Research

jhn

Journal of Holistic Nursing
American Holistic Nurses Association
Volume 30 Number 3
September 2012 170-185

10.1177/0898010111435949
http://jhn.sagepub.com

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

Cecile A. Lengacher, PhD, RN, FAAN
Kevin E. Kip, PhD
Michelle Barta, BS, MPH
University of South Florida, College of Nursing, Tampa
Janice Post-White, PhD, RN, FAAN
University of Minnesota, School of Nursing, Minneapolis
Paul B. Jacobsen, PhD
H. Lee Moffitt Cancer Center and Research Institute, Tampa
Maureen Groer, PhD, RN, FAAN
Brandy Lehman, PhD, RN
Manolete S. Moscoso, PhD, PA
Rajendra Kadel, MS
Nancy Le, BS
University of South Florida, College of Nursing, Tampa
Loretta Loftus, MD, MBA
Craig A. Stevens, MD, PhD
Mokenge P. Malafa, MD, FACS
H. Lee Moffitt Cancer Center and Research Institute, Tampa
Melissa Molinari Shelton, PhD, RN
University of South Florida, College of Nursing, Tampa

Purpose: To investigate whether a mindfulness-based stress reduction program for cancer (MBSR-C) improved psychological and physical symptoms, quality of life (QOL), and stress markers among advanced-stage cancer patients and caregivers. **Design:** A pilot within-subject design was used. **Method:** Patients previously diagnosed with advanced-stage breast, colon, lung, or prostate cancer and on treatment were recruited from the Moffitt Cancer Center and Research Institute. Twenty-six patient–caregiver dyads completed a modified 6-week, self-study MBSR-C program based on the Kabat–Zinn model. Psychological and physical symptoms and QOL were compared pre– and post–MBSR-C sessions. Salivary cortisol and interleukin-6 were assessed pre– and post–MBSR-C session at 1, 3, and 6 weeks. **Findings:** Following the 6-week MBSR program, patients showed improvements in stress and anxiety ($p < .05$); caregivers' psychological and QOL also improved but were not statistically significant. Both patients and caregivers had decreases in cortisol at Weeks 1 and 3 ($p < .05$) but not at Week 6. Similar to cortisol levels at Week 6, salivary interleukin-6 levels were lower overall (before/after an

MBSR-C session), compared with Week 1 for patients and caregivers. **Conclusions:** MBSR-C may be a beneficial intervention for reducing stress, anxiety, cortisol levels, and symptoms in advanced-stage cancer patients and may also benefit caregivers.

Keywords: *MBSR; advanced-stage cancer patients; caregivers; cortisol; IL-6*

Background and Literature Review

Lung, prostate, breast, and colon cancers have the highest incidence and estimated mortality rates nationally and in Florida. Progress in the treatment of advanced-stage cancer has simultaneously increased life expectancy and extended length of time in the home care setting, thus increasing caregiver burden (Schulz & Beach, 1999). It is estimated that approximately 28.5% (65.7 million) of the U.S. population are in an unpaid caregiving role to either a friend or a relative, with 8% of caregiver recipients having cancer (National Alliance for Caregiving & American Association of Retired Persons, 2009).

Advanced-stage cancer survivors experience multiple symptoms and progressive decline in quality of life (QOL). Patients with advanced-stage cancer report lack of energy, drowsiness, and pain as the most frequently occurring and distressing symptoms (Lobchuk & Degner, 2002). Decreased quality of sleep in Stage IV cancer has been associated with pain and decreased QOL (Mystakidou, Parpa, et al., 2007), and emotional, physical, social, and role functioning are predictors of depression and anxiety (Mystakidou et al., 2005; Shapiro et al., 2001).

Caregiving requires time, effort, and changes in roles and responsibilities. In one study, 76% of cancer caregivers reported caregiver distress, with more than 25% seeking treatment for either depression or anxiety (Golant & Haskins, 2008). Caregivers also report chronic sleep disturbances, which affect their emotions and their ability to function adequately in their caregiving role (Carter, 2006). Caregiver depression has been correlated with patient depression (Mystakidou, Tsilika, Parpa, Galanos, & Vlahos, 2007) and a greater perceived level of burden (Adejumo, 2009). Caregivers of patients undergoing pain experience more tension, depression, and mood disturbance than caregivers of painfree cancer patients (Miaskowski, Kragness, Dibble, & Wallhagen, 1997).

Caregiving creates stress, resulting in increased interleukin-6 (IL-6), a proinflammatory cytokine measured in spouses of patients with dementia (Kiecolt-Glaser et al., 2003); increased C-reactive protein, a marker for systemic inflammation, in caregivers of patients with brain cancer (Rohleder, Marin, Ma, & Miller, 2009); and cardiovascular and autonomic dysregulation in caregivers of other cancer patients (Lucini et al., 2008). Caregiver strain has also been associated with a 63% increased risk of mortality within 5 years (Schulz & Beach, 1999).

Several cognitive and behavioral intervention studies, designed to reduce the stress of caregiving of patients with advanced cancer, have measured improvements in marital functioning and depression (McLean et al., 2008), lower caregiver task burden, and increased caregiver QOL (McMillan et al., 2006). Patients also benefited, with decreased distress (McMillan & Small, 2007) and lower symptom burden (McMillan et al., 2006).

These studies demonstrate a role for interventions to reduce short-term distress and caregiver burden in advanced cancer. However, there continues to be limited empirical data testing the feasibility and effectiveness of stress-reducing interventions for advanced-stage cancer patients and their caregivers (Harding & Higginson, 2003; Hodges, Humphris, & Macfarlane, 2005; McWilliams, 2004; Northouse, 2005). With this void in mind, mindfulness-based stress reduction (MBSR) was proposed to help caregivers manage the stress and to reduce the perceived burden for caregivers and symptom distress for patients.

Authors' Note: We would like to give special recognition to the late Dr. Cynthia D. Myers, Director of Integrative Medicine at the H. Lee Moffitt Cancer Center and Research Institute. Without Dr. Myers's efforts, our pilot study would not have been possible. This project was funded by the H. Lee Moffitt Cancer Center Integrative Medicine Pilot Research Grant Program, Grant No. 15259.
Please address correspondence to Cecile A. Lengacher, University of South Florida, College of Nursing, MDC 22, 12901 Bruce B. Downs Boulevard, Tampa, FL 33612-4476; e-mail: clengach@health.usf.edu.

MBSR is a standardized form of meditation and yoga that has been shown to be effective in reducing anxiety (Kabat-Zinn et al., 1992; Miller, Fletcher, & Kabat-Zinn, 1995), depression (Teasdale et al., 2000), and stress in patients with chronic pain (Kabat-Zinn, Lipworth, & Burney, 1985). MBSR has had widespread clinical use in the cancer population and has established efficacy for reducing both psychological and physical symptoms in this population. To date, there have been 16 MBSR studies conducted among patients with cancer that have consistently found reductions in stress and cancer-related symptoms(Altschuler, Rosenbaum, Gordon, Canales, & Avins, 2011; Birnie, Garland, & Carlson, 2010; Campbell, Labelle, Bacon, Faris, & Carlson, 2011; Carlson & Garland, 2005; Carlson, Speca, Faris, & Patel, 2007; Carlson, Speca, Patel, & Goodey, 2003, 2004; Dobkin, 2008; Garland, Carlson, Cook, Lansdell, & Speca, 2007; Lengacher et al., 2009; Matchim, Armer, & Stewart, 2011; Matousek, Pruessner, & Dobkin, 2011; Monti et al., 2006; Saxe et al., 2001; Shapiro, Bootzin, Figueredo, Lopez, & Schwartz, 2003; Speca, Carlson, Goodey, & Angen, 2000; Tacon, Caldera, & Ronaghan, 2004; Witek-Janusek et al., 2008). Four of these studies were randomized controlled trials, and compared with a control group, MBSR participants had less depression, anxiety, fear of recurrence, symptom distress, stress, and mood disturbance and higher QOL, sleep quality, energy, and physical functioning (Lengacher et al., 2009; Monti et al., 2006; Shapiro et al., 2003; Speca et al., 2000). Additionally, 3 of these studies included patients with advanced cancer, and results showed improvements in mindfulness, rumination, anxiety, overall stress, anger, and mood disturbance and a decrease in the rate of prostate specific antigen among prostate cancer patients (Campbell et al., 2011; Garland et al., 2007; Saxe et al., 2001). Only 1 study included caregivers of cancer patients and resulted in significant reductions in mood disturbance post-MBSR for both patients and caregivers (Birnie et al., 2010). However, there have been 2 reported studies that have examined MBSR with caregivers, both in non-cancer populations. One study provided MBSR training for parents of children with special needs; results showed significant decreases in stress symptoms and mood disturbances in parent caregivers (Minor, Carlson, Mackenzie, Zernicke, & Jones, 2006). A second study found increased levels of happiness in adults with multiple disabilities when their caregivers received MBSR compared with those with the control caregivers (Singh et al., 2004). Neither of these studies included training for the patient along with the caregiver.

Furthermore, evidence exists that MBSR may affect positively cytokines and cortisol (Carlson et al., 2003, 2004; Carlson et al., 2007; Matchim et al., 2011; Witek-Janusek et al., 2008). Matchim et al. (2011) found reductions in morning cortisol among early-stage breast cancer survivors post-MBSR. Results from Carlson et al. (2007; Carlson et al., 2003, 2004) among breast and prostate cancer outpatients showed an increase in T cell production of IL-4 and a decrease in T cell production of interferon-gamma, natural killer cell production of IL-10 and cortisol levels, which continued through 6- and 12-month follow-ups. Additionally, breast cancer patients receiving MBSR had reestablished natural killer cell cytotoxicity and cytokine production and reduced cortisol levels (Witek-Janusek et al., 2008).

This pilot study tested MBSR in advanced-stage cancer patients and their caregivers to determine the following: (a) the feasibility of recruiting and retaining patients and their caregivers in the 6-week MBSR program; (b) the short-term effects of the MBSR program on psychological symptoms, physical symptoms, and QOL; and (c) the acute effects of the MBSR program on salivary cortisol and salivary IL-6 levels as measures of acute stress. The exploratory and theoretical logic model (Evans, 1992; Figure 1) postulated that MBSR-C would improve psychological and physical symptoms and QOL over the course of a 6-week program and also would reduce stress-related salivary cortisol and IL-6 immediately following each individual session.

Materials and Method

Subjects, Sample Setting, and Design

This study was approved by the Scientific Review Committee of the H. Lee Moffitt Cancer Center and Research Institute and the University of South Florida Institutional Review Board. Inclusion criteria for patients were women and men aged 21 years or older diagnosed with Stage III or IV breast, colon, lung, or prostate cancer; had completed surgery; were undergoing treatment with radiation and/or chemotherapy; and had a family caregiver who was caring for the patient at home and/or assisting in

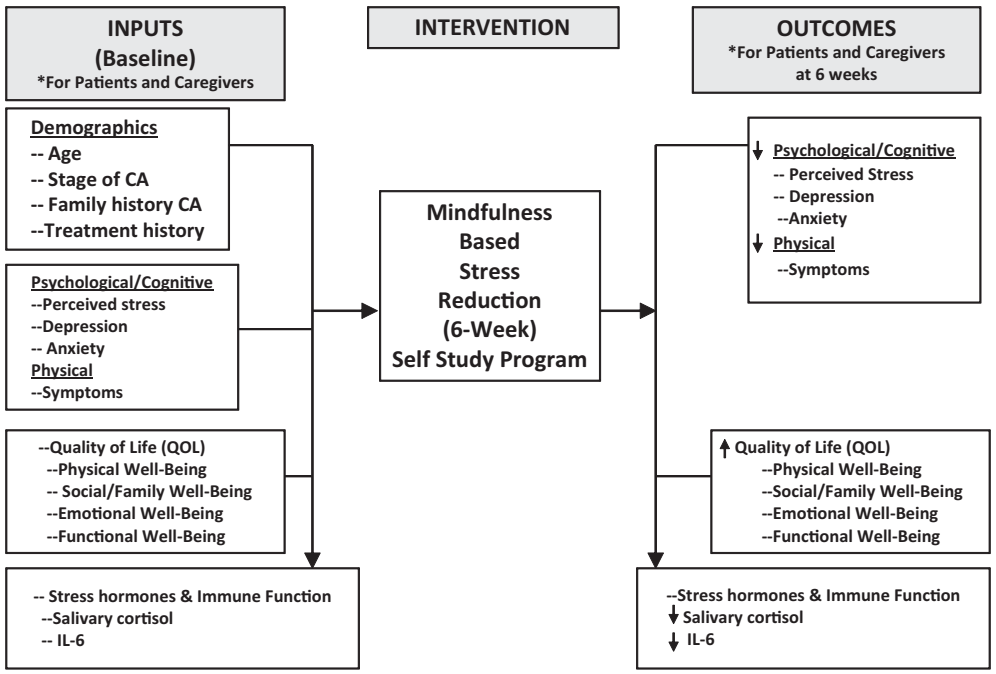

Figure 1. Hypothesized Biobehavioral MBSR-C Patient and Caregiver Logic Model
Note: MBSR-C = mindfulness-based stress reduction for cancer. The figure hypothesizes that the MBSR-C program will favorably improve variables (psychological symptoms, physical symptoms, and quality of life) for both patients and family caregivers following the program (at 6 weeks).

accompanying the patient for clinic appointments. Inclusion criteria for the caregiver included being at least 18 years old, having the ability to read and speak English at an eighth-grade level, and with no cancer diagnosis within the past 4 years. Patients and caregivers with cognitive deficits or a severe psychiatric diagnosis (e.g., bipolar disorder) were excluded. This pilot study investigated the feasibility and preliminary efficacy of a modified MBSR program (MBSR program for cancer; MBSR-C) using a one-group, quasi-experimental, pre–post test design with 26 patients and 26 primary caregivers of these patients. Caregivers and patients were expected to attend three classes, listen to the CDs, and practice MBSR at home.

Procedures

Recruitment and screening. Twenty-six patients with cancer (breast, colon, lung, and prostate) and 26 family caregivers of these patients were recruited from the H. Lee Moffitt Cancer Center and Research Institute at the University of South Florida between September 2007 and February 2008. Eligible patients were identified by health care providers after patient completion of surgery and while they were on treatment with chemotherapy and/or radiation. Patients and caregivers who expressed an interest in the study were met by research staff at a scheduled clinic visit and were invited to an orientation session.

Assessments. At the orientation session following consent into the study, patients and caregivers completed baseline measures of psychological and physical symptom status and QOL and (subset of all patients and caregivers) provided saliva for cortisol and IL-6 measurement. Patients and caregivers were scheduled for three in-person sessions where additional assessments of salivary cortisol and IL-6 were taken pre– and post–MBSR-C class sessions at Weeks 1, 3, and 6. Following the final class meeting, patients completed survey assessments of psychological and physical symptom status and QOL identical to those at baseline.

Intervention and study materials. The MBSR-C intervention is modeled on a program developed by Jon Kabat-Zinn and colleagues at the Stress Reduction

and Relaxation Clinic, Massachusetts Medical Center (Kabat-Zinn et al., 1985; Kabat-Zinn et al., 1992). Mindfulness is the capacity to bring full attention (not just thinking) into moment-to-moment awareness. MBSR is a clinical program that provides systematic training to promote stress reduction by self-regulating arousal to stressful circumstances or symptoms (Kabat-Zinn et al., 1985; Kabat-Zinn et al., 1992). The goal of training is to teach patients and caregivers to become more aware of their thoughts and feelings through meditation practice and to pay attention and observe, but not react to, their thoughts or feelings during stressful situations that contribute to emotional distress (Kabat-Zinn et al., 1985).

The MBSR-C program was modified from the original 8-week program to a 6-week program that has been implemented and tested in previous pilot work with breast cancer patients (Lengacher et al., 2009). The delivery of the MBSR-C program was further modified for this study to include three in-person sessions and three audiotaped sessions provided on CDs. To ensure that all content was covered from the original 8-week program and the MBSR-C CDs, a content validity index score of .944 was computed by a licensed clinical psychologist and research associate. All sessions focused on the weekly content of the 8-week Kabat-Zinn program and included emotional/psychological responses (e.g., anxiety and depression) and physical symptoms (e.g., pain and sleep), which are common concerns to advanced-stage patients and caregivers. Caregivers and patients were taught sitting and walking meditation, body scan, and yoga; these techniques were used to raise awareness to physical responses and emotional responses during stressful situations (Kabat-Zinn et al., 1985).

Patients and caregivers received a manual containing descriptions of exercises, visual diagrams of yoga poses, homework, and a set of CDs of the 6-weekly sessions. Patients and caregivers attended live classes taught by a licensed clinical psychologist who was trained in MBSR on Weeks 1, 3, and 6 and used the CDs and patient manual that contained 2 hours of material (including 60 minutes of content and 60 minutes of practice examples) for at-home practice on Weeks 2, 4, and 5. At the first session, patients and caregivers were instructed to practice for a minimum of 15 to 45 minutes formally and a minimum of 15 to 45 minutes informally daily and were encouraged to record their meditation, yoga, walking meditation, and body scan practice time in a diary for 6 days per week for 6 weeks following the orientation. This information was reinforced on the third week when they returned for their second live session. On the 6th week, the patients and caregivers attended a 2-hour session that included a practice session and a discussion on nutrition similar to the Kabat-Zinn's program.

Measurements

Patients and caregivers completed the following assessments:

Perceived stress. The Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983) is a 14-item, Likert-type instrument that assesses how often in the past month one appraises life situations as "stressful." Internal consistency reliability is reported to range from .84 to .86.

Depression. Depression was measured by the Center for Epidemiological Studies Depression Scale, a 20-item measure of depressive symptomatology (Radloff, 1977). Respondents rate how frequently they have experienced each depressive symptom during the previous week on a 4-point scale. Reported coefficient α reliability is .92 for cancer participants.

Anxiety. The State–Trait Anxiety Inventory contains two 20-item Likert-type scales that measure both ***state anxiety*** (Y1: present experience of anxiety) and ***trait anxiety*** (Y2: trait anxiety, the potential of the individual to experience anxiety symptoms when confronted with a threatening situation). Internal consistency reliability is .95 (Spielberger, Gorsuch, & Luschene, 1983).

Physical and psychological symptoms. Symptoms were measured using the Memorial Symptom Assessment Scale (MSAS), which contains 32 physical and psychological symptoms (Chang, Hwang, Feuerman, Kasimis, & Thaler, 2000). Each symptom is evaluated by three categories that assess how often the patient had the symptom, how severe the symptom was, and how much distress the symptom caused. Cronbach's α coefficients range from .58 to .88 for MSAS subscales (Portenoy et al., 1994).

QOL. The Medical Outcomes Studies Short-Form General Health Survey (MOS SF-36), a 36-item

QOL health status measure, uses Likert-type response formats (Ware, Kosinski, & Keller, 1994). The MOS SF-36 includes eight subscales: Physical Functioning, Physical Role Functioning, Bodily Pain, General Health, Vitality, Social Functioning, Emotional Role Functioning, and Mental Health. Reliability estimates of internal consistency range from .62 to .94, with the majority of scores exceeding .80 (Ware, Snow, Kosinski, & Gandek, 1993).

Demographic data. A standard demographic data form and detailed clinical history form were completed by self-report at baseline.

Cortisol and Immune (IL-6) Measures

For analysis of cortisol and IL-6, saliva time was standardized and collected at two time points between 10:00 a.m. and 12:00 p.m. (i.e., to make valid pre- and post-MBSR comparisons) from patients and caregivers via the "drool method" (drooling saliva into a 50 mL conical tube for 5 minutes without coughing or clearing their throat). To control for contamination in saliva, researchers followed recommendations from the Salimetrics® kit. Patients and caregivers were advised to avoid caffeine, alcohol, and nicotine; not to brush or floss their teeth; and not to use mouthwash, drink anything except water, or eat 1 hour prior to sample collection. In the 5 minutes prior to saliva collection, patients and caregivers were instructed to rinse their mouths out with water.

Samples were transported to the lab, transferred into 15 mL conical tubes, and centrifuged at 3,000 rpm for 15 minutes; supernatants were pipetted into Fisherbrand siliconized/low-retention microcentrifuge tubes (Fisher Scientific) and stored in the −80° C freezer until assayed, in duplicate, using a High-Sensitivity Salivary Cortisol Enzyme Immunoassay Kit from Salimetrics, Inc. (State College, PA) according to kit instructions (Salimetrics Inc., Catalog No. 1-0102/1-0112 96-Well Kit, Updated: 6/23/04) and an IL-6 ELISA kit (EBioscience). The lowest limit of detection for cortisol was 0.006 μg/dL, with an intra- and interassay coefficient of variation less than 3.65% and less than 7%, respectively. The lowest limit of detection for IL-6 ELISA was between 0 and 2 pg/mL, with both intra- and interassay coefficients of variation of less than 10%. This evaluation was implemented after half the MBSR groups had been enrolled; hence, we report herein on a subset of the full sample.

Statistical Analysis

All outcome distributions were evaluated for normality. Those with skewed distributions were transformed to permit use of parametric statistical methods. For patients and caregivers, demographic and presenting clinical characteristics were described by means (±standard deviations) for continuous variables and percentages for categorical variables. Paired t tests were used to compare pre- and post-MBSR measures of psychological status, QOL subscale scores, and symptom subscale scores, stratified by patient versus caregiver status. In addition, for both caregivers and patients, measures of salivary cortisol and IL-6 were compared before and after individual MBSR sessions at Weeks 1, 3, and 6 by use of paired t tests. The $\log_{10}$ transformation method was used to correct for skewness of the original cortisol and IL-6 data and to achieve a normal distribution prior to final analysis. Salivary levels reported in this article are the original, raw values, although statistical outcomes are based on the transformed data. To assess the degree of concordance among dyads, correlation coefficients (Pearson or Spearman depending on distributional properties) were calculated for baseline and pre- and post-MBSR outcome difference scores.

Results

Participants

A total of 26 patients and 26 primary caregivers were enrolled into the study. The mean age of patients and their primary caregivers were 53.5 ± 10.4 and 51.5 ± 14.6 years, respectively (Table 1). The majority of patients and caregivers were female, married, and White, non-Hispanic. Among patients, the leading cancer type was colon (42.3%), followed by breast (30.8%), lung (19.2%), and prostate (7.7%), with 77% of all cancer diagnoses being Stage IV. The majority of patients (61.5%) received chemotherapy only, whereas the remaining 38.5% received combination chemotherapy and radiation treatment. Overall, only 13.5% of participants were on corticosteroids, including 5 out of 26 patients and 2 out of 26 caregivers. Of the 7 participants who were on corticosteroids, 3 participants were included in immune analyses. Figure 2 depicts the experimental design and study flow. Of the 26 dyads enrolled into the study, 24 patients and 23 caregivers completed

Table 1. Demographic and Clinical Characteristics of Patients and Caregivers

Characteristics	Patients (*n* = 26)	Caregivers (*n* = 26)
Age, mean (*SD*)	53.5 (10.4)	51.5 (14.6)
Female gender, *n* (%)	18 (69.2)	16 (61.5)
Lives with patient/caregiver, *n* (%)	14 (53.8)	14 (53.8)
Race/ethnicity, *n* (%)		
White, non-Hispanic	19 (73.1)	23 (88.5)
White, Hispanic	4 (15.4)	1 (3.8)
Black, non-Hispanic	3 (11.5)	1 (3.8)
Black, Hispanic	0 (0.0)	1 (3.8)
Marital status, *n* (%)		
Married	18 (69.2)	22 (84.6)
Single	1 (3.8)	3 (11.5)
Widowed	1 (3.8)	0 (0.0
Divorced	4 (15.4)	0 (0.0
Other	2 (7.7)	1 (3.8)
Education attainment, *n* (%)		
High school or less	10 (38.5)	7 (26.9)
Some college	10 (38.5)	10 (38.5)
College or professional degree	6 (23.1)	9 (34.6)
Cancer type, *n* (%)		
Breast	8 (30.8)	—
Colon	11 (42.3)	—
Lung	5 (19.2)	—
Prostate	2 (7.7)	—
Cancer stage, *n* (%)		
III	6 (23.1)	—
IV	20 (76.9)	—
Treatment(s) received, *n* (%)		
Chemotherapy	16 (61.5)	—
Chemotherapy + radiation	10 (38.5)	—
Support group, *n* (%)	5 (19.2)	4 (16.0)

the study with a total of 23 whole dyads (88.5%) finishing the study. Of the 26 dyads enrolled, 10 dyads participated in the immune analyses, as this outcome was added after 17 patients and caregivers were already enrolled.

Feasibility and Compliance

In terms of feasibility, 23 of the 26 dyads (88.5%) completed the full 6-week program. Of the 23 dyads who completed the MBSR-C program, 21 (91.3%) attended at least two of the three classes, and among all dyads, 88.5% recorded their practice times in a daily diary. In terms of compliance, participants practiced an average of 603 ± 543 minutes (10.0 ± 9.0 hours) over the 6-week intervention period and a range of zero to 2,683 minutes practiced, reflecting highly variable rates across patients and caregivers. Relationships between practice time (i.e., compliance) and assessments of symptoms were analyzed by Spearman correlations. The most consistent finding was that increased yoga practice time associated with better social functioning in patients ($r = .39$, $p = .06$) and caregivers ($r = .39$, $p = .07$). In addition, whereas daily practice was not associated with improvement overall among caregivers, in patients, yoga was associated with a decrease in perceived stress ($r = .47$, $p = .02$) and state anxiety ($r = .67$, $p = .0003$). Likewise, sitting meditation was associated with a decrease in state anxiety in patients ($r = .53$, $p = .008$).

Change in Psychological and Physical Symptoms and QOL Following the MBSR-C Program

Among the 24 patients, mean changes pre–MBSR-C and post–6 weeks on measures of perceived stress (19.5 vs. 16.8), trait anxiety (42.7 vs. 39.3), MSAS subscale, and total score (3.6 vs. 2.9) all improved significantly ($p < .05$) after participating in the 6-week MBSR-C program (Table 2). There was also an

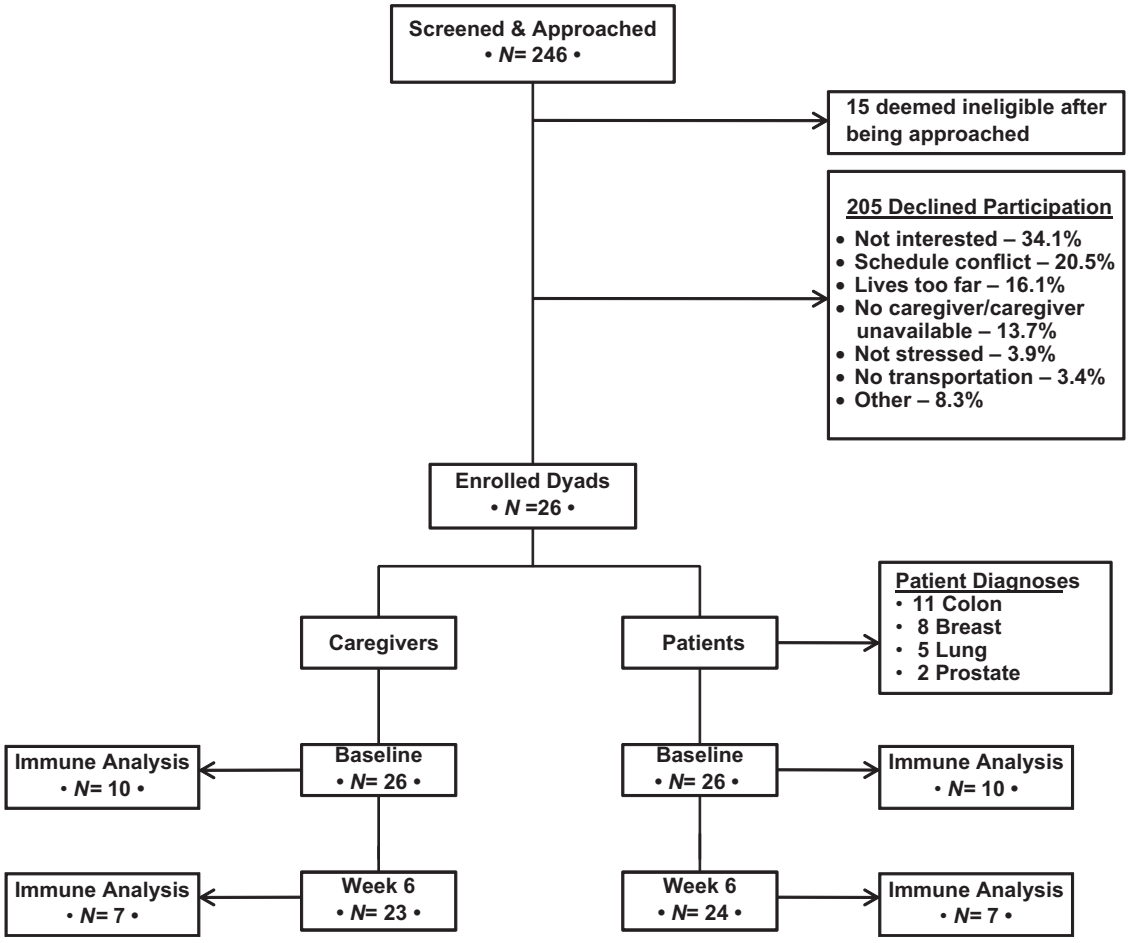

Figure 2. Study Flow and Subject Retention
Note: The figure is a flowchart showing recruitment and enrollment of 26 patient–caregiver dyads into the trial, of which 24 patients and 23 caregivers completed the study and were included in outcome analyses.

indication of improvement in depression (16.5 vs. 20.4; p = .07), state anxiety (36.9 vs. 41.3; p = .08) and emotional well-being (49.0 vs. 45.3; p = .07) subscale of the MOS SF-36. Patients who reported favorable changes in depression scores on the Center for Epidemiological Studies Depression Scale also tended to have caregivers who reported favorable changes (r = 0.48, p = .02). Among caregivers, changes in psychological status and QOL after MBSR were consistently in the direction of improvement, but they were relatively small and did not achieve statistical significance.

Acute Changes in Salivary Cortisol and IL-6 After Individual MBSR-C Sessions

Figure 3 shows pre- and postsession cortisol levels among patients and caregivers after individual MBSR-C sessions at Weeks 1, 3, and 6 of the program. Both patients and caregivers had significant decreases in cortisol at Week 1 of the MBSR-C program (p = .042, p = .005, respectively) and at Week 3 (p = .065, p = .029, respectively). No significant pre- and postsession differences were observed at Week 6; however, it is notable that baseline (presession) cortisol levels at Week 6 were much lower (roughly half) than those measured at Week 1.

Figure 4 shows $\log_{10}$ transformed data for IL-6 levels among patients and caregivers after individual MBSR-C sessions. Although not as consistent as cortisol results, caregivers, in particular, showed a larger reduction in IL-6 levels after Week 1 MBSR-C session (p = .029), and patients had lower IL-6 levels at Week 6. Similar to cortisol levels at Week 6, salivary IL-6 levels were lower overall (before and after an MBSR-C session), compared

Table 2. Baseline and Post-MBSR Mean Scores of Psychological, Quality of Life, and Symptom Measures

	Patients (n = 24)			Caregivers (n = 23)		
Measure	Baseline	Post-MBSR	p Value	Baseline	Post-MBSR	p Value
Depression (CESD)	20.4 (11.7)	16.5 (11.4)	.07	13.3 (9.1)	11.4 (9.3)	.30
Perceived Stress (PSS)	19.5 (7.1)	16.8 (6.0)	.04*	18.1 (6.6)	17.1 (6.4)	.29
Trait Anxiety (STAI)	42.7 (12.6)	39.3 (10.2)	.05*	38.5 (12.5)	37.8 (11.9)	.61
State Anxiety (STAI)	41.3 (13.3)	36.9 (13.6)	.08	36.5 (13.4)	35.4 (14.8)	.51
Quality of Life (SF-36)						
Pain	45.0 (10.0)	45.0 (9.7)	.99	53.9 (8.5)	54.2 (8.7)	.82
Energy	43.8 (8.4)	45.0 (8.6)	.36	52.8 (8.3)	54.5 (9.7)	.33
Physical functioning	42.2 (8.5)	43.2 (8.9)	.24	55.7 (7.3)	56.6 (6.7)	.27
RL: Physical health	42.4 (7.1)	44.1 (7.3)	.30	54.7 (8.6)	55.7 (8.1)	.54
General health	42.9 (9.0)	44.3 (9.7)	.21	54.9 (7.6)	54.5 (8.5)	.75
Emotional well being	45.3 (11.9)	49.0 (11.5)	.07	49.8 (9.7)	50.2 (10.3)	.71
RL: Emotional problems	47.6 (10.8)	46.3 (11.7)	.60	49.3 (9.9)	52.2 (9.4)	.13
Social functioning	45.4 (11.8)	46.3 (9.7)	.57	53.3 (8.0)	52.2 (8.2)	.47
Aggregate physical health	42.1 (7.0)	42.9 (7.7)	.38	57.3 (7.9)	57.3 (7.6)	.99
Aggregate mental health	47.3 (10.9)	48.6 (10.6)	.51	48.8 (10.5)	50.1 (10.3)	.34
Symptom Assessment (MSAS)						
Global score	3.1 (1.8)	2.4 (1.6)	.01*	2.2 (1.4)	1.9 (1.4)	.26
Physical score	4.0 (2.0)	3.1 (1.9)	.02*	1.8 (1.5)	1.6 (1.1)	.43
Psychological score	4.6 (2.9)	3.7 (2.4)	.02*	4.1 (2.6)	3.5 (2.4)	.04*
Total score	3.6 (1.8)	2.9 (1.5)	.006*	2.0 (1.4)	1.6 (1.0)	.07

Note: CESD = Center for Epidemiological Studies Depression Scale; PSS = Perceived Stress Scale; STAI = State–Trait Anxiety Inventory; SF -36 = Medical Outcomes Studies–Short-Form General Health Survey; RL = role limitations; MSAS = Memorial Symptom Assessment Scale.
*p Value calculated by paired t test.

with Week 1, when participants began the MBSR program.

Discussion

There is lack of empirical data related to improving the care of patients with advanced illness. Results from this pilot study suggest that a modified MBSR-C program that can be partially completed at home with a CD may be beneficial for some patients with advanced cancer. In this pilot study, cancer patients reported greater benefit from the MBSR-C program than did their primary caregivers. Without a control group or a specific measure of mindfulness, however, improvements cannot be attributed to the MBSR-C program alone.

Feasibility and Compliance

Based on program completion rates, the modified MBSR-C program appears suitable and feasible for advanced-stage cancer patients and their primary caregiver. This is encouraging in that there is a growing number of studies that present the difficulty of recruiting sick patients (e.g., Steinhauser et al., 2006). Although recruitment rates were lower than a study of patients with earlier stage cancer (Lengacher et al., 2009), retention was high, with 23 of the 26 enrolled dyads completing all outcome measures, 21 dyads attending at least two of the three classes, and 20 dyads participating in home practice. In terms of compliance, the prescribed amount of practice per day was 15 to 45 minutes; however, the actual mean amount performed was 18.4 minutes/day, which is at the lower end of the recommended amount. We postulate that providing the MBSR intervention to patients and caregivers simultaneously may boost study adherence with encouragement and accountability between patient and caregiver. In addition, we postulate that the highly variable amount of MBSR practice reported may be most related to characteristics of this patient population, including transient physical and psychological symptoms that incur limitations in functioning, as well as time conflicts such as those related to treatment activities (e.g., scheduled chemotherapy and doctor appointments). In this realm, future

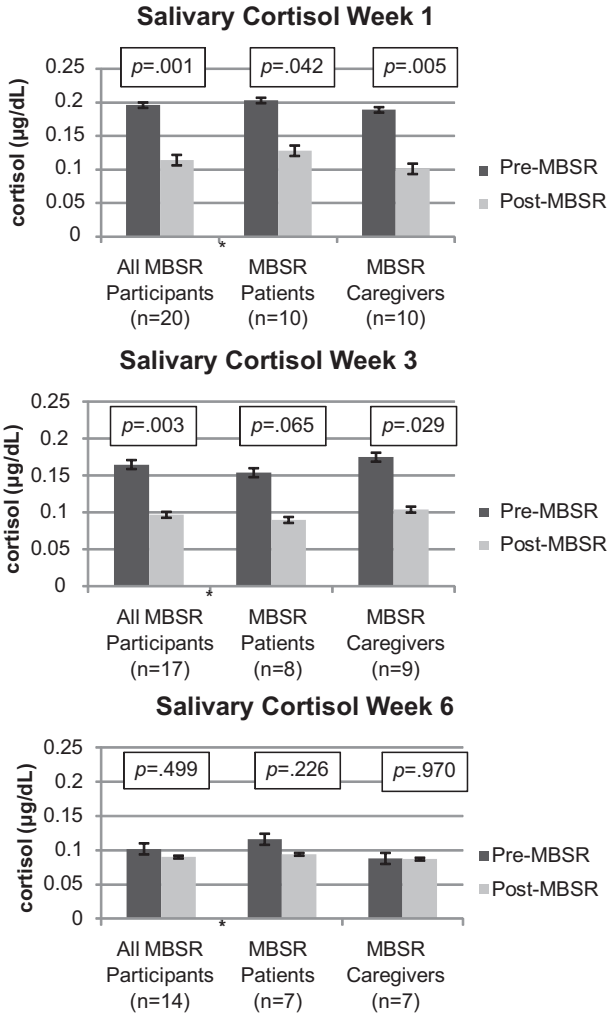

Figure 3. Salivary Cortisol Pre-MBSR and Post-MBSR
Note: MBSR = mindfulness-based stress reduction. The figure shows cortisol levels among patients and caregivers after individual MBSR-C sessions at Weeks 1, 3, and 6 of the program. All bars show the raw data. The p values are from the $\log_{10}$ transformed data. Error bars are standard errors.
*Immune analyses were implemented after half the MBSR groups had been enrolled, hence, we report herein on a subset of the full sample. Saliva was first allocated to cortisol analysis, and any remaining sample was then evaluated for interleukin-6.

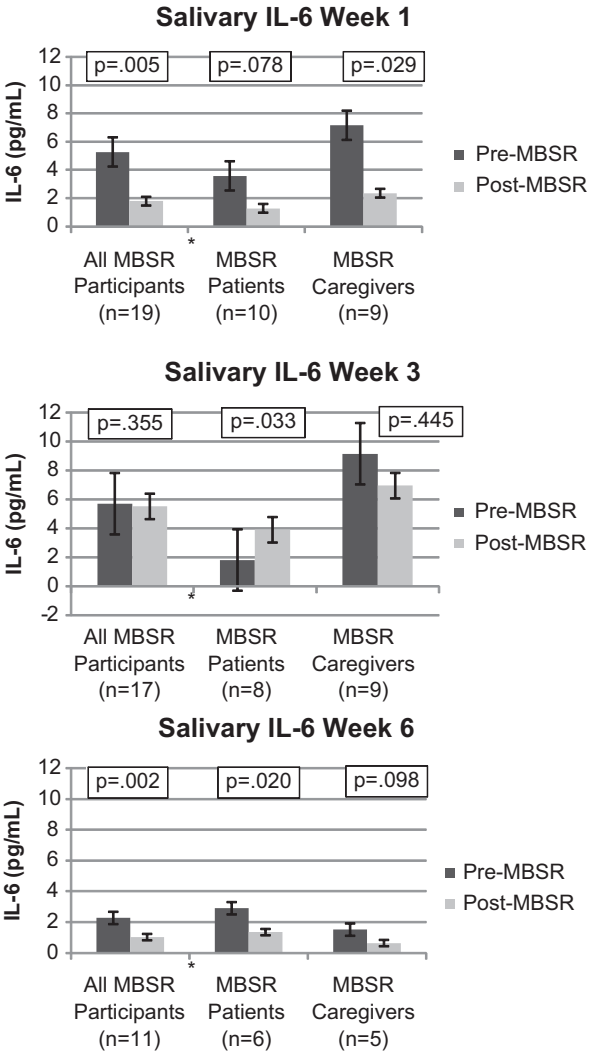

Figure 4. Salivary IL-6 Pre- and Post-MBSR
Note: MBSR = mindfulness-based stress reduction; IL-6 = interleukin-6. The figure shows log10 transformed data for IL-6 levels among patients and caregivers after individual MBSR-C sessions. All bars show the raw data. The p values are from the log10 transformed data. Error bars are standard error.
*Immune analyses were implemented after half the MBSR groups had been enrolled, hence, we report herein on a subset of the full sample. Saliva was first allocated to cortisol analysis, and any remaining sample was then evaluated for IL-6.

studies may consider incentives and use of "telehealth" technology to maximize participation among advanced-stage cancer patients.

In a recent meta-analysis of MBSR studies in cancer patients, approximately 19% of all patients across the nine studies had advanced-stage cancer, and advanced stage patients were not more likely to drop out than early-stage patients (Ledesma & Kumano, 2009). Almost half (43% to 49%) of subjects in two randomized, wait-listed controlled trials testing MBSR (Speca et al., 2000) and mindfulness-based art therapy were advanced-stage cancer patients (Monti et al., 2006; Speca et al., 2000). These studies therefore, and in addition to ours, demonstrate that effective recruitment and a high rate of retention are achievable in an advanced-stage cancer population.

Psychological and Physical Symptom Benefit of MBSR-C for Advanced-Stage Cancer Patients

Over the 6-week MBSR-C intervention, advanced-stage cancer patients in this study had significantly less perceived stress and trait anxiety, a trend toward greater emotional well-being, and less state anxiety and depression. These data suggest a potential benefit of MBSR-C for advanced-stage cancer patients and the need for future randomized controlled studies to determine efficacy of MBSR, reduce symptoms, and improve QOL. The benefits to caregivers are less clear.

In the study by Speca et al. (2000), MBSR reduced total mood disturbance and specific symptoms of anxiety, depression, anger, and confusion. Mindfulness-based art therapy also resulted in less distress and significant improvements in QOL (Monti et al., 2006). These limited studies, along with our findings, suggest that MBSR and its various adaptations can be feasibly offered and completed by some advanced-stage cancer patients and can contribute to improved symptoms and aspects of QOL. Further study is needed, however, to determine if MBSR alone is responsible for the perceived benefits.

Benefits of MBSR for Caregivers

Caregivers had improvements in psychological status and QOL, although the effects were small and not statistically significant. The larger improvements seen in patients versus their caregivers may be because of greater symptom burden seen at baseline by patients. Only one other study has investigated the potential benefit of MBSR in reducing psychological symptoms in the caregiver population (Minor et al., 2006). This study included 44 caregivers of children with chronic illness and found that the traditional 8-week MBSR reduced stress symptoms and mood disturbance in caregivers. A larger study sample would provide a more robust sample, and it is possible that the conventional 8-week MBSR program may provide greater benefit to caregivers. Our rationale for the MBSR-C 6-week program, of which three sessions were in class and three sessions were self-study, was to decrease patient burden of class attendance.

Biological Measures Pre- and Post-MBSR in Advanced-Stage Cancer Patients and Caregivers

For the small subset of both patients and caregivers, salivary cortisol was significantly reduced pre- to post-MBSR-C sessions at Weeks 1 and 3 but not at Week 6; however, cortisol was significantly reduced over the 6-week MBSR-C program. This improvement suggests that by Week 6 of the MBSR-C program, both patients and caregivers had less stress, thereby precluding the ability to observe significant additional reductions following participation in an individual MBSR-C session. Salivary cortisol is an indirect measure of hypothalamic-hypophyseal-adrenocortical activation. Chronic elevations in hypothalamic-hypophyseal-adrenocortical activation with high levels of cortisol may suppress immune function and contribute to fatigue and metabolic dysregulation. Because there was no control group, the reductions in stress and cortisol cannot be attributed solely to the MBSR-C program.

Changes in IL-6 were inconsistent before and after each MBSR-C session; however, a significant reduction in IL-6 overall was observed in both patients and caregivers pre– to post–6-week MBSR-C program. Although these findings are intriguing, we cannot determine clinical relevance, and changes in salivary IL-6 do not necessarily indicate systemic change. IL-6 is an inflammatory cytokine with both pro- and antiinflammatory effects; high levels are associated with poorer prognosis and increased invasiveness in the tumor microenvironment (Goldberg & Schwertfeger, 2010). Although the immediate effect was to lower IL-6 and cortisol at Time 1 and Time 3 (suggesting reductions in perceived stress following the MBSR-C intervention), the longer term effects and the clinical benefits of reducing cortisol and IL-6 have yet to be determined. The sample size is too small to infer definitive outcomes. Further studies are needed to clarify the importance of salivary levels of IL-6 and other contributing factors, such as gum and dental disease, lack of hygiene, smoking, toothbrushing, and dry mouth.

Although inconclusive, results are similar to one study that observed lower cortisol and IL-6 in breast cancer patients post-MBSR intervention compared with a nonrandomized control group; of note, the difference in IL-6 between intervention and control group became significant 1-month post–MBSR

intervention (Witek-Janusek et al., 2008). In a different study, "normalization" of cortisol levels was observed in a group of breast and prostate cancer patients post–MBSR intervention, where initially high cortisol levels were reduced post-MBSR and initially low cortisol levels were elevated post-MBSR (Carlson et al., 2004). However, at 6- and 12-month follow-up, linear decreases in cortisol were observed (Carlson et al., 2007). Although not definitive, our findings, along with outcomes from other studies, suggest that MBSR may influence certain stress hormones (i.e., cortisol) and cytokine levels (i.e., IL-6). Salivary measures are noninvasive and can provide a window on stress and immune function. Cortisol is free and active in saliva and positively correlated with serum levels. Many studies have found relationships between stress and elevated salivary cortisol (Hellhammer, Wust, & Kudielka, 2009) and IL-6 (Cox, Pyne, Gleson, & Callister, 2008; Groer et al. 2010; Minetto et al., 2005; Sjogren, Leanderson, Kristenson, & Ernerudh, 2006). Including biological measures of stress reduction in future randomized controlled studies will help determine the differential effects of MBSR. Additionally, follow-up evaluations are critical to detect whether or not changes in biological measures are sustainable.

Limitations

This pilot study is limited by a small sample size, particularly for the biological data, which included a subset of the total sample; reliance on self-reported outcomes (despite use of validated measures); lack of follow-up after the intervention; lack of a comparison group; and no measure of mindfulness or perceived caregiver burden. Regarding lack of follow-up and sustainability, a family intervention directed at advanced-stage breast cancer patients and caregivers showed improvements in negative appraisal of illness for both patients and caregivers and less hopelessness for patients at 3 months; however, the benefits of the intervention were not sustained at 6 months (Northouse, Kershaw, Mood, & Schafenacker, 2005).

Although this study was composed of a heterogeneous cancer population, it was a homogeneous population because the patients shared similar stages of cancer and physical and psychological symptoms. Without a control group, we cannot confirm that the effects were related to the MBSR-C intervention per se, as opposed to change over time or changes in treatment circumstances. As a pilot study, we did not attempt to control for other explanatory variables that might affect cortisol and IL-6, including acute illness, daily stressors, or changes to treatments. In addition, 3 out of 20 participants (15%) were taking corticosteroids, which, although not ideal for pure immunological analyses, is sufficiently small not to bias the overall study results. Although these factors would influence cortisol and IL-6 over the course of the program, they are not likely to explain the acute pre–post session effects.

Although not suggested by our data, we cannot exclude the possibility that at least some of the positive outcomes of MBSR-C in patients and their caregivers are a result of group support benefits and patient–caregiver relationships that are nonspecific to the program. Furthermore, it should be mentioned that study results achieving statistical significance do not guarantee clinical significance.

Conclusion

Our study indicates that select patients with advanced cancer and their caregivers are interested in MBSR, are willing to participate in a research study and contribute outcome data, and are able to comply with some degree to the practice expectations of the program. We conclude that MBSR-C may be a beneficial intervention for advanced stage cancer patients and, although inconclusive, may also benefit caregivers.

References

Adejumo, A. (2009). Influence of social support, depression, and self-esteem on burden of care among caregivers of oncology patients. *World Hospitals and Health Services, 45*(3), 19-21.

Altschuler, A., Rosenbaum, E., Gordon, P., Canales, S., & Avins, A. L. (2011). Audio recordings of mindfulness-based stress reduction training to improve cancer patients' mood and quality of life-a pilot feasibility study. *Supportive Care in Cancer*. Advance online publication. doi:10.1007/s00520-011-1216-7

Birnie, K., Garland, S. N., & Carlson, L. E. (2010). Psychological benefits for cancer patients and their partners participating in mindfulness-based stress reduction (MBSR). *Psycho-Oncology, 19*, 1004-1009.

Campbell, T. S., Labelle, L. E., Bacon, S. L., Faris, P., & Carlson, L. E. (2011). Impact of mindfulness-based stress

reduction (MBSR) on attention, rumination and resting blood pressure in women with cancer: A waitlist-controlled study. *Journal of Behavioral Medicine*. Advance online publication. doi:10.1007/s10865-011-9357-1

Carlson, L. E., & Garland, S. N. (2005). Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients. *International Journal of Behavioral Medicine, 12*, 278-285.

Carlson, L. E., Speca, M., Faris, P., & Patel, K. D. (2007). 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, Behavior, and Immunity, 21*, 1038-1049.

Carlson, L. E., Speca, M., Patel, K. D., & Goodey, E. (2003). Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress, and immune parameters in breast and prostate cancer outpatients. *Psychosomatic Medicine, 65*, 571-581.

Carlson, L. E., Speca, M., Patel, K. D., & Goodey, E. (2004). 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.

Carter, P. A. (2006). A brief behavioral sleep intervention for family caregivers of persons with cancer. *Cancer Nursing, 29*, 95-103.

Chang, V. T., Hwang, S. S., Feuerman, M., Kasimis, B. S., & Thaler, H. T. (2000). The Memorial Symptom Assessment Scale–Short Form (MSAS-SF). *Cancer, 89*, 1162-1171.

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior, 24*, 385-396.

Cox, A. J., Pyne, D. B., Gleson, M., & Callister, R. (2008). Resting plasma and salivary IL-6 concentrations are not correlated in distance runners. *European Journal of Applied Physiology, 103*, 477-479.

Dobkin, P. L. (2008). Mindfulness-based stress reduction: What processes are at work? *Complementary Therapies in Clinical Practice, 14*(1), 8-16.

Evans, M. E. (1992). Using a model to structure psychosocial nursing [corrected]. *Journal of Psychosocial Nursing and Mental Health Services, 30*(8), 27-32.

Garland, S. N., Carlson, L. E., Cook, S., Lansdell, L., & Speca, M. (2007). A non-randomized comparison of mindfulness-based stress reduction and healing arts programs for facilitating post-traumatic growth and spirituality in cancer outpatients. *Supportive Care in Cancer, 15*, 949-961.

Golant, M., & Haskins, N. V. (2008). "Other cancer survivors": The impact on family and caregivers. *Cancer Journal, 14*, 420-424.

Goldberg, J. E., & Schwertfeger, K. L. (2010). Proinflammatory cytokines in breast cancer: Mechanisms of action and potential targets for therapeutics. *Current Drug Targets, 11*, 1133-1146.

Groer, M., Murphy, R., Bunnell, W., Salomon, K., Van Eepoel, J., Rankin, B., . . . Bykowski, C. (2010). Salivary measures of stress and immunity in police officers engaged in simulated critical incident scenarios. *Journal of Occupational and Environmental Medicine, 52*, 595-602.

Harding, R., & Higginson, I. J. (2003). What is the best way to help caregivers in cancer and palliative care? A systematic literature review of interventions and their effectiveness. *Palliative Medicine, 17*, 63-74.

Hellhammer, D. H., Wust, S., & Kudielka, B. M. (2009). Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinology, 34*, 163-171.

Hodges, L. J., Humphris, G. M., & Macfarlane, G. (2005). A meta-analytic investigation of the relationship between the psychological distress of cancer patients and their carers. *Social Science & Medicine, 60*(1), 1-12.

Kabat-Zinn, J., Lipworth, L., & Burney, R. (1985). The clinical use of mindfulness meditation for the self-regulation of chronic pain. *Journal of Behavioral Medicine, 8*, 163-190.

Kabat-Zinn, J., Massion, A. O., Kristeller, J., Peterson, L. G., Fletcher, K. E., Pbert, L., . . . Santorelli, S. F. (1992). Effectiveness of a meditation-based stress reduction program in the treatment of anxiety disorders. *American Journal of Psychiatry, 149*, 936-943.

Kiecolt-Glaser, J. K., Preacher, K. J., MacCallum, R. C., Atkinson, C., Malarkey, W. B., & Glaser, R. (2003). Chronic stress and age-related increases in the proinflammatory cytokine IL-6. *Proceedings of the National Academy of Sciences of the United States of America, 100*, 9090-9095.

Ledesma, D., & Kumano, H. (2009). Mindfulness-based stress reduction and cancer: A meta-analysis. *Psycho-Oncology, 18*, 571-579.

Lengacher, C. A., Johnson-Mallard, V., Post-White, J., Moscoso, M. S., Jacobsen, P. B., Klein, T. W., . . . Kip, K. E. (2009). Randomized controlled trial of mindfulness-based stress reduction (MBSR) for survivors of breast cancer. *Psycho-Oncology*, *18*, 1261-1272.

Lobchuk, M. M., & Degner, L. F. (2002). Symptom experiences: Perceptual accuracy between advanced-stage cancer patients and family caregivers in the home care setting. *Journal of Clinical Oncology, 20*, 3495-3507.

Lucini, D., Cannone, V., Malacarne, M., Bruno, D., Beltrami, S., Pizzinelli, P., . . . Pagani, M. (2008). Evidence of autonomic dysregulation in otherwise healthy cancer caregivers: A possible link with health hazard. *European Journal of Cancer, 44*, 2437-2443.

Matchim, Y., Armer, J. M., & Stewart, B. R. (2011). Effects of mindfulness-based stress reduction (MBSR) on health among breast cancer survivors. *Western Journal of Nursing Research*, *33*, 996-1016.

Matousek, R. H., Pruessner, J. C., & Dobkin, P. L. (2011). Changes in the cortisol awakening response (CAR) following participation in mindfulness-based stress reduction in

women who completed treatment for breast cancer. *Complementary Therapies in Clinical Practice, 17*(2), 65-70.

McLean, L. M., Jones, J. M., Rydall, A. C., Walsh, A., Esplen, M. J., Zimmermann, C., & Roodin, G. M. (2008). A couples intervention for patients facing advanced cancer and their spouse caregivers: Outcomes of a pilot study. *Psycho-Oncology, 17*, 1152-1156.

McMillan, S., & Small, B. (2007). Using the COPE intervention for family caregivers to improve symptoms of hospice homecare patients: A clinical trial. *Oncology Nursing Forum, 34*, 313-321.

McMillan, S., Small, B. J., Weitzner, M., Schonwetter, R., Tittle, M., Moody, L., & Haley, W. E. (2006). Impact of coping skills intervention with family caregivers of hospice patients with cancer: A randomized clinical trial. *Cancer, 106*, 214-222.

McWilliams, A. E. (2004). Couple psychotherapy from an attachment theory perspective: A case study approach to challenging the dual nihilism of being an older person and someone with a terminal illness. *European Journal of Cancer Care (England), 13*, 464-472.

Miaskowski, C., Kragness, L., Dibble, S., & Wallhagen, M. (1997). Differences in mood states, health status, and caregiver strain between family caregivers of oncology outpatients with and without cancer-related pain. *Journal of Pain and Symptom Management, 13*, 138-147.

Miller, J. J., Fletcher, K., & Kabat-Zinn, J. (1995). Three-year follow-up and clinical implications of a mindfulness meditation-based stress reduction intervention in the treatment of anxiety disorders. *General Hospital Psychiatry, 17*, 192-200.

Minetto, M., Rainoldi, A., Gazzoni, M., Terzolo, M., Borrione, P., Termine, A., . . . Paccotti, P. (2005). Differential responses of serum and salivary interleukin-6 to acute strenuous exercise. *European Journal of Applied Physiology, 93*, 679-686.

Minor, H. G., Carlson, L. E., Mackenzie, M. J., Zernicke, K., & Jones, L. (2006). Evaluation of a mindfulness-based stress reduction program for caregivers of children with chronic conditions. *Social Work in Health Care, 43*(1), 91-109.

Monti, D. A., Peterson, C., Kunkel, E. J., Hauck, W. W., Pequignot, E., Rhodes, L., & Brainard, G. (2006). A randomized, controlled trial of mindfulness-based art therapy (MBAT) for women with cancer. *Psycho-Oncology, 15*, 363-373.

Mystakidou, K., Parpa, E., Tsilika, E., Pathiaki, M., Gennatas, K., Smyrniotis, V., & Vassiliou, L. (2007). The relationship of subjective sleep quality, pain, and quality of life in advanced cancer patients. *Sleep, 30*, 737-742.

Mystakidou, K., Tsilika, E., Parpa, E., Galanos, A., & Vlahos, L. (2007). Caregivers of advanced cancer patients: Feelings of hopelessness and depression. *Cancer Nursing, 30*, 412-418.

Mystakidou, K., Tsilika, E., Parpa, E., Katsouda, E., Galanos, A., & Vlahos, L. (2005). Assessment of anxiety and depression in advanced cancer patients and their relationship with quality of life. *Quality of Life Research, 14*, 1825-1833.

National Alliance for Caregiving & American Association of Retired Persons. (2009). *Caregiving in the U.S.* Washington, DC: Author.

Northouse, L. (2005). Helping families of patients with cancer. *Oncology Nursing Forum, 32*, 743-750.

Northouse, L., Kershaw, T., Mood, D., & Schafenacker, A. (2005). Effects of a family intervention on the quality of life of women with recurrent breast cancer and their family caregivers. *Psycho-Oncology, 14*, 478-491.

Portenoy, R. K., Thaler, H. T., Kornblith, A. B., Lepore, J. M., Friedlander-Klar, H., Kiyasu, E., . . . Scher, H. (1994). The Memorial Symptom Assessment Scale: An instrument for the evaluation of symptom prevalence, characteristics, and distress. *European Journal of Cancer, 30A*, 1326-1336.

Radloff, L. (1977). The CES-D scale: A self-report depression scale for researching the general population. *Application of Psychological Measures, 1*, 385-401.

Rohleder, N., Marin, T. J., Ma, R., & Miller, G. E. (2009). Biologic cost of caring for a cancer patient: Dysregulation of pro- and anti-inflammatory signaling pathways. *Journal of Clinical Oncology, 27*, 2909-2915.

Saxe, G. A., Hebert, J. R., Carmody, J. F., Kabat-Zinn, J., Rosenzweig, P. H., Jarzobski, D., . . . Blute, R. D. (2001). Can diet in conjunction with stress reduction affect the rate of increase in prostate specific antigen after biochemical recurrence of prostate cancer? *Journal of Urology, 166*, 2202-2207.

Schulz, R., & Beach, S. R. (1999). Caregiving as a risk factor for mortality: The Caregiver Health Effects Study. *Journal of the American Medical Association, 282*, 2215-2219.

Shapiro, S. L., Bootzin, R. R., Figueredo, A. J., Lopez, A. M., & Schwartz, G. E. (2003). The efficacy of mindfulness-based stress reduction in the treatment of sleep disturbance in women with breast cancer: An exploratory study. *Journal of Psychosomatic Research, 54*(1), 85-91.

Shapiro, S. L., Lopez, A. M., Schwartz, G. E., Bootzin, R., Figueredo, A. J., Braden, C. J., & Kurker, S. E. (2001). Quality of life and breast cancer: Relationship to psychosocial variables. *Journal of Clinical Psychology, 57*, 501-519.

Singh, N. N., Lancioni, G. E., Winton, A. S., Wahler, R. G., Singh, J., & Sage, M. (2004). Mindful caregiving increases happiness among individuals with profound multiple disabilities. *Research in the Developmental Disabilities, 25*, 207-218.

Sjogren, E., Leanderson, P., Kristenson, M., & Ernerudh, J. (2006). Interleukin-6 levels in relation to psychosocial factors: Studies on serum, saliva, and in vitro production by blood mononuclear cells. *Brain, Behavior, and Immunity, 20*, 270-278.

Speca, M., Carlson, L. E., Goodey, E., & Angen, M. (2000). 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. *Psychosomatic Medicine, 62*, 613-622.

Spielberger, C. D., Gorsuch, R. L., & Luschene, R. E. (1983). *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists.

Steinhauser, K. E., Clipp, E. C., Hays, J. C., Olsen, M., Arnold, R., Christakis, N. A., . . . Tulsky, J. A. (2006). Identifying, recruiting, and retaining seriously-ill patients and their caregivers in longitudinal research. *Palliative Medicine, 20*, 745-754.

Tacon, A. M., Caldera, Y. M., & Ronaghan, C. (2004). Mindfulness-based stress reduction in women with breast cancer. *Families, Systems, & Health, 22*, 193.

Teasdale, J. D., Segal, Z. V., Williams, J. M., Ridgeway, V. A., Soulsby, J. M., & Lau, M. A. (2000). Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *Journal of Consulting and Clinical Psychology, 68*, 615-623.

Ware, J. E., Kosinski, M., & Keller, M. (1994). *SF36 Physical and mental health summary scales: User's manual* (2nd ed.). Boston, MA: Health Institute.

Ware, J. E., Snow, K. K., Kosinski, M., & Gandek, B. (1993). *SF-36 survey manual and interpretation guide*. Boston, MA: New England Medical Center.

Witek-Janusek, L., Albuquerque, K., Chroniak, K. R., Chroniak, C., Durazo-Arvizu, R., & Mathews, H. L. (2008). Effect of mindfulness based stress reduction on immune function, quality of life and coping in women newly diagnosed with early stage breast cancer. *Brain, Behavior, and Immunity, 22*, 969-981.

Cecile A. Lengacher, PhD, RN, FAAN is the Professor and Director of the BS-PHD Program at the University of South Florida's College of Nursing. Her expertise spans the program of research in women's health, including psycho-oncology, psychoneuroimmunology, complementary alternative medicine, along with expertise in clinical trials and translational research.

Kevin E. Kip, PhD, FAHA is the Executive Director of the University of South Florida College of Nursing Research Center. Dr Kip is an epidemiologist and focuses on significantly broadening the research portfolio of the nursing college, including multidisciplinary and multi-institution collaborations, and expanding and upgrading research infrastructure and capacity.

Michelle Barta, BS, MPH is a PharmD student at the University of Florida. She is a research associate and assists with in the recruitment, orientation and consent processes for the clinical trial, as well as daily implementation of the study activities.

Janice Post-White, PhD, RN, FAAN is an adjunct associate professor at the University of Minnesota and a research consultant in complementary and alternative therapies, and Bio-behavioral approaches.

Paul B. Jacobsen, PhD is the Program Leader and Chair of the Department of Health Outcomes & Behavior at H. Lee Moffitt Cancer Center and Research Institute. His research interest is in behavioral and psychological aspects of cancer. The goal of his work is to demonstrate how an understanding of psychological principles can be used to reduce cancer-related morbidity and mortality.

Maureen Groer, PhD, RN, FAAN is a Gordon Keller Professor and Director of the Biobehavioral & Psychoneuroimmunology Laboratory at the University of South Florida's College of Nursing. Dr Groer's lab in the College of Nursing is currently conducting studies on exercise and inflammation, immune function of preterm infants, menstrual cycle immune function, and postpartum immunology. Her research interests have focused on psychoneuroimmunology with a special focus on women and children.

Brandy Lehman, PhD, RN was a former faculty member at the University of South Florida's College of Nursing. Her area of research focused on accessing stress hormones in caregivers.

Manolete S. Moscoso, PhD, PA is a psychologist and currently a Stress Research Faculty at the University of South Florida, where he provides a six-week training program on Mindfulness Meditation to breast cancer patients, as part of a series of clinical trials aimed to explore the effects of mindfulness meditation training on the immune and endocrine systems.

Rajendra Kadel, MS is a PhD candidate of Biostatics at the University of South Florida's College of Public Health. His primary area of research includes modeling zero-inflated ordered categorical longitudinal data in the specific area of social and behavioral health studies. In addition his research interests include survival analysis and micro-array analysis of gene expressions of cancer patients.

Nancy Le, BS was a former research associate that assisted with the recruitment, orientation and consent processes for the clinical trial, as well as daily implementation of the study realted activities.

Loretta Loftus, MD, MBA is a medical oncologist and Senior Member of the Breast Program at H. Lee Moffitt's Cancer Center and Research Institute's Department of Women's Oncology. Dr Loftus is also a Professor of Medicine at the Unveristy of South Florida's College of Medicine. Her clinical and research area of interests are in Breast Cancer Risk Reduction and Prevention, Ductal Carcinoma in Situ of the Breast, and Bisphosphanate Therapy and Breast Cancer.

Craig W. Stevens, MD, PhD is the Chair and Senior Member in the Department of Radiation Oncology at H. Lee Moffitt's Cancer Center and Research Institute. Dr Steven's research focus on Mesothelioma, lung cancer, radiation treatment planning for lung cancer, predicting tumor/normal tissue response to radiation, and DNA repair.

Mokenge P. Malafa, MD, FACS is a surgical oncologist and Chair of the Department of Gastrointestinal Oncology and Program Leader of the Gastrointestinal Tumor Program at the H. Lee Moffitt's Cancer Center and Research Institute. Dr Malafa's clincal and research areas of interest include surgical management of GI malignancies with particular interest in complex pancreatic, liver and bile duct tumors; translational research in the development of bioactive vitamin E compounds for cancer prevention and therapy.

Melissa Molinari Shelton, PhD, RN is an Assistant Professor and Director of the Nursing Education Master's Concentration at the University of South Florida's College of Nursing. Her research focuses on stress and immune markers in pregnancy as a means of predicting adverse pregnancy outcomes.