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## Sleep/Wake Disturbances in People With Cancer and Their Caregivers: State of the Science

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**Purpose/Objectives:** To review the state of the science on sleep/wake disturbances in people with cancer and their caregivers.

**Data Sources:** Published articles, books and book chapters, conference proceedings, and MEDLINE<sup>®</sup>, the *Cumulative Index to Nursing and Allied Health Literature*<sup>®</sup>, PsycINFO, and the Cochrane Library computerized databases.

**Data Synthesis:** Scientists have initiated studies on the prevalence of sleep/wake disturbances and the etiology of sleep disturbances specific to cancer. Measurement has been limited by lack of clear definitions of sleep/wake variables, use of a variety of instruments, and inconsistent reporting of sleep parameters. Findings related to use of nonpharmacologic interventions were limited to 20 studies, and the quality of the evidence remains poor. Few pharmacologic approaches have been studied, and evidence for use of herbal and complementary supplements is almost nonexistent.

**Conclusions:** Current knowledge indicates that sleep/wake disturbances are prevalent in cancer populations. Few instruments have been validated in this population. Nonpharmacologic interventions show positive outcomes, but design issues and small samples limit generalizability. Little is known regarding use of pharmacologic and herbal and complementary supplements and potential adverse outcomes or interactions with cancer therapies.

**Implications for Nursing:** All patients and caregivers need initial and ongoing screening for sleep/wake disturbances. When disturbed sleep/wakefulness is evident, further assessment and treatment are warranted. Nursing educational programs should include content regarding healthy and disrupted sleep/wake patterns. Research on sleep/wake disturbances in people with cancer should have high priority.

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### Key Points . . .

- ▶ Sleep/wake disturbances in people with cancer and their caregivers can occur alone or as part of symptom clusters but have received little attention from healthcare providers.
- ▶ Several models offer approaches to examine the numerous factors that may underlie sleep/wake disturbances in people with cancer and their caregivers.
- ▶ A need exists to screen and assess sleep and wakefulness and to establish evidence for the reliability and validity of instruments used in this population.
- ▶ Randomized clinical trials to test interventions to promote sleep in this population are needed, but nonpharmacologic approaches found to be effective in people with insomnia can be included in patient-teaching materials.
- ▶ Future directions for research on sleep/wake disturbances have been identified and are ready for study.

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**D**espite the evidence suggesting that sleep/wake disturbances, particularly insomnia, are among the most common complaints of people with cancer, sleep problems have received little attention from healthcare providers (Savard & Morin, 2001). Data suggest that patients with cancer have twice the prevalence of sleep problems as that reported in the general population (Savard, Laroche, Simard, Ivers, & Morin, 2003), with the majority of people reporting maintenance insomnia with several awakenings during the night (Davidson, MacLean, Brundage, & Schulze, 2002; Lee, 2003). Insomnia is associated with increased rates of medical and psychiatric illnesses and decreased quality of life (QOL) in the general population (Sateia & Pigeon, 2004). The disturbances compound the many challenges faced by people with cancer. The much-needed research on sleep/wake disturbances in people with cancer needs to build on the extensive body of knowledge that exists regarding sleep/wake disturbances in the general population and specific sleep disorders such as sleep apnea, periodic leg movement syndrome, restless leg syndrome, narcolepsy, and insomnia.

This article summarizes participants' contributions to the Oncology Nursing Society (ONS) State-of-the-Science Conference on Sleep/Wake Disturbances in People With Cancer and Their Caregivers, which was held at ONS headquarters in Pittsburgh, PA, July 15–17, 2004. This article presents the state of the science on sleep/wake disturbances in people with cancer and their caregivers. It is divided into four main sections: sleep/wake disturbances in people with cancer, measurement of sleep/wake disturbances, nonpharmacologic and pharmacologic interventions, and implications for practice, education, and research. This article lays the foundation for directing increased attention to sleep/wake disturbances in clinical, educational, and research environments. As a result, the authors anticipate that patients with cancer and their caregivers will experience improved assessment and treatment.

## Sleep/Wake Disturbances in People With Cancer

Adults and children report that sleep/wake disturbances occur during all phases of cancer care (Clark, Cunningham, McMillan, Vena, & Parker, 2004; Gibson, Garnett, Richard-

son, Edwards, & Sepion, 2005; Hockenberry-Eaton et al., 1998; Vena, Parker, Cunningham, Clark, & McMillan, 2004). They occur before treatment has begun (Ancoli-Israel, Moore, & Jones, 2001) and often seem to be directly related to the cancer diagnosis (Lee, Cho, Miaskowski, & Dodd, 2004; Savard, Simard, Blanchet, Ivers, & Morin, 2001).

The sleep of caregivers, who often are family members, also is disrupted. Problems with insomnia, other nocturnal sleep disturbances, and daytime fatigue are common among caregivers of people with cancer and other chronic illnesses (Carter, 2003; Carter & Chang, 2000; Hinds et al., 1999; Jepson, McCorkle, Adler, Nuamah, & Lusk, 1999; Kozachik et al., 2001; McGrath, Paton, & Huff, 2004; Nijboer et al., 2000; Nijboer, Triemstra, Tempelaar, Sanderman, & van den Bos, 1999). Reactive depression is very prevalent and can interfere with daily function, QOL, and ability to continue to provide care (Jepson et al.; Kozachik et al.; Nijboer et al., 1999, 2000). Only recently has chronic sleep loss related to stress and the 24-hour-per-day demands of caregiving been described as a significant problem (Carter & Chang). In addition, caregivers may be at risk for sleep problems after the loss of a loved one. A recent study demonstrated that the risk for long-term psychological morbidity, including sleep/wake disturbances, in a surviving partner significantly increased if a patient's symptoms were unrelieved during the last three months of life (Valdimarsdottir, Helgason, Furst, Adolfsson, & Steineck, 2004).

Many nurses are aware that people with cancer have problems getting a good night's sleep but do not realize the effects that poor sleep can have on daytime wakefulness, functional ability, and QOL (Vena et al., 2004). Furthermore, the assessment of sleep/wake disturbances and treatment of problems have not been integrated into routine clinical practice (Savard & Morin, 2001; Sherman et al., 2004). Barriers to integration of current knowledge about sleep are similar to those that commonly occur when working to translate knowledge of pain. The barriers occur at the level of patients, families, care providers, and healthcare systems. Nonetheless, as part of a comprehensive care plan, nurses should assess the sleep needs of patients and caregivers regularly and tailor interventions to meet their needs (Steele & Fitch, 1996). Sleep/wake disturbances increasingly are recognized as significant side effects of cancer treatment that affect physiologic as well as psychological function. In fact, the U.S. Department of Health and Human Services, the National Institutes of Health, and the National Heart, Lung, and Blood Institute (2003); the Institute of Medicine (2005); and ONS (2003) have identified sleep disturbances as a priority research area.

## Sleep/Wake-Related Terminology

Recently, an increasing number of descriptive studies have included one or more sleep variables or terms indicating sleep/wake disturbances in some context in people with cancer. Unfortunately, the lack of consistency in terminology makes it difficult to compare and contrast studies and optimally evaluate their quality. Therefore, the authors recommend that, when possible, the terminology employed by the American Academy of Sleep Medicine (AASM) in the *International Classification of Sleep Disorders* (AASM, 2005) be used to provide consistency (Clark et al., 2004). For example, a primary sleep disorder is a specific diagnostic entity that includes a wide array of problems characterized by the symptoms of insomnia, excessive daytime sleepiness, or

abnormal movements, behaviors, or sensations during sleep. Eight groups of sleep disorders are described by AASM.

- **Insomnias:** disorders that produce repeated difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate time and opportunity for sleep and results in some form of daytime impairment
- **Sleep-related breathing disorders:** characterized by disordered respiration during sleep
- **Hypersomnias of central origin:** characterized by the primary complaint of daytime sleepiness not related to circadian rhythm sleep disorders, sleep-related breathing disorders, or other causes of disturbed nocturnal sleep
- **Circadian rhythm sleep disorders:** recurrent or chronic patterns of sleep disturbance resulting from alterations of the circadian timing system or misalignment between an individual's rhythm and the 24-hour social and physical environments
- **Parasomnias:** undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousal from sleep
- **Sleep-related movement disorders:** conditions that are characterized primarily by relatively simple, usually stereotyped movements that disturb sleep (e.g., periodic limb movements)
- **Isolated symptoms, apparently normal variants, and unresolved issues:** symptoms that either lie at the borderline between normal and abnormal sleep or that exist on a continuum of normal to abnormal events in sleep (e.g., snoring)
- **Other sleep disorders:** disorders that cannot be classified elsewhere (e.g., other physiologic [organic] sleep disorders)

In contrast, terms such as sleep/wake disturbances, sleep problems, alterations in sleep, or impaired sleep are more general terms and often are used to describe complaints, symptoms, or groups of symptoms experienced by individuals. They are not diagnostic entities as defined by the AASM and often are used when a specific diagnosis has not or cannot be made. Nonetheless, two of the most common complaints or symptoms experienced by the general public that are defined in the *International Classification of Sleep Disorders* are insomnia and excessive daytime sleepiness. Insomnia may be a primary sleep disorder or a symptom of one of many other sleep disorders, such as sleep-related breathing disorders. Daytime sleepiness is defined as the inability to stay awake and alert during the major waking episodes of the day, resulting in unintended lapses into drowsiness or sleep; it also may be seen in a wide range of sleep disorders. Thus, understanding the causes of insomnia and excessive daytime sleepiness is essential to providing effective interventions. Numerous additional sleep-related terms can help characterize sleep/wake disturbances, including total sleep time, sleep latency, awakenings during sleep, and wake after sleep onset.

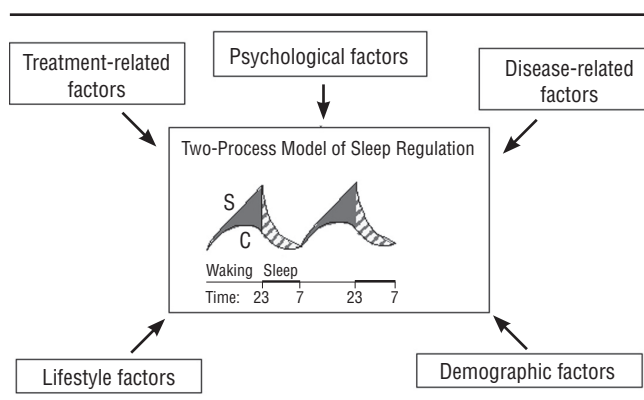
## Understanding Sleep/Wake Disturbances in People With Cancer and Their Caregivers

Most organisms, including humans, exhibit a daily rest/activity (sleep/wake) pattern. The pattern is a functional property of all living matter, including humans, and is controlled by two primary factors: the amount, timing, and placement of sleep across the day (i.e., sleep homeostasis) and the underlying

intrinsic circadian rhythm (Lazuna & Farr, 2003). The role of homeostatic factors and circadian rhythm in sleep regulation is best understood when sleep is examined as a physiologic as well as a behavioral process controlled by a system based in the brain and central nervous system. The sleep-regulation system provides an engine that drives sleep and wakefulness.

One model commonly used to help understand sleep is the Two-Process Model of Sleep Regulation (see Figure 1) (Achermann & Borbely, 2003; Borbely, 1982). According to the Two-Process Model, sleep begins (sleep onset) when the homeostatic (somnostat) component or need to sleep (Process S) is high. The need to sleep (Process S) increases as the time of prior wakefulness increases. The process of sleep onset also is modulated by the sympathetic nervous system (Lichstein, Wilson, Noe, Aguiard, & Bellur, 1994; Lushington, Dawson, & Lack, 2000; Vgontzas et al., 1998) and by the hypothalamic-pituitary-adrenal (HPA) axis (Vgontzas et al.). Increased activation of the sympathetic nervous system and the HPA axis can elevate arousal levels and delay the onset of sleep. Input from the systems is filtered out by the thalamus as sleep occurs, a process that must be filtered continually to maintain uninterrupted sleep.

In addition to Process S, there is Process C, the circadian process. The circadian oscillator resides in the suprachiasmatic nuclei, where rhythms are generated and synchronized with the environment by light and dark cues from the retina of the eye. Additional timing modifications are provided by interaction with the paraventricular nuclei and the ventromedial hypothalamus. Marker rhythms of the circadian oscillator are the core temperature rhythm and the rhythmic secretion of the hormone melatonin. At sleep onset, sleep initiation is most likely to occur during the falling phase of the endogenous component of the temperature rhythm (Strogatz, Kononaur, & Czeisler, 1986; Zullay, Weaver, & Aschoff, 1981). This occurs approximately five to six hours before the daily body temperature minimum is at its lowest point and one to two hours after the evening rise in plasma melatonin levels (Duffy, Dijk, Klerman, & Czeisler, 1998). Timing of the circadian component is adjusted by melatonin secreted from the pineal gland during the dark and inhibited by light exposure (Claustrate, Brun, & Chazot, 2005). Circadian timing also is adjusted by levels of plasma and central nervous system neurotransmitters and neuroendocrine factors such as gamma-amino-butyric acid; dopamine;



**Figure 1. Factors That Affect Sleep Regulation in Patients With Cancer**

Note. Based on information from Vena et al., 2004.

growth hormone releasing hormone; prostaglandins D<sub>2</sub>, E<sub>2</sub>, and F<sub>2α</sub>; vasoactive inhibitory peptide; and growth hormone (Harrington & Mistlberger, 2003; Kunz & Achermann, 2003; Lazuna & Farr, 2003; Mignot, Taheri, & Nishino, 2002; Obal & Krueger, 2004; Ouyang, Hellman, Abel, & Thomas, 2004; Pace-Schott & Hobson, 2002).

Final awakening typically occurs when body temperature is rising (approximately one to two hours after the minimum temperature of the endogenous circadian rhythm) and sleep pressure (Process S) has decreased (Czeisler & Dijk, 2001). Therefore, the result is that sleep is regulated and sleep consolidation is achieved by an interaction between the circadian oscillator (Process C) and the homeostatic somnostat (Process S) (Czeisler & Dijk). The two processes appear to interact continuously throughout the day to drive physiologic and psychophysiological variables (Borbely, Dijk, Acherman, & Tobler, 2001). Thus, the coordination between the two dynamic processes modulates the onset and offset of sleep as well as the rhythms of sleep propensity, wake propensity, and the degree of daytime alertness (Czeisler & Dijk; Dijk & Czeisler, 1994, 1995). In addition to the two processes, numerous demographic, lifestyle and environmental, psychological, and disease- and treatment-related factors are likely to contribute to poor sleep and daytime sleepiness experienced by people with cancer and their caregivers (see Figure 2).

For people with cancer, altered physiology directly related to the disease may play a prominent role in disrupting sleep and circadian regulatory processes. For example, abnormalities in the circadian production of cortisol have been reported in patients with cancer (Mazzoccoli et al., 2003; Raida et al., 2002). An absent or blunted rhythm of melatonin secretion also has been noted in patients with lung or colorectal cancer (Bartsch & Bartsch, 1999; Khoory & Stemme, 1988; Viviani, Bidoli, Spinazze, Rovelli, & Lissoni, 1992). Changes over time in nighttime melatonin levels in patients with breast or ovarian cancer also have been reported (Payne, 2002). In addition, cancer cells produce and induce production of cytokines, substances that promote sleep (Ardestani, Inserra, Solkoff, & Watson, 1999). More detailed summaries have been published (Clark et al., 2004; Lee, Dantzer, et al., 2004; Lee, Landis, et al., 2004; Vena et al., 2004). Further research is needed to understand more fully the extent to which the pathophysiology of cancer affects sleep and wakefulness.

Other models derived from or related to the Two-Process Model of Sleep Regulation have been proposed and address sleep/wake disturbances or health outcomes. The Conceptual Model of Impaired Sleep (Lee, 2003) describes impaired sleep as being related primarily to either sleep deprivation or sleep disruption, both of which can lead to adverse health outcomes in physiologic, cognitive-behavioral, emotional, and social domains. The PPP Model (Spielman & Glovinsky, 2004) proposes three main categories affecting sleep, particularly insomnia: predisposing, precipitating, and perpetuating factors. Predisposing factors are the biologic, genetic, and demographic traits that increase a person's risk and susceptibility to insomnia. Precipitating factors are situations and conditions that, although they may be temporary, actually trigger insomnia. Perpetuating factors are those that reinforce insomnia over longer periods of time. The Two-Process Model of Sleep Regulation, the Conceptual Model of Impaired Sleep, and the PPP Model offer various approaches to examining factors that

### Demographic Factors

- Age: Although increased age is associated with poorer quality of sleep, comorbidities may play a more important role.
- Gender: Women typically report poorer sleep quality than men.
- Race: Caucasian race has been associated with increased sleep complaints.

### Lifestyle and Environmental Factors

- Poor sleep hygiene: detrimental lifestyle factors such as irregular sleep/wake schedules and prolonged naps
- Caffeine intake disrupts sleep and causes arousals from sleep.
- Alcohol intake initially causes sedation but can disrupt sleep later in the night.
- Smoking may act as a central nervous system stimulant.
- Environment for sleeping: Excess light, noise, temperature extremes, and other stimuli (e.g., phone, pets) disrupt sleep.

### Psychological Factors

- Depression and anxiety are common responses to the diagnosis of or treatment for cancer and are associated with disturbed sleep.
- Stress and coping: work and family responsibilities, rigorous therapeutic schedules
- Social support and loneliness: number of people available to provide supportive assistance to change in self-image

### Disease-Related Factors

- Symptoms: Pain is experienced by as many as 80% of patients with cancer and may significantly interfere with sleep; multiple symptoms occurring in clusters have been linked to poor sleep.
- Hormone and cytokine secretion: Factors produced by tumor cells such as growth factors and other humoral factors can affect the timing, duration, and quality of sleep. Tumor-related factors, such as tumor growth factor, have been shown to inhibit sleep. Cytokines, such as interleukin (IL)-1, IL-2, IL-6, tumor necrosis factor (TNF), and interferon produced by the immune system in response to tumors, also interfere with sleep and circadian regulation.
- Site and stage of cancer: progression of disease

### Disease- and Treatment-Related Factors

- Surgery produces pain and inflammatory responses that can affect sleep; anesthetics also may adversely affect sleep and waking for prolonged periods.
- Chemotherapy: Problems with sleep, particularly night awakenings, have been described, but the etiology is unknown; hot flashes are common.
- Radiation therapy: Problems with nocturnal sleep and daytime sleepiness are documented.
- Biotherapy: Cytokines (IL-2, TNF-α) are associated with daytime sleepiness, disturbed sleep, and depression.
- Medication use: Many medications such as analgesics, antidepressants, antiemetics, anxiolytics, and corticosteroids may adversely affect sleep.

## Figure 2. Factors That Can Interfere With Normal Sleep Regulation in Patients With Cancer and Their Caregivers

Note. Based on information from Vena et al., 2004.

may underlie sleep/wake disturbances in people with cancer and their caregivers. Use of a particular model is dependent on the focus of a specific research study.

### Symptom Clusters

Clinical experience suggests that patients with cancer often present with multiple symptoms, which Dodd, Miaskowski, and Paul (2001) labeled a symptom cluster. Findings from several studies suggest that sleep disturbance may be part of a symptom cluster that includes pain, depression, and fatigue (Dodd et al.; Gift, Jablonski, Stommel, & Given, 2004; Gift, Stommel, Jablonski, & Given, 2003; Given et al., 2002; Given,

Given, Azzouz, Kozachik, & Stommel, 2001). In most of the studies to date, the symptom cluster of pain, fatigue, and sleep disturbance was associated with poorer functional status or decreased QOL. The question of which comes first remains unknown.

## Genetics and Sleep

Most sleep disturbances in healthy people result from complex interactions between an individual's genes and his or her environment (Taheri, 2004). Modern techniques in molecular genetics are being used in insect and animal models to begin to elucidate the genetic basis for circadian rhythms and sleep disturbances. Studies in animals and humans have shown that the sleep/wake and circadian clock systems are linked closely with each other on the molecular and systems levels (Turek, 2004). An excellent review on the genetics of sleep disorders (Taheri) described studies in animals that are beginning to elucidate the molecular mechanisms that underlie narcolepsy, obstructive sleep apnea, and restless leg syndrome. At least 10 circadian clock core genes have been identified in mammals to date, including findings related to diurnal preferences (morningness and eveningness) (Archer et al., 2003). Undoubtedly, future studies will help to determine the molecular basis for sleep disturbances that occur in the context of other medical conditions such as cancer.

# Measurement of Sleep/Wake Disturbances

## Key Sleep Parameters

One of the major challenges facing sleep research is measurement. "Difficulty sleeping," a term commonly used by patients, caregivers, and practitioners, can have very different meanings and causes. Symptoms of sleep/wake disturbances may include difficulty getting to sleep; difficulty staying asleep; restless sleep or the feeling that sleep is not refreshing; or sleepiness, the inability to stay awake when desired. In otherwise healthy populations, relatively little is known about the various manifestations of sleep disturbances and how they interact to result in a patient's report of "difficulty sleeping." In patients with cancer, particularly children, even less is known. Between one-third and three-quarters of adult patients with cancer experience difficulty sleeping (Andrykowski et al., 1997; Davidson et al., 2002; Engstrom, Strohl, Rose, Lewandowski, & Stefanek, 1999; Fortner, Stepanski, Wang, Kasprovicz, & Durrence, 2002; Miaskowski & Lee, 1999). Children with cancer and their caregivers or parents also report sleep disturbances, but the actual incidence of disturbed sleep in children is unknown (Ferrell, Rhiner, Shapiro, & Dierkes, 1994; Gedaly-Duff et al., 2002; Hockenberry-Eaton et al., 1998).

In each of the descriptive studies described in the earlier paragraph, different parameters were used to define difficulty sleeping. Daytime sleepiness that may be a result of nocturnal sleep difficulties has not been included in the studies yet, but it is an important component of poor sleep, as well as an indicator of poor QOL. As researchers and clinicians attempt to explore sleep quality and its importance to health, their efforts would be advanced significantly if consensus were achieved regarding which sleep parameters to measure and which measurement instruments to use in a standard fashion. Based on a review of the literature and consensus of the expert clinicians

and researchers participating in the ONS State-of-the-Science Conference on Sleep/Wake Disturbances in People With Cancer and Their Caregivers, nine parameters of sleep disturbance are proposed to provide a common language of sleep disturbance for measurement of the problem in all studies involving adults and children with cancer as well as their caregivers. The parameters are total sleep time, sleep latency, awakenings, wake time after sleep onset, napping during the day, excessive daytime sleepiness, quality of perceived sleep, stability of circadian rhythms, and sleep efficiency (see Table 1). No single parameter is recommended because poor sleep cannot be captured in its totality by any one parameter. Instead, the nine parameters collectively describe the characteristics of a sleep/wake disturbance.

Table 1 includes clinical tools and research instruments to assess the nine sleep parameters. In addition to the few sleep tools or instruments that have been validated in patients with cancer (e.g., the Pittsburgh Sleep Quality Index [PSQI]), clinical tools and research instruments that have been used with other patient populations also have been included. Clinical tools were chosen based on their ease of use in busy clinical settings and the ability to modify therapy quickly based on findings. Research instruments were chosen based on what is known about reliability (precision), validity (accuracy), and sensitivity of the instruments in research settings (Beck, Schwartz, Towsley, Dudley, & Barsevick, 2004; Carpenter & Andrykowski, 1998).

Of note, the Clinical Sleep Assessment for Adults and the Clinical Sleep Assessment for Children were developed as brief assessments for sleep problems in clinical settings (see Figure 3) (Lee & Ward, 2005). The tools were derived from an extensive clinical assessment protocol called BEARS, an acronym that stands for bedtime issues, excessive daytime sleepiness, night awakenings, regularity and duration of sleep, and snoring (Owens & Dalzell, 2005). Both need extensive testing in clinical practice but are administered easily, can be scored for research purposes, and have excellent face validity. They are useful for obtaining a brief sleep history in inpatient and ambulatory care settings, as well as for identifying people in need of specific intervention strategies such as improvements in sleep hygiene, changes in lifestyle, or referrals to sleep disorder specialists. When time is limited, a subset of four of the seven questions can be used (see notes in Figure 3). Using the tools can facilitate a focused approach to understanding sleep disturbances, improving sleep, and maximizing QOL for all people with cancer during and after treatment.

As with any tool or instrument, each of the clinical tools and research instruments listed in Table 1 has limitations. Clinicians and researchers are urged to read more about a particular tool or instrument before using it in practice or research. Validation of clinical tools and research instruments in patients with cancer and their caregivers is highly encouraged.

## Considerations for Assessment of Sleep

One consideration in the choice of a sleep measurement is the temporal nature of the sleep/wake cycle. The assessment of a biologic process that normally fluctuates in a circadian pattern is inherently challenging. Instruments that are easy to administer and interpret are needed to more fully appreciate the nature of sleep and sleep disturbance.

Although sleep/wake disturbances can be assessed subjectively and objectively, the subjective and objective measurements do not necessarily correlate (Berger & Johnson, 2004; Young-

**Table 1. Recommended Sleep Parameter Tools for Clinical and Research Settings**

Sleep Parameter	Normal	Tools in Clinical Settings	Tools in Research Settings
Total sleep time while in bed: number of minutes of sleep while in bed	Adults normally attempt to sleep 7–9 hours (420–540 minutes) in 24 hours. Newborns normally sleep 16–20 hours in a 24-hour period. Infants normally sleep 13–16 hours in a 24-hour period. Children 2–5 years old normally sleep 11–13 hours in a 24-hour period. Children 6–12 years old normally sleep 10 hours in a 24-hour period. Adolescents 13–18 years old normally sleep 8.5–9.25 hours in a 24-hour period (Grigg-Damberger, 2004; Hoban, 2004).	Adults: Clinical Sleep Assessment (Adult) (Lee & Ward, 2005), parent/caregiver interview, and Sleep Diary (Ellis et al., 1981; Kryger, 2004; Morin & Espie, 2003; National Sleep Foundation, 1999; Rogers et al., 1993) Children and adolescents: Clinical Sleep Assessment (Child) (Lee & Ward, 2005) and parent/caregiver interview	Adults: actigraph (Littner, Kushida, et al., 2003; Sadeh et al., 1995), Pittsburgh Sleep Quality Index <sup>a</sup> (Buysse et al., 1989), polysomnography, and time-lapse video recordings (Anders & Sostek, 1976) Children and adolescents: actigraph (Littner, Hirshkowitz, et al., 2003; Sadeh et al., 1995), Children's Sleep Habits Questionnaire (Owens & Dalzell, 2005), and polysomnography
Latency: number of minutes between when someone lays down to bed and actually goes to sleep	Adult latency normally is less than 20 minutes. Children and adolescent latency normally is 30–60 minutes (Glaze, 2004). Preadolescent children's latency averages 19 minutes ± 1.6 minutes (Hoban & Chervin, 2001).	Adults: BEARS (B–bedtime) (Owens & Dalzell, 2005), Clinical Sleep Assessment (Adult) (Lee & Ward, 2005), parent/caregiver interview, and sleep diary (Ellis et al., 1981; Kryger, 2004; Morin, 1993; Morin & Espie, 2003; National Sleep Foundation, 1999; Rogers et al., 1993) Children and adolescents: Clinical Sleep Assessment (Child) (Lee & Ward, 2005) and parent/caregiver interview	Adults: actigraph (Littner, Kushida, et al., 2003), Pittsburgh Sleep Quality Index <sup>a</sup> (Buysse et al., 1989), and polysomnography Children and adolescents: actigraph (Littner, Kushida, et al., 2003; Sadeh et al., 1995), Children's Sleep Habits Questionnaire (Owens & Dalzell, 2005), and polysomnography
Awakenings during sleep period: the number of awakenings during a sleep period	Adults normally awaken two to six times during a typical night's sleep of 420 minutes. Children normally awaken one to five times (an average of three times) during a typical night's sleep (Riter & Wills, 2004). Night awakenings gradually decrease in children two to five years of age (Glaze, 2004).	Adults: BEARS (A–night awakenings, S–snoring) (Owens & Dalzell, 2005), Clinical Sleep Assessment (Adult) (Lee & Ward, 2005), parent/caregiver interview, and sleep diary (Ellis et al., 1981; Kryger, 2004; Morin & Espie, 2003; National Sleep Foundation, 1999; Rogers et al., 1993) Children and adolescents: Clinical Sleep Assessment (Child) (Lee & Ward, 2005), parent/caregiver interview, and sleep diary (parent reports) (D'Andrea, 2004)	Adults: actigraph (Littner, Kushida, et al., 2003), Pittsburgh Sleep Quality Index <sup>a</sup> (Buysse et al., 1989), and polysomnography Children and adolescents: actigraph (Littner, Kushida, et al., 2003; Sadeh et al., 1995), Children's Sleep Habits Questionnaire (Owens & Dalzell, 2005), Pediatric Sleep Questionnaire (Chervin et al., 2000), and polysomnography
Wake after sleep onset (WASO): number of minutes awake or percentage of time awake after sleep onset during the sleep period	Adult WASO time normally is less than 10% of the total sleep minutes, or 42 minutes if the person sleeps 420 minutes (seven hours) during the night. Children's WASO time normally is less than 20 minutes for each awakening.	Adults: No tools assessing WASO in the clinical setting were identified. Children and adolescents: No tools assessing WASO in the clinical setting were identified.	Adults: actigraph (Littner, Kushida, et al., 2003), Pittsburgh Sleep Quality Index <sup>a</sup> (Buysse et al., 1989), and polysomnography Children and adolescents: actigraph (Littner, Kushida, et al., 2003; Sadeh et al., 1995), Children's Sleep Habits Questionnaire (Owens & Dalzell, 2005), and polysomnography
Napping during the day: total number of minutes of sleep during the daytime; can be intentional or unintentional sleep	Adult napping normally can vary from five minutes to two hours. Napping for children tends to conclude at about age six (Weissbluth, 1995).	Adults: parent/caregiver interview, Sleep Diary (Ellis et al., 1981; Kryger, 2004; Morin & Espie, 2003; National Sleep Foundation, 1999; Rogers et al., 1993) Children and adolescents: parent/caregiver interview, sleep diary, parent report, or sleep logs	Adults: actigraph (Littner, Kushida, et al., 2003) and Pittsburgh Sleep Quality Index <sup>a</sup> (Buysse et al., 1989) Children and adolescents: actigraph (Littner, Kushida, et al., 2003; Sadeh et al., 1995) and Children's Sleep Habits Questionnaire (Owens & Dalzell, 2005)

<sup>a</sup> These tools are highly recommended.

<sup>b</sup> Although commonly reported, sleep efficiency was not believed to be the most helpful factor to assess because it is difficult to determine without polysomnography.

*(Continued on next page)*

**Table 1. Recommended Sleep Parameter Tools for Clinical and Research Settings (Continued)**

Sleep Parameter	Normal	Tools in Clinical Settings	Tools in Research Settings
Excessive daytime sleepiness: episodes of lapses into sleep of short duration, usually in situations in which the person is inactive for even brief periods; excessive daytime sleepiness can result from acute or chronic sleep deprivation or loss or other pathophysiologic causes.	Adults normally have a minimal chance of dozing while engaged in routine activities. 1.7% of children 4–12 years old experience excessive daytime sleepiness.	Adults: BEARS (E–excessive daytime sleepiness, S–snoring) (Owens & Dalzell, 2005), Clinical Sleep Assessment (Adult) (Lee & Ward, 2005), parent/caregiver interview, and sleep diary (Ellis et al., 1981; Kryger, 2004; Morin & Espie, 2003; National Sleep Foundation, 1999; Rogers et al., 1993) Children and adolescents: Clinical Sleep Assessment (Child) (Lee & Ward, 2005), parent/caregiver interview, and visual analog scale (Fallone et al., 2002)	Adults: actigraph (Littner, Kushida, et al., 2003), Epworth Sleepiness Scale <sup>a</sup> (Johns, 1992), Maldonado Sleepiness Scale With Cartoon Faces (Maldonado et al., 2004), Multiple Sleep Latency Test as measured with polysomnography, Pittsburgh Sleep Quality Index <sup>a</sup> (Buysse et al., 1989), and Stanford Sleepiness Scale (Hoddes et al., 1972) Children and adolescents: actigraph (Littner, Kushida, et al., 2003; Sadeh et al., 1995), Children's Sleep Habits Questionnaire (Owens & Dalzell, 2005), and Multiple Sleep Latency Test as measured with polysomnography
Quality of perceived sleep: multidimensional perceptions of length and depth of sleep and feelings of being rested upon awakening; subjective assessment of sufficiency of sleep for daytime functioning	Adults normally feel satisfied or very satisfied with their usual sleep patterns and believe that their sleep enhances their daily functioning. This has not been defined for children.	Adults: Clinical Sleep Assessment (Adult) (Lee & Ward, 2005), parent/caregiver interview, and sleep diary (Ellis et al., 1981; Kryger, 2004; Morin & Espie, 2003; National Sleep Foundation, 1999; Rogers et al., 1993) Children and adolescents: Clinical Sleep Assessment (Child) (Lee & Ward, 2005) and parent/caregiver interview	Adults: Pittsburgh Sleep Quality Index <sup>a</sup> (Buysse et al., 1989) Children and adolescents: Children's Sleep Habits Questionnaire (Owens & Dalzell, 2005)
Circadian rhythm: biobehavioral phenomenon associated with fluctuations in light, hormones, eating, or socializing that repeats approximately every 24 hours	Adults, children, and adolescents: Circadian rhythm peaks and troughs within a 24-hour period.	Adults: BEARS (R–regularity and duration of sleep) (Owens & Dalzell, 2005) and parent/caregiver interview Children and adolescents: parent/caregiver interview	Adults: actigraph (Littner, Kushida, et al., 2003), dim light melatonin onset, Morningness/Eveningness Scale <sup>a</sup> (Taillard et al., 2004), Pittsburgh Sleep Quality Index <sup>a</sup> (Buysse et al., 1989), social rhythm metric, and 24-hour core temperatures Children and adolescents: actigraph (Littner, Kushida, et al., 2003; Sadeh et al., 1995) and Children's Sleep Habits Questionnaire (Owens & Dalzell, 2005)
Sleep efficiency <sup>b</sup> : the number of minutes of sleep divided by the total number of minutes in bed, multiplied by 100	In adults, 95% sleep efficiency indicates a good night's sleep; less than 80% indicates a bad night's sleep; in a night's sleep of 420 minutes (7 hours), this would be equivalent to 20 minutes to fall asleep and three awakenings of 10 minutes each. No references were found for children.	Adults: No tools assessing sleep efficiency in the clinical setting were identified. Children and adolescents: No tools assessing sleep efficiency in the clinical setting were identified.	Adults: actigraph (Littner, Kushida, et al., 2003) and polysomnography Children and adolescents: actigraph (Littner, Kushida, et al., 2003; Sadeh et al., 1995), Children's Sleep Habits Questionnaire (Owens & Dalzell, 2005), and Pediatric Sleep Questionnaire (Chervin et al., 2000)

<sup>a</sup> These tools are highly recommended.

<sup>b</sup> Although commonly reported, sleep efficiency was not believed to be the most helpful factor to assess because it is difficult to determine without polysomnography.

McCaughan et al., 2003). Certain research instruments, such as sleep diaries, assess individuals' perceptions of problems falling asleep and sleep quality, whereas others, such as wrist actigraphy, assess actual physical movements during sleep-activity periods.

Valuable sleep information can be obtained from bed partners, parents of children, and caregivers. For example, the final

section of the PSQI includes specific questions to be answered by bed partners, and the Clinical Sleep Assessment (Child) is completed by parents of young or otherwise nonverbal children. Understandably, sleep information obtained from bed partners or caregivers is affected by their own sleep patterns. Skilled clinicians are able to synthesize the data as treatments plans are

### Clinical Sleep Assessment (Adult)

1. What is your employment status?  
 Retired or unemployed  
 Self-employed or homemaker  
 Employed  
 Day shift  
 Night shift  
 Rotating shifts  
Work hours: \_\_\_ am/pm to \_\_\_ am/pm
2. In the past month, have you taken medication or alcohol to help you sleep?  
 No  Yes  
If yes, list name. \_\_\_\_\_  
Did you take it  
 Fewer than one time per week?  
 One or two nights per week?  
 Three or more nights per week?
3. Considering the past month, how would you rate your sleep quality?  
 Very good  
 Fairly good  
 Fairly bad  
 Very bad
4. In the past week, what time did you typically turn out the light to go to sleep?  
 \_\_\_ am/pm on weeknights/workdays  
 \_\_\_ am/pm on weekends/days off
5. In the past week, what time was your typical final awakening?  
 \_\_\_ am/pm on weeknights/workdays  
Total hours of sleep on weeknights \_\_\_  
 \_\_\_ am/pm on weekends/days off  
Total hours of sleep on weekends/days off \_\_\_
6. In the past week, how many times did you typically wake up during the night?  
 Never or once  
 One or two times, depending on the night  
Total minutes \_\_\_  
 Two or three times, depending on the night  
Total minutes \_\_\_  
 Three to four times, depending on the night  
Total minutes \_\_\_  
 Always three or more times  
Total minutes \_\_\_  
What is the main reason for waking up?  
 Bladder  
 Other (Please note snoring, choking, suffocating, kicking, hitting, etc.)
7. In the past week, how sleepy did you feel during the day?  
 Not at all sleepy  
 A little sleepy  
 Very sleepy  
 I would fall asleep when I did not really want to or plan to fall asleep.

*Note.* A short form of this screen should include items 2, 3, 6, and 7. For the long or short form, a referral to a sleep specialist is indicated for any of the following responses: #2, medication taken three or more nights/week; #3, sleep quality is very bad; #6, wake up three or four times depending on night; or wake up three or more times/night; #7, fall asleep when not planned.

*Note.* For content validity, questions were reviewed by a panel of sleep experts in research and clinical practice. Neither this seven-item assessment tool nor the essential four items for rapid screening have been rigorously tested in clinical practice.

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### Clinical Sleep Assessment (Child)

1. Does your child attend  
 Day care (part-time)?  
 Day care (full time)?  
 School?  
School starts at \_\_\_ am/pm  
School ends at \_\_\_ am/pm
2. In the past month, has your child taken a medication or alcohol to sleep?  
 No  Yes  
If yes, list name \_\_\_\_\_  
Was it taken  
 Fewer than one time per week?  
 One or two nights per week?  
 Three or more nights per week?
3. Considering the past month, how would you rate your child's sleep quality?  
 Very good  
 Fairly good  
 Fairly bad  
 Very bad
4. In the past week, what time did your child typically go to bed?  
 \_\_\_ am/pm weeknights/school days  
 \_\_\_ am/pm on weekends  
How difficult was it for your child to settle and fall asleep after bedtime rituals?  
 Not at all difficult  
 A little difficult  
 Somewhat of a struggle  
 A constant struggle
5. In the past week, what time was your child's typical final awakening?  
 \_\_\_ am/pm on weeknights/school days  
 \_\_\_ am/pm on weekends  
How difficult was it for your child to get up in the morning?  
 Not at all difficult  
 A little difficult  
 Somewhat of a struggle  
 A constant struggle
6. In the past week, how many times did your child wake up during the night?  
 Never or once  
 One or two times, depending on the night  
 Two to three times, depending on the night  
 Three to four times, depending on the night  
 Always three or more times  
What is the main reason for waking up?  
 Thirst  
 Bladder  
 Other (Please note snoring, choking, kicking, hitting, head banging, teeth grinding, bed wetting, sleep walking or talking, nightmares, night terrors, etc.)
7. In the past week, how sleepy was your child during the day?  
 Not at all sleepy  
 A little sleepy  
 Very sleepy  
 Takes a nap most days  
 Falls asleep during class  
 Falls asleep on the way home from school

*Note.* A short form of this screen should include items 2, 3, 6, and 7. For the long or short form, referral to a sleep specialist is indicated for any of the following responses: #2, medication taken three or more nights/week; #3, sleep quality is very bad; #6, wake up three or four times depending on night or wake up three or more times/night; #7, fall asleep on the way home from school.

*Note.* For content validity, questions were reviewed by a panel of sleep experts in research and clinical practice. Neither this seven-item assessment tool nor the essential four items for rapid screening have been rigorously tested in clinical practice.

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**Figure 3. Clinical Sleep Assessment for Adults and Children**



developed in clinical settings; however, quantitative methods to handle the data should be developed for research purposes.

Time frame is an important consideration in the choice of a sleep measurement. For example, the two most frequently used measurements of daytime sleepiness are the Stanford Sleepiness Scale (Hoddes, Zarcone, & Dement, 1972) and the Epworth Sleepiness Scale (Johns, 1992), both self-report measurements. The Stanford Sleepiness Scale was developed to assess sleepiness several times throughout a day in conjunction with the multiple sleep onset latency test (a polysomnography study of daytime sleepiness) and can be performed on an hourly basis to examine change in sleepiness during the day as well as time of day when sleepiness is greatest. The Epworth Sleepiness Scale, on the other hand, asks about how likely it would be for a person to doze off in various activities that typically are performed over the course of a day (e.g., watching TV), week (e.g., as a passenger in a car), or month (e.g., attending the theater). Prospective measurements, such as a sleep diary or the Stanford Sleepiness Scale, and retrospective measurements, such as the Epworth Sleepiness Scale, have strengths and weaknesses related to reliability that clinicians and researchers need to consider when matching a research instrument to a specific research question or clinical concern.

## Interventions

### Nonpharmacologic

Since 1985, psychological and behavioral factors increasingly have been recognized as contributing to the development of insomnia. More than a dozen nonpharmacologic, cognitive, and behavioral interventions have been developed; however, the populations in which they have been tested have been otherwise healthy people with insomnia. Only discussion of interventions for insomnia in adults is possible because information is limited in regard to children. To identify commonly used nonpharmacologic interventions to promote sleep or prevent insomnia, a two-step search of the literature indexed was conducted using the major literature search engines (MEDLINE®, Cumulative Index to Nursing and Allied Health Literature®, and PsycINFO). Key words used for the primary search included sleep, sleep disturbance, intervention, and insomnia. From the findings, primary research, research summary, and meta-analysis articles were selected.

The secondary search of the literature was conducted using the names of the interventions used in the articles identified in the primary search (e.g., sleep restriction, sleep hygiene, relaxation therapy, massage, yoga). When possible, classic sources were identified and retrieved for each intervention and compared with recent sources to provide definitions, rationale, and recommendations or strategies for each intervention. The findings are summarized in Table 2. Although the authors recognize the limitations of the generalizability of the studies, the body of knowledge provides a foundation from which to generate knowledge of interventions that are effective in people with cancer and their caregivers.

Nonpharmacologic interventions to promote sleep and prevent or treat insomnia often were used as combination therapies (cognitive and behavioral therapies) depending on the needs or restrictions of the study populations. The use of different combinations of interventions may explain some of the differences across studies in terms of the recommenda-

tions or strategies suggested for implementation. However, definitions and rationales for the use of interventions were consistent across sources.

**Meta-analyses of nonpharmacologic interventions for disturbances in sleep:** To determine possible therapeutic modalities to improve sleep in people with cancer and their caregivers, a search was conducted for meta-analyses of nonpharmacologic cognitive and behavioral interventions for insomnia in noncancer populations. Searches of MEDLINE, CINAHL, PsycINFO, and the Cochrane Library from 1994–2004 were conducted using the key term sleep interventions and limit of meta-analysis. Five analyses were found that provided the state-of-the-science information on the effectiveness of nonpharmacologic interventions to improve sleep in presumably healthy noncancer populations (see Table 3). None of the reviews addressed insomnia interventions in populations with cancer.

The Cochrane Database has published highly controlled, systematic reviews on bright light therapy, physical exercise, and cognitive and behavioral interventions to improve sleep. Each systematic review includes information about the search strategy used. Cognitive and behavioral interventions are defined as treatments that aim to improve sleep by changing poor sleep habits and challenging negative thoughts, attitudes, and beliefs about sleep. The interventions include a broad range of treatments, from educational packages to those that employ behavioral strategies. Only cognitive and behavioral treatments provided level 1 (strongest) evidence of short-term effects in reducing sleep onset latency and wake after sleep onset; however, the treatment effects were not durable over time (Montgomery & Dennis, 2003). Two earlier meta-analyses (Morin, Culbert, & Schwartz, 1994; Murtagh & Greenwood, 1995) provided stronger evidence that nonpharmacologic interventions produced reliable and durable clinical benefits in reducing sleep onset latency and wake after sleep onset. Differences in the conclusions of the two earlier meta-analyses compared to a more recent report by Montgomery and Dennis (2003) may be attributed, in part, to more rigorous inclusion criteria that resulted in fewer studies being included in the recent analysis. Larger effects were found for people who were referred by clinicians and not regular users of hypnotics (Murtagh & Greenwood). Current reviews are limited by the lack of randomized, controlled trials of sleep in people with cancer and their caregivers. As evidence grows regarding the effects of interventions for insomnia and other sleep/wake disturbances in cancer and noncancer populations, additional meta-analyses are recommended.

**Nonpharmacologic intervention studies of sleep/wake disturbances in patients with cancer:** Clark et al. (2004) examined research published from 1980–2003 on sleep/wake disturbances in people with cancer. Fifty-two pieces of evidence, including descriptive and intervention studies, were used in the evidence tables and rated from level 1 (strongest) to level 3 (weakest) of evidence. Readers are encouraged to review the evidence tables to gain perspective on the state of the science.

From 2003–2004, an increasing volume of descriptive studies was published that included the variable of sleep in some context in patients with cancer. A search of MEDLINE, CINAHL, and PsycINFO was conducted to identify all nonpharmacologic intervention studies that examined sleep disturbance or sleep quality outcomes in adults with cancer; the search revealed 20 studies (as of March 2005) that met the criteria (see Table 4).

**Table 2. Cognitive and Behavioral Interventions Used to Promote Sleep**

Intervention	Definition and Rationale	Recommendations and Strategies
Stimulus control (Bootzin et al., 1991)	<p>Definition: reassociating the bed and bedroom with rapid sleep onset by limiting sleep-incompatible activities that cue wakefulness and by enforcing a consistent sleep-wake schedule</p> <p>Rationale: based on the theory that insomnia is an altered conditioned response to time and environmental cues that usually are associated with sleep</p>	<ul style="list-style-type: none"> <li>• Go to bed only when sleepy.</li> <li>• Use the bedroom only for sleep and sex.</li> <li>• Maintain a regular arising time in the morning regardless of sleep duration the previous night.</li> <li>• Get out of bed and go into another room whenever unable to fall asleep or return to sleep within 15–20 minutes, and return to bed only when sleepy again.</li> <li>• Avoid daytime napping.</li> </ul>
Sleep restriction (Morin et al., 1999; Petit et al., 2003; Spielman et al., 1987)	<p>Definition: limiting the amount of time spent in bed to closer approximate the amount of time asleep</p> <p>Rationale: creates a mild state of sleep deprivation and promotes more rapid sleep onset, more efficient sleep, and less inter-night variability</p>	<ul style="list-style-type: none"> <li>• Log sleep efficiency for one week.</li> <li>• Prescribe the amount of time in bed to match the time slept on the log.</li> <li>• Evaluate sleep efficiency weekly.</li> <li>• If <math>\geq 90\%</math>, increase time in bed by 15 minutes.</li> <li>• If <math>&lt; 80\%</math>, decrease time in bed by 15 minutes.</li> <li>• If <math>80\%–89\%</math>, keep the same sleep time.</li> <li>• To avoid excessive daytime sleepiness, do not prescribe less than five hours in bed per night.</li> </ul>
Paradoxical intention (Morin et al., 1999)	<p>Definition: encouragement of patients to engage in their most feared activity, staying awake</p> <p>Rationale: based on the theory that performance anxiety inhibits sleep onset. Thus, if a patient stops trying to sleep and instead genuinely attempts to stay awake, performance anxiety will be lessened and sleep may come more easily.</p>	<ul style="list-style-type: none"> <li>• Instruct patient to attempt to stay awake without the use of stimulants.</li> </ul>
Sleep hygiene (healthy sleep practices) (Hauri, 1991; Lacks & Rotert, 1986)	<p>Definition: health practices and environmental factors that may be either barriers to or facilitators for sleep</p> <p>Rationale: If patients are able to identify factors (internal and external) that are affecting their sleep, they will be able to choose to remove barriers and increase facilitators of their sleep.</p>	<ul style="list-style-type: none"> <li>• Avoid caffeine and nicotine a minimum of four to six hours before bed.</li> <li>• Avoid strenuous exercise five to six hours before bed.</li> <li>• Avoid use of alcohol as a sleep aid.</li> <li>• Reduce noise, light, and temperature in bedroom.</li> <li>• Keep a regular sleep schedule.</li> <li>• Participate in relaxing activities prior to bed.</li> </ul>
Cognitive therapy for insomnia (cognitive restructuring) (Morin, 1993)	<p>Definition: use of restructuring techniques such as decatastrophizing, hypothesis testing, reappraisal, and attention shifting to alter false beliefs and attitudes about sleep</p> <p>Rationale: short-circuits the vicious cycle of insomnia, emotional distress, dysfunctional cognitions, and further sleep disturbances by identifying patient-specific dysfunctional sleep thoughts, challenging their validity, and replacing them with more adaptive substitutes</p>	<ul style="list-style-type: none"> <li>• Target current perceptions of sleep to be addressed by cognitive therapy</li> <li>• Avoid unrealistic sleep expectations (e.g., “I must get eight hours of sleep every night.”).</li> <li>• Avoid misconceptions about the causes of insomnia (e.g., “My insomnia is entirely due to a chemical imbalance.”).</li> <li>• Avoid amplifications of the consequences of insomnia (e.g., “I cannot accomplish anything after a poor night’s sleep.”).</li> <li>• Avoid performance anxiety resulting from excessive attempts at controlling the sleep process (e.g., “I just need to try harder to sleep.”).</li> </ul>
Relaxation therapy (Benson & Stark, 1996; Lichstein, 1988; Seaward, 2002)	<p>Definition: activities that reduce somatic or cognitive arousal. Somatic: Therapies focus on reducing physiologic arousal (e.g., muscle tension, hypertension), including but not limited to progressive muscle relaxation, massage, biofeedback, autogenic training, and self-hypnosis. Cognitive: Therapies focus on reducing cognitive arousal (e.g., intrusive thoughts, racing mind), including but not limited to imagery and visualization training, thought stopping, and mindfulness meditation.</p> <p>Rationale: Patients with insomnia often have high levels of somatic and cognitive arousal, both at night and during the daytime. Relaxation methods are used to deactivate the arousal system and promote sleep.</p>	<ul style="list-style-type: none"> <li>• Selection of specific techniques varies depending on whether somatic or cognitive arousal is targeted for treatment. Duration, frequency, and intensity of treatments are dependent on particular therapies selected.</li> </ul>

*(Continued on next page)*

**Table 2. Cognitive and Behavioral Interventions Used to Promote Sleep (Continued)**

Intervention	Definition and Rationale	Recommendations and Strategies
Phototherapy, bright light therapy (Smith et al., 2003)	<p>Definition: Phototherapy is the use of bright light to influence the circadian rhythm. Phototherapy often is accomplished via a light box that generates blue spectrum light at 4,000–10,000 lux. The dose is adjusted by altering the distance and duration of light exposure.</p> <p>Rationale: Bright light in the morning advances the timing of the circadian phase, whereas exposure in the evening delays the circadian phase. The sleep-promoting effects of bright light may occur via several mechanisms, including shifting the circadian system, enhancing the amplitude of the circadian pacemaker, promoting wakefulness during the day and sleep at night, or indirectly, via its antidepressant effects.</p>	<ul style="list-style-type: none"> <li>• Phase delay insomnia (go to bed late and wake up late)—Bright light exposure in the morning for a minimum of 30 minutes is recommended.</li> <li>• Phase advance insomnia (go to bed early and wake up early)—Bright light exposure in the late evening/early night for a minimum of 30 minutes is recommended.</li> </ul>
Exercise (Buxton et al., 2003; Li et al., 2004; National Center for Complementary and Alternative Medicine, 2004; Neubauer, 1999)	<p>Definition: bodily exertion at regular intervals for sustained periods of time</p> <p>Rationale: Regular exercise, such as brisk walking, may help to improve sleep quality and shorten sleep latency. Other types of exercise have been linked to improved overall sleep quality, decreased sleep latency, and decreased daytime sleepiness. Exercise also has been shown to be effective as an intervention for circadian phase resetting.</p>	<ul style="list-style-type: none"> <li>• Exercise that incorporates stretching, concentration, and strength may improve mood as well as provide circadian influences. Recommendations are for 60-minute sessions at least three times per week.</li> <li>• Timing of exercise can affect circadian phase. <ul style="list-style-type: none"> <li>– Significant phase delays were reported for nocturnal exercise.</li> <li>– Significant phase advances were reported for evening exercise.</li> </ul> </li> <li>• Duration and intensity recommendations vary—typically, study exercise activities last for 60 minutes and are of the intensity of 60%–75% <math>VO_{2max}</math>.</li> </ul>
Yoga (Cohen et al., 2004; National Center for Complementary and Alternative Medicine, 2004; Seaward, 2002)	<p>Definition: Yoga is a comprehensive discipline that includes physical exercises, postures, breathing techniques, and meditation for the purpose of improving health and well-being.</p> <p>Rationale: Yoga is used to decrease cognitive and physiologic arousal, thus improving sleep onset latency times.</p>	<ul style="list-style-type: none"> <li>• Daily practice is encouraged. Can be done at the beginning or end of each day to release stress and frustration.</li> </ul>
Acupuncture (National Center for Complementary and Alternative Medicine, 2004; Seaward, 2002; Sok et al., 2003; Spence et al., 2004)	<p>Definition: Acupuncture is a family of procedures involving stimulation of anatomical points on the body for the purpose of regulating energy (Qi) flow.</p> <p>Rationale: Insomnia is a result of stagnated Qi. Acupuncture regulates Qi, resulting in improved duration, latency, and efficiency measures.</p>	<p>Recommended method, duration, frequency, and total number of treatments vary widely. All treatments need to be administered by an individual trained in traditional Chinese medicine techniques.</p>

All of the interventions employed combinations of cognitive or behavioral techniques. The most commonly used intervention technique was training in relaxation strategies (Allison et al., 2004; Berger et al., 2002, 2003; Cannici, Malcolm, & Peek, 1983; Carlson, Specia, Patel, & Goodey, 2003, 2004; Davidson, Waisberg, Brundage, & MacLean, 2001; Simeit, Deck, & Conta-Marx, 2004). All of the studies reported improvement in or stability with some sleep parameters. Four studies tested the effect of mindfulness meditation techniques (Carlson et al., 2003, 2004; Cohen, Warneke, Fouladi, Rodriguez, & Chaoul-Reich, 2004; Shapiro, Bootzin, Figueredo, Lopez, & Schwartz, 2003) and reported similar improvements in some sleep parameters. Exercise was tested in three studies (Coleman et al., 2003; Mock et al., 2001; Young-McCaughan et al., 2003). Most of the interventions were conducted in three to

eight sessions; exercise interventions (Mock et al.; Young-McCaughan et al.) and mindfulness stress reduction (Carlson et al., 2003, 2004) included practice two to seven times per week. The individualized sleep-promotion plan (Berger et al., 2002, 2003) was reinforced and revised every 21–30 days.

Notwithstanding the positive findings of most of the cited studies, the quality of the evidence in support of cognitive and behavioral interventions for sleep was generally consistent but lacking in randomized multicenter trials with at least 100 participants (Hadorn, Baker, Hodges, & Hicks, 1996). Only six of the 20 studies used randomized clinical trial designs (Cannici et al., 1983; Coleman et al., 2003; Dalton, Keefe, Carlson, & Youngblood, 2004; de Moor et al., 2002; Kim, Roscoe, & Morrow, 2002; Shapiro et al., 2003); four used quasiexperimental designs (Cohen et al., 2004; Mock et al., 2001; Simeit et al.,

**Table 3. Meta-Analyses of Nonpharmacologic Interventions for Sleep Disturbances in Noncancer Populations**

Author	Study Information	Conclusions and Implications
Montgomery & Dennis, 2002a	<p>Search strategy: MEDLINE (1966–January 2001); EMBASE (1980–January 2001); <i>Cumulative Index to Nursing and Allied Health Literature</i> (CINAHL) (1982–January 2001); PsycINFO (1970–2001); the Cochrane Library Issue 1, (2001); National Research Register (NRR [2001]). Bibliographies of existing reviews in the area, as well as of all trial reports obtained, were searched. Experts in the field were consulted.</p> <p>Sample: no studies of bright light therapy for older adults (age &gt; 60) with primary insomnia</p>	No trials met the inclusion criteria for this review by the Cochrane Collaboration.
Montgomery & Dennis, 2002b	<p>Search strategy: MEDLINE (1966–January 2001); EMBASE (1980–January 2002); CINAHL (1982–January 2002); PsycINFO (1987–2002); the Cochrane Library Issue 1, (2002); NRR (2002). Bibliographies of existing reviews in the area, as well as of all trial reports obtained, were searched. Experts in the field were consulted.</p> <p>Sample: one study of physical exercise for older adults (&gt; 60 years) with primary insomnia</p> <p>Outcomes: sleep onset latency, total sleep time, and sleep efficiency</p> <p>Treatment evaluated: 16 weeks of moderate-intensity, community-based exercise (4 x 40 minutes of endurance training per week)</p>	<p>Only one study met the criteria for review by the Cochrane Collaboration.</p> <p>Insufficient evidence exists to determine the effectiveness of physical exercise for the treatment of sleep problems in healthy older adults.</p>
Montgomery & Dennis, 2003	<p>Search strategy: MEDLINE (1966–October 2001); EMBASE (1980–January 2002); CINAHL (1982–January 2002); PsycINFO (1970–2002); the Cochrane Library Issue 1, (2002); NRR (2002). Bibliographies of existing reviews in the area, as well as of all trial reports obtained, were searched. Experts in the field were consulted.</p> <p>Sample: six trials of cognitive and behavioral interventions for older adults (&gt; 60 years) with primary insomnia</p> <p>Outcomes: sleep onset latency, total sleep time, sleep efficiency, wake after sleep onset, total wake time, early morning awakening, and sleep quality</p> <p>Treatments evaluated: sleep hygiene, stimulus control, muscle relaxation, sleep restriction, and cognitive therapy</p>	<p>Cognitive and behavioral treatments for sleep problems are mildly effective for some aspects of sleep in the short term; the treatments are not always durable.</p> <p>The interventions had the following effects.</p> <ul style="list-style-type: none"> <li>• Sleep onset latency (three studies) for the treated group improved slightly after treatment, three minutes less than the control group; after one year, it was 11.5 minutes better than the control group.</li> <li>• Wake after sleep onset (four studies) improved modestly immediately after treatment, 21.9 minutes less for the treated group; at three months post-treatment (two studies), wake time was 33 minutes less for the treated group; after one year (one study) wake time was only 13 minutes less for the treated group.</li> <li>• Total wake time (one study) lessened for the treated group immediately after treatment, one hour less by sleep diary, and 38 minutes less by polysomnography (PSG).</li> <li>• Sleep duration (four studies) improved mildly, 14.6 minutes more sleep by sleep diary; however, by PSG, it decreased by 19 minutes; at three months (one study), treated people had 14.8 minutes less sleep; after one year (one study), treated people had 32 minutes more sleep; however, by PSG, the control group was sleeping almost seven minutes more per night.</li> <li>• Early morning awakening (one study) improved modestly after treatment, with the treated group waking 17 minutes later than the control group by sleep diary; by PSG, waking was 14.9 minutes later.</li> <li>• Sleep efficiency (three studies) improved modestly post-treatment with 7.5% improvement; at three months (one study), the effect was stronger, 9.6%; after one year (one study), the effect was weaker, 4.4%.</li> <li>• Sleep quality (one study) measured by the Pittsburgh Sleep Quality Index was modestly improved, score = 7.8 for the treated group compared with 10.6 for the control group; at three months, score for the treated group was 6.2 compared with 10.2 for the control group; however, all scores were higher than the 5.0 cut-off indicating sleep disturbance.</li> </ul>

*(Continued on next page)*

**Table 3. Meta-Analyses of Nonpharmacologic Interventions for Sleep Disturbances in Noncancer Populations (Continued)**

Author	Study Information	Conclusions and Implications
Morin et al., 1994	<p>Search strategy: computer search of studies that met the following criteria</p> <ul style="list-style-type: none"> <li>• The primary target problem was sleep onset, maintenance, or mixed insomnia.</li> <li>• The treatment was nonpharmacologic.</li> <li>• The study used a group design.</li> <li>• The outcome measures consisted of one or more of the following: sleep onset latency, time awake after sleep onset, number of awakenings, and total sleep time.</li> </ul> <p>Case reports or studies based on a single-subject design and studies evaluating pharmacologic treatments were excluded.</p> <p>Sample: 59 nonpharmacologic treatment outcomes studies of people with sleep onset, maintenance, or mixed insomnia</p> <p>Outcomes: sleep onset latency, total sleep time, number of awakenings, and time awake after sleep onset</p> <p>Improvement rates evaluated from pre- to post-treatment and from post-treatment to follow-up</p> <p>Treatments evaluated: nonpharmacologic treatment, including stimulus control, sleep restriction, relaxation, paradoxical intention, sleep hygiene education, and other therapies</p>	<p>Nonpharmacologic interventions provide reliable and durable clinical benefits. The average treated person had</p> <ul style="list-style-type: none"> <li>• Shorter sleep onset latency than 81% of untreated people.</li> <li>• Less time awake after sleep onset latency than 74% of untreated people.</li> <li>• Fewer number of awakenings than 70% of untreated people.</li> <li>• Longer total sleep time than 66% of untreated people.</li> </ul> <p>Clinical gains at the end of treatment were maintained at follow-ups averaging six months in duration.</p> <p>Comparison of treatments determined that stimulus control was the most effective single therapy for sleep onset or maintenance difficulties.</p>
Murtagh & Greenwood, 1995	<p>Search strategy: Key word “insomnia”; MEDLINE and PsycLIT (1973–1993) and the reference lists of relevant review articles and books. Unpublished studies were identified from listings of dissertations and theses over the same period.</p> <p>Sample: 66 treatment outcome studies of healthy people with insomnia</p> <p>Outcomes: sleep onset latency, total sleep time, nightly awakenings, and sleep quality ratings</p> <p>Treatments evaluated: relaxation-based therapies such as progressive muscle relaxation, meditation, desensitization, imagery relaxation, hypnosis, and autogenic training</p> <p>Nonrelaxation therapies, such as stimulus control, paradoxical intention, sleep restriction, and combination treatments</p>	<p>Psychological treatments of insomnia enhanced sleep patterns and subjective sleep experience.</p> <p>Average treatment effects for the hypothetical average case of insomnia may be expected to</p> <ul style="list-style-type: none"> <li>• Reduce sleep onset latency from 61 to 37 minutes.</li> <li>• Increase total sleep time from 5.65 to 6.18 hours.</li> <li>• Decrease number of nightly awakenings from 1.63 to 0.44.</li> </ul> <p>The majority of active treatment effect sizes was greater than corresponding placebo effect sizes but did not differ greatly in efficacy.</p> <p>Greater gains were found for participants who were clinically referred and who were not regular users of hypnotics.</p>

2004; Smith, Kemp, Hemphill, & Vojir, 2002). Only three studies had sample sizes greater than 100 participants (Dalton et al., 2004; Kim et al.; Simeit et al.), a criterion for the strongest level of evidence (Hadorn et al.; Ropka & Spencer-Cisek, 2001). Because combinations of intervention strategies were used, specifying the essential elements that accounted for the success of a given intervention is difficult. Future studies need to disentangle such issues by statistical methods before conclusions can be drawn about the most effective interventions to improve sleep in patients with cancer. The studies also were limited by a lack of clear definition of terms regarding sleep or use of measurements that may contain only a single-item rating of sleep.

### Pharmacologic

Numerous pharmacologic approaches can be used to enhance sleep. Few of the approaches have been studied in populations with cancer, although the drugs are used commonly clinically in people with cancer. Table 5 summarizes specific medications by class or category, hypnotic dose, and onset and duration of action. Specific features of drugs also are noted.

Hypnotics are the most commonly prescribed medications and include benzodiazepines and nonbenzodiazepine hypnotics, sometimes referred to as Z drugs. The drugs vary in their

half-lives. Those with longer half-lives can cause daytime sleepiness and impair waking cognitive and motor function, and those with shorter half-lives may wear off before desired or scheduled wake-up times.

Antidepressants including serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants also may aid sleep, depending on dosages used. They have demonstrated some benefit for treatment of concomitant depression, neuropathic pain, hot flashes, and night sweats. SSRIs have varying effects on anxiety and daytime activity. The drugs have a narrow therapeutic index, and signs of toxicity should be monitored closely.

To evaluate the efficacy of current pharmacologic approaches, a search was conducted to identify meta-analyses. The search strategy included MEDLINE, CINAHL, PsycINFO, and the Cochrane Library covering 1994–2004, using the key terms insomnia, sleep disturbance, hypnotics, pharmacotherapy, and meta-analysis. Stimulants were not included in the search; however, they are being tested to improve daytime sleepiness and fatigue in people with cancer. The efficacy of hypnotic drugs has been evaluated in five meta-analyses published from 1997–2004. None of them was specific to the use of the drugs in patients with cancer or their caregivers. Specific details are summarized in Table 6. The reports were

**Table 4. Nonpharmacologic Intervention Studies in Patients With Cancer**

Author and Year	Intervention Tested or Compared	Design	Sample, Setting, and Treatment Phase	Outcomes	Evidence Rating
Allison et al., 2004	NuCare Coping Strategies Program: self-study book and audiocassette designed to enhance personal control and teach emotional and instrumental coping responses Training in <ul style="list-style-type: none"> <li>• Problem solving</li> <li>• Relaxation</li> <li>• Coping skills</li> <li>• Goal setting</li> <li>• Communication</li> <li>• Social support</li> <li>• Lifestyle factors</li> </ul>	Pilot feasibility study Prospective nonrandomized design; no control group; one group	66 patients with head and neck cancer enrolled; 59 completed; 50 gave outcome data. Groups: choice of small group (n = 3), one on one (n = 33), or home format without therapist (n = 23) Setting: Canada Treatment phase: not described Compliance: 59 of 66 completed the study.	Statistically significant improvement in <ul style="list-style-type: none"> <li>• Sleep disturbance</li> <li>• Global quality of life</li> <li>• Fatigue</li> <li>• Depression</li> </ul>	Priority Symptom Management (PRISM) level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) <ul style="list-style-type: none"> <li>• No placebo control group</li> <li>• Small sample size</li> <li>• Feasibility study not designed to test efficacy</li> <li>• No objective sleep measure</li> </ul>
Berger et al., 2002	Individualized sleep promotion plan <ul style="list-style-type: none"> <li>• Sleep hygiene</li> <li>• Relaxation therapy</li> <li>• Stimulus control</li> <li>• Sleep restriction</li> </ul> One two-hour session; four 15-minute problem-solving sessions; three 30-minute revision sessions	Pilot feasibility study One group; pre- and post-test design	25 patients with breast cancer Setting: midwestern United States, oncology clinics and patient homes Treatment phase: active treatment Compliance: 22 of 25 completed the study; moderate to high adherence (46%–80%) with components of sleep plan	Sleep latency, efficiency, total rest, and rating of awakening were consistently within the desired range. Time awake after sleep onset and nighttime awakenings exceeded desired levels. No statistically significant changes over time in any variables Conclusion: intervention feasible, adherence improved over time, most sleep/wake patterns consistent with normal values	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) <ul style="list-style-type: none"> <li>• No placebo control group</li> <li>• Small sample size</li> <li>• Feasibility study not designed to test efficacy</li> </ul>
Berger et al., 2003	Individualized sleep-promotion plan <ul style="list-style-type: none"> <li>• Sleep hygiene</li> <li>• Relaxation therapy</li> <li>• Stimulus control</li> <li>• Sleep restriction</li> </ul> One two-hour session; four 15-minute problem-solving sessions; three 30-minute revision sessions	One group; pre- and post-test design	21 patients with breast cancer Setting: midwestern United States, patient homes Treatment phase: long-term follow-up Adherence to components of intervention: <ul style="list-style-type: none"> <li>• 77%–88% for sleep hygiene counseling</li> <li>• 83%–88% for relaxation therapy</li> <li>• 36%–56% for stimulus control</li> <li>• 83%–88% for sleep restriction</li> </ul>	Self-reported and actigraph readings of sleep latency demonstrated that it was stable and within desired range. Actigraph readings demonstrated that 74%–88% were awake for more than the desired 30 minutes after sleep onset. Awakenings were more frequent than six per night. Number of nighttime awakenings and length of daytime naps decreased over time.	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) <ul style="list-style-type: none"> <li>• No placebo control group</li> <li>• Small sample size</li> <li>• Feasibility study not designed to test efficacy</li> </ul> Intervention may be beneficial in reducing nighttime awakenings and daytime naps.
Cannici et al., 1983	Muscle relaxation training Three sessions	Randomized clinical trial	30 patients with cancer Groups: relaxation, n = 15; usual care, n = 15	Sleep onset latency reduced in relaxation group compared with usual care group.	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6)

*(Continued on next page)*

**Table 4. Nonpharmacologic Intervention Studies in Patients With Cancer (Continued)**

Author and Year	Intervention Tested or Compared	Design	Sample, Setting, and Treatment Phase	Outcomes	Evidence Rating
			Setting: southeastern United States, hospital or patient's home Treatment phase: active treatment or long-term follow-up Compliance: 26 of 30 completed the study.	After three months, differences in sleep latency were maintained. No differences in hours of sleep, number of night awakenings, sleep satisfaction, or feeling rested	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• No objective sleep measure</li> </ul> Intervention may be effective in reducing sleep onset latency.
Carlson et al., 2003	Mindfulness-based stress-reduction meditation program <ul style="list-style-type: none"> <li>• Relaxation</li> <li>• Meditation</li> <li>• Gentle yoga</li> </ul> Nine sessions, daily practice	One group; pre- and post-test design	Pretest: n = 59 patients with breast and prostate cancer Setting: Canada, outpatient department Treatment phase: long-term follow-up Compliance: <ul style="list-style-type: none"> <li>• 42 of 59 completed the study.</li> <li>• 52 of 59 completed five or more intervention sessions.</li> <li>• Median sessions attended = eight</li> <li>• Average practice time per day = 24 minutes (meditation) and 13 minutes (yoga)</li> </ul>	Data were presented for 42 participants who completed the study. Significant improvements in <ul style="list-style-type: none"> <li>• Overall quality of life</li> <li>• Symptom of appetite loss</li> <li>• Stress symptoms</li> </ul> No significant change in sleep quality Immune cells: <ul style="list-style-type: none"> <li>• No change occurred in overall number of lymphocytes.</li> <li>• T-cell production of interleukin-4 increased.</li> <li>• Interferon-gamma decreased.</li> <li>• Nonkiller cell production of interleukin-10 decreased.</li> </ul> Shift in immune profile was consistent with shift in depressive symptoms to a more normal profile.	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) <ul style="list-style-type: none"> <li>• No placebo control group</li> <li>• Small sample size</li> <li>• Findings were not correlated with program attendance or home practice.</li> <li>• Compliance problems</li> <li>• No objective sleep measures</li> </ul>
Carlson et al., 2004	Mindfulness-based stress-reduction meditation program <ul style="list-style-type: none"> <li>• Relaxation</li> <li>• Meditation</li> <li>• Gentle yoga</li> </ul> Nine sessions, daily practice	One group; pre- and post-test design	59 patients with breast cancer and 10 patients with prostate cancer Setting: Canada, outpatient department Treatment phase: long-term follow-up Compliance: <ul style="list-style-type: none"> <li>• 42 of 59 completed the study.</li> <li>• 52 of 59 completed the intervention.</li> <li>• Median sessions attended = eight</li> <li>• Average practice time per day = 24 minutes (meditation) and 13 minutes (yoga)</li> </ul>	Postintervention data available for 31 of 42 participants Significant improvements from pre- and post-test intervention in <ul style="list-style-type: none"> <li>• Overall quality of life</li> <li>• Symptoms of stress</li> <li>• Sleep quality</li> </ul> Improvements not significantly correlated with the degree of program attendance or minutes of home practice. Average daily cortisol level did not change from pre- to post-test intervention.	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) <ul style="list-style-type: none"> <li>• No placebo control group</li> <li>• Small sample size</li> <li>• Findings were not correlated with program attendance or home practice.</li> <li>• Compliance problems</li> <li>• No objective sleep measure</li> </ul> Intervention may be effective in improving sleep quality.
Cohen et al., 2004	Tibetan yoga (TY) versus wait list control group	Quasiexperimental two-group design with sequential assignment	39 patients with lymphoma Groups: TY, n = 20;	TY group reported lower sleep disturbance	PRISM level of evidence (Ropka & <i>(Continued on next page)</i>

**Table 4. Nonpharmacologic Intervention Studies in Patients With Cancer (Continued)**

Author and Year	Intervention Tested or Compared	Design	Sample, Setting, and Treatment Phase	Outcomes	Evidence Rating
	<p>TY</p> <ul style="list-style-type: none"> <li>Controlled breathing</li> <li>Visualization</li> <li>Mindfulness techniques</li> <li>Low-impact postures</li> </ul> <p>Seven sessions</p>		<p>control, n = 19 (wait list)</p> <p>Setting: southern United States, outpatient department</p> <p>Treatment phase: active treatment or long-term follow-up (15 of 39)</p> <p>Compliance:</p> <ul style="list-style-type: none"> <li>38 of 39 completed the study.</li> <li>32% attended seven sessions.</li> <li>26% attended five or six sessions.</li> <li>32% attended two or three sessions.</li> <li>10% attended one session.</li> </ul>	<p>scores than control group.</p> <ul style="list-style-type: none"> <li>Better subjective sleep quality</li> <li>Faster sleep latency</li> <li>Longer sleep duration</li> <li>Less use of sleep medicine</li> </ul> <p>No differences in</p> <ul style="list-style-type: none"> <li>Intrusion</li> <li>Avoidance</li> <li>State anxiety</li> <li>Depression</li> <li>Fatigue</li> </ul>	<p>Spencer-Cisek, 2001) = II (6)</p> <ul style="list-style-type: none"> <li>No randomization</li> <li>Small sample size</li> <li>No objective sleep measure</li> <li>Compliance problems</li> </ul> <p>Intervention may be effective for subjective sleep quality, latency, duration, and less use of sleep drugs.</p>
Coleman et al., 2003	<p>Home-based exercise versus control group</p> <p>Exercise</p> <ul style="list-style-type: none"> <li>Warm-up walking</li> <li>Stretching</li> <li>Endurance walking</li> <li>Strength resistance training</li> <li>Cool down</li> </ul> <p>Frequency and length of program not described</p>	Randomized clinical trial	<p>24 patients with multiple myeloma receiving high-dose chemotherapy and autologous peripheral blood stem cell transplant</p> <p>Groups: exercise = 14; control = 10 (usual care)</p> <p>Setting: midwestern United States, outpatient setting</p> <p>Treatment phase: active treatment</p> <p>Compliance: 58% completed study; no information on compliance with exercise</p>	<p>Compared with control group, exercise group had lower weight loss than control group (p = 0.01).</p> <p>No patient injuries</p> <p>Individualized exercise program during aggressive treatment is feasible.</p>	<p>PRISM level of evidence (Ropka &amp; Spencer-Cisek, 2001) = II (6)</p> <ul style="list-style-type: none"> <li>Small sample size</li> <li>Compliance problems</li> <li>Analysis poorly described</li> </ul>
Dalton et al., 2004	<p>Standard cognitive behavioral therapy (CBT), profile-tailored CBT, or usual care</p> <p>Standard CBT</p> <p>Profile-tailored CBT: matched to modules based on score on Biobehavioral Pain Profile (BPP) (Dalton et al., 1994)</p> <p>Usual care: five one-hour sessions</p>	Three-group, experimental, repeated measures, randomized clinical trial design	<p>131 patients who had elevated scores on the BPP and who were receiving treatment for cancer pain at three cancer treatment centers and one hospital in three southeastern states</p> <p>Groups: Standard, CBT = 47; profile-tailored, CBT = 50; usual care = 34</p> <p>Setting: southeastern United States, inpatient and outpatient settings</p> <p>Treatment phase: Active treatment for cancer pain</p> <p>Retention:</p>	<p>Compared with standard CBT, profile-tailored CBT led to substantial improvement from baseline to postintervention in</p> <ul style="list-style-type: none"> <li>Worst pain</li> <li>Least pain</li> <li>Less interference of pain with sleep</li> <li>Less confusion.</li> </ul> <p>From baseline to one month postintervention, profile-tailored patients saw greater improvement in</p> <ul style="list-style-type: none"> <li>Less interference of pain with activities</li> <li>Walking</li> <li>Relationships</li> <li>Sleep.</li> </ul>	<p>PRISM level of evidence (Ropka &amp; Spencer-Cisek, 2001) = II (6)</p> <p>Significant attrition</p> <p>Intervention may be beneficial for less interference of pain with sleep.</p>

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**Table 4. Nonpharmacologic Intervention Studies in Patients With Cancer (Continued)**

Author and Year	Intervention Tested or Compared	Design	Sample, Setting, and Treatment Phase	Outcomes	Evidence Rating
			<ul style="list-style-type: none"> <li>• 121 of 131 completed preintervention.</li> <li>• 53 of 131 completed immediate follow-up.</li> <li>• 43 of 131 completed one-month follow-up.</li> <li>• 28 of 131 completed six-month follow-up.</li> </ul>		
Davidson et al., 2001	Sleep therapy program <ul style="list-style-type: none"> <li>• Stimulus control therapy</li> <li>• Relaxation training</li> <li>• Strategies to consolidate sleep</li> <li>• Strategies to reduce arousal</li> </ul> Six sessions	One-group; pre- and post-test design	14 patients; eight with breast cancer, one with cervical cancer, two with lymphoma, and one with melanoma Setting: central Canada, outpatient clinics Treatment phase: long-term follow-up Compliance: 12 of 14 completed the intervention.	Significant improvement over baseline in <ul style="list-style-type: none"> <li>• Number of awakenings</li> <li>• Time awake after sleep onset</li> <li>• Total sleep time</li> <li>• Sleep efficiency</li> <li>• Rating of feeling rested</li> <li>• Rating of sleep quality</li> </ul>	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) <ul style="list-style-type: none"> <li>• No placebo control group</li> <li>• Small sample size</li> <li>• No objective sleep measure</li> </ul> Intervention may be effective for improving number of awakenings, time awake after sleep onset, total sleep time, sleep efficiency, and ratings of feeling rested and sleep quality.
de Moor et al., 2002	Expressive writing (EW) versus neutral writing (NW) Four sessions	Randomized clinical trial	42 patients with metastatic renal cell carcinoma receiving vaccine therapy Groups: EW, n = 21; NW, n = 21 Setting: southwestern United States, outpatient clinic Treatment phase: active treatment Compliance: <ul style="list-style-type: none"> <li>• 35 of 42 completed four writing assignments.</li> <li>• 42 of 42 completed at least one writing assignment.</li> </ul>	Compared with the NW group, the EW group reported <ul style="list-style-type: none"> <li>• Less sleep disturbance</li> <li>• Better sleep quality and duration</li> <li>• Less daytime dysfunction</li> <li>• Increased vigor.</li> </ul> No differences between groups in <ul style="list-style-type: none"> <li>• Distress</li> <li>• Perceived stress</li> <li>• Mood disturbance</li> </ul>	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) Small sample size Intervention may be effective in improving sleep quality and duration and feelings of vigor; it may reduce sleep disturbance and daytime dysfunction.
Fobair et al., 2002	Supportive-expressive group therapy discussion <ul style="list-style-type: none"> <li>• Problem of new diagnosis</li> <li>• Coping with illness, treatment, and mood changes</li> <li>• Self-efficacy</li> <li>• Improving relationships</li> <li>• Managing pain, sleep, body image, and sexuality</li> </ul>	One group; pre- and post-test design	20 lesbians diagnosed with early-stage breast cancer within the previous 12 months Setting: western United States, outpatient clinic Treatment phase: active treatment or long-term follow-up Compliance: <ul style="list-style-type: none"> <li>• 20 of 20 completed baseline, three- and six-month measures, and participated in</li> </ul>	Improved sleep, less pain Decreased emotional distress, intrusiveness, and avoidance Improved coping Reduced social support Trend toward more family cohesiveness and expressiveness No change in body image, sexuality, or attitude toward health-care providers	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) <ul style="list-style-type: none"> <li>• No placebo control group</li> <li>• Small sample size</li> <li>• No objective sleep measure</li> </ul> Intervention may be effective in improving sleep.

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**Table 4. Nonpharmacologic Intervention Studies in Patients With Cancer (Continued)**

Author and Year	Intervention Tested or Compared	Design	Sample, Setting, and Treatment Phase	Outcomes	Evidence Rating
Kim et al., 2002	Informational intervention on severity of side effects of radiation therapy for prostate cancer Two audiocassettes, 8 and 12 minutes	Randomized clinical trial	group intervention • 17 of 20 completed 12-month measure.  184 patients with prostate cancer receiving radiotherapy Groups: information, n = 77; control, n = 75 (general information) Setting: northeastern United States, outpatient setting Treatment phase: active treatment Compliance: 152 of 184 were fully evaluable.	Information group had • Fewer sleep problems • Less fatigue. No difference in negative attitude	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) • No baseline measurements • No objective sleep measure Intervention may be effective in reducing sleep problems.
Mock et al., 1997	Moderate, self-paced, progressive, home-based exercise program Walking exercise versus usual care Individualized walking program based on age, level of fitness, and history of exercise • 20–30 minute brisk walk • Five-minute slow walk cool down • Four to five sessions a week for six weeks	Two-group; pre- and post-test experimental design	46 patients with breast cancer receiving outpatient radiation therapy Groups: exercise, n = 22; usual care, n = 24 Setting: eastern United States Treatment phase: active Compliance: 152 of 184 were fully evaluable; issues with adherence to five-day-per-week regimen	Exercise group reported positive findings as compared to the control group. • Improved physical functioning • Reduced symptom intensity (fatigue, anxiety, and difficulty sleeping)	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) • Small sample • Possible diffusion between groups • Lack of control over intervention in home setting Issues with adherence to five-day-per-week regimen
Quesnel et al., 2003	Multimodal cognitive-behavioral therapy for insomnia (eight sessions) • Stimulus control • Sleep restriction • Coping strategies for fatigue • Reframing maladaptive cognitions • Sleep hygiene	Prospective, nonrandomized, repeated measure design (21 data points; as long as six months follow-up); single case research comparing each individual over this time	10 patients with chronic insomnia and nonmetastatic breast cancer (stages I–III) who had completed chemotherapy and radiation therapy 2–175 months prior; all had a diagnosis of chronic insomnia per <i>Diagnostic and Statistical Manual IV</i> . Setting: Canada Treatment phase: long-term follow-up Compliance: 8 of 10 completed the study.	Daily variability in sleep decreased after initiation of the intervention. Significant improvement in sleep efficiency and total wake time Significant improvements in mood, general and physical fatigue, and global and cognitive dimensions of quality of life	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) • Small sample • Inconsistent completion of sleep diaries
Shapiro et al., 2003	Mindfulness-based stress reduction (MBSR) • Sitting meditation • Body scan • Hatha yoga (stretches and postures)	Randomized clinical trial	63 women with a history of breast cancer Groups: MBSR, n = 31; free-choice control, n = 32 Setting: western United States	Both MBSR and free-choice groups had significant improvement in sleep quality. Neither group had improvement in sleep efficiency.	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) • Small sample • Inconsistent compliance with MBSR

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**Table 4. Nonpharmacologic Intervention Studies in Patients With Cancer (Continued)**

Author and Year	Intervention Tested or Compared	Design	Sample, Setting, and Treatment Phase	Outcomes	Evidence Rating
	Six sessions and a one-day silent retreat		Treatment phase: long-term follow-up	MBSR group members who practiced more improved more on sleep measure associated with distress.	techniques • Wide range of relaxation techniques accepted
Simeit et al., 2004	Progressive muscle relaxation (PMR) versus autogenic training (AT) Information: myths, relaxation technique (PMR or AT), sleep hygiene, stimulus control; three one-hour sessions Practice session: relapse prevention and motivation	Quasiexperimental design; sequential recruitment of groups; patient choice for PMR or AT	239 patients with breast, kidney, or prostate cancer staying for three to four weeks in oncology rehabilitation center Groups: PMR, n = 80; AT, n = 71; control, n = 78 Setting: Germany Treatment phase: long-term follow-up Compliance: not described	Compared with the control group, both intervention groups had improvement in • Sleep latency • Duration • Efficiency • Quality. Quality-of-life scales showed improvement over time.	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) • Compliance with MBSR techniques not described • Covariates like hormone therapy not described or controlled • Sleep tool translated; no information about validity and reliability
Smith, Kemp, et al., 2002	Therapeutic massage: 15–30 minutes of light Swedish massage, three sessions per week	Quasiexperimental design; sequential recruitment of groups	41 patients admitted to inpatient oncology unit for chemotherapy or radiation therapy Groups: massage, n = 20; control, n = 21 (nurse interaction) Setting: midwestern United States, veterans' hospital Treatment phase: active Compliance: 18 patients were withdrawn or lost from the study because of their discharge before the end of the one-week period or because of death (8 from massage group and 10 from control group).	Mean scores for pain, sleep quality, symptom distress, and anxiety improved from baseline for the massage group. Only anxiety improved for control group. Sleep deteriorated for the control group. Interactions were found for pain, symptom distress, and sleep quality.	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) • Small sample • Lack of randomization; cohorts treated sequentially • High withdrawal rate
Weze et al., 2004	Healing touch, a non-invasive, noncondition-specific method involving placing of hands on various parts of the body for about 40 minutes, giving particular attention to areas of pain or discomfort Four one-hour sessions within four to six weeks (or withdrawn)	One group; pre- and post-test design	35 patients with variety of cancers, males and females, half had less than one-year duration of cancer, half had one to five years. Setting: Outpatient Centre for Complementary Care in Eskdale, Cumbria, United Kingdom Treatment phase: 40% at advanced stage of disease; at various stages of treatment;	Statistically significant improvement pre- to post-test on sleep disturbances per Wilcoxon Signed Rank Test	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) • Small sample • One group design

(Continued on next page)

**Table 4. Nonpharmacologic Intervention Studies in Patients With Cancer (Continued)**

Author and Year	Intervention Tested or Compared	Design	Sample, Setting, and Treatment Phase	Outcomes	Evidence Rating
Wright et al., 2002	Autogenic training <ul style="list-style-type: none"> <li>• Deep relaxation</li> <li>• Self-hypnosis</li> </ul> 10 weekly sessions; told to practice three times per week	One group; pre- and post-test design	18 patients with cancer who attended an outpatient cancer center Setting: Ireland Treatment phase: either in treatment or long-term follow-up Compliance: All 18 fully participated.	94% had received treatment Compliance: All completed the program. Subjective report of improved sleep and sense of well-being Reduction in anxiety Increase in “fighting spirit”	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = III (8) <ul style="list-style-type: none"> <li>• Qualitative comments only regarding improved sleep</li> <li>• Training not well defined</li> </ul>
Young-McCaughan et al., 2003	Aerobic exercise program patterned after phase II cardiac rehabilitation program, providing exercise and education Two days per week for 12 weeks	One group; pre- and post-test design	62 patients with various cancer diagnoses within previous two years, one-half men, one-half women Setting: southwest United States, military medical centers Treatment phase: active and long-term follow-up Compliance: 46 (74%) participants completed the program.	Exercise tolerance, activity and sleep patterns, and quality of life improved over time for those who completed the program.	PRISM level of evidence (Ropka & Spencer-Cisek, 2001) = II (6) <ul style="list-style-type: none"> <li>• Feasibility study</li> <li>• No control group</li> <li>• Small sample</li> <li>• Missing actigraph data</li> </ul>

limited by the diversity of outcomes and variable methods of summarizing results that made it difficult to pool findings. Most studies were of short duration; thus, limited knowledge exists about long-term efficacy and side effects of the drugs.

Consistent evidence exists that benzodiazepines and nonbenzodiazepine hypnotics reduce self-reported sleep onset latency time and number of awakenings and improve self-reported sleep duration, total sleep time, and sleep quality. No clear evidence has been found that one type of hypnotic is superior to another. Benzodiazepines were associated with increased daytime sleepiness, dizziness, or lightheadedness but not discontinuation of drug. One meta-analysis examined behavioral and pharmacologic approaches and concluded that the duration of effects from behavioral therapy was significantly longer than those from pharmacotherapy (Smith, Perlis, et al., 2002). Because of a lack of evidence specific to cancer populations, clinicians should evaluate systematically how each patient responds to a prescribed agent with regard to insomnia and side effects of the medication (Clark et al., 2004).

**Herbal and complementary supplements used to promote sleep:** To examine the evidence for complementary and alternative pharmacologic substances to improve sleep in people with cancer, a search was conducted for studies and reviews of research published from 1990–2005. CINAHL and PsycINFO were searched, using the key terms cancer and sleep and complementary therapy, cancer and insomnia and complementary therapy, and insomnia and complementary therapy. The identified substances primarily included the herbal supplements va-

lerian, kava, and St. John’s wort, plus the hormone supplement melatonin. Milder sedatives identified as needing clinical study included chamomile, lavender, lemon balm, and passionflower. A summary of the findings is presented in Table 7.

Although patients with cancer were included as participants in a few studies, research testing pharmacologic complementary and alternative substances to treat sleep disturbances that focused specifically on people with cancer is almost nonexistent. In addition, most of the studies have had major design flaws, small sample sizes, uncontrolled confounding variables, and other threats to internal and external validity (Block, Gyllenhaal, & Mead, 2004; Gyllenhaal, Merritt, Peterson, Block, & Gochenour, 2000; Stevinson & Ernst, 2000).

A meta-analysis of the effects of melatonin on sleep revealed only minimal clinical benefits, with sleep onset latency reduced by 3.9 minutes, sleep duration increased by 13.7 minutes, and sleep efficiency increased by 3% (Brzezinski et al., 2005). Studies of effects of valerian on sleep have used weak designs and produced inconsistent results, leading the U.S. Pharmacopoeia to conclude that insufficient evidence exists in the scientific literature to recommend valerian for insomnia (Stevinson & Ernst, 2000). Kava studies have revealed mixed results. Adverse reactions and safety concerns, including a number of cases of hepatic failure that required liver transplantation, prompted a U.S. Food and Drug Administration alert in 2002. In particular, patients with cancer were instructed not to take kava (Block et al., 2004; Memorial Sloan-Kettering Cancer Center, 2005), and the

**Table 5. Medications Commonly Used to Promote Sleep**

Drug	Hypnotic Dose	Onset (Duration of Action)	Notes
<b>Benzodiazepines</b>			
Diazepam	5–10 mg (capsule, tablet)	30–60 minutes (6–8 hours)	May need to decrease opioid levels
Temazepam	15–30 mg (capsule)	60 minutes, minimum (6–8 hours)	Biphasic half-life can cause residual daytime sleepiness and dysfunction.
Triazolam	0.125–0.5 mg (tablet)	30 minutes (peaks 1–1.5 hours)	Patient may have anterograde amnesia and rebound insomnia.
Clonazepam	0.5–2.0 mg (tablet)	30–60 minutes (8–12 hours)	May be used during concomitant treatment of seizure disorder
<b>Nonbenzodiazepine hypnotics (Z drugs)</b>			
Zolpidem tartrate	5–20 mg (tablet)	30 minutes (4–6 hours)	–
Zaleplon	10–20 mg (capsule)	30 minutes (4–6 hours)	Do not give with or immediately after a meal.
Eszopiclone	1–3 mg (tablet)	30 minutes (5–7 hours)	–
<b>Tricyclic antidepressants (TCAs)</b>			
Doxepin	10–150 mg (capsule, liquid)	30 minutes	One of the most sedating TCAs
Amitriptyline	10–300 mg (tablet, injection)	30 minutes	Good for concomitant depression or neuropathic pain
Nortriptyline	10–50 mg (capsule)	30 minutes	Narrow therapeutic index (i.e., very small changes in dose can cause toxic results)
<b>Second-generation antidepressants</b>			
Trazodone	25–150 mg (tablet)	30 minutes	Risk of hypotension, risk of priapism, and lower seizure threshold
Nefazadone	50–100 mg (tablet)	30 minutes	Risk of postural hypotension; can induce mania
<b>Antihistamines</b>			
Diphenhydramine	25–100 mg (tablet, capsule, syrup)	10–30 minutes (4–6 hours)	Available over the counter and inexpensive; can increase digoxin and levodopa levels because of delayed gastric emptying
Hydroxyzine	10–100 mg (tablet, capsule, syrup)	15–30 minutes (4–6 hours)	Numerous other effects (antipruritic, muscle relaxant, bronchodilator, and antiemetic); can potentiate central nervous system depressants; may interact with other drugs, caution in hepatic impairment
<b>Chloral derivatives</b>			
Chloral hydrate	0.5–1.0 g (capsule, syrup, suppository)	30–60 minutes (4–8 hours)	Second-line agent in older patients; can increase warfarin levels; narrow therapeutic index; active metabolite: half-life is 8–11 hours.
<b>Neuroleptics</b>			
Chlorpromazine	10–50 mg (tablet)	30–60 minutes	Biphasic half-life is 2 hours and 30 hours; effective for hiccoughs; avoid with severe cardiac disease or agents that may compound hypotensive effect; caution in hepatic impairment

*Note.* Based on information from National Cancer Institute, 2005; Szuba et al., 2003.

supplement is banned in several countries (Consumer Reports, 2004). St. John's wort may have anxiolytic effects with relevance to sleep, but herb-drug interactions with chemotherapeutic agents and other common drugs make the herb a potentially dangerous choice for use in patients with cancer (Block et al.).

To summarize, the evidence to support the use of herbal sedatives is weak and inconsistent, whereas data on adverse effects are not collected and reported regularly. In fact, the lack of pure, standardized ingredients in available compounds is a major limitation to research and clinical use of the supple-

ments. In many cases, patients are at risk for adverse outcomes related to herbal substances or their contaminants.

Despite the limitations, consumers who are eager for help with sleep disturbances increasingly are turning to over-the-counter and Internet sales of complementary and alternative therapies advertised as "natural" and safe. An Institute Of Medicine report released in January 2005 revealed that one-third of American adults have used such therapies and that they are untested and often unsafe (Use of Complementary and Alternative Medicine Committee, 2005).

**Table 6. Meta-Analysis of Pharmacologic Interventions for Sleep/Wake Disturbances in Noncancer Populations**

Author	Study Information	Conclusions and Implications
Dandar et al., 2004	<p>Search strategy: extremely detailed and included six databases (MEDLINE, EMBASE, PsycINFO, SCI, SCI/ISI Proceedings, and the Cochrane Library) covering 1966–2003; multiple languages included</p> <p>Sample: 24 randomized clinical trials representing 3,909 patients, primarily female; 13 studies had fewer than 100 patients.</p> <p>Outcomes: sleep onset latency, total sleep duration, number of awakenings, quality of sleep, adverse events, and rebound insomnia</p> <p>Treatments evaluated: benzodiazepine receptor agonists such as Z drugs (zaleplon, zolpidem, or zopiclone) with benzodiazepines (n = 17) or with each other (n = 7); meta-analysis only possible on a small number of outcomes</p>	<p>No convincing evidence that Z drugs have better efficacy than benzodiazepines</p> <p>In six studies, some evidence suggests that zaleplon results in shorter sleep latency than zolpidem, but zolpidem results in longer sleep duration.</p> <p>None of the existing trials adequately compares these medications.</p>
Holbrook et al., 2000	<p>Search strategy: MEDLINE and Cochrane Controlled Trials Registry from 1966–1998; randomized clinical trials of benzodiazepines for insomnia; English only</p> <p>Sample: 45 randomized clinical trials representing 2,672 patients, 47% were women; few studies were pooled; no studies with &gt; 100 subjects</p> <p>Outcomes: sleep latency, total sleep duration, and adverse events</p> <p>Treatments evaluated: benzodiazepine versus placebo (n = 27) or another agent (n = 13) or a combination (n = 5)</p>	<p>Diversity of outcomes and variable methods of summarizing results made it difficult to pool findings.</p> <p>Pooled differences in sleep latency records from four studies indicate a decrease in 4.2 minutes for benzodiazepine versus placebo.</p> <p>Patient estimates of sleep latency from eight studies estimate the superiority of benzodiazepines at 14.3 minutes.</p> <p>Recorded sleep duration from two studies (n = 39 patients) indicated an average increase of 61.8 minutes.</p> <p>Patient estimates from eight studies indicated an average increased sleep duration of 48.4 minutes.</p> <p>Benzodiazepines were associated with increased daytime sleepiness, dizziness, or lightheadedness but not discontinuation of drug.</p> <p>Data regarding cognitive impairment were insufficient.</p>
Nowell et al., 1997	<p>Search strategy: MEDLINE from 1966–1996; manual review of relevant journals and bibliographies</p> <p>Sample: 22 randomized clinical trials or crossover design studies in adults &lt; 65 years with primary chronic insomnia representing 1,894 patients, 60% women; six studies &gt; 100 patients</p> <p>Outcomes: reported or recorded sleep latency, total sleep time, number of awakenings, and sleep quality</p> <p>Treatments evaluated: zolpidem and benzodiazepines used clinically in the United States versus placebo</p>	<p>Median treatment duration was seven days.</p> <p>Both benzodiazepines and zolpidem result in reliable improvement in sleep onset latency, total sleep time, number of awakenings, and sleep quality.</p> <p>Average effect sizes were moderate: range = 0.56–0.71.</p>
Smith, Perlis, et al., 2002	<p>Search strategy: MEDLINE, PsycINFO, and bibliographies from 1966–2000</p> <p>Sample: 21 studies (prospective, within-subject designs) representing 470 patients; no studies had &gt; 100 patients; 55% female</p> <p>Outcomes: sleep diary measures of sleep latency, number of awakenings, wake time after asleep, and total sleep time</p> <p>Treatments: Benzodiazepines or benzodiazepine receptor agonists (n = 7), or behavioral treatments (including stimulus control or sleep restriction) (n = 13), and one comparative (n = 1) for primary insomnia of one month or longer</p>	<p>Wake time after sleep onset was reduced by 46% with pharmacotherapy and 56% with behavior therapy.</p> <p>Both interventions demonstrated moderate improvement in total sleep time.</p>
Soldatos et al., 1999	<p>Search strategy: MEDLINE from 1966–1997; sleep laboratory studies of benzodiazepines, zolpidem, and zopiclone</p> <p>Sample: 75 studies representing 1,276 people (804 insomniacs and 472 healthy volunteers)</p> <p>Outcomes: tolerance and rebound insomnia</p> <p>Treatments evaluated: brotizolam, midazolam, triazolam, zolpidem, and zopiclone</p>	<p>Tolerance with intermediate and long-term use was developed with triazolam and marginally with midazolam and zolpidem.</p> <p>Rebound insomnia on first withdrawal night was significant with triazolam and mild with zolpidem.</p> <p>Insufficient evidence for brotizolam and zopiclone</p> <p>Duration of behavioral therapy was significantly longer than pharmacotherapy.</p> <p>Sleep latency was reduced by 30% with pharmacologic treatments, compared to 43% with behavioral interventions.</p> <p>Both treatments reduced number of awakenings by one.</p>

Currently, the National Center for Complementary and Alternative Medicine Web site (National Center for Complementary and Alternative Medicine, 2005) lists more than

30 cancer clinical trials ([www.nccam.nih.gov/clinicaltrials/cancer](http://www.nccam.nih.gov/clinicaltrials/cancer)) and three cancer side-effect clinical trials in progress using complementary and alternative medicines with people

**Table 7. Complementary and Alternative Therapy Sedatives**

Herb	Dose (Oral)	Action	Evidence of Efficacy	Advantages and Disadvantages	Precautions in Cancer Care
Valerian: <i>Valeriana officinalis</i> and other variants	400–600 mg ethanol extract and valerianic acid	Inhibits the catabolism of gamma-aminobutyric acid. Binds to benzodiazepine receptors in vitro	Multiple randomized trials, most with important design limitations, demonstrated relief of insomnia with one to two weeks of therapy, although not with single doses. Sleep quality improvement was found in several uncontrolled trials (Block et al., 2004; Stevinson & Ernst, 2000).	No significant residual morning effects No evidence of drug interaction with chemotherapy or alcohol	Recommendation: insufficient evidence to recommend Not well standardized; variation in content; unstable compound May potentiate sedatives, hypnotics, tranquilizers, or anesthesia Not recommended during pregnancy, mutagenic potential
Kava: <i>Piper methysticum</i>	60–120 mg/kg ground kava root extract (WS 1490)	Kava pyrones produce skeletal muscle relaxation and local and general anesthetic effects.	Several randomized, controlled trials showed decreased anxiety and insomnia. Beneficial effects were suggested in several uncontrolled studies (Consumer Reports, 2004; Lehl, 2004).	Adverse effects: kava dermatopathy, thrombocytopenia, leukopenia, and hepatotoxicity Hepatotoxicity with liver failure was reported in numerous cases.	Recommendation: not recommended British, Canadian, and French governments have banned use of kava and its derivatives. Hepatotoxicity is a concern; may have additive effect with alcohol and other central nervous system depressants; may reduce reaction time and affect driving ability.
St. John's Wort: <i>Hypericum perforatum</i>	500–900 mg once a day	Antidepressant effects may improve sleep where insomnia is related to depression. Inhibits norepinephrine, serotonin, and dopamine uptake	Although multiple randomized, controlled trials demonstrated relief of depression, only one uncontrolled study suggested a beneficial effect on insomnia (Assemi, 2001; Block et al., 2004; Cauffman & Forbes, 1999; Wheatley, 1999).	Well-documented interactions with chemotherapeutic agents and other drugs (e.g., busulfan, cyclophosphamide, docetaxel, tamoxifen) (Assemi, 2001) Side effects: gastrointestinal upset, dizziness, sedation, fatigue, confusion, photosensitivity	Recommendation: not recommended Strong potential for interaction with chemotherapy and other drugs Potentiates barbiturate effects Avoid prolonged sun exposure.
Melatonin: <i>N-acetylmethoxytryptamine</i>	0.3–5.0 mg	A neurohormone produced by the pineal gland; also found in grains and beans as a phytochemical; accelerates adaptation of circadian rhythm	Clinical studies suggest that ingestion 30 minutes to four hours before bedtime may decrease sleep latency and improve overall sleep (Brzezinski et al., 2005; Sack et al., 1998). Optimal dose, length of therapy, and effect on endogenous melatonin are unknown (Sack et al., 1998).	Adverse effects: rare, but include drowsiness, depression, disorientation, headache, hypothermia, pruritis, abdominal cramps, and tachycardia May cause vasoconstriction in coronary arteries. Need eight hours set aside for sleep after ingestion	Recommendation: insufficient evidence to recommend May interact with nifedipine, resulting in elevated blood pressure and heart rate; antiproliferative effects in breast cancer and melanoma; contaminants have caused eosinophilia myalgia syndrome.

with cancer ([www.nccam.nih.gov/clinicaltrials/cancersideeffects](http://www.nccam.nih.gov/clinicaltrials/cancersideeffects)). Results from the studies will provide researchers and clinicians with more scientifically rigorous information about the outcomes of the use of complementary and alternative medicines in patients with cancer.

Oncology nurses should be familiar with the research evidence concerning complementary and alternative therapy medicine and supplements and assess their use for people with cancer to better assist patients and caregivers to make informed decisions. A continued need exists for well-designed, large-sample, double-blind, placebo-controlled clinical trials to determine the efficacy and safety of complementary and alternative therapies for sleep/wake disturbances in people with cancer.

## Nursing Implications

### Practice

This state-of-the-science summary of sleep/wake disturbances in people with cancer and their caregivers provides information to guide evidence-based practice, the “conscientious explicit and judicious use of theory-derived research-based information in making decisions about care delivery to people or groups of patients and in consideration of people needs and preferences” (Ingersoll, 2000, p. 152). This article addresses all steps of an evidence-based practice process: Clinical nurses and advanced practice nurses often are the first healthcare team members to hear patient complaints of sleep disturbances. Complaints of sleep disturbance can emanate from a variety of problems (Berger, 1998; Carpenter et al., 2004; Clark et al., 2004; Davidson et al., 2002; Montplaisir & Godbout, 1990; Montplaisir, Lorrain, & Godbout, 1991; Parker, 2004; Roscoe et al., 2002; Vena et al., 2004). To understand the nature of sleep complaints, clinicians should perform assessments in a systematic manner using valid and reliable tools to obtain information needed to target interventions or appropriate referrals such as sleep specialists (Clark et al.; Vena et al.).

Because of the high incidence of sleep/wake disturbances in people with cancer, sleep-screening tools, such as the Clinical Sleep Assessment (Adult) and Clinical Sleep Assessment (Child), should be integrated into oncology clinical practice. The challenge is to determine when and how to perform screening. Not all patients report disturbed sleep; however, a subset of patients report problems at varying times throughout the cancer experience (Berger et al., 2003; Carpenter et al., 2004; Davidson et al., 2002; Engstrom et al., 1999; Koopman et al., 2002; Lee, Landis, et al., 2004). Clinicians can initiate sleep assessments by routinely asking a preliminary question during each clinical contact: “Are you having sleep problems or difficulty staying awake during the day?” If a patient offers an affirmative response, standardized assessments can be performed.

Data generated from screening tools can prove beneficial for specific patients as well as for groups of patients. At the individual patient level, clinicians can use assessment data to make appropriate patient referrals for further evaluation as necessary. In addition, clinical assessment data for a specific patient can be used to design and prescribe a tailored intervention that increases the skills of self-assessment, self-management (e.g., sleep hygiene), or self-monitoring of negative effects of sleep disturbance (e.g., excessive daytime sleepiness). At the group level, clinical screening data can be used as a benchmark, prior to intervening, as part of quality-

improvement projects. Group-level screening data also can be used to provide prevalence and intensity information about sleep disturbances that can be compared within or across patient populations and ultimately enable more appropriate selection and testing of interventions.

The Joint Commission on Accreditation of Healthcare Organizations recommends that hospitals and clinics complete periodic quality-improvement projects. Clinical sleep tools for screening can provide an excellent means to report on assessments of the nine sleep parameters and on interventions designed to reduce sleep disturbances.

### Education

Nursing education has not included sufficient information about sleep and circadian rhythms in undergraduate curriculum content, despite the fact that considerable emphasis has been placed on physical activity, nutrition, and stress management as key components of health and wellness (Lee, Landis, et al., 2004). A nursing task force, including members of the Association of Professional Sleep Societies, recently developed educational competencies for sleep and chronobiology (Lee, Landis, et al.). Educators are encouraged to learn more about the recommendations and to incorporate the competencies into curricula. Undergraduate objectives are organized into learning objectives, clinical competency objectives, and clinical evaluation methods that can be integrated into medical-surgical and psychiatric nursing courses. Graduate-level learning activities are designed to prepare advanced practice nurses to work as members of interdisciplinary teams at accredited sleep disorder centers or in general practice settings. The content also can be used to organize staff development offerings for clinical nurses, advanced practice clinical nurses, nurse educators, and researchers.

Specific education implications related to sleep/wake disturbances include the following.

- Nursing education programs should include an overview of normal sleep, the prevalence of sleep/wake disturbances in cancer populations, a conceptual understanding of the processes that regulate sleep and waking, the measurement of sleep and waking (clinical and research), and currently available evidence-based therapies and interventions.
- Nursing education programs and staff development programs should include the importance of patient education regarding general strategies, such as good sleep hygiene, to optimize sleep and waking.

### Research

Studies in cancer populations are a high research priority because sleep disturbances are common in people with cancer, and poor sleep may be hazardous to health and safety. Issues that currently are being addressed by the larger sleep scientific community include the lack of a standard procedure to determine and document outcomes of successful sleep intervention. Criteria beyond sufficiency of sleep time that also need consideration include definition of intervention endpoint (single or multiple), how best to measure intended outcomes, and whether a patient’s self-report of perceived quality of sleep is a more appropriate endpoint than biologic outcomes.

Sleep scientists recognize that a critical component of randomized clinical trials is the selection of reliable, valid, conceptually sound, sensitive, and clinically relevant outcome instruments. Evidence-based guidelines depend on the



## Etiology and Treatment

1. Determine the prevalence, characteristics, and severity of sleep disturbances in distinct populations of patients with cancer in the clinical setting.
2. Further characterize the sleep disturbances of formal and informal caregivers and contributing and alleviating factors.
3. Explore in greater detail specific factors involved in normal sleep and circadian regulation that are disrupted by cancer or cancer treatment.
4. Describe the effects of nocturnal sleep disturbances and daytime sleepiness on the health outcomes (i.e., morbidity and mortality) of patients with cancer and caregivers.
5. Explore relationships among disturbances in sleep and wakefulness and other symptoms such as pain, depression, anxiety, and fatigue.
6. Explore the genetic basis of sleep disturbances in patients with cancer.
7. Develop and test interventions designed to enhance the sleep and daytime wakefulness of patients with cancer and their caregivers.

## Measurement

1. Estimate reliability and validity of established sleep and wakefulness instruments for use in patients with cancer and their caregivers.
2. Identify a recommended core battery of standard instruments for inclusion in sleep clinical trials as well as a standard approach for clinical assessments of sleep and wakefulness; identify a common minimum data set for quality-improvement projects.
3. Include subjective and objective instruments to measure sleep (researchers should not expect strong correlations between them, but reliability and validity should be examined for the population in which they are being used).
4. Evaluate the use and implications of biomarkers related to sleep: melatonin, cortisol, C-reactive protein, core body temperature, circadian rhythm markers, and immune and genetic markers.
5. Identify relationships and their variations among sleep disturbances and comorbidities, functional status and perceived quality of life, and related symptoms (e.g., daytime sleepiness or wakefulness, fatigue, neurocognitive function, pain, mood).
6. Design studies with careful attention to theoretical models that include antecedents and consequences of impaired sleep to increase knowledge of the etiology and outcomes of disturbances in sleep and wakefulness.

## Figure 4. Implications for Multidisciplinary Research of Disturbances in Sleep and Wakefulness

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development and use of such instruments in a standardized manner. Sleep scientists also are aware that they need to move beyond insomnia as the exclusive focus of their research and link sleep research with other related symptoms such as pain, depression, fatigue, and anxiety that are applicable to the population being studied (Morin, 2003). A summary of directions for future research related to sleep disturbances in people with cancer and their caregivers appears in Figure 4.

## Summary

Much remains to be learned about the nature and purposes of sleep in the general population, making the assessment and treatment of sleep disturbances in patients with cancer and their caregivers especially challenging. Nonetheless, the state of the science and theory development have evolved to a beginning understanding of the complexities of the problems in cancer populations. Numerous factors have been identified that can contribute to sleep/wake disturbances in people with cancer, providing the initial descriptive work needed to guide the development and testing of population-specific interventions designed to enhance sleep. In addition, an exploration of how sleep may affect other symptoms experienced by people with cancer, how it may affect their tolerance of treatment, and how genetics plays a role in the expression of sleep/wake disturbances may be especially relevant to long-term survival rates and QOL. The information could guide the identification of people at high risk for sleep/wake disturbances as well as the development of new interventions.

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