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### Title

Survivorship: sleep disorders, version 1.2014.

### Permalink

<https://escholarship.org/uc/item/6j7856qn>

### Journal

Journal of the National Comprehensive Cancer Network : JNCCN, 12(5)

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### Publication Date

2014-05-01

### DOI

10.6004/jnccn.2014.0067

Peer reviewed



# HHS Public Access

Author manuscript

*J Natl Compr Canc Netw*. Author manuscript; available in PMC 2016 February 29.

Published in final edited form as:

*J Natl Compr Canc Netw*. 2014 May ; 12(5): 630–642.

## Survivorship: Sleep Disorders, Version 1.2014:

### Clinical Practice Guidelines in Oncology

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### 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.

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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.<sup>1</sup> Sleep disorders affect 30% to 50% of patients with cancer and survivors, often in combination with fatigue, anxiety, or depression.<sup>1–10</sup> Improvements in sleep lead to improvements in fatigue, mood, and quality of life.<sup>11</sup> Most clinicians, however, do not know how best to evaluate and treat sleep disorders.<sup>1</sup>

Sleep disorders are common in patients with cancer as a result of multiple factors, including biologic changes, the stress of diagnosis and treatment, and side effects of therapy (eg, pain, fatigue).<sup>12</sup> In addition, evidence suggests that changes in inflammatory processes from cancer and its treatment play a role in sleep disorders. These sleep disturbances can be perpetuated in the survivorship phase by chronic side effects, anxiety, depression, medications, and maladaptive behaviors such as shifting sleep times, excessive time in bed because of fatigue, and unplanned naps.<sup>12</sup>

Additional information about sleep disorders in patients with cancer can be found in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Palliative Care and the NCCN Guidelines for Cancer-Related Fatigue (available at [NCCN.org](http://NCCN.org)). These guidelines may be modified to fit the individual survivor's circumstances.

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Survivors should be screened for possible sleep disorders at regular intervals, especially					
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The NCCN Guidelines Staff have no conflicts to disclose.

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.<sup>13,14</sup>

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).<sup>15</sup> Other screening tools for OSA risk have also been validated.<sup>16</sup> 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.<sup>17,18</sup>

## Management of Sleep Disorders

OSA should be treated with continuous positive airway pressure, surgery, or oral appliances. 19–21 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.<sup>22–30</sup> 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.<sup>30,31</sup>

For other types of sleep disturbances, several types of interventions are recommended.<sup>1,32,33</sup> 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.<sup>34–36</sup> 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.<sup>37–43</sup> 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.<sup>40</sup> 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.<sup>38</sup> 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.<sup>44</sup> In particular, several randomized controlled trials have shown that CBT improves sleep in the survivor population.<sup>45–48</sup> 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.<sup>45</sup>

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.<sup>49</sup>

### **Pharmacologic Interventions**

Many pharmacologic treatments for sleep disturbances are available, including psychostimulants for narcolepsy (eg, modafinil, methylphenidate) and hypnotics for insomnia (eg, zolpidem, ramelteon).<sup>33,50,51</sup> 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.<sup>52</sup> Overall, however, data on pharmacologic interventions aimed at improving sleep in patients with cancer and survivors are lacking.<sup>10</sup>

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## References

- Berger AM, Mitchell SA. Modifying cancer-related fatigue by optimizing sleep quality. *J Natl Compr Canc Netw*. 2008; 6:3–13. [PubMed: 18267055]
- Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: a review. *Eur J Cancer Care (Engl)*. 2001; 10:245–255. [PubMed: 11806675]
- Ancoli-Israel S. Recognition and treatment of sleep disturbances in cancer. *J Clin Oncol*. 2009; 27:5864–5866. [PubMed: 19884528]
- Carney S, Koettters T, Cho M, et al. Differences in sleep disturbance parameters between oncology outpatients and their family caregivers. *J Clin Oncol*. 2011; 29:1001–1006. [PubMed: 21282549]

5. Fiorentino L, Ancoli-Israel S. Insomnia and its treatment in women with breast cancer. *Sleep Med Rev.* 2006; 10:419–429. [PubMed: 16963293]
6. Fiorentino L, Ancoli-Israel S. Sleep dysfunction in patients with cancer. *Curr Treat Options Neurol.* 2007; 9:337–346. [PubMed: 17716597]
7. Flynn KE, Shelby RA, Mitchell SA, et al. Sleep-wake functioning along the cancer continuum: focus group results from the Patient-Reported Outcomes Measurement Information System (PROMIS®). *Psychooncology.* 2010; 19:1086–1093. [PubMed: 20013938]
8. Forsythe LP, Helzlsouer KJ, MacDonald R, Gallicchio L. Daytime sleepiness and sleep duration in long-term cancer survivors and non-cancer controls: results from a registry-based survey study. *Support Care Cancer.* 2012; 20:2425–2432. [PubMed: 22218738]
9. Liu L, Ancoli-Israel S. Sleep disturbances in cancer. *Psychiatr Ann.* 2008; 38:627–634. [PubMed: 21243092]
10. Zee PC, Ancoli-Israel S. Does effective management of sleep disorders reduce cancer-related fatigue? *Drugs.* 2009; 69(Suppl 2):29–41. [PubMed: 20047349]
11. Dirksen SR, Epstein DR. Efficacy of an insomnia intervention on fatigue, mood and quality of life in breast cancer survivors. *J Adv Nurs.* 2008; 61:664–675. [PubMed: 18302607]
12. Palesh O, Aldridge-Gerry A, Ulusakarya A, et al. Sleep disruption in breast cancer patients and survivors. *J Natl Compr Canc Netw.* 2013; 11:1523–1530. [PubMed: 24335687]
13. Omachi TA. Measures of sleep in rheumatologic diseases: Epworth Sleepiness Scale (ESS), Functional Outcome of Sleep Questionnaire (FOSQ), Insomnia Severity Index (ISI), and Pittsburgh Sleep Quality Index (PSQI). *Arthritis Care Res (Hoboken).* 2011; 63(Suppl 11):S287–S296. [PubMed: 22588751]
14. Savard MH, Savard J, Simard S, Ivers H. Empirical validation of the Insomnia Severity Index in cancer patients. *Psychooncology.* 2005; 14:429–441. [PubMed: 15376284]
15. Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology.* 2008; 108:812–821. [PubMed: 18431116]
16. Silva GE, Vana KD, Goodwin JL, et al. Identification of patients with sleep disordered breathing: comparing the four-variable screening tool, STOP, STOP-Bang, and Epworth Sleepiness Scales. *J Clin Sleep Med.* 2011; 7:467–472. [PubMed: 22003341]
17. Buchfuhrer MJ. Strategies for the treatment of restless legs syndrome. *Neurotherapeutics.* 2012; 9:776–790. [PubMed: 22923001]
18. Moyer DE, Zayas-Bazan J, Reese G. Restless legs syndrome: diagnostic time-savers, Tx tips. *J Fam Pract.* 2009; 58:415–423. [PubMed: 19679021]
19. Antonescu-Turcu A, Parthasarathy S. CPAP and bi-level PAP therapy: new and established roles. *Respir Care.* 2010; 55:1216–1229. [PubMed: 20800002]
20. Ballard RD. Management of patients with obstructive sleep apnea. *J Fam Pract.* 2008; 57:S24–S30. [PubMed: 18687236]
21. Weingarten JA, Basner RC. Advances in the management of adult obstructive sleep apnea. *F1000 Med Rep.* 2009; 1
22. Bassetti CL, Bornatico F, Fuhr P, et al. Pramipexole versus dual release levodopa in restless legs syndrome: a double blind, randomised, cross-over trial. *Swiss Med Wkly.* 2011; 141:w13274. [PubMed: 22101745]
23. Ferini-Strambi L, Aarskog D, Partinen M, et al. Effect of pramipexole on RLS symptoms and sleep: a randomized, double-blind, placebo-controlled trial. *Sleep Med.* 2008; 9:874–881. [PubMed: 18952497]
24. Kaplan PW, Allen RP, Buchholz DW, Walters JK. A double-blind, placebo-controlled study of the treatment of periodic limb movements in sleep using carbidopa/levodopa and propoxyphene. *Sleep.* 1993; 16:717–723. [PubMed: 8165385]
25. Manconi M, Ferri R, Zucconi M, et al. Pramipexole versus ropinirole: polysomnographic acute effects in restless legs syndrome. *Mov Disord.* 2011; 26:892–895. [PubMed: 21370262]
26. Montplaisir J, Nicolas A, Denesle R, Gomez-Mancilla B. Restless legs syndrome improved by pramipexole: a double-blind randomized trial. *Neurology.* 1999; 52:938–943. [PubMed: 10102409]



27. Oertel WH, Stiasny-Kolster K, Bergtholdt B, et al. Efficacy of pramipexole in restless legs syndrome: a six-week, multicenter, randomized, double-blind study (effect-RLS study). *Mov Disord.* 2007; 22:213–219. [PubMed: 17133582]
28. Trenkwalder C, Garcia-Borreguero D, Montagna P, et al. Ropinirole in the treatment of restless legs syndrome: results from the TREAT RLS 1 study, a 12 week, randomised, placebo controlled study in 10 European countries. *J Neurol Neurosurg Psychiatry.* 2004; 75:92–97. [PubMed: 14707315]
29. Walters AS, Ondo WG, Dreykluft T, et al. Ropinirole is effective in the treatment of restless legs syndrome. TREAT RLS 2: a 12-week, double-blind, randomized, parallel-group, placebo-controlled study. *Mov Disord.* 2004; 19:1414–1423. [PubMed: 15390050]
30. Wilt TJ, MacDonald R, Ouellette J, et al. Pharmacologic therapy for primary restless legs syndrome: a systematic review and meta-analysis. *JAMA Intern Med.* 2013; 173:496–505. [PubMed: 23460396]
31. Hornyak M, Scholz H, Kohnen R, et al. What treatment works best for restless legs syndrome? Meta-analyses of dopaminergic and non-dopaminergic medications. *Sleep Med Rev.* 2013
32. Morgenthaler T, Kramer M, Alessi C, et al. Practice parameters for the psychological and behavioral treatment of insomnia: an update. An American Academy of Sleep Medicine report. *Sleep.* 2006; 29:1415–1419. [PubMed: 17162987]
33. Morgenthaler TI, Kapur VK, Brown T, et al. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. *Sleep.* 2007; 30:1705–1711. [PubMed: 18246980]
34. Insomnia: assessment and management in primary care. National Heart, Lung, and Blood Institute Working Group on Insomnia. *Am Fam Physician.* 1999; 59:3029–3038. [PubMed: 10392587]
35. Kupfer DJ, Reynolds CF 3rd. Management of insomnia. *N Engl J Med.* 1997; 336:341–346. [PubMed: 9011788]
36. Lippmann S, Mazour I, Shahab H. Insomnia: therapeutic approach. *South Med J.* 2001; 94:866–873. [PubMed: 11592743]
37. Cheville AL, Kollasch J, Vandenberg J, et al. A home-based exercise program to improve function, fatigue, and sleep quality in patients with stage IV lung and colorectal cancer: a randomized controlled trial. *J Pain Symptom Manage.* 2013; 45:811–821. [PubMed: 23017624]
38. Mishra SI, Scherer RW, Geigle PM, et al. Exercise interventions on health-related quality of life for cancer survivors. *Cochrane Database Syst Rev.* 2012; 8:CD007566. [PubMed: 22895961]
39. Mishra SI, Scherer RW, Snyder C, et al. Exercise interventions on health-related quality of life for people with cancer during active treatment. *Cochrane Database Syst Rev.* 2012; 8:CD008465. [PubMed: 22895974]
40. Mustian KM, Sprod LK, Janelsins M, et al. Multicenter, randomized controlled trial of yoga for sleep quality among cancer survivors. *J Clin Oncol.* 2013; 31:3233–3241. [PubMed: 23940231]
41. Payne JK, Held J, Thorpe J, Shaw H. Effect of exercise on biomarkers, fatigue, sleep disturbances, and depressive symptoms in older women with breast cancer receiving hormonal therapy. *Oncol Nurs Forum.* 2008; 35:635–642. [PubMed: 18591167]
42. Rogers LQ, Fogleman A, Trammell R, et al. Effects of a physical activity behavior change intervention on inflammation and related health outcomes in breast cancer survivors: pilot randomized trial. *Integr Cancer Ther.* 2013; 12:323–335. [PubMed: 22831916]
43. Van Gerpen RE, Becker BJ. Development of an evidence-based exercise and education cancer recovery program. *Clin J Oncol Nurs.* 2013; 17:539–543. [PubMed: 24080053]
44. Bootzin RR, Perlis ML. Nonpharmacologic treatments of insomnia. *J Clin Psychiatry.* 1992; 53(Suppl):37–41. [PubMed: 1613018]
45. Espie CA, Fleming L, Cassidy J, et al. Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer. *J Clin Oncol.* 2008; 26:4651–4658. [PubMed: 18591549]
46. Epstein DR, Dirksen SR. Randomized trial of a cognitive-behavioral intervention for insomnia in breast cancer survivors. *Oncol Nurs Forum.* 2007; 34:E51–E59. [PubMed: 17878117]
47. Gielissen MF, Verhagen S, Witjes F, Bleijenberg G. Effects of cognitive behavior therapy in severely fatigued disease-free cancer patients compared with patients waiting for cognitive

- behavior therapy: a randomized controlled trial. *J Clin Oncol.* 2006; 24:4882–4887. [PubMed: 17050873]
48. Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: sleep and psychological effects. *J Clin Oncol.* 2005; 23:6083–6096. [PubMed: 16135475]
  49. Nakamura Y, Lipschitz DL, Kuhn R, et al. Investigating efficacy of two brief mind-body intervention programs for managing sleep disturbance in cancer survivors: a pilot randomized controlled trial. *J Cancer Surviv.* 2013; 7:165–182. [PubMed: 23338490]
  50. National Institutes of Health. National Institutes of Health State of the Science Conference statement on Manifestations and Management of Chronic Insomnia in Adults, June 13–15, 2005. *Sleep.* 2005; 28:1049–1057. [PubMed: 16268373]
  51. Neubauer DN. The evolution and development of insomnia pharmacotherapies. *J Clin Sleep Med.* 2007; 3:S11–S15. [PubMed: 17824496]
  52. Kim SW, Shin IS, Kim JM, et al. Effectiveness of mirtazapine for nausea and insomnia in cancer patients with depression. *Psychiatry Clin Neurosci.* 2008; 62:75–83. [PubMed: 18289144]

**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.

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The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) are a statement of consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult the NCCN Guidelines<sup>®</sup> is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment. The National Comprehensive Cancer Network<sup>®</sup> (NCCN<sup>®</sup>) makes no representation or warranties of any kind regarding their content, use, or application and disclaims any responsibility for their applications or use in any way. The full NCCN Guidelines for Survivorship are not printed in this issue of *JNCCN* but can be accessed online at [NCCN.org](http://NCCN.org).

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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<sup>a</sup>
  - ▶ Do you snore, gasp for breath, or stop breathing during sleep?
- Restless legs syndrome (RLS)<sup>a</sup>
  - ▶ Do you have the urge to move the legs, usually accompanied by an uncomfortable, deep-seated sensation that is brought on by rest?
- Parasomnias<sup>a,b</sup>
  - ▶ Do you sleep walk, wake up screaming, or have violent movements during sleep?

No concerns for sleep disorder/disturbance

Reevaluate at subsequent visits/post-therapy

Concerns for sleep disorder/disturbance

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)

- Sleep disturbance and/or excessive sleepiness
  - ▶ Narcolepsy and other hypersomnias
  - ▶ Obstructive sleep apnea<sup>a</sup>
  - ▶ RLS<sup>a,c</sup>
  - ▶ Circadian rhythm sleep disorders<sup>a,b</sup>
  - ▶ Parasomnias<sup>a,b</sup>

See SSD-2

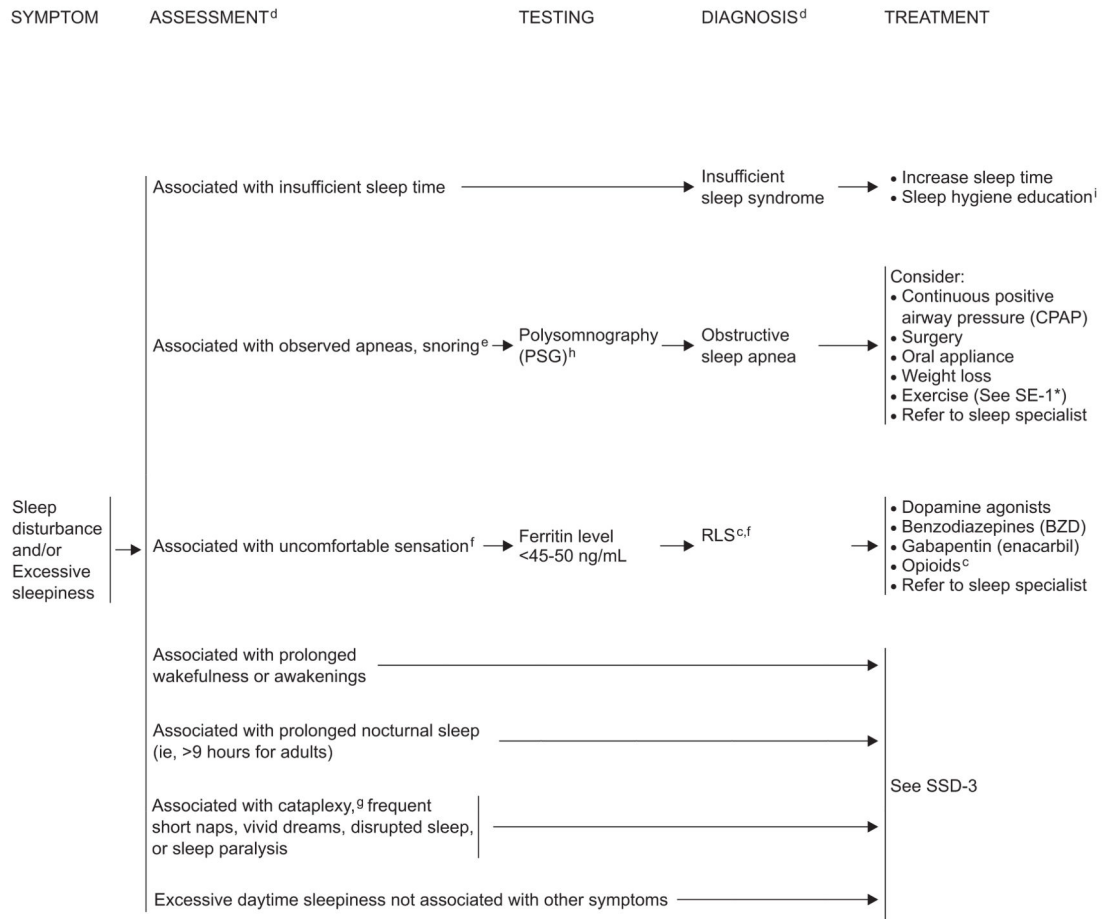
- Insomnia symptoms (difficulty falling asleep and/or maintaining sleep):
  - Duration >4 weeks
  - Occurring at least 3 times per week

See SSD-4

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

<sup>a</sup>Note that obstructive sleep apnea, RLS, circadian rhythm sleep disorders, and parasomnia may also present with symptoms of insomnia.  
<sup>b</sup>For circadian rhythm sleep disorders and parasomnias, refer to a sleep specialist.  
<sup>c</sup>RLS is also known as *Willis-Ekbom disease*.

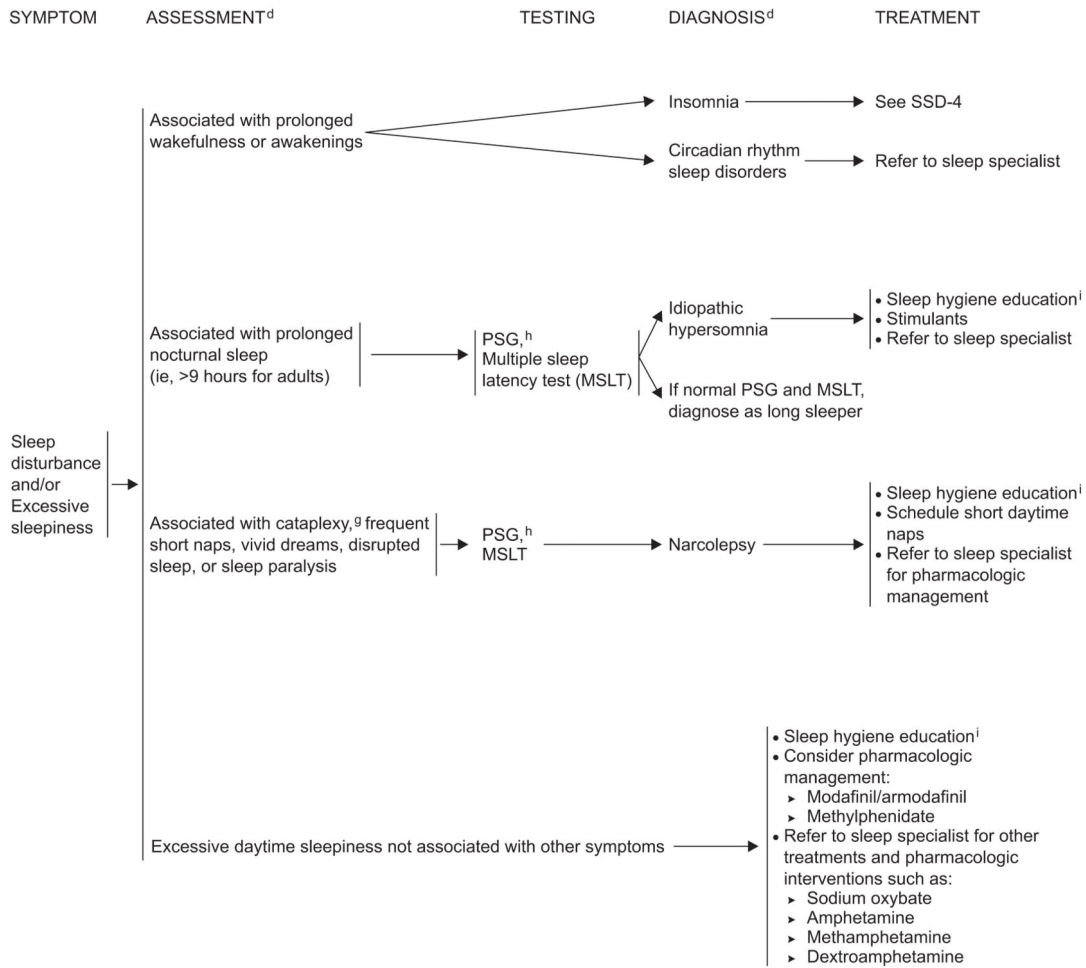
SSD-1



\*To view the most recent version of these guidelines, visit NCCN.org.

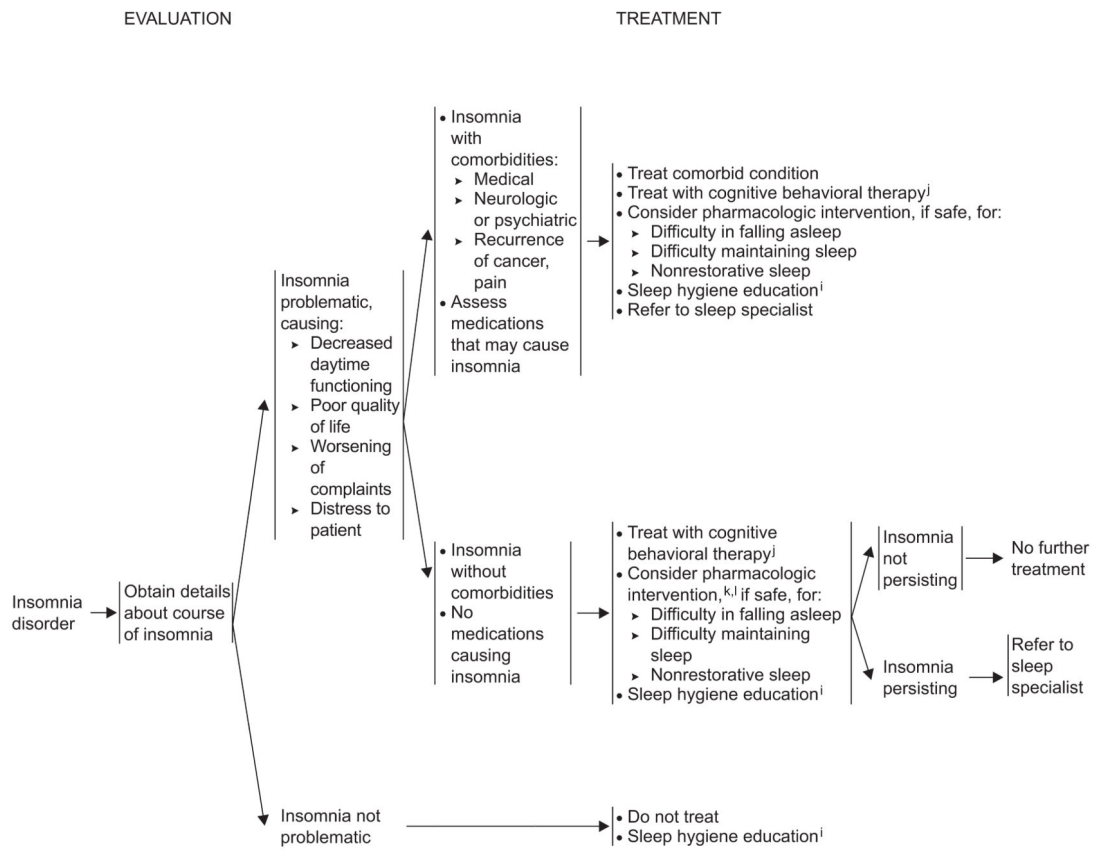
<sup>c</sup>RLS is also known as *Willis-Ekbom disease*.  
<sup>d</sup>For other less frequent syndromes, refer to sleep specialist.  
<sup>e</sup>See STOP Questionnaire: A Tool to Screen Patients for Obstructive Sleep Apnea (SSD-A).  
<sup>f</sup>See Essential Diagnostic Criteria for Restless Legs Syndrome (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).

SSD-2



<sup>d</sup>For other less frequent syndromes, refer to sleep specialist.  
<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).

SSD-3



<sup>i</sup>See General Sleep Hygiene Measures (SSD-C).  
<sup>j</sup>See Cognitive Behavioral Treatments (SSD-D).  
<sup>k</sup>See Principles for Choosing an FDA-Approved Hypnotic (SSD-E).  
<sup>l</sup>See Other Commonly Used Medications For Insomnia (SSD-F).

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STOP Questionnaire: A Tool to Screen Patients for Obstructive Sleep Apnea (OSA)<sup>1,2</sup>

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<sup>3</sup>

- 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 urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching.
- The symptoms are more pronounced in the evening or night or may only occur in the evening or night.

<sup>1</sup>Reproduced and modified with permission from Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology* 2008;108:812-821.

<sup>2</sup>This screening tool and other similar tools are not diagnostic, but have been shown to be useful to assess risk for OSA.

<sup>3</sup>Reproduced with permission from Allen RP, Picchiotti D, Hening WA, et al. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med* 2003;4:101-119.

SSD-A

SSD-B

GENERAL SLEEP HYGIENE MEASURES<sup>1,2,3</sup>

- 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<sup>4</sup>

STRATEGY	GOAL
Cognitive therapy	<ul style="list-style-type: none"> <li>• Challenge patient's dysfunctional beliefs and misconceptions about sleep disturbances</li> <li>• Promote positive thoughts</li> </ul>
Relaxation training	<ul style="list-style-type: none"> <li>• Reduce physiologic and cognitive arousal at bedtime</li> <li>• Techniques include progressive muscular relaxation, transcendental meditation, yoga, biofeedback</li> </ul>
Sleep restriction	<ul style="list-style-type: none"> <li>• Improve sleep continuity by limiting time spent in bed and maintaining a regular sleep schedule</li> </ul>
Stimulus control	<ul style="list-style-type: none"> <li>• Associate the bed/bedroom as a place for sleep or sexual activity only</li> </ul>

<sup>1</sup>National Heart, Lung, and Blood Institute Working Group on Insomnia. Insomnia: Assessment and Management in Primary Care. 1998. Available at: [https://www.nhlbi.nih.gov/guidelines/archives/insom\\_pc/insom\\_pc\\_archive.pdf](https://www.nhlbi.nih.gov/guidelines/archives/insom_pc/insom_pc_archive.pdf). Accessed April 21, 2014.

<sup>2</sup>Kupfer DJ, Reynolds CF. Management of insomnia. N Engl J Med 1997;336:341-346

<sup>3</sup>Lippmann S, Mazour I, Shahab H. Insomnia: therapeutic approach. South Med J 2001;94:866-873.

<sup>4</sup>Data from Bootzin RR, Perlis ML. Nonpharmacologic treatments of insomnia. J Clin Psychiatry 1992;53(Suppl):37-41.

SSD-C

SSD-D

PRINCIPLES FOR CHOOSING AN FDA-APPROVED HYPNOTIC:<sup>1</sup>

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

<u>AGENT</u>	<u>HELPS WITH SLEEP INITIATION</u>	<u>INCREASES TOTAL SLEEP TIME</u>	<u>INDICATED FOR SLEEP ONSET AND MAINTENANCE</u>
Zolpidem	+	+	-
Zolpidem CR	+	+	+
Zaleplon	+	-	-
Eszopiclone	+	+	+
Ramelteon	+	+/-	-
Temazepam	+	+	+
Doxepin (3-6 mg)	-	+	+
Lorazepam	+	-	-

OTHER COMMONLY USED MEDICATIONS FOR INSOMNIA<sup>2</sup>

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<sup>3</sup>

- Trazodone
- Amitriptyline
- Trimipramine
- Mirtazapine
- Doxepin

Antihistamines<sup>3</sup>

- Diphenhydramine

Antiepileptics<sup>3</sup>

- Gabapentin
- Tiagabine

Atypical antipsychotics<sup>3</sup>

- Quetiapine

Nutritional/herbal supplements

- Melatonin
- Valerian

<sup>1</sup>Data from the Physicians' Desk Reference, 6th ed. Montvale, NJ: PDR Network, LLC; 2012.

<sup>2</sup>From Neubauer, D. Evolution and Development of Insomnia Pharmacotherapies. J Clin Sleep Med 2007;3(5 Suppl):S11-16. and National Institutes of Health State of the Science Conference Statement: Manifestations and Management of Chronic Insomnia in Adults June 13-15, 2005. Sleep 2005;28:1049-1057.

<sup>3</sup>Although they are commonly prescribed, antidepressants, antihistamines, antiepileptics, and antipsychotics have significant risks and should be used with caution.

SSD-E

SSD-F