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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

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Abstract

Objectives: This study investigated the relationships between a mindfulness-based stress reduction meditation program for early stage breast and prostate cancer patients and quality of life, mood states, stress symptoms, and levels of cortisol, dehydroepiandrosterone-sulfate (DHEAS) and melatonin.

Methods: Fifty-nine patients with breast cancer and 10 with prostate cancer enrolled in an eight-week Mindfulness-Based Stress Reduction (MBSR) program that incorporated relaxation, meditation, gentle yoga, and daily home practice. Demographic and health behavior variables, quality of life, mood, stress, and the hormone measures of salivary cortisol (assessed three times/day), plasma DHEAS, and salivary melatonin were assessed pre- and post-intervention.

Results: Fifty-eight and 42 patients were assessed pre- and post-intervention, respectively. Significant improvements were seen in overall quality of life, symptoms of stress, and sleep quality, but these improvements were not significantly correlated with the degree of program

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attendance or minutes of home practice. No significant improvements were seen in mood disturbance. Improvements in quality of life were associated with decreases in afternoon cortisol levels, but not with morning or evening levels. Changes in stress symptoms or mood were not related to changes in hormone levels. Approximately 40% of the sample demonstrated abnormal cortisol secretion patterns both pre- and post-intervention, but within that group patterns shifted from "inverted-V-shaped" patterns towards more "V-shaped" patterns of secretion. No overall changes in DHEAS or melatonin were found, but nonsignificant shifts in DHEAS patterns were consistent with healthier profiles for both men and women.

Conclusions: MBSR program enrollment was associated with enhanced quality of life and decreased stress symptoms in breast and prostate cancer patients, and resulted in possibly beneficial changes in hypothalamic-pituitary-adrenal (HPA) axis functioning. These pilot data represent a preliminary investigation of the relationships between MBSR program participation and hormone levels, highlighting the need for better-controlled studies in this area.

Keywords: Psychoneuroendocrinology; Cortisol; DHEAS; Melatonin; Meditation; Cancer; Stress; Quality of life; MSBR

1. Introduction

Recently, there has been a growth of clinical treatment and wellness programs based on mindfulness meditation and yoga modeled after the Mindfulness-Based Stress Reduction (MBSR) program of Jon Kabat-Zinn and colleagues at the Stress Reduction Clinic of the University of Massachusetts Medical Centre (Kabat-Zinn, 1990). Since their initial inception in 1979, there are now over 240 such programs across North America.

MBSR is rooted in the contemplative spiritual traditions in which the experience of conscious awareness is actively cultivated. Within a framework of non-judging, acceptance, and patience, meditative practice often focuses awareness on one's own breathing. Typically, this leads to a state of relaxation and alert observant detachment. The body of research investigating MBSR's efficacy for the treatment of health problems has also grown. Studies have shown its efficacy for problems as various as chronic pain (Kabat-Zinn, 1982; Kabat-Zinn et al., 1987), anxiety disorders (Kabat-Zinn et al., 1992; Miller et al., 1995), fibromyalgia (Kaplan et al., 1993; Singh et al., 1998), epilepsy (Deepak et al., 1994), psoriasis (Kabat-Zinn et al., 1998), and hypertension (Schneider et al., 1995). Enhancement of health-related quality of life with improved vitality, less bodily pain, fewer role limitations caused by physical health, greater social functioning, and decreased anxiety and depression have been shown recently in a group of mixed diagnosis medical patients (Reibel et al., 2001).

Considering the high degree of emotional distress following receipt of a cancer diagnosis (Strain, 1998; Derogatis et al., 1983; Zabora et al., 1997), and the efficacy of MBSR in other medical populations, it seemed logical to offer the MBSR program to cancer patients. Indeed, within the population of cancer patients, there is a growing interest in mind–body medicine and complementary and alternative therapies, as well as a desire to be proactive and take initiative in personal care (Cassileth and Chap-

man, 1998; Ernst and Cassileth, 1998). Thus, the MBSR program provides not only an efficacious treatment for distress, but fits with patients' own framework of positive health behavior. Our initial work with MBSR showed substantial improvements in symptoms of stress and mood disturbance in a randomized controlled trial of a mixed group of cancer patients (Speca et al., 2000), which were maintained six months later (Carlson et al., 2001). Another report of results on immune system parameters from the current study is in press (Carlson et al., in press). Here, we focus on the effects of the program on hormone levels.

Cortisol, the primary stress hormone secreted from the adrenals, is known to have immunosuppressive effects (for reviews, see Andersen et al., 1994; Cohen and Williamson, 1991; Spiegel et al., 1998) and is largely responsible for the downregulation of immune function as a result of stress. Its hypersecretion may also result in depressed mood (Sikes and Lasley, 1989; Wolkowitz, 1994). Additionally, cortisol levels have been reported to be elevated in breast cancer patients both prior to and following treatment (Aragona et al., 1996; van der Pompe et al., 1997; McEwen and Sapolsky, 1995). Abnormal patterns of cortisol secretion have also been reported in up to 75% of a sample of metastatic breast and ovarian cancer patients (Touitou et al., 1996). The slope of the rate of change of cortisol levels throughout the day was associated with survival time in a group of women with metastatic breast cancer, with those women who displayed less variation in cortisol levels, expressed as a flatter slope, experiencing earlier mortality (Sephton et al., 2000). This relationship held even when other prognostic medical variables were taken into account. The authors speculate that these abnormal circadian rhythms of cortisol secretion represent compromised hypothalamic–pituitary–adrenal (HPA) axis functioning, which may be responsible for the earlier mortality. Indeed, other studies have found that circadian abnormalities had prognostic value in predicting initial occurrences of breast cancer (Ticher et al., 1996), as well as associations with later stages of cancer development and with other prognostic indicators (Mormont and Levi, 1997; Touitou et al., 1996).

Meditation has been shown to decrease cortisol levels in populations of healthy volunteers (MacLean et al., 1994; Sudsuang et al., 1991), but the effect of meditation training or the MBSR program on cortisol levels has not previously been evaluated in people with cancer. However, there has been some investigation of the effects of other types of psychosocial intervention on cortisol levels in cancer patients. One study of a 10-week behavioral intervention for early stage breast cancer patients combined relaxation techniques, information about the mind–body connection, health education, and coping skills (Schedlowski et al., 1994). Decreases in cortisol levels in the intervention compared to the control group were seen within two weeks, and these differences were maintained at the end of the intervention. However, women were not randomly assigned to groups, and plasma samples of cortisol were collected only in the evenings. A randomized trial of an experiential–existential therapy intervention including relaxation, emotional self-disclosure, and social support provided to later stage breast cancer patients reported decreases in levels of cortisol post-intervention in the treatment group, but only for those who had high levels of cortisol at the start of the program (van der Pompe et al., 1997). Again, only one measure

of plasma cortisol was taken at each test time, and in this case the time of day was not specified and presumably not controlled. Another study that randomly assigned women with early stage breast cancer to a post-surgery 10-week cognitive-behavioral stress management intervention found decreased cortisol levels that were related to increases in the ability to find positive benefits of the breast cancer experience (Cruess et al., 2000). As in the other studies, one sample of plasma cortisol was obtained at each assessment period, at 18:00 h in this case. Improving on these designs, in the current study, cortisol was assessed at three time periods both pre- and post-intervention. Salivary cortisol measurement was used, as it is more convenient for multiple daily assessment, and has been shown to accurately reflect blood levels (Kirschbaum and Hellhammer, 1994). The method of using cotton collection swabs has also been shown not to affect the validity of cortisol immunoassays (Shirtcliff et al., 2001)

Dehydroepiandrosterone (DHEA) and its sulfate (DHEAS), too, are adrenal hormones, androgens that have antiglucocorticoid properties on cells of the immune system (Blauer et al., 1991). DHEAS is more commonly measured than DHEA due to its much higher blood levels, long half-life, and most importantly, its absence of diurnal variation, making it possible to take only one blood sample and attain an accurate reading regardless of the time of day (Hornsby, 1995). DHEAS is the most abundant product of the adrenal gland and has been identified as the most prevalent steroid hormones in the brains of both rats and humans, where it was found upon postmortem analysis at levels many times higher than in the plasma (Majewska, 1995), although the CSF levels of DHEAS in humans were reported as much lower than those in the blood (Guazzo et al., 1996). In both men and women, DHEAS is derived almost exclusively from the adrenal gland and shows tremendous variation throughout the lifespan and between individuals, with systemic age-related decreases (Vermeulen, 1995). Higher levels of DHEAS have been associated with enhanced immune function and mood in humans (Morales et al., 1994), although not all studies have found lower DHEAS levels in depressed patients (Heuser et al., 1998; Wolkowitz et al., 1997; Morales et al., 1994). A study of healthy long-term meditation practitioners found higher levels of DHEAS and lower levels of cortisol compared to healthy controls (Walton et al., 1995), and in the women practising meditation, cortisol correlated inversely, and DHEAS directly, with months of meditation practice. Another study found higher DHEAS in meditators compared to non-meditators in all age groups for women, but only in the older men, suggesting a modification of the age-related decreases in DHEAS for males (Glaser et al., 1992). In terms of intervention effects, in a group of HIV positive men who participated in a 10-week cognitive-behavioral stress reduction intervention, the ratio of cortisol/DHEAS increased, and was associated with changes in mood disturbance over the course of the intervention (Cruess et al., 1999). DHEAS measurement in the current study was done via serum, since only one sample was required.

The pineal hormone melatonin has been implicated recently in the development and treatment of many types of cancers (Kanno et al., 1997; Esterling et al., 1996). Animal research has shown it to be immune enhancing, increasing T lymphocyte proliferation and NK cell response to the mitogen concanavalin (Liebmann et al.,

1997). Melatonin also has oncostatic actions, suppressing tumor growth and even shrinking the size of tumors in vitro (Cos et al., 1998). In humans, a series of clinical trials using melatonin in conjunction with standard treatment found superior survival response in patients with advanced cancer receiving adjuvant melatonin (Lissoni et al., 1999a), and higher tolerance of standard chemotherapy regimes (Lissoni et al., 1999b; Lissoni et al., 1997). A recent large review in the Journal of Clinical Oncology concluded that converging evidence points to antioxidant and oncostatic actions of melatonin and provides a rationale for large transnational research-based clinical trials of melatonin therapy for a wide variety of cancers (Vijayalaxmi et al., 2002). Considering this growing body of evidence implicating melatonin as a potentially important factor in carcinogenesis, the demonstration in healthy people that consistent meditators produced higher levels of melatonin after a night-time meditation session compared to a control night (Tooley et al., 2000; Henderson, 1989), and that meditation practice in breast cancer patients was effective in increasing melatonin levels (Massion et al., 1995), is provocative. Melatonin was measured in this study via salivary assays. Studies have shown very high correlations between plasma and salivary levels of melatonin, using cotton saliva collection techniques (Voultsios et al., 1997; Laakso et al., 1990; McIntyre et al., 1987). The convergence of this endocrinological research suggests that the measurement of cortisol, DHEAS, and melatonin may be important to understand the mechanisms underlying the physiological effects of these psychosocial interventions.

This paper reports the results of pre–post-intervention study of an eight-week MBSR intervention provided to breast and prostate cancer patients. We focused on breast and prostate patients because these two cancers have similar good prognoses in the early disease stages, and a similar, although often differently expressed, degree of physical and psychological impairment (DeFlorio and Masie, 1995; Keller and Henrich, 1999; Riska and Ettorre, 1999). Both cancers are also often hormonally dependent, and thought to be responsive to psychosocial intervention. In addition, breast and prostate cancer are the most prevalent carcinomas reported today in women and men, respectively (National Cancer Institute of Canada, 2001). The outcome variables of quality of life, stress symptoms, mood, and the hormonal measures of cortisol, DHEAS, and melatonin are reported. Results of the same trial on immune function are currently in press (Carlson et al., in press).

2. Methods

2.1. Subjects

Patients were eligible to participate in the study if they met the following inclusion criteria: (1) age 18 years or older; (2) a diagnosis of Stage 0, I, or II breast or early stage (localized to the prostate) prostate cancer at any time in the past (using standardized TNM diagnostic criteria); and (3) a minimum of three months since surgery (mastectomy/lumpectomy/prostatectomy/cryotherapy). Exclusion criteria were: (1) treatment with chemotherapy, radiation therapy, or hormone therapy

(except tamoxifen or goserelin) currently or within the past three months; (2) a concurrent DSM-IV Axis I mood, anxiety, or psychotic disorder (not in full or partial remission); (3) a concurrent autoimmune disorder; and (4) past participation in an MBSR group. Psychiatric diagnoses were determined by the first author (a clinical psychologist) during the initial interview based on the Structured Clinical Interview for DSM-IV (SCID) mood, anxiety, and psychotic disorders modules. Medical conditions and medications were determined using a Medical History Questionnaire designed for this study. Charts were reviewed to determine cancer-related diagnoses and treatments.

A total of 59 breast and prostate cancer patients were enrolled in the study. One individual did not complete the time 1 measures. Sixteen individuals did not complete the time 2 measures, and of these, seven did not complete the intervention itself: four due to work demands, two due to scheduling difficulties, and one due to lack of interest. Of the other nine subjects who participated in the intervention but did not complete time 2 measures, most (six) had problems with scheduling, as the assessments had to take place early in the morning. One had to work early mornings, and two had problems finding a drive to the centre at that time. As such, data from 42 individuals were available for the pre–post analyses.

2.2. Instruments

2.2.1. Demographics and medical history form

Demographic information including age, education, marital status, occupation, and current employment status was obtained on a form created for this study. Medical history including type of illness, dates of diagnosis, and types of treatments was collected. Areas specifically assessed included heart disease, vascular disorders, autoimmune disorders, epilepsy, and psychiatric disorders. All current medications were recorded.

2.2.2. Health behaviors form

Health behaviors that could potentially affect the immune and/or endocrine systems were recorded, including amount of coffee, tea, and caffeinated soft-drink consumption (servings/week), alcohol consumption (servings/week), smoking (cigarettes/day), exercise (times/week), average hours of sleep per night, self-rated quality of sleep (poor, adequate, good), and self-rated quality of diet (poor, adequate, good).

2.2.3. Weekly meditation form

This form collected daily information on minutes spent in home practice of mediation and yoga from each participant and was collected each week during class.

2.2.4. European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) (Aaronson et al., 1993)

This 30-item quality of life questionnaire includes five functional domains of quality of life: physical, role, emotional, cognitive, and social function, and two items

that assess global quality of life. It has become the gold-standard of QL assessment in clinical trials in both Europe and North America, with much normative data available for comparison (Aaronson et al., 1993; Aaronson et al., 1991). Only the global QL score will be reported in this paper.

2.2.5. Profile of mood states (POMS) (McNair et al., 1971)

The POMS is a 65-item scale which assesses six affective dimensions. It has been widely used in the assessment of mood changes resulting from a variety of interventions due to its responsiveness, and has been used extensively with cancer populations (Cassileth et al., 1985). The Total Mood Disturbance (TMD) score will be reported here.

2.2.6. Symptoms of Stress Inventory (SOSI) (Leckie and Thompson, 1979)

The SOSI was designed to measure physical, psychological, and behavioral responses to stressful situations. The respondent is instructed to rate the frequency with which they experience various stress-related symptoms on a 5-point scale ranging from never to frequently during the past week. Ten subscale scores can be calculated, but only the total stress score will be reported here. Readers are directed to our paper currently in press for details of the psychological measures' subscales (Carlson et al., in press)

2.3. Procedures

2.3.1. Recruitment

Patients were recruited from the Tom Baker Cancer Centre. Patients were primarily recruited with pamphlets and posters around the centre, in each of the breast and prostate clinic areas, and were able to self-refer. With the approval and cooperation of the breast tumor group staff, eligible breast cancer patients were also invited to participate in the study and given a summary of the research during their clinic visit, or were phoned and invited to participate. If patients were interested in participating, their name was placed on a waiting list administered by the research assistant.

2.3.2. Testing

Once 15 patients accrued on the waiting list using the recruitment strategy detailed above, they were scheduled for an individual interview with the principal investigator (PI) during the week prior to the start of the group to further explain the study, determine eligibility, and provide informed consent. During this interview, the Medical History Form, Health Behaviors Form, and the SCID were completed by the PI. A maximum of three patients were assessed daily between 08:00 and 10:00 h, to control as much as possible for time of day, and the blood samples were all taken before 10:00 h. Appointments were set for 08:00, 08:30, and 09:00 h. After the approximately 30-min initial interview with the PI, subjects proceed to the research assistant (RA), who drew a blood sample for DHEAS levels. The samples were sent to the laboratory on the same day by 10:00 h. The patients then completed the

assessment battery of questionnaires, supervised by the RA, who clarified instructions and answered any questions, which took approximately one-half hour.

For the cortisol and melatonin assays, participants were instructed to collect salivary samples at three times on the day prior to the first group session: 08:00, 14:00, and 20:00 h, using cotton saliva swabs (Sali-Savers®, ALPCO Diagnostics, Windham, NH) packaged with a cotton swab and plastic tube with sealing cap. They were instructed in detail how to collect and store the samples, and required to bring the three samples with them to the first session on the day following saliva sampling. Any variation in the collection times was noted when patients delivered the completed samples, and if variation was greater than 1 h earlier or later than the designated times, all three samples were re-taken later that same week. The sample for the melatonin assay was taken from the 14:00 h saliva collection, and cortisol levels were measured at each collection time. In retrospect, it would have been more theoretically logical to measure melatonin from the later sample, given its circadian rhythm of increasing throughout the day to peak during sleep, but the initial decision was guided by practical concerns of obtaining a large enough sample to perform the assay.

Beginning the week after the completion of the intervention, the same procedure was followed as prior to the intervention, with the patients returning to the hospital to have blood drawn and complete the questionnaires. For the salivary assays, participants were given the cotton swabs on the last day of the intervention, and asked to provide saliva samples on the day preceding their scheduled appointment, bringing the refrigerated swabs with them to the post-intervention assessment. They completed the Health Behavior Form without the assistance of the PI for this assessment. All participants were assessed within two weeks of completion of the intervention (three each morning).

2.3.3. Intervention

Details of the intervention, including objectives, structure, components, and content, have previously been described (Speca et al., 2000). Our program was modeled after the Mindfulness-Based Stress Reduction program at the Stress Reduction and Relaxation Clinic, Massachusetts Medical Center, as described by Kabat-Zinn (1990). A few changes have been made to the program since our last publication in order to make our program more consistent with the Kabat-Zinn MBSR format. The intervention was provided over the course of eight (rather than seven) weekly, 90-min group sessions with a maximum of 15 participants each, and we added in a 3-h silent retreat on the Saturday between weeks six and seven. The Saturday retreat combined participants from all of our ongoing MBSR groups, and usually consisted of about 40 participants. The program consisted of three primary components: (1) theoretical material related to mindfulness, relaxation, meditation, yoga, and the body–mind connection, (2) experiential practice of meditation and yoga during the group meetings and home-based practice, and (3) group process focused on solving problems concerning impediments to effective practice, practical day to day applications of mindfulness, and supportive interaction between group members.

In addition, we produced and provided patients with a 52-page booklet containing

information pertinent to each week's instruction, including a bibliography for those wishing to pursue relevant themes in greater depth, and an audio tape with a sensate focused body scan meditation on one side and a guided sitting meditation on the other. Patients were instructed to practise daily. Didactic, inductive, and experiential modes of learning were employed to implement the intervention and convey the informational content.

2.3.4. Hormone assays

Cortisol and melatonin levels present in saliva were assayed using solid-phase ELISAs according to the manufacturer's instructions (ALPCO Diagnostics, Widham, NH). Saliva was collected at 08:00, 14:00 and 20:00 h using Sali-Savers (ALPCO Diagnostics, Widham, NH) and stored at 4 °C overnight. Saliva was extracted from the Sali-Savers by centrifugation at 300 × *g* for 10 min. The 08:00 and 20:00 h samples were immediately frozen and subsequently stored at −20 °C. Two hundred microlitres of saliva from the 14:00 h sample were removed for melatonin assays, and the remainder of the sample was stored at −20 °C. The 200 μl of saliva to be used in the melatonin assay were pre-treated for 10 min with 0.25 N NaOH according to the manufacturer's instructions. After 10 min, the solution was neutralized with an equivalent concentration of HCl and then stored at −20 °C.

DHEAS was assayed from serum using solid-phase ELISA according to the manufacturer's instructions (ALPCO Diagnostics, Widham, NH). Blood was collected in serum tubes (VWR, Mississagua, ON), allowed to clot and then centrifuged for 10 min at 500 × *g*. The serum was removed and stored at −20 °C.

2.4. Data analysis

All data analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 11.0, for the PC in Windows NT.

The demographic, medical history, and health behavior variables were described pre-intervention for the complete sample using frequency and descriptive statistics. The cortisol data were normally distributed so no transformations were necessary. Mean daily cortisol level pre- and post-intervention was calculated by summing the three daily measures and calculating a mean for each person. Because previous work had shown the rate of change of cortisol levels throughout the day to be a potentially important measure (Turner-Cobb et al., 2000; Sephton et al., 2000), the slope of diurnal change in salivary cortisol levels was calculated as an estimate of diurnal variability for each patient both pre- and post-intervention. The cortisol slope was calculated by regressing the cortisol values as the DV on the time of day that each sample was collected. Patients were classified as having one of four types of cortisol slope profiles at each time period: (1) normal, which represented a continual decrease across the assessment periods from morning to evening; (2) up then down (inverted V-shape), an increase from morning to afternoon followed by a decrease from afternoon to evening; (3) down then up (V-shape), a decrease from morning to afternoon followed by an increase from afternoon to evening; and (4) continual up, continually increasing levels throughout the day. Following the procedures used by Touitou et

al. (1996), the latter three groups were collapsed and referred to as the "abnormal" profile group, and compared to the "normal" group on demographic, cancer history, and psychological variables using independent samples *t*-tests.

The mean cortisol slopes were compared pre- and post-intervention using the Chow test, which determines whether the slopes of two regression equations are different. The error sums of squares of each of the individual slopes (pre- and post-) were summed and divided into the pooled error sums of squares resulting from performing the regression on the pooled pre- and post-data (all of which were adjusted for degrees of freedom). The resultant ratio (*Q*-statistic) was compared to the *F* value for the overall regression, and if it was smaller than this value, the null hypothesis of equality of the slopes was accepted. The ratio of cortisol/DHEAS was calculated at each time by dividing each patient's mean daily cortisol value by their 08:00 h DHEAS value, then multiplied by 100 to express cortisol as a percentage of DHEAS. Both were measured in the same units so no metric conversion was required.

All variables were tested for normalcy of the distributions. Melatonin levels were positively skewed (skewness >2.0) at both test times, and were thus transformed using the natural-log transformation prior to analyses. The other hormone levels at each test time were normally distributed. Of the health behavior and demographic continuous variables, only alcohol servings/week was significantly positively skewed at both time periods (skewness >2.0). On the EORTC, SOSI, and POMS, all variables were normal. Therefore, the natural-log transformation was applied to the skewed variables, at both time periods, which resulted in normal distributions for all variables. These transformed variables were subsequently used in all calculations. Non-transformed values are reported in the tables.

To evaluate the effects of the intervention, paired-samples *t*-tests were used to compare pre- and post-intervention scores on the health behaviors, EORTC, POMS, and SOSI subscales, and total scores, as well as on the hormone levels. To analyze change across the two time points, change scores were calculated on each subscale and total score, and on the hormone variables by subtracting the time 1 values from the time 2 values for each participant.

To investigate whether levels of hormones or changes in hormonal measures were related to changes in quality of life, mood, or stress symptoms, Pearson product–moment correlations were performed between the hormone levels and psychological scores at each time period, and between change scores on each of the hormone measures and each of the overall total scores of the psychological measures. Similar correlations were also performed between class attendance, home practice, and both psychological and hormonal change scores. To determine if health behaviors or other therapies influenced initial hormone parameters, multiple regressions were performed with each of the time 1 hormone parameters as the dependant variable, first entering demographic and disease-related variables, followed by caffeine and alcohol consumption, exercise, sleep hours, sleep quality, and diet quality.

3. Results

3.1. Subjects

Demographic characteristics and health behaviors of participants at time 1 are presented in Table 1. Most participants were 50 years of age or older, mean 54.5 years, SD 10.9 years. Most ($n = 42$) were married or co-habiting at the time of study entry. Participants were generally well-educated, with a mean of 14.7 years of formal education. They had been diagnosed with cancer a median of 1.1 years previously (range 3 months–20 years). Six participants were greater than five years post-diagnosis. Just over two-thirds had Stage II cancer (64.4%), with the remainder having a diagnosis of Stage I. Data were collected on the type and timing of the last treatment each patient had received. Radiation was the last treatment for 28 patients, chemotherapy for seven, hormones for five, nine patients had no treatment at all, and the type of last treatment was unavailable for 10 patients. The median time for

Table 1
Demographic characteristics

	Pre-intervention (*N* (%))			Post-intervention (*N* (%))		
	Overall	Women	Men	Overall	Women	Men
Stage of cancer						
1	21/59 (35.6)	19 (38.8)	2 (20.0)	15/42 (34.9)	13 (38.2)	2 (22.2)
2	38/59 (64.4)	30 (61.2)	8 (80.0)	28/42 (65.1)	21 (61.8)	7 (77.8)
Sleep quality						
Poor	24/58 (41.4)	22 (45.8)	2 (20.0)	6/32 (19.4)*	6 (26.1)	0
Adequate	20/58 (34.5)	15 (31.3)	5 (50.0)	13.32 (41.9)*	8 (34.8)	5 (55.6)
Good	14/58 (24.1)	11 (22.9)	3 (30.0)	12/32 (38.7)*	9 (39.1)	4 (44.4)
Diet quality						
Poor	5/58 (8.6)	5 (10.4)	0	0/32	0	0
Adequate	14/58 (24.1)	11 (22.9)	3 (30.0)	8/32 (25.8)	7 (30.4)	1 (11.1)
Good	39/58 (67.2)	32 (66.7)	7 (70.0)	23/32 (74.2)	16 (69.6)	8 (88.9)
Smoking status: nonsmokers	52/58 (88.1)	42 (87.5)	10 (100)	41/42 (97.7)	32 (97.0)	9 (100)
	Mean	SD		Mean	SD	
Cigarettes/day smokers (pre *n*=6; post *n*=1)	14.8	9.7		25.0	0	
Alcohol (servings/week)	1.8	3.4		1.8	3.1	
Caffeine (servings/week)	17.8	15.2		17.0*	14.4	
Exercise (times/week)	4.0	2.5		4.8*	2.3	
Sleep (hours/night)	7.1	1.5		7.6	1.4	

* Indicates improvement pre- to post-intervention, $p < 0.05$.

completion of last treatment was six months previously, with a range of 3 months–20 years.

Sixteen of the women were currently taking tamoxifen and continued to do so through the course of the study. Tamoxifen treatment has been associated with elevated cortisol levels in some studies (van der Pompe et al., 1996; Kailajarvi et al., 2000), but it had no effect on DHEAS levels (Lonning et al., 1995). Two of the men were taking goserelin (Zolodex), a gonadotrophic releasing hormone (GnRH) analog. No differences were found in initial hormone levels when those taking either tamoxifen or goserelin were compared to the rest of the participants within each sex. Fourteen patients were also taking antidepressant medication, both at time 1 and time 2, with no changes in dosage occurring. Patients had all started the medication at least three months prior to participation in the program. Medications used included: sertrailne (Zoloft, three patients), venlafaxine (Effexor, three), paroxetine (Paxil, two), fluoxetine (Prozac, two), and one each of amitriptyline (Elavil), buproprion (Wellbutrin), nefazodone (Serzone), and fluvoxamine (Luvox). When patients using antidepressants were compared to the others on initial hormone levels, values were very similar with no significant differences.

Of the 42 patients who completed the time 2 measures, 33 had breast cancer and nine had prostate cancer. Fifteen patients had Stage I cancers and 28 patients had Stage II cancers. Fourteen of the tamoxifen/goserelin users and 11 of the antidepressant users provided time 2 data. Chi-square and *t*-tests compared the 17 patients with incomplete data with the rest of the sample on all demographic, medical, and psychological variables collected at baseline, or pre-intervention. Participants with complete data were more likely to be married or co-habitating rather than single, divorced, or widowed, $\chi^2(1) = 9.20$, $p < 0.005$. No other differences on the demographic or medical variables were found. Non-completers had higher scores than completers on several of the baseline Profile of Mood States subscales: depression, $t(56) = 3.65$, $p < 0.001$; anger, $t(56) = 2.87$, $p < 0.01$, and confusion, $t(56) = 2.17$, $p < 0.05$. Such differences are consistent with other research, which has found that cancer patients experiencing emotional and cognitive disturbance appear less likely to comply with medical treatment regimens and to participate in research (Spiegel, 1996).

3.2. Compliance

The 59 patients in this study attended a median of eight of a possible nine sessions over the eight weeks (range 1–9). Seven participants attended four or fewer session, while the majority (46 patients, 78%) attended seven or more sessions. They also practised at home as instructed, reporting an average of 24 min/day of meditation and 13 min/day of yoga over the course of the eight weeks.

3.3. Health behaviors

Health behavior data were available pre-intervention for 58 of the participants. The initial sample reported consumption of about 2.5 cups of caffeinated beverages each day. They drank a small amount of alcohol (1.8 drinks/week), and exercised

on average four times a week. They were sleeping an average of 7.1 h per night, but many (40.7%) reported sleep of poor quality. A third of the sample reported adequate sleep, while less than a quarter reported having a good quality of sleep. One-quarter of the patients reported their diet quality as generally adequate, and two-thirds rated their diet as good quality. Only 12% of the sample were smokers, and of those they smoked an average of 15 cigarettes/day.

Post-data were available regarding health behavior for 31 of the 42 patients who completed the assessments. These missing data were due to a procedural oversight in that the participants of our first cohort were not asked to provide these data. However, paired-sample *t*-tests and chi-squared non-parametric tests investigating changes in health behaviors for those for whom we had pre–post data found that sleep quality improved over the course of the intervention ($\chi^2 = 6.81$, $p < 0.05$), with 80% of the sample reporting adequate or good sleep on the post-assessment. Caffeine servings per week decreased significantly ($t(31) = 2.38$, $p < 0.05$), and exercise increased ($t(30) = -2.10$, $p < 0.05$).

3.4. Psychological tests

The psychological effects of the program on the EORTC, POMS, and SOSI subscale scores are fully described in our other paper (Carlson et al., in press). Here, we report only global scores, which are also presented in Table 2. The raw scores for the entire group are presented pre- and post-intervention, and change scores for those who completed both assessments are also presented. The calculations were also made excluding those taking tamoxifen or goserelin, without those who were taking antidepressants, and without those who attended five or fewer sessions.

3.5. Quality of life

In the sample of 42 patients who completed both the pre- and post-intervention questionnaires, changes were seen on the overall global quality of life score ($t = -2.23$, $p < 0.05$), indicating greater overall quality of life. None of the correlations between quality of life global change scores and home practice or attendance were significant at the $p < 0.05$ level.

3.6. Mood scores

There were no significant changes in any of the POMS scores over the course of the intervention. The TMD score at time 1 was 15.93, which is already quite low, indicating minimal mood disturbance. The change in TMD scores represented a 13% reduction of overall mood disturbance for these participants.

None of the correlations between overall mood disturbance scores and home practice or attendance were significant at the $p < 0.05$ level.

Table 2
QL, mood, and stress scores

	Pre-intervention		Post-intervention		Change score	
	Mean	SD	Mean	SD	Mean	SD
EORTC global QL						
Overall sample	63.79 ($n = 58$)	16.71	71.71 ($n = 43$)	14.68	5.56* ($n = 42$)	16.12
Without those taking hormones	62.40 ($n = 41$)	14.21	70.40 ($n = 29$)	15.20	5.46* ($n = 29$)	14.31
Without those taking antidepressants	65.72 ($n = 44$)	16.30	71.61 ($n = 32$)	15.53	3.23 ($n = 31$)	14.01
Without those who attended ≤5 sessions	65.36 ($n = 51$)	16.53	71.14 ($n = 41$)	14.33	3.96 ($n = 40$)	13.99
POMS total mood disturbance						
Overall sample	22.62 ($n = 58$)	33.16	13.65 ($n = 43$)	32.66	−2.07 ($n = 42$)	25.02
Without those taking hormones	21.39 ($n = 41$)	31.71	13.97 ($n = 29$)	33.56	1.41 ($n = 29$)	26.51
Without those taking antidepressants	18.48 ($n = 44$)	30.14	14.44 ($n = 32$)	35.60	1.35 ($n = 31$)	25.76
Without those who attended ≤5 sessions	21.02 ($n = 51$)	33.68	14.00 ($n = 41$)	33.39	0.23 ($n = 40$)	23.33
SOSI total stress score						
Overall sample	88.43 ($n = 58$)	52.01	66.12 ($n = 43$)	42.10	−15.26** ($n = 42$)	29.73
Without those taking hormones	89.29 ($n = 41$)	55.69	70.03 ($n = 29$)	46.63	−10.27 ($n = 29$)	29.19
Without those taking antidepressants	84.50 ($n = 44$)	46.87	67.06 ($n = 32$)	42.61	−11.51 ($n = 31$)	28.03
Without those who attended ≤5 sessions	87.43 ($n = 51$)	53.08	65.02 ($n = 41$)	42.18	−13.30** ($n = 40$)	28.52

* Significant change pre- to post-intervention using paired t-tests, $p < 0.05$.
** Significant change pre- to post-intervention using paired t-tests, $p < 0.01$.

3.7. Stress scores

The mean SOSI total score showed a significant reduction ($t = 3.23$, $p < 0.01$), representing a decrease in stress symptoms over the course of the intervention. These participants achieved a 19.3% mean reduction in total symptoms of stress as measured by the SOSI upon completion of the intervention.

None of the correlations between stress change scores and home practice or attendance were significant at the $p < 0.05$ level.

3.8. Hormone levels

Hormone levels for all measures pre-intervention, post-intervention, and change scores are presented for the overall group and by sex in Table 3. Measures for those using or not using either tamoxifen or goserelin are presented in Table 4. Independent samples *t*-tests were used to compare the two groups on the measures and change

Table 3
Hormonal levels by sex

	Pre-intervention		Post-intervention		Change score	
Cortisol slope	Beta = −0.481		Beta = −0.511			
	Mean	SD	Mean	SD	Mean	SD
Mean daily cortisol (ng/ml)	6.34	2.77	6.13	2.03	−0.31	3.10
Men	7.95	3.69	7.67*	1.90	−0.85	4.68
Women	5.98	2.43	5.81	1.93	−0.20	2.72
08.00 Cortisol (ng/ml)	9.60	4.76	9.69	4.36	0.11	5.98
Men	12.87	6.80	12.53	5.93	−0.51	9.03
Women	8.90	3.97	9.04	3.71	0.26	5.16
14:00 Cortisol (ng/ml)	5.09	3.38	4.68	2.12	−0.57	3.15
Men	4.97	2.25	5.07	1.96	−0.30	1.86
Women	5.12	3.60	4.59	2.17	−0.49	2.99
20:00 Cortisol (ng/ml)	4.18	3.46	3.94	2.52	−0.25	4.01
Men	5.99	4.94	4.58	3.69	−1.63	6.43
Women	3.79	2.98	3.81	2.26	0.05	3.33
09:00 DHEAS (ng/ml)	817.76	642.37	840.19	663.19	15.36	493.74
Men	592.40	399.17	778.89	492.16	155.00	230.89
Women	863.76	675.27	852.73	697.04	−13.20	529.12
Cortisol/DHEAS ratio	1.78	2.43	1.70	2.32	0.00	2.14
Men	2.50	3.66	2.03	2.42	−0.70	2.03
Women	1.47	1.92	1.59	2.27	0.15	2.16
14:00 Melatonin (pg/ml)	8.62	15.52	6.52	9.10	−1.20	11.81
Men	14.83	22.24	3.04*	2.59	−3.98	8.27
Women	7.27	13.60	7.30	9.85	0.40	6.66

* Men different levels than women, $p < 0.05$.

Table 4
Hormone levels by tamoxifen/goserelin usage

	Pre-intervention		Post-intervention		Change score	
	Mean	SD	Mean	SD	Mean	SD
Mean daily cortisol (ng/ml)						
Users	6.24	2.06	6.69	2.17	0.27	2.59
Non-users	6.38	3.06	5.86	1.94	−0.60	3.32
08:00 Cortisol (ng/ml)						
Users	9.81	3.87	11.01	5.14	1.08	6.02
Non-users	9.51	5.14	9.06	3.87	−0.35	6.00
14:00 Cortisol (ng/ml)						
Users	5.27	2.67	5.01	1.34	−0.42	2.64
Non-users	5.01	3.67	4.53	2.41	−0.47	2.90
20:00 Cortisol (ng/ml)						
Users	3.62	2.53	3.97	3.03	0.13	2.34
Non-users	4.42	3.80	3.92	2.30	−0.43	4.56
09:00 DHEAS (ng/ml)						
Users	767.89	526.33	924.69	847.84	145.63	403.37
Non-users	839.66	692.09	803.65	579.19	−40.97	523.00
Cortisol/DHEAS ratio						
Users	1.87	3.05	1.63	2.02	−0.39	1.44
Non-users	1.56	1.96	1.68	2.42	0.19	2.41
14:00 Melatonin (pg/ml)						
Users	7.41	13.14	5.57	5.68	−0.71	8.18
Non-users	9.15	16.58	6.90	10.20	−0.31	6.74

No significant differences between users and non-users of tamoxifen or goserelin.

scores, and paired-samples *t*-tests evaluated the pre–post scores within only the group not taking these medications, as well as for the full sample.

3.9. Cortisol levels

The average daily mean of the three cortisol values did not change from pre- to post-intervention, with values of 6.34 and 6.13 ng/ml, respectively. Neither did the overall slope of the diurnal rate of change differ pre- to post-intervention, nor did any of the three assessment time period means. The only significant differences between the men and the women was that men had higher mean daily cortisol post-intervention than the women ($t = -2.49$, $p < 0.05$). The slope Beta values indicated an overall negative slope of cortisol values at both time periods. However, when the slope of the diurnal cortisol levels was assessed for each individual, the four distinct patterns emerged: (1) continually decreasing (58.9% of the sample); (2) inverted V-shape—up then down (17.9%), (3) V-shape—down then up (19.6%); and (4) continually increasing (3.6%). Because the numbers of patients in groups 2 and 4 were low, and following the classification procedure used by Touitou et al. (1996), patients were divided into “normal” and “abnormal” cortisol profile groups at each time period. At both time periods, approximately 58% of the sample demonstrated “normal”

profiles, while the other approximately 42% displayed one of the three "abnormal" profiles. However, people did shift between categories pre- to post-intervention. The most frequent switches occurred away from the "inverted-V" pattern and to the "V-shaped" pattern. This indicates that the pattern characterized by afternoon elevation of cortisol was less prevalent after the intervention.

When compared on demographic, cancer history, and psychological variables pre-intervention, the patients with normal profiles at the start of the study were not different from those with abnormal profiles on the variables of age, education, time since diagnosis, alcohol or caffeine consumption, exercise, or nightly hours of sleep. Those with abnormal patterns did show a trend to report more symptoms of stress, mood disturbance, and lower global QL scores. These results are presented in Table 5. However, even though the mean scores appear to be quite different, only the SOSI total scores were marginally statistically significantly different ($t = -1.78$, $p = 0.08$). Of note are the high standard deviations for the abnormal profile group, indicating significant variability and contributing to the lack of statistical significant differences between groups. Those with initially abnormal profiles also appear to have improved more on the SOSI, but these change scores of −11 vs. −22 points were not significantly different.

When patients were divided using a median split on mean daily cortisol levels into high and low initial cortisol level groups, and compared using independent samples *t*-tests on subsequent cortisol change scores, it was found that the change scores were significantly different, in that those with initially higher levels decreased over time on mean cortisol levels ($t = 4.43$, $p < 0.00l$), as well as on cortisol values at 08:00 h ($t = 3.55$, $p < 0.001$), 14:00 h ($t = 2.15$, $p < 0.05$), and 20:00 h ($t = 2.36$, $p < 0.05$), while the group with lower cortisol levels had overall *increased* values. This pattern of change suggests a "normalization" of mean cortisol levels for participants overall, with lower scores increasing and higher scores decreasing. It is also not

Table 5
Relationship of mood, stress, and QL scores to cortisol pattern

	POMS total score		SOSI total score		Global QL total score	
	Mean	SD	Mean	SD	Mean	SD
Time 1						
Normal pattern	18.45 ($n = 33$)	30.50	77.88	41.39	66.67	13.98
Abnormal pattern	30.41 ($n = 23$)	37.60	105.09	63.45	60.98	18.07
Time 2						
Normal pattern	17.79 ($n = 26$)	34.22	69.13	44.45	70.14	13.88
Abnormal pattern	9.94 ($n = 15$)	31.56	59.88	39.15	74.02	16.64
Change scores						
Normal pattern	−4.12 ($n = 26$)	27.26	−10.85	26.75	3.21	16.17
Abnormal pattern	2.29 ($n = 26$)	22.27	−21.84	35.06	8.93	16.17

surprising considering the statistical tendency of extreme scores to regress toward the mean over time.

None of the correlations between cortisol levels at time 2 or change scores, and home practice or attendance were significant.

3.10. DHEAS levels and cortisol/DHEAS ratio

DHEAS levels did not change significantly pre- to post-intervention, with values of 818 (SD = 642) and 840 (SD = 663) ng/ml, respectively. The range of values was from 68 to 3264 ng/ml. There were no significant differences between the men and the women. The ratio of cortisol/DHEAS similarly did not change over time. None of the correlations between DHEAS levels or the cortisol/DHEAS ratio, and change scores at time 2, home practice, or attendance were significant.

3.11. Melatonin levels

Melatonin levels similarly did not change significantly pre- to post-intervention, with values of 1.59 and 1.86 pg/ml, respectively. There were no significant differences between the men and the women. None of the correlations between melatonin levels at time 2 or melatonin change scores, and home practice or attendance were significant.

3.12. Relationships between psychological and hormonal variables

Correlations between hormone measures and psychological measures at time 1 were nonsignificant, indicating that scores on stress, quality of life, and mood were not related to initial levels of cortisol, DHEAS, or melatonin. At time 2, the same pattern was seen, in that none of the hormone levels were related to psychological measures after the program. Only the change score of cortisol at 14:00 h and the change in global quality of life score were significantly related ($r = -0.326$, $p < 0.05$), such that larger decreases in afternoon cortisol levels pre- to post-intervention were related to greater increases in global QL following the program. This relationship was not due to outliers, as the data were truncated such that any scores greater than 2 SD from the mean were assigned the value equivalent to 2 SD from the mean in that direction. Only two values had to be truncated in this manner.

3.13. Relationships between health behaviors and hormonal variables

Regression equations were performed using each of the time 1 hormone measures as the dependent variable, regressing the predictor variables of alcohol servings per week, caffeine servings per week, smoking status, exercise times per week, sleep hours per night, sleep quality, and diet quality in one block, after first entering the demographic and disease variables of age, years of education, cancer stage, and duration of illness as a block. Several equations were significant, including that for DHEAS ($F = 2.75$, $p < 0.01$) and the cortisol/DHEAS ratio ($F = 3.15$, $p < 0.0l$).

Greater age was related to lower values of DHEAS ($t = -4.01$, $p < 0.00l$) and a higher cortisol/DHEAS ratio ($t = 4.20$, $p < 0.00l$). Smoking status was also related to both DHEAS levels and the ratio, with smokers having lower levels of DHEAS (-2.63, $p < 0.05$), and a higher cortisol/DHEAS ratio ($t = 2.93$, $p < 0.0l$).

4. Discussion

The results of this pre–post-intervention study indicate that this eight-week mindfulness-based stress reduction program was effective in decreasing symptoms of stress and improving overall quality of life in this group of breast and prostate cancer patients. No change was seen on the POMS scores of these patients, which may be explained by the low level of initial mood disturbance. In fact, the initial level of total mood disturbance in this sample was similar to the post-intervention level of distress reported in our previous samples (Speca et al., 2000; Carlson et al., 2001). This low level of mood disturbance could be explained by the study inclusion criteria that patients be in early stage disease and at least three months post-treatment. The period of diagnosis and active treatment is often associated with greater distress, and since our previous group was very heterogeneous with respect to both type and stage of cancer, and treatment regimen, it is reasonable to see these differences. With such low initial levels of mood disturbance in the current sample creating a floor effect and with significant variance in scores, it would be difficult to attain statistically significant improvements. Consistent with the lower scores on the POMS, initial scores on the SOSI were somewhat lower in this group of patients compared to our previous study group, but still significantly higher than the post-intervention scores. However, the post-intervention scores were quite similar in both groups. This indicates that the end point for both groups was similar in terms of both stress symptoms and mood, but that the current group began with somewhat less distress.

Of note also was the finding that certain health behaviors changed over the course of the program, most notably sleep quality, which improved in many patients. Approximately one-third of the sample who provided post-intervention data reported poor sleep prior to the program, while less than 20% continued to report poor sleep quality after the program. The total number of hours of sleep increased by 1/2 h per night. This difference was not statistically significant. Improvements were also seen in exercise times/week, which increased from four to five, and servings of caffeine, which decreased from 18 to 17. Aerobic and weight training exercise has been associated with many quality of life and biological benefits for cancer patients (Courneya, 2001; Courneya and Friedenreich, 1999), and moderate exercise, including walking, household tasks, and occupational exercise, may reduce risk for the development of breast cancer (Friedenreich et al., 2001). Considering that one goal of the study was to encourage regular yoga exercises, it is heartening that the exercise frequency did appear to increase somewhat. Indeed, patients reported practising an average of 13 min of yoga and 24 min of meditation daily, very close to the targets we set of 45 min daily home practice.

The major methodological limitation of this study is the lack of a control or com-

parison group. It could be argued that the observed changes may have occurred spontaneously as part of the cancer recovery trajectory or healing. Another possibility is that stress and/or hormone levels could have been artifactually elevated prior to program participation due to the novelty of beginning a new treatment program. This possibility cannot be ruled out within this study design, and the results reported must necessarily be considered preliminary and hypothesis generating. However, one point that argues in favour of treatment effects is that the patients in this sample were an average of two years post-diagnosis, with a median time of about 14 months post, so it is unlikely that any significant return to normal hormone levels would still be occurring in this sample of patients. Another issue related to the non-specificity of the intervention is that even if the beneficial effects were due to the intervention and not natural history or recovery, the relative importance of the different components of the program cannot yet be ascertained. Whether the most effective components are the meditation, yoga, social support, group processes, professional attention, or other factors will have to await further "dismantling" studies of MBSR. In all likelihood, the most useful aspects vary from person to person depending on the individual's needs, background, and personality.

One further limitation of the study is the lack of correction for multiple comparisons, as the significance value applied was $\alpha = 0.05$. This was chosen primarily due to the exploratory and hypothesis-generating nature of the study, so the chances of making a Type I error (rejecting the null hypothesis of no treatment effect when it is in fact the case) are elevated. Therefore, the need for controlled clinical trials with a limited number of hypotheses in this area is evident.

The QL scores reported by this group represent quite high initial QL levels. Compared to a Swedish normative sample of the same age range whose average global QL score was 77 (Michelson et al., 2000), our patients scored an average global QL pre-intervention of 66. This is higher than other patient groups that have reported scores in the 50s (Aaronson et al., 1993). This may indicate that, similar to the floor effects seen in the POMS mood disturbance scores, our participants had relatively good QL prior to participation in the intervention, making it more difficult to incite enhancement of these already quite healthy levels.

Despite the beneficial effects associated with participation in the program on stress symptoms, quality of life, and sleep quality, no associated changes in hormone levels were observed in these patients. This is in contrast to other studies that have reported decreases in cortisol levels after stress management-type programs in breast cancer patients (Schedlowski et al., 1994; Cruess et al., 2000; van der Pompe et al., 1997), but only for those who had high levels of cortisol at the start of the program in the latter study. There were, in fact, no overall changes in cortisol levels in that study (van der Pompe et al., 1997). When we similarly divided our sample by initial mean daily cortisol level and compared the degree of change in mood, stress symptoms, QL, and subsequent cortisol levels, we found that indeed those people with initially elevated cortisol levels did show significant decreases in cortisol over time at each time point, compared to those with lower initial levels, who in fact displayed *increases* in their cortisol levels. This is interesting as it points to the possibility that the intervention had a regulatory effect on the participants, resulting perhaps in

normalization of the HPA axis functioning. However, this tempered effect also makes sense from a statistical perspective, taking into consideration regression towards the mean of more extreme values. That is, if a woman began the intervention with elevated cortisol levels, it would be more likely that woman would show decreases over the course of the intervention than would a woman who began the study with average or low levels. Thus, whether the changes observed were related to program participation or statistical artifact cannot be definitively stated.

This study also confirmed previous reports of a high percentage of breast cancer patients who displayed abnormal diurnal cortisol secretion patterns (Touitou et al., 1996). In this sample, approximately 40% of these early stage breast and prostate cancer patients displayed atypical patterns. This percentage was similar both pre- and post-intervention, but a shift did occur from more people displaying a pattern with elevated afternoon cortisol levels, to a sharper decrease after wakening associated with a lower afternoon level, and similar evening levels. The potential significance of this finding was highlighted by an association between decreases in the afternoon cortisol level and increases in overall global quality of life. Thus, those who showed greater declines in the afternoon cortisol level, without an elevation in evening levels, also improved more on quality of life. This measure may therefore be meaningful in terms of its relationship to quality of life.

Levels of DHEAS did not change over the course of the program. There was very large variation in the levels of DHEAS measured in our sample, which has similarly been reported by other researchers (Vermeulen, 1995), but the range in our sample was even broader than that reported by other investigators. Also replicated was the often reported finding of decreasing DHEAS levels by age (Vermeulen, 1995; Hornsby, 1995), but no significant gender differences were found. Most other studies have reported 10–30% higher DHEAS levels in men than in women (Vermeulen, 1995; Carlson and Sherwin, 1999; Mazat et al., 2001). Our finding is unusual not only in that there were no significant differences, but the women also had consistently higher values than the men. Comparatively, our sample had much lower DHEAS values than a large community sample of women who were an average age of 52 years (Johannes et al., 1999).

DHEAS may have different effects on health in men compared to women. In one example, higher levels of DHEAS were associated with protection from cardiovascular disease in men (Feldman et al., 2001), but in women the opposite was found: lower DHEAS was associated with lower cardiovascular disease risk (Johannes et al., 1999). Similarly, and more importantly in this context, in two studies, women with higher DHEAS levels were at greater risk for developing breast cancer after menopause than those with lower endogenous levels (Gordon et al., 1990; Dorgan et al., 1997). This seems to be the case primarily in postmenopausal women, in whom peripheral DHEAS conversion is the primary source of estrogens. It may be, then, that DHEAS is protective against some diseases in men, but higher levels are detrimental to women, particularly after menopause. Unfortunately, we did not collect information on menopausal status from the women in this sample. Still, in this light, our findings of a small decrease in DHEAS levels in women of menopausal age over the course of the MBSR program, but a larger increase in men, may again

be an indication of a differential shift towards a healthier pattern of hormonal secretion in both genders. More troubling, though, is the consideration that the men in this study may be at greater risk for other diseases in association with their lower than normal DHEAS levels.

Levels of melatonin similarly did not change over the course of the intervention. The melatonin levels reported in this group were within the range of daytime values found in normal healthy populations. The usual daytime range is from 0 to 20 pg/ml, with peak secretion occurring during the night of about 50–200 pg/ml (Vijayalaxmi et al., 2002). Our patients secreted an average of 8.6 and 6.5 pg/ml of melatonin pre- and post-intervention at the 14:00 h collection time, within this normal daytime range. For years, reports have indicated that both men with prostate cancer (Bartsch et al., 1985) and women with breast cancer (Tamarkin et al., 1982) had suppressed or absent nocturnal melatonin peaks. It may have been interesting to investigate levels of melatonin later in the day or night, as this peak secretion has been related to health outcomes. The studies that have found increases in melatonin secretion associated with meditation have measured plasma nighttime melatonin directly following a meditation session (Tooley et al., 2000), or urinary secretion over the 12-h nighttime period (Massion et al., 1995). It may be that these effects are temporary, and following a night of sleep, the levels decrease back to the usual level. Indeed, even in the experienced meditators who were assessed on a control night when they did not meditate, lower melatonin secretion was recorded compared to after a meditation session (Tooley et al., 2000). It may be, then, that the effects of meditation on melatonin are twofold: increasing baseline peak nighttime levels, and further enhancing melatonin levels immediately following practice. Since we did not sample saliva for melatonin in relation to the meditation practice or sample evening levels, it is difficult to determine whether the levels may have changed subsequent to practice or not. We can conclude, however, that no changes did occur pre- to post-intervention for the 14:00 h measure. Whether peak nighttime melatonin levels changed cannot be determined from the methodology used. Future studies would benefit from methodology measuring nighttime secretion levels perhaps after meditation and on a day without meditation.

In summary, this study confirmed our previous findings of decreases in stress symptoms after participation in an MBSR program, and further demonstrated small improvements in overall quality of life of these early stage breast and prostate cancer patients. Sleep quality, a common problem for cancer patients, improved over the course of the intervention, and other health behaviors such as exercise and caffeine consumption also improved. Diurnal cortisol secretion patterns changed in that more extreme levels were attenuated, and patterns of secretion indicated a shift towards possibly healthier HPA axis functioning. DHEAS levels, although unchanged overall, also showed some gender-specific shifts consistent with healthier patterns. Changes seen in these patients were moderate. This may have been due to the high levels of patient functioning at the start of the study, but could also indicate that this type of program is only moderately effective for early stage breast and prostate cancer patients who are three months or more post-treatment. Nonetheless, these data are intriguing for a preliminary uncontrolled study of the hormonal effects of the MBSR

program in cancer patients. Future studies of this nature would benefit from a randomized control group, fewer statistical comparisons, and screening for more distressed individuals at the start of the program, as those individuals are more likely to benefit in terms of improvements in stress symptoms, mood, and quality of life, as well as, perhaps, in enhancement of hormonal functioning.

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References

Aaronson, N.K., Ahmedzai, S., Bullinger, M., Crabeels, D., Estape, J., Filiberti, A., Flechtner, H., Frick, U., Hurny, C., Kaasa, S., Klee, M., Mastilica, M., Osoba, D., Pfausler, B., Razavi, D., Rofe, P.B., Schraub, S., Sullivan, M., Takeda, F., 1991. The EORTC core quality of life questionnaire: interim results of an international field study. In: Osoba, D. (Ed.), Effect of Cancer on Quality of Life. CRC Press, London, pp. 185–203.

Aaronson, N.K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N.J., Filiberti, A., Flechtner, H., Fleishman, S.B., deHaes, J.C.J.M., Kaasa, S., Klee, M., Osoba, D., Razavi, D., Rofe, P.B., Schraub, S., Sneeuw, K., Sullivan, M., Takeda, F., 1993. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J. Natl. Cancer Inst. 85, 365–376.

Andersen, B.L., Kiecolt-Glaser, J.K., Glaser, R., 1994. A biobehavioral model of cancer stress and disease course. Am. Psychol. 49 (5), 389–404.

Aragona, M., Muscatello, M.R., Losi, E., Panetta, S., La, T.F., Pastura, G., Bertolani, S., Mesiti, M., 1996. Lymphocyte number and stress parameter modifications in untreated breast cancer patients with depressive mood and previous life stress. J. Exp. Ther. Oncol. 1 (6), 354–360.

Bartsch, C., Bartsch, H., Fluchter, S.H., Attanasio, A., Gupta, D., 1985. Evidence for modulation of melatonin secretion in men with benign and malignant tumors of the prostate: relationship with the pituitary hormones. J. Pineal Res. 2 (2), 121–132.

Blauer, K.L., Poth, M., Rogers, W.M., Bernton, E.W., 1991. Dehydroepiandrosterone antagonizes the suppressive effects of dexamethasone on lymphocyte proliferation. Endocrinology 129, 3174–3179.

Carlson, L.E., Sherwin, B.B., 1999. Relationships among cortisol (CRT), dehydroepiandrosterone-sulfate (DHEAS), and memory in a longitudinal study of healthy elderly men and women. Neurobiol. Aging 20 (3), 315–324.

Carlson, L.E., Ursuliak, Z., Goodey, E., Angen, M., Speca, M., 2001. 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 (2), 112–123.

Carlson, L.E., Speca, M., Patel, K.D., Goodey, E., in press. 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.

Cassileth, B.R., Chapman, C.C., 1998. Alternative and complementary cancer therapies. Cancer 77 (6), 1026–1034.

Cassileth, B.R., Lusk, E.J., Brown, L.L., Cross, P.A., 1985. Psychosocial status of cancer patients and next of kin: normative data from the profile of mood states. J. Psychosoc. Oncol. 3 (3), 99–105.

Cohen, S., Williamson, G.M., 1991. Stress and infectious diseases in humans. Psychol. Bull. 109, 5–24.

Cos, S., Fernandez, R., Guezmes, A., Sanchez-Barcelo, E.J., 1998. Influence of melatonin on invasive and metastatic properties of MCF-7 human breast cancer cells. Cancer Res. 58, 4383–4390.

Courneya, K.S., 2001. Exercise interventions during cancer treatment: biopsychosocial outcomes. Exerc. Sport Sci. Rev. 29 (2), 60–64.

Courneya, K.S., Friedenreich, C.M., 1999. Physical exercise and quality of life following cancer diagnosis: a literature review. Ann. Behav. Med. 21 (2), 171–179.

Cruess, D.G., Antoni, M.H., Kumar, M., Ironson, G., McCabe, P., Fernandez, J.B., Fletcher, M., Schneiderman, N., 1999. Cognitive-behavioral stress management buffers decreases in dehydroepiandrosterone sulfate (DHEAS) and increases in the cortisol/DHEAS ratio and reduces mood disturbance and perceived stress among HIV-seropostive men. Psychoneuroendocrinology 24, 537–549.

Cruess, D.G., Antoni, M.H., McGregor, B.A., Kilbourn, K.M., Boyers, A.E., Alferi, S.M., Carver, C.S., Kumar, M., 2000. Cognitive-behavioral stress management reduces serum cortisol by enhancing benefit finding among women being treated for early stage breast cancer. Psychosom. Med. 62 (3), 304–308.

Deepak, K.K., Manchanda, S.K., Maheshwari, M.C., 1994. Meditation improves clinicoelectroencephalographic measures in drug-resistant epileptics. Biofeedback Self Regul. 19 (1), 25–40.

DeFlorio, M., Masie, M.J., 1995. Review of depression in cancer: gender differences. Depression 3, 66–80.

Derogatis, L.R., Morrow, G.R., Fetting, J., 1983. The prevalence of psychiatric disorders among cancer patients. J. Am. Med. Assoc. 249, 751–757.

Dorgan, J.F., Stanczyk, F.Z., Longcope, C., Stephenson, H.E. Jr., Chang, L., Miller, R., Franz, C., Falk, R.T., Kahle, L., 1997. Relationship of serum dehydroepiandrosterone (DHEA), DHEA sulfate, and 5-androstene-3 beta, 17 beta-diol to risk of breast cancer in postmenopausal women. Cancer Epidemiol. Biomarkers Prev. 6 (3), 177–181.

Ernst, E., Cassileth, B.R., 1998. The prevalence of complementary/alternative medicine in cancer: a systematic review. Cancer 83, 777–782.

Esterling, B.A., Kiecolt-Glaser, J.K., Glaser, R., 1996. Psychosocial modulation of cytokine-induced natural killer cell activity in older adults. Psychosom. Med. 58 (3), 264–272.

Feldman, H.A., Johannes, C.B., Araujo, A.B., Mohr, B.A., Longcope, C., McKinlay, J.B., 2001. Low dehydroepiandrosterone and ischemic heart disease in middle-aged men: prospective results from the Massachusetts Male Aging Study. Am. J. Epidemiol. 153 (1), 79–89.

Friedenreich, C.M., Courneya, K.S., Bryant, H.E., 2001. Relation between intensity of physical activity and breast cancer risk reduction. Med. Sci. Sports Exerc. 33 (9), 1538–1545.

Glaser, J.L., Brind, J.L., Vogelman, J.H., Eisner, M.J., Dillbeck, M.C., Wallace, R.K., Chopra, D., Orentreich, N., 1992. Elevated serum dehydroepiandrosterone sulfate levels in practitioners of the Transcendental Meditation (TM) and TM-Sidhi programs. J. Behav. Med. 15 (4), 327–341.

Gordon, G.B., Bush, T.L., Helzlsouer, K.J., Miller, S.R., Comstock, G.W., 1990. Relationship of serum levels of dehydroepiandrosterone and dehydroepiandrosterone-sulfate to the risk of developing postmenopausal breast cancer. Cancer Res. 50, 3859–3862.

Guazzo, E.P., Kirkpatrick, P.J., Goodyer, I.M., Shiers, H.M., Herbert, J., 1996. Cortisol, dehydroepiandrosterone (DHEA), and DHEA sulfate in the cerebrospinal fluid of man: relation to blood levels and the effects of age. J. Clin. Endocrinol. Metab. 81 (11), 3951–3960.

Henderson, L.E., 1989. Characteristics and Immune Function of Meditators and Non-Meditators: An Exploratory Study. University of Calgary.

Heuser, I.F., Deuschle, M.F., Luppa, P.F., Schweiger, U.F., Standhardt, H.F., Weber, B., 1998. Increased diurnal plasma concentrations of dehydroepiandrosterone in depressed patients. J. Clin. Endocrinol. Metab. 83 (9), 3130–3133.

Hornsby, P.J., 1995. Biosynthesis of DHEAS by the human adrenal cortex and its age-related decline. Ann. N. Y. Acad. Sci. 774, 29–46.

Johannes, C.B., Stellato, R.K., Feldman, H.A., Longcope, C., McKinlay, J.B., 1999. Relation of dehydroe-

piandrosterone and dehydroepiandrosterone sulfate with cardiovascular disease risk factors in women: longitudinal results from the Massachusetts Women's Health Study. J. Clin. Epidemiol. 52 (2), 95–103.
Kabat-Zinn, J., 1982. An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. Gen. Hosp. Psychiatry 4, 33–42.
Kabat-Zinn, J., 1990. Full Catastrophe Living: Using the Wisdom of your Body and Mind to face Stress, Pain and Illness. Delacourt, New York.
Kabat-Zinn, J., Lipworth, L., Burney, R., Sellers, W., 1987. Four-year follow-up of a meditation based program for the self-regulation of chronic pain: treatment outcomes and compliance. Clin. J. Pain 2, 159–173.
Kabat-Zinn, J., Massion, A.O., Kristeller, J., Peterson, L.G., Fletcher, D.E., Pbert, O., Lenderking, W.R., Santorelli, S.F., 1992. Effectivenes of a meditation-based stress reduction program in the treatment of anxiety disorders. Am. J. Psychiatry 149 (7), 943–963.
Kabat-Zinn, J., Wheeler, E., Light, T., Skillings, A., Scharf, M.J., Croplwy, T.G., Hosmer, D., Bernhard, J.D., 1998. Influence of a mindfulness meditation-based stress reduction intervention on rates of skin clearing in patients with moderate to sever psoriasis undergoing phototherpay (UVB) and photochemotherapy (PUVA). Psychosom. Med. 60, 625–632.
Kailajarvi, M.F., Ahokoski, O.F., Virtanen, A.F., Salminen, E.F., Irjala, K., 2000. Early effects of adjuvant tamoxifen therapy on serum hormones, proteins and lipids. Anticancer Res. 20 (2B), 1323–1327.
Kanno, J., Wakikawa, A., Utsuyama, M., Hirokawa, K., 1997. Effect of restraint stress on immune system and experimental B melanoma metastasis in aged mice. Mech. Ageing Dev. 93 (1-3), 107–117.
Kaplan, K.H., Goldenberg, D.L., Galvin-Nadeau, M., 1993. The impact of a meditation-based stress reduction program on fibromyalgia. Gen. Hosp. Psychiatry 15 (5), 284–289.
Keller, M., Henrich, G., 1999. Ilness-related distress: does it mean the same for men and women? Acta Oncol. 38 (6), 747–755.
Kirschbaum, C., Hellhamer, D.H., 1994. Salivary cortisol in psychoneuroendocrine research: recent developments and applications. Psychoneuroendocrinology 19, 313–333.
Laakso, M.L., Porkka-Heiskanen, T.F., Alila, A.F., Stenberg, D.F., Johansson, G., 1990. Correlation between salivary and serum melatonin: dependence on serum melatonin levels. J. Pineal Res. 9 (1), 39–50.
Leckie, M.S., Thompson, E., 1979. Symptoms of Stress Inventory. University of Washington, Seattle, WA.
Liebmann, P.M., Wolfler, A., Hofer, D., Schauenstein, K., 1997. Melatonin and immune system. Arch. Allergy Immunol. 112, 203–211.
Lissoni, P., Cazzaniga, M., Tancini, G., Scardino, E., Musci, R., Barni, S., Maffezzini, M., Meroni, T., Rocco, F., Conti, A., Maestroni, G., 1997. Reversal of clinical resistance to LHRH analogue in metastatic prostate cancer by the pineal hormone melatonin: efficacy of LHRH analogue plus melatonin in patients progressing on LHRH analogue alone. Eur. Urol. 31, 178–181.
Lissoni, P., Barni, S., Mandala, M., Ardizzoia, A., Paolorossi, F., Vaghi, M., Longarini, R., Malugani, F., Tancini, G., 1999a. Decreased toxicity and increased efficacy of cancer chemotherapy using the pineal hormone melatonin in metastatic solid tumour patients with poor clinical status. Eur. J. Cancer 35 (12), 1688–1692.
Lissoni, P., Tancini, G., Paolorossi, F., Mandala, M., Ardizzoia, A., Malugani, F., Giani, L., Barni, S., 1999b. Chemoneuroendocrine therapy of metastatic breast cancer with persistent thrombocytopenia with weekly low-dose epirubicin plus melatonin: a phase II study. J. Pineal Res. 26 (3), 169–173.
Lonning, P.E., Johannessen, D.C., Lien, E.A., Ekse, D., Fotsis, T., Adlercreutz, H., 1995. Influence of tamoxifen on sex hormones, gonadotrophins and sex hormone binding globulin in postmenopausal breast cancer patients. J. Steroid Biochem. Mol. Biol. 52 (5), 491–496.
MacLean, C.R., Walton, K.G., Wenneberg, S.R., Levitsky, D.K., Mandarino, J.P., Waziri, R., Schneider, R.H., 1994. Altered responses of cortisol, GH, TSH and testosterone to acute stress after four months' practice of transcendental meditation (TM). Ann. N. Y. Acad. Sci. 746, 381–384.
Majewska, M.D., 1995. Neuronal action of dehydroepiandrosterone: possible roles in brain development, aging, memory and affect. Ann. N. Y. Acad. Sci. 774, 111–120.
Massion, A.O., Hebert, J.R., Wertheimer, M.D., Kabat-Zinn, J., 1995. Meditation, melatonin and breast/prostate cancer: hypothesis and preliminary data. Med. Hypotheses 44, 39–46.

Mazat, L., Lafont, S., Berr, C., Debuire, B., Tessier, J.F., Dartigues, J.F., Baulieu, E.E., 2001. Prospective measurements of dehydroepiandrosterone sulfate in a cohort of elderly subjects: relationship to gender, subjective health, smoking habits, and 10-year mortality. Proc. Natl. Acad. Sci. U.S.A. 98 (14), 8145–8150.

McEwen, B.S., Sapolsky, R.M., 1995. Stress and cognitive function. Curr. Opin. Neurobiol. 5 (2), 205–216.

McIntyre, I.M., Norman, T.R., Burrows, G.D., Armstrong, S.M., 1987. Melatonin rhythm in human plasma and saliva. J. Pineal Res. 4 (2), 177–183.

McNair, D.A., Lorr, M., Droppelman, L.F., 1971. Profile of Mood States. Educational and Industrial Testing Service, San Diego.

Michelson, H., Bolund, C., Nilsson, B., Brandberg, Y., 2000. Health-related quality of life measured by the EORTC QLQ-C30--reference values from a large sample of Swedish population. Acta Oncol. 39 (4), 477–484.

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. Gen. Hosp. Psychiatry 17, 192–200.

Morales, A.J., Nolan, J.J., Jerald, C., Nelson, S., Yen, S.C., 1994. Effects of replacement dose of dehydroepiandrosterone in men and women of advancing age. J. Clin. Endocrinol. Metab. 78 (6), 1360–1367.

Mormont, M.C., Levi, F., 1997. Circadian-system alterations during cancer processes: a review. Int. J. Cancer 70 (2), 241–247.

National Cancer Institute of Canada, 2001. Canadian Cancer Statistics 2001. Toronto, Ontario: National Cancer Institute of Canada.

Reibel, D.K., Greeson, J.M., Brainard, G.C., Rosenzweig, S., 2001. Mindfulness-based stress reduction and health-related quality of life in a heterogeneous patient population. Gen. Hosp. Psychiatry 23 (4), 183–192.

Riska, E., Ettorre, E., 1999. Mental distress: gender aspects of symptoms and coping. Acta Oncol. 38 (6), 757–761.

Schedlowski, M., Jung, C., Schimanski, G., Tewes, U., Schedlowski, M., Schmoll, H.-J., 1994. Effects of behavioral intervention on plasma cortisol and lymphocytes in breast cancer patients: an exploratory study. Psycho-Oncology 3, 181–187.

Schneider, R.H., Staggers, F., Alexander, C.N., Sheppard, W., Rainforth, M., Kondwani, K., Smith, S., King, C.G., 1995. A randomised controlled trial of stress reduction for hypertension in older African Americans. Hypertension 26 (5), 820–827.

Sephton, S.E., Sapolsky, R.M., Kraemer, H.C., Spiegel, D., 2000. Diurnal cortisol rhythm as a predictor of breast cancer survival. J. Natl. Cancer Inst. 92 (12), 944–1000.

Shirtcliff, E.A., Granger, D.A., Schwartz, E., Curran, M.J., 2001. Use of salivary biomarkers in biobehavioral research: cotton-based sample collection methods can interfere with salivary immunoassay results. Psychoneuroendocrinology 26 (2), 165–173.

Sikes, C.R.A., Lasley, B.J., 1989. Cognitive sequelae of hypothalamic-pituitary-adrenal (HPA) dysregulation in depression. Biol. Psychiatry 25, 148A–149A.

Singh, B.B., Berman, B.M., Hadhazy, V.A., Creamer, P., 1998. A pilot study of cognitive behavioral therapy in fibromyalgia. Altern. Ther. Health Med. 4 (2), 67–70.

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. Psychosom. Med. 62 (5), 613–622.

Spiegel, D., 1996. Cancer and depression. Br. J. Psychiatry Suppl. (30), 109–116.

Spiegel, D., Sephton, S.E., Terr, A.I., Sittes, D.P., 1998. Effects of psychosocial treatment in prolonging cancer survival may be mediated by neuroimmune pathways. Ann. N. Y. Acad. Sci. 840, 674–683.

Strain, J.J., 1998. Adjustment disorders. In: Holland, J.F. (Ed.), Psycho-oncology. Oxford University Press, New York, pp. 509–517.

Sudsuang, R., Chentanez, V., Veluvan, K., 1991. Effect of Buddhist meditation on serum cortisol and total protein levels, blood pressure, pulse rate, lung volume and reaction time. Physiol. Behav. 50 (3), 543–548.

Tamarkin, L., Danforth, D., Lichter, A., DeMoss, E., Cohen, M., Chabner, B., Lippman, M., 1982.

Decreased nocturnal plasma melatonin peak in patients with estrogen receptor positive breast cancer. Science 216 (4549), 1003–1005.
Ticher, A., Haus, E., Ron, I.G., Sackett-Lundeen, L., Ashkenazi, I.E., 1996. The pattern of hormonal circadian time structure (acrophase) as an assessor of breast-cancer risk. Int. J. Cancer 65 (5), 591–593.
Tooley, G.A., Armstrong, S.M., Norman, T.R., Sali, A., 2000. Acute increases in night-time plasma melatonin levels following a period of meditation. Biol. Psychol. 53 (1), 69–78.
Touitou, Y., Bogdan, A., Levi, F., Benavides, M., Auzeby, A., 1996. Disruption of the circadian patterns of serum cortisol in breast and ovarian cancer patients: relationships with tumour marker antigens. Br. J. Cancer 74 (8), 1248–1252.
Turner-Cobb, J.M., Sephton, S.E., Koopman, C., Blake-Mortimer, J., Spiegel, D., 2000. Social support and salivary cortisol in women with metastatic breast cancer. Psychosom. Med. 62 (3), 337–345.
van der Pompe, G., Duivenvoorden, H.J., Antoni, M.H., Visser, A., Hejinen, C.J., 1997. Effectiveness of a short-term group psychotherapy program on endocrine and immune function in breast cancer patients: an exploratory study. J. Psychosom. Res. 42 (5), 453–466.
van der Pompe, G.F., Antoni, M.H., Heijnen, C.J., 1996. Elevated basal cortisol levels and attenuated ACTH and cortisol responses to a behavioral challenge in women with metastatic breast cancer. Psychoneuroendocrinology 21 (4), 361–374.
Vermeulen, A., 1995. Dehydroepiandrosterone sulfate and aging. Ann. N. Y. Acad. Sci. 774, 121–127.
Vijayalaxmi, Thomas, C.R. Jr., Reiter, R.J., Herman, T.S., 2002. Melatonin: from basic research to cancer treatment clinics. J. Clin. Oncol. 20 (10), 2575–2601.
Voultsios, A.F., Kennaway, D.J., Dawson, D., 1997. Salivary melatonin as a circadian phase marker: validation and comparison to plasma melatonin. J. Biol. Rhythms 12 (5), 457–466.
Walton, K.G., Pugh, N.D., Gelderloos, P., Macrae, P., 1995. Stress reduction and preventing hypertension: preliminary support for a psychoneuroendocrine mechanism. J. Altern. Complement. Med. 1 (3), 263–283.
Wolkowitz, O.M., 1994. Prospective controlled studies of the behavioral and biological effects of exogenous corticosteroids. Psychoneuroendocrinology 3 (19), 233–255.
Wolkowitz, O.M., Reus, V.I., Roberts, E., Manfredi, F., Chan, T., Raum, W.J., Ormiston, S., Johnson, R., Canick, J., Brizendine, L., Weingartner, H., 1997. DHEA treatment of depression. Biol. Psychiatry 41, 311–318.
Zabora, J.R., Blanchard, C.G., Smith, E.D., Roberts, C.S., Glajchen, M., Sharp, J.M., Brintzenhofeszoc, K.M., Locher, J.W., Carr, E.W., Best-Castner, S., Smith, P.M., Dozier-Hall, D., Polinsky, M.L., Hedlund, S.C., 1997. Prevalence of psychological distress among cancer patients across the disease continuum. J. Psychosoc. Oncol. 15 (2), 73–86.