Sleep Across Chemotherapy Treatment: A Growing Concern for Women Older Than 50 With Breast Cancer

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Purpose/Objectives: To conduct a metasynthesis of human sleep studies that included women aged 50 years and older with breast cancer across chemotherapy treatment.

Data Sources: English publications were searched with the terms *sleep* and *breast cancer* via Ovid, PubMed, and EBSCOhost databases. Human studies that used sleep-specific instruments published from January 1974–May 2009 were included. Intervention studies also were included if they provided baseline sleep data. Studies that used quality-of-life or symptom instruments or in which patients were prescreened for insomnia were not included.

Data Synthesis: 382 publications were found; 17 met inclusion criteria, and 3 additional studies were located from the literature on fatigue. Two articles reported on the same study, so a total of 19 studies were included in the review. In women with nonmetastatic breast cancer, subjective and objective sleep quality appear to be poor and nocturnal awakenings frequent across chemotherapy treatment. Daytime sleepiness increases in the active phase of chemotherapy, and insomnia symptoms are common before and following chemotherapy treatment. In women with recurrent or metastatic breast cancer, difficulty falling asleep, nocturnal awakenings, difficulty awakening, and daytime sleepiness are problematic at different points in chemotherapy treatment.

Conclusions: Sleep for women, including those older than 50 years, appears to be impaired across chemotherapy treatment, although replication of findings is very limited.

Implications for Nursing: Future research should investigate sleep in specific age and minority groups, include daytime sleep and sleepiness, and use standard sleep nomenclature and objective measures.

As women age, their risk for neoplastic disorders such as breast cancer rises, with 66% of cases occurring in those aged 55 years or older (American Cancer Society, 2009). Estimated risk for developing breast cancer from age 60–69 years is 1 in 27 and continues to increase with age; about 126,964 of the estimated 192,370 new cases of breast cancer diagnosed in 2009 were anticipated in women aged 55 years or older (National Cancer Institute, 2009). With the increasing numbers of breast cancer cases in older women, an urgent need exists for a better understanding of their symptoms, including sleep impairment.

Women are at higher risk for developing sleep impairment because of increased age alone. Sleep changes including an increased number of night-time awakenings, decreased sleep efficiency (percentage of time spent asleep when in bed), increased daytime naps, and decreased ability to phase shift (change the routine sleep time backward or forward) all are characteristic of normal aging (Bliwise, 2005). Among adults older than 65 years, sleep-phase advance such as lark tendencies or early awakening and sleep disorders such as insomnia, prolonged sleep-onset latency (time from going to bed to sleep onset), and sleep-maintenance (staying asleep) issues are common (Bliwise, 2005).

Sleep in women aged 50 years or older is complicated further by menopause, which occurs at about age 51 (National Institute on Aging, 2009), although it may occur earlier or as late as age 58 (Moe, 2005). Common complaints associated with menopause include difficulty falling asleep, increased awakenings, and daytime sleepiness. However, menopause has not been demonstrated to be a strong predictor of specific sleep disorder symptoms, although perimenopausal and postmenopausal women have described their sleep as less satisfactory than premenopausal women (Young, Rabago, Zgierska, Austin, & Laurel, 2003). Hot flashes may be severe enough to awaken women during menopause (National Institute on Aging, 2009) and are likely to be experienced by women with breast cancer as a side effect of chemotherapy-induced ovarian disruption or of hormonal therapy following chemotherapy

(Carpenter et al., 1998). Forty percent of female survivors of breast cancer ($\bar{X}$ age = 57 years; $\bar{X}$ time postdiagnosis = 3 years) have reported that hot flashes moderately or severely disturb sleep (Carpenter, Johnson, Wagner, & Andrykowski, 2002).

Sleep issues are twice as prevalent in patients with cancer than the general population (Savard, Laroche, Simard, Ivers, & Morin, 2003), yet impaired sleep receives limited healthcare provider attention (Savard & Morin, 2001). Although sleep difficulty has long been known as one of the most common concerns of patients with cancer (Whelan et al., 1997), the understanding of sleep in specific cancers and age groups is limited (Berger et al., 2005). In addition, changes in physical function among patients aged 65 years or older have been predicted by insomnia (Given, Given, Sikorski, & Hadar, 2007). Therefore, impaired sleep appears to be problematic for many patients with cancer and has functional implications for the older adult population. Although sleep changes in women with breast cancer have been the subject of research in the past several decades, the sleep of women aged 50 years or older with breast cancer has not been addressed specifically. This article reviews findings from the past 35 years of studies that included women aged 50 years or older with breast cancer across (before, during, and following) chemotherapy treatment.

Methods

The review was guided by Cooper (1998) and Stock (1994). A search was conducted for publications in English reporting human studies with the terms *sleep* and *breast cancer* in the Ovid, PubMed, and EBSCOhost (including Health Source®: Nursing/Academic Edition and Psychology and Behavioral Sciences Collection™) databases.

Inclusion criteria were studies that employed sleep-specific instruments to assess sleep-related issues among patients with breast cancer across chemotherapy treatment. Intervention studies were included if they provided pre-intervention baseline data regarding the prevalence of sleep difficulties among patients with breast cancer. Because no studies were found that focused exclusively on women aged 50 years or older with breast cancer, no age restrictions were used for this review, given that the sample included women aged 50 years or older. Although several studies had a mean age slightly younger than 50 years, they were included if women aged 50 years or older were participants in the studies. Publications from January 1974–May 2009 were selected as representing the period in which sleep medicine evolved, sleep-specific instruments were developed, and studies of sleep within different clinical populations emerged (Dement, 2005).

Studies that included diverse disease sites were excluded if data for patients with breast cancer were not reported separately. Studies using quality-of-life or symptom measures that assessed sleep with a single item or several items only and studies that included only patients preselected for insomnia or impaired sleep were not included in the review.

The selected studies were analyzed, summarized, and synthesized to answer two questions about sleep in women with breast cancer aged 50 years or older: (a) What are the methodologic characteristics of research conducted over the past 35 years? and (b) What do research findings report about sleep quality, nocturnal and daytime sleep, daytime sleepiness, and insomnia in this population?

Results

Two hundred fifty-eight articles were located from OVID, 140 from EBSCOhost, and 306 from PubMed. After deletion of duplicates, 382 articles remained. Seventeen human sleep studies met inclusion criteria. Three additional studies were located through a previous search of the literature on fatigue. Because two articles reported findings from the same study, 19 studies actually were reviewed.

The 365 excluded publications included 43 general articles (commentaries, research briefs, etc.); 50 feasibility, interventional methodologic, or epidemiologic studies; and 1 literature review. The remainder of the articles excluded addressed topics that were not the primary focus of the review, including menstrual cycle, cyclical mastalgia, menopause, or fertility (59); symptoms, correlates, or quality of life (95); risk factors, biomarkers, or mammography (44); information or support (1); breast cancer treatments (22); quality indicators (1); metastatic or recurrent breast cancer (6); general cancer or mixed cancers (8); physiology or biology (8); caregivers (2); cancer in men (4); and unrelated topics (21).

Selected Study Characteristics

Designs: The 19 studies selected included 10 cross-sectional (Ancoli-Israel et al., 2006; Bardwell et al., 2008; Berger, Farr, Kuhn, Fischer, & Agrawal, 2007; Carpenter et al., 2004; Davidson, MacLean, Brundage, & Schulze, 2002; Fortner, Stepanski, Wang, Kasprowicz, & Durrence, 2002; Haghighat, Akbari, Holakouei, Rahimi, & Montazeri, 2003; Koopman et al., 2002; Savard, Simard, Blanchet, Ivers, & Morin, 2001; Silberfarb, Hauri, Oxman, & Schnurr, 1993) and nine longitudinal (Andrykowski, Curran, & Lightner, 1998; Berger, 1998; Berger et al., 2002, 2009; Berger & Farr, 1999; Berger & Higginbotham, 2000; Kuo, Chiu, Liao, & Hwang, 2006; Liu et al., 2008; Palesh et al., 2008; Payne, Piper, Rabinowitz, & Zimmerman, 2006) designs. Comparison groups were included in five studies. One longitudinal study included a comparison group of age-matched

women with benign breast disease (Andrykowski et al., 1998). One cross-sectional study included an age- and sex-matched comparison group (Silberfarb et al., 1993), two included demographically matched comparison groups of healthy women (Carpenter et al., 2004; Payne et al., 2006), and one included a comparison group of patients from an internal medicine clinic (Fortner et al., 2002).

Sample races and ethnicities: The study samples were derived from populations representing four countries and several races or ethnicities. Study populations were American and predominantly Caucasian or unspecified (15), Canadian and Caucasian or unspecified (2), Taiwanese (1), and Iranian (1).

Sample ages: Mean ages in years of four samples were in their late 40s, 13 samples were in their 50s, and two samples were in their 60s. The age of participants across studies ranged from 18–90 years. As noted, none of the studies focused solely on the sleep of women older than 50 years with breast cancer, but all included women aged 50 years or older as participants.

Sleep measures: Ten studies used self-report measures only to assess sleep (Andrykowski et al., 1998; Bardwell et al., 2008; Carpenter et al., 2002; Davidson et al., 2002; Fortner et al., 2002; Haghighat et al., 2003; Koopman et al., 2002; Liu et al., 2008; Palesh et al., 2008; Savard et al., 2001), whereas seven used objective measures in addition to self-report measures (Ancoli-Israel et al., 2006; Berger & Higginbotham, 2000; Berger et al., 2002, 2007, 2009; Kuo et al., 2006; Silberfarb et al., 1993). Two studies (three articles) used only objective measures (Berger, 1998; Berger & Farr, 1999; Payne et al., 2006).

Self-report measures included the following. The Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1991; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) was used in eight studies (Ancoli-Israel et al., 2006; Andrykowski et al., 1998; Berger et al., 2002, 2007, 2009; Carpenter et al., 2004; Fortner et al., 2002; Liu et al., 2008). The Morin Sleep Diary (Morin, 1993) or the World Health Organization's Education Kit for Sleep Disorders sleep log (World Health Organization Worldwide Project on Sleep and Health Mental and Behavioural Disorders Team, 2000) were used in three studies (Berger et al., 2002; Berger & Higginbotham, 2000; Kuo et al., 2006). The Epworth Sleepiness Scale (Johns, 1991, 1992) was used in one study (Kuo et al., 2006). The Women's Health Initiative Insomnia Rating Scale, based on the Sleep Disturbance Scale (Levine et al., 2003), was used in one study (Bardwell et al., 2008). The Insomnia Screening Questionnaire, which incorporates the Sleep Impairment Index and the Insomnia Interval Schedule-R (Morin, 1993), was used in one study (Savard et al., 2001). Finally, the Brief Sleep History (Libbus, Baker, Osgood, Phillips, & Valentine, 1995) was used by Berger et al. (2002). Seven studies used author-derived sleep diaries or questionnaires (Berger et al., 2002, 2009; Davidson et al., 2002; Haghighat et al., 2003; Koopman et al., 2002; Palesh et al., 2008; Silberfarb et al., 1993).

Studies that employed objective measures included polysomnography and actigraphy. Polysomnography, the gold standard for assessing sleep that yields data on sleep stages, was used in one study (Silberfarb et al., 1993). An actigraph, a wristwatch-sized device measuring activity or the absence of activity interpreted as wake or sleep time (Ambulatory Monitoring, Inc., 2007), was used in seven studies (eight articles) (Ancoli-Israel et al., 2006; Berger, 1998; Berger & Farr, 1999; Berger et al., 2002, 2007, 2009; Kuo et al., 2006; Payne et al., 2006). In addition, biomarkers (serum cortisol, serotonin, melatonin, and bilirubin) were used in one study (Payne et al., 2006).

Treatment and cancer categories: Five studies described sleep prior to the initiation of chemotherapy (Ancoli-Israel et al., 2006; Berger et al., 2002, 2007, 2009; Liu et al., 2008), five described sleep during chemotherapy (Berger, 1998; Berger & Farr, 1999; Berger & Higginbotham, 2000; Kuo et al., 2006; Liu et al., 2008; Payne et al., 2006), three described sleep following chemotherapy (Andrykowski et al., 1998; Bardwell et al., 2008; Carpenter et al., 2004), and four described sleep at variable points of chemotherapy (Davidson et al., 2002; Fortner et al., 2002; Haghighat et al., 2003; Savard et al., 2001) in women with nonmetastatic breast cancer. Two studies described sleep in women with recurrent or metastatic breast cancer at different points in chemotherapy treatment (Koopman et al., 2002; Palesh et al., 2008).

Sleep variables: Sleep variables described in the studies included one or more of the following: subjective sleep quality, objective sleep quality (sleep efficiency), nocturnal sleep characteristics (nocturnal sleep time, sleep-onset latency, nocturnal awakenings), day sleep time, daytime sleepiness, and insomnia symptoms. The sleep variables of interest and the expected normal parameters described for adults and older adults are briefly defined, where available, in Table 1. Note that some studies assessed more variables than were reported and, therefore, only the variables reported can be included in this review. To view summaries of the reviewed studies, see Appendix A in the online version of this article at http://ons.metapress.com/content/0190-535X.

Suggested Sleep Findings

Subjective sleep quality: Subjective sleep quality, the perception of sleep as restorative and sufficient for function, was reported as poor prior to the initiation of chemotherapy treatment (PSQI global sleep quality scores = 6.6–8.8), exceeding the recommended clinical cut-off score of 5 as indicative of poor sleep (Ancoli-Israel et al., 2006; Berger et al., 2002, 2007, 2009; Liu et al., 2008).

At different points in chemotherapy treatment, subjective sleep quality was described as fair or very bad by 20% of women ($\bar{X}$ PSQI global sleep score = 6.8), although it was similar for those receiving and not receiving

Table 1. Sleep Variables and Expected Normal Values

Variable	Definition	Expected Normal Values
Sleep quality	Multidimensional perceptions of length and depth of sleep and feelings of being rested upon awakening	Perception of sleep as restorative and sufficient for function
Subjective sleep quality	The assessment of sleep as sufficient for daytime function (Berger et al., 2005)	A global sleep score lower than 5 indicates good sleep quality (Buysse et al., 1989).
Objective sleep quality	Sleep efficiency is a common measure (Van Cauter & Allostatic Load Working Group, 1997).	See sleep efficiency.
Sleep efficiency	The number of minutes of sleep divided by the total number of minutes in bed, multiplied by 100 to obtain a percentage (Berger et al., 2005)	Higher than 95% in adults indicates good sleep; lower than 80% indicates poor sleep (Berger et al., 2005).
Nocturnal sleep time	Minutes of sleep during the night (total sleep time minus day sleep time)	Seven to nine hours of attempted sleep for adults (Berger et al., 2005); seven hours per night is the mean for older adults (National Sleep Foundation, 2003), and 7.1 has been reported in older adult women (Huang et al., 2002).
Sleep-onset latency	Number of minutes between when a person lies down to bed and actually falls asleep (Berger et al., 2005)	Less than 20 minutes in adults (Berger et al., 2005); a mean of 35 minutes has been reported for older adult women (Ohayon et al., 2004).
Nocturnal awakenings	The number of awakenings during a sleep period (Berger et al., 2005)	Two to six awakenings in seven hours of sleep (Berger et al., 2005)
Day sleep time (napping)	Number of minutes spent resting during the day, intentional or unintentional (Berger et al., 2005)	Five minutes to two hours in adults (Berger et al., 2005); older women have been reported to nap 13.5–31 minutes per day (Ohayon et al., 2004).
Daytime sleepiness	Inability to stay awake and alert during major daytime wake episodes, resulting in unintentional lapses into drowsiness or sleep (American Academy of Sleep Medicine, 2005)	Slight or no chance of dozing unintentionally; a mean of 5.85 on the Epworth Sleepiness Scale (Johns, 1991) has been reported for community-dwelling older adults (Whitney et al., 1998).
Insomnia	Repeated difficulty with sleep initiation, duration, consolidation, or quality, despite adequate time and opportunity for sleep, resulting in daytime impairment (American Academy of Sleep Medicine, 2005)	The absence of insomnia; see sleep-onset latency, nocturnal sleep time, and nocturnal awakenings.

chemotherapy (Fortner et al., 2002). Subjective sleep quality based on sleep log recordings was described as decreased ($p < 0.05$) in the active (days 8–9 of a 21-day third cycle) as compared to recovery (two days prior to a 21-day fourth cycle) phases of treatment in a small prospective study (Kuo et al., 2006).

At an average of two years post-treatment, subjective sleep quality was perceived as poor and did not differ between breast cancer survivors and an age-matched comparison group of women with benign breast disease ($\bar{X}$ PSQI global sleep score = 7.12 versus 6.13, respectively). In addition, the PSQI subjective sleep quality subscale was significantly poorer ($\bar{X}$ scores = 1.06 versus 0.79) in breast cancer survivors relative to the comparison group ($p < 0.05$) at the initial post-treatment assessment (Andrykowski et al., 1998). Similar results were obtained in a study comparing a small sample of breast cancer survivors experiencing hot flashes (assessed three months to 14 years post-treatment) with a control group of healthy women matched for age, ethnicity, and menopausal status (Carpenter et al., 2004). The groups did not differ in their perceptions of subjective sleep quality ($\bar{X}$ PSQI global sleep scores = 7.3 and 6.9, respectively), and scores for both groups indicated poor sleep. In addition, subjective sleep quality was not associated with hot flash frequency, despite almost twice the number of objectively measured hot flashes in breast cancer cases versus control (Carpenter et al., 2004).

Objective sleep quality: Objective sleep quality, often assessed with sleep efficiency (time spent asleep over time in bed attempting to sleep multiplied by 100), was described as poor to normal prior to the initiation of chemotherapy treatment ($\bar{X}$ sleep efficiency = 76%–89%; expected = 80% or higher) based on actigraphy recordings (Ancoli-Israel et al., 2006; Berger et al., 2002, 2007, 2009; Liu et al., 2008). Based on sleep diary recordings, sleep efficiency was found to be 85% or higher (Berger et al., 2002).

Objective sleep quality (sleep efficiency) measured by actigraphy was poor and similar (82.1% versus 79.9%) during the active and recovery phases of the third chemotherapy cycle (Kuo et al., 2006). Based on Morin Sleep Diary recordings, sleep efficiency was found to

be about 90% during treatment, with half of the women reporting less than 85% in the recovery phase (Berger & Higginbotham, 2000).

Nocturnal sleep time: Nocturnal sleep time (minutes of sleep during the night) was characterized as averaging 6–6.6 hours (normal adult range = 7–9 hours) prior to chemotherapy treatment based on actigraphy recordings (Ancoli-Israel et al., 2006; Berger et al., 2007). By sleep diary, nocturnal sleep time before treatment averaged 6–8.5 hours (Berger et al., 2002).

Nocturnal sleep time during the first two days of the first chemotherapy cycle was shorter in patients with breast cancer than in demographically matched comparisons without breast cancer (5.95 hours versus 6.97 hours; $p = 0.037$) but not by the beginning of the fourth cycle, as assessed by actigraphy recordings (Payne et al., 2006). In addition, mean nocturnal sleep times (6.6 hours versus 6.5 hours) were reported as similar during the active and recovery phases of chemotherapy in women evaluated with actigraphy during their third cycle of treatment (Kuo et al., 2006).

Sleep-onset latency: Sleep-onset latency (the number of minutes between lying down in bed to go to sleep and actually going to sleep) was reported as 11 minutes (normal adult time = 20–35 minutes or less) prior to chemotherapy treatment based on actigraphy recordings (Ancoli-Israel et al., 2006; Berger et al., 2007). By sleep diary, sleep-onset latency was found to be less than 30 minutes (Berger et al., 2002) before treatment.

At different points in chemotherapy treatment, sleep-onset latency appeared to be prolonged. Half of the women reported sleep-onset latency exceeding 30 minutes as assessed by Morin Sleep Diary recordings (Berger & Higginbotham, 2000).

Nocturnal awakenings: Nocturnal awakenings (the number of awakenings during a sleep period) prior to chemotherapy were found to be frequent (10–60 per night; expected adult range = 2–6 per night) based on actigraphy recordings (Ancoli-Israel et al., 2006; Berger et al., 2007). However, nocturnal awakenings were recalled as occurring less often (2 versus 10 times per night) by sleep diary compared to actigraphy recordings (Berger et al., 2009).

Over the course of the first three adjuvant chemotherapy cycles, frequent nocturnal awakenings (22 or more per night) were reported in a small sample of women assessed repeatedly (Berger, 1998). As might be expected, the nocturnal awakenings were significantly greater ($p < 0.007$) during the beginning of each treatment cycle (days 1–4 after chemotherapy) than the midpoints of each cycle (three days midcycle when women were removed from chemotherapy). However, no significant difference was found between different chemotherapy regimens (Berger, 1998). At different points in chemotherapy treatment, frequent sleep disturbance because of pain, nocturia, feeling too hot, coughing, or snoring loudly were assessed by the PSQI, although the number of actual nocturnal awakenings was not reported. However, the sleep disturbance reported by women with breast cancer was described as similar to that of women without cancer seen for general medical conditions (Fortner et al., 2002).

Nocturnal awakenings were described as an issue by 42% of women with recurrent or metastatic breast cancer at different points in chemotherapy treatment as assessed by sleep questionnaire, although the actual number of nocturnal awakenings was not reported (Koopman et al., 2002; Palesh et al., 2008).

Day sleep time: Day sleep time (the number of minutes spent resting during the day) was reported as within expected limits for age prior to chemotherapy treatment (66 minutes; normal adult range = 5 minutes to 2 hours) as assessed by actigraphy recordings. However, actigraphy cannot detect the difference between nonmoving behavior and sleep.

Daytime sleepiness: Issues with subjective daytime sleepiness (assessed via the Epworth Sleepiness Scale) were significantly more pronounced during the active as compared to recovery phases of chemotherapy ($p < 0.05$) among women evaluated during the third cycle of treatment (Kuo et al., 2006). Daytime sleepiness scores were indicative of a light doze ($\bar{X} = 6$) during active treatment (days 8–9) but were within normal limits ($\bar{X} = 4.3$) during the recovery phase (prior to the next cycle of chemotherapy) of the third cycle (Kuo et al., 2006).

Difficulty waking and getting up was reported by 30%–31% of women with recurrent or metastatic breast cancer based on sleep questionnaire, although actual severity of daytime sleepiness was not assessed (Koopman et al., 2002; Palesh et al., 2008).

Insomnia symptoms: Current insomnia symptoms (repeated difficulty with sleep initiation, duration, consolidation, or quality, despite adequate time and opportunity for sleep) were reported by 51% of women with stage I–III breast cancer ($\bar{X} = 48.6$ months postdiagnosis). Of the women with insomnia symptoms who completed a retrospective insomnia interview, 33% reported that the symptoms began within six months of breast cancer diagnosis and frequently were caused or aggravated by cancer and its treatments, whereas 67% reported that the symptoms preceded breast cancer diagnosis (Savard et al., 2001). The duration of preexisting insomnia symptoms was noted as a mean of about 20 years (Savard et al., 2001).

At variable points in chemotherapy treatment, insomnia symptoms were reported by 60% of women with breast cancer (Haghighat et al., 2003). In addition, insomnia symptoms were described as severe in about 14% of women undergoing or having completed initial chemotherapy treatment (Haghighat et al., 2003).

About four years following chemotherapy treatment, insomnia symptoms were reported by 33%–50% of

women with breast cancer (Bardwell et al., 2008; Savard et al., 2001). Insomnia syndrome was diagnosed in about 19% of women and was characterized by issues with sleep onset (75%), sleep maintenance (86%), awakening too early in the morning (73%), or mixed difficulties initiating and maintaining sleep (71%) (Savard et al., 2001). The median duration of sleep difficulties in breast cancer survivors with insomnia syndrome was 60 months, and 95% indicated chronic insomnia for 6 months or longer (Savard et al., 2001).

In women with recurrent or metastatic breast cancer at different points in chemotherapy treatment, actual assessment of insomnia symptoms was not reported. However, issues falling asleep were reported by 22%–25% of women and awakening during the night by 42%, although awakening too early was not described as problematic (Koopman et al., 2002; Palesh et al., 2008).

Suggested Sleep Findings Across Chemotherapy Treatment

Sleep appears to be impaired in many women with nonmetastatic, metastatic, or recurrent breast cancer before, during, and after the chemotherapy treatment experience (see Table 2). Poor subjective and objective quality of sleep, frequent nocturnal awakenings, and increased insomnia symptoms appear pervasive in women with nonmetastatic breast cancer. However, subjective sleep quality in women with breast cancer does not appear to be associated with frequency of hot flashes, despite more frequent hot flashes being reported than in women without cancer. Issues with sleep initiation, maintenance, and getting up appear common in women with recurrent or metastatic breast cancer. Daytime sleepiness increases during chemotherapy treatment in women with nonmetastatic breast cancer and is an issue in a substantial number of women with recurrent or metastatic breast cancer.

Table 2. Sleep Findings Across Chemotherapy Treatment in Women With Breast Cancer

Sleep Variable	Before Treatment	During Treatment	After Treatment
Subjective sleep quality	Poor	Poor	Poor
Objective sleep quality (sleep efficiency)	Poor to normal	Poor	–
Nocturnal sleep time	Below average for age	Below average for age	–
Sleep-onset latency	In normal limits	Prolonged	–
Nocturnal wake episodes	Frequent	Frequent	–
Daytime sleep	In expected limits	–	–
Daytime sleepiness	–	Increased in active phase[a]	–
Insomnia symptoms	Present in 30%	Present in 30%–60%	Present in 30%–50%
Insomnia syndrome	–	–	Present in 19%

[a] Women with nonmetastatic or metastatic breast cancer

Although the studies reviewed suggest certain issues in the sleep of women with breast cancer, the findings must be considered within the context of the limited number of studies available that address specific sleep variables and the wide age range of women with breast cancer included. Variation in demographic characteristics of samples, types of chemotherapy treatment, treatment status, and other clinical factors that differed between studies may have influenced the overall suggested sleep findings of this review. In addition, although the studies reviewed did include women aged 50 years or older, the suggested findings are not representative of sleep only in women aged 50 years or older. However, the suggested sleep findings of this review do provide information regarding what is known to date about sleep in women with breast cancer, including those aged 50 years or older.

Methodologic Limitations

Almost half of the studies reviewed used cross-sectional designs, although slightly more than half were longitudinal studies. A number of studies had very small sample sizes, samples were predominantly Caucasian, the age range in most samples was quite broad, and most studies did not include comparison groups or age-matched population norms. Many studies also did not note exclusion criteria or covariates, such as menopausal status, medical comorbidities, or concurrent depression, which might have influenced the findings. Menopausal symptoms such as hot flashes, which are commonly experienced by women during and following chemotherapy, were rarely described in the sleep studies reviewed. In addition, the intensity and frequency of menopausal symptoms, which may differ when induced by chemotherapy or hormonal therapy as compared to natural menopause, were not addressed. Finally, basic descriptive information such as accrual or refusal and attrition rates were not provided by several studies.

Some studies subjectively assessed sleep only, although findings were strengthened by the use of standardized measures of sleep. Sleep was examined at different points in cancer treatment within and among samples,

and sleep evaluations during treatment were limited to the first few chemotherapy cycles rather than across the full span of treatment. The type of chemotherapy regimen also was not reported in all studies.

The studies often did not note whether the data were distributed normally or whether transformations or nonparametric analyses might have been more appropriate analytic strategies. In addition, differences between case and control groups (e.g., income) were not always controlled for in the analysis. Many studies reported mean responses but not the percentage of participants who exceeded cut-off values. A number of studies also reported limited data, such as total sleep time, but not other common basic sleep variables.

Conclusions, Nursing Implications, and Research Recommendations

Sleep has been described as impaired for many women with breast cancer across the treatment experience. Particular areas of concern include diminished sleep quality, frequent nocturnal awakenings, and insomnia symptoms across chemotherapy treatment. Other areas of concern include increased sleep latency, decreased sleep efficiency, increased daytime sleepiness, and increased insomnia symptoms during chemotherapy. Sleep changes in women aged 50 years or older may be compounded by breast cancer and its treatment; however, the current review lacks adequate age-specific evidence to say whether women aged 50 years or older with breast cancer experience greater sleep impairment than younger women. However, the current evidence is sufficient to warrant routine assessment of prediagnosis sleep history before chemotherapy. Subjective sleep quality, daytime sleepiness, and insomnia symptoms should be assessed before and during chemotherapy treatment at intervals to promote early sleep intervention before impairment becomes severe or chronic. Objective sleep assessment through actigraphy may provide useful clarification of client reports, and referral to a sleep specialist may be indicated if a sleep disorder is suspected. Sleep also should be assessed following chemotherapy because evidence suggests that sleep impairment may be a continuing issue for many breast cancer survivors.

Future research should investigate sleep in women with breast cancer in particular age and minority groups across chemotherapy treatment and should include a prediagnosis sleep history. Examination of daytime sleep and daytime sleepiness also may contribute to a greater understanding of night-time sleep in this population. Additional considerations for investigation include obstructive sleep apnea and restless-leg syndrome, which may be associated with poor sleep quality, poor sleep efficiency, and excessive daytime sleepiness in this population. Standard sleep nomenclature and objective measures are essential to strengthen research findings.

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Appendix A. Studies Investigating Sleep in Women Aged 50 Years or Older With Breast Cancer

Study	Design and Sample	Tools	Findings	Limitations
Ancoli-Israel et al., 2006	Cross-sectional; 85 Americans with stage I–IIIA cancer; $\bar{X}$ age = 51 years, range = 34–79; 74% Caucasian; $\bar{X}$ days preadjuvant or neoadjuvant anthracycline-based chemotherapy = 7; 83% accrual rate	PSQI, FOSQ, and actigraphy	Sleep quality was poor ($\bar{X}$ = 7); $\bar{X}$ nocturnal sleep time by actigraph = 6 hours per night; $\bar{X}$ sleep efficiency = 76%; $\bar{X}$ night awakenings = 60; $\bar{X}$ day sleep time = 66 minutes	No control group; lack of information on covariates (e.g., length of time since surgery, menopausal status)
Andrykowski et al., 1998	Longitudinal with comparison group; 88 Americans with stage 0–IIIA breast cancer; $\bar{X}$ age = 54 years, range = 35–76; 91% Caucasian; $\bar{X}$ years after chemotherapy = 2; 88 controls with benign breast issues; 81% accrual rate	PSQI	Sleep quality was similar in cases versus controls at initial assessments (PSQI global scores of 7.12 and 6.13, respectively); sleep quality subscale was less ($p < 0.05$) in cases versus controls.	Predominance of women who received mastectomies; mixture of treatments; current tamoxifen therapy
Bardwell et al., 2008	Cross-sectional; 2,645 Americans with stage I–IIIA cancer; $\bar{X}$ age = 53 years, range = 28–74; 85% Caucasian, non-Hispanic; 4 years or less since initial treatment; no accrual rate data	WHI-IRS based on SDS	Insomnia was reported by 39% (exceeded the cutoff score of 9 or higher).	Predominance of well-educated, married women; possible recall bias; lack of information about sleep history, anxiety, use of sleep aids, and hormonal therapy
Berger, 1998; Berger & Farr, 1999	Longitudinal; 72 Americans with stage I–II cancer; $\bar{X}$ age = 50 years, range = 33–69; receiving doxorubicin and cyclophosphamide; cyclophosphamide, methotrexate, and 5-fluorouracil; or cyclophosphamide, doxorubicin, and 5-fluorouracil; 94% accrual rate	Actigraphy	Nocturnal awakenings were elevated but similar between treatment groups at chemotherapy cycles 1, 2, and 3; nocturnal awakenings were higher at treatment (days 1–4 after chemotherapy) and lower at chemotherapy cycle midpoints (3 days midcycle) during the first three cycles.	Lack of baseline rest pattern data; actigraphy data regarding nocturnal awakenings were available only for a small subset (17 of 72) of the total sample.
Berger et al., 2002	Longitudinal; 25 Americans with stage I–II cancer; $\bar{X}$ age = 54 years, range = 40–65;100% Caucasian; prior to adjuvant doxorubicin-based chemotherapy; 89% accrual rate	PSQI, daily diary based on MSD, and actigraphy	Baseline sleep quality was poor (PSQI global $\bar{X}$ score = 8.8; 50% scored higher than 8); $\bar{X}$ sleep latency by diary was less than 30 minutes per night, sleep efficiency was 85% or higher, and total sleep time was 6–8.5 hours.	Missing data or data that were not in agreement (sleep diary or actigraphy)
Berger et al., 2007	Cross-sectional; 130 Americans with stage I–IIIA cancer; $\bar{X}$ age = 51 years, range = 34–83; 92% Caucasian; 48 hours prior to adjuvant anthracycline-based chemotherapy; no accrual rate data	Actigraphy and PSQI	Sleep quality was poor ($\bar{X}$ = 6 before chemotherapy; 57% exceeded 5 and 26% exceeded 8); sleep variables by actigraphy were in normal limits ($\bar{X}$ nocturnal sleep time = 6.6 hours; $\bar{X}$ sleep-onset latency = 11 minutes, $\bar{X}$ sleep efficiency = 86%; $\bar{X}$ day sleep time = 64 minutes), except for frequent nocturnal awakenings ($\bar{X}$ = 10) and wake after sleep onset of 63 minutes.	Lack of correspondence between timing of subjective and objective sleep assessments; less than 72 hours of actigraphy recording
Berger et al., 2009	Longitudinal; 219 patients with stage I–IIIA cancer; $\bar{X}$ age = 52 years, range = 29–79; 97% Caucasian, non-Hispanic; prior to initial anthracycline-based chemotherapy; 41% accrual rate	Actigraphy, PSQI, and daily diary	Poor sleep quality pretreatment ($\bar{X}$ = 7); normal nocturnal sleep variables by sleep diary and actigraphy (total sleep time = 432 and 416 minutes, nocturnal awakenings = 2 and 10, wake after sleep onset = 32 and 52 minutes, and sleep efficiency after onset = 90% and 89%, respectively)	Baseline values of mild fatigue and poor sleep quality may have created a ceiling effect; sleep diary recording may have influenced sleep behavior; delivery of intervention by nonsleep specialist may have caused dose-response effect

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ESS—Epworth Sleepiness Scale; FOSQ—Functional Outcome of Sleep Questionnaire; IIS-R—Insomnia Interview Schedule-Revised; ISQ—Insomnia Screening Questionnaire; MSD—Morin Sleep Diary; PSQI—Pittsburgh Sleep Quality Index; SDS—Sleep Disturbance Scale; SII—Structured Insomnia Interview; WHI-IRS—Women's Health Initiative Insomnia Rating Scale; WHO-EKSD—World Health Organization Education Kit for Sleep Disorders

Appendix A. Studies Investigating Sleep in Women Aged 50 Years or Older With Breast Cancer *(Continued)*

Study	Design and Sample	Tools	Findings	Limitations
Berger & Higginbotham, 2000	Longitudinal; 14 Americans with stage I–II cancer; $\bar{X}$ age = 52 years, range = 32–69; race unspecified; receiving doxorubicin or cyclophosphamide; no accrual rate data	MSD	Total sleep time exceeded 8 hours per 24 hours at all points, returning to 8 hours or less by recovery (2 months after chemotherapy); sleep-onset latency exceeded 30 minutes in 50%; $\bar{X}$ sleep efficiency = 90% during treatment, but half dropped below 85% by recovery.	Lack of baseline rest pattern data; incomplete actigraphy data
Carpenter et al., 2004	Cross-sectional with comparison group; 15 Americans with hot flashes and predominantly stage I–II cancer; $\bar{X}$ age = 47 years (SD = 7.4); 73% Caucasian; 15 matched controls; $\bar{X}$ years postdiagnosis = 5; 33% accrual rate	PSQI	Poor sleep quality (73% exceeded 5 and 53% exceeded 8); sleep quality was similar in controls (67% exceeded 5 and 40% exceeded 8). Nocturnal sleep duration was shorter for cases ($p < 0.05$) than controls.	Small sample size
Davidson et al., 2002	Cross-sectional; 302 Canadians (breast cancer group only); $\bar{X}$ age = 65 years (SD = 12.5); 99% women; 0%–10% received chemotherapy treatment in previous 6 months; 87% accrual rate	Brief sleep survey questionnaire	Sleep issues included insomnia (38%), excessive sleepiness (27%), sleeping more than usual (14%), repetitive leg movements (14%), and breathing interruptions during sleep (10%).	Varying points in treatment status; possible recall bias regarding sleep issues, medical status, and medication use
Fortner et al., 2002	Cross-sectional with comparison group; 72 Americans with breast cancer (stage unspecified); $\bar{X}$ age = 51 years (breast cancer group) and 38 years (control), range = 38–65 years; 82% Caucasian; 50 general medical patients; varying phases of treatment, with 41% receiving chemotherapy or radiation; no accrual rate data	PSQI	Sleep quality was poor; 61% of cases exceeded 5; $\bar{X}$ sleep-onset latency = 21 minutes; $\bar{X}$ nocturnal sleep time = 6.9 hours per night (less than 6 hours in 36%); $\bar{X}$ sleep efficiency was less than 85% in 46%; sleep quality was "fairly bad" or "very bad" in 29%; getting up to use the bathroom and pain were the most common disturbances; sleep medication-use subscore was higher ($p = 0.03$) for cases; sleep disturbance subscore was higher for cases receiving versus not receiving treatment but similar for different regimens.	Age differences between groups; patients were at different points of treatment; single self-report sleep measure; no baseline sleep data
Haghighat et al., 2003	Cross-sectional; 112 Iranians with stage I (9%), II (67%), or III–IV (24%) cancer; $\bar{X}$ age = 46 years, range = 22–76; 55% receiving treatment; 45% completed initial treatment; no accrual data	Insomnia symptoms (single item)	Insomnia symptoms were reported by 60% of women.	No ethics committee approval or written informed consent; differences in treatment completion
Koopman et al., 2002	Cross-sectional; 97 Americans with locally recurrent or metastatic cancer; $\bar{X}$ age = 53 years, range = 33–80 years; 90% Caucasian; 31% received chemotherapy within the prior 2 months.	27-item sleep questionnaire based on SII	Patients had issues falling asleep at night (25%), nocturnal awakenings (44%), issues waking and getting up in the morning (30%), and daytime sleepiness (21%); 37% used sleep medication in the past 30 days.	Exclusion of current severe depression; lack of objective sleep measures
Kuo et al., 2006	Longitudinal; 16 Taiwanese patients with stage I–II cancer; $\bar{X}$ age = 45 years, range = 18–65; receiving third cycle of cyclophosphamide, epirubicin, and fluorouracil or cyclophosphamide, methotrexate, and fluorouracil; no accrual rate data	Actigraphy, WHO-EKSD sleep logs, and ESS	Sleep quality was better in recovery than active phase (6 versus 4.3; $p < 0.05$); $\bar{X}$ sleep latency = 35 minutes (sleep log) and 23 minutes (actigraphy); nocturnal awakenings = 2 (sleep log); $\bar{X}$ sleep efficiency = 82% (actigraphy); daytime sleepiness was higher in active ($p < 0.05$) than recovery phase.	Small sample; short time period of investigation

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ESS—Epworth Sleepiness Scale; FOSQ—Functional Outcome of Sleep Questionnaire; IIS-R—Insomnia Interview Schedule-Revised; ISQ—Insomnia Screening Questionnaire; MSD—Morin Sleep Diary; PSQI—Pittsburgh Sleep Quality Index; SDS—Sleep Disturbance Scale; SII—Structured Insomnia Interview; WHI-IRS—Women's Health Initiative Insomnia Rating Scale; WHO-EKSD—World Health Organization Education Kit for Sleep Disorders

Appendix A. Studies Investigating Sleep in Women Aged 50 Years or Older With Breast Cancer *(Continued)*

Study	Design and Sample	Tools	Findings	Limitations
Liu et al., 2008	Longitudinal; 76 Americans with stage I–III cancer; $\bar{X}$ age = 51 years, range = 34–79; 72% Caucasian; newly diagnosed; prior to and during cycles 1–4 of anthracycline-based chemotherapy; no accrual rate data	PSQI	66% reported poor sleep quality (PSQI score higher than 5) at baseline; all women reported worse sleep during treatment versus baseline ($p < 0.01$).	Predominance of well-educated, married women; lack of information on sleep history, comorbidities, and medications, which may have influenced findings; possible influence of multiple sleep assessments on findings
Palesh et al., 2008	Longitudinal; 93 Americans with metastatic breast cancer; $\bar{X}$ age = 54 years, range = 33–80; 90% Caucasian; no accrual rate data	Sleep questionnaire based on SII	64% reported one or more sleep disturbances, with moderate to severe issues falling sleep (22%), awakening during the night (42%), waking and getting up in the morning (31%), and daytime sleepiness (23%).	Possible influence of high baseline stress levels and pain on sleep of some participants; possible recall bias
Payne et al., 2006	Longitudinal with comparison group; 11 Americans with stage II cancer; $\bar{X}$ age = 47 years; 55% Caucasian; 11 matched controls; receiving adjuvant chemotherapy (unspecified regimen)	Actigraphy, biomarkers (serum cortisol, serotonin, melatonin, and bilirubin)	$\bar{X}$ nocturnal sleep time by wrist actigraphy was lower ($p = 0.037$) for cases than controls over the two nights of cycle 1 but not at other measurement points; nocturnal sleep time differed most the night after chemotherapy cycle 1; $\bar{X}$ serum melatonin was similar across cycles 1–4, $\bar{X}$ serum serotonin was lower ($p < 0.001$) between cycles 1–4; cortisol levels decreased ($p < 0.0001$) the day after chemotherapy in cases.	Small sample; limited chemotherapy cycles may have influenced cumulative effect.
Savard et al., 2001	Cross-sectional; 300 Canadians with stage I–III cancer; $\bar{X}$ age = 60 years, range = 28–90; 100% Caucasian; $\bar{X}$ months postdiagnosis = 48.6; 38% previously received chemotherapy; 95% accrual rate	ISQ and IIS-R	51% reported insomnia symptoms; of them, 33% reported symptoms occurred following breast cancer diagnosis and 67% reported preexisting symptoms. 19% percent met diagnostic criteria for insomnia syndrome; 95% of insomnia was chronic; 58% reported that cancer caused or aggravated insomnia symptoms.	Phone interview only of patients reporting sleep difficulty or medications; inability to differentiate insomnia subtypes; lack of pain assessment; possible recall bias
Silberfarb et al., 1993	Cross-sectional; 15 Americans with stage I–III cancer; $\bar{X}$ age = 58 years, range = 38–70 years; $\bar{X}$= 8.7 months following diagnosis; age- and gender-matched comparison groups; 32 comparisons without insomnia and 32 comparisons with insomnia; no accrual rate data	Polysomnography (three nights) and sleep log including sleep satisfaction assessment	Findings for breast cancer cases versus comparisons without insomnia versus comparisons with insomnia were as follows: $\bar{X}$ total sleep time (minutes) = 384 versus 387 versus 338; $\bar{X}$ sleep efficiency = 85% versus 90% versus 78%; sleep-onset latency (minutes) = 37 versus 26 versus 56; nocturnal awakenings (times per night) = 12 versus 15 versus 17. 53% of breast cancer cases reported satisfaction with sleep by sleep log versus 100% of comparisons without insomnia.	Small number of breast cancer cases; possible influence of two-week period of sleep medication withdrawal and radiation therapy; lack of clinical treatment status data

ESS—Epworth Sleepiness Scale; FOSQ—Functional Outcome of Sleep Questionnaire; IIS-R—Insomnia Interview Schedule-Revised; ISQ—Insomnia Screening Questionnaire; MSD—Morin Sleep Diary; PSQI—Pittsburgh Sleep Quality Index; SDS—Sleep Disturbance Scale; SII—Structured Insomnia Interview; WHI-IRS—Women's Health Initiative Insomnia Rating Scale; WHO-EKSD—World Health Organization Education Kit for Sleep Disorders