, 1996
42. Sherbourne CD, Stewart AL: The MOS social support survey. Soc Sci Med 32:705-714, 1991
43. Benjamini Y, Hochberg Y: Controlling the false discovery rate: A practical and powerful approach to multiple testing. J R Stat Soc B 57:289-300, 1995
44. Perneger TV: What's wrong with Bonferroni adjustments. BMJ 316:1236-1238, 1998
45. Mormon MC, Bogdan A, Cormont S, et al: Cortisol diurnal variation in blood and saliva of patients with metastatic colorectal cancer: Relevance for clinical outcome. Anticancer Res 22:1243-1249, 2002
46. Lutgendorf SK, Weinrib AZ, Penedo F, et al: Interleukin-6, cortisol, and depressive symptoms in ovarian cancer patients. J Clin Oncol 26:4820-4827, 2008
47. Sephton SE, Lush E, Dedert EA, et al: Diurnal cortisol rhythm as a predictor of lung cancer survival. Brain Behav Immun 30:S163-S170, 2013 (suppl)
48. Cohen L, Cole SW, Sood AK, et al: Depressive symptoms and cortisol rhythmicity predict survival in patients with renal cell carcinoma: Role of inflammatory signaling. PLoS One 7:e42324, 2012
49. Labelle LE, Campbell TS, Carlson LE: Mindfulness-based stress reduction in oncology: Evaluating mindfulness and rumination as mediators of change in depressive symptoms. Mindfulness 1:28-40, 2010
50. Labelle LE: How does mindfulness-based stress reduction (MBSR) improve psychological functioning in cancer patients? [doctoral thesis] University of Calgary, Calgary, Alberta, Canada, 2012

 © 2013 by American Society of Clinical Oncology

Information downloaded from jco.ascopubs.org and provided by at MEMORIAL SLOAN KETTERING on February 24, 2016
Copyright © 2013 American Society of Clinical Oncology. All rights reserved.

Acknowledgment

We thank all of the research staff who worked on this project, including Beth DeBruyn, Barbara Pickering, Linnette Lawlor-Savage, Kimberley Burris, Heather Bowden, and Dale Dirkse. We also thank the program facilitators—Shirley MacMillan, Lisa Lamont, Sarah Sample, Andrea Grabovac, and Heather Rennie. Finally, none of this work would be possible without the open-hearted participation of the survivors of breast cancer.

© 2013 by American Society of Clinical Oncology

Information downloaded from jco.ascopubs.org and provided by at MEMORIAL SLOAN KETTERING on February 24, 2016
Copyright © 2013 American Society of Clinical Oncology. All rights reserved.

ERRATA

The November 20, 2007, article by Burger et al, entitled "Phase II Trial of Bevacizumab in Persistent or Recurrent Epithelial Ovarian Cancer or Primary Peritoneal Cancer: A Gynecologic Oncology Group Study" (J Clin Oncol 32:5165-5171, 2007), contained an error.

In the Results section of the Abstract, the first sentence gave the number of patients considered platinum resistant as 26 (41.9%), whereas it should have been 36 (58.1%) as follows:

"The study consisted of 62 eligible and assessable patients, median age 57 years, 41 (66.1%) having received two prior regimens and **36 (58.1%)** considered platinum resistant."

The online version has been corrected in departure from the print. The authors apologize for the error.

DOI: 10.1200/JCO.2014.59.6320; published November 10, 2014

The September 1, 2013, article by Carlson et al, entitled "Randomized Controlled Trial of Mindfulness-Based Cancer Recovery Versus Supportive Expressive Group Therapy for Distressed Survivors of Breast Cancer (MINDSET)" (J Clin Oncol 31:3119-3126, 2013), contained errors. After further analysis of the dataset, the authors identified discrepancies in statistical values for effect sizes and confidence intervals.

In the Abstract, the first sentence of the Conclusion was given as:

"In the largest trial to date, MBCR was superior for improving a range of psychological outcomes for distressed survivors of breast cancer."

whereas it should have been:

"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."

In the Results section, under "Primary Outcomes: Mood and Cortisol Slopes," the second sentence of the first paragraph gave the *P* value for group × time interaction as .037, whereas it should have been .042 as follows:

"Linear mixed-effects modeling showed a significant group × time interaction for the POMS Total Mood Disturbance score ($P = .042$; Table 2; Fig 2A)."

Also, the third sentence of the first paragraph gave the *P* values for SET as .020 and for SMS as .050, whereas they should have been .024 and .051, respectively, as follows:

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

Also in the same section, the third sentence of the last paragraph gave the *P* value for the group × time interaction as .007, whereas it should have been .009 as follows:

"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)."

Also, the fourth sentence of the last paragraph gave the *P* values for SET as .002 and for MCBR as .011, whereas they should have been .003 and .014, respectively, as follows:

"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)."

Also in the Results section, under "Secondary Outcomes: Stress Symptoms, Quality of Life, and Social Support," the first sentence gave the mean change for SET as −9.39, whereas it should have been −9.46; the mean change for SMS as −8.96, whereas it should have been −8.87; the *P* value for SMS as .024 whereas it should have been .023; and the effect size as large whereas it should have been small to medium, as follows:

"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."

In the Discussion section, the last sentence of the first paragraph was given as:

"Improvements were clinically meaningful and similar to those reported in our previous work with mixed groups of patients with cancer."

whereas it should have been:

"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**."

Also in the Discussion section, the second sentence of the second paragraph gave the between-group effect size as medium, whereas it should have been small, as follows:

"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."

Also in the Discussion section, the second- and third-to-last sentences of the last paragraph were given as:

 © 2014 by American Society of Clinical Oncology

"Once corrected for multiple comparisons, the primary analysis of the POMS may have been slightly underpowered, because despite large and clinically meaningful 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 a wide range of relevant psychosocial and biologic outcome measures,"

whereas they should have been:

"Once corrected for multiple comparisons, the primary analysis of the POMS may have been slightly underpowered, because despite **small effect sizes**, 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**."

In addition, effect sizes and confidence intervals in Tables 2 and 3 were recalculated; some *P* values (group, time and/or group × time), mean, and N values were also amended. Revised tables 2 and 3 are available in the online version of the article.

Finally, the authors provided a Statistical Report which has been uploaded as a Data Supplement.

The online version has been corrected in departure from the print. The authors apologize for the mistakes.

DOI: 10.1200/JCO.2014.59.6338; published November 10, 2014

The May 10, 2014, article by Russell et al, entitled "IGH@ Translocations Are Prevalent in Teenagers and Young Adults With Acute Lymphoblastic Leukemia and Are Associated With a Poor Outcome" (J Clin Oncol 32:1453-1462, 2014), contained errors. In Tables 1 and A9, the row labels for given for high and low minimal residual disease (MRD) risk were reversed.

The online version has been corrected in departure from the print. The authors apologize for the errors.

DOI: 10.1200/JCO.2014.59.6346; published November 10, 2014

© 2014 by American Society of Clinical Oncology