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Incorporating Measures of Sleep Quality into Cancer Studies

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Abstract

Introduction/background—Sleep disturbance may influence the development of cancer and responses to treatment. It is also closely tied to recovery and quality of life in cancer patients, survivors, and caregivers, and recent studies have begun to show beneficial effects of sleep promoting interventions. Despite the importance of sleep to cancer and its treatment and the availability of numerous tools for measuring sleep quality and quantity, sleep measurements are underutilized in cancer studies.

Methods—This review, written for cancer researchers interested in incorporating sleep measures into their studies, is designed to raise awareness about the importance of sleep and suggest strategies for including sleep evaluation in cancer studies.

Conclusions—Inclusion of readily available sleep measures may ultimately improve cancer care by facilitating studies that lead to a greater understanding of how sleep and sleep disturbance influence all aspects of cancer care and the patient experience.

Introduction

Sleep disturbance is a common component of the cancer experience in adult and child cancer patients, survivors, and caregivers. There is beginning evidence that some aspects of sleep disturbance may contribute to the development of cancer and substantial evidence that sleep disturbance is associated with many aspects of cancer treatment, cancer symptoms and morbidity, mortality and quality of life. Although there is growth in understanding of the importance of sleep and its relevance cancer care, there is a continued need to improve scientific knowledge about the relationships among sleep disturbance, cancer biology, and

the experience of cancer. Better knowledge of these relationships may contribute to the development and uptake of interventions to promote sleep and improve sleep-related outcomes in this large group of patients, survivors, and their caregivers [1]. However, barriers to achieving this goal include the lack of discussion between health care providers and patients about sleep [2], lack of sleep treatments with documented efficacy [1], lack of familiarity regarding the impact of sleep on cancer, and limited knowledge among oncology clinicians and oncology scientists about the importance of sleep and the tools available for measuring its attributes. Therefore, the purposes of this paper are to provide clinical and behavioral cancer researchers who are non-sleep specialists with an understanding of the importance of sleep in cancer; the most commonly used and validated sleep measures and their properties, and suggest strategies for incorporating these measures into cancer studies. The ultimate goal is to facilitate research that will lead to improved identification and more aggressive treatment of sleep disturbances among patients with cancer.

Background

Sleep is a recurrent multi-dimensional phenomenon with distinct and measurable biological, behavioral, perceptual, and temporal attributes (See table 1). Sleep attributes reflect underlying behavioral and physiological processes that are the mechanisms through which sleep disturbance influences cancer biology, recovery, quality of life, and morbidity and mortality. Cancer therapies, cancer symptoms, and psychological and behavioral stressors associated with cancer and its treatment contribute to sleep disturbance that, in turn, may contribute to morbidity, mortality, and decrements in function and quality of life. While the importance of sleep is becoming more widely recognized, efficacious interventions are needed [1]. Examples of the importance of sleep to cancer, including the potential contributions of sleep disturbance to the development of cancer, the role of sleep disturbance during the course of cancer treatment and recovery, and the associations of sleep disturbance with other common and distressing cancer-related symptoms (e.g., fatigue and pain) and quality of life outcomes, are outlined below to emphasize the importance of this problem. Evident in this literature is the multi-dimensional nature of sleep disturbance that require measures that capture its complexity.

Growing evidence suggests that excessively long or short sleep duration [3] may increase the risk for developing cancer; and sleep-wake alterations may contribute to cancer mortality [4]. However, the mechanisms are not well-known.

Obstructive sleep apnea (OSA) may also increase the risk of cancer through its influence on intermittent hypoxia and angiogenesis [5–7], although conflicting data are available [8, 9]. OSA is also associated with short sleep duration and fragmentation that may contribute to cancer. Although the mechanisms are not completely understood, sleep disruption leads to increases in inflammatory mediators [10], that may contribute to excess morbidity and mortality among people with cancer. Unknown is the extent to which treatment of these aspects of sleep disturbance may prevent cancer or its negative consequences.

There are growing efforts to understand the relationships between the epigenetics of sleep, circadian rhythms, and cancer biology [11]. Altered timing in the sleep-wake cycle

contributes to cancer risk [12, 13]. Circadian processes influence most physiologic processes, such as hormone secretion, metabolism, and patterns of alertness. For example, the protein products of the Per1 and Per2 genes [14] regulate the cell cycle and play a fundamental role in circadian control. These genes have been linked with response to DNA damage [15], a step in the genesis of some cancers.

Melatonin, a hormone secreted by the pineal gland, is a key component of the circadian system. Studies have linked melatonin with reduction in the development and growth of tumors. [For good reviews see [16, 17]]. Mechanisms explaining this relationship may include: (1) scavenging of free-radicals [18] and stimulation of anti-oxidant enzymes [19], (2) stimulation of apoptosis in cancer cells [16], and (3) inhibition of angiogenesis and proliferation of malignant endothelial cells [17, 20]. The oncostatic properties of melatonin have been demonstrated in a wide range of cancer cell types including reproductive tumors, lymphomas, leukemias, and neural cell tumors [16]. Other data suggest that melatonin may influence the regulation of clock genes [21] and that it can correct circadian disruption in cancer cells [22, 23]. The relationships between key components of the circadian system and oncostasis suggest possible mechanisms to explain increased cancer in shift-workers who have disrupted circadian cycles [24] and why response to cancer treatment appears to be influenced by the time of day at which the therapy is administered [25, 26]. These promising findings have important implications for clinical cancer care and suggest the importance of measurement of circadian timing of sleep and wake among cancer patients or those at risk for cancer.

Insomnia, a disorder of initiating and maintaining sleep, accompanied by daytime dysfunction, is detected by self-report and often wrist actigraphy. Insomnia is common across the course of cancer diagnosis, treatment, and survivorship in adults [1, 3, 27– 34]. Insomnia is also an important concern in palliative care patients [35], children with cancer, adult survivors of childhood cancer [33] and among caregivers of cancer patients [36, 37]. Although prevalence rates vary widely based on criteria used, time frame relative to treatment, and populations studied, review of a large data base revealed that 33–50% of patients undergoing chemotherapy for a variety of cancers reported clinically significant insomnia, with the highest rates in lung cancer patients [34]. These rates were approximately three times as high as those in the general population.

Emotional distress, uncertainty, and cancer symptoms themselves (e.g., pain) contribute to poor sleep quality, including insomnia symptoms during the diagnostic process. Likewise, side- effects of common cancer treatments including chemotherapy [38] radiotherapy, surgery, hormone blocking drugs [39], and cancer symptoms often contribute to including insomnia symptoms. Sleep disturbance is also usually a component of cancer symptom clusters [36, 40, 41], for which the biological underpinnings and consequences are just beginning to be understood [42]. Sleep disturbance and sleep-related symptoms are also well-documented contributors to poor function [43] and quality of life in cancer patients [44].

Sleep quality is closely tied with the pain response [45, 46]. While it is often assumed that poor sleep quality is a result of pain, the converse is often also true: Poor sleep, included

sleep fragmentation and decreased rapid eye movement (REM) and slow wave sleep, leads to decreased pain thresholds and increased pain perception [45, 47]. Opioids, a mainstay of cancer pain treatment, have a negative impact on sleep architecture [48], but may also lead to drowsiness, daytime fatigue and napping that in turn may contribute to worsening sleep disruption [49]. Evidence is emerging that opioids may also contribute to central sleep apnea, a form of sleep disordered breathing [48] that may further contribute to daytime symptoms and hypoxia. Sleep fragmentation and nocturnal hypoxia, common in advanced cancer, may also contribute to daytime dysfunction [50]. These findings suggest the importance of improved understanding of the interplay among sleep and pain, as well as the need for pharmacological and non-pharmacologic strategies that reduce pain [47] but do not have negative effects on sleep. Research is especially needed on sleep and cancer pain.

Sleep disturbance is a well-documented contributor to daytime fatigue in cancer [51–55] and daytime sleepiness among cancer patients. It is important to recognize that fatigue and sleepiness are distinct constructs; fatigue may contribute to sleepiness [55] and vice [56], but despite the overlap, distinguishing the two phenomena is necessary to guide clinical care [57]. Sleepiness is usually related to sleep loss and specific sleep disorders associated with sleep loss, such as sleep apnea, while fatigue is more often associated with systemic conditions [58] and the presence of insomnia.

Treatment of sleep disturbance may be an important pathway to fatigue management in cancer patients. While both pharmacological and non-pharmacological interventions may be useful in addressing insomnia symptoms in cancer, a number of studies of non-pharmacological interventions have been of mixed quality and did not consistently document improvements in sleep or sleep-related outcomes [1, 36]. However, cognitive behavioral therapy for insomnia (CBT-I) has consistently improved sleep quality manifested in insomnia symptoms in several studies [59–62]. Although the effects on fatigue have not been as consistent or as frequently studied [59, 60], a large trial in the UK demonstrated improvements in this important outcome [61, 62]. Therefore, CBT-I may be an important adjunct to fatigue management in cancer patients. On the other hand, few studies have addressed daytime sleepiness in cancer populations. Given the high prevalence of sleep disturbance, including insomnia symptoms, fatigue and possibly sleepiness in cancer populations, further studies of the clinical efficacy of CBT-I and other interventions, as well as comparative effectiveness and translation into practice are of critical importance to the field.

Taken together, these examples selected from the growing body of evidence of the role of sleep in cancer suggest several directions for future research and underscore the multi-dimensional nature of sleep disturbance. Understanding the conceptual and practical underpinning of sleep measurement methods is critical to this body of science.

Sleep measurement methods

Sleep is a recurrent multi-dimensional phenomenon with distinct and measurable biological, behavioral, perceptual, and temporal (circadian, infradian, ultradian) attributes. A list of

sleep terminology as it pertains to cancer patients has been published [36], and table 1 includes a list of the primary measurable attributes of sleep.

Choice of sleep measurement methods should be guided by understanding of the sleep attributes of relevance to the study (e.g., duration, continuity, temporal patterns, associated physiological events), the physical and psychometric properties of available measures, scoring methods, optimal frequency and duration of monitoring, characteristics of the patient population (e.g., acuity of illness, ability to cooperate, developmental stage), ecological validity, the nature of the setting (e.g., hospital, home, community) in which the study takes place. For example, hospitals are well-known causes of sleep disturbance due to unfamiliar surroundings, excessive and poorly timed lighting, and frequent awakenings for patient care activities noise, and therefore, may have a particular impact on the sleep of adults, children, and caregivers with cancer for whom sleep is already compromised [37, 53, 63].

Additional concerns regarding sleep measurement include subject burden/intrusiveness and feasibility relative to available human and financial resources. The measures described here and in table 1 elicit biological (polysomnography), behavioral (actigraphy, self-report), perceptual (self-report), and temporal (multiple measures) aspects of sleep.

Polysomnography (PSG), the “gold standard” of sleep measurement, can be conducted in the sleep laboratory or in ambulatory settings with electronic devices. The key elements of PSG include electrophysiological (EEG) monitoring obtained in multiple leads and electromyography obtained with sensors placed on the chin to evaluate changes in muscle tension associated with sleep stage changes. Electro-oculography (EOG) is used to evaluate eye movements, in conjunction with EEG and EMG in order to score sleep stages [64].

Additional measures of cardiac (electrocardiography), respiratory (oxygen saturation, respiratory effort, airflow obstruction), and neurological events (periodic limb movements) are often obtained to evaluate the association of sleep with cardiorespiratory events and to diagnose sleep-related breathing disorders and periodic limb movements during sleep. In addition to PSG obtained while attended by a sleep technician or unattended PSG studies, cardiorespiratory measures of sleep relevant to the diagnosis of sleep disordered breathing may be obtained with ambulatory devices that are used unattended in home and institutional settings [65]. These devices present a more cost-effective alternative to full PSG, but do not include direct EEG measures of sleep. However, some incorporate accelerometers to approximate the sleep period.

The primary advantage of PSG is the ability to measure the physiological properties of sleep and sleep architecture as well as accompanying physiological and pathophysiological parameters. Recent advances in ambulatory monitoring that enable sleep studies to be conducted in home and hospital bedside environments have increased the ecological validity of PSG monitoring, and computerized scoring algorithms have simplified data analysis, although there continues to be a need for human interaction with these algorithms. Intra- and inter-scorer reliability within and between trained sleep personnel are critical to obtaining high quality sleep data.

Disadvantages of PSG include the need for special training and skills to apply the sensors and score the sleep studies; the intrusive nature of sleep recordings, given the need for attached sensors; and the high cost of the equipment; sensors, and personnel needed to obtain and score the sleep studies. Recent examples of the use of PSG in the human cancer literature include studies of women undergoing lumpectomy for breast cancer [66], chemotherapy for multiple myeloma [38], and the relationship between hot flashes and sleep disturbance in women with breast cancer [39]. PSG is especially useful in studies where sleep architecture and/or cardiorespiratory events (e.g., apneas, ECG changes) are of major interest. However, PSG is not a diagnostic tool for insomnia, except to rule-out other sleep disorders.

Wrist actigraphy, obtained with the use of miniaturized accelerometers, is a reliable and valid measure of activity-rest in adults [67] and adolescents [68] and has frequently been used to measure sleep of children with cancer and others, despite concerns about sensitivity to wake and measurement of naps [69]. Sleep is estimated from the patterns of activity-rest using commercially available computer algorithms in specialized software. Sleep duration and sleep efficiency measured with wrist actigraphs and scored with commercial algorithms are reliable and valid relative to PSG, but these associations are generally higher in people who have good sleep continuity and those without insomnia.

Several types of wrist actigraphs are currently available from a number of vendors for research and clinical purposes. Accelerometers designed to measure physical activity and sleep are also available to the public for personal use, although there is a need to establish the reliability and validity of these devices prior to widespread use for research and clinical purposes. Actigraphs must be programmed and downloaded using commercially available software; and sleep characteristics can be estimated from these data.

For interpretation of actigraph data, it is helpful to have the patient depress the event marker to determine lights out time in order to evaluate sleep latency, and instruction is needed to obtain high quality data. Advanced devices have light sensors that record changes in lighting, such as those occurring at bedtime. Sleep diaries are usually used concurrently to assist in interpreting actigraph data to guide understanding of the behaviors occurring relative to changes in activity.

Recent advances in wrist actigraphy include reductions in size and larger data storage capacity; inclusion of light sensors; and event markers. Advantages of wrist actigraphy include their non-intrusive nature and the capability of obtaining several weeks or longer of data. The ability of actigraphs to acquire 24-hour activity-rest data enables evaluation of temporal characteristics of sleep and activity-rest, as well as day-day changes, with the duration of monitoring dependent upon epoch length, battery life, and storage capacity.

There are several challenges to use of actigraphy in research [70]. Disadvantages of actigraphy include the inability to evaluate sleep architecture and the potential for missing data if the patient fails to wear the device. Actigraphs also overestimate sleep time in individuals who lie awake for long periods of time without moving, such as those who have insomnia. Actigraphs are more expensive than self-report measures, but considerably less

expensive than PSG. Although there are a number of accelerometer-based actigraphs on the market, it is important to note that they each have different physical properties, use different software, and are not interchangeable due to these characteristics.

Wrist actigraphy has frequently been used to evaluate the sleep and circadian patterning of activity-rest among cancer patients, including adults [59, 71–73], adolescents, [68, 74], children [75], and family caregivers [76]. Given the ability to monitor activity-rest and sleep over many days depending on storage capacity and epoch length, actigraphs are especially useful in monitoring changes over the trajectory of cancer treatment and recovery. As noted in the examples above, actigraphs are also frequently-used measures of the rhythmicity of activity-rest, an important measure in studies of shift-work and other studies where chronobiologic attributes are important to cancer

Self-report sleep measures include questionnaires and diaries that elicit perceptions of quantitative (e.g., duration) and qualitative aspects of sleep (e.g., perceived sleep quality and satisfaction with sleep). Self-report measures may also be used to elicit the presence of insomnia symptoms, risk factors for specific sleep disorders (e.g., sleep disordered breathing, restless legs syndrome), sleep habits, and perceptions about sleep-relate behaviors. Self-report measures utilize various time frames (e.g., past month, past week) and must be carefully selected to represent the time period of interest. Some frequently used self-reported measures are summarized in table 1.

Critical considerations when selecting self-report measures include the conceptual consistency between the sleep characteristics of interest (e.g., global sleep quality vs. specific sleep disorders symptoms) and the measure, psychometric characteristics, reading level, language, length, and the time frame of interest (e.g., chronic sleep disturbance vs. sleep disturbance occurring in real time or over the short term). Use of standardized instruments where possible allows for comparability between studies. The PROMIS initiative (http://www.nihpromis.org/) has produced standardized measures of sleep quality and sleep-related impairment [77, 78] that can be administered over the internet or with pen and paper.

Self-report measures are generally inexpensive and non-intrusive, compared with objective sleep measures, but perceptions of sleep, like other symptoms, do not always correlate highly with these objective measures. Examples of reliable and valid sleep questionnaires used in cancer research include the General Sleep Disturbances Questionnaire [32, 79] and the Pittsburgh Sleep Quality Index [79–81], and the insomnia severity index [81]. Additional measures have been reviewed for use in adult, child, adolescent, and caregiver cancer populations [36, 68].

Sleep diaries are often used in sleep research as daily measures of sleep completed upon awakening. Sleep diaries are also used in tandem with wrist actigraphy to assist in interpreting the data. Although a variety of sleep variables may be included, diaries typically include time taken to fall asleep (sleep latency - SL), minutes of wakefulness after sleep onset (WASO), number of awakenings (NOA), total sleep time (TST), and sleep efficiency percent (SE); the values can be used as daily measures or can be summed and averaged over

a period of one week or more. Diaries may also elicit additional information about symptoms (e.g., pain and fatigue) and activity occurring on a daily basis, as well as medications and other variables.

Sleep diaries are reliable and valid measures of sleep. Due to the variety of sleep diary formats available, however, there are numerous ways in which stem questions for each of the common variables can be asked and answers provided. To achieve more consistency, a consensus sleep diary has been developed and proposed for use in insomnia research [82]. It contains the standard core elements above (e.g., time to fall asleep) as well as the capacity to individualize non-core elements.

Self-reported measures of sleep and sleep-related outcomes have traditionally been administered in paper and pencil format, but are increasingly administered with electronic methods (e.g., web-based, smart phone). Advantages of electronic methods include the ability capture of data in real time, rather than retrospective completion of forms and the ability to electronically capture the data in a database without the need for data entry.

Advantages of self-report measures of sleep are their non-intrusiveness and low cost. However, these measures rarely correspond well with objective measures, such as PSG or actigraphy due to the need for recall and the subjective nature of perception. This may be especially true for patients with insomnia who may perceive that their sleep quality to be poorer than when measured objectively. Although this discrepancy may be viewed as a disadvantage, patient perceptions about sleep are key components of the diagnosis of insomnia and important determinants of quality of life. Thus, perception of sleep is important to assess, in addition to objective measures.

Measures of excessive daytime sleepiness and fatigue. Many outcomes relevant to the cancer experience are sensitive to the effects of sleep loss (e.g., fatigue, depression, cognitive dysfunction). However, the primary sleep-specific neurobiological outcome is thought to be excessive daytime sleepiness (tendency to fall asleep). The circadian tendency for sleepiness occurs in the mid-afternoon and in the early morning hours, but sleepiness also occurs as sleep debt increases (homeostatic process).

Excessive daytime sleepiness, can be measured with self-report [e.g., Epworth Sleepiness Scale [83, 84] and the Stanford Sleepiness Scale [85]] and objective measures, including the multiple sleep latency test (MSLT) [86]; the Maintenance of Wakefulness Test MWT [87] and the Psychomotor Vigilance Task (PVT) [88].

The MSLT is a daytime polysomnographic procedure that measures sleep propensity in a bedroom environment that is conducive to sleep. The test consists of a series of five ‘nap’ opportunities provided every two hours beginning at 10:00 am. The measured outcome is the average latency to sleep onset across all naps (with a maximum of 20 minutes to attain sleep before the test ends). Conversely, the MWT is a measure of the ability to remain awake while resisting the pressure to fall asleep while seated quietly in a darkened room. Like the MSLT, the MWT consists of a series of five 20-minute tests every two hours beginning at 10:00 a.m. Both the MSLT and the MWT are administered during the day but require a PSG study on the previous night, making them somewhat burdensome.

The PVT is a sustained-attention, reaction-timed task that measures the speed with which subjects respond to a visual stimulus; sleep deficit is associated with poorer performance on these tasks. Despite their potential usefulness as objective measures of the effects of sleep loss, these objective measures have rarely been used to study sleepiness in cancer patients [89].

Fatigue, a frequent outcome of sleep loss, is common in cancer patients and often studied by cancer researchers. A number of well-validated fatigue instruments are available, including several constructed specifically for cancer populations [e.g., Brief Fatigue Inventory [90]; Cancer Fatigue Scale [91]; and the Functional Assessment of Chronic Illness Therapy-Fatigue [92]]. PROMIS measures are also available to measure fatigue (http://www.nihpromis.org/). Interestingly, there is no consensus on a gold standard cancer-related fatigue instrument, but the selection of a fatigue instrument should be tailored to the goals of the research [93].

Because sleepiness and fatigue are overlapping, but distinct constructs, both fatigue and sleepiness should be measured as consequences of sleep loss, sleep disorders and/or systemic disturbance, rather than using one as a proxy for the other [57]. However, some have suggested that using separate sleepiness and fatigue scales may not be adequate to measure change in each construct over time as changes in one may not parallel changes of similar magnitude in the other [94].To address this problem, the FACES Checklist is a scale that measures both states concomitantly. (See Table 1).

Ready availability of standard sleep measurement methods, such as those described in this paper, may improve opportunities to design and conduct studies to address important questions regarding sleep disturbance and cancer. Collaboration between the community of oncology providers and scientists and sleep specialists to conduct sleep-related studies is essential. In addition to the conduct of studies with the primary aim of addressing sleep in cancer patients, judicious inclusion of sleep measures in ongoing and emerging cancer trials designed for broader purposes may be a cost-effective way to improve knowledge of sleep. Inclusion of common data elements to measure sleep across studies may facilitate comparison across populations and settings. These studies may add to the growing science regarding the biological and behavioral importance of sleep, sleep loss and circadian rhythms to the development of cancer; the impact of treatments; and quality of life for cancer patients, survivors, and their families. Better understanding of the role of sleep in cancer development, progression, and quality of life, as well as clinical trials to test interventions to improve sleep and sleep-related outcomes is needed in the diverse populations of people who are cancer patients, survivors, and caregivers, as well as those who are at particular risk for cancer (e.g., shift workers).

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Table 1

Attributes of sleep, sleep measures, time to complete, and comments

	Sleep measure	Time to complete	Comments
Sleep architecture/sleep stages - Wake, Stage N1-N3, and Stage REM	Polysomnography (PSG)	Full night (~12 hrs)	Laboratory-based PSG is the gold standard method to capture EEG data from which to score sleep stages. There are ambulatory units that can perform full polysomnographic recordings, which can be used in the home setting; these require technicians to set-up the device or considerable patient education.
Sleep-related physiology	Polysomnography	Full night (8–9 hrs)	PSG includes cardiorespiratory measures.
- Cardiorespiratory (apneas, hypopneas, oxygenation, ECG	Level III or IV ambulatory devices	Full night (~12 hrs)	Type III/IV devices do not measure EEG activity. Type IV devices usually include oximetry and a measure of respiratory effort measure; Type III devices include oximetry as well as 2 respiratory effort and/or airflow measures, and a measure of heart rate or an ECG.
- Limb movements	Polysomnography	Full night (~12 hrs)	
Sleep continuity and Sleep duration	Polysomnography	Full night (~12 hrs)	PSG is the gold standard measure of sleep continuity.
- Sleep latency (duration of time from lights out to sleep onset)	Wrist-actigraphy	Worn 24 hrs/day; typically over 1–2 weeks	Actigraphy is a valid and reliable objective alternative to PSG for capturing sleep continuity.
- Time awake after sleep onset - Total sleep time - Sleep efficiency (% of time in bed spent asleep) - Number of awakenings	Self-report (sleep diary)	5 minutes per day; typically over 1–2 weeks	Sleep diaries are standard self-report measures of sleep continuity. There is often a subjective-objective discrepancy between diaries and both actigraphy and PSG. Adherence can be improved by having patients/subjects use phone or web-based daily data entry.
Electrophysiologic arousals	Polysomnography	Full night (~12 hrs)	Changes in EEG lasting < 15 seconds, which can be scored as being a spontaneous arousal or related to a respiratory event.
Sleep quality/sleep satisfaction	Pittsburgh Sleep Quality Index [95] http://www.sleep.pitt.edu/content.asp?id=1484	5–10 minutes	19-item self-report questionnaire that assesses sleep quality and sleep disturbances over a one-month period of time. Seven component scores that range from 0–3 are summed to produce a global score with higher scores representing poorer sleep quality. A global score > 5 indicates the presence of a clinically
	Patient Reported Outcomes Measurement Information System (PROMIS) – Sleep [96] http://www.nihpromis.org/	5–15 minutes depending on the version	The PROMIS sleep measure is drawn from an item bank of 27 items for sleep disturbance and 16 items for sleep-related impairment. Each domain may be used with Computerized Adaptive Testing that tailors the questionnaire to the individual by selecting the

Support Care Cancer. Author manuscript; available in PMC 2016 April 01.

	Sleep measure	Time to complete	Comments
			most informative set of questions based on the individual's prior responses. Alternatively, 4-, 6- and 8-item versions of the sleep disturbance measure have been validated. Scores are t-transformed and higher scores indicate greater disturbance.
	General Sleep Disturbance Scale [97]	10 minutes	21-item self-report scale that assesses overall sleep disturbance. All items are on a 0–7 scale and there are seven subscales with their own cut points. The total score can range from 0–147 and a total score ≥ 43 indicate a clinically meaningful level of sleep disturbance.
	Single item measures	1 minute	Single likert-scale items can be added to other instruments (e.g., a sleep diary) to assess perceived sleep quality or sleep satisfaction.
Risk for sleep disordered breathing	Berlin Questionnaire [98]	< 5 minutes	11-item self-report questionnaire including a BMI calculation; 10 items are multiple choice with responses varying form yes/no to a 1–5 scale. There are 3 categories (snoring, fatigue/sleepiness, and somnolence). Scoring 'positive' on ≥ 2 categories indicates a high risk of OSA.
	STOP-BANG Questionnaire [99]	< 5 minutes	8-item self-report instrument with yes/no responses. Requires knowing BMI and neck circumference. Answering 'yes' to ≥ 3 items indicates a high risk of OSA:
Insomnia symptoms	Insomnia Severity Index [100]	< 5 minutes	7-item self-report scale for assessing difficulty initiating and maintaining sleep, daytime consequences, worry about sleep, and satisfaction with sleep quality. Each item can be rated on a 0–4 scale with total score ranging from 0–28 and higher scores indicating more severe insomnia. There is an established clinical cutoff of ≥ 10 in general population (≥ 11 in clinical samples).
	Insomnia Symptom Questionnaire [101]	5 minutes	13-item self-report scale to identify chronic insomnia. Items 1–5 contain multiple choices on an ordinal 0–5 scale to assess the presence, frequency and/or severity of the complaint with follow-up questions for the problem's duration. Items 6–13 assess the sleep complaints effect on daytime activities on a 0–4 scale. Higher scores indicate more severe symptoms.
	Athens Insomnia Scale [102]	< 5 minutes	8-item self-report scale based on the International Classification of Sleep Disorders criteria to diagnose insomnia. Each item is rated on 0–3 scale with a total score ranging from 0–24 and higher scores indicating more severe insomnia.
Sleep Habits: Children	Children's Sleep Habits Questionnaire [103]	10–15 minutes	35-item (reduced from 45 items) self-report parent questionnaire that assesses a number of sleep

	Sleep measure	Time to complete	Comments
			behaviors in young children. Questions are anchored to a recent 'typical' week with items rated on a 3-point producing eight subscale scores and a total sleep disturbance score.
Adults	Sleep Hygiene Index [104]	< 5 minutes	13-item self-report measure designed to assess the practice of sleep hygiene behaviors. Each item is rated on a 0–4 scale with a total score ranging from 0 to 52 and a higher score representing poorer sleep hygiene.
Sleepiness	Epworth Sleepiness Scale [83]	< 5 minutes	8-item self-report measure of daytime sleepiness that assess the likelihood of falling asleep in various daily situations (e.g., watching television) on a 0–3 scale, providing a summed score ranging from 0–24. A cutoff of 10 has been established as a marker of excessive daytime sleepiness.
	Stanford Sleepiness Scale [85]	1 minute	A single item measure of sleepiness in the moment on a 1–7 scale.
	Multiple sleep Latency Test[105]	Full day following overnight polysomnography	An objective measure of sleep propensity that uses a series of daytime nap tests to determine mean time to fall asleep with lower scores indicating greater sleepiness and a score < 5 minutes indicating pathological sleepiness.
	Maintenance of Wakefulness Test [87]	Full day following overnight polysomnography	An alternative objective means of assessing sleepiness via a series of daytime tests of the ability to remain awake with impairment associated with mean latency to sleep of < 12 minutes.
	Psychomotor Vigilance Test [88]	10 minutes	A computer-delivered, sustained-attention, reaction-timed task with stimuli presented every 2–10 seconds. A higher number of lapses correspond to greater sleepiness.
Fatigue	Brief Fatigue Inventory [90]	< 5 minutes	9-item self-report measure that assesses ratings of fatigue severity (3 times) and its interference in life activities (6 items) in the past 24 hours. Items responses are on a 0–10 scale with a total score range of 0–10 based on a mean of all items. Higher scores indicate greater fatigue with scores of 4–6 indicating moderate fatigue and ≥ 7 severe fatigue.
	Cancer Fatigue Scale [91]	< 5 minutes	15-item self-report with three subscales that assess physical, affective and cognitive fatigue. 'right now.' Items responses are on a 1–5 scale with some items reverse scored. The total score range is 15–75 and higher scores indicating greater fatigue.
	Functional Assessment of Chronic Illness Therapy-Fatigue [92]	< 5 minutes	13-item self-report measure that assesses ratings of fatigue severity and its interference in the last week. Items responses are on a 0–4 scale with higher item scores representing greater severity except for two

	Sleep measure	Time to complete	Comments
			positively worded items. All items are then reverse scored so that lower scores indicate less fatigue in a total range of 0–52.
	FACES of Fatigue and Sleepiness Adjective Checklist (Shapiro et al, 2002)	10 minutes	50-item self-report measure with 5 subscales including one for fatigue (15 items) and one for sleepiness (9 items). Item responses are anchored to intensity of fatigue-related adjectives experienced in the past week on a 0–3 scale from “not at all” to “strongly” with higher item scores representing greater severity and items for each subscale summed for a total subscale scores.