

Insomnia Guideline

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Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

Major Changes as of December 2021

- Use of the **STOP-BANG** tool is recommended when sleep apnea is suspected and is required prior to referral to Sleep Medicine.
- The **Insomnia Severity Index (ISI)** tool is recommended for determining initial insomnia severity as well as for monitoring changes in insomnia over time. Prescribing medication is not recommended unless insomnia is severe (ISI score ≥ 22) or if behavioral treatments have not been successful.
- **Ramelteon** is no longer recommended as first-line treatment for the elderly because there is only weak evidence of its effectiveness over melatonin, and it is non-formulary for most patients.

Guideline Summary

- Insomnia may be concurrent with or caused by other medical conditions, which should be thoroughly evaluated before the diagnosis of insomnia is made. See Conditions to Rule Out/When to Refer, below.
- **Behavioral treatment is recommended as first-line treatment** for chronic insomnia and includes cognitive behavioral therapy for insomnia (CBT-I) and sleep hygiene.
- Complementary and alternative treatment options that are recommended for insomnia include acupuncture, mindfulness meditation, light box therapy, listening to music, and moderate exercise.
- Short-term (not to exceed 6 weeks) **pharmacologic treatment may be considered** if insomnia is severe (ISI score 22 or higher) or if behavioral treatment alone has been ineffective.
 - Melatonin
 - Trazodone
 - Doxepin
- The following pharmacologic treatments are **not** recommended for insomnia:
 - Benzodiazepines and Z-drugs
 - Diphenhydramine (Benadryl)
 - Cannabinoids (CBD or THC)
 - Clonidine
 - Amitriptyline or nortriptyline (may be helpful for patients who have both insomnia and depression)
- Changes in sleep patterns, such as difficulty in sleep initiation and reductions in total sleep time and sleep efficiency, are a normal part of the aging process.

Background

The recommendations in this guideline apply to adults aged 18 years or older. Pregnant patients are out of scope for this guideline; consider consultation with Women's Health.

This guideline is in alignment with the National Permanente Medical Group 2021 Practice Recommendations for Benzodiazepines & Non-Benzodiazepine Sedative-Hypnotics/Z drugs.

Insomnia is a sleep disorder characterized by difficulty falling and/or staying asleep for a month or longer. Individuals with insomnia may have one or more of the following symptoms:

- Difficulty falling asleep
- Waking up often during the night and having trouble going back to sleep
- Waking up too early in the morning
- Feeling tired upon waking

Acute insomnia is insomnia lasting 1–3 months.

Chronic insomnia is insomnia occurring at least 3 nights a week for more than 3 months (International Classification of Sleep Disorders 3rd edition 2014).

Conditions to Rule Out/When to Refer

Patients who report difficulty initiating sleep, difficulty maintaining sleep, waking too early, or experiencing non-restorative sleep should be assessed to evaluate for comorbid medical conditions, comorbid psychiatric disorders, use of medications that interfere with sleep, and other sleep disorders.

Patients should be encouraged to keep a sleep diary—such as this one from the [Sleep Foundation](#)—for 1 to 2 weeks to help identify sleep-wake times, general patterns, and day-to-day variation.

Comorbid medical conditions

Identify any underlying medical conditions—such as pulmonary disease, heart failure, or chronic pain—that may be interfering with the patient's sleep, and treat as indicated prior to initiating treatment for insomnia.

Comorbid psychiatric disorders

Identify any psychiatric disorders—such as depression, anxiety, post-traumatic stress disorder and substance abuse—that may be interfering with the patient's sleep. It is important to **screen the patient for depression, substance use, and alcohol use** using the MHW Screening Tool, as about 1 in 3 patients reporting insomnia have co-occurring psychiatric illness (typically depression or anxiety) and 1 in 6 have alcohol- or drug-induced sleep problems.

Consider a referral to an **integrated mental health social worker** for any of the following:

- Patient is interested in cognitive behavioral therapy.
- Patient exhibits significant anxiety and/or depression in addition to insomnia.
- Patient is using alcohol or illicit drugs.

Use of medications that may interfere with sleep

It is also important to **review the patient's current medications**. Table 1 (next page) lists medications that may interfere with sleep.

- Medication effects on sleep are complex. Medications can cause sleep disturbances via:
 - Stimulating or activating properties
 - Changes in sleep architecture (e.g., slow wave sleep and REM suppression)
 - Physiological changes (e.g., increased urination)
- Medication effects on sleep vary greatly by individual. For example, some patients who take fluoxetine report insomnia as an adverse effect, whereas other patients experience daytime somnolence.
- For patients who are having difficulty falling or staying asleep, consider:
 - The time of day the patient takes the medication
 - Whether there is an appropriate alternative
- For patients who are experiencing medication withdrawal effects, advise that the related sleep disturbance is temporary.

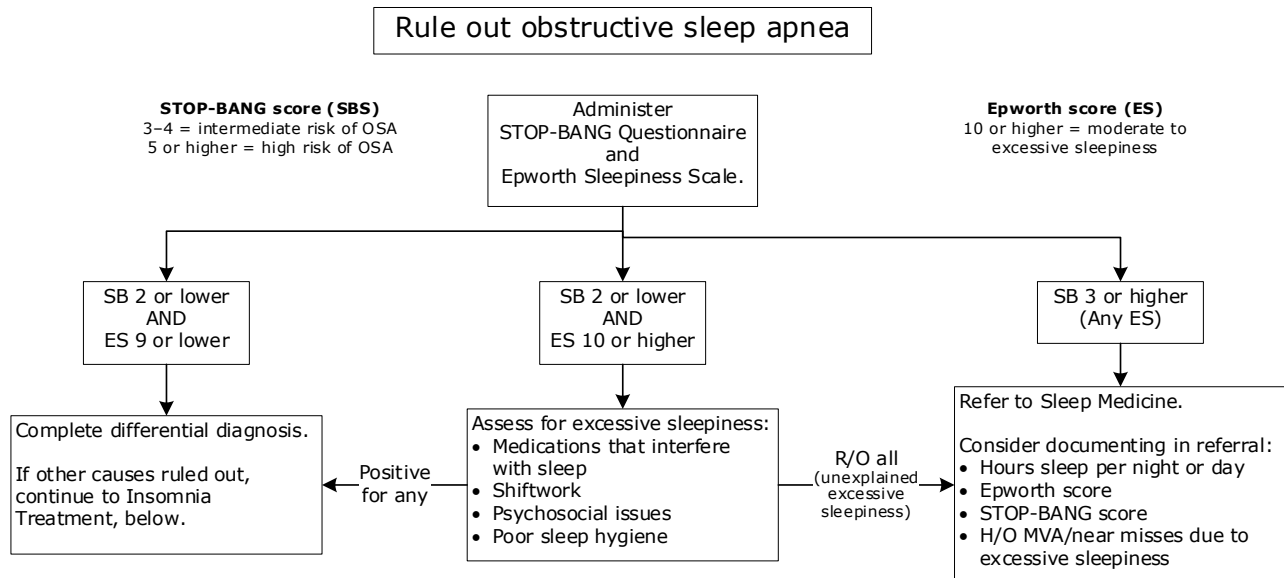
Table 1. Medications that may interfere with sleep

Drug class	Difficulty falling asleep	Difficulty staying asleep	Medication withdrawal effects
Albuterol	X	X	
Alpha-receptor agonists			X
Antidepressants: SSRIs, SNRIs, bupropion	X (particularly fluoxetine, venlafaxine, duloxetine, bupropion)	X	X
Beta-blockers		X	X
Corticosteroids	X	X	
Diuretics		X	
Opioids			X
Stimulants (see below)	X	X	

Patients taking stimulant medication

- Consider taking stimulant earlier in the day or a shorter-acting formulation to minimize evening exposure.
- Sleep hygiene and relaxation therapies may be beneficial for children with ADHD.
- Clonidine is not recommended for stimulant-induced insomnia due to a lack of evidence of safety or effectiveness.

Suspected obstructive sleep apnea



Other suspected sleep disorders

Within KPWA, see the **Sleep Medicine Quick Care Guide** prior to referral.

Consider a referral to **Sleep Medicine** for any of the following:

- Acting out dreams
- Sleepwalking
- Narcolepsy
- Shifted sleep schedule (delayed sleep phase, shift work)
- Restless leg syndrome

Insomnia Treatment

Assessing insomnia severity

The Insomnia Severity Index (ISI) is recommended for determining initial insomnia severity and for monitoring changes in insomnia over time. The seven-question ISI is available as a KP HealthConnect documentation flowsheet and asks patients to subjectively rate aspects of their insomnia, such as impact on daily activities and their level of anxiety about it.

The ISI is a primary measure of the severity of insomnia used to monitor changes in symptoms over time; it is not intended to be used for diagnosis. One study (Yang 2009) found that a 6-point reduction in ISI score represents a clinically meaningful improvement in insomnia. The ISI is useful for evaluating whether behavioral and pharmacologic treatment has improved a patient's insomnia symptoms.

Insomnia Severity Index

1. In the past 2 weeks, have you experienced difficulty falling asleep? (none, mild, moderate, severe, very severe)
2. In the past 2 weeks, have you experienced difficulty staying asleep? (none, mild, moderate, severe, very severe)
3. In the past 2 weeks, have you experienced problems with waking up too early? (none, mild, moderate, severe, very severe)
4. How SATISFIED/DISSATISFIED are you with your current sleep pattern? (very satisfied, satisfied, moderately satisfied, dissatisfied, very dissatisfied)
5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life? (not at all noticeable, a little, somewhat, much, very much noticeable)
6. How WORRIED/DISTRESSED are you about your current sleep problem? (not at all worried, a little, somewhat, much, very much worried)
7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g., daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood) CURRENTLY? (not at all interfering, a little, somewhat, much, very much interfering).

Normal sleep pattern changes in healthy elderly individuals

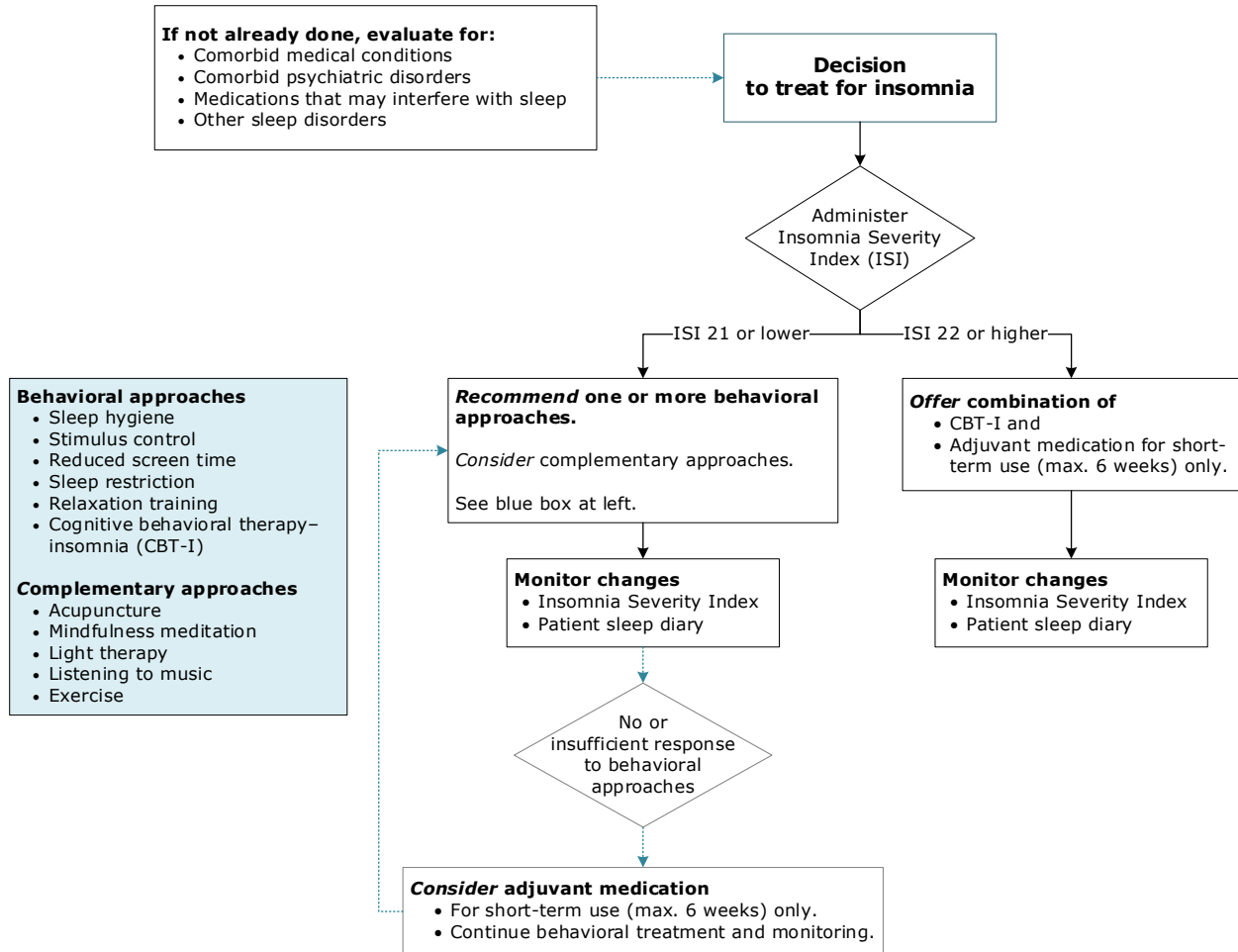
It is important to set expectations with patients about the normal changes in sleep patterns that occur in healthy elderly individuals. These changes include:

- More difficulty with sleep initiation
- Reduced total sleep time and sleep efficiency
- Decreased delta wave or slow wave sleep
- Increased sleep fragmentation
- Increased time spent in bed awake after retiring
- Changes in circadian rhythm that cause sleepiness in the early evening and earlier waking
- Increased frequency of daytime naps, which makes it harder to sleep at night

Approach to insomnia treatment

The following approach is recommended for treatment of insomnia. **Note that prescribing medication is only appropriate if insomnia is severe (ISI score ≥ 22) or if behavioral treatments have not been successful.**

The SmartPhrase **.AVSINSOMNIAPTINFO** provides an overview of insomnia therapies for patients.



Special populations

Perimenopausal patients

- Recommended therapeutic options include CBT-I and moderate exercise.
- Treatment options with limited or insufficient evidence include low-dose hormonal therapy, herbal medications, and soy.
- **Note:** Perimenopausal hot flashes must be treated separately from insomnia.

Shift workers

- To promote daytime sleep, recommendations include: modifying the sleep environment by using blackout shades and reducing ambient noise with a white noise machine; minimizing exposure to light on the way home; and going directly to sleep to prevent activating wakefulness.
- To promote a regular sleep schedule with a stable circadian rhythm, recommended schedule adjustments include: limiting the number of night shifts worked in a row to 4 or fewer, taking 48 hours off work after a string of night shifts, and avoiding frequently rotating shifts.
- Advise patients to get enough sleep on days off and adjust to a slightly later bedtime (1–2 hours later) on the 2 days before the start of night shifts.

Behavioral treatment

Behavioral therapy is recommended as the initial treatment for insomnia. There is good evidence that behavioral therapy is effective in treating insomnia and that the improvement gained is long-term.

Behavioral strategies can include:

- Sleep hygiene
- Stimulus control
- Reducing screen time
- Sleep restriction
- Relaxation training
- Cognitive behavioral therapy – insomnia (CBT-I)

Sleep hygiene

Sleep hygiene focuses on teaching good sleeping habits to patients (e.g., keeping a regular schedule, exercising during the day, avoiding napping) and can help to identify and address specific habits, behaviors, and environmental factors that can impact sleep.

- Create a bedtime routine. Get ready for bed, get into bed, and get up at the same time every day, even on weekends. Establishing a routine helps regulate your inner clock. Try not to take naps during the day.
- Avoid too much mental or physical stimulation an hour or so before going to bed. Don't finish office work or get into a big discussion about finances or other stressful topics right before getting ready to sleep. For many people, this includes reducing screen time before bed.
- Get some exercise each day. You might find that exercising 3 to 4 hours before going to bed helps you to sleep better. However, don't exercise vigorously later than 3 hours before your bedtime.
- Follow a healthy diet. Don't drink beverages that have caffeine, even soft drinks, after 2 p.m. Drinking alcohol, using tobacco, and taking certain medicines can also make it hard to fall asleep. If you drink alcohol before bed, you might have periods of wakefulness during the night, after the alcohol wears off.

Stimulus control

Stimulus control helps the patient to form a positive, clear association between the bed and sleep, and to establish a stable sleep-wake schedule.

- Take time to relax before getting into bed. Doing something you enjoy, like reading, taking a warm bath, or using other relaxation techniques can reduce stress and quiet your mind for sleep.
- Your bedroom should be cool, dark, and quiet for sleeping. If street lights shine in your room, or you need to sleep during the day because of your work schedule, put room-darkening shades, blinds, or drapes on the windows.
- Your bedroom should be as quiet as possible. If you can't block outside noise, cover it up with familiar inside sounds, like the steady hum of a fan.
- Move the clock away from your bed so you can't see it easily. Try putting it out of sight, such as safely on the floor, so you can still hear the alarm when it goes off.
- If you share your room or bed with someone who is restless, snores, keeps the light on late for reading, or steals your covers, arrange to sleep separately until you establish a regular sleeping pattern.
- Only use your bedroom for sleeping and sexual activity. Don't use your bedroom for working, having discussions, watching TV, or using your computer.
- If, after 30 minutes of trying, you have trouble falling asleep or getting back to sleep, get up and leave the room for a while. Doing something relaxing in another room, such as reading or listening to calming music, might help you feel sleepy so you can go back to bed.

Reducing screen time

Observational studies show an association between screen time and mobile phone use during the day or at bedtime and an increase in sleep disturbances among school age children, adolescents, and adults. Limiting screen exposure 2 hours before bedtime is recommended to minimize any harmful effects on sleep and well-being. There is no evidence that blue light modulation provides any benefit in decreasing sleep problems related to screen time.

Sleep restriction

The goal of sleep restriction is to increase sleep efficiency as close to 100% as possible, so that most of the time in bed is spent sleeping versus lying awake or tossing and turning. Current baseline sleeping time is recorded in sleep logs (e.g., of the 8 hours spent in bed, 5 hours were restful sleep). Then the patient restricts their total time in bed to their baseline sleeping time, staying up later at night but getting up at the same time each day. The purpose of this therapy is to increase the level of tiredness before sleep so that patients can break the mindset that they have difficulty falling asleep. Once a good sleep pattern is established, the amount of sleep can gradually be increased each night.

Relaxation training

Relaxation training includes techniques such as progressive muscle relaxation, guided imagery, and abdominal breathing. The purpose is to lower physical and mental stimulation that can interfere with sleep.

Cognitive behavioral therapy – insomnia (CBT-I)

CBT-I is a combination of cognitive therapy and behavioral treatments. The goal is to change unrealistic expectations and negative thoughts about sleep. There is evidence that CBT-I for insomnia is effective for adults, including perimenopausal women and the elderly.

Face-to-face CBT-I

Patients who are interested in CBT-I may be referred to Mental Health and Wellness for individual CBT-I treatment. However, availability of face-to-face CBT-I at KPWA is limited.

Online CBT-I

Online CBT-I may be an attractive option, as in-person access may be a significant barrier to care. Evidence suggests that internet-delivered CBT-I leads to improvements in sleep efficiency, sleep onset latency, total sleep time, and wake time after sleep, as well as improvements in depression and anxiety.

The effects were comparable to those found for face-to-face CBT-I and were generally maintained at 4–48 weeks follow-up.

Internet-delivered CBT-I programs include:

- CALM (free app for all Kaiser Permanente members): Use the .DIGITALSELFCARE SmartPhrase. Available in English and Spanish.
- CBTi coach (free app from Veterans Affairs) <https://mobile.va.gov/app/cbt-i-coach>
- CBT for Insomnia (\$) <https://www.cbtforinsomnia.com/>

Use .AVSINSOMNIA for additional resources.

Complementary/alternative therapy

- **Acupuncture** is recommended, used alone or with antidepressants, for improving the sleep quality of adults with depression-related insomnia. Acupuncture may also be effective for perimenopausal patients without depression.
- **Mindfulness meditation** is recommended for improving sleep quality.
- **Listening to music** is recommended for improving subjective sleep quality.
- **Light therapy** may have a small to moderate effect on improving some insomnia outcomes.
- **Exercise** is recommended for a minimum of 150 minutes per week at moderate intensity, preferably broken into 20- to 30-minute sessions, at least 5 days per week.

Adjunctive pharmacologic treatment

If insomnia is severe (ISI score \geq 22) or if behavioral treatments have not been successful, short-term (not to exceed 6 weeks) pharmacologic treatment may be considered.

Safety considerations and sleep outcomes of common insomnia medications

Table 2 provides information on potential benefits and safety considerations for the most commonly used medications for sleep and may be useful in conversations with patients who request specific medications, particularly those that are **not recommended** in this guideline. The table compares over the counter (OTC) medications, benzodiazepines and Z-drugs, and sedating antidepressants.

- Antidepressants show the greatest improvement in sleep length (sleep duration up to 80 minutes longer than with placebo).
- Improvement in sleep latency is similar for all pharmacologic options (sleep onset 10–20 minutes faster than with placebo).

Table 2. Safety considerations and sleep outcomes of common insomnia medications				
Medication	Category	Sleep latency¹	Sleep length²	Safety considerations³
Preferred medications for refractory insomnia (See Table 3.)				
Melatonin	OTC – supplement	7 min	8 min	No data on long-term use
Trazodone	Antidepressant	10 min	80 min	Orthostatic hypotension
Doxepin	Antidepressant	10 min	80 min	HRME Limit ≤ 6 mg/day if aged ≥ 65 years.
Medications that are <i>not</i> recommended for insomnia				
Ramelteon	Melatonin agonist	10–15 min	No difference	Somnolence, fatigue, dizziness, nausea, exacerbation of insomnia, abnormal thinking/behavioral changes (e.g., sleep driving)
Mirtazapine	Antidepressant	10 min	80 min	CNS depression, weight gain
Diphenhydramine	OTC – antihistamine	No change	11 min	HRME Limit use to 2–3 days. May impair physical or mental abilities
Doxylamine	OTC – antihistamine	Not available	Not available	HRME Limit use to 2–3 days. May impair physical or mental abilities
Temazepam	Benzodiazepine ⁴	15 min	33 min	Risk of next-day impairment, unawareness of activities during sleep (e.g., driving), fracture, falls, stroke
Zolpidem ⁵	Z-drug	22 min	11 min	HRME Risk of next-day impairment, unawareness of activities during sleep (e.g., driving), fracture, falls, stroke
¹ Reduction from placebo. ² Increase from placebo. ³ HRME = high-risk medication in the elderly. ⁴ The only benzodiazepines FDA approved for insomnia are temazepam, flurazepam, and triazolam. ⁵ Dosage adjustment is recommended for females; pharmacokinetic studies involving zolpidem showed a significant increase in maximum concentration and exposure in females compared to males at the same dose.				

Pharmacologic options for refractory insomnia in adults

Table 3 shows dosing information for medications that may be used for short-term relief of insomnia that has not improved with behavioral treatment. The medication treatment period should not exceed 6 weeks, as sleep studies have shown that sleep patterns return to pretreatment levels after only a few weeks of regular medication use.

Table 3. Recommended pharmacologic options for refractory insomnia in adults ¹				
Medication	Category	Initial dose ²	Older adult dose ²	Max. dose ²
Melatonin ³	OTC - supplement	3 mg	2 mg	5 mg
Trazodone ⁴	Antidepressant	25–50 mg	25–50 mg	200 mg
Doxepin ⁵	Antidepressant	3–6 mg (10 mg/mL oral solution)	3–6 mg (10 mg/mL oral solution)	10 mg
¹ Pharmacologic therapy is recommended for intermittent short-term use only. ² Doses are daily before bedtime. ³ First-line option for elderly and for general population. Best for advanced phase sleep disorders or circadian rhythm disorders. ⁴ Not FDA-approved for insomnia. ⁵ Preferred when insomnia is related to depression or anxiety. Contraindicated with glaucoma or urinary retention and during use of MAO inhibitors.				

A note about ramelteon: Ramelteon is an option for older adults as weak evidence shows that it may be more effective than melatonin due to a stronger binding affinity to the melatonin receptor. However, ramelteon is considered non-formulary for many patients at KPWA and may be more costly than over-the-counter melatonin. Advise patients to contact Member Services with coverage questions.

There is no evidence that ramelteon is superior to melatonin in other age groups.

Medications that are *not* recommended for insomnia due to harms or lack of evidence

Medications with insufficient evidence of efficacy

- Amitriptyline or nortriptyline: There is a lack of evidence to determine efficacy and safety for insomnia, but these medications may be helpful for patients who have both insomnia and depression. These agents also have some added risks because of anticholinergic activity. These agents are also considered HRME.
- Doxylamine
- Mirtazapine
- Supplements and herbals: 5-HTP, tryptophan, valerian, chamomile, hops, kava-kava, passionflower
- THC or CBD: Evidence is insufficient to recommend the use of THC or CBD for adult patients with insomnia. There is evidence that regular use of cannabis can lead to worsening depression. See the [KPWA Depression Guideline](#).

Medication that causes rebound insomnia and next-day performance impairment

- Diphenhydramine (Benadryl): The SmartPhrase .AVSBENADRYLNOTRECOMFORINSOMNIA provides information to patients on why diphenhydramine is not recommended.

Medications with significant harms

- Z-drugs
- Benzodiazepines

See the [KPWA Benzodiazepine and Z-drug Safety Guideline](#) for more information.

Adverse effects of benzodiazepines and Z-drugs include:

- Particularly high risk of overdose and death when combined with sedative drugs, such as opioids or alcohol
- Psychological or physical dependence, which can develop over a few weeks or months
- Tolerance to hypnotic effects, which can develop after only a few days of regular use
- Daytime somnolence
- Dizziness
- Impaired driving performance leading to an increased risk of road traffic accidents
- Depression and increased anxiety
- Slowness of mental processes and body movements
- Increased risk of mortality
- Increased risk of cognitive impairment and delirium
- Increased risk of falls and fractures, especially among older adults

Note: Z-drugs are not “safer” than benzodiazepines, and patients on benzodiazepines should not be switched to Z-drugs to try to improve safety.

Monitoring

Assess for improvement in insomnia severity using the Insomnia Severity Index (ISI, see p. 6). Do not continue any insomnia medication for longer than 6 weeks.

Evidence Summary

The Insomnia Guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

As part of our improvement process, the Kaiser Permanente Washington guideline team is working towards developing new clinical guidelines and updating the current guidelines every 2–3 years. To achieve this goal, we are adapting evidence-based recommendations from high-quality national and international external guidelines, if available and appropriate. The external guidelines should meet several quality standards to be considered for adaptation. They must: be developed by a multidisciplinary team with no or minimal conflicts of interest; be evidence-based; address a population that is reasonably similar to our population; and be transparent about the frequency of updates and the date the current version was completed.

In addition to identifying the recently published guidelines that meet the above standards, a literature search was conducted to identify studies relevant to the key questions that are not addressed by the external guidelines.

External guidelines meeting KPWA criteria for adaptation/adoption

- 2021 [Behavioral and psychological treatments for chronic insomnia disorder in adults: an American Academy of Sleep Medicine clinical practice guideline](#)
- 2021 [KP National Permanente Medical Groups Clinician Practice Recommendations for Benzodiazepines & Non-Benzodiazepine Sedative-Hypnotics/Z Drugs](#)
- 2019 [VA/DoD Clinical Practice Guidelines for the Management of Chronic Insomnia Disorder and Obstructive Sleep Apnea](#)
- 2019 [AGS 2019 Updated Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults](#)

Key questions addressed in the KPWA guideline

1. **What is the comparative effectiveness and safety of benzodiazepines and Z-drugs, cognitive behavioral therapy (CBT), and other alternative drugs or therapies used for the treatment of insomnia?**

The 2021 KP National guideline and the 2021 AASM guideline have been adopted. Low-quality evidence (Feng 2020) suggests that the effectiveness of CBT-I is comparable to that of hypnotics.

2. **What is the comparative effectiveness of internet-based cognitive behavioral therapy (CBT) and face-to-face cognitive behavioral therapy for insomnia (CBT-I) in improving sleep efficiency and reducing the severity of insomnia in the short and long term among adults? What is the effectiveness of video/telephone/internet-based CBT among adults with insomnia?**

The 2021 KP National guideline and the 2021 AASM guideline have been adopted. Low-quality evidence (Feng 2020) suggests that the effectiveness of CBT-I is comparable to that of hypnotics.

3. **What is the effectiveness and safety of tricyclic antidepressants (amitriptyline, nortriptyline) for the management of insomnia in adults?**

There is a lack of evidence to determine the efficacy and safety of amitriptyline or nortriptyline for insomnia.

4. **What is the effectiveness and safety of melatonin and ramelteon in managing insomnia in adults?**

Four systematic reviews (Jafari-Koulaee 2021, McCleery 2020, Baglioni 2020, Besag 2020) were assessed. Adult patients with insomnia with or without comorbidities were included in the studies. Dose and treatment duration varied. The findings indicated that melatonin may be effective (in sleep quality, total nocturnal sleep time, and sleep-onset latency) in the short term, but it is not clear if this is

clinically meaningful. Melatonin may be safe in the short term (≤ 4 weeks), but there is insufficient evidence to determine its safety in the long term.

There is low evidence (Baglioni 2020) showing that the short-term use of ramelteon was associated with improvement in some sleep parameters in patients with insomnia. The reported significant adverse effect of ramelteon was somnolence (based on evidence review 2018).

Adverse events were assessed in a systematic review (Besag 2020) wherein the authors found that melatonin was safe in the short term (≤ 4 weeks), with mild to moderate adverse effects that resolved without adjustment of the dose. Low-quality evidence suggests that CBT-I is more effective than melatonin.

5. What is the effectiveness and safety of acupuncture for the management of insomnia in adults?

Three systematic reviews and meta-analyses (Kim 2021, Zhao 2021, Zhang 2021) were reviewed. The population consisted of adult patients with primary or secondary insomnia. Included studies compared acupuncture to sham/placebo, no treatment, or hypnotics. Type of acupuncture and follow-up varied. The findings suggest acupuncture may be more effective than sham or hypnotics. It seems to be safe. However, the quality of the evidence is low. Better-quality studies are warranted. In one meta-analysis (Kim 2021), the findings were mixed at weeks 3 and 4.

6. What pharmacological and non-pharmacological therapies are effective and safe for managing insomnia in the elderly?

Four systematic reviews were appraised (Kwon 2020, Samara 2020, Chiu 2021, Sys 2020). The population consisted of elderly patients with insomnia. Non-pharmacological interventions or medications were compared to placebo, active controls, or wait list. The included studies were of low to very low quality, lowering the quality of the evidence overall. The findings did not change the conclusion of the KPWA evidence review performed in 2018. Therefore, no changes were made. AGS Beers criteria should be considered.

7. What are the adverse effects of Z-drugs for sleep disturbance in patients with dementia?

The evidence is insufficient. Only two observational studies (Richardson 2020, Richardson 2021) were reviewed. The population consisted of adult patients living with dementia and sleep disturbance. Interventions consisted primarily of Z-drugs, including zopiclone, zolpidem and zaleplon. Patients were secondarily exposed to benzodiazepines, low-dose tricyclic antidepressants, and antipsychotics. Follow-up varied.

The findings indicated that Z-drugs may increase the risk of fracture, and there was a dose-dependent pattern. Mortality risk increased with Z-drugs in this population, but this is not a causal association. Higher-dose Z-drugs (≥ 7.5 mg zopiclone) were associated with increased risks of fracture and stroke, similar or greater to that for higher-dose benzodiazepines. No impact on cognitive function was identified. The overall quality of the evidence is low.

8. What is the effectiveness and safety of clonidine and non-pharmacological treatment in managing stimulant-induced insomnia?

Evidence is lacking. There is a lack of high-quality evidence to determine the effectiveness and safety of clonidine and non-pharmacological treatment in managing stimulant-induced insomnia.

9. What is the effectiveness and safety of THC, CBD (THC versus CBD) in managing insomnia in adults?

A systematic review and meta-analysis of randomized controlled trials (RCTs) and non-RCTs (Bhagavan 2020) assessed the effects of cannabinoids on insomnia. Inclusion criteria were adults (≥ 18 years) with insomnia disorder in studies comparing cannabis-based products with the standard of care, placebo, or a sedative. Patients with primary and secondary insomnia were included, but

most patients had secondary insomnia. Average age was 47.7 years (range 18–72). Different orally administered cannabis-based products were included (THC at varying dose, nabilone, THC as add-on treatment in olive oil, CBD as adjunct treatment). Five studies (2 RCTs and 3 non-RCTs) representing 219 patients were included.

The findings suggested cannabinoids may improve sleep outcomes, including Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and sleep-onset latency. However, the quality of included studies was very low. Despite some efficacy, evidence is insufficient for or against the clinical use of THC or CBD for adult patients with insomnia.

References

- Baglioni C, Bostanova Z, Bacaro V, et al. A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials Evaluating the Evidence Base of Melatonin, Light Exposure, Exercise, and Complementary and Alternative Medicine for Patients with Insomnia Disorder. *J Clin Med*. 2020;9(6):1949. Published 2020 Jun 22. doi.org/10.3390/jcm9061949
- Besag FMC, Vasey MJ, Lao KSJ, Wong ICK. Adverse Events Associated with Melatonin for the Treatment of Primary or Secondary Sleep Disorders: A Systematic Review. *CNS Drugs*. 2019;33(12):1167-1186. doi.org/10.1007/s40263-019-00680-w
- Bhagavan C, Kung S, Doppen M, et al. Cannabinoids in the Treatment of Insomnia Disorder: A Systematic Review and Meta-Analysis. *CNS Drugs*. 2020;34(12):1217-1228. doi:10.1007/s40263-020-00773-x
- Chiu HY, Lee HC, Liu JW, et al. Comparative efficacy and safety of hypnotics for insomnia in older adults: a systematic review and network meta-analysis. *Sleep*. 2021;44(5):zsaa260. doi:10.1093/sleep/zsaa260
- Feng F, Zhang Y, Hou J, et al. Can music improve sleep quality in adults with primary insomnia? A systematic review and network meta-analysis. *Int J Nurs Stud*. 2018 Jan;77:189-196.
- Jafari-Koulaee A, Bagheri-Nesami M. The effect of melatonin on sleep quality and insomnia in patients with cancer: a systematic review study. *Sleep Med*. 2021;82:96-103. doi.org/10.1016/j.sleep.2021.03.040
- Kim SA, Lee SH, Kim JH, et al. Efficacy of Acupuncture for Insomnia: A Systematic Review and Meta-Analysis. *Am J Chin Med*. 2021;49(5):1135-1150. doi.org/10.1142/S0192415X21500543
- Kwon CY, Lee B, Cheong MJ, et al. Non-pharmacological Treatment for Elderly Individuals With Insomnia: A Systematic Review and Network Meta-Analysis. *Front Psychiatry*. 2021;11:608896. Published 2021 Jan 28. doi:10.3389/fpsy.2020.608896
- McCleery J, Sharpley AL. Pharmacotherapies for sleep disturbances in dementia. *Cochrane Database Syst Rev*. 2020;11(11):CD009178. Published 2020 Nov 15. doi.org/10.1002/14651858.CD009178.pub4
- Richardson K, Loke YK, Fox C, et al. Adverse effects of Z-drugs for sleep disturbance in people living with dementia: a population-based cohort study. *BMC Med*. 2020;18(1):351. Published 2020 Nov 24. doi:10.1186/s12916-020-01821-5
- Richardson K, Savva GM, Boyd PJ, et al. Non-benzodiazepine hypnotic use for sleep disturbance in people aged over 55 years living with dementia: a series of cohort studies. *Health Technol Assess*. 2021;25(1):1-202. doi:10.3310/hta25010
- Samara MT, Huhn M, Chiochia V, et al. Efficacy, acceptability, and tolerability of all available treatments for insomnia in the elderly: a systematic review and network meta-analysis. *Acta Psychiatr Scand*. 2020;142(1):6-17. doi:10.1111/acps.13201
- Sys J, Van Cleynebreugel S, Deschodt M, Van der Linden L, Tournoy J. Efficacy and safety of non-benzodiazepine and non-Z-drug hypnotic medication for insomnia in older people: a systematic literature review. *Eur J Clin Pharmacol*. 2020;76(3):363-381. doi:10.1007/s00228-019-02812-z
- Yang M, Morin CM, Schaefer K, Wallenstein GV. Interpreting score differences in the Insomnia Severity Index: using health-related outcomes to define the minimally important difference. *Curr Med Res Opin*. 2009 Oct;25(10):2487-2494.
- Zhang J, He Y, Huang X, Liu Y, Yu H. The effects of acupuncture versus sham/placebo acupuncture for insomnia: A systematic review and meta-analysis of randomized controlled trials. *Complement Ther Clin Pract*. 2020;41:101253. doi:10.1016/j.ctcp.2020.101253
- Zhao FY, Fu QQ, Kennedy GA, et al. Comparative Utility of Acupuncture and Western Medication in the Management of Perimenopausal Insomnia: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med*. 2021;2021:5566742. Published 2021 Apr 26. doi.org/10.1155/2021/5566742

Guideline Development Process and Team

Development process

The guideline team developed the Insomnia Guideline using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in December 2021.

Team

The Insomnia Guideline development team included representatives from the following specialties: family medicine, geriatrics, mental health and wellness, neurology, pharmacy, residency, and social work.

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