Sleep disturbances include insomnia (trouble falling or staying asleep resulting in daytime dysfunction), excessive sleepiness (which can result from insufficient sleep opportunity, insomnia, or other sleep disorders), sleep-related movement or breathing disorders, and parasomnias. Sleep disorders affect 30% to 50% of patients with cancer and survivors, often in combination with fatigue, anxiety, or depression. Improvements in sleep lead to improvements in fatigue, mood, and quality of life.

**Abstract**

Sleep disorders, including insomnia and excessive sleepiness, affect a significant proportion of patients with cancer and survivors, often in combination with fatigue, anxiety, and depression. Improvements in sleep lead to improvements in fatigue, mood, and quality of life. This section of the NCCN Guidelines for Survivorship provides screening, diagnosis, and management recommendations for sleep disorders in survivors. Management includes combinations of sleep hygiene education, physical activity, psychosocial interventions, and pharmacologic treatments. (J Natl Compr Canc Netw 2014;12:630–642)

**NCCN Categories of Evidence and Consensus**

**Category 1:** Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

**Category 2A:** Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

**Category 2B:** Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

**Category 3:** Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise noted.

**Clinical trials:** NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

**Please Note**

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Disclosures for the NCCN Survivorship Panel

At the beginning of each NCCN Guidelines panel meeting, panel members review all potential conflicts of interest. NCCN, in keeping with its commitment to public transparency, publishes these disclosures for panel members, staff, and NCCN itself.

Individual disclosures for the NCCN Survivorship Panel members can be found on page 642. (The most recent version of these guidelines and accompanying disclosures are available on the NCCN Web site at NCCN.org.)

These guidelines are also available on the Internet. For the latest update, visit NCCN.org.
Survivorship
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Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Palliative Care and the NCCN Guidelines for Cancer-Related Fatigue (available at NCCN.org). These guidelines may be modified to fit the individual survivor’s circumstances.

Screening for and Assessment of Sleep Disorders

Survivors should be screened for possible sleep disorders at regular intervals, especially when they experience a change in clinical status or treatment. The panel lists screening questions that can help determine whether concerns about sleep disorders or disturbances warrant further assessment. Other tools to screen for sleep problems have been validated,13,14 Text cont. on page 639.

NCCN Sleep Disorders Panel Members

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Subcommittees: *Anxiety and Depression; *Cognitive Function; *Exercise; *Fatigue; *Immunizations and Infections; *Pain; *Sexual Function; *Sleep Disorders

Specialties: ΝBone Marrow Transplantation; ΠCardiology; ΞCephalometrics; ΞExercise/Physiology; ΞGynecology; ΞGynecologic Oncology; ΞHematology/Hematology Oncology; ΞInfectious Diseases; ΞInternal Medicine; ΞMedical Oncology; ΞNeurology/Neuro-Oncology; ΞNursing; ΞNutrition Science/Dietician; ΞPatient Advocacy; ΞPediatric Oncology; ΞPsychiatry, Psychology, Including Health Behavior; ΞSupportive Care Including Palliative, Pain Management, Pastoral Care, and Oncology Social Work; ΞSurgery/Surgical Oncology; ΞUrology

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Specialties: ΝBone Marrow Transplantation; ΠCardiology; ΞCephalometrics; ΞExercise/Physiology; ΞGynecology; ΞGynecologic Oncology; ΞHematology/Hematology Oncology; ΞInfectious Diseases; ΞInternal Medicine; ΞMedical Oncology; ΞNeurology/Neuro-Oncology; ΞNursing; ΞNutrition Science/Dietician; ΞPatient Advocacy; ΞPediatric Oncology; ΞPsychiatry, Psychology, Including Health Behavior; ΞSupportive Care Including Palliative, Pain Management, Pastoral Care, and Oncology Social Work; ΞSurgery/Surgical Oncology; ΞUrology

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Survivorship: Sleep Disorders, Version 1.2014

SCREENING

Screening/assessment questions to be asked at regular intervals, especially when there is a change in clinical status or treatment:

- Insomnia
  - Do you have difficulty falling or staying asleep?
  - How long does it take to fall asleep?
  - How many times do you wake up every night?
  - How long have you had difficulty falling or staying asleep?
- Excessive sleepiness
  - Do you fall asleep while reading, watching television, talking to friends, or driving?
- Obstructive sleep apnea
  - Do you snore, gasp for breath, or stop breathing during sleep?
- Restless legs syndrome (RLS)
  - Do you have the urge to move the legs, usually accompanied by an uncomfortable, deep-seated sensation that is brought on by rest?
- Parasomnias
  - Do you sleep walk, wake up screaming, or have violent movements during sleep?

H&P

- Assessment of treatable contributing factors:
  - Comorbidities
  - Alcohol and/or substance abuse
  - Obesity
  - Cardiac dysfunction
  - Endocrine dysfunction (eg, hypothyroidism)
  - Anemia
  - Emotional distress: screen for anxiety and depression (See SANXDE-1* and NCCN Guidelines for Distress Management)
  - Neurologic disorders
  - Psychiatric disorders
  - Medications (consider persistent use of sleep aids, pain medications, antiemetics, stimulants, sedative/hypnotics, over-the-counter sleep aids, or antihistamines)
  - Review history of chemotherapy
  - Pain (See SPAIN-1*)
  - Fatigue (See SFAT-1*)
  - Shift work
  - Current coping strategies (eg, relaxation techniques, meditation)

No concerns for sleep disorder/disturbance

Concerns for sleep disorder/disturbance

Reevaluate at subsequent visits/post-therapy

Sleep disturbance and/or excessive sleepiness
  - Narcolepsy and other hypersomnias
  - Obstructive sleep apnea
  - RLS
  - Circadian rhythm sleep disorders
  - Parasomnias

Insomnia symptoms (difficulty falling asleep and/or maintaining sleep):
  - Duration >4 weeks
  - Occurring at least 3 times per week

See SSD-2

See SSD-4

*Available online, in these guidelines, at NCCN.org.
†To view the most recent version of these guidelines, visit NCCN.org.

Note that obstructive sleep apnea, RLS, circadian rhythm sleep disorders, and parasomnias may also present with symptoms of insomnia.

For circadian rhythm sleep disorders and parasomnias, refer to a sleep specialist.

RLS is also known as Willis-Ekbom disease.
Survivorship: Sleep Disorders, Version 1.2014

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>ASSESSMENT</th>
<th>TESTING</th>
<th>DIAGNOSIS</th>
<th>TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated with insufficient sleep time</td>
<td></td>
<td>Insufficient sleep syndrome</td>
<td>Increase sleep time, Sleep hygiene education</td>
<td>Consider: Continuous positive airway pressure (CPAP), Surgery, Oral appliance, Weight loss, Exercise (See SE-1*), Refer to sleep specialist</td>
</tr>
<tr>
<td>Associated with observed apneas, snoring</td>
<td>Polysomnography (PSG)</td>
<td>Obstructive sleep apnea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associated with uncomfortable sensation</td>
<td>Ferritin level &lt;45-50 ng/mL</td>
<td>RLS&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td>Dopamine agonists, Benzodiazepines (BZD), Gabapentin (enacarbil), Opioids&lt;sup&gt;c&lt;/sup&gt;, Refer to sleep specialist</td>
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<tr>
<td>Associated with prolonged wakefulness or awakenings</td>
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<tr>
<td>Associated with prolonged nocturnal sleep (ie, &gt;9 hours for adults)</td>
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<tr>
<td>Associated with cataplexy, frequent short naps, vivid dreams, disrupted sleep, or sleep paralysis</td>
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<tr>
<td>Excessive daytime sleepiness not associated with other symptoms</td>
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</table>

<sup>c</sup>RLS is also known as Willis-Ekbom disease.
<sup>d</sup>For other less frequent syndromes, refer to sleep specialist.
<sup>e</sup>See STOP Questionnaire: A Tool to Screen Patients for Obstructive Sleep Apnea (SSD-A).
<sup>f</sup>See Essential Diagnostic Criteria for Restless Legs Syndrome (SSD-B).
<sup>g</sup>Cataplexy: Sudden loss of muscle tone. Typically triggered by strong emotions, such as laughter or anger. Cataplexy is the most specific diagnostic feature of narcolepsy.
<sup>h</sup>Sleep studies can be done as laboratory PSG or as home sleep study.
<sup>i</sup>See General Sleep Hygiene Measures (SSD-C).

*To view the most recent version of these guidelines, visit NCCN.org.
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**Clinical trials:** NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged. All recommendations are category 2A unless otherwise indicated.

---

**SYMPTOM**  
**ASSESSMENT**
- Associated with prolonged wakefulness or awakenings
- Associated with prolonged nocturnal sleep, (i.e., >9 hours for adults)
- Associated with cataplexy, frequent short naps, vivid dreams, disrupted sleep, or sleep paralysis

**TESTING**
- PSG, Multiple sleep latency test (MSLT)

**DIAGNOSIS**
- Insomnia
- Circadian rhythm sleep disorders
- Idiopathic hypersomnia

**TREATMENT**
- Sleep hygiene education
- Stimulants
- Refer to sleep specialist
- Sleep hygiene education
- Schedule short daytime naps
- Refer to sleep specialist for pharmacologic management

---

**Excessive daytime sleepiness not associated with other symptoms**

---

**For other less frequent syndromes, refer to sleep specialist.**
**Cataplexy:** sudden loss of muscle tone. Typically triggered by strong emotions, such as laughter or anger. Cataplexy is the most specific diagnostic feature of narcolepsy.

**Sleep studies can be done as laboratory PSG or as home sleep study.**

See General Sleep Hygiene Measures (SSD-C)

---

SSD-3
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**EVALUATION**
- Insomnia problematic, causing:
  - Decreased daytime functioning
  - Poor quality of life
  - Worsening of complaints
  - Distress to patient

- Insomnia not problematic

**TREATMENT**
- Insomnia with comorbidities:
  - Medical
  - Neurologic or psychiatric
  - Recurrence of cancer, pain
  - Assess medications that may cause insomnia

- Insomnia without comorbidities
  - No medications causing insomnia

- Insomnia not persisting
  - Do not treat
  - Sleep hygiene education

- Insomnia persisting
  - Refer to sleep specialist
  - No further treatment

- Treat comorbid condition
  - Treat with cognitive behavioral therapy
  - Consider pharmacologic intervention, if safe, for:
    - Difficulty in falling asleep
    - Difficulty maintaining sleep
    - Nonrestorative sleep
    - Sleep hygiene education
    - Refer to sleep specialist

- Insomnia not persisting
  - No further treatment

---

1See General Sleep Hygiene Measures (SSD-C).
2See Cognitive Behavioral Treatments (SSD-D).
3See Principles for Choosing an FDA-Approved Hypnotic (SSD-E).
4See Other Commonly Used Medications For Insomnia (SSD-F).

SSD-4
STOP Questionnaire: A Tool to Screen Patients for Obstructive Sleep Apnea (OSA)\textsuperscript{1,2}

1. **Snoring**
   - Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?
     - Yes
     - No

2. **Tired**
   - Do you often feel tired, fatigued, or sleepy during daytime?
     - Yes
     - No

3. **Observed**
   - Has anyone observed you stop breathing during your sleep?
     - Yes
     - No

4. **Blood pressure**
   - Do you have or are you being treated for high blood pressure?
     - Yes
     - No

**PROVIDER KEY**

High risk of OSA: Answering yes to 2 or more questions
Low risk of OSA: Answering yes to less than 2 questions

---

**ESSENTIAL DIAGNOSTIC CRITERIA FOR RESTLESS LEGS SYNDROME**\textsuperscript{3}

- An urge to move the legs usually accompanied by uncomfortable and unpleasant sensations in the legs, and sometimes the arms or other body parts.
- The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting.
- The symptoms are more pronounced in the evening or night or may only occur in the evening or night.


\textsuperscript{2} This screening tool and other similar tools are not diagnostic, but have been shown to be useful to assess risk for OSA.

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GENERAL SLEEP HYGIENE MEASURES

- Regular exercise in the morning and/or afternoon
- Increase exposure to bright light during the day
- Avoid exposure to bright light during the night
- Avoid heavy meals or drinking within 3 hours of bed
- Avoid alcohol, caffeine, nicotine too close to bedtime
- Enhance sleep environment (dark, quiet room, comfortable temperature)
- Set aside a worry time
- Avoid looking at the clock

COGNITIVE BEHAVIORAL TREATMENTS

<table>
<thead>
<tr>
<th>STRATEGY</th>
<th>GOAL</th>
</tr>
</thead>
</table>
| Cognitive therapy| • Challenge patient’s dysfunctional beliefs and misconceptions about sleep disturbances  
|                  | • Promote positive thoughts                                           |
| Relaxation training| • Reduce physiologic and cognitive arousal at bedtime       
|                  | • Techniques include progressive muscular relaxation, transcendental meditation, yoga, biofeedback |
| Sleep restriction | • Improve sleep continuity by limiting time spent in bed and maintaining a regular sleep schedule |
| Stimulus control  | • Associate the bed/bedroom as a place for sleep or sexual activity only |

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Clinical trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged. All recommendations are category 2A unless otherwise indicated.

**PRINCIPLES FOR CHOOSING AN FDA-APPROVED HYPNOTIC:**

- Does the patient have difficulty initiating or maintaining sleep?
- Does the patient have both sleep onset and sleep maintenance difficulty?

<table>
<thead>
<tr>
<th>AGENT</th>
<th>HELPS WITH SLEEP INITIATION</th>
<th>INCREASES TOTAL SLEEP TIME</th>
<th>INDICATED FOR SLEEP ONSET AND MAINTENANCE</th>
</tr>
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<tbody>
<tr>
<td>Zolpidem</td>
<td>+</td>
<td>+</td>
<td>–</td>
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<tr>
<td>Zolpidem CR</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Zaleplon</td>
<td>+</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Eszopiclone</td>
<td>+</td>
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<td>+</td>
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<tr>
<td>Ramelteon</td>
<td>+</td>
<td>+/-</td>
<td>–</td>
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<tr>
<td>Temazepam</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Doxepin (3-6 mg)</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

**OTHER COMMONLY USED MEDICATIONS FOR INSOMNIA**

This is a list of agents that do not have an FDA-approved indication for the treatment of insomnia and that do not have enough data to be recommended for routine use. They have none to limited efficacy or effectiveness data for the treatment of insomnia disorder.

- **Antidepressants**
  - Trazodone
  - Amitriptyline
  - Trimipramine
  - Mirtazapine
  - Doxepin

- **Antiepileptics**
  - Gabapentin
  - Tiagabine

- **Atypical antipsychotics**
  - Quetiapine

- **Antihistamines**
  - Diphenhydramine

- **Nutritional/herbal supplements**
  - Melatonin
  - Valerian

---

3Although they are commonly prescribed, antidepressants, antihistamines, antiepileptics, and antipsychotics have significant risks and should be used with caution.
If concerns regarding sleep are significant, the panel recommends that treatable contributing factors be assessed and managed. Comorbidities that can contribute to sleep problems include alcohol and substance abuse, obesity, cardiac dysfunction, endocrine dysfunction, anemia, neurologic disorders, pain, fatigue, and emotional distress. In addition, some medications, both prescription and over-the-counter, can contribute to sleep issues. For instance, pain medication, antiemetics, and antihistamines can all contribute to sleep disturbance, as can the persistent use of sleep aids.

**Diagnosis of Sleep Disorders**

The panel divided sleep disorders into 2 general categories: insomnia, and sleep disturbance and/or excessive sleepiness.

Insomnia is diagnosed when patients have difficulty falling asleep and/or maintaining sleep at least 3 times per week for at least 4 weeks, accompanied by distress.

Diagnosing patients with excessive sleepiness can be challenging, because it can be caused by a variety of factors. When excessive sleepiness is associated with observed apneas or snoring, the STOP questionnaire can be used as a screening tool to determine the risk of obstructive sleep apnea (OSA). Other screening tools for OSA risk have also been validated. Sleep studies (ie, laboratory polysomnography [PSG] or home sleep studies) can confirm the diagnosis of OSA. Multiple sleep latency tests (MSLTs) and PSG can also be useful in diagnosing narcolepsy, idiopathic hypersomnia, and parasomnias. Narcolepsy should be considered when excessive sleepiness is accompanied by cataplexy, frequent short naps, vivid dreams, disrupted sleep, or sleep paralysis.

Excessive sleepiness can also be associated with uncomfortable sensations or an urge to move the legs (and sometimes the arms or other body parts). These symptoms are usually worse at night and with inactivity, may be improved or relieved with movement such as walking or stretching, and indicate restless legs syndrome (RLS; also known as Willis-Ekbom disease). In these patients, ferritin levels should be checked; levels less than 45 to 50 ng/mL indicate a treatable cause of RLS.

**Management of Sleep Disorders**

OSA should be treated with continuous positive airway pressure, surgery, or oral appliances. Additionally, weight loss and exercise should be recommended, and patients should be referred to a sleep specialist.

RLS is treated with dopamine agonists, benzodiazepines, gabapentin, and/or opioids, and referral to a sleep specialist. Two separate recent meta-analyses found dopamine agonists and calcium channel alpha-2-delta ligands (eg, gabapentin) to be helpful in reducing RLS symptoms and improving sleep in the noncancer setting.

For other types of sleep disturbances, several types of interventions are recommended. In addition, referral to a sleep specialist can be considered in most cases.

**Sleep Hygiene Education**

Educating survivors about general sleep hygiene is recommended, especially for the treatment of insomnia. Key points are listed in the guidelines and include regular morning or afternoon exercise; daytime exposure to bright light; keeping the sleep environment dark, quiet, and comfortable; and avoiding heavy meals, alcohol, and nicotine near bedtime.

**Physical Activity**

Physical activity may improve sleep in patients with cancer and survivors. One recent randomized controlled trial compared a standardized yoga intervention plus standard care with standard care alone in 410 survivors (75% breast cancer; 96% women) with moderate to severe sleep disruption. Participants in the yoga arm experienced greater improvements in global and subjective sleep quality, daytime functioning, and sleep efficiency (all P≤.05). In addition, the use of sleep medication declined in the intervention arm (P=.05).

A recent meta-analysis of randomized controlled trials in patients who had completed active cancer treatment showed that exercise improved sleep at a 12-week follow-up. Overall, however, data supporting improvement in sleep with physical activity are limited in the survivorship population.

**Psychosocial Interventions**

Psychosocial interventions such as cognitive behavioral therapy (CBT), psychoeducational therapy, and supportive expressive therapy are recommended to treat sleep disturbances in cancer survivors.
particular, several randomized controlled trials have shown that CBT improves sleep in the survivor population.\textsuperscript{45–48} For example, a randomized controlled trial in 150 survivors (58% breast cancer; 23% prostate cancer; 16% bowel cancer; 69% women) found that a series of 5 weekly group CBT sessions was associated with a reduction in mean wakefulness of almost 1 hour per night, whereas usual care (in which physicians could treat insomnia as they would in normal clinical practice) had no effect on wakefulness.\textsuperscript{45}

In addition, a small randomized controlled trial of 57 survivors (54% breast cancer; 75% women) found that mind–body interventions (mindfulness meditation or mind–body bridging), decreased sleep disturbance more than sleep hygiene education did.\textsuperscript{49}

**Pharmacologic Interventions**

Many pharmacologic treatments for sleep disturbances are available, including psychotherapies for narcolepsy (eg, modafinil, methylphenidate) and hypnotics for insomnia (eg, zolpidem, ramelteon).\textsuperscript{33,50,51} In addition, antidepressants, antihistamines, antiepileptics, and antipsychotics are often used off-label for the treatment of insomnia, even though limited to no efficacy or effectiveness data are available for this use. The panel also noted that these medications are associated with significant risks and should be used with caution. One small, open-label study found that the antidepressant mirtazapine increased the total amount of nighttime sleep in patients with cancer.\textsuperscript{32} Overall, however, data on pharmacologic interventions aimed at improving sleep in patients with cancer and survivors are lacking.\textsuperscript{10}

**References**


<table>
<thead>
<tr>
<th>Panel Member</th>
<th>Clinical Research Support/Data Safety Monitoring Board</th>
<th>Advisory Boards, Speakers Bureau, Expert Witness, or Consultant</th>
<th>Patent, Equity, or Royalty</th>
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<td>Jose G. Montoya, MD</td>
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<td>Kathi Mooney, RN, PhD</td>
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<td>Mary Ann Morgan, PhD, FNP-BC</td>
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<td>Javid J. Mosleh, MD</td>
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<td>Linda Overholser, MD, MPH</td>
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The NCCN Guidelines Staff have no conflicts to disclose.