# Sleep problems in breast cancer survivors 1-10 years posttreatment

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(RECEIVED February 13, 2017; ACCEPTED March 23, 2017)

# ABSTRACT

*Objective:* Sleep can affect quality of life (QoL) during cancer survivorship, and symptoms related to poor sleep can be exacerbated. We examined the prevalence, severity, and nature of subjective sleep complaints in women surviving stage I–III breast cancer who were 1–10 years posttreatment. We also examined the demographic, medical, physical, and psychosocial correlates of poor sleep in these women in order to identify the subgroups that may be most in need of intervention.

*Method:* A total of 200 patients at a comprehensive cancer center who were 1–10 years posttreatment for primary stage I–III breast cancer with no evidence of disease at the time of enrollment completed a battery of questionnaires on demographics, sleep, physical symptoms, mood, cancer-specific fears, and QoL.

*Results:* The women had a mean age of 57 years (SD = 10.0), with a mean of 63.3 months (SD = 28.8) of post-cancer treatment. Some 38% of these patients were identified as having poor-quality sleep. Women with poor sleep took longer to fall asleep, had more awakenings, and acquired 2 hours less sleep per night than those with good sleep. They also had a lower QoL, greater severity of pain, more concerns about health and recurrence, and increased vasomotor symptoms (p < 0.05). Daytime sleepiness and depression were found to be not significantly correlated with sleep quality.

*Significance of results:* Many breast cancer survivors had severe subjective insomnia, and several breast cancer survivor subgroups were identified as having members who might be most in need of sleep-improvement interventions. Addressing physical symptoms (e.g., vasomotor symptoms and pain) and providing education about the behavioral, social, environmental, and medical factors that affect sleep could result in substantial improvement in the life course of breast cancer survivors.

KEYWORDS: Breast cancer, Survivor, Sleep, Vasomotor symptoms, Quality of life

# **INTRODUCTION**

Poor sleep is a common problem in people who have been treated for cancer, yet, unlike other symptoms

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(e.g., pain and fatigue), it is largely overlooked in the medical and supportive care of these patients. Across all cancers, the prevalence rates of sleep disturbance are consistently high (59-79%) (Davidson et al., 2002; Palesh et al., 2010; Savard et al., 2011); however, breast cancer patients have been found to be particularly vulnerable to sleep disturbances compared to patients with other types of cancers (Colagiuri et al., 2011). Breast cancer patients have often reported that poor-quality sleep and staying asleep throughout the night are their greatest challenges (Beck et al., 2010; Davidson et al., 2002; Kotronoulas et al., 2012). Impaired daytime functioning—including low activity levels, fatigue, and naps-are also frequently reported (Berger et al., 2009a; Kotronoulas et al., 2012). Although several studies have found that sleep disturbances begin or worsen during cancer treatment (Beck et al., 2010; Enderlin et al., 2010; Kotronoulas et al., 2012; Savard & Morin, 2001), some research has demonstrated that, even after cessation of cancer treatment, breast cancer survivors continue to experience sleep problems for many years (Lindley et al., 1998; Savard & Morin, 2001). This is a matter for concern, given that there are serious negative physical and psychological consequences of long-term sleep disturbance (Colten & Altevogt, 2007). The quality of sleep of breast cancer patients who are surviving for years posttreatment has not been well-studied, despite this being one of the largest survivorship populations. By increased research focused on this area, sleep problems can become mainstream in terms of symptom screening and management as part of comprehensive supportive cancer care.

There are a number of physical and psychological variables thought to contribute to the high rate of sleep disturbances in breast cancer survivors (Palesh et al., 2010; Savard et al., 2004; Ellis et al., 2014). Some 40–70% of breast cancer survivors experience vasomotor symptoms (such as night sweats and hot flashes) and report a greater symptom burden at night (Carpenter et al., 2004; Harris et al., 2002). Tamoxifen, typically given to breast cancer survivors for 5 years following treatment, is known to increase the frequency of hot flashes (Colagiuri et al., 2011; Savard et al., 2004; 2001). In fact, Mourits et al. (2002) found that as many as 50% of women taking tamoxifen reported multiple awakenings through the night. Such physical symptoms as pain can also impact sleep (Miaskowski et al., 2004). In addition, when patients cannot sleep, they expose themselves to stressful and upsetting thoughts. Some studies have found that most patients attribute their sleep disturbance to negative thoughts, worry, and anxiety (Dupont et al., 2014; Hall et al., 2014; Rumble et al., 2010). In a study of cancer patients, Rumble and colleagues (2010) found that higher levels of sleep-inhibitory thoughts and behaviors are antecedents of insomnia, as well as higher levels of pain, fatigue, and hot flashes and lower levels of positive mood as consequences of insomnia. Carpenter et al. (2004) found that self-reported sleep disturbances were more common in breast cancer patients than in agematched healthy controls; however, sleep disturbances were more strongly correlated with depression and fatigue than to frequency of hot flashes. The evidence is not clear as to which factors contribute most to sleep disturbances.

Poor sleep can negatively impact quality of life (QoL) during survivorship and exacerbate such symptoms commonly seen in breast cancer survivors as pain, depression, anxiety/worry, and hot flashes (Davidson et al., 2002). A vast body of literature has shown that untreated chronic insomnia negatively impacts mood, physical symptoms, pain sensitivity, fatigue, and QoL (Colten & Altevogt, 2007). Insomnia is increasingly viewed as an independent risk factor for future depression (Irwin et al., 2013; Jim et al., 2013). Breast cancer patients have also reported on sleep disturbance as part of a dietary intervention study (Bardwell et al., 2008), where the authors found that demographic, medical, and health behavior variables were not significant risk factors for sleep disturbance (only worse depressive and vasomotor symptoms were meaningful predictors). Further research is needed to better understand the interaction of the above factors and their impact on sleep in posttreatment survivors of breast cancer. Engaging in a sleep-improvement intervention has the potential to enhance breast cancer survivors' QoL. reduce physical symptoms, improve mood (Berger et al., 2009a; Espie et al., 2008; Savard et al., 2005), and even affect the disease course and survival (Palesh et al., 2014; Savard et al., 2003; Colten & Altevogt, 2007; Spiegel et al., 2002). The importance of understanding sleep disturbances in cancer populations has been highlighted by national agencies and professional societies (Colten & Altevogt, 2007). The U.S. Department of Health and Human Services has recognized sleep disorders as warranting further scientific investigation, with cancer named specifically as a high-priority research focus (Buscemi et al., 2005).

In the current study, we examined the prevalence, severity, and nature of subjective sleep complaints in women who had survived stage I–III breast cancer and were 1–10 years posttreatment. We also examined the demographic, medical, physical, and psychosocial correlates of poor sleep in order to describe identifiable subgroups of breast cancer survivors. The study included a subset of participants (n = 27) who underwent polysomnography sleep studies in

order to enhance our understanding of the physiological nature of the sleep disturbances experienced. Those findings are reported in a separate article (Reinsel et al., 2015).

## **METHODS**

# **Participants**

Our sample included 200 female adult breast cancer survivors who were receiving follow-up care at the Breast Cancer Service at the Memorial Sloan Kettering Cancer Center. The eligibility criteria included: (1) a diagnosis of primary stage I, II, or III breast cancer; (2) being at least 1 year and no more than 10 years posttreatment; (3) having no evidence of disease at the time of assessment; (4) showing no evidence of acute or chronic encephalopathy; (5) no evidence of psychiatric disease severe enough to compromise data collection; (6) being at least 18 years of age; and (7) having the ability to speak and read English.

## Measures

#### Sociodemographic Characteristics

Participants completed a demographics questionnaire that included questions related to age, race/ ethnicity, marital status, education level, employment status, and income.

#### Medical Characteristics

Participants' medical data were reviewed upon entry into the study to obtain site and stage of disease, Eastern Cooperative Oncology Group rating, current medications, present oncologic therapy, and medications for palliative care.

#### Subjective Sleep Assessments

The Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) is a 24-item questionnaire about a patient's sleep habits. It describes sleep disturbance in terms of seven domains along with a global score. It has good reliability and validity and has been used in psychiatric and general medical as well as oncology studies (Carpenter & Andrykowski, 1998). The Insomnia Severity Index (ISI) (Bastien et al., 2001) is a 7-item self-report measure of perceived severity of insomnia symptoms over the course of the previous two weeks. The overall severity of insomnia can be calculated by summing individual items (difficulties with falling asleep, maintaining sleep, and early morning awakenings, as well as degree of dissatisfaction with current sleep). The Epworth Sleepiness Scale (ESS) (Johns, 1991) is an 8-item self-report questionnaire employed to assess daytime sleepiness in adults.

#### Associated Symptoms and Quality of Life

The Numeric Rating Scale (NRS) (Paice & Cohen, 1997) is a pain symptom inventory that assesses a range of symptoms associated with pain severity (e.g., energy level, pain, and daytime sedation) on a 0-to-10 Likert-type scale. The Quality of Life Cancer Survivor Summary (QoL-CS) (Ferrell et al., 1995) is a 41-item instrument that assesses four domains of QoL: physical, psychological, social, and spiritual well-being. The Postmenopausal Estrogen/Progestin Intervention Scale (PEPI) (Greendale et al., 1998) is a 47-item self-report measure of postmenopausal symptoms. For the current study, we adapted the original version of the PEPI by asking women to respond on a 0 (not at all) to 4 (extremely) Likert-type scale about the impact of their menopausal symptoms during the previous week. It has been used in several large-scale clinical trials with healthy and medically ill populations and has good reliability and a wide distribution of responses (Espeland et al., 1995; Greendale et al., 1998).

#### **Psychological Distress Measures**

The Brief Zung Self-Rating Depression Scale (BZSDS) (Dugan et al., 1998) is an 11-item measure of depressive symptoms (e.g., anhedonia, dysphoria, concentration, and hopelessness) that does not assess the somatic symptoms of depression that are often confounded by cancer and its treatment (e.g., fatigue, appetite changes, and insomnia). In the current sample, the BZSDS demonstrated good internal consistency ( $\alpha = 0.86$ ). The Concerns About Recurrence Scale (CARS) (Vickberg, 2003) is a 30-item scale designed to assess women's fears about the possibility of recurrence of breast cancer. This scale assesses overall fear of recurrence by asking about the frequency, potential for upset, consistency, and intensity of fears, in addition to the nature of women's fears, including health, womanhood, role, and death worries.

#### Procedure

Our protocol was submitted and approved by the institutional review board at Memorial Sloan Kettering. All the procedures performed involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments, or comparable ethical standards. A list of participants based on study eligibility criteria was generated by querying our institutional database. Breast cancer survivors who met the eligibility criteria were randomly selected for participation. A trained research study assistant reviewed patients' electronic medical records, confirmed survivor eligibility status with the clinic's attending physician, and obtained permission to approach the survivor. Informed consent was obtained from all the individual participants included in the study.

Eligible participants who gave informed consent completed the battery of questionnaires in person at the time of their clinic appointment, at their own home, and returned it by mail, or via telephone with the assistance of a trained research study assistant. A \$20 stipend was provided upon completion of the battery of questionnaires.

#### Statistical Analysis

Descriptive statistics were calculated to characterize the current sample of breast cancer survivors with respect to sleep variables, as well as demographic, medical, physical, and psychosocial variables. Correlation analysis was conducted to understand bivariate associations among study variables. To examine group differences, breast cancer survivors were categorized into good and poor sleepers, based on a PSQI global cutoff score of 8 (Carpenter & Andrykowski, 1998). Differences were analyzed using independent-means t or chi-square tests, as appropriate.

## RESULTS

For our analysis, questionnaires were completed by 200 breast cancer survivors. The majority of women were Caucasian (88.5%), married (68.5%), employed (58%), had a college degree (75%), were postmenopausal (81.5%), and were 50 years of age or older (73%). More than half of the women (55%) in our study were diagnosed with stage II breast cancer. Additional demographic and medical characteristics of the sample are presented in Table 1.

Using a PSQI global score of 8 as a conservative cutoff (as suggested by Carpenter & Andrykowski [1998]) for use in cancer populations), we found that 38% of breast cancer survivors were categorized as having very poor-quality sleep (PSQI global score >8). Among these women, 54% reported difficulty falling asleep (10% rated this problem as severe or very severe), 67% had difficulty staying asleep (24% rated this as severe or very severe), and 58% reported problems waking up too early (16% rated this as severe or very severe). Compared to those with good-quality sleep, women with poor-quality sleep took more than twice as much time to fall asleep (M = 39 vs. 15 min; t(86) = -5.68, p < 0.001, d = 0.90),

**Table 1.** Demographic variables in breast cancer survivors (N = 200)

Variable	n	%
Age	200	100
21-35	2	1
35 - 50	54	27
50 - 65	103	51.5
65 - 80	41	20.5
Race		
White	177	88.5
Black/African American	8	4
Asian/Pacific Islander	5	2.5
Spanish/Hispanic/Latino	6	3
Other	4	2
Marital status		
Married	137	68.5
Not married	63	31.5
Education		
High school or less	25	12.5
Partial college	25	12.5
College degree	69	34.5
Graduate degree	81	40.5
Employment		
Employed	116	58
Retired	56	28
Unemployed	28	14
Income (UŠ\$)		
<50,000	33	16.5
50,000-89,000	38	19
>89,000	28	14

had almost double the number of nighttime awakenings (M = 2.7 vs. 1.6 awakenings per night; t(197) =-7.84, p < 0.001, d = 1.07), and slept a total of 2 hours less each night (M = 5.1 vs. 7.0 hours; t(86) = 10.96, p < 0.001, d = 1.72).

Chi-square analyses revealed that good and poor sleepers did not differ on such demographic variables as marital status  $(X^2(3,200) = 4.12, p > 0.05)$ , race  $(X^{2}(4,200) = 4.93, p > 0.05)$ , and education level  $(X^{2}(5,200) = 9.12, p > 0.05)$ , but poor sleepers were less likely to be working  $(X^2(6,200) = 14.5, p <$ 0.05). Moreover, poor sleepers were more likely to endorse such behaviors as smoking cigarettes  $(X^2(1,199) = 5.85, p < 0.05)$  and drinking alcohol  $(X^2(3,198) = 3.93, p < 0.05)$ , but they did not differ when compared to good sleepers with respect to caffeine use  $(X^2(3,200) = 0.887, p > 0.05)$ . Chi-square tests revealed that good and poor sleepers did not differ on such medical factors as disease stage  $(X^2(2,184) = 1.30, p > 0.05)$  or cancer treatment types: surgery  $(X^2(1,199) = 5.85, p < 0.05)$ , chemotherapy  $(X^2(1,200) = 0.327, p > 0.05)$ , radiation  $(X^{2}(1,200) = 0.966, p > 0.05)$ , hormonal  $(X^{2}(1,200) =$ 0.644, p > 0.05), and biologic ( $X^2(1,200) = 0.584$ , p > 0.05) 0.05). Menopausal status, however, did appear to play a role in sleep quality. Poor sleep quality was reported in 33% of postmenopausal women, in 50% of perimenopausal women, and in only 9% of premenopausal women.

Means, standard deviations, and correlations among age, psychosocial, QoL, and sleep variables can be found in Table 2. PSQI global score, daytime sleepiness (based on ESS score), and severity of insomnia (based on ISI score) were all significantly positively correlated with menopausal symptoms, pain symptoms, and concerns about recurrence, and negatively correlated with cancer-related QoL. Depressive symptoms were unrelated to severity of insomnia, daytime sleepiness, and PSQI global score. PSQI global score was significantly positively associated with severity of insomnia but unrelated to ratings of daytime sleepiness. Correlation analyses also revealed that PSQI global score was significantly associated with increased concerns about recurrence and increased menopausal symptoms.

Mean differences in QoL, depressive symptoms, pain symptoms, concerns about recurrence, insomnia severity, and daytime sleepiness between those with good- and poor-quality sleep are given in Table 3. Compared to women with good-quality sleep, women with poor sleep had significantly more symptoms of insomnia, a poorer QoL, more concerns about cancer recurrence, and greater pain severity, but they did not differ significantly with regard to daytime sleepiness ratings or depressive symptoms.

Given that vasomotor symptoms are common among breast cancer survivors and can impact their sleep, we wanted to understand the associations of

**Table 2.** Treatment and medical variables in breast cancer survivors (N = 200)

Variable	N	%
Disease stage		
I	64	32
II	111	55.5
III	25	12.5
Time since treatment		
1-2 (years)	20	10
2-5 (years)	82	41
5-10 (years)	98	49
Treatment type		
Surgery	175	87.5
Chemotherapy	194	97
Radiation	138	69
Hormonal	120	60
Menopausal status		
Premenopausal	19	9.5
Perimenopausal	14	7.0
Postmenopausal	163	81.5

Treatment type total percentage is greater than 100% because some women received multiple treatments.

hot flashes and night sweats, as well as associated tamoxifen use, with sleep in our sample. Compared to women with good-quality sleep, those with poorquality sleep reported more hot flashes (t = 4.3, p <0.001, d = 0.46) and night sweats (t = 3.1, p < 1000.001, d = 0.66). Difficulties with falling and staying asleep and problems with waking up too early were all positively associated with night sweats and hot flashes (p < 0.05). The strongest association between insomnia symptoms and vasomotor symptoms was for difficulties staying asleep and both hot flashes (r = 0.38, p < 0.001) and night sweats (r = 0.45, p < 0.001)0.001). A total of 122 women, some 61% of the sample, were taking hormones. Women taking tamoxifen (13.5%) reported a larger number of hot flashes (t =-3.96, p < 0.001) and night sweats (t = -3.13, p < 0.001) 0.001). Tamoxifen use was also significantly correlated with worse sleep on the PSQI (r = 0.14, p <0.05).

Finally, we wanted to understand if women who reported good- versus poor-quality sleep differed on the psychosocial factors commonly reported by breast cancer survivors (e.g., difficulty coping, concerns about appearance, social isolation, purpose in life, and concerns about health, recurrence, and death). Women with poor-quality sleep reported greater difficulty coping (t = 3.9, p < 0.001, d = 0.61), more concerns about their appearance (t = 3.1, p < 0.01, d = 0.23), and were more socially isolated (t = 3.5, p < 0.001, d = 0.52). They also reported greater concerns about their overall health (t = -1.98, p = 0.05, d = 0.29) and recurrence (t = 3.64, p < 0.001, d = 0.53). There were no differences with respect to purpose

**Table 3.** Mean differences between good and poorsleepers on psychosocial and quality of life variables

	Good sleeper (PSQI $\leq 8$ ) ( $n = 124$ )	Poor sleeper (PSQI $> 8$ ) ( $n = 76$ )	<i>t</i> value	<i>p</i> value
ISI ESS CARS BZDSD QoL-CS NRS	$5.2 \pm 4.5 \\ 5.9 \pm 3.4 \\ 2.7 \pm 1.2 \\ 19.5 \pm 6.1 \\ 282.3 \pm 49.9 \\ 1.3 \pm 1.4$	$\begin{array}{c} 13.9 \pm 5.2 \\ 6.3 \pm 4.4 \\ 3.3 \pm 1.4 \\ 19.8 \pm 6.9 \\ 240.9 \pm 57.0 \\ 3.2 \pm 1.8 \end{array}$	$12.0 \\ 0.68 \\ 3.5 \\ 0.37 \\ 5.2 \\ 7.8$	$<\!\!\!\!\!\begin{array}{c} <\!$
PEPI	$18.7 \pm 11.1$	$34.6 \pm 19.3$	6.3	< 0.001

Values are given as mean  $\pm$  standard deviation. The given *p* value is for a two-tailed test.

ns = nonsignificant; PSQI = Pittsburgh Sleep Quality Index; ISI = Insomnia Severity Index; ESS = Epworth Sleepiness Scale; BZSDS = Brief Zung Self-Rating Depression Scale; CARS = Concerns About Recurrence Scale; NRS = Numerical Rating Scale; PEPI = Postmenopausal Estrogen/Progestin Intervention Scale; QoL-CS = Quality of Life Cancer Survivor Summary. in life (t = 0.387, ns, d = 0.06) or concerns about death (t = 0.37, ns, d = 0.05 (see Table 4).

# DISCUSSION

The primary goal of our study was to describe the prevalence, severity, and nature of sleep disturbance in a sample of breast cancer survivors up to 10 years posttreatment. More than a third of them had subjectively poor sleep, with clinically important differences. They reported taking more than twice as long to fall asleep. They also had twice as many awakenings during the night, and they slept 2 hours less on average every night. That equates to an average of 14 hours, or two full nights, less sleep every week. This suggests that these women had only 5 hours of total sleep time per night. By that subjective assessment, they were very sleep-deprived compared to those with good-quality sleep, and that could have enormous consequences. Of the 38% of women with poor-quality sleep, trouble staying asleep was the most common sleep complaint (67%), with 24% rating this problem as severe or very severe. This is consistent with the findings from several studies of breast cancer patients undergoing treatment (Beck et al., 2010; Davidson et al., 2002; Kotronoulas et al., 2012), as well as a recent review focused on sleep during the posttreatment survivorship period (Budhrani et al., 2015).

Our secondary goal was to identify the demographic, medical, physical, and psychosocial correlates of poor sleep among survivors. We found that women who were unemployed or retired were more likely to report poor-quality sleep, but this was not merely due to age, as age was not related to sleep quality. There are very few studies on sleep and aging

in cancer patients, and the existing evidence is mixed. Some studies have found poorer sleep in older individuals, and other research has found an association with younger age (see Palesh et al. [2013] for a review). There are multiple potential explanations for such mixed associations, such as confounding factors, including psychosocial burden and employment status. Perimenopausal breast cancer survivors may also gain particular benefit from sleep interventions, as they are more likely to report poor sleep. This may be due to the greater likelihood of experiencing hot flashes and night sweats, as well as tamoxifen use, which we found to be associated with more sleep disturbances, especially nighttime awakenings. These results are consistent with Berger et al.'s (2009b)findings that interrupted sleep from hot flashes varies by menopausal status. Vasomotor symptoms have been reported to affect sleep in breast cancer survivors (Savard et al., 2004), and healthy women with hot flashes have reported poor sleep (Carpenter et al., 2002). Breast cancer survivors tend to have more severe and distressing hot flashes than women without cancer (Carpenter & Andrykowski, 1998; Carpenter et al., 2002). These findings support the importance of addressing vasomotor symptoms.

Individuals who engaged in such behaviors as smoking and drinking alcohol reported poorer overall sleep quality. Further research is needed to examine the possible explanations for this association, such as whether the smoking and drinking behaviors developed as an attempt to self-medicate for the poor sleep. Interestingly, caffeine use was not significantly related to reported sleep quality. In a previous study of 20-year survival in 96 women with breast cancer (Lehrer et al., 2013), coffee consumption was found to have a significant effect on overall survival

Variable	1	2	3	4	5	6	7	8	9
1. Age	_	0.038	0.008	-0.162*	0.018	-0.181**	-0.097	-0.041	$0.153^{*}$
2. PSQI		-	$0.824^{**}$	0.088	0.015	$0.300^{**}$	$0.640^{**}$	$0.548^{**}$	$-0.423^{**}$
3. ISI			-	0.184	0.003	$0.361^{**}$	$0.679^{**}$	$0.629^{**}$	-0.540 **
4. ESS				_	0.030	0.201	0.267	$0.309^{**}$	-0.324*
5. BZSDS					_	-0.016	-0.007	0.053	-0.024
6. CARS						_	$0.404^{**}$	$0.426^{**}$	$-0.666^{**}$
7. NRS							_	$0.699^{**}$	$-0.602^{**}$
8. PEPI									$-0.730^{**}$
9. QoL-CS								—	_
Mean	57.01	7.47	8.52	6.08	19.66	2.93	1.98	23.26	266.5
Standard deviation	10.0	4.459	6.34	3.87	6.40	1.29	1.83	16.37	56.44

Table 4. Correlations, means, and standard deviations among study variables

PSQI = Pittsburgh Sleep Quality Index Global Score; ISI = Insomnia Severity Index; ESS = Epworth Sleepiness Scale; BZSDS = Brief Zung Self-Rating Depression Scale; CARS = Concerns About Recurrence Scale; NRS = Numerical Rating Scale; PEPI = Postmenopausal Estrogen/Progestin Intervention Scale; QoL-CS = Quality of Life Cancer Survivor Summary.

\* p < 0.05. \*\* p < 0.01.

independent of the effects of lymph node involvement, age at diagnosis, and smoking history. The authors of that study suggested that coffee consumption may have been an attempt to self-medicate for persistent fatigue. Taken together, these results suggest that breast cancer survivors may have a poor understanding of how these substances impact sleep and how they themselves might benefit from interventions that promote sleep education (e.g., sleep hygiene).

With regard to psychosocial variables, there was an association between poor sleep and concerns about health and cancer recurrence. Previous research has found inconsistent evidence regarding such associations in breast cancer survivors. Hall et al. (2014) found that, among younger women 2-4years post-breast cancer treatment, subsyndromal insomnia was common and associated with cancerrelated anxiety. Dupont et al. (2014) followed breast cancer survivors for a year posttreatment and found that cancer-related worry was not associated with sleep disturbance. Although there is limited relevant research on long-term posttreatment survivors, there is some evidence linking worry and rumination with insomnia in cancer patient populations (Rumble et al., 2010), as well as prior research on general adult populations (Carney et al., 2010). Thus, further examination of potential associations between cancer-related worry and sleep is warranted in future studies of sleep correlates in posttreatment breast cancer survivors.

Higher levels of pain have been reported by women with poorer-quality sleep. This finding is consistent with prior research in cancer patients (Miaskowski et al., 2012; Syrjala et al., 2014) and in other populations (Vitiello et al., 2014). Breast cancer survivors with chronic pain may have impaired sleep and might benefit from sleep interventions that incorporate pain management techniques (Syrjala et al., 2014). However, further research exploring the relationship between pain and sleep in posttreatment survivors is required.

Reported sleep quality was not associated with daytime sleepiness in our participants. Although the relationship between daytime sleepiness and sleep quality has not been well-studied in cancer survivors (Forsythe et al., 2012), a similar lack of association has been found in studies of other medical populations (Lu et al., 2015; Setthawatcharawanich et al., 2014). The populations in which a relationship has been found include newly diagnosed lung cancer patients (Le Guen et al., 2007) and individuals with such breathing-related sleep disorders as sleep apnea (Vanaparthy et al., 2015), suggesting that a more complex relationship may exist between sleep quality and daytime sleepiness that should be examined in future research.

We also found no association between sleep quality and depression. Previous research has yielded inconsistent evidence regarding such associations in both cancer patients and the general population. In a longitudinal study of postsurgery breast cancer patients (Van Onselen et al., 2013), women with lower depression scores immediately following surgery experienced more sleep disturbances (compared to women with higher depression scores), but their sleep had improved at the 3-month follow-up assessment. In Ellis et al.'s (2014) longitudinal study of healthy participants, acute insomnia was associated with firstonset depression 3 months later. In a study of 419 older adults (Lee et al., 2013), persistent sleep disturbance during a year-long period was associated with depression during the following year in older adults with a history of depression; however, depression did not develop in any individuals who had no history of depression. Future study is certainly needed to examine the association between depression and sleep quality over time in posttreatment breast cancer survivors.

In addition, we found that women reporting poor sleep had poorer QoL. Combining this knowledge with other results presented in our present research, there is a clear need to implement routine sleep disturbance screening and interventions in supportive cancer care, particularly for breast cancer survivors. The practice of identifying and effectively treating sleep disturbances as a part of cancer care is currently suboptimal due to numerous barriers (Savard & Morin, 2001). Further efforts are needed to increase awareness via education, to develop brief validated sleep questionnaires, and to integrate screening (using multiple tools, if necessary) and treatment of sleep disturbances in cancer care. Interventions should take into account the fact that breast cancer survivors are often peri- or postmenopausal, taking tamoxifen, and may be experiencing hot flashes, night sweats, and pain along with impaired QoL (Berger et al., 2012; Otte et al., 2010; Van Onselen et al., 2013). Interventions that promote sleep education and relaxation training may be particularly beneficial for breast cancer survivors, offering new skills and awareness that may have been lacking. Medications for sleep should also be considered. Future research is needed to examine specific therapeutic techniques with regard to sleep that would be most beneficial for and preferred by breast cancer survivors.

#### STUDY LIMITATIONS AND STRENGTHS

Our study findings should be considered in the context of several limitations. The sample consisted primarily of women who were well-educated, non-Hispanic, white, and married, so that our results may not extrapolate to breast cancer survivor groups with other demographic and medical profiles. In addition, our study relied mostly on self-report, which is subject to response bias. However, sleep quality is ultimately a subjective experience, and objectively measured sleep does not always correlate with outcomes as successfully as subjective reports of sleep do. Finally, with a cross-sectional design, the direction of causation of the relationships between variables could not be determined. The relationships examined in our study should be further tested in future longitudinal descriptive and interventional research. The strengths of the current study include its focus on an understudied cancer survivorship period (up to 10 years posttreatment) and its examination of a comprehensive set of the demographic, medical, physical, and psychosocial correlates of sleep.

#### CONCLUSIONS

The present study provides novel and important information regarding the correlates of sleep in longterm breast cancer survivors. Our results highlight several subgroups of breast cancer survivors who may be most in need of sleep interventions. Furthermore, by identifying multiple physical, psychosocial, and behavioral correlates of poor sleep, our study provides valuable information that should be targeted in future sleep interventions for breast cancer survivors. Such interventions have the potential to enhance breast cancer survivors' quality of life, overall well-being, and possibly even survival.

### REFERENCES

- Bardwell, W.A., Profant, J., Casden, D.R., et al. (2008). The relative importance of specific risk factors for insomnia in women treated for early-stage breast cancer. *Psy-cho-Oncology*, *17*(1), 9–18. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2575103/pdf/nihms-73982.pdf.
- Bastien, C.H., Vallieres, A. & Morin, C.M. (2001). Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Medicine*, 2(4), 297–307.
- Beck, S.L., Berger, A.M., Barsevick, A.M., et al. (2010). Sleep quality after initial chemotherapy for breast cancer. Supportive Care in Cancer, 18(6), 679-689. Epub ahead of print Jun 13, 2009. Available from https:// www.ncbi.nlm.nih.gov/pmc/articles/PMC2874643/.
- Berger, A.M., Kuhn, B.R., Farr, L.A., et al. (2009a). Oneyear outcomes of a behavioral therapy intervention trial on sleep quality and cancer-related fatigue. *Journal of Clinical Oncology*, 27(35), 6033–6040.
- Berger, A.M., Treat Marunda, H.A. & Agrawal, S. (2009b). Influence of menopausal status on sleep and hot flashes throughout breast cancer adjuvant chemotherapy. *Jour*-

nal of Obstetric, Gynecologic, and Neonatal Nursing, 38(3), 353–366.

- Berger, A.M., Visovsky, C., Hertzog, M., et al. (2012). Usual and worst symptom severity and interference with function in breast cancer survivors. *The Journal of Supportive Oncology*, *10*(3), 112–118. Epub ahead of print Jan 24.
- Budhrani, P.H., Lengacher, C.A., Kip, K., et al. (2015). An integrative review of subjective and objective measures of sleep disturbances in breast cancer survivors. *Clinical Journal of Oncology Nursing*, *19*(2), 185–191.
- Buscemi, N., Vandermeer, B., Friesen, C., et al. (2005). Manifestations and Management of Chronic Insomnia in Adults. Rockville, MD: Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. Available from https://www.ncbi.nlm. nih.gov/books/NBK11906/.
- Buysse, D.J., Reynolds., C.F., 3rd, Monk, T.H., et al. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research*, 28(2), 193–213.
- Carney, C.E., Harris, A.L., Moss, T.G., et al. (2010). Distinguishing rumination from worry in clinical insomnia. *Behaviour Research and Therapy*, 48(6), 540–546. Epub ahead of print Mar 11. Available from https:// www.ncbi.nlm.nih.gov/pmc/articles/PMC2871974/.
- Carpenter, J.S. & Andrykowski, M.A. (1998). Psychometric evaluation of the Pittsburgh Sleep Quality Index. Journal of Psychosomatic Research, 45(1), 5–13.
- Carpenter, J.S., Johnson, D., Wagner, L., et al. (2002). Hot flashes and related outcomes in breast cancer survivors and matched comparison women. *Oncology Nursing Forum*, 29(3), E16–E25.
- Carpenter, J.S., Elam, J.L., Ridner, S.H., et al. (2004). Sleep, fatigue, and depressive symptoms in breast cancer survivors and matched healthy women experiencing hot flashes. *Oncology Nursing Forum*, 31(3), 591–598.
- Colagiuri, B., Christensen, S., Jensen, A.B., et al. (2011). Prevalence and predictors of sleep difficulty in a national cohort of women with primary breast cancer three to four months postsurgery. *Journal of Pain and Symptom Management*, 42(5), 710–720. Epub ahead of print May 26.
- Colten, H.R. & Altevogt, B.M., eds. (2007). Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem. Washington, DC: National Academies Press.
- Davidson, J.R., MacLean, A.W., Brundage, M.D., et al. (2002). Sleep disturbance in cancer patients. Social Science & Medicine, 54(9), 1309–1321.
- Dugan, W., McDonald, M.V., Passik, S.D., et al. (1998). Use of the Zung Self-Rating Depression Scale in cancer patients: Feasibility as a screening tool. *Psycho-Oncology*, 7(6), 483–493.
- Dupont, A., Bower, J.E., Stanton, A.L., et al. (2014). Cancer-related intrusive thoughts predict behavioral symptoms following breast cancer treatment. *Health Psychology*, 33(2), 155–163. Epub ahead of print Feb 4, 2013. Available from https://www.ncbi.nlm.nih.gov/ pmc/articles/PMC3796187/.
- Ellis, J.G., Perlis, M.L., Bastien, C.H., et al. (2014). The natural history of insomnia: Acute insomnia and first-onset depression. *Sleep*, *37*(1), 97–106. Available from https:// www.ncbi.nlm.nih.gov/pmc/articles/PMC3902876/.
- Enderlin, C.A., Coleman, E.A., Cole, C., et al. (2010). Sleep across chemotherapy treatment: A growing concern for women older than 50 with breast cancer. Oncology Nursing Forum, 37(4), 461–463.

- Espeland, M.A., Bush, T.L., Mebane-Sims, I., et al. (1995). Rationale, design, and conduct of the PEPI Trial: Postmenopausal Estrogen/Progestin Interventions. Controlled Clinical Trials, 16(Suppl. 4), 3S-19S.
- Espie, C.A., Fleming, L., Cassidy, J., et al. (2008). Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer. *Journal* of Clinical Oncology, 26(28), 4651–4658. Epub ahead of print Jun 30.
- Ferrell, B.R., Dow, K.H. & Grant, M. (1995). Measurement of the quality of life in cancer survivors. *Quality of Life Research*, 4(6), 523–531.
- Forsythe, L.P., Helzlsouer, K.J., MacDonald, R., et al. (2012). Daytime sleepiness and sleep duration in long-term cancer survivors and non-cancer controls: Results from a registry-based survey study. *Supportive Care in Cancer*, 20(10), 2425–2432. Epub ahead of print Jan 5.
- Greendale, G.A., Reboussin, B.A., Hogan, P., et al. (1998). Symptom relief and side effects of postmenopausal hormones: Results from the Postmenopausal Estrogen/Progestin Interventions Trial. Obstetrics and Gynecology, 92(6), 982–988.
- Hall, D.L., Mishel, M.H. & Germino, B.B. (2014). Living with cancer-related uncertainty: Associations with fatigue, insomnia, and affect in younger breast cancer survivors. Supportive Care in Cancer, 22(9), 2489–2495. Epub ahead of print Apr 12.
- Harris, P.F., Remington, P.L., Trentham-Dietz, A., et al. (2002). Prevalence and treatment of menopausal symptoms among breast cancer survivors. *Journal of Pain* and Symptom Management, 23(6), 501-509.
- Irwin, M.R., Olmstead, R.E., Ganz, P.A., et al. (2013). Sleep disturbance, inflammation and depression risk in cancer survivors. *Brain, Behavior, and Immunity*, 30(Suppl.), S58–S67. Epub ahead of print May 24, 2012. Available from https://www.ncbi.nlm.nih.gov/ pmc/articles/PMC3435451/.
- Jim, H.S., Jacobsen, P.B., Phillips, K.M., et al. (2013). Lagged relationships among sleep disturbance, fatigue, and depressed mood during chemotherapy. *Health Psychol*ogy, 32(7), 768–774. Epub ahead of print Feb 25. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC3700563/.
- Johns, M.W. (1991). A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. *Sleep*, 14(6), 540–545.
- Kotronoulas, G., Wengstrom, Y. & Kearney, N. (2012). A critical review of women's sleep-wake patterns in the context of neo-/adjuvant chemotherapy for early-stage breast cancer. *Breast*, 21(2), 128–141. Epub ahead of print Dec 20, 2011.
- Lee, E., Cho, H.J., Olmstead, R., et al. (2013). Persistent sleep disturbance: A risk factor for recurrent depression in community-dwelling older adults. *Sleep*, *36*(11), 1685–1691. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3792386/.
- Le Guen, Y., Gagnadoux, F., Hureaux, J., et al. (2007). Sleep disturbances and impaired daytime functioning in outpatients with newly diagnosed lung cancer. *Lung Cancer*, 58(1), 139–143. Epub ahead of print Jul 5.
- Lehrer, S., Green, S. & Rosenzweig, K.E. (2013). Coffee consumption associated with increased mortality of women with breast cancer. *Journal of Caffeine Research*, 3(1), 38–40. Available from https://www.ncbi.nlm.nih.gov/ pmc/articles/PMC3643262/.

- Lindley, C., Vasa, S., Sawyer, W.T., et al. (1998). Quality of life and preferences for treatment following systemic adjuvant therapy for early-stage breast cancer. *Journal of Clinical Oncology*, 16(4), 1380–1387.
- Lu, W., Cantor, J.B., Aurora, R.N., et al. (2015). The relationship between self-reported sleep disturbance and polysomnography in individuals with traumatic brain injury. *Brain Injury*, 29(11), 1342–1350. Epub ahead of print Jul 23.
- Miaskowski, C., Dodd, M. & Lee, K. (2004). Symptom clusters: The new frontier in symptom management research. Journal of the National Cancer Institute, Monographs, 2004(32), 17-21. Available from https://academic.oup.com/jncimono/article/2004/32/17/1021847/Symptom-Clusters-The-New-Frontier-in-Symptom.
- Miaskowski, C., Cooper, B., Paul, S.M., et al. (2012). Identification of patient subgroups and risk factors for persistent breast pain following breast cancer surgery. *Journal of Pain*, 13(12), 1172–1187. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3511823/.
- Mourits, M.J., Bockermann, I., de Vries, E.G., et al. (2002). Tamoxifen effects on subjective and psychosexual wellbeing, in a randomised breast cancer study comparing high-dose and standard-dose chemotherapy. British Journal of Cancer, 86(10), 1546-1550. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2746594/.
- Otte, J.L., Carpenter, J.S., Russell, K.M., et al. (2010). Prevalence, severity, and correlates of sleep-wake disturbances in long-term breast cancer survivors. Journal of Pain and Symptom Management, 39(3), 535-547. Epub ahead of print Jan 18. Available from https:// www.ncbi.nlm.nih.gov/pmc/articles/PMC2843803/.
- Paice, J.A. & Cohen, F.L. (1997). Validity of a verbally administered numeric rating scale to measure cancer pain intensity. *Cancer Nursing*, 20(2), 88–93.
- Palesh, O.G., Roscoe, J.A., Mustian, K.M., et al. (2010). Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. Journal of Clinical Oncology, 28(2), 292–298. Epub ahead of print Nov 23, 2009. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC2815717/.
- Palesh, O., Aldridge-Gerry, A., Ulusakarya, A., et al. (2013). Sleep disruption in breast cancer patients and survivors. *Journal of the National Comprehensive Can*cer Network, 11(12), 1523–1530.
- Palesh, O., Aldridge-Gerry, A., Zeitzer, J.M., et al. (2014). Actigraphy-measured sleep disruption as a predictor of survival among women with advanced breast cancer. *Sleep*, 37(5), 837–842. Available from https://www. ncbi.nlm.nih.gov/pmc/articles/PMC3985107/.
- Reinsel, R.A., Starr, T.D., O'Sullivan, B., et al. (2015). Polysomnographic study of sleep in survivors of breast cancer. *Journal of Clinical Sleep Medicine*, 11(12), 1361–1370. Available from https://www.ncbi.nlm.nih. gov/pmc/articles/PMC4661327/.
- Rumble, M.E., Keefe, F.J., Edinger, J.D., et al. (2010). Contribution of cancer symptoms, dysfunctional sleep related thoughts, and sleep inhibitory behaviors to the insomnia process in breast cancer survivors: A daily process analysis. *Sleep*, 33(11), 1501–1509. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC2954700/.
- Savard, J. & Morin, C.M. (2001). Insomnia in the context of cancer: A review of a neglected problem. *Journal of Clin*ical Oncology, 19(3), 895–908.

- Savard, J., Simard, S., Blanchet, J., et al. (2001). Prevalence, clinical characteristics, and risk factors for insomnia in the context of breast cancer. *Sleep*, 24(5), 583-590.
- Savard, J., Laroche, L., Simard, S., et al. (2003). Chronic insomnia and immune functioning. *Psychosomatic Medicine*, 65(2), 211–221.
- Savard, J., Davidson, J.R., Ivers, H., et al. (2004). The association between nocturnal hot flashes and sleep in breast cancer survivors. *Journal of Pain and Symptom Management*, 27(6), 513–522.
- Savard, J., Simard, S., Ivers, H., et al. (2005). Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects. *Journal of Clinical Oncology*, 23(25), 6083–6096.
- Savard, J., Ivers, H., Villa, J., et al. (2011). Natural course of insomnia comorbid with cancer: An 18-month longitudinal study. *Journal of Clinical Oncology*, 29(26), 3580–3586. Epub ahead of print Aug 8.
- Setthawatcharawanich, S., Limapichat, K., Sathirapanya, P., et al. (2014). Excessive daytime sleepiness and nighttime sleep quality in Thai patients with Parkinson's disease. Journal of the Medical Association of Thailand, 97(10), 1022-1027.
- Spiegel, K., Sheridan, J.F. & Van Cauter, E. (2002). Effect of sleep deprivation on response to immunization. *The*

Journal of the American Medical Association, 288(12), 1471–1472.

- Syrjala, K.L., Jensen, M.P., Mendoza, M.E., et al. (2014). Psychological and behavioral approaches to cancer pain management. *Journal of Clinical Oncology*, 32(16), 1703–1711.
- Vanaparthy, R., Mota, P., Khan, R., et al. (2015). A longitudinal assessment of sleep variables during exacerbations of chronic obstructive pulmonary disease. *Chronic Respiratory Disease*, 12(4), 299–304. Epub ahead of print May 31.
- Van Onselen, C., Paul, S.M., Lee, K., et al. (2013). Trajectories of sleep disturbance and daytime sleepiness in women before and after surgery for breast cancer. *Journal of Pain and Symptom Management*, 45(2), 244–260. Epub ahead of print Aug 24, 2012. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3561473/.
- Vickberg, S.M. (2003). The Concerns About Recurrence Scale (CARS): A systematic measure of women's fears about the possibility of breast cancer recurrence. *Annals* of *Behavioral Medicine*, 25(1), 16–24.
- Vitiello, M.V., McCurry, S.M., Shortreed, S.M., et al. (2014). Short-term improvement in insomnia symptoms predicts long-term improvements in sleep, pain, and fatigue in older adults with comorbid osteoarthritis and insomnia. *Pain*, 155(8), 1547–1554. Epub ahead of print May 1. Available from https://www.ncbi.nlm.nih.gov/pmc/ articles/PMC4104256/.