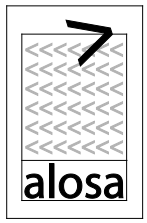
Insomnia: habits, help, and hazards



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These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient's clinical condition.

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Introduction

Insomnia is a common problem in the US, and a very frequent complaint brought to primary care physicians. It can result in decreased quality of life, lost productivity, and increased morbidity.[1] Older people are at particular risk of insomnia, partly because of age-related changes in sleep physiology. The elderly have lower sleep efficiency and spend less time in deep sleep, and have higher sleep latency (time to sleep onset). They also often have circadian rhythm disturbances, with earlier bedtimes and wake times. These sleep disturbances can result in excessive daytime sleepiness with an increased risk of fatigue and falls, and decreased memory and concentration. Insomnia leads to considerable health care utilization, with direct and indirect costs estimated to be $77 to $92 billion annually in the US, although it is difficult to discern the cost of the insomnia, versus the co-morbid conditions that often co-exist.[1]

Despite its high prevalence, morbidity, and costs, up to 50% of patients with sleep problems do not report insomnia symptoms to their physicians. Up to 85% of patients remain untreated,[2] or treat themselves with remedies of questionable efficacy and safety (such as alcohol and over-the-counter drugs).[3] A number of factors contribute to the rate of under-treatment of insomnia, including low reporting by patients, limited physician training, office time constraints, and misconceptions about the seriousness of insomnia, the advantages of addressing it, and the risks associated with sedatives.[4]

This document presents an evidence-based approach for the evaluation and management of insomnia, including a discussion of underlying conditions and medications that can cause or worsen insomnia.

Burden of disease

Epidemiology

One in three adults intermittently have sleep problems, and one in ten suffer from insomnia chronically.[1, 5, 6] It is most common in the elderly, where the prevalence is 25-35% in those >65 years old.[6] Despite its high prevalence, only 6% of Americans with insomnia symptoms report being diagnosed with insomnia, and only 4% report ever being treated for it.[7]

Risk factors

Risk factors for insomnia include:[5-7, 9, 10]

- female gender (women are 1.5 times more likely to report insomnia than men)
- increasing age
- medical comorbidities (listed)
- psychiatric comorbidities (listed later in the document)
- substance abuse

- emotional stress (e.g. separation from a partner, impaired social relationships)
- work-related conditions (e.g. unemployment, working at night, frequent major shifts in work hours)
- circadian rhythm disturbances (e.g., jet lag)
- low socioeconomic status

Consequences

Insomnia can cause excessive daytime sleepiness, irritability, and lethargy. Chronic insomnia can lead to depression, inattention, learning and memory problems, and underperformance at school or work.[6,7,11,12] Insomnia is associated with frequent use of medical services, increased drug use, and medical problems including heart disease, hypertension, and musculoskeletal problems.[5,6,8]

Definitions of insomnia

Diagnostic criteria

The International Classification of Sleep Disorders, 2nd Edition (ICSD-2) criteria for the diagnosis of insomnia are provided in the table below.[9,10]

Table 1. Criteria for the diagnosis of insomnia

A complaint of difficulty initiating sleep, difficulty maintaining sleep, or waking up too early, or sleep that is chronically non-restorative or poor in quality. Sleep difficulty occurs despite adequate opportunity and circumstances for sleep.
AND
At least one of the following forms of daytime impairment related to the nighttime sleep difficulty is reported by the patient: • Fatigue or malaise; • Attention, concentration, or memory impairment; • Social or vocational dysfunction or poor school performance; • Mood disturbance or irritability; • Daytime sleepiness; • Motivation, energy, or initiative reduction; • Proneness to errors/accidents at work or while driving; • Tension, headaches, or gastrointestinal symptoms in response to sleep loss; and • Concerns or worries about sleep.

Acute versus chronic insomnia

Acute insomnia is insomnia that lasts for less than 4 weeks and is usually caused by acute stressors such as:[9,10]

- situational stress (e.g., occupational, interpersonal, financial, medical)
- environmental stressors (e.g., noise, extreme temperatures, caring for a newborn)
- death or illness of a loved one
- disruption of the sleep/wake cycle (e.g., jet lag).

Chronic insomnia is insomnia that lasts for 4 weeks or more.[5,9,10] About 80% of patients with chronic insomnia will have a contributing comorbidity.[5,10]

Primary versus secondary (co-morbid) insomnia

Primary insomnia (also known as psychophysiologic insomnia) has been described as a disorder of somatized tension and learned sleep-preventing associations. Conditioned negative associations regarding sleep perpetuate difficulty sleeping and are exacerbated by the patient's concern about sleep.[9] Secondary insomnia is difficulty initiating and/or maintaining sleep due to a medical or psychiatric process.[6,9]

Evaluation of insomnia

Take a good history

Determining the frequency of sleep disruption and the degree to which it affects daytime function (e.g., work, mood, social life) is the most important guide to the need for further evaluation and treatment.[10] In order to determine the frequency, severity, and causes of the insomnia, assess the general medical, psychiatric, medication, and substance abuse history (Table 2) and obtain a thorough sleep history[7](Table 3).

Table 2. Medical/psychiatric conditions and medications that can cause insomnia [5, 9,10,12,13]

MEDICAL CONDITIONS	
Musculoskeletal • arthropathies	**Cardiovascular** • congestive heart failure
Respiratory • asthma • COPD	**Endocrine** • diabetes • hypo-/hyper-thyroidism • menopause
Neurologic • Parkinson's disease • stroke • traumatic brain injury	**Gastrointestinal** • gastroesophageal reflux disease • peptic ulcer disease
Other • benign prostatic hypertrophy • cancer • chronic pain syndromes • end-stage renal disease • HIV/AIDs	**Primary sleep disorders** • Circadian rhythm disorder • Sleep Apnea • Movement disorder (restless legs syndrome, periodic limb movement disorder) • Parasomnias (sleep walking/talking)

<table>
<tr><th colspan="2">PSYCHIATRIC CONDITIONS</th></tr>
<tr><td>anxiety disorders
bipolar disorder
schizophrenia</td><td>major depressive or dysthymic disorders
personality disorders
post-traumatic stress disorder</td></tr>
<tr><th colspan="2">MEDICATIONS / DRUGS</th></tr>
<tr><td>Recreational/lifestyle
alcohol
amphetamines
caffeine
cigarettes
nicotine (including replacement therapies)
cocaine</td><td>Hormones
thyroid hormone
oral contraceptives
progesterone
corticosteroids</td></tr>
<tr><td>Respiratory
bronchodilators (beta agonists)
theophylline</td><td>Cardiovascular
beta-blockers
alpha-receptor agonists and antagonists
atorvastatin
diuretics</td></tr>
<tr><td>Neurologic/psychotropic
CNS stimulants (methylphenidate, dextroamphetamine)
antiepileptics (lamotrigine, phenytoin)
antidepressants (SSRIs, SNRIs, bupropion, monoamine oxidase inhibitors). SSRIs can exacerbate restless legs syndrome.
levodopa</td><td>Analgesics
oxycodone
codeine
propoxyphene</td></tr>
<tr><td>Decongestants
pseudoephedrine
phenylephrine</td><td>Other
anticholinergic agents
antineoplastics
interferon alfa
quinidine</td></tr>
</table>

Table 3: Sample questions to obtain an adequate sleep history[9]

Evaluation category	Helpful questions	What the questions identify
What is the nature and severity of the problem?	• Do you have difficulty falling asleep? • Do you have difficulty staying asleep? • When you wake during the night do you have trouble getting back to sleep? • Do you take anything to help you sleep? • Does your insomnia affect your ability to function through the day?	These questions help categorize whether the problem is sleep onset vs. sleep maintenance, and assess the daytime consequences of the problem.
Is the sleep environment hostile to sleep?	• Is there anything in your home that disrupts your sleep such as infants, noise, lights, partner snoring, TV, pets? • Do you feel safe in your sleep environment?	Positive answers here indicate possible environmental interventions (see Treatment section).
Does the sleep routine perpetuate the conditioned insomnia?	• What time do you go to bed and try to sleep? • What time do you get out of bed for the day? • That represents xx hours in bed trying to sleep, is that correct? • Out of the total hours in bed, how many are you actually sleeping? • Do you go to bed and get up at the same time every day, including holidays and weekends? • How much sleep do you believe you need per night? • Do you fall asleep during the day or evening (watching TV, after eating)?	Positive answers here indicate that the patient may benefit from sleep hygiene and/or sleep restriction therapy (see Treatment section).
Does the patient have behaviors and/or beliefs that create arousal?	• Do you use/consume nicotine, caffeine, alcohol, or other stimulants (e.g. ginseng or Sudafed) prior to bedtime? • When you wake up in the night do you eat or smoke? • What is your pre-bedtime routine? (e.g., exercise, computer use, eating) • When you wake up at night do you watch or check the clock?	Positive answers here indicate that the patient may benefit from specific behavior-change strategies (see Treatment section).

Additional Diagnostic tools

In selected patients, additional diagnostic tools can help further define the insomnia. These are easily administered and interpreted by primary care physicians, and can easily be found on-line:

1. the Epworth Sleepiness Scale can assess the severity of daytime sleepiness (scale of 0-24; see Appendix 2, available at http://www.epworthsleepinessscale.com)
2. the Insomnia Screening Questionnaire can help diagnose the type (primary or secondary) and the causes of insomnia (Appendix 3, available at http://www.centreforsleep.com/assets/images/pdf/insomnia_assessment_guideline07.pdf)[9]
3. a 2-week sleep diary can identify sleep-wake times, general patterns, and day-to-day variability (Appendix 4, available at http://www.sleepeducation.com/pdf/sleepdiary.pdf)

Consider sleep studies in specific circumstances

Sleep studies should not be routinely used in the evaluation of insomnia in primary care.[5, 6] However, they may be useful in some patients with comorbidities associated with insomnia, or with signs and symptoms that strongly suggest specific sleep disorders (see below).[6, 9] These include reports (often from the bed partner) of very loud snoring accompanied by periods of gasping or apnea; or abnormal leg movements.

Polysomnography or Multiple Sleep Latency Test

The American Academy of Sleep Medicine recommends using polysomnography or a multiple sleep latency test (MSLT), or both, to evaluate patients with breathing disorders (such as sleep apnea), movement disorders (such as periodic limb movement disorder), or insomnia resistant to initial therapy.[6,9] Polysomnography is usually performed overnight in a sleep laboratory.[11] The test objectively records a number of sleep parameters, including sleep latency (time to get to sleep), sleep efficiency and the number and/or duration of awakenings during sleep.[5] Polysomnography may also record hemoglobin saturation, airflow at the nose and mouth, respiratory effort, and leg movements. The MSLT is conducted in a sleep laboratory after an overnight sleep study. The test involves a series of four 20-minute naps to measure daytime sleepiness and the onset of REM sleep.[6]

Sleep Actigraphy

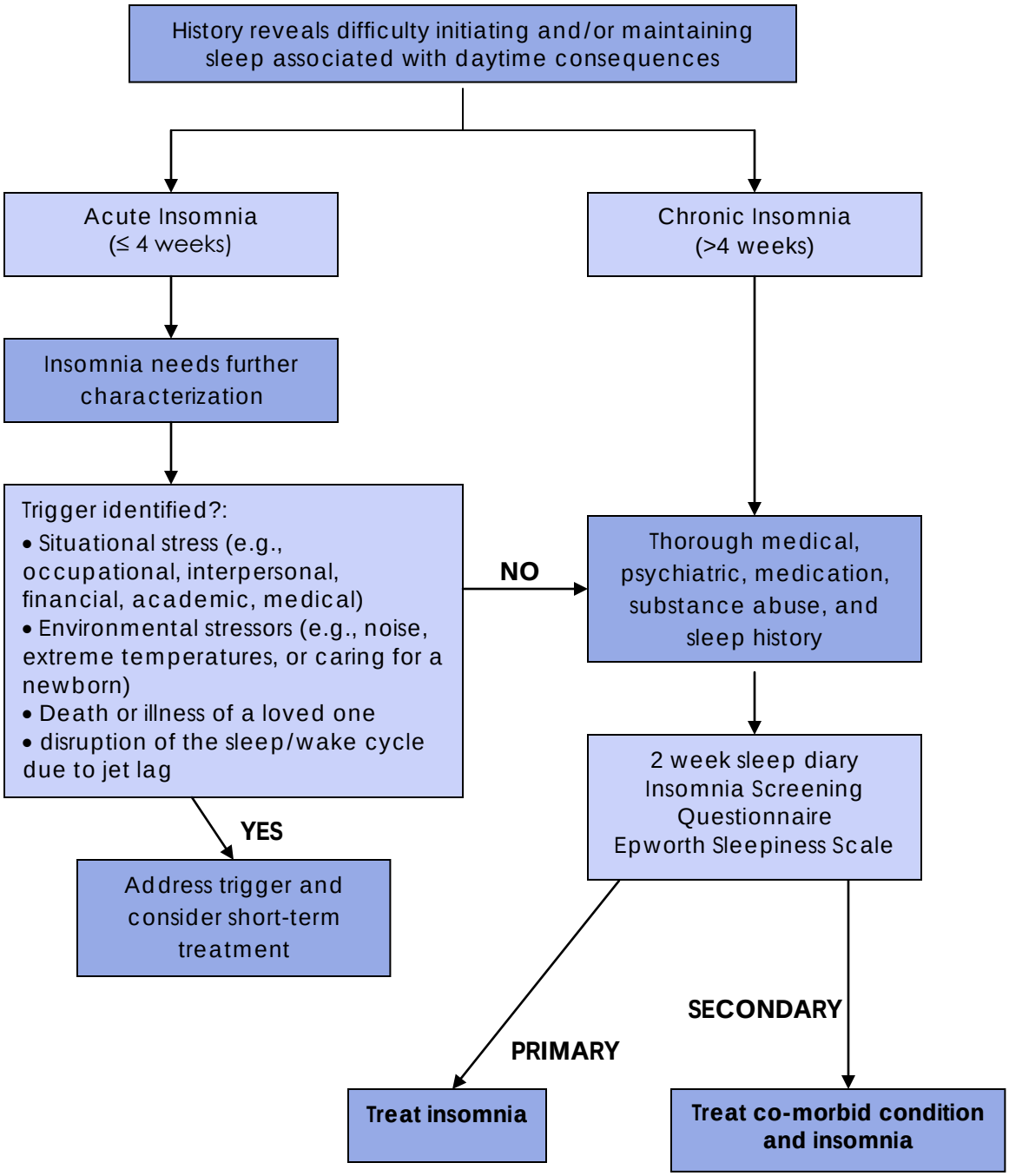
In this test, the patient wears a small, watch-like device around the wrist to record movement.[5, 6] The absence of movement for a given continuous period is consistent with sleep.[10] Actigraphy provides a recording of sleep patterns, but may underestimate insomnia severity in patients who remain inactive while awake. Sleep actigraphs are most often used in research settings,[6] but may be indicated to characterize circadian rhythm patterns in individuals with insomnia.[9]

Other testing

Other testing (e.g., laboratory, radiology) is not indicated for the routine evaluation of insomnia unless it is intended to evaluate other suspected comorbid conditions.[9]

Bottom line: Evaluation of insomnia should include a comprehensive sleep history and assessment of contributing medical/psychiatric conditions and medication use. Other helpful aids include a 2-week patient sleep diary, the Epworth sleepiness scale, and the Insomnia screening questionnaire. Sleep studies or other tests are not routinely needed for the evaluation of insomnia in primary care.

Algorithm for the diagnosis of insomnia



Non-pharmacological therapies

It was once thought that patients with secondary insomnia would not respond well to insomnia treatment. But patients with either primary or secondary insomnia can benefit from non-pharmacologic and pharmacologic therapies.[12] Most patients will benefit from non-drug approaches, discussed below. Those who don't respond adequately can then be considered for short term drug treatment.

The most common measures of sleep used in studies evaluating treatments include total sleep time, sleep latency (time to fall asleep), and sleep efficiency (the proportion of time asleep vs. total time in bed). Most effective interventions improve total sleep time and sleep latency by about 20-30 minutes (more detail below). Other less commonly reported measures of efficacy include wake after sleep onset, sleep quality, and next-day symptoms such as alertness, quality of life, or work functioning. Sleep parameters can be subjectively and objectively assessed, usually by sleep diary and polysomnography (PSG), respectively. Although objective measures do not depend on patient recall, subjective measures are more reflective of what is clinically relevant to the patient, and both are often reported in clinical trials. The following sections review the efficacy and safety of non-pharmacologic and pharmacologic interventions for insomnia.

Cognitive Behavioral Therapy (CBT):

When patients worry about not getting enough sleep, this worry can trigger increased arousal and further hinder sleep, creating a cycle of chronic insomnia. CBT helps patients understand and alleviate anxious thoughts about sleep, and addresses factors that can perpetuate the insomnia cycle regardless of the cause.[13] CBT is usually delivered as a "package" of interventions, with each individual intervention addressing a different component of the insomnia cycle. The efficacy of the individual components of CBT, as well as a CBT package of interventions is presented below. May kinds of behavioral therapy can be performed by a PCP, though some usually require referral to a sleep specialist.

CBT that can be delivered by PCPs

Sleep hygiene

External distractions and disruptions can reduce sleep quality or quantity; sleep hygiene education instructs patients how to change these external factors to enhance sleep quality and quantity (Table 4). Sleep hygiene alone has not been directly compared to control interventions. One small trial compared sleep hygiene to multi-component CBT and found improvements in both groups, but more so in the CBT group; sleep latency decreased 8 minutes in both groups, sleep efficiency increased 8% in CBT and 1% in sleep hygiene, and wake after sleep onset decreased 43 minutes in CBT, but did not change in the sleep hygiene group.[14] Sleep hygiene is not endorsed by the

American Association of Sleep Medicine (AASM) as a stand-alone therapy, but is often included as a component of CBT.[13]

Stimulus control

Insomnia is sometimes a maladaptive response to the bed/bedroom. Stimulus control retrains the patient to associate the bed/bedroom with sleep, and to become sleepy when lying down (Table 4). Several randomized trials have found significant improvements in sleep outcomes with stimulus control compared to placebo or wait-list controls. A recent trial randomized patients taking chronic insomnia medications to stimulus control (with or without medication withdrawal) or wait-list control and found significant improvements in most sleep outcomes and reduction in daytime sleepiness in the stimulus control groups.[12,15] Stimulus control is recommended as effective individual therapy by the AASM.[13]

Sleep restriction

Sometimes insomnia can be exacerbated by patients trying to "make up" lost sleep by spending extra non-sleep time in bed. Sleep restriction can increase sleep efficiency by reducing the amount of non-sleep time spent in bed (Table 4). Several randomized trials have found improvements in sleep parameters with sleep restriction compared to placebo. A recent trial found significant improvements in awake time after sleep onset (decreased from 67 to 38 minutes), but no improvements in daytime functioning.[12,16] A subsequent evidence-based review found sleep restriction therapy had the strongest evidence-base for efficacy in improving sleep parameters in older patients with insomnia, compared to all the other individual behavioral therapies.[17] This therapy is also recommended as effective individual therapy by the AASM.[13]

Table 4. Cognitive behavioral therapy (CBT) components that can be administered by a PCP

Component of CBT	Patient Instructions	Which patients benefit
Sleep hygiene and stimulus control*	• Set room temperature between 68-72°F • Restrict smoking, alcohol, caffeine, and exercise within 4-5 hours of bedtime • Remove bedroom distractions (i.e., bedside clock) • Remove bedroom disruptions (i.e., snoring partner, pets) • Do not nap • Only go to bed when sleepy • Maintain the same daily wake time (including weekends) • Use bed only for sleep and sex (not reading, eating, watching TV, etc.) • If unable to sleep within 20 minutes, get out of bed and do something relaxing in another room (and only return when sleepy)	• Those whose sleep is disturbed by external factors • Those who sleep better away from home • Those who do many other things in bed • Those with sleep onset insomnia
Sleep restriction	• To start, only allow the amount of time in bed that is *usually spent asleep* (but not <4 hours) • Do not nap • Record daily time in bed and daily time asleep • Once sleep efficiency is >85%, increase the time in bed 15 minutes a week, until sleep time is at least 7 hours and daytime somnolence is alleviated	• Those currently not severely sleep deprived • Those trying to reduce need for sleeping pills

* Handouts available at http://www.sleepeducation.com/Hygiene.asp

CBT delivered by specialists (**To locate a sleep center in your area that may offer these services or training: http://www.sleepcenters.org)

Paradoxical intention

Insomnia may result from the "performance anxiety" of trying to get to sleep; paradoxical intention improves this anxiety by paradoxically avoiding any active attempts to get to sleep. It is a cognitive technique intended to reduce sleep effort. Several randomized trials have found significant improvements in sleep parameters with paradoxical intention compared to placebo or wait list controls.[12] This therapy is also recommended as effective individual therapy by the AASM.[13]

Relaxation therapy

Insomnia may be associated with hyper-arousal, and physical and mental relaxation can reduce this arousal state. Several randomized trials have compared relaxation therapy to control therapy and found modest improvements in sleep parameters.[12] A meta-analysis found no significant difference in sleep latency, sleep efficiency or sleep quality between relaxation therapy and placebo, but relaxation therapy significantly improved total sleep time (by about 20 minutes).[5] Relaxation therapy is also recommended as effective individual therapy by the AASM.[13]

Cognitive therapy

Patients with insomnia can have inaccurate understandings of sleep expectations, or exaggerated fears about the effects of a poor night of sleep; cognitive therapy educates them about realistic sleep expectations, and teaches them to reduce the anxiety and negative expectations about the effects of a poor night of sleep. It can also help them understand and cope with anxious thoughts and worries that can hinder sleep onset or maintenance. No studies have evaluated the individual efficacy of cognitive therapy on sleep parameters.[12] Cognitive therapy is not recommended by the AASM as stand-alone therapy, but is often included as a component of CBT.[13]

Multi component CBT

In multi-component CBT, several behavioral therapies (such as sleep hygiene, stimulus control, paradoxical intention, sleep restriction, or relaxation therapy) are combined with cognitive therapy to improve insomnia symptoms. CBT is usually delivered by a practitioner with specialized sleep training, in group or individual sessions over the course of several weeks. Several randomized trials have found a beneficial effect of multi-component CBT on sleep outcomes. One large meta-analysis found CBT reduced mean sleep latency by 28 minutes (compared to 8 minutes in controls) and increased mean total sleep time by 29 minutes (compared to 4 minutes in controls). This translated into the average treated patient falling asleep faster than 81% of untreated patients, and staying asleep longer than 66% of untreated patients.[18] A more recent meta-analysis of randomized trials found CBT did not significantly reduce sleep latency or increase total sleep time compared to controls, but it did significantly improve mean wake after sleep onset by 18 minutes (CI 6-30), sleep efficiency by 6% (95% CI, 1-10%), and sleep quality by 0.38 (95% CI, 0.09-0.67) standard deviations compared to placebo.[5] A recent Cochrane review in patients >age 60 also found very similar results; CBT had no significant effects on sleep latency or total sleep time, but significant improvements in wake after sleep onset by 22 minutes (95% CI, 6-37), sleep efficiency by 6% (95% CI, 2-10%) and significant improvements in sleep quality scales.[19] A systematic review found CBT was significantly better than placebo in improving sleep parameters in patients with both primary and secondary insomnia[12] and a subsequent systematic review of psychological treatments for insomnia in older patients found CBT was an effective means of treating insomnia.[17]

CBT is also effective in reducing the quantity of sedative-hypnotic use; in a randomized trial of patients with insomnia on chronic sedative-hypnotics, CBT significantly reduced the frequency and dose of hypnotic use, with almost a third of the intervention group reporting no drug use at 3 and 6 month follow-up.[20]

CBT safety and cost

There are no significant adverse effects of CBT, although there is a time and cost investment. Some CBT elements can be delivered by practitioners who are familiar with them (sleep hygiene, stimulus control, paradoxical intention, and possibly sleep restriction therapy), but others (cognitive therapy, relaxation therapy, and multi-component CBT) might require professionals with specialized training, which is not always locally available.[21] The cost of therapy depends on the number of sessions,

whether it is delivered in an individual or group setting, and whether it is covered by insurance. A systematic review found the mean amount of CBT delivered in published studies was 6 weekly visits, of which 54% were delivered by individual sessions, 30% by group sessions, and the remainder by self-help materials with or without telephone consultations.[12] One small study did find abbreviated "PCP-friendly" CBT (2 sessions) was effective in improving sleep parameters compared to a control group, but no studies have determined the effective "dose" of CBT.[14]

CBT comparative efficacy

There are only a few studies that directly compared the relative efficacy of individual components of CBT.[12] Based on these randomized trials:

- Multi-component CBT may be more effective than relaxation[22]
- Multi-component CBT may be more effective than sleep hygiene[14]
- Relaxation may be more effective than sleep restriction or sleep hygiene for sleep latency insomnia[23]
- Sleep restriction may be more effective than relaxation for sleep maintenance insomnia[16, 23]

Summary of CBT

The American Academy of Sleep Medicine recommends stimulus control, sleep restriction, paradoxical intention, relaxation, and multi-component CBT as effective interventions to reduce sleep problems. Based on lack of qualifying evidence, sleep hygiene and cognitive therapy are not recommended as individual therapies, but are often combined within a CBT "package".[13] Multi-component CBT is effective in the treatment of primary insomnia, secondary insomnia, and for patients taking chronic insomnia medication who need or want to reduce their medication use.[13] There is no evidence to determine the efficacy of group versus individual therapy, or the efficacy of face-to-face instruction versus other modalities (internet-based training, handouts, instructional videos, etc). The amount of practitioner training needed for competency in delivering the content to patients is also unknown.

Exercise

Exercise can be an effective treatment for insomnia. A Cochrane review found only 1 high-quality randomized trial of exercise; patients assigned moderate-intensity exercise 4 days a week fell asleep 11 minutes faster and slept for 42 minutes longer than those in the control group.[24, 25] Exercise is not recommended within 4-5 hours of bedtime, so morning or early afternoon is best.

Bright light therapy

Light therapy can be used to correct circadian rhythm disturbances. An artificial light source provides intense light for a period (can we give a rough range of times) of wake time, and is removed a few hours before expected sleep. Light therapy is sometimes used with melatonin therapy to re-train the central nervous system back to a more normal circadian cycle, or to maintain an abnormal circadian cycle for those that must do so (i.e. for work). In a systematic review, the AASM found light therapy to

be of variable success in circadian rhythm sleep disorders.[26] There is no data to support the use of light therapy in non-circadian disorder insomnia.[26,27] Light therapy does not appear to have harmful effects, although minor side effects can occur (eye irritation/dryness, skin dryness, nausea, and headache) (www.sleepeducation.com).

Acupuncture

A Cochrane review of acupuncture for the treatment of insomnia found it was more effective than placebo or control treatments in improving sleep quality, but was no more effective than placebo or control in improving total sleep time or sleep latency. Only one study reported adverse events, including a 6% withdrawal rate due to pain. Based on overall poor methodological quality, no conclusions can be made on the effectiveness of acupuncture for insomnia.[28]

Bottom line: CBT is effective for improving sleep in both primary insomnia and secondary insomnia, and may reduce the use of medication. Many CBT components can be delivered by primary care physicians, but more advanced CBT requires specialty referral which may not always be available. Morning or early afternoon exercise is also effective, but exercise within 4-5 hours of bedtime should be avoided. Bright light therapy is indicated only for circadian rhythm disorders, and acupuncture lacks evidence of efficacy for insomnia.

Pharmacological therapies

Three classes of prescription medications have been approved by the FDA for insomnia: benzodiazepines (BZDs), benzodiazepine receptor agonists (BZD-agonists), and a melatonin receptor agonist. Other prescription and non-prescription medications used to treat insomnia are not well supported by evidence, and will be mentioned only briefly.

Benzodiazepines (BZDs)

BZDs bind several gamma-aminobutyric acid (GABA) type A receptor subtypes to reduce sleep latency and increase total sleep time. Five 5 BZDs have been FDA approved for treating insomnia; they differ primarily by half-life (see Table 5). All are available in generic form (other than quazepam), and all are schedule IV drugs regulated by the Drug Enforcement Agency (DEA). Several other BZDs are widely used, but these agents have not been FDA approved for treatment of insomnia.

Table 5. BZD drugs FDA approved for short-term treatment of insomnia.

Name	Half life Dose Ranges	Indications	Available as a generic?
Triazolam (generics, Halcion)	Short 0.125mg-0.5mg	Sleep onset	Yes
Temazepam (generics, Restoril)	Intermediate 15mg-30mg	Sleep maintenance	Yes
Estazolam (generics)	Intermediate 0.5mg-2mg	Sleep maintenance	Yes
Flurazepam (generics, Dalmane)	Long 15mg-30mg	None	Yes
Quazepam (Doral)	Long 7.5mg-15mg	None	No

BZD efficacy

A meta-analysis of 22 studies found sedative-hypnotics (including BZDs and zolpidem) significantly improved short-term sleep measures compared to placebo, with moderate treatment effect sizes for sleep onset latency and sleep quality, and large treatment effect sizes for total sleep time and number of awakenings. With a median treatment duration of 7 days, 3 out of every 4 medication-treated patients had better sleep measures than placebo-treated patients.[29] Four subsequent meta-analyses further quantified sleep improvement with BZDs. Collectively, they found mean increases in total sleep time of 33-62 minutes, mean reductions in sleep latency of 4-20 minutes, and mean improvements in sleep efficiency of 6-8%, with all outcomes significantly better than placebo.[5,13, 30,31] One of the meta-analyses (which only included patients >age 60) also found BZDs significantly reduced the mean number of night awakenings by 0.63 (95% confidence interval [CI], 0.48 to 0.77) compared to placebo.[30] Another meta-analysis found BZDs significantly increased the standard mean difference in sleep quality (0.8 standard deviations higher than placebo).[5]

BZD comparative efficacy

There is no good evidence that any one BZD is better than another in improving sleep parameters. The agents most commonly recommended for insomnia have a short or intermediate duration of action (triazolam, temazepam, and estazolam). Those with longer durations (flurazepam and quazepam) have a higher incidence of next-day side effects, which limits their usefulness in most patients, especially the elderly. Based on half life, triazolam is often prescribed for sleep latency insomnia, and temazepam and estazolam are often prescribed for sleep maintenance insomnia.[21]

BZD safety

One meta-analysis found that BZDs were associated with almost twice as many total adverse effects (odds ratio 1.8, 95% CI, 1.4-2.4), particularly daytime drowsiness

(odds ratio 2.4, 95% CI, 1.8-3.4) compared to placebo.[32] Another meta-analysis found that for every 7 patients treated with a BZD, one would experience a side-effect (i.e. number needed to harm of 7).[5,31] Another meta-analysis of patients over age 60 found sedative-hypnotics (primarily BZDs) nearly quintupled the risk of cognitive symptoms (odds ratio 4.8, 95% CI, 1.5-15.5) and nearly quadrupled the risk of daytime fatigue (odds ratio 3.8, 95% CI, 1.9-7.8) compared to placebo, with an overall number needed to harm of 6.[30] There is no evidence that any one BZD is safer than another.

Rebound insomnia often occurs for 1-3 nights after cessation of the shorter acting BZDs, but occurs infrequently after cessation of the intermediate or longer acting BZDs. Daytime sleepiness, on the other hand, occurs frequently with the longer acting BZDs but infrequently with the shorter acting BZDs. Fall risk and hip fractures have been associated with use of longer acting BZDs in the elderly. BZDs should not be used in patients required to make decisions at night (such as those on-call for work or those with dependents at home). BZDs should be also be avoided in those with:[33]

- Hepatic or renal disease (delayed drug clearance)
- Sleep apnea or hypoventilation
- Pregnancy (first trimester fetal malformation risk)
- Concomitant CNS depressant use (including alcohol)

The BZDs indicated for insomnia are metabolized by the CYP3A4 enzyme (except temazepam); inhibitors of this enzyme (e.g., macrolide antibiotics) will increase drug levels while inducers (e.g., rifampin) will decrease drug levels. A full list of inhibitors and inducers is available at http://www.pharmacytimes.com/issue/pharmacy/2008/2008-09/2008-09-8687. BZD dependence occurs in about 30% of patients who take them for >4 weeks. Dependence is more likely to occur in older patients taking daily or shorter acting BZDs.[33]

Bottom line: BZDs improve total sleep time, sleep latency, sleep efficiency, and sleep quality. However, they also increase the risk of adverse cognitive events, falls, and fractures, especially in elderly patients. BZDs should be completely avoided in some patients, limited in the elderly, and prescribed with careful attention to adverse effects and drug interactions. Long-term use is discouraged because of side effects and risk of dependence.

BZD-agonists

BZD-agonists bind to one of the GABA type A receptor subtypes, with more targeted effects on sleep, and less anxiolytic/anticonvulsant effects than the BZDs. Four BZD-agonists are FDA approved for the treatment of insomnia; they differ by half life (see Table 6). All are approved only for short-term use, except eszopiclone, which is approved for longer-term use (>35 days). Generics are available for the shorter acting agents (zolpidem and zaleplon) but not the longer acting agents (zolpidem CR and eszopiclone). All are schedule IV drugs regulated by the DEA.

Table 6. FDA approved BZD-agonists

Name	Half life Dose Ranges	Indications	Duration	Generic
Eszopiclone (Lunesta)	6 hours (intermediate) 1mg-3mg	Sleep maintenance	Long term	No#
Zolpidem CR (Ambien CR)	3 hours (short) 6.25mg-12.5mg	Sleep onset Sleep maintenance	Short term	No
Zolpidem (generics, Ambien, Edluar)	3 hours (short) 5mg-10mg	Sleep onset	Short term	Yes
Zaleplon (generics, Sonata)	1 hour (ultrashort) 5mg-20mg	Sleep onset Sleep maintenance*	Short term	Yes

A generic version of Lunesta is expected to be available in 2010-2011
*If re-dosed with >4 hours of expected sleep time remaining

BZD-agonist efficacy

A meta-analysis of 22 studies found BZD-agonists significantly improved short term sleep parameters compared to placebo, with moderate treatment effect sizes for sleep onset latency and sleep quality, and large treatment effect sizes for total sleep time and night time awakenings.[29] Two subsequent meta-analyses further quantified sleep improvements with BZD-agonists. Collectively they found mean increases in total sleep time of 11-32 minutes, mean reductions in sleep latency of 13-18 minutes, and mean improvements in sleep efficiency of 5-6%, all significantly better than placebo.[5,31] One of the meta-analyses also found significant improvements in sleep quality and quality of life in the treatment groups compared to placebo (with standard mean differences of 0.48 and 0.45 respectively).[5] Three subsequent, longer-term placebo controlled trials of eszopiclone and zolpidem ER found these agents not only significantly improved sleep parameters, but also improved daytime symptoms including quality of life, work performance, and daytime concentration, compared to an inert pill.[34-36]

BZD-agonists **do not necessarily need to be used on an every-night basis**. Intermittent dosing of BZD-agonists works just as well as every-night dosing.[37] Based on long-term studies conducted primarily in non-elderly people, BZD-agonists dosed nightly or as needed can remain effective (without tolerance) in long term use (6-12 months).[38]

BZD-agonist comparative efficacy

A systematic review found 6 studies directly comparing zolpidem to zaleplon; they found zaleplon had significantly shorter sleep latency (by about 10 minutes), and less rebound insomnia, but zolpidem had significantly longer total sleep time (by about 20 minutes) and better subjective sleep quality.[39] One subsequent trial randomized patients to eszopiclone, zolpidem, or placebo and found no significant differences in objective sleep outcomes between the active treatment groups.[36] Based on half-life,

the longer-acting agents (eszopiclone and zolpidem CR) work best for sleep maintenance insomnia; the shorter acting agents (zolpidem and zaleplon) work best for sleep onset insomnia. Zolpidem CR is both rapid acting (for sleep onset) and controlled released (for sleep maintenance). Zaleplon (ultra-short acting) can also be re-administered during the night for nocturnal awakenings, if 4 or more hours of sleep time remain.

BZD-agonist safety

Two meta-analyses found a significantly higher risk of adverse events in BZD-agonists compared to placebo, with a number needed to harm of about 20.[5,35] The most commonly reported side effects of these drugs include headache, dizziness, nausea, and somnolence; less common side effects included abdominal pain, unpleasant taste, and dry mouth.[31] A number of widely reported instances have made it clear that zolpidem can cause significant amnesia, such that patients may wake up in the middle of the night and engage in complex activities, such as preparing and consuming a meal, or going driving, with no memory for the event the next day.[40] Hangover effects, rebound insomnia, and abuse/dependence have not been reported with these drugs, other than occasional sleep disruption the first night after discontinuation of the longer-acting agents. There is no evidence that any one BZD-agonist is safer than another.

BZD-agonists should never be combined with other CNS depressants, including alcohol or BZDs. All of these agents are metabolized by the CYP3A4 enzyme; inhibitors of this enzyme will increase drug levels (e.g., macrolide antibiotics) while inducers will decrease drug levels (e.g., rifampin). A full list of inhibitors and inducers is available at http://www.pharmacytimes.com/issue/pharmacy/2008/2008-09/2008-09-8687. Doses should be reduced in patients with hepatic dysfunction. Long term use of BZD-agonists confers ongoing risk of side effects, especially in older people. As with any medication, regularly reassess potential harms and benefits. Eszopiclone is the only BZD-agonists FDA approved for long term use (>35 days).

Bottom line: Compared to placebo, BZD-agonists improve total sleep time, sleep latency, sleep efficiency, sleep quality, quality of life, work performance, and daytime concentration, but can also cause amnesia. BZD-agonists should not be taken with other CNS depressants. Treat sleep onset insomnia with a shorter-acting agent, and sleep maintenance insomnia with a longer-acting agent. Only eszopiclone is approved for long-term use.

Melatonin agonist

Ramelteon (Rozerem) is the only FDA approved melatonin agonist. This medication binds to melatonin receptors in the suprachiasmatic nucleus of the brain to decrease sleep latency and increase total sleep time.

Melatonin agonist efficacy

A randomized trial against placebo found significant improvements in sleep latency and total sleep time of about 13 minutes each.[41] Another trial found these improvements in sleep latency and total sleep time were sustained at 1 year.[42]

Melatonin agonist safety

No adverse events or next day effects have been reported above rates seen with placebo (headache, somnolence, and sore throat were reported in <1% of patients).[41] Mild hyperprolactinemia has been associated with short-term use, but the clinical significance is not known. There are no reports of withdrawal symptoms or rebound insomnia. Ramelteon is the only FDA approved sleep aid that is not a scheduled substance by the DEA. It is metabolized by the CYP1A2 enzyme; inhibitors of this enzyme will increase drug levels (e.g., ciprofloxacin) while inducers will decrease drug levels (e.g., rifampin). A full list of inhibitors and inducers is available at http://www.pharmacytimes.com/issue/pharmacy/2007/2007-11/2007-11-8279.

Table 7. Summary of sleep measure improvements among the insomnia drug classes

Medication type	Increase Total Sleep Time	Decrease Sleep Latency	Increase Sleep Efficiency	Number Needed to Harm
BZD	33-62 minutes	4-20 minutes	6-8%	6 (elderly) 7 (other)
BZD-agonist	11-32 minutes	13-18 minutes	5-6%	14-20
Melatonin agonist	13 minutes	13 minutes	NA	NA

Bottom line: Ramelteon (Rozerem) has been shown to improve sleep latency and total sleep time compared with placebo. It is the only FDA approved melatonin agonist, and is the only FDA approved sleep aid that is not a DEA scheduled substance.

Other medications

Several other prescription and over-the-counter medications have sedating effects. All have limited evidence of efficacy and in some cases have important side-effects. They are discussed briefly below.

Anti-histamines

The sedating histamine-1 receptor antagonists (anti-histamines), such as diphenhydramine (e.g., Benadryl, Sominex) are marketed for the treatment of insomnia, but evidence supporting their use is limited by small participant numbers and subjective outcomes. Adverse outcomes include anticholinergic effects (dry mouth, blurry vision,

urinary retention) and morning sedation. Use of these agents for insomnia is not recommended by the AASM.[5]

Antidepressants / Antipsychotics

Sedating anti-depressants (trazadone, doxepin, amitriptyline) and anti-psychotics (conventional and atypical) are sometimes used to treat insomnia in patients *without* co-morbid depression or psychosis. Use of these agents in these patients should be discouraged, primarily due lack of efficacy data in non-depressed/psychotic patients. Although one meta-analysis found sedating anti-depressants significantly improved sleep parameters (improved sleep latency by 7 minutes, sleep efficiency by 14%, total sleep time by 53 minutes, and moderately increased sleep quality), they also cause a pooled risk difference of adverse events of 0.09 (95% CI 0.01-0.18), translating into a number needed to harm of 11.[31] Their use is reasonable in patients with insomnia who also have depression or psychosis, but a full discussion of this specialized population is beyond the scope of this review.

Melatonin

Melatonin is a hormone produced by the pineal gland. Higher levels are released after dark and signal that night is approaching. Melatonin is available in the US as a nutritional supplement in doses generally between 1mg – 5mg (although physiologic doses of melatonin are only around 0.3mg). The primary use for melatonin is with circadian rhythm disorders, in which normal rhythm has been disrupted (such as jet lag, night shift work, or blindness); taking melatonin for a period of time can "trick" the body back into a normal rhythm. A meta-analysis found melatonin significantly reduced sleep latency compared to placebo by 8 minutes (95% CI, 2-14), but no significant effect was seen on sleep efficiency, total sleep time, or sleep quality.[31] The analysis did not find significant differences in adverse effects between melatonin and placebo, but formulations are not regulated by the FDA and the quantity and quality of ingredients may vary by brand. A long-acting prescription formulation of melatonin is approved in Europe, but is not available in the US.

Valerian

Valerian is an over-the-counter remedy purported to improve sleep quality, but rigorous studies supporting its use are lacking. A meta-analysis found no significant difference between valerian and placebo in sleep latency, sleep efficiency, or sleep quality.[31] It also found no significant differences in adverse effects between valerian and placebo, as with melatonin, formulations are not regulated by the FDA and the quality and quantity of ingredients may vary by brand.

Alcohol

Alcohol is commonly used by patients with insomnia to reduce sleep latency. Although it can reduce short-term sleep latency, it disrupts overall sleep quality, increases wakefulness after sleep onset, and reduces REM sleep time. It is therefore not recommended as short or long-term treatment for insomnia. It is important for

physicians to ask patients whether they are self-medicating their insomnia with alcohol, as it can have dangerous interactions with prescription sleep medications.

Comparative efficacy

Table 7 presents some indirect comparisons of efficacy among various medications for insomnia. This section will review direct comparative efficacy data for these choices. No comparative efficacy or safety data are available for ramelteon.

CBT versus Drug Therapy:

One small trial randomized 46 patients to 6 weeks of CBT, zopiclone, or placebo. At both short-term (6 week) and long-term (6 month) follow-up, patients in the CBT group fared better, with significantly less total wake time (51 vs. 98 minutes at 6 weeks, and 47 vs. 93 minutes at 6 months), higher sleep efficiency (89% vs. 82% at 6 weeks, and 90% vs. 82% at 6 months), and slow wave sleep (80 vs. 62 minutes at 6 weeks and 84 vs. 59 minutes at 6 months), compared to the zopiclone group.[2]

CBT versus Drug Therapy versus CBT+Drug Therapy:

Several randomized trials have compared the effects of multi-component CBT, medication, or both on sleep parameters. The first randomized patients to multi-component CBT, temazepam, or both for 8 weeks. All 3 active treatments performed better than placebo in short- and long-term follow up. In short term follow-up, the combination group overall performed the best. For example, the proportion of patients achieving sleep efficiency >85% was 68% in the combination group, 56% in the CBT group, 47% in medication group, and just 22% in the placebo group. In long-term follow-up, both behavioral treatment groups performed the best, with more sustained sleep parameter improvements compared to medication alone. The CBT group performed best in improving the sleep impairment index (short- and long-term), followed by the combination group, then the medication group.[43]

Another small trial randomized 63 patients to 8 weeks of CBT, zolpidem, both, or neither. Mean sleep efficiency was highest in the CBT group (89%) followed by the combined group (86%), then the medication group (83%) and placebo (77%). Total sleep time was highest in the combined group (407 minutes) followed by CBT alone (365 minutes) medication alone (315 minutes) vs. placebo (303 minutes). Sleep latency was best for CBT (23 minutes) followed by medication or both (each 42 minutes), and then placebo (58 minutes).[44]

Another trial randomized patients to CBT vs. CBT + zolpidem for 6 weeks. Patients then underwent a secondary randomization to continue CBT +/- zolpidem as needed for 6 months of maintenance therapy. The best long term outcome (remission of insomnia) was found in patients initially treated with combination therapy, followed by CBT alone, indicating a benefit to tapering medication after initial combination

therapy.[3] Other studies have confirmed that BZD tapering is much more successful with CBT than without, in patients with chronic insomnia on long term BZD.[20,45,46]

BZD-agonists versus BZDs:

A systematic review found 4 studies directly comparing zolpidem to BZDs. One found zolpidem improved sleep latency better than BZDs (39 vs. 62 minutes, P=.05) with no other significant differences in total sleep time or sleep quality.[39] Indirect comparisons by meta-analyses have not found significant differences in sleep outcomes between any of the BZDs or BZD-agonists (see Table 7).[5,29,31]

Bottom Line: Comparative efficacy studies suggest that CBT is as or more effective than pharmacological therapy. CBT combined with pharmacologic agents may offer additional benefit. CBT can also be used to reduce medication need in those already on insomnia medications. There are no significant differences in efficacy between the BZDs and BZD-agonists.

Comparative safety

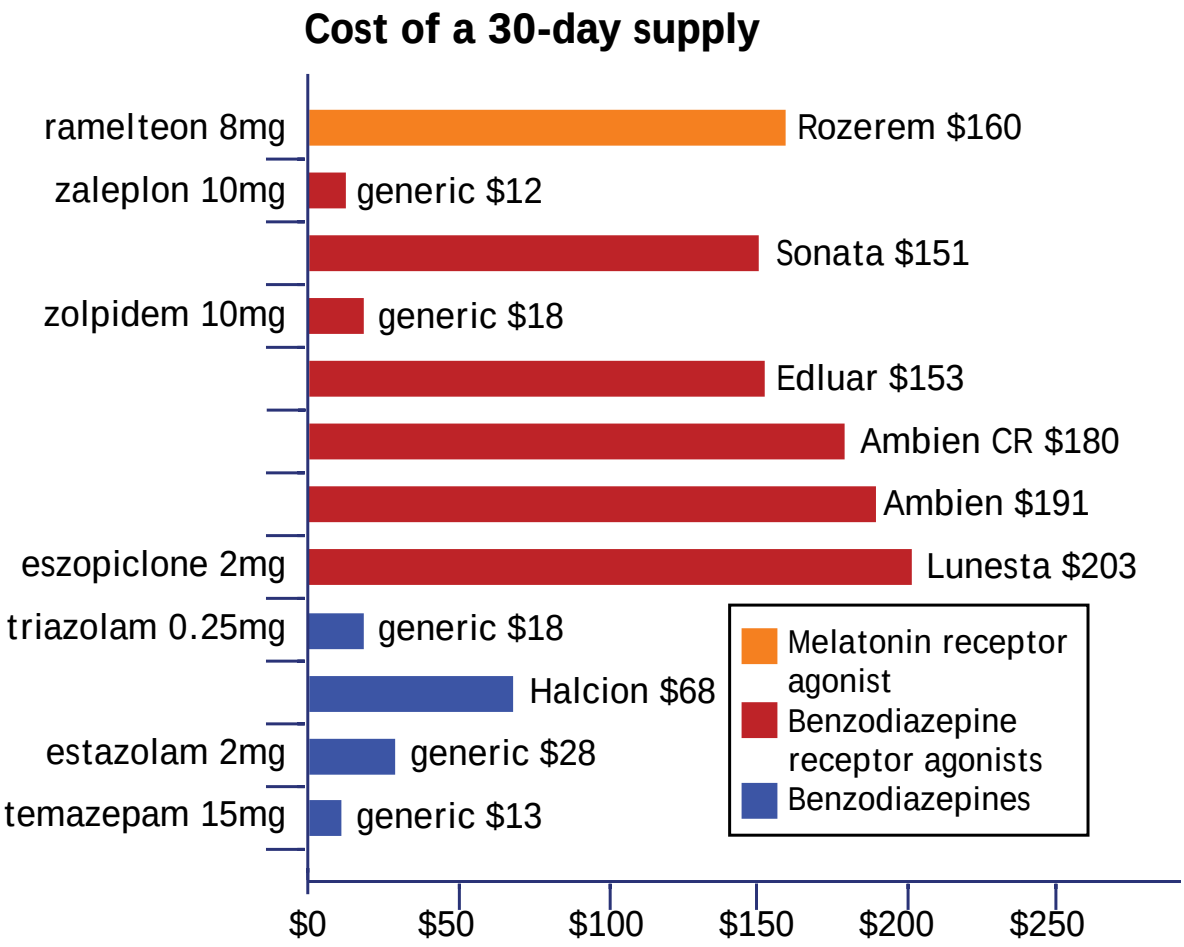
No comparative safety data are available for CBT or ramelteon.

BZD-agonists appear to have a better safety profile than BZDs. Indirect comparison by meta-analyses found adverse effects occurred significantly more often in BZDs than BZD-agonists, with a risk difference of harm versus placebo of 0.15 for BZDs and 0.05 for BZD-agonists.[5] Another meta-analysis found similar adverse effect risks with a risk difference of harm versus placebo of 0.15 for BZDs and 0.07 for BZD-agonists, with a number needed to harm of 7 for BZD (and 6 in the elderly) and 14-20 for BZD-agonists (Table 7).[5, 31]

Costs and overall value

Generic forms of several medications for insomnia can make treatment more affordable. The costs of a 30-day supply of the defined daily dose for prescription medications used to treat insomnia are in Figure 1.

Figure 1. Cost of medications used in the treatment of osteoporosis



Prices obtained from www.epocrates.com and www.drugstore.com October 2010

Figure 2. Efficacy, safety and cost of prescription drugs for insomnia

Key:	Best outcome	Intermediate	Problem

Therapy	Efficacy	Adverse effect profile	Cost	Overall value
CBT			*	
Benzodiazepines				
Benzodiazepine receptor agonists				
Melatonin receptor agonists				

*Some elements of CBT can be inexpensive to implement; formal CBT programs can be expensive and limited in availability.

Putting it all together

The evaluation of insomnia should include a comprehensive medical, psychiatric, medication, substance abuse, and sleep history. Insomnia can be further characterized by the use of:

1. the Epworth Sleepiness Scale to assess the severity of daytime sleepiness (Appendix 2)
2. the Insomnia Screening Questionnaire to help diagnose the type (primary or secondary) and the causes of insomnia (Appendix 3)[12]
3. a 2-week sleep diary to identify sleep-wake times, general patterns, and day-to-day variability (Appendix 4)

Sleep studies are not routinely needed for the evaluation of insomnia in primary care, but may be useful in some patients with specific symptoms such as those suggesting sleep apnea or movement disorders (such as restless legs or periodic limb movement disorder), and in patients whose insomnia is resistant to initial therapy.[6, 9]

Treatment should be tailored to its type (sleep onset or sleep maintenance), severity (and impact on daily life), risk/benefits of the treatment options (including availability and cost), and patient preferences.

For most patients, initial treatment should consist of behavioral therapies such as sleep hygiene and stimulus control education that can be taught by primary care physicians. These are easily presented through instruction, handouts, or videos, and carry little risk or cost. Paradoxical intention and sleep restriction can also be initiated early in the treatment course for patients with sleep onset insomnia, if the practitioner is comfortable with these approaches. Moderate intensity exercise should also be performed several days of the week, preferably in the morning or early afternoon. For circadian rhythm disturbances, bright light therapy and melatonin may be useful.

Patients with continued symptoms can be started on a trial of medication, with instructions that the drugs do not necessarily need to be used on an every-night basis. The medication should be tailored to the type of insomnia, balancing the risk of adverse events and cost (see Table 8 and Figure 1). Referral to a sleep specialist may be necessary for patients with refractory symptoms.

Table 8. Treatment options for insomnia

	First line	Second line	Third line	Fourth line
Sleep onset insomnia	CBT	Shorter-acting BZD-agonists (zaleplon or zolpidem)	Shorter-acting BZDs (triazolam)	Ramelteon*
Sleep maintenance insomnia	CBT	Longer-acting BZD-agonists (zolpidem ER or eszopiclone)* or shorter acting zaleplon (dosed in the night if >4 hours of remaining sleep time)	Intermediate-acting BZDs (temazepam or estazolam)	n/a

*Not available in generic form

There are no significant differences in efficacy among the BZDs, among the BZD-agonists, or between the BZDs and BZD-agonists. The BZDs have a higher risk of adverse events compared to the BZD-agonists, and are therefore third-line agents for most patients. Ramelteon has the least amount of efficacy data, and is not available in generic form. However, since it has an adverse effects profile similar to placebo, it can reasonably be used as a fourth-line agent in patients with sleep onset insomnia. Generic formulations for all agents should be chosen when available.

For patients whose symptoms improve after a trial of drugs plus behavioral therapy, the medication should be tapered as feasible, while the patient continues to perform the behavioral interventions initially recommended. BZD-agonists remain effective (without evidence of tolerance) even after several months of use (6-12 months). However, continued use confers ongoing risk of side effects, especially in older patients. As with any medication, regularly reassess potential harms and benefits.

Those with continued symptoms despite a combination of CBT and medication may require referral to a specialty sleep clinic for more advanced diagnostic (polysomnography) and therapeutic (advanced CBT and medication management) interventions.

Appendix 1. Underlying causes of insomnia

Disorder	Characteristics	Notes
Psychophysiologic insomnia	Disturbed sleep from conditioned arousal, usually to the bedroom	Look for a history of sleep improvement when away from the bedroom; patients may have an inordinate concern over sleep.
Restless leg syndrome (RLS)	An uncomfortable or restless feeling in legs most prominent at night and at rest; alleviated by movement	Look for a family history of RLS, history of caffeine abuse, iron deficiency, renal disease, pregnancy, attention deficit hyperactivity disorder, and, less likely, vitamin B12 or folate deficiency. RLS may also be present with colon adenocarcinoma (I always learned that was due to the resulting iron deficiency, but can leave it in here). Approximately 80% of patients with RLS have periodic leg movements in sleep on polysomnography. Occurs in 11% of general population.
Periodic limb movement disorder	Repetitive stereotypic leg movement during sleep	Look for a history of repetitive leg movements during sleep that leads to disturbed sleep. Polysomnography is necessary for diagnosis.
Sleep-state misperception	Objectively normal sleep in the face of the patient's complaint of insufficient sleep	Polysomnography will document normal sleep. The factor(s) that generate the complaint are unclear. Patients have no obvious psychopathology.
Idiopathic insomnia	Lifelong sleep problems with suspected neurologic abnormality of sleep-wake system	Look for lifelong persistent insomnia.
Central sleep apnea syndrome	Repetitive pauses in breathing during sleep without upper airway occlusion	Look for associated history of congestive heart failure or central nervous system disease. Polysomnography is necessary for diagnosis.
obstructive sleep apnea syndrome	Upper airway obstruction during inspiration in sleep	Look for a history of snoring, respiratory pauses, and daytime sleepiness. Is body habitus a criterion here? Polysomnography is needed for diagnosis. OSAS occurs in about 2% of middle-aged females and 4% of middle-aged males.
Inadequate sleep hygiene	Disturbed sleep associated with caffeine, tobacco, alcohol use, or irregular sleep habits	Comprehensive sleep history will facilitate the diagnosis. Believed to be a common factor in insomnia.
Environmental sleep disorder	Disturbed sleep associated with environmental elements	Comprehensive sleep history will facilitate the diagnosis.

Appendix 1. (continued)

Altitude insomnia	Disturbed sleep associated with altitude	Look for a history of ascent to high altitudes. Can begin as low as 2000 meters for persons from sea level and is common above 4000 meters. Characterized by periodic breathing and central apnea events
Hypnotic-dependent sleep disorder	Disturbed sleep associated with tolerance to or withdrawal from hypnotic drugs	Ask for positive history of sustained hypnotic use with development of tolerance leading to increased dose.
Stimulant-dependent sleep disorder	Disturbed sleep associated with stimulant drug use	Comprehensive sleep history will facilitate the diagnosis.
Alcohol-dependent sleep disorder	Alcohol used to initiate sleep; sleep that follows is fragmented	Ask for patient's history of alcohol use to facilitate sleep for at least the last 30 days. May be preceded by other sleep-disturbing factors.
Toxin-induced sleep disorder	Disturbed sleep associated with arsenic, copper, lead, or mercury ingestion	The clinician must be alert to chronic or acute ingestion. Diagnosed with tests for heavy metals, complete blood count, hepatic, and renal testing.
Shift-work sleep disorder	Sleep occurs at times that are counter to normal circadian rhythm and environmental factors	Look for a history of insomnia associated with shift work. Remember that shift work includes those patients working a permanent night shift. Occurs in approximately 2% to 5% of population.
Delayed sleep-phase syndrome	A circadian rhythm disorder in which the major sleep phase is delayed relative to clock time	Look for a history of sleep-onset insomnia and difficulty awakening at the desired time. Patients have no difficulty maintaining sleep once asleep. Most common in adolescents (tell me about it).
Advanced sleep-phase syndrome	A circadian rhythm disorder in which the major sleep phase is advanced relative to clock time	Look for a history of inability to stay awake until desired bedtime and early morning awakening. Occurs most commonly in the elderly.
Time zone change syndrome (jet lag)	Travel leads to complaints of poor sleep, daytime sleepiness, or both. Physical complaints may ensue (e.g., GI upset)	Look for a history of recent travel across multiple time zones.

Adapted from: Wilson JF. In the clinic. Insomnia. *Ann Intern Med.* Jan 1 2008;148(1):ITC13-1-ITC13-16

Appendix 2. Epworth Sleepiness Scale

The Epworth scale is used to check for daytime sleepiness, especially for people with sleep apnea.

Epworth Sleepiness Scale

Name: _____ Today's date: _____

Your age (Yrs): _____ Your sex (Male = M, Female = F): _____

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired?

This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the **most appropriate number** for each situation:

0 = would **never** doze
1 = **slight chance** of dozing
2 = **moderate chance** of dozing
3 = **high chance** of dozing

It is important that you answer each question as best you can.

Situation	Chance of Dozing (0-3)
Sitting and reading	___
Watching TV	___
Sitting, inactive in a public place (e.g. a theatre or a meeting)	___
As a passenger in a car for an hour without a break	___
Lying down to rest in the afternoon when circumstances permit	___
Sitting and talking to someone	___
Sitting quietly after a lunch without alcohol	___
In a car, while stopped for a few minutes in the traffic	

THANK YOU FOR YOUR COOPERATION

Scoring

6-9	**Sleepy**
10-17	**Very sleepy**
≥ 18	**Dangerously sleepy**

Reproduced from: http://epworthsleepinessscale.com/

Appendix 3. The insomnia screening questionnaire

The insomnia screening questionnaire can be used to help diagnose the causes of insomnia, including primary sleep disorders.[47] It can be found online at: http://www.centreforsleep.com/assets/images/pdf/insomnia_assessment_guideline07.pdf

	Circle the best answer				
Over the past month:	**Never**	**Rarely**	**Occasionally**	**Most nights/days**	**Always**
1. Do you have trouble falling asleep?	1	2	3	4	5
2. Do you have trouble staying asleep?	1	2	3	4	5
3. Do you wake up unrefreshed?	1	2	3	4	5
4. Do you take anything to help you sleep?	1	2	3	4	5
5. Do you use alcohol to help you sleep?	1	2	3	4	5
6. Do you have any medical conditions that disrupt your sleep?	1	2	3	4	5
7. Have you lost interest in hobbies or activities?	1	2	3	4	5
8. Do you feel sad, irritable, or hopeless?	1	2	3	4	5
9. Do you feel nervous or worried?	1	2	3	4	5
10. Do you think something is wrong with your body?	1	2	3	4	5
11. Are you a shift worker or is your sleep schedule irregular?	1	2	3	4	5
12. Are your legs restless and/or uncomfortable before bed?	1	2	3	4	5
13. Have you been told that you are restless or that you kick your legs in your sleep?	1	2	3	4	5
14. Do you have any unusual behaviors or movements during sleep?	1	2	3	4	5
15. Do you snore?	1	2	3	4	5
16. Has anyone said that you stop breathing, gasp, snort, or choke in your sleep?	1	2	3	4	5
17. Do you have difficulty staying awake during the day?	1	2	3	4	5

Guidelines for Interpreting the Insomnia Screening Questionnaire.

- Insomnia: Q1-5
- Medical/Psychiatric Disorders: Q6-10
- Circadian Rhythm Disorder: Q11
- Movement Disorders: Q12-13
- Parasomnias: Q14
- Sleep Apnea: Q15-17

1: Patients who answer 3, 4 or 5 on any question likely suffer from insomnia. If they answer 3, 4 or 5 to two or more items and have significant daytime impairment the insomnia requires further evaluation and management. If there is no evidence of a primary sleep disorder and/or no identifiable secondary cause of insomnia, this is primary insomnia.

2: Patients who answer 4 or 5 on Questions 7-9 should be further screened for psychiatric disorders. Question 10 refers to somatization which is commonly associated with insomnia and may reflect an underlying somatoform disorder which requires specific treatment.

3: Patients who answer 4 or 5 on question 11 likely have a circadian rhythm disorder. Further questioning about shift work or a preference for a delayed sleep phase should be done.

4: Question 12 refers to restless legs syndrome and question 13 refers to periodic limb movement disorder. An answer of 4 or 5 on either item is significant and likely contributing to the patient's symptoms of insomnia or non-restorative sleep.

5: An answer of 2-5 on question 14 should raise concern especially if the event or movement is violent or potentially injurious to the patient or bed partner.

6: Answering 4 or 5 on questions 15 or 16 requires further clinical evaluation for sleep apnea. An answer of > 3 on questions 15 and 17 is also suspicious for sleep apnea and further evaluation should be done.

Appendix 4: Two week sleep diary

An example of a sleep diary from the American Academy of Sleep Medicine is provided below and as a tear-off pad from iDiS.

TWO WEEK SLEEP DIARY

INSTRUCTIONS:
1. Write the date, day of the week, and type of day: Work, School, Day Off, or Vacation.
2. Put the letter "C" in the box when you have coffee, cola or tea. Put "M" when you take any medicine. Put "A" when you drink alcohol. Put "E" when you exercise.
3. Put a line (I) to show when you go to bed. Shade in the box that shows when you think you fell asleep.
4. Shade in all the boxes that show when you are asleep at night or when you take a nap during the day.
5. Leave boxes unshaded to show when you wake up at night and when you are awake during the day.

SAMPLE ENTRY BELOW: On a Monday when I worked, I jogged on my lunch break at 1 PM, had a glass of wine with dinner at 6 PM, fell asleep watching TV from 7 to 8 PM, went to bed at 10:30 PM, fell asleep around Midnight, woke up and couldn't get back to sleep at about 4 AM, went back to sleep from 5 to 7 AM, and had coffee and medicine at 7:00 in the morning.

Today's Date	Day of the week	Type of Day Work, School, Off, Vacation	Noon	1PM	2	3	4	5	6PM	7	8	9	10	11PM	Midnight	1AM	2	3	4	5	6AM	7	8	9	10	11AM
sample	Mon.	Work		E					A				I									C M				

week 1

week 2

Available at: http://www.sleepeducation.com/pdf/sleepdiary.pdf

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