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INSOMNIA

A Primary Care Primer on Diagnosis and Treatment

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NEEDS ASSESSMENT

Sleep disorders affect 50-70 million Americans,[1] yet symptoms often go unmentioned. For most sufferers, the problem is not just getting to sleep but staying asleep. Night awakenings are the most common reported symptom of insomnia.[2] The National Sleep Foundation reports that 1 in 3 of its survey respondents has frequent awakenings a few nights each week; 1 in 4 wakes up too early and can't get back to sleep; and 38% awaken unrefreshed.[3]

Insomnia and other sleep disorders diminish quality of life to much the same degree as in persons with depression or heart failure.[4] Sleep disorders are associated with decrements in daytime performance. Persistent insomnia predicts the onset of psychiatric disorders, notably depression and substance use. In addition to insomnia, many people are affected by a myriad of disorders that disturb sleep, including obstructive sleep apnea syndrome.[5]

Other disorders include restless legs syndrome, whose prevalence increases in iron deficiency states, and circadian rhythm disorders.[5] Despite the prevalence and impact of insomnia and associated sleep disorders, some 70% of patients say their doctors don't take time to ask about sleep symptoms, but 89% want them to do so.[3] In a community clinic study, prevalence of diagnosed sleep disorders was just 0.1%.[6]

The past few years have seen a refinement of cognitive behavioral treatments for insomnia and other sleep disorders. However, these treatments are underutilized, largely due to a lack of trained professionals. For insomnia, a variety of pharmacologic agents are also available. Most of these agents are $GABA_A$ receptor agonists, and recently melatonin receptor agonists have been introduced.[7,8] Agents in development include antagonists/inverse-agonists of the serotonin 2A receptor ($5\text{-}HT_{2A}$), orexin/hypocretin receptor antagonists, H_1 antagonists, among others.[9,10] This monograph will explore insomnia and related sleep disorders in patients; clarify the nature of sleep and its architecture; and review the various treatment modalities available to family physicians as well as those in development.

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LEARNING OBJECTIVES

Participants who complete this activity should be able to:

- Discuss the role of sleep-wake cycle processes and their effect on neurologic and physiologic processes on daytime functioning
- Discern patients' common complaints associated with sleep disorders
- Recognize the impact of insomnia and related symptoms on comorbid medical and psychiatric disorders
- Implement evidence-based behavioral and pharmacologic strategies in managing sleep disorders, targeted to the patient's chief complaint

INTENDED AUDIENCE

This monograph is intended for family physicians.

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Insomnia: A Primary Care Primer on Diagnosis and Treatment

Insomnia: A Primary Care Primer on Diagnosis and Treatment is a monograph based on material presented at a symposium, *Sleep: The Golden Chain That Ties Health and Our Bodies Together,* on October 14, 2009, in Boston, Massachusetts. This monograph is intended for family physicians.

For an activity that is generally quiet and sedate, sleeping can play a powerful role in a person's health and well-being. Improper sleep—too much or too little—has been proven to cause more than tiredness. Proper sleep is critical for learning and memory, particularly long-term memory, and it enhances cognition and physical health.[1,2]

Compromised sleep quality has been associated with, among other conditions, depression, heart failure, coronary heart disease, gastroesophageal reflux disease, and irritable bowel syndrome, excessive alcohol consumption, and stress.[3] Sleep loss can also negatively affect workplace performance, personal relationships, and mood.

How important is sleep? Some experts think it is so important that it should be added to the list of vital signs.[4]

Its importance notwithstanding, sleep is often relegated to low priority in today's 24/7 world. Up to 50% of adults suffer from disrupted sleep, and 10% to 15% can be diagnosed with insomnia.[5,6]

Self-reported sleep problems are even more widespread. In the 2009 Sleep in America Poll, 64% of respondents reported experiencing any sleep problem at least a few nights a week, with 41% saying problems occurred every night or almost every night.[7]

Despite the high prevalence, sleep disorders remain severely underreported and underdiagnosed, and public and professional awareness of the health burden surrounding sleep disorders is low.[8]

Primary-care physicians (PCPs) are in a position to diagnose and treat a host of sleep disorders, but both patients and physicians often fail to take advantage of that position. The 2009 Sleep in America Poll reported that 68% of respondents had never discussed sleep issues with a healthcare professional.[7] A study found that the overall prevalence of sleep-related disorders in a community-based clinic was a mere 0.1%.[9]

On a hopeful note, another study implemented a sleep education program

for clinicians in a community clinic and more than doubled rates of recognition and diagnosis of sleep disorders.[10]

Several factors contribute to the lack of recognition and treatment of sleep disorders. Physicians spend little if any time during medical school and training learning about sleep disorders and may not feel confident in this area. One survey asking PCPs about their knowledge of sleep medicine found that of 105 respondents, none rated themselves as excellent, 10% rated themselves as good, 60% as fair, and 30% as poor.[11]

Time pressures faced by today's PCPs also discourage active pursuit of sleep disorder diagnosis and treatment, which by their nature, can be time-consuming and involve extensive counseling and follow-through.[6]

Patients also seem reluctant to pursue sleep issues, chalking them up as a cost of today's fast-paced world and simply living with the consequences. Of those who described sleeping difficulties in one study, only 9% reported the problems to a physician.[6]

It is undeniable that there are many sleep issues to report and that Americans are sleeping less than in the past. In 2009, 20% of respondents to the Sleep in America Poll reported sleeping less than 6 hours a night on weekdays vs. 12% in 1998.[7]

Subjective evidence also is dramatic. More than 11% of surveyed Americans recently reported that they did not get enough sleep for even 1 night in the past month, and only 31% said they got enough sleep every day during the previous month.[12]

SLEEP-WAKE CYCLES

Sleep and wake cycles are regulated by the interaction of homeostatic and circadian processes. The homeostatic process for sleep increases as a function of the time awake and dissipates during sleep. The circadian clock located in the suprachiasmatic nucleus (SCN) of the hypothalamus plays an important role in consolidating sleep during the night and wakefulness during the day.

As the sleep homeostatic pressure builds with ensuing wakefulness during the day, SCN neuronal activity increases, peaking in the early evening to maintain wakefulness until bedtime. After peaking in the early evening, SCN activity decreases and enters a quiescent phase that lasts through the night. Therefore, sleep is most consolidated at night, when there is a low circadian alerting signal and a high homeostatic drive, allowing people to sleep continuously for 7 to 8 hours in the night. Once asleep, the accumulated sleep drive begins to dissipate.

This is not to say that all sleep is the same. Throughout sleep the brain is quite active. Sleep architecture includes non-rapid eye movement (REM) sleep (stage 1, stage 2, slow wave sleep) and rapid eye movement (REM) sleep, where most dreaming takes place. Slow wave sleep is thought to be somatically restorative.[13] After age 50, people will experience major reductions in the amount of slow wave sleep.

During a typical night's sleep, the brain makes transitions between REM and non-REM stages about every 90 minutes. There are also a couple of brief episodes of awakening (***Figure 1***).[14]

CONSEQUENCES OF SLEEP DISTURBANCES

Lack of sleep results in much more than yawning and tiredness; it can significantly affect mood, performance, and overall health. In one study, investigators studied sleep restriction's impact on performance as measured by reaction time.

After establishing baseline values with normal sleep, investigators restricted sleep to 7, 5, and 3 hours in some and augmented sleep to 9 hours in another group. Performance slowed immediately and severely when sleep was incrementally restricted, and restricting sleep even to 7 hours measurably impaired performance. The 5- and 3-hour groups experienced further impairment.[15]

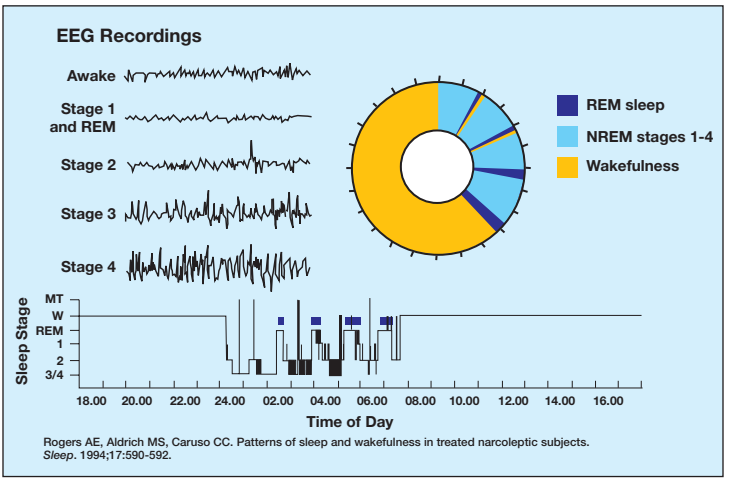

Figure 1. Sleep-Wake Cycle: A Dynamic Process

Interestingly, it took more than 3 days of normal, extended sleep for subjects to recover their baseline performance after 1 week of restricted sleep.[15] For some severely sleepy individuals, it may take up to 2 weeks to become fully alert.[16]

Safety is also at issue when sleep is lost. Studies have found that sleep deprivation can produce diminished performance equivalent to that exhibited by someone who is impaired after drinking alcohol, bringing to the forefront problems with driving and other activities that are dangerous when attention is lacking.[17]

Too much or too little sleep has been associated with increased mortality risk. United Kingdom (UK) investigators found higher rates of all-cause mortality among study participants who consistently slept either ≤5 hours or ≥9 hours.[18] Similarly, a Japanese study reported a U-shaped relationship of sleep time with total mortality, with 7 hours of sleep at the nadir.[19]

A Finnish study echoed the results of the UK and Japanese researchers regarding sleep duration, but added the surprising finding that poor sleep quality did not independently affect mortality risk.[20]

MEDICAL CONDITIONS AND SLEEP

The relationship of sleep and health is bidirectional: poor health leads to poor sleep, and poor sleep leads to poor health. Conversely, good sleep leads to good health.

Medical conditions that can cause sleep abnormalities include chronic obstructive pulmonary disease and other lung disease, gastroesophageal reflux disease, chronic renal disease, fibromyalgia and other chronic pain conditions, and certain infectious diseases, including HIV and Lyme disease.[21]

In the other direction, sleep disorders can lead to myriad physical impairments. For example, in normal adults, restriction of sleep to only 4 hours a night was found to:

- impair glucose control
- increase cortisol level
- increase sympathetic activation
- increase blood pressure
- increase inflammation markers such as C-reactive protein (CRP)
- decrease leptin levels, thus increasing hunger[22]

Clinical evidence is mounting regarding how poor sleep is associated with numerous specific medical conditions and psychiatric disorders. Among the recent findings:

Hypertension. At least 2 studies in the past year have found direct links between short sleep duration and hypertension risk.[23,24] In one, researchers reported that each hour of reduced sleep time increased the odds of incident hypertension by 37%.[24]

In the other study, authors concluded that chronic insomnia associated with objectively measured short sleep time is a significant risk factor for hypertension, independent of comorbid conditions usually associated with insomnia or hypertension.[23]

A third study found that low sleep efficiency (SE) is associated with prehypertension and hypertension in healthy adolescents, perhaps more so than sleep duration.[25] The importance of this finding takes on increasing significance when one considers that cell phones, music players, and other technology have become commonplace bed companions for teens.[26]

Diabetes. Numerous studies have shown that too much or too little sleep is associated with insulin resistance, reduced glucose tolerance, and diabetes.[27-30] One study found that participants who slept ≤5 hours were almost twice as likely as those who slept 7 hours to have incident diabetes over the follow-up period.[27]

A small study found that insulin resistance and reduced glucose tolerance developed after only 2 weeks in which sleep was restricted to 5.5 hours a night.[28]

A recent study looked at reduced slow wave sleep but with no change in total sleep time. Investigators found that the reduced sleep quality led to reduced glucose tolerance and increased diabetes risk.[13] Moreover, the lower the levels of slow wave sleep, the higher the impact on insulin sensitivity.

Obesity. Reduced total sleep time has been associated with obesity in adults and adolescents in various settings (***Figure 2***).[31-35] Studies have linked sleep deprivation to neuroendocrine changes affecting appetite and energy expenditure.[36,37] Specifically, lack of sleep lowers levels of leptin, which inhibits appetite and increases energy expenditure, and increases ghrelin, which stimulates hunger.[36]

One small study found leptin levels decreased 18% and ghrelin levels increased 28% after only 2 days of sleep restricted to 4 hours. In addition, sleep-deprived subjects experienced increased appetite, most notably for calorie-dense foods with high carbohydrate content.[38]

Cardiovascular (CV) risk. A number of studies have shown that sleep disorders increase such CV risk factors as coronary artery calcification.

A recent investigation found that longer sleep was associated with lower calcification incidence. In fact, 1 more hour of sleep a night decreased the estimated odds of calcification by 33%.[39]

Japanese researchers studied older patients with hypertension and found that sleepers of short duration (<7.5 hours) had a 1.68 times increased risk of CV disease.[40]

Common cold. Participants in a study who slept <7 hours per night were 2.94 times more likely to develop a cold after exposure to a rhinovirus than those who slept ≥8 hours. In addition, subjects with <92% SE were 5.5 times more likely to develop a cold than those with ≥98% efficiency.[41]

Depression and other psychiatric disorders. Approximately half of insomnia sufferers are saddled with a comorbid psychiatric disorder, the most common of which are major depressive disorder (MDD) and anxiety.[42] In the primary care setting, insomnia is associated with depression more than it is with any medical disorder.[6] Other psychiatric disorders associated with insomnia include drug and alcohol abuse and dysthymia.

The relationship between insomnia and psychiatric disorders, particularly MDD, is bidirectional. It is well established that insomnia is an early indicator of increased risk of MDD. Insomnia sufferers have a 3 to 4 times increased risk over the next several years of developing MDD.[43]

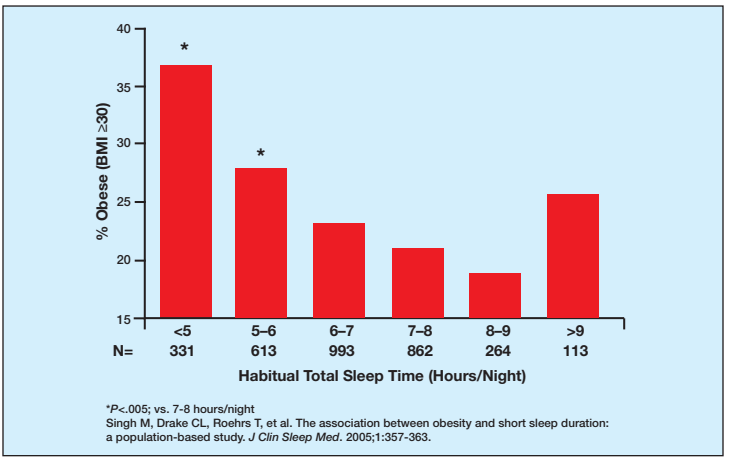

Figure 2. Reduced Total Sleep Time Is Associated With Increased Prevalence of Obesity

In the other direction, one study found that the most prominent residual symptom of patients with depression successfully treated with fluoxetine was disturbed sleep; the second-most was fatigue, typically a component of insomnia.[44]

Antidepressants are often used to treat insomnia, giving a clinician a choice of using 1 or 2 medications—one addressing each of the conditions—when treating a patient with both insomnia and MDD. When researchers added the sleep agent eszopiclone to the antidepressant fluoxetine for patients with MDD and insomnia, they found the combination was associated with significant sleep improvement. Also, the time to response to, and effect of, the antidepressant improved markedly.[45]

Combining antidepressants and hypnotics allows physicians to target more sleep-wake mechanisms than a single agent. Since combined therapy typically involves lower doses of each medication, side effects are minimized.[5]

A recent small pilot study treated MDD and insomnia by adding cognitive-behavioral therapy (CBT) for insomnia to the use of escitalopram for 12 weeks. Researchers reported markedly higher remission rates for both MDD and insomnia in treated patients vs. controls.[46]

Medications. A number of drugs are associated with sleep-wake disorders, including β-blockers, dopamine agonists, selective serotonin reuptake inhibitors, and anticholinergics (***Table 1***).[47]

EVALUATION FOR INSOMNIA

Insomnia is by far the most common sleep disorder.[48,49]

According to clinical guidelines, insomnia is defined as "a subjective report of difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity for sleep, and that results in some form of daytime impairment." (***Table 2***)[5]

Acute insomnia, usually defined as lasting less than 2 weeks, is typically associated with specific factors such as jet lag, acute illness, menstrual cycle, or unusual stress. Chronic insomnia, occurring an average of 3 nights a week for more than a month, can be complex and requires a well-thought-out treatment plan.[48,50]

Some 85% of insomnia cases are comorbid with a host of medical and psychological conditions, including other sleeping disorders such as restless legs syndrome (RLS) and obstructive sleep apnea (OSA) (***Tables 3 and***

Table 1. Medications Associated With Sleep-Wake Disturbances
Anticholinergics
Antihypertensives
Antihistamines*
Bronchodilators
ß-blockers
Decongestants
Diuretics
Dopamine agonists*
Hypnotics*
MAO inhibitors
Phenytoin
Quinidine
Selegiline
SSRIs
Thyroid hormone
Xanthines
*Causes excessive sleepiness; other listed agents are associated with insomnia; hydrophilic, lipophilic. MAO = monoamine oxidase; SSRI = selective serotonin reuptake inhibitor Zagaria ME. Insomnia, depression, and suicide risk in the elderly: raising awareness. *US Pharm*. 2004;5:30-37.

4).[42] (A statement by the National Institute of Health [NIH] suggests calling these cases "comorbid insomnia" instead of the more common "secondary insomnia," which the NIH suggests could lead to undertreatment.)[49]

The first step in evaluating a patient for insomnia is to determine whether the sleeping difficulties are decreasing daytime functioning and quality of life.

If the answer is Yes, the next step is to establish whether the insomnia is primary or comorbid. If an underlying comorbid condition exists, that condition and the insomnia should be treated concurrently.

Determine the precise nature of the sleep complaint. Patients may be having trouble falling asleep, staying asleep, or getting back to sleep after awakening during the night, or they may not feel rested and restored in the morning.

The most common complaint overall is nonrestorative sleep; the most frequent nocturnal complaint is waking up in the night and experiencing dif-

ficulty getting back to sleep.[51] Nocturnal awakenings plague about one third of the general population[52] and have more impact on daytime functioning than other insomnia symptoms.[53]

Often patients will present with a combination of symptoms.[5] For each, determine the onset, duration, frequency, and severity to get a clear picture of the patient's situation.

Details of the patient's sleep-wake pattern will help point to the next steps. Questions to ask include:

- What is your habitual daily sleep duration?
- Do you have problems falling asleep or staying asleep?
- What is the frequency and duration of your nocturnal awakenings?
- How long have you been experiencing insomnia symptoms?
- Do you feel sleepy, drowsy, or tired during the day?
- Do you snore, have hypertension, or stop-breathing episodes?

Table 2. Diagnostic Criteria for Insomnia Based on The International Classification of Sleep Disorders, 2nd Edition (ICSD-2)

A. A complaint of difficulty initiating sleep, difficulty maintaining sleep, or waking up too early, or sleep that is chronically nonrestorative or poor in quality.
B. The above sleep difficulty occurs despite adequate opportunity and circumstances for sleep.
C. At least one of the following forms of daytime impairment related to the nighttime sleep difficulty is reported by the patient: 1. Fatigue or malaise 2. Attention, concentration, or memory impairment 3. Social or vocational dysfunction or poor school performance 4. Mood disturbance or irritability 5. Daytime sleepiness 6. Motivation, energy, or initiative reduction 7. Proneness for errors/accidents at work or while driving 8. Tension, headaches, or gastrointestinal symptoms in response to sleep loss 9. Concerns or worries about sleep.

Schutte-Rodin S, Broch L, Buysse D, et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med*. 2008;4:487-504.

Table 3. Common Comorbid Medical Disorders, Conditions, and Symptoms
Neurologic: Stroke, dementia, Parkinson disease, seizure disorders, headache disorders, traumatic brain injury, peripheral neuropathy, chronic pain disorders, neuromuscular disorders
Cardiovascular: Angina, congestive heart failure, dyspnea, dysrhythmias
Pulmonary: Chronic obstructive pulmonary disease, emphysema, asthma, laryngospasm
Digestive: Gastroesophagral reflux disease, peptic ulcer disease, cholelithiasis, colitis, irritable bowel syndrome
Genitourinary: Incontinence, benign prostatic hypertrophy, nocturia, enuresis, interstitial cystitis
Endocrine: Hypothyroidism, hyperthyroidism, diabetes mellitus
Musculoskeletal: Rheumatoid arthritis, osteoarthritis, fibromyalgia, Sjögren syndrome, kyphosis
Reproductive: Pregnancy, menopause, menstrual cycle variations
Sleep disorders: Obstructive sleep apnea, central sleep apnea, restless legs syndrome, periodic limb movement disorder, circadian rhythm sleep disorders, parasomnias
Other: Allergies, rhinitis, sinusitis, bruxism, alcohol and other substance use/dependence/withdrawal

- Have you ever had to fight to stay alert while driving?
- Do you ever have unpleasant, restless feelings in your limbs when you are trying to sleep?
- What medications are you currently taking?

If possible, interview a patient's bed partner, who can often add important information the patient is not aware of. Also ask about napping and daytime consequences of sleep disturbance, such as fatigue and sleepiness, mood disturbances, cognitive difficulties, and quality-of-life deterioration.

Diagnostic tools can help ascertain the extent of a patient's sleep problems. The Epworth Sleepiness Scale, for example, helps to assess how easily the patient falls asleep during everyday activities such as reading, watching television, and riding in a car as a passenger (***Table 5***).[54]

Finally, a physical exam may provide clues as to the cause of sleeping problems and should take only 5 minutes (***Table 6***).[48]

GETTING TO KNOW THE PATIENT'S HABITS

Understanding and treating insomnia can be broken into 3 discrete "P factors": predisposing, precipitating, and perpetuating (***Figure 3***).[55]

Patients with predisposing factors would include those with anxiety or depression, individuals who react with sleep disturbance when stressed, those with decreased homeostatic sleep drive. Precipitating factors can be various comorbid medical or psychiatric conditions, prescription or nonprescription drugs, shift work, or stressful life events. Perpetuating factors move an acute case of insomnia into a chronic one and include counterproductive efforts to solve the problem, poor sleep hygiene, and psychological conditioning.[55]

Much of insomnia treatment, particularly CBT, tries to break the cycle between precipitating and perpetuating factors.

Before starting treatment, get a picture of the patient's sleep habits. A several-week sleep log or diary will show, for example, that the patient goes to bed at 10:30 PM and awakes at 6:30 AM during the week,

Table 4. Common Comorbid Psychiatric Disorders and Symptoms

Disorders	Category Examples
Mood	Major depressive disorder, bipolar mood disorder, dysthymia
Anxiety	Generalized anxiety disorder, panic disorder, posttraumatic stress disorder, obsessive compulsive disorder
Psychotic	Schizophrenia, schizoaffective disorder
Amnestic	Alzheimer disease, other dementias
Disorders usually seen in childhood and adolescence	Attention deficit disorder
Other disorders and symptoms	Adjustment disorders, personality disorders, bereavement, stress

Schutte-Rodin S, Broch L, Buysse D, et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med*. 2008;4:487-504.

but goes to bed well after midnight and sleeps until late morning on weekends.

Primary measures obtained from a sleep log include:

- bedtime
- sleep latency (SL: time to fall asleep following bedtime)
- number of awakenings and duration of each awakening
- wake after sleep onset (WASO: the sum of wake times from sleep onset to the final awakening)
- time in bed (TIB: time from bedtime to getting out of bed)
- total sleep time (TST: time in bed minus SL and minus WASO)
- sleep efficiency percent (SE equals TST divided by TIB times 100)
- nap times (frequency, times, durations)

Table 5. The Epworth Sleepiness Scale

The Epworth Sleepiness Scale	
Name	Age
Today's Date	M/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 have not 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	
Situation	**Chance of dozing**
1. Sitting and reading	
2. Watching TV	
3. Sitting, inactive in a public place (eg, a movie theatre or a meeting)	
4. As a passenger in a car for an hour without a break	
5. Lying down to rest in the afternoon when circumstances permit	
6. Sitting and talking to someone	
7. Sitting quietly after lunch without alcohol	
8. In a car, while stopped for a few minutes in traffic	
TOTAL SCORE	
Source: Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*. 1991;14:540-545.	

Sleep logs may also include daily reports of sleep quality, medications, and caffeine and alcohol consumption.[5]

The diary can be useful in diagnosing circadian rhythm disorders, such as phase advance syndrome, which is more common in elderly patients. Also, it will establish a baseline of sleep data for use in tracking the patient's response to therapy.[56]

At this time, discuss goals with the patient. General goals would be to improve sleep duration and quality and to reduce daytime impairments associated with poor sleep. More specific goals could be to aim for SL <30 minutes, WASO <30 minutes, TST >7 hours, and a decreased number of nocturnal awakenings.

Table 6. Elements of a Physical Exam When Sleep Problems Are Present

Vital signs. Hypertension and respiratory diseases are associated with insomnia.
Head and neck. Examine for signs of possible hindrance to breathing, like retrognathia, tonsillar hypertrophy, and enlarged soft palate. Also note the size and consistency of the tongue, the size of the airway in the pharynx, the appearance of the soft palate, the uvula's size, shape, and position, and evidence of trauma. The nose should be examined for obstruction, either from a septal deviation, polyps, or engorgement of the turbinates as in chronic allergic rhinitis. Note if the nares collapse with inspiration, especially when the patient is supine.
Neck. Examine for thyroid enlargement or nodules.
Heart. Auscultate for signs of congestive heart failure.
Lung. Auscultate for degree of asthma and chronic obstructive pulmonary disease.
Extremities. Examine for signs of arthritis or any other causes of pain.
Neurologic system. Conduct a brief neurologic exam that includes the extraocular muscles and peripheral nerves.

Doghramji PP. Detection of insomnia in primary case. *J Clin Psychiatry*. 2001;62(suppl 10):18-26.

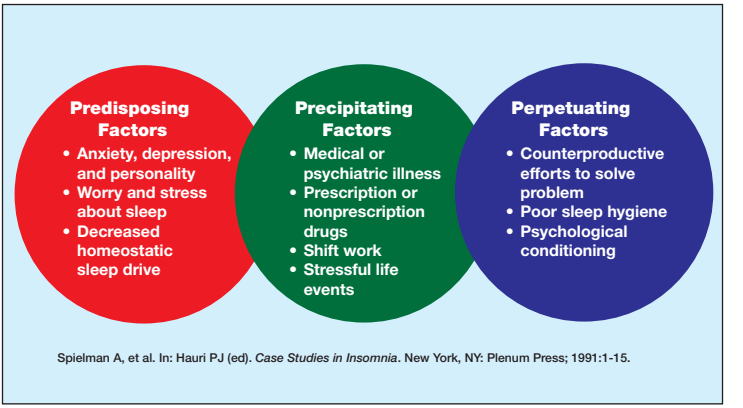

Figure 3. Spielman's Model of Insomnia: The 3 P's

COGNITIVE-BEHAVIORAL THERAPY

CBT has been found to be beneficial for both primary and comorbid insomnia and is particularly effective in improving nocturnal wakefulness.[57] Its positive effects typically last longer than those of pharmacotherapy, and no side effects have been associated with the treatment.[49]

The main CBT techniques for treating chronic insomnia include sleep hygiene, stimulus-control therapy, sleep restriction, relaxation therapy, and cognitive therapy (***Table 7***).[58]

Sleep hygiene. The goal of improving sleep hygiene is to promote habits that help sleep and to provide a rationale for subsequent instructions. Encourage the patient to create a sleep-enhancing environment: dark, quiet, and a comfortable temperature. This will allow the brain to be quiet, relaxed, and sleepy.

Patients should use the bedroom only for sleep—no reading, watching television, talking, or working. Sex is allowed, but not if it contains elements of frustration. The bedroom should be restricted to things that are relaxing and conducive to sleep.

Restrict consumption of sleep-disrupting substances, particularly near bedtime. No caffeine after lunch is a general rule. Alcohol makes patients sleepy initially but wakes them up as it leaves their bloodstream during the night. Nicotine intake can also disturb sleep.

Other items to avoid: eating a heavy meal within 3 hours of bedtime; looking at the clock when you awaken in the night, resulting in making it

harder to go back to sleep; and exposure to bright light during the night.

On the flip side, activities that promote sleep are regular exercise (though not too close to bedtime) and setting aside a time during the day for worrying. While the latter strategy may sound simplistic, patients often find it effective in stopping their minds from swirling when they first get into bed or awaken in the night. They know that they will have a specified opportunity to worry the next day.

Bedtime and wake time consistency should be highly encouraged. This is important for routine and to enhance circadian rhythm.

Stimulus-control therapy. The goal of this tactic is to strengthen the association between sleep and bed. Tell patients to go to bed only when they are sleepy, no matter the time—that is, when they can fall asleep within 20 minutes, which is a normal sleep latency.[48]

If the patient does not fall asleep within 20 minutes (an *estimated*

Table 7. Nonpharmacologic Treatments

Techniques	Goals
Sleep Hygiene	Promote habits that help sleep; provide rationale for subsequent instructions
Stimulus-Control Therapy	Strengthen bed and bedroom as sleep stimulus
Sleep Restriction	Improve sleep continuity by limiting time spent in bed
Relaxation	Reduce arousal and decrease anxiety (progressive muscular relaxation, transcendental meditation, yoga, biofeedback)
Cognitive-Behavioral Therapy	Combines sleep reduction, stimulus control techniques, sleep restriction with cognitive therapy, challenged dysfunctional beliefs and misperceptions about sleep and insomnia
Circadian Rhythm Entrainment	Reset or reinforce biological rhythm

Bootzin RR, Perlis ML. Nonpharmacologic treatments of insomnia. *J Clin Psychiatry*. 1992;53(suppl 6):37-41.

20 minutes if the patient is following the hygiene rule of not looking at the clock), the patient should get out of bed, leave the room, and do something quiet and conducive to sleep. Television is permitted as long as watching does not stimulate the patient or encourage staying up longer than he/she would otherwise.

The patient should then try to sleep again, getting out of bed once again if sleep does not come within 20 minutes. No matter what time the patient eventually falls asleep, he/she must awaken at the same time as any other day.

Patients should not be surprised if they have to get out of bed 7 or 8 times in the first couple of days. By the third night, the sleep drive should be high and the number of times in and out of bed should decrease, though it can take as long as a month for full effect.

During that time, try to keep in some contact with the patient to oversee the process, whether by e-mail or a faxed sleep log. That will allow the physician to make any needed adjustments to the approach.

Sleep restriction. This aims to improve sleep continuity by limiting time spent in bed (and therefore cutting overall sleep time) until sleep efficiency (SE) improves. Begin by limiting time in bed to the actual amount the patient reports sleeping, but not fewer than 4 hours per night. Prohibit sleep outside of these hours; naps are not allowed.

Ask the patient to report daily the amount of sleep he/she has obtained. Compute SE based on a moving average of 5 nights. Once a patient is asleep for 85-90% of his/her time in bed, he/she can go to bed 15 minutes earlier (always rising at the same time each morning). Elderly patients' goal is 80% SE, and they are allowed a 30-minute nap during the day.[59]

For example, if a patient has been waking up at 6 AM after sleeping 5 hours, but being in bed for 8 hours (an SE of 63%), the patient is not allowed to go to bed until 1 AM at the start of sleep-restriction therapy. As SE improves, bed time can be moved (advanced) earlier until time in bed has increased to 8 hours or some other mutually decided figure, with a SE of 90% or better. This therapy is not without significant adverse events and one must attend to the potential for increased sleepiness that may be induced during treatment. Sleep restrictions may be contraindicated among patients with major mood disorders.

Relaxation therapy. This strategy can be particularly effective for patients with naturally elevated arousal levels and is often combined with cognitive therapy. Techniques such as progressive muscle relaxation, guided imagery, biofeedback, breathing exercises, yoga, meditation, and abdominal

breathing aim to lower cognitive arousal states that interfere with sleep.[5,58]

Cognitive therapy. This method seeks to implement cognitive restructuring and takes aim at anxiety-producing and erroneous beliefs about sleep and sleep loss.[49]

Psychotherapeutic sessions focus on factors that predispose (eg, hyperarousal) and perpetuate insomnia, including excessive worry about the inability to sleep and the daytime consequences of poor sleep, ineffective strategies to improve sleep, and excessive time spent in bed trying to fall asleep. The last factor can be particularly debilitating as the patient associates bed with a frustrating, unproductive, and ultimately failed effort.[5]

Given time constraints, many primary care practices would be hard-pressed to enter into long-term counseling programs for their patients with sleep disorders. Recently, abbreviated cognitive therapy has shown promise.

A study by Edinger and Sampson used a brief 2-session program and found that 52% of patients reported at least a 50% reduction in wake time after sleep onset. Moreover, 56% of patients in the study with pathologic scores on a sleep-assessment tool achieved normal scores at the end of the study.[60]

In a more recent study, Edinger and colleagues determined that 4 individual biweekly sessions constituted the optimal dosing for cognitive therapy intervention.[61] Among patients with that dosing, 58% met criteria for clinically significant improvement by the end of the treatment compared with 44% of those receiving 1 session, 35% of those receiving 8 sessions, and 22% of those receiving 2 sessions.[61]

Even more significantly, only the 4-session patients exhibited long-term improvements in objective wake time and SE measures at the 6-month follow-up.[61]

Delivery of abbreviated cognitive therapy takes training, but it need not be done by a psychologist or physician. Nurse practitioners, physician assistants, and nurses can be adequately trained in proper sleep concepts.

PHARMACOTHERAPY OPTIONS

There are currently 10 Food and Drug Administration (FDA)-approved hypnotics for insomnia, all of which act as benzodiazepine receptor agonists (BzRAs).[62,63] They can be broken into 3 categories:

Older benzodiazepines

- Estazolam (ProSom)

- Flurazepam HCl (Dalmane)
- Quazepam (Doral)
- Temazepam (Restoril)
- Triazolam (Halcion)

Newer nonbenzodiazepines
- Eszopiclone (Lunesta)
- Zaleplon (Sonata)
- Zolpidem (Ambien)
- Zolpidem extended release (Ambien CR)

Melatonin receptor agonist
- Ramelteon (Rozerem)

The most consistent trend in pharmacologic agents for insomnia has been the progressive reduction in sedative half-life. This reflects emerging understanding that daytime carryover of the sedative effect represents the most important side effect for these medications. Half-lives of fewer than 4 hours are associated with reduced risk of residual sedation.

Though all the newer approved agents have been proven safe and effective in clinical trials, none is considered superior to all others in a general sense; physicians should match patients' complaints with the characteristics of individual agents.

For example, eszopiclone's half-life is slightly longer than that of other new agents (though shorter than older benzodiazepines), making it a good choice for patients having difficulty staying asleep. Zolpidem is approved only for difficulty falling asleep, but zolpidem extended release is approved for difficulty falling and staying asleep. Zaleplon's short half-life means that it can be taken in the middle of the night when the patient has at least 4 hours left in bed.

Most older benzodiazepine hypnotics have a relatively long half-life, making them effective in helping patients sleep through the night but potentially impairing next-day cognitive and psychomotor function with lasting sedation.[6]

In selecting an insomnia agent, consider:
- symptom pattern
- treatment goals

- past treatment responses
- patient preference
- cost
- availability of other treatments
- comorbid conditions
- contraindications
- concurrent medication interactions
- side effects[5]

Potential adverse effects of BzRAs include residual sedation, memory and performance impairment, falls, undesired behaviors during sleep, somatic symptoms, drug interactions, and withdrawal and rebound insomnia with rapid dose decrease or discontinuation.[5]

The only approved melatonin receptor agonist, ramelteon, unlike the BzRAs, does not cause withdrawal or residual drowsiness.[64] However, it has limited efficacy in maintaining sleep due to its short half-life.[64]

Another class of drugs commonly used to treat insomnia is antidepressants. Trazodone is most prescribed, despite a relative paucity of efficacy evidence and a lengthy half-life, particularly in the elderly.[6,65] Its popularity may be related to perceived safety, generic availability, unscheduled status, and lack of restrictions on prescription duration.

Antidepressants are potentially advantageous for patients experiencing chronic insomnia comorbid with depression, but efficacy is not consistent, they have a poor side-effect profile, including cardiovascular effects and other residual effects, and there is no well-defined effective dose.[50,66]

Antihistamines, other OTC medicines, and melatonin supplements are commonly used by patients to aid sleep, primarily because of their low cost and easy availability. Adverse effects include dry mouth, blurred vision, urinary retention, constipation, risk of increased intraocular pressure in individuals with narrow-angle glaucoma, residual daytime sedation, diminished cognitive function, and delirium (of particular concern in the elderly).[67,68]

Other antihistamine disadvantages include inconsistent efficacy, development of tolerance to sedative effects within a few days, potential for residual effects, and no well-defined effective dose.

Not surprisingly, guidelines promulgated in 2008 specifically do not recommend antihistamines or other OTC sleep aids for treating insomnia because of the relative lack of efficacy and safety data.[5]

Novel agents being studied for insomnia treatment include:

- 5-HT_{2A} antagonists
- Low-dose mirtazapine and doxepin
- Melatonin receptor agonists
- Mixed 5-HT_{2A} and melatonin receptor agonist
- Modified sustained-release formulations
- Substance P antagonists
- Hypocretin/orexin receptor antagonists
- H_1 receptor antagonists (selective)

CBT AND PHARMACOTHERAPY COMBINED

Data from combining CBT and medication to treat chronic insomnia indicate that using both is not consistently advantageous or disadvantageous vs. CBT alone.[5,69]

There is some support for combined CBT and pharmacotherapy for chronic insomnia. Morin and colleagues found in a 1999 study that combined therapy improved wake time somewhat better than either therapy alone in the short term, but in the long term it did not perform as well as CBT alone.[70]

A more recent study by Morin and colleagues found that the best long-range outcome for patients with persistent insomnia was obtained by using combined therapy during the initial 6 weeks, then employing CBT only during long-term maintenance.[71] In that initial period, combined therapy increased sleep time more than either therapy alone.[71]

OTHER TYPES OF SLEEP DISORDERS

Restless legs syndrome (RLS). An irresistible and powerful urge to move the legs—sometimes described as a "creepy-crawly" feeling—characterizes RLS and manifests most strongly at night when resting. Patients with RLS often have difficulty falling and staying asleep.[48,72]

The overall prevalence of RLS is 5-10%, though a study of one primary care practice in Idaho found that 24% of patients presenting during the course of 1 year had all 4 essential symptoms for an RLS diagnosis.[73]

Studies have shown that RLS increases with age until 60-79 years and has greater prevalence in women than in men; pregnancy is a risk factor.[73-75]

The FDA has approved 2 agents to treat RLS: ropinirole (Requip) and pramipexole (Mirapex). Certain dopaminergic agents, sleeping aids, anticonvulsants, and pain relievers have been found in clinical studies to effec-

tively relieve RLS symptoms.[76,77]

Circadian rhythm disorders. Patients with circadian rhythm disorders have a biological, internal clock that is out of sync with the environmental clock.

Types of circadian difficulties can be advanced sleep phase syndrome (getting sleepy early in the evening and awakening in the very early morning hours), delayed sleep phase syndrome (not getting sleepy until the very early morning hours and sleeping until the late morning or early afternoon), jet lag, and shift work disorder.

Treatment centers on bright-light therapy to delay or advance sleep schedules. A 10,000-lux light box exposes a patient to bright light at specific times to improve sleep timing.

Obstructive sleep apnea (OSA). This common disorder involves breathing stoppages during sleep. During a physical exam, the physician should look for specific OSA risk factors, such as snoring, obesity, male gender, older age, increased neck circumference, hypertension, sleepiness and fatigue, and upper airway restrictions. Suspected OSA can only be diagnosed in a formal sleep study in a qualified laboratory.

First-line treatment is continuous positive airway pressure; other treatments can involve dental appliances and surgery.

Weight loss can sometimes effectively reduce OSA and its effects. In a recent study, obese patients with type 2 diabetes who lost weight enjoyed significant improvement in OSA symptoms. Patients in the study who lost weight through lifestyle interventions had a mean decrease of 9.7 apnea-hypopnea events per hour vs. patients receiving only education. At 1 year, 3 times more participants in the weight-loss group experienced complete remission of OSA compared with the education-only group.[78] Weight loss, however, is not always effective in treating OSA.

SPECIAL POPULATIONS: WOMEN AND THE ELDERLY

Women. Meta-analysis has shown that women experience sleep disturbances more often than men.[79] Menstrual-related problems including cramping and heavy flow have been associated with increased insomnia-related symptoms, such as daytime sleepiness.[80] Many of the hormonal, body, and lifestyle changes surrounding pregnancy and childbirth often lead to sleep deprivation, fragmented sleep, and circadian rhythm disruption.

Some 60% of menopausal women report that they suffer from insomnia.[81]

Nocturnal hot flashes have been associated with more frequent nighttime awakenings, less efficient sleep, and a decrease in deep, slow wave sleep.[82] Severe hot flashes have been associated with chronic insomnia for women in midlife.[83]

Studies have found that women taking hormonal therapy have fewer sleep disturbances and better sleep quality than those not taking hormonal therapy, which could signal a hormonal cause of menopausal insomnia.[84,85] This is still an area of debate, however.

Sleep disturbances in women can cause particular problems. In one recent study, investigators reported that poor sleep quality, more frequent problems falling asleep, and long sleep latency were associated with higher fasting insulin, fibrinogen, and inflammatory biomarkers—but only for women.[86]

Another study concluded that cognitive decline was associated with sleep disturbance in nondemented community-dwelling elderly women.[87]

The elderly. Sleep complaints rise with age, driven primarily by high comorbidity (***Figure 4***).[88] Sleep architecture in the elderly is markedly different than that in younger patients. Older patients awake much more frequently and more often complain of difficultly falling back asleep. Compared with younger patients, the elderly will experience a relatively small percentage of slow wave sleep, the most restorative of the sleep levels.

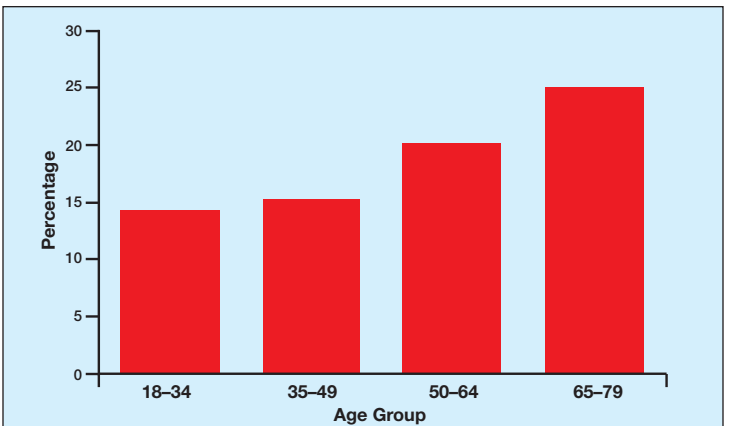

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Figure 4. Insomnia by Age Group

Several factors can increase wake time after sleep onset, including nocturia, OSA, periodic limb movement disorder, pain, and medical conditions such as chronic obstructive pulmonary disease. Among clinical correlates are daytime sleepiness and falls in the elderly.

One study looked at more than 34,000 nursing-home residents to evaluate the relationship between insomnia, hypnotic use, and falls. Insomnia, but not hypnotic use, was associated with a greater risk (52% more likely) of subsequent falls.[89]

Another study examined sleep disturbance and falls among community-dwelling women ≥70 years and found that short sleep duration and fragmented sleep were associated with an increased risk of falls.[90] The increased risk was independent of medication use.

In some cases, elderly patients, because of their frequent nighttime awakenings, will ambulate, putting themselves at considerable risk for falling.

CONCLUSION

Referral to a sleep specialist or for polysomnography is appropriate in certain cases, such as for patients who have indicators of RLS, OSA, or narcolepsy, and patients who exhibit violent arousals or severe daytime impairment. Also, patients who fail to respond to treatment may benefit from seeing a sleep specialist.

Largely, though, primary care clinicians can successfully diagnose and treat sleep disorders. Be vigilant for signs of sleep disorders in patients, and take the initiative to routinely ask about sleep habits. Uncovering and treating sleep disorders can profoundly improve a patient's overall health status and quality of life.

CASE STUDY

Mrs. M is a 55-year-old woman presenting with a primary complaint of difficulty staying asleep and early-morning awakening for about 3-4 months. She reported waking up several times each night, almost every 2 hours. Her scheduled bedtime is 10:30 PM; her wake time is 7:00 AM.

She attributed her sleeplessness in part to hot flashes and her husband's snoring. Her husband has commented on her snoring.

Mrs. M complained of tiredness, poor concentration, and increased frequency of migraines. She drinks 3 cups of coffee in the morning and 1 cup in the afternoon. Ten years ago, she had a bout of depression after a close

friend's death.

She has high blood pressure and takes a "diuretic," multivitamin, and calcium supplement. Her body mass index is 29 kg/m^2.

To illustrate the challenge of treating patients with sleep complaints, when this case was presented to an audience of family physicians, 31% believed insomnia associated with menopause was the primary diagnosis, 29% voted for insomnia associated with OSA, 27% for psychophysiologic insomnia, and 13% for insomnia associated with depression.

Because of her snoring and history of hypertension, Mrs. M was sent for a sleep study, which found OSA. She was diagnosed with psychophysiologic insomnia.

Initial treatment focused on improving Mrs. M's sleep hygiene by restricting her sleep and using stimulus-control therapy. She was advised not to go to bed until 1:45 AM, giving her 5 hours and 15 minutes before she must awaken at 7:00 AM. She was not to nap during the day.

Once Mrs. M is able to sleep for 85-90% of the time she is in bed, she should go to bed 15 minutes earlier and while still getting up at 7:00 AM. She should slowly increase the amount of time in bed by 15-minute intervals until she reaches 8 or 8.5 hours and while sleeping at least 90% of the time.

She was instructed to use the time in bed for sleep only; no reading or watching television or another activity.

Mrs. M began sleeping better within 3 weeks of initiating sleep restriction and stimulus-control therapy.

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AECOM Course Number: 3565

POSTTEST

1. According to a recent poll, what percentage of Americans experienced any sleep problem at least a few nights a week?
a. 18%
b. 45%
c. 64%
d. 80%

2. Which part of sleep is the most restorative?
a. Rapid eye movement
b. Stage 1
c. Stage 2
d. Slow wave sleep

3. Sleeping 9 hours or more a night has been associated with which of the following?
a. Increased mortality
b. Increased risk of alcoholism
c. Decreased blood pressure
d. Excessive daytime sleepiness

4. Longer sleep has been associated with lower calcification incidence. One extra hour of sleep a night can decrease the estimated odds of calcification by
a. 10%
b. 25%
c. 33%
d. 50%

5. Many insomnia sufferers are also diagnosed with major depressive disorder (MDD). Giving such patients both an antidepressant for MDD and a hypnotic for insomnia is
a. Often efficacious with few adverse effects
b. Rarely effective
c. Useful under very specific circumstances
d. Dangerous and not recommended

6. The definition of insomnia in clinical guidelines includes all of the following except

a. An adequate opportunity to sleep
b. Daytime impairment
c. Difficulty with sleep initiation
d. Sleep duration <6 hours per night

7. Cognitive therapy seeks to reduce anxiety-producing and erroneous beliefs about sleep and sleep loss. According to a recent study recent study by Edinger and colleagues, how many biweekly sessions constituted optimal dosing?

a. 2
b. 4
c. 6
d. 8

8. Which of the following is not a risk factor for obstructive sleep apnea?

a. Female gender
b. Older age
c. Hypertension
d. Increased neck circumference

9. What percentage of menopausal women report sleep problems?

a. 25%
b. 50%
c. 60%
d. 75%

10. In the elderly, insomnia has been associated with which of the following?

a. Obstructive sleep apnea
b. Overuse of medications
c. Increased risk of falls
d. Increased heart disease