

# Sleep, Fatigue, and Depressive Symptoms in Breast Cancer Survivors and Matched Healthy Women Experiencing Hot Flashes

Janet S. Carpenter, PhD, RN, Julie L. Elam, MSN, RN, Sheila H. Ridner, PhD, RN, Pam H. Carney, BSN, RN, Gloria J. Cherry, BA, RN, and Heather L. Cucullu, BSN, RN

**Purposes/Objectives:** To compare sleep quality and disturbance, fatigue, and depressive symptoms between breast cancer survivors and healthy women experiencing hot flashes and to examine relationships among sleep and remaining variables (fatigue, depressive symptoms, and frequency of hot flashes).

**Design:** Cross-sectional, descriptive, comparative pilot study.

**Setting:** University-based outpatient setting.

**Sample:** 15 breast cancer survivors and 15 healthy women matched on age, race, and menopausal status. All women had untreated hot flashes (no hormone replacement therapy or other hot flash treatments).

**Methods:** Questionnaires (sleep quality and disturbance, fatigue, and depression); two ambulatory, 24-hour sternal skin conductance monitoring sessions (hot flash frequency); and medical records review.

**Main Research Variables:** Sleep quality and disturbance, fatigue, depressive symptoms, and objective hot flash frequency.

**Findings:** The majority of participants evidenced poor sleep quality and high sleep disturbance (73% of breast cancer survivors and 67% of healthy women above a cutoff score of 5). Sleep duration was significantly shorter for breast cancer survivors in contrast to healthy women. Nighttime flashes were experienced by 67% of breast cancer survivors and 37% of healthy women. No group differences were found in fatigue, depressive symptoms, or objective hot flash frequency. Global sleep scores were significantly positively correlated with fatigue and depression but not with hot flash frequency.

**Conclusions:** Findings suggest that sleep disturbance is common in menopausal breast cancer survivors and healthy women, is not necessarily related to hot flashes, and may stem from a multifactorial etiology.

**Implications for Nursing:** Menopausal breast cancer survivors who present with any one of these symptoms should be screened for all symptoms both during and after treatment.

Although breast cancer survivors with untreated hot flashes have reported sleep problems (Carpenter, Johnson, Wagner, & Andrykowski, 2002; Couzi, Helzlsouer, & Fetting, 1995; Finck, Barton, Loprinzi, Quella, & Sloan, 1998; Knopf, 2001), the extent of these sleep problems has not been fully documented. Among breast cancer survivors, sleep research has not included empirically validated measures of hot flashes, such as sternal skin conductance monitoring (Broeckel, Jacobsen, Horton, Balducci, & Lyman, 1998; Carpenter & Andrykowski, 1998; Okuyama et al., 2000; Servaes, Prins, Verhagen, & Bleijenbergh, 2002; Servaes,

## Key Points . . .

- Oncology nurses should be aware of sleep problems, fatigue, and depressive symptoms in women who have been treated for breast cancer and are experiencing hot flashes.
- Sleep problems may be related to fatigue and depressive symptoms.

Verhagen, & Bleijenbergh, 2002). Conversely, researchers examining hot flashes have tended to assess sleep problems using single items rather than empirically validated measures (Carpenter et al., 2002; Couzi et al.; Harris, Remington, Trentham-Dietz, Allen, & Newcomb, 2002; Stein, Jacobsen, Hann, Greenberg, & Lyman, 2000). Sleep in breast cancer survivors with objectively documented hot flashes warrants attention because sleep disruptions may be related to post-treatment fatigue (Broeckel et al.; Carpenter & Andrykowski; Okuyama et al.) and depressive symptoms (Carpenter & Andrykowski; Okuyama et al.; Servaes, Prins, et al.).

The purposes of this study were to compare sleep quality and disturbance, fatigue, and depressive symptoms between breast cancer survivors and matched healthy women experiencing hot flashes and to examine the potential relationships among sleep and remaining variables (fatigue, depressive symptoms, and frequency of hot flashes).

*Janet S. Carpenter, PhD, RN, is an associate professor, and Julie L. Elam, MSN, RN, is a research nurse, both in the School of Nursing at Indiana University in Indianapolis; Sheila H. Ridner, PhD, RN, is a postdoctoral fellow in the School of Nursing, Pam H. Carney, BSN, RN, is a research nurse in the Clinical Trials Office, Gloria J. Cherry, BA, RN, is a research nurse for the Cancer Information Service, and Heather L. Cucullu, BSN, RN, is a research nurse in the Clinical Trials Office, all at Vanderbilt University in Nashville, TN. Data from the breast cancer survivors group were supported by National Institute for Nursing Research grant R01 NR05261. Data from the healthy women group were supported by a grant from Merck & Co., Inc. (Submitted April 2003. Accepted for publication September 15, 2003.)*

Digital Object Identifier: 10.1188/04.ONF.591-598

## Literature Review

Sleep problems are common in people diagnosed with cancer, including women with breast cancer. Sleep problems are measured in terms of sleep quality and sleep disturbance. Sleep quality includes quantitative aspects of sleep, such as the number of minutes of sleep (duration), time in minutes to fall asleep (latency), number of awakenings, and subjective reports of restlessness or disturbance (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Others define poor sleep quality in terms of inability to function fully during the day without a need for naps (Miaskowski & Lee, 1999). Poor sleep quality and sleep disturbance are problematic for people undergoing cancer treatment, as well as for those who have completed treatment.

Research suggests that patients with breast cancer experience sleep changes while undergoing initial treatment (e.g., chemotherapy, radiation therapy) (Ancoli-Israel, Moore, & Jones, 2001; Berger, 1998; Berger et al., 2002; Berger & Farr, 1999; Berger & Higginbotham, 2000; Berger & Walker, 2001; Broeckel et al., 1998; Mourits et al., 2002; Redeker, Lev, & Ruggiero, 2000; Roscoe et al., 2002) and while receiving treatment for metastatic disease (Ancoli-Israel et al.; Miaskowski & Lee). Sleep changes, which can occur at varying time points during treatment, include sleeping more during the day and less at night, overall poor sleep quality, poor sleep efficiency, and sleep disturbance. More daytime and less nighttime sleeping are related to higher on-treatment fatigue (Berger & Farr; Roscoe et al.) and higher depressive symptomatology (Roscoe et al.). Findings across studies have been largely consistent despite differences in time points selected for study, types of sleep measures used (e.g., questionnaires, wrist actigraphy), and specific treatment groups studied (e.g., radiation plus chemotherapy, chemotherapy alone, primary versus metastatic treatment).

Research also suggests that sleep changes initially encountered during cancer treatment may become chronic (Ancoli-Israel et al., 2001) and that the relationships between sleep and fatigue and between sleep and depressive symptoms continue after treatment and into the period of cancer survivorship. Despite differences in measures, findings across studies of breast cancer survivors have indicated that chronic poor sleep quality does occur and is correlated moderately with post-treatment fatigue ( $r = \pm 0.38\text{--}0.68$ ,  $p < 0.05$ ) (Broeckel et al., 1998; Carpenter & Andrykowski, 1998; Okuyama et al., 2000) and with post-treatment depressive symptoms ( $r = 0.50\text{--}0.63$ ,  $p < 0.001$ ) (Carpenter & Andrykowski; Okuyama et al.). Similarly, comparative research suggests that sleep problems and depressive symptoms are significantly higher among very fatigued breast cancer survivors in comparison to those who are not as fatigued (Servaes, Prins, et al., 2002).

In addition to being experienced by women who have been treated for breast cancer, sleep problems also are commonly experienced by menopausal women in general (Baker, Simpson, & Dawson, 1997; Clark, Flowers, Boots, & Shettar, 1995; Dennerstein, Dudley, Hopper, Guthrie, & Burger, 2000; Owens & Matthews, 1998; Shaver & Zenk, 2000). In fact, sleep problems and hot flashes have been defined as "classic" symptoms of menopause (Porter, Penney, Russell, Russell, & Templeton, 1996). In healthy women, poor sleep quality and sleep disturbance may stem from several factors, including

hormonal changes (Empson & Purdie, 1999; Manber & Armitage, 1999; Polo-Kantola, Erkkola, Helenius, Irjala, & Polo, 1998; Shaver & Zenk), vasomotor symptoms such as hot flashes and night sweats (Baker et al.; Erlik et al., 1981; Hollander et al., 2001; Woodward & Freedman, 1994), or psychological distress such as depression (Avis, Crawford, Stellato, & Longcope, 2001; Harlow, Cohen, Otto, Spiegelman, & Cramer, 1999; Joffe et al., 2002; Kingsberg, 2002).

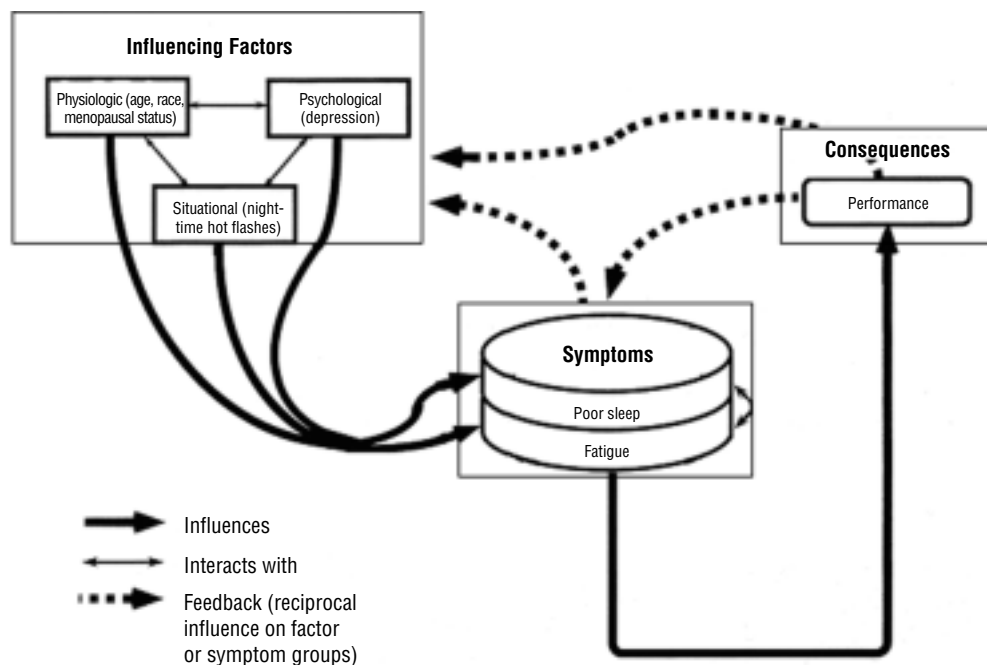
Whether sleep problems experienced by breast cancer survivors are more severe than those experienced by healthy menopausal women of the same age is unclear because of a lack of comparative studies. Breast cancer survivors with untreated hot flashes may experience poorer sleep quality and higher sleep disturbance in comparison to their age-matched counterparts without cancer as a result of additional hormonal changes related to tamoxifen use (Mourits et al., 2002); more frequent, severe, and distressing hot flashes compared to naturally menopausal healthy women (Carpenter et al., 2002); or greater psychological distress related to diagnosis and treatment. Therefore, this study sought to examine sleep, fatigue, and depressive symptoms in breast cancer survivors and matched healthy women experiencing hot flashes. This pilot study was designed to improve on previous research by (a) measuring sleep, fatigue, and depression using standard, validated instruments rather than single-item scales; (b) measuring hot flashes objectively, rather than using subjective reports, and (c) including a comparison group of healthy women matched on age, race, and menopausal status to aid in quantifying and understanding the severity of sleep problems experienced by breast cancer survivors with hot flashes.

## Conceptual Framework

The Lenz Theory of Unpleasant Symptoms served as the conceptual framework for this study (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). The theory has three interrelated components: symptoms that a person experiences, influencing factors that cause or affect the nature of the symptoms, and consequences of the symptom experience (Lenz et al., 1997; Lenz, Suppe, Gift, Pugh, & Milligan, 1995). Symptoms and influencing factors related to this study will be described in more detail. Consequences, defined as the impact of symptoms on an individual's performance ability, such as a decline in job performance related to sleep problems, were not addressed in this study.

According to the theory, symptoms are indicators of a change in normal functioning (Lenz et al., 1995, 1997). For this study, sleep problems were considered the primary symptom and fatigue the secondary symptom. The model posits that symptoms can occur simultaneously, such as sleep problems occurring with fatigue, or develop sequentially, such as sleep problems leading to fatigue. In either case, the model depicts symptoms as stacked on top of one another, as shown in Figure 1. In this study, several aspects of sleep problems were assessed, including overall sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleeping medications, and daytime dysfunction. In addition, severity of fatigue was assessed.

Influencing factors can be physiologic, psychological, or situational (Lenz et al., 1995, 1997). For this study, physiologic factors potentially influencing sleep that were controlled were



**Figure 1. Theoretical Framework: Adapted Lenz Model**

age and menopausal status. Because African American women may experience more hot flashes than Caucasian women (Avis, Stellato, et al., 2001), groups also were matched on race. A psychological factor potentially influencing sleep that was considered in this study was depression, measured in terms of the intensity of depressive symptomatology. A situational factor potentially influencing sleep that was considered was the number of nighttime hot flashes experienced, measured objectively using sternal skin conductance monitoring.

## Methods

### Sample

Eligible women were at least 21 years of age; willing and able to provide informed consent; able to read, write, and speak English; peri- or postmenopausal; experiencing daily hot flashes; in good general health; not taking any type of prescription or nonprescription treatments for hot flashes (e.g., antidepressants, hormone replacement therapy, high-dose vitamin E, herbs); and not currently depressed (i.e., no antidepressants and no evidence of a major depressive episode). Breast cancer survivors participated in psychological screening as part of the funded intervention study to rule out major depressive episodes, but resources did not permit similar screening of healthy women. Breast cancer survivors had additional criteria: first-time diagnosis of cancer, no other cancer, considered disease-free at time of study enrollment, and at least four weeks past completion of surgery, radiation, or chemotherapy. In addition, if the women were taking tamoxifen, they were required to have been taking the drug for at least six weeks.

### Recruitment and Setting

The research was approved by the institutional review board, and all participants provided written informed consent prior to the start of any study procedures. Survivors were recruited from outpatient breast care centers in the southeastern

United States as part of a larger hot flash intervention study. Women were contacted in person in the clinic or via the telephone, informed of the purpose and nature of the study, and invited to participate. Of 140 eligible women identified, 56 consented to the study (40%) and 46 had complete baseline data to include in this article. Of those 46 women, a subset of 15 who were matched to the healthy women was chosen for this analysis.

Healthy women were recruited using an advertisement sent via e-mail to university employees. Interested women phoned a project office (n = 52) and were screened for eligibility and informed of the purpose and nature of the study. Eligible and interested women then were scheduled for their first monitoring session (n = 17). A total of 15 healthy women completed the study.

### Procedures

Women wore a small, lightweight sternal skin conductance monitor for two ambulatory, 24-hour recording sessions separated in time by one week. They also maintained a hot flash diary to assist in interpreting the sternal skin conductance data and completed demographic, sleep, fatigue, and depression questionnaires. To complete the hot flash monitoring sessions, study nurses traveled to participants' homes or workplaces to connect the monitor and then returned 24 hours later to disconnect it. Demographic questionnaires were completed during the first monitoring session. Sleep, fatigue, and depressive symptom questionnaires were completed during the second monitoring session. All women were compensated \$50 for their time and effort in participating in the pilot study. Breast cancer survivors then went on to complete the intervention portion of the study.

### Measures

**Sample description:** Demographic information included age, race, marital status, income, education, employment status, presence of noncancer comorbidities such as arthritis or high blood pressure, and current medication use. For the breast cancer group, disease and treatment information was obtained from medical records. Data included date and stage at diagnosis, types and dates of treatment (i.e., surgery, chemotherapy, or radiation), and tamoxifen use. For both groups, menopausal status was assessed using questions adapted from the Massachusetts Women's Health Study (Brambilla, McKinlay, & Johannes, 1994). Questions assessed the time of a woman's last menstrual cycle (i.e., number of weeks, months, or years ago) and whether menses were regular or irregular. The following definitions were

used: (a) premenopausal—had a menstrual period in the past three months, (b) perimenopausal—3–11 months of amenorrhea or increased menstrual irregularity if still cycling, and (c) postmenopausal—12 or more months of amenorrhea.

**Sleep:** Sleep quality and disturbance were assessed using the **Pittsburgh Sleep Quality Index (PSQI)** (Buysse et al., 1989). The PSQI originally was designed for use in clinical populations as a simple and valid assessment of sleep quality and disturbance that might affect sleep quality. The PSQI consists of 19 items that produce a global sleep quality score and seven component scores: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medications, and daytime dysfunction. Items and component scores represent standard areas assessed by clinicians when individuals report sleep complaints. Global scores range from 0–21 and reflect the number and severity of sleep problems. Global scores of 5 or greater indicate poor sleep quality and high sleep disturbance (Buysse et al., 1989). In addition to being indicative of poor sleep quality and high sleep disturbance, global scores of 8 or more have been linked to cancer-related fatigue in survivors of breast cancer and other cancers (Carpenter & Andrykowski, 1998). PSQI items use varying response categories that include recording usual bed time, usual wake time, number of actual hours slept, and number of minutes to fall asleep, as well as forced-choice, Likert-type responses. Responses are based on habits during the prior week or month. Psychometric properties of the PSQI have been supported widely in a variety of populations, including healthy individuals and breast cancer survivors (Buysse et al., 1989, 1991; Carpenter & Andrykowski; Gentili, Weiner, Kuchibhatla, & Edinger, 1995; Pasternak et al., 1994; Tiffin, Ashton, Marsh, & Kamali, 1995).

**Fatigue:** Fatigue was measured using the fatigue subscale of the **Profile of Mood States–Short Form (POMS–SF)** (McNair, Lorr, & Droppleman, 1992; Shacham, 1983). The POMS–SF fatigue subscale contains five items from the 37-item POMS–SF. The fatigue subscale was combined with the six-item POMS–SF vigor subscale to help avoid response bias because items could alternate between positive and negative words. Participants responded by using the prior two weeks as a time frame. The five-item subscale is a valid measure of cancer-related fatigue, internally consistent (Cronbach's  $\alpha = 0.89\text{--}0.90$ ), one-dimensional on factor analysis, and sensitive to differences in patient groups selected as being high and low on cancer-related fatigue (Andrykowski et al., 1997; Curran, Andrykowski, & Studts, 1995; Meek et al., 2000; Schwartz et al., 2002). This measure is advantageous over others because it poses minimal response burden.

**Depressive symptoms:** The **Center for Epidemiologic Studies–Depression Scale (CES–D)** is a 20-item, self-report instrument assessing the presence and severity of depressive symptoms occurring over the prior week (Radloff, 1977). Respondents rate each item using a four-point scale: 0 = rarely or none of the time, 1 = some or a little of the time, 2 = occasionally or a moderate amount of the time, and 3 = most or all of the time. After reverse scoring four positive items, responses are summed to obtain total scores of 0–60. Scores of 16 or greater indicate high levels of depressive symptoms but are not diagnostic of clinical depression (Berkman et al., 1986; Comstock & Helsing, 1976). The cut-off point of 16 has been used extensively in other studies, including studies of breast cancer survivors (Carpenter et al., 1998).

**Hot flashes:** Hot flash frequency was assessed using sternal skin conductance monitoring. Because frequency can vary considerably from day to day (Carpenter, unpublished data), hot flash frequency was based on the average number of hot flashes recorded during two (rather than one) 24-hour recording sessions separated in time by one week. Means for total hot flashes, daytime flashes, and nighttime flashes were calculated for each individual woman. Prior research suggests that sternal skin conductance monitoring is a valid and reliable measure of hot flashes (Carpenter, Andrykowski, Freedman, & Munn, 1999; Freedman, 1989).

Skin conductance levels were monitored using Medi-Trace silver/silver chloride electrodes (S'offset, Graphic Controls, Buffalo, NY) and a 0.5 constant voltage circuit (Lykken & Venables, 1971) built into the front end of a single channel of a Biolog ambulatory recorder (UFI, Model 3991 SCL, Morro Bay, CA). Electrodes were 1.5 cm in diameter and filled with 0.05 M potassium chloride velvachol/glycol gel (Dormire & Carpenter, 2002). Electrodes were attached 1.5" below the collarbone and 2" on either side of the sternal midline. The Biolog monitor contains a microprocessor and 4 megabytes of memory. It is powered by a standard 9-volt battery and is programmed to sample 12-bit skin conductance data at 1 Hz (once per second). The Biolog 3991 measures 1.3" x 2.8" x 5" and weighs 8 oz. The monitor was placed in a bag and worn around the waist or across the shoulders.

At the conclusion of a monitoring session, the monitor was connected to a personal computer through the Biolog Interface Box (UFI) and data were downloaded. Customized software (DPS v4.1, UFI) and standardized procedures were used to evaluate data in the context of subjective reports of hot flashes assessed using an event marker on the monitor and a diary. When pressed, the monitor event marker time-stamped the data to signal the perception of a hot flash. Diary entries indicated hot flashes as well as activity. Data from the Biolog were displayed graphically during analysis by the downloading and plotting software (DPS v4.1). Based on prior research (Carpenter et al., 1999; Freedman, 1989), a hot flash was defined as an increase in skin conductance of 2  $\mu\text{mho}$  or more within a 30-second period.

## Data Analysis

Data analysis proceeded using four steps. First, demographic information was analyzed. Using nonparametric Mann-Whitney tests and chi-square analyses, group differences in demographic variables were examined to determine the success of matching efforts and to identify any potential group differences. Disease and treatment information for breast cancer survivors was examined using descriptive statistics. Second, group means for the various measures were compared using Mann-Whitney tests. Third, scale frequencies were examined by group to determine: (a) the percentage of women scoring above established cutoff scores on the PSQI (both 5 and 8 used as cutoff scores), (b) frequency of daytime and nighttime hot flashes, (c) a median split score for each group on the POMS–SF fatigue subscale because this scale has no established cutoff score indicating high fatigue, and (d) the percentage of women scoring the CES–D cutoff score of 16 or higher. Step 3 was performed to provide additional information beyond the simple comparison of group means performed in step 2. Fourth, correlations

among sleep and the remaining variables were examined using nonparametric Spearman's rho statistics. Nonparametric statistics were used because of the small sample and pilot nature of this study.

## Results

### Sample Description

The sample is described in Table 1. Because participants were matched on age (within two years), race (all except one participant), and menopausal status, no significant group differences in these variables were noted. Groups also were matched on other variables, including education, body mass index, marital status, income, employment status, and presence of noncancer comorbidities. The majority of breast cancer survivors were stage II or less at diagnosis (66%) and less than five years after completion of treatment (66%). However, breast cancer survivors ranged from 3 months to 14 years post-treatment. Treatments received included surgery alone (20%), surgery plus radiation therapy (13%), surgery plus chemotherapy (27%), and surgery plus radiation plus chemotherapy (40%). None of the healthy women was taking tamoxifen; 40% of the breast cancer survivors were.

### Group Differences

Group differences on study variables are shown in Table 2. Sleep duration was significantly shorter for breast cancer survivors in comparison to healthy women ( $p < 0.05$ ). Group differences in the number of hot flashes experienced during

**Table 2. Group Differences in Sleep, Hot Flashes, Fatigue, and Depressive Symptoms**

Variable	Breast Cancer Survivors (n = 15)		Healthy Women (n = 15)		p
	$\bar{X}$	SD	$\bar{X}$	SD	
Pittsburgh Sleep Quality Index	7.33	2.74	6.93	3.39	0.68
Global score					
Sleep quality	1.20	0.68	1.07	0.80	0.62
Sleep latency	1.13	1.06	1.00	1.00	0.74
Sleep duration	0.87	0.64	1.47	0.64	0.05
Sleep disturbance	1.67	0.62	1.40	0.51	0.31
Sleep medication	0.33	0.72	0.33	0.72	1.00
Daytime dysfunction	0.80	0.56	0.80	0.68	0.97
Sleep efficiency	1.33	1.23	0.87	0.92	0.37
Mean daytime hot flashes	4.07	3.96	2.50	2.53	0.25
Mean nighttime hot flashes	1.47	1.81	0.43	0.88	0.05
Mean 24-hour hot flashes	5.53	5.16	2.93	3.36	0.29
Profile of Mood States–Short	8.60	5.04	7.80	4.43	0.65
Form fatigue subscale					
Center for Epidemiologic Studies–Depression Scale depressive symptoms	8.40	6.59	12.93	10.03	0.22

**Table 1. Sample Characteristics**

Variable	Breast Cancer Survivors (n = 15)		Healthy Women (n = 15)		p
	$\bar{X}$	SD	$\bar{X}$	SD	
Age (years)	46.6	7.4	48.4	4.3	0.43
Education (years)	14.3	2.3	14.3	2.7	1.00
Body mass index	27.2	6.9	29.6	8.6	0.42
Variable	n	%	n	%	p
Race					0.69
Caucasian	11	73	10	67	
Other <sup>a</sup>	4	27	5	33	
Marital status					0.14
Married or living with partner	14	93	11	73	
Other	1	7	4	27	
Household income					0.18
\$40,000 per year	3	20	6	40	
More than \$40,000 per year	12	80	9	60	
Employment status					0.28
Working full- or part-time	12	80	14	93	
No work outside the home	3	20	1	7	
Reporting noncancer comorbidities	8	53	7	47	0.72
Menopausal status					0.71
Perimenopausal	6	40	7	47	
Postmenopausal	9	60	8	53	
Current tamoxifen use	6	40	–	–	0.01

<sup>a</sup> Includes three African Americans and one Asian in the group of breast cancer survivors and four African Americans and one Asian in the group of healthy women

sleep did not reach statistical significance ( $p = 0.05$ ). No other group differences in total or waking hot flashes, fatigue, or depressive symptoms were noted. However, a trend was noted for breast cancer survivors to report more problems on all measures.

### Frequencies by Group

Using the PSQI, women were grouped into good and poor sleepers using the previously established cutoff score of 5 or higher to indicate poor sleep quality and high sleep disturbance (Buysse et al., 1989). The majority of women in each group (73% of breast cancer survivors and 67% of healthy women) had global scores above 5. Using the higher cutoff score of 8 proposed by Carpenter and Andrykowski (1998), the women again were grouped into good and poor sleepers. The majority of women in each group (53% of breast cancer survivors and 40% of healthy women) exceeded this higher cutoff score as well.

Frequencies by group for the remaining measures were as follows. For the POMS–SF fatigue subscale, the median score for each group was identified in lieu of an established cutoff score. The median score was found to be the same in each group. Half of the women (50%) in each group scored above 7 on the POMS–SF, with a range of 0–17 in the breast cancer survivors group and 0–15 in the healthy women group. Using the CES–D, 13% of breast cancer survivors ( $n = 2$ ) and 33% of healthy women ( $n = 5$ ) scored higher than the cutoff point. Hot flash frequencies during waking and sleeping hours were examined separately. Almost half of the breast cancer survivors (47%) experienced a mean of four or more daytime hot flashes compared to 13% of healthy women. Similarly, a majority of breast cancer survivors (67%) experienced nighttime hot flashes (defined as  $\geq 1$  hot flash during  $\geq 1$  monitoring night) compared to a minority of healthy women (37%).

Correlations Among Measures

Correlations among sleep and remaining variables (fatigue, depressive symptoms, and hot flashes) are shown in Table 3. Both PSQI global and sleep duration scores were used given that group differences emerged in sleep duration. Global sleep quality was significantly correlated with fatigue and depressive symptoms but not with hot flashes. Sleep duration was not significantly related to fatigue or hot flashes but was correlated with depressive symptoms.

Discussion

This study was the first to examine sleep problems, fatigue, and depressive symptoms in breast cancer survivors and healthy women with untreated, objectively documented hot flashes. Overall, sleep frequency data and the lack of group differences on sleep variables indicated that a majority of women in each group were experiencing poor sleep quality and high sleep disturbance. Although breast cancer survivors tended to experience more nighttime hot flashes ( $p = 0.05$ ), their sleep quality was not worse than the healthy women's. These findings support previous research that sleep disturbance is common in menopausal women (Baker et al., 1997; Clark et al., 1995; Dennerstein et al., 2000; Owens & Matthews, 1998; Shaver & Zenk, 2000). Findings also support research suggesting that sleep problems in menopausal women stem from a multifactorial etiology, not just from hot flashes (Avis, Crawford, et al., 2001; Empson & Purdie, 1999; Harlow et al., 1999; Joffe et al., 2002; Kingsberg, 2002; Manber & Armitage, 1999; Polo-Kantola et al., 1998). Although some researchers consider both sleep problems and hot flashes to be "classic" menopausal symptoms (Porter et al., 1996), others argue against a menopausal syndrome. For example, Avis, Stellato, et al. (2001) evaluated 14,906 peri- and postmenopausal women and found no consistent pattern of symptoms that occurred during menopause. However, although Avis, Stellato, et al. argued against a menopausal syndrome, their data omitted the important variable of sleep problems because of missing information. Given the current study's findings that sleep problems in this sample of longer-term breast cancer survivors were not significantly different than those of matched healthy women, and that sleep quality and sleep disturbance were poor in both groups, this work should be conducted on larger samples of healthy women and breast cancer survivors to determine whether results can be replicated.

The lack of group differences in sleep, fatigue, depressive symptoms, and hot flashes may have been related to several factors. First, the group of breast cancer survivors contained

long-term survivors (e.g., 34% were > 5 years postdiagnosis). Because cancer-related symptoms tend to abate over time, the group of breast cancer survivors may have been more similar to the group of healthy women than dissimilar. For example, although fatigue is the most commonly reported symptom during cancer treatment, only a minority of breast cancer survivors continues to have persistent fatigue after treatment completion (Winningham, 1996). Future research should take time since treatment into consideration through sample stratification, limits on inclusion criteria, or statistical control.

Second, the lack of group differences may have been the result of a tendency for breast cancer survivors to underreport symptoms post-treatment. Research suggests that women undergoing treatment for breast cancer tend to underreport sleep problems (personal communication, Ann M. Berger, PhD, RN, AOCN®, December 10, 2002), hot flashes (Carpenter et al., 1999), other symptoms such as pain (Turk & Fernandez, 1990), and possibly fatigue and depressive symptoms as examined in the current study. This under-reporting of symptoms may be the result of a phenomenon known as response shift, which is defined as a change in a respondent's values or standards (Myers, Allen, & Baile, 1996; Schwartz, 1996). Interestingly, the only group difference that approached statistical significance ( $p = 0.05$ ) was based on an objective measure (e.g., hot flash frequency) that could not be affected by a response shift. Objective measures are not affected by a change in perception and, in terms of hot flashes, are more accurate than subjective methods such as daily diaries (Carpenter et al., 1999). To avoid a potential response bias, future research could focus on objective measurement of hot flashes as well as sleep (e.g., polysomnography, actigraphy) and depression (e.g., Hamilton rating scale).

Finally, the larger percentage of healthy women scoring above the CES-D cutoff point may have contributed to the lack of group differences in sleep and fatigue. If the healthy women had been a truly nondepressed sample, or if breast cancer survivors with high depressive symptoms had not been excluded, group differences may have emerged. Future research should focus on more detailed screening of depressive symptoms and depression with plans to exclude such patients from the sample, statistically control for depression, or otherwise account for variability in depressive symptoms.

Correlations among sleep, fatigue, and depressive symptoms were similar to those found in previous research among breast cancer survivors (Broeckel et al., 1998; Carpenter & Andrykowski, 1998; Okuyama et al., 2000). These findings provide evidence for a symptom cluster of poor sleep, fatigue, and depressive symptoms in both groups of menopausal women. The lack of correlation between sleep and hot flashes may have been related to the lack of variability in the samples. Inclusion of women without sleep problems who were not having hot flashes may have increased sample variability and resulted in a positive correlation between hot flashes and sleep.

Implications for Practice

Nursing research has prompted awareness of sleep problems in people with cancer. Although various factors can lead to sleep problems, nurses play a vital role in assessment and development of interventions for such health-related issues. Assessment of sleep problems can facilitate the development of effective nursing interventions.

Table 3. Spearman's Rho Correlations Among Sleep and Fatigue, Depressive Symptoms, and Hot Flashes

	Pittsburgh Sleep Quality Index (PSQI) Global Score	PSQI Sleep Duration
Fatigue	0.43*	0.21
Depressive symptoms	0.47*	0.37*
Mean daytime hot flash frequency	0.17	-0.02
Mean nighttime hot flash frequency	-0.04	-0.18
Mean total hot flash frequency	0.13	-0.04

\*  $p < 0.05$  (two tailed)

Sleep problems, fatigue, depression, and hot flashes can affect survivorship and quality of life. Nurses who care for healthy menopausal women may have more awareness to assess such issues than oncology nurses, who may encounter menopausal symptoms less often. Incorporating standard assessment tools, such as those used in the current study, can help nurses target specific symptoms and positively influence patients' quality of life. Although these symptoms can be problematic during treatment, oncology nurses must recognize that they may be attributed to other nontreatment-related factors and, as such, may continue to be a problem in the post-treatment period. Thus, formulating an assessment tool that incorporates a cluster of health issues such as sleep problems, fatigue, depression, and hot flashes may be beneficial to oncology nurses treating patients during all phases of the cancer experience, even into long-term survivorship.

After assessment, nurses can educate patients and family members about specific symptoms and how certain behaviors can affect the severity of those symptoms. For example,

teaching patients about the impact that sleep problems can have on daily activities, fatigue, or depression can bring awareness to these problems and prompt patients to change their health-seeking behaviors and relay information to the oncology care team. Education should incorporate information about the long-term prevalence and effects of these symptoms and should be sensitive to ethnic and cultural needs. Nurses then can plan interventions in conjunction with patients and families to help manage the impact of these symptoms in their daily lives. For example, standard sleep hygiene interventions could be implemented. Appropriate referrals to other members of the healthcare team may be necessary. Follow-up should continue until problems are addressed appropriately.

*The authors thank Liguu Yu, PhD, for database support.*

**Author Contact:** Janet S. Carpenter, PhD, RN, can be reached at carpentj@iupui.edu, with copy to editor at rose\_mary@earthlink.net.

## References

- Ancoli-Israel, S., Moore, P.J., & Jones, V. (2001). The relationship between fatigue and sleep in cancer patients: A review. *European Journal of Cancer Care*, 10, 245–255.
- Andrykowski, M.A., Carpenter, J.S., Greiner, C.B., Altmair, E.M., Burish, T.G., Antin, J.H., et al. (1997). Energy level and sleep quality following bone marrow transplantation. *Bone Marrow Transplantation*, 20, 669–679.
- Avis, N.E., Crawford, S., Stellato, R., & Longcope, C. (2001). Longitudinal study of hormone levels and depression among women transitioning through menopause. *Climacteric*, 4, 243–249.
- Avis, N.E., Stellato, R., Crawford, S., Bromberger, J., Ganz, P., Cain, V., et al. (2001). Is there a menopausal syndrome? Menopausal status and symptoms across racial/ethnic groups. *Social Science and Medicine*, 52, 345–356.
- Baker, A., Simpson, S., & Dawson, D. (1997). Sleep disruption and mood changes associated with menopause. *Journal of Psychosomatic Research*, 43, 359–369.
- Berger, A.M. (1998). Patterns of fatigue and activity and rest during adjuvant breast cancer chemotherapy. *Oncology Nursing Forum*, 25, 51–62.
- Berger, A.M., & Farr, L. (1999). The influence of daytime inactivity and nighttime restlessness on cancer-related fatigue. *Oncology Nursing Forum*, 26, 1663–1671.
- Berger, A.M., & Higginbotham, P. (2000). Correlates of fatigue during and following adjuvant breast cancer chemotherapy: A pilot study. *Oncology Nursing Forum*, 27, 1443–1448.
- Berger, A.M., VonEssen, S., Khun, B.R., Piper, B.F., Farr, L., Agrawal, S., et al. (2002). Feasibility of a sleep intervention during adjuvant breast cancer chemotherapy. *Oncology Nursing Forum*, 29, 1431–1441.
- Berger, A.M., & Walker, S.N. (2001). An explanatory model of fatigue in women receiving adjuvant breast cancer chemotherapy. *Nursing Research*, 50, 42–52.
- Berkman, L.F., Berkman, C.S., Kasl, S., Freeman, D.H., Jr., Leo, L., Ostfeld, A.M., et al. (1986). Depressive symptoms in relation to physical health and functioning in the elderly. *American Journal of Epidemiology*, 124, 372–388.
- Brambilla, D.J., McKinlay, S.M., & Johannes, C.B. (1994). Defining the perimenopause for application in epidemiologic investigations. *American Journal of Epidemiology*, 140, 1091–1095.
- Broeckel, J.A., Jacobsen, P.B., Horton, J., Balducci, L., & Lyman, G.H. (1998). Characteristics and correlates of fatigue after adjuvant chemotherapy for breast cancer. *Journal of Clinical Oncology*, 16, 1689–1696.
- Busse, D.J., Reynolds, C.F., III, Monk, T.H., Berman, S.R., & Kupfer, D.J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research*, 28, 193–213.
- Busse, D.J., Reynolds, C.F., III, Monk, T.H., Hoch, C.C., Yeager, A.L., & Kupfer, D.J. (1991). Quantification of subjective sleep quality in healthy elderly men and women using the Pittsburgh Sleep Quality Index (PSQI). *Sleep*, 14, 331–338.
- Carpenter, J.S., & Andrykowski, M.A. (1998). Psychometric evaluation of the Pittsburgh Sleep Quality Index. *Journal of Psychosomatic Research*, 45, 5–13.
- Carpenter, J.S., Andrykowski, M.A., Freedman, R.R., & Munn, R. (1999). Feasibility and psychometrics of an ambulatory hot flash monitoring device. *Menopause*, 6, 209–215.
- Carpenter, J.S., Andrykowski, M.A., Wilson, J., Hall, L.A., Rayens, M.K., Sachs, B., et al. (1998). Psychometrics for two short forms of the Center for Epidemiologic Studies–Depression Scale. *Issues in Mental Health Nursing*, 19, 481–494.
- Carpenter, J.S., Johnson, D., Wagner, L., & Andrykowski, M. (2002). Hot flashes and related outcomes in breast cancer survivors and matched comparison women. *Oncology Nursing Forum*, 29, E16–E25. Retrieved March 2, 2004, from [http://www.ons.org/xp6/ONS/Library.xml/ONS\\_Publications.xml/ONF.xml/ONF2002.xml/April\\_2002.xml/Members\\_Only/Carpenter\\_article.xml](http://www.ons.org/xp6/ONS/Library.xml/ONS_Publications.xml/ONF.xml/ONF2002.xml/April_2002.xml/Members_Only/Carpenter_article.xml)
- Clark, A.J., Flowers, J., Boots, L., & Shettar, S. (1995). Sleep disturbance in mid-life women. *Journal of Advanced Nursing*, 22, 562–568.
- Comstock, G.W., & Helsing, K.J. (1976). Symptoms of depression in two communities. *Psychological Medicine*, 6, 551–563.
- Couzi, R.J., Helzlsouer, K.J., & Fetting, J.H. (1995). Prevalence of menopausal symptoms among women with a history of breast cancer and attitudes toward estrogen replacement therapy. *Journal of Clinical Oncology*, 13, 2737–2744.
- Curran, S.L., Andrykowski, M.A., & Studts, J.L. (1995). Short form of the Profile of Mood States (POMS–SF): Psychometric information. *Psychological Assessment*, 7, 80–83.
- Dennerstein, L., Dudley, E.C., Hopper, J.L., Guthrie, J.R., & Burger, H.G. (2000). A prospective population-based study of menopausal symptoms. *Obstetrics and Gynecology*, 96, 351–358.
- Dormire, S.L., & Carpenter, J.S. (2002). An alternative to unibase/glycol as an effective nonhydrating electrolyte medium for the measurement of electrodermal activity. *Psychophysiology*, 39, 423–426.
- Empson, J.A., & Purdie, D.W. (1999). Effects of sex steroids on sleep. *Annals of Medicine*, 31, 141–145.
- Erlik, Y., Tataryn, I.V., Meldrum, D.R., Lomax, P., Bajorek, J.G., & Judd, H.L. (1981). Association of waking episodes with menopausal hot flashes. *JAMA*, 245, 1741–1744.
- Finck, G., Barton, D.L., Loprinzi, C.L., Quella, S.K., & Sloan, J.A. (1998).

- Definitions of hot flashes in breast cancer survivors. *Journal of Pain and Symptom Management*, 16, 327–333.
- Freedman, R.R. (1989). Laboratory and ambulatory monitoring of menopausal hot flashes. *Psychophysiology*, 26, 573–579.
- Gentili, A., Weiner, D.K., Kuchibhatla, M., & Edinger, J.D. (1995). Test-retest reliability of the Pittsburgh Sleep Quality Index in nursing home residents [Letter to the editor]. *Journal of the American Geriatrics Society*, 43, 1317–1318.
- Harlow, B.L., Cohen, L.S., Otto, M.W., Spiegelman, D., & Cramer, D.W. (1999). Prevalence and predictors of depressive symptoms in older premenopausal women: The Harvard Study of Moods and Cycles. *Archives of General Psychiatry*, 56, 418–424.
- Harris, P.F., Remington, P.L., Trentham-Dietz, A., Allen, C.I., & Newcomb, P.A. (2002). Prevalence and treatment of menopausal symptoms among breast cancer survivors. *Journal of Pain and Symptom Management*, 23, 501–509.
- Hollander, L.E., Freeman, E.W., Sammel, M.D., Berlin, J.A., Grisso, J.A., & Battistini, M. (2001). Sleep quality, estradiol levels, and behavioral factors in late reproductive age women. *Obstetrics and Gynecology*, 98, 391–397.
- Joffe, H., Hall, J.E., Soares, C.N., Hennen, J., Reilly, C.J., Carlson, K., et al. (2002). Vasomotor symptoms are associated with depression in perimenopausal women seeking primary care. *Menopause*, 9, 392–398.
- Kingsberg, S.A. (2002). Reproductive senescence and depression revisited (again) [Editorial]. *Menopause*, 9, 389–391.
- Knobf, M.T. (2001). The menopausal symptom experience in young mid-life women with breast cancer. *Cancer Nursing*, 24, 201–211.
- Lenz, E.R., Pugh, L.C., Milligan, R.A., Gift, A., & Suppe, F. (1997). The middle-range theory of unpleasant symptoms: An update. *Advances in Nursing Science*, 19(3), 14–27.
- Lenz, E.R., Suppe, F., Gift, A.G., Pugh, L.C., & Milligan, R.A. (1995). Collaborative development of middle-range nursing theories: Toward a theory of unpleasant symptoms. *Advances in Nursing Science*, 17(3), 1–13.
- Lykken, D.T., & Venables, P.H. (1971). Direct measurement of skin conductance: A proposal for standardization. *Psychophysiology*, 8, 656–672.
- Manber, R., & Armitage, R. (1999). Sex, steroids, and sleep: A review. *Sleep*, 22, 540–555.
- McNair, D.M., Lorr, M., & Droppleman, L.F. (1992). *EdITS manual for the Profile of Mood States*. San Diego, CA: Educational and Industrial Testing Service.
- Meek, P.M., Nail, L.M., Barsevick, A., Schwartz, A.L., Stephen, S., Whitmer, K., et al. (2000). Psychometric testing of fatigue instruments for use with cancer patients. *Nursing Research*, 49, 181–190.
- Miaskowski, C., & Lee, K.A. (1999). Pain, fatigue, and sleep disturbances in oncology outpatients receiving radiation therapy for bone metastasis: A pilot study. *Journal of Pain and Symptom Management*, 17, 320–332.
- Mourits, M.J., Bockermann, I., de Vries, E.G., van der Zee, A.G., ten Hoor, K.A., van der Graaf, W.T., et al. (2002). Tamoxifen effects on subjective and psychosexual well-being, in a randomized breast cancer study comparing high-dose and standard-dose chemotherapy. *British Journal of Cancer*, 86, 1546–1550.
- Myers, E.G., Allen, R.A., & Baile, W.F. (1996). Pain less than zero: Response-shift theory applied to pain measurement [Abstract]. *Proceedings of the Third World Congress of Psycho-Oncology, USA*, 3, 50.
- Okuyama, T., Akechi, T., Kugaya, A., Okamura, H., Imoto, S., Nakano, T., et al. (2000). Factors correlated with fatigue in disease-free breast cancer patients: Application of the Cancer Fatigue Scale. *Supportive Care in Cancer*, 8, 215–222.
- Owens, J.F., & Matthews, K.A. (1998). Sleep disturbance in healthy middle-aged women. *Maturitas*, 30(1), 41–50.
- Pasternak, R.E., Reynolds, C.F., III, Houck, P.R., Schlermitzauer, M., Buysse, D.J., Hoch, C.C., et al. (1994). Sleep in bereavement-related depression during and after pharmacotherapy with nortriptyline. *Journal of Geriatric Psychiatry and Neurology*, 7(2), 69–73.
- Polo-Kantola, P., Erkkola, R., Helenius, H., Irjala, K., & Polo, O. (1998). When does estrogen replacement therapy improve sleep quality? *American Journal of Obstetrics and Gynecology*, 178, 1002–1009.
- Porter, M., Penney, G.C., Russell, D., Russell, E., & Templeton, A. (1996). A population based survey of women's experience of the menopause. *British Journal of Obstetrics and Gynaecology*, 103, 1025–1028.
- Radloff, L.S. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, 1, 385–401.
- Redeker, N.S., Lev, E.L., & Ruggiero, J. (2000). Insomnia, fatigue, anxiety, depression, and quality of life of cancer patients undergoing chemotherapy. *Scholarly Inquiry for Nursing Practice*, 14, 275–290.
- Roscoe, J.A., Morrow, G.R., Hickok, J.T., Bushnow, P., Matteson, S., Rakita, D., et al. (2002). Temporal interrelationships among fatigue, circadian rhythm and depression in breast cancer patients undergoing chemotherapy treatment. *Supportive Care in Cancer*, 10, 329–336.
- Schwartz, A.L., Meek, P.M., Nail, L.M., Fargo, J., Lundquist, M., Donofrio, M., et al. (2002). Measurement of fatigue. Determining minimally important clinical differences. *Journal of Clinical Epidemiology*, 55, 239–244.
- Schwartz, C.E. (1996). Examining response shift in adaptation to chronic health stressors: Quantitative and qualitative evidence [Abstract]. *Annals of Behavioral Medicine: Nineteenth Annual Meeting*, 20(Suppl. 1), S035.
- Servaes, P., Prins, J., Verhagen, S., & Bleijenberg, G. (2002). Fatigue after breast cancer and in chronic fatigue syndrome. Similarities and differences. *Journal of Psychosomatic Research*, 52, 453–459.
- Servaes, P., Verhagen, S., & Bleijenberg, G. (2002). Determinants of chronic fatigue in disease-free breast cancer patients: A cross-sectional study. *Annals of Oncology*, 13, 589–598.
- Shacham, S. (1983). A shortened version of the Profile of Mood States. *Journal of Personality Assessment*, 47, 305–306.
- Shaver, J.L., & Zenk, S.N. (2000). Sleep disturbance in menopause. *Journal of Women's Health and Gender-Based Medicine*, 9, 109–118.
- Stein, K.D., Jacobsen, P.B., Hann, D.M., Greenberg, H., & Lyman, G. (2000). Impact of hot flashes on quality of life among postmenopausal women being treated for breast cancer. *Journal of Pain and Symptom Management*, 19, 436–445.
- Tiffin, P., Ashton, H., Marsh, R., & Kamali, F. (1995). Pharmacokinetic and pharmacodynamic responses to caffeine in poor and normal sleepers. *Psychopharmacology*, 121, 494–502.
- Turk, D.C., & Fernandez, E. (1990). On the putative uniqueness of cancer pain: Do psychological principles apply? *Behaviour Research and Therapy*, 28(1), 1–13.
- Winningham, M.L. (1996). Fatigue. In S.L. Groenwald, M.H. Frogge, M. Goodman, & C.H. Yarbrow (Eds.), *Cancer symptom management* (pp. 42–58). Sudbury, MA: Jones and Bartlett.
- Woodward, S., & Freedman, R.R. (1994). The thermoregulatory effects of menopausal hot flashes on sleep. *Sleep*, 17, 497–501.