



Insomnia Related to Stress

Insomnia Prevalence

Insomnia refers to a subjective complaint of difficulty falling asleep or maintaining sleep and/or unrestorative sleep that is accompanied by daytime consequences such as sleepiness, irritability or cognitive impairment. Occasional insomnia affects approximately one-third of adults in the U.S. and 10% to 15% have the clinical diagnosis of insomnia, making it more common than heart disease or cancer.¹ The prevalence of insomnia in the primary care population is even higher, possibly due to the high rates of concomitant illnesses.² A recent survey found that the prevalence of insomnia among primary care patients was 69%, with 50% reporting occasional insomnia and 19% reporting chronic insomnia.³

Insomnia in Women

Women are at higher risk of insomnia than men.⁴ The specific factors that increase the risk of insomnia among women are unclear, but evidence suggests that female reproductive biology may contribute to insomnia throughout the life span. The higher prevalence of insomnia in women may also be explained by higher rates of depression, which is strongly associated with insomnia, among women. Psychosocial factors and having the dual responsibility of career and caregiver/homemaker may also increase the risk of insomnia in women.

Primary vs. Comorbid Insomnia

Primary insomnia is a diagnosis of exclusion, given when a sleep difficulty persists for more than three weeks and no other condition is identified as the cause. Primary insomnia may be brought on by stress, worry, poor sleep hygiene, environmental factors, jet lag, alcohol, or caffeine. Life events may also cause insomnia; a recent study found that the most common precipitating factors for primary insomnia are events related to work, family, and health.⁵ Insomnia may also be comorbid with other medical or psychiatric illnesses such as depression, anxiety, Parkinson's disease, Alzheimer's disease, rheumatoid arthritis, heart failure, stroke and cancer.⁶

Insomnia with Comorbid Depression

Depression is the most common insomnia comorbidity; evidence suggests that people with insomnia are nearly ten times more likely to develop depression than those who sleep well.⁷ The relationship between insomnia and depression is complex and multidirectional; insomnia may be a symptom of depression, a predisposing factor for it or the two conditions may have parallel etiology.^{8 9} Depressed patients may suffer from a range of insomnia symptoms, including difficulty falling asleep (sleep onset insomnia), difficulty staying asleep (sleep maintenance insomnia), unrefreshing sleep, and daytime sleepiness. Research suggests that the risk of developing depression is highest among people with both sleep onset and sleep maintenance insomnia.¹⁰

Insomnia Comorbid with Other Sleep Disorders

Insomnia is often comorbid with other sleep disorders such as obstructive sleep apnea (OSA), which causes breathing pauses during sleep and nocturnal awakenings that may be mistaken for sleep maintenance insomnia. OSA is more common in men, though the risk of OSA increases for older women. Post-menopausal women are three times more likely than their younger female counterparts to suffer from OSA.¹¹ Restless legs syndrome (RLS) is another primary cause of insomnia. RLS is more common among older adults and more common in women than men.¹²

Insomnia Related to Lifestyle Factors

Alcohol is a common self-treatment for insomnia. Its sedative properties may help some patients with sleep onset insomnia. However, alcohol causes shallow and fragmented sleep throughout the night and may lead to dependency and abuse.¹³ Use of caffeine is also a primary cause of insomnia. Caffeine may also exacerbate feelings of stress and worry, which contribute to sleep problems. A lack of physical activity and poor sleep habits such as watching television in bed may also cause insomnia. Regular exercise may improve insomnia symptoms; a recent study involving more than 4,000 adults found that daily exercise was negatively correlated with insomnia.¹⁴ Stressful life events may also cause insomnia. One study found that people with chronic insomnia experience a greater number of stressful life events during the year of insomnia onset compared with other years and compared with good sleepers.¹⁵ In cases where the stressful life event is short-lived, sleep problems usually resolve once the stressor is resolved.

Insomnia Related to Menopause

Sleep disturbances are common in middle-aged and older women, especially during the transition to menopause.¹⁶ A recent study of more than 2,000 middle-aged women revealed that menopause was independently associated with insomnia even after adjusting for confounding factors such as depression.¹⁷ Little is known about the underlying pathology of insomnia related to menopause, but it is likely caused by hormonal changes. Menopausal symptoms such as hot flashes and night sweats are predictive of subjective complaints of insomnia. Menopause may also mediate the relationship between insomnia and depression. That is, the onset of menopause symptoms may cause depression in women who are predisposed to it.¹⁸

Insomnia Caused by Work Stress

Exposure to chronic workplace stress is a risk factor for insomnia, especially among people whose work involves high demands, a high degree of risk, long hours, and excessive work loads.^{19 20} Being in a supervisory role and having a high degree of immersion in work may also contribute to insomnia.²¹ In addition, research suggests that an inability to stop worrying about work during free time may be an important link in the relationship between stress and insomnia, especially for women and older adults.²²

Consequences of Untreated Insomnia

Insomnia is associated with fatigue, sleepiness, irritability, concentration problems, and impairments in work performance. People with insomnia also have higher rates of work absenteeism, lower work productivity, and are more likely to make mistakes on the job compared to good sleepers.^{23 24} Insomnia patients also have a three-fold increase in risk of car crashes.²⁵ Health-related quality of life is also lower for insomnia patients. In a recent study of 3,445 primary care patients, quality of life ratings among people with severe insomnia were similar to those of patients with congestive heart failure and depression.²⁶

The Role of the Primary Care Physician

The primary care physician is on the front lines of insomnia therapy, as patients with sleep problems are most likely to address those issues in the primary care setting. However, a recent study found that only about half of insomnia patients reported discussing the problem with a physician.²⁷ Research also suggests that most practitioners do not routinely ask their patients about their sleep.²⁸ However, physicians who receive sleep disorders training are far more likely (81%) to initiate a conversation about sleep with their patients.²⁹

Differential Diagnosis

Evaluating a patient for insomnia begins by asking patients whether they have difficulty falling asleep, difficulty staying asleep or waking up unrefreshed. Patients should also be asked about their daytime symptoms such as sleepiness and irritability. Questions about snoring and leg discomfort may reveal the presence of obstructive sleep apnea and restless legs syndrome, respectively. Inquiring about the patient's sleep environment, caffeine and alcohol consumption, sleep schedule and bedtime routine may also reveal precipitating factors for insomnia. Insomnia patients should use a sleep diary for a period of two weeks in order to provide practitioners with a detailed view of their sleep habits. Evaluation of insomnia does not require polysomnography except in cases where other sleep problems such as obstructive sleep apnea are suspected. Rather, insomnia is diagnosed based on patient history and subjective complaints.

Sleep Hygiene and Behavioral/Psychological Therapies

The essential components of an insomnia treatment plan include sleep hygiene, behavioral/psychological therapy, and pharmacological treatment. Sleep hygiene involves adopting habits that promote sleep such as keeping a regular sleep/wake schedule, having a relaxing bedtime routine, avoiding caffeine and alcohol, and creating a sleep environment that is cool, dark, quiet, and comfortable. Behavioral/psychological therapy for insomnia focuses on addressing the maladaptive beliefs that perpetuate sleep difficulty, including feelings of hopelessness about one's ability to achieve healthy sleep and the belief that needing a full night's sleep is a sign of weakness. Such beliefs may confound behavioral therapies for insomnia, especially when it is comorbid with depression.³⁰ Behavioral treatments such as cognitive restructuring (see cognitive behavioral therapy) that target these beliefs may improve patient outcomes.

Sleep hygiene and behavioral remedies are usually employed before the use of medications, but pharmacological therapies may also be a first-line treatment in patients with more severe insomnia, which generally refers to sleep difficulty that occurs every night and causes significant daytime impairment.³¹ When used alone, behavioral strategies have been shown to be an effective long-term treatment for insomnia.³² However, evidence suggests that pharmacological therapies used in combination with behavioral strategies are more effective at treating short-term sleep difficulties than behavioral strategies alone.³³

Cognitive Behavioral Therapy

Cognitive behavioral therapy (CBT) has been shown to produce significant and lasting improvements in all measures of insomnia with no side effects or risk of dependency.³⁴ CBT for insomnia is also generally less expensive than pharmacological therapy.³⁵ CBT for insomnia typically requires multiple sessions with a practitioner over a period of 6-8 weeks, though research suggests that even brief

behavioral interventions can significantly improve insomnia as well as daytime symptoms of sleepiness and anxiety.³⁶ Research also suggests that as many as one-third of insomnia patients become good sleepers as a result of CBT for insomnia.³⁷

Cognitive behavioral therapy (CBT) for insomnia typically consists of the following components, and physicians may use one or a combination of them:

- Cognitive restructuring - targets the patient's maladaptive beliefs about sleep, such as excessive worry about the effects of not sleeping.
- Sleep restriction – limits the patient's time in bed to the amount of time he or she typically sleeps, and then gradually increases time in bed as sleep time increases.
- Stimulus control – allows the patient to re-associate the bedroom with sleep. It involves going to bed only when sleepy, limiting the bedroom activities to sleep and sex, getting out of bed if sleep is not achieved within 15 minutes and avoiding naps.
- Relaxation therapy – reduces stress and anxiety, relaxes the body, and prepares the patient for sleep.

Pharmacological Therapies

Pharmacological treatments are recommended for patients in whom behavioral strategies alone are not effective. There are currently ten drugs with approval by the U.S. Food and Drug Administration (FDA) for the treatment of insomnia (see Table 1), and all are recommended for short-term use. Those that have received FDA approval since 2005 (ramelteon, eszopiclone and zolpidem CR) may be prescribed without limitation on the duration of their use.

Pharmacological Therapies

Table 1 – FDA-Approved Medications for the Treatment of Insomnia

Drug	Chemical Class	Recommended Dose in Adults, in Older Adults	Half Life (hours)
Estazolam	Benzodiazepine	2 mg, 1 mg	8 - 24
Eszopiclone	Non-benzodiazepine	2 mg, 3 mg, 1 mg	5 - 7
Flurazepam	Benzodiazepine	30 mg, 15 mg	48 - 120
Quazepam	Benzodiazepine	15 mg, 7.5 mg	48 - 120
Temazepam	Benzodiazepine	30 mg, 15 mg	8 - 20
Triazolam	Benzodiazepine	0.25 mg, 0.125 mg	2 - 4
Zaleplon	Non-benzodiazepine	10 mg, 5 mg	~1.0
Zolpidem	Non-benzodiazepine	10 mg, 5 mg	1.5 – 2.4
Zolpidem CR	Non-benzodiazepine	12.5 mg, 6.25 mg	6.26 – 12.5
Ramelteon	Melatonin agonist	8 mg, 8 mg	1.5 - 5

Pharmacological Therapies – Potential for Adverse Effects

Each of the medications approved for the treatment of insomnia have the potential for adverse effects, which may include daytime drowsiness, cognitive impairment, ataxia, dependence, and rebound insomnia. A recent NIH consensus conference concluded that the occurrence of these effects may be lower for the newer sleep medications (e.g., ramelteon, eszopiclone and zolpidem CR), most likely because these agents have shorter half-lives.³⁸ Additionally, the FDA recently requested that manufacturers of insomnia medications revise their product labels to include stronger language concerning potential risks. These risks include severe allergic reactions and

complex sleep-related behaviors, which may include sleep driving. Sleep driving is defined as driving while not fully awake after ingestion of a sedative-hypnotic product, with no memory of the event.

Pharmacological Therapy for Insomnia with Comorbid Depression

Treatment for insomnia may be complicated by comorbid depression. Because insomnia and depression commonly coexist, patients with both conditions are often treated with sedating antidepressant medications. In fact, the antidepressant trazodone is now the most commonly prescribed medication for insomnia.³⁹ In the short-term, evidence suggests that sedating antidepressants improve symptoms of insomnia. However, sedating antidepressants carry a risk of side effects such as residual sedation and weight gain. The potential benefits of sedating antidepressants should be evaluated by practitioners against the potential for adverse effects. It is important to keep in mind that treating comorbid depression or any other comorbid condition may not resolve a patient's insomnia. Rather, insomnia treatment may need to be considered separately or in combination with therapies for the comorbid condition.

Treatment of Menopausal Insomnia

Symptoms of menopause such as hot flashes, night sweats and the gradual decrease in progesterone and estrogen may contribute to poor sleep and an inability to cope with stress in middle-aged women.⁴⁰ Treatment of insomnia related to menopause should focus on sleep hygiene and behavioral therapies and may include hormone replacement therapy and treatment with insomnia medications.⁴¹ Evidence suggests that treating menopause symptoms can significantly improve sleep quality and minimize the adverse effects of insomnia, including depression.⁴²

The Case of a Female Business Executive Presentation, Personal history and Sleep Complaints

A 55 year-old married female business executive presents with worsening insomnia over the previous 9 months, which coincided with a major promotion at work. She works 10-12 hour days and commonly drinks several glasses of wine in the evening while watching television in bed, falling asleep between 10:30 pm and 2:00 am. Once asleep, she wakes up 2-3 times per night as a result of her husband's snoring or due to a need to urinate and often cannot fall back to sleep due to worry about the demands of the coming work day. She sometimes experiences hot flashes during her nighttime arousals. She does not nap, mostly because she cannot afford the time. Since her promotion, her total sleep time has decreased to about 5 hours on most nights. She is worried about her sleep and fears losing her job as a result of her insomnia.

The patient drinks two double lattes upon waking and consumes several additional cups of coffee throughout the day. She notes increasing daytime sleepiness and concentration problems, particularly in low-stimulus situations like meetings. In the past she would exercise a few times per week, but has given it up since receiving her promotion. Since the onset of her sleep problems, she is irritable and impatient and feels an increasing burden of stress and worry. She notes having been treated by a therapist briefly during college for depressive symptoms and that her father suffered from depression and insomnia. The patient is also experiencing stressors in her home life. Her husband is unhappy with her increasing work load and increasing irritability. In addition, she recently had the responsibility of placing her ailing mother in a nursing home and sending her youngest child to college.

The Case of a Female Business Executive Differential Diagnosis

The patient has symptoms of major depression (poor concentration, irritability, sleep maintenance insomnia with early awakening) and a family history of both depression and insomnia. She is also experiencing major life stressors that can cause a depressive episode in a susceptible patient. Poor sleep hygiene (strong dependence on alcohol and caffeine) also contributes to the patient's sleep difficulties. In addition, having a variable sleep schedule, using the television to fall asleep, and a lack of exercise are likely contributing to her insomnia. Symptoms of menopause may also be contributory. There is also a component of sleep phase delay, probably related to hyperarousal in the evening.

The Case of a Female Business Executive Treatment

The patient was instructed regarding proper sleep hygiene, with specific instructions to gradually reduce caffeine to 1 cup of coffee in the morning, to discontinue alcohol and to avoid using the television to fall asleep. Assessment of her sleep environment suggested that the bedroom was too warm at night, contributing to her hot flashes. She was advised to reduce the temperature and to wear earplugs or move to another room because of her husband's snoring. She was also advised to begin an exercise program of 30 minutes per day of brisk walking.

The patient met the criteria for mild major depressive episode and was referred to a psychologist for cognitive behavior therapy for depression and stress management. The psychologist also worked with her on cognitive behavior approaches to insomnia. This led to some improvement in her insomnia, but she continued to experience insomnia and was interested in pursuing pharmacological therapy. Issues to consider when prescribing insomnia medication for this patient are residual sedation, weight gain and the patient's history of alcohol abuse. With her history of mild depression, a sedating antidepressant is one choice, although the potential side effects (e.g., residual sedation and weight gain) could be limiting factors. Longer-acting insomnia medications (eszopiclone and zolpidem CR) might be helpful for her sleep maintenance symptoms. With her sleep onset difficulties and potential component of a phase delay, ramelteon may also be considered.

Summary

There is significant overlap between insomnia and depression and both may be exacerbated by stress. Insomnia and depression are both more common in women than men and the risk of developing both insomnia and depression increase with age. Primary care physicians are critical to the early diagnosis and treatment of insomnia as well as stress and depression. Insomnia, including insomnia comorbid with depression, is treatable and evidence suggests that early intervention increases functioning and improves quality of life.



Go to www.BriefCaseCME.com for another valuable CME opportunity.

References

- ¹ Morin CM, et al., Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors *Sleep Medicine* 2006 Vol. 7, No. 2
- ² Shochat T et al., Insomnia in primary care patients *Sleep* 1999 Vol. 22, Suppl 2
- ³ Shochat T et al., Insomnia in primary care patients *Sleep* 1999 Vol. 22, Suppl 2
- ⁴ Ohayon MM, Epidemiology of insomnia: what we know and what we still need to learn *Sleep Medicine Review* 2002 Vol. 6, No. 2
- ⁵ Bastien CH et al., Precipitating factors of insomnia *Behavioral Sleep Medicine* 2004 Vol. 2, No. 1
- ⁶ National Institutes of Health State of the Science Conference Statement on Manifestations and Management of Chronic Insomnia in Adults June 13-15, 2005 *Sleep* 2005 Vol. 28
- ⁷ Taylor DJ, et al., Epidemiology of Depression, Insomnia and Anxiety *Sleep* 2005 Vol. 28, No. 11
- ⁸ Perlis M, et al., Insomnia as a risk factor for onset of depression in the elderly *Behavioral Sleep Medicine* 2006 Vol. 4, No. 2
- ⁹ Buysse DJ, Insomnia, depression and aging - assessing sleep and mood interactions in older adults *Geriatrics* 2004 Vol. 59, No. 2
- ¹⁰ Taylor DJ, et al., Epidemiology of Depression, Insomnia and Anxiety *Sleep* 2005 Vol. 28, No. 11
- ¹¹ Scientific Workshop on Women and Sleep, National Sleep Foundation March 2007
- ¹² Phillips P, et al. Prevalence and Correlates of Restless Legs Syndrome: Results from the 2005 National Sleep Foundation Poll *Chest* 2006 Vol. 128
- ¹³ Crum RM, et al., Association of sleep disturbance with chronicity and remission of alcohol dependence: data from a population-based prospective study *Alcoholism: Clinical and Experimental Research* 2004 Vol. 28, No. 10
- ¹⁴ Kim K et al., Lifestyles and sleep disorders among the Japanese adult population *Psychiatry and Clinical Neuroscience* 1999 Vol. 53, No. 2
- ¹⁵ Healey ES et al., Onset of insomnia: role of life-stress events *Psychosomatic Medicine* 1981 Vol. 43, No. 5
- ¹⁶ Owens JF and Matthews KA, Sleep disturbance in healthy middle-aged women *Maturitas* 1998 Vol. 30, No. 1
- ¹⁷ Shin C, et al., Prevalence of insomnia and its relationship to menopausal status in middle-aged Korean women *Psychiatry & Clinical Neurosciences* 2006 Vol. 59, No. 4
- ¹⁸ Parry BL et al., Sleep, rhythms and women's mood. Part II. Menopause *Sleep Medicine Reviews* 2006 Vol. 10, No. 3
- ¹⁹ Utsugi M et al., Relationships of occupational stress to insomnia and short sleep in Japanese workers *Sleep* 2005 Vol. 28, No. 6
- ²⁰ Ribet C and Derriennic F, Age, working conditions and sleep disorders: a longitudinal analysis in the French cohort E.S.T.E.V. *Sleep* 1999 Vol. 22, No. 4
- ²¹ Akerstedt T, et al., Mental fatigue, work and sleep *Psychosomatic Research* 2004 Vol. 57, No. 5
- ²² Akerstedt T et al., Sleep disturbances, work stress and work hours: a cross-sectional study *Psychosomatic Research* 2002 Vol. 53, No. 3

-
- ²³ Leger D et al., Professional correlates of insomnia *Sleep* Vol. 29, No. 2
- ²⁴ Leger D et al., Professional correlates of insomnia *Sleep* 2006 Vol. 29, No. 2
- ²⁵ Leger D et al., Professional correlates of insomnia *Sleep* 2006 Vol. 29, No. 2
- ²⁶ Katz, DA and CA McHorney, The relationship between insomnia and health-related quality of life in patients with chronic illness *Family Practice* 2002 Vol. 51, No. 3
- ²⁷ Aikens JE and Rouse ME, Help-seeking for insomnia among adult patients in primary care *Journal of the American Board of Family Practice* 2005 Vol. 18, No. 4
- ²⁸ Haponik EF et al., Sleep history is neglected diagnostic information. Challenges for primary care physicians *Journal of General Internal Medicine* Vol. 11, No. 12
- ²⁹ Haponik EF et al., Sleep history is neglected diagnostic information. Challenges for primary care physicians *Journal of General Internal Medicine* Vol. 11, No. 12
- ³⁰ Carney CE, et al., Beliefs about sleep in disorders characterized by sleep and mood disturbance *Psychosomatic Research* 2007 Vol. 62, No. 2
- ³¹ Holbrook AM et al., The diagnosis and management of insomnia in clinical practice: a practical evidence-based approach *Canadian Medical Association Journal* 2000 Vol. 162, No. 2
- ³² Lee KA, Sleep dysfunction in women and its management *Current Treatment Options in Neurology* 2006 Vol. 8, No. 5
- ³³ Morin CM, et al., Behavioral and pharmacological therapies for late-life insomnia: a randomized controlled trial *Journal of the American Medical Association* 1999 Vol. 281, No. 11
- ³⁴ Edinger JD et al., Cognitive behavioral therapy for treatment of chronic primary insomnia: a randomized controlled trial *Journal of the American Medical Association* 2001 Vol. 285, No. 14
- ³⁵ Ozminkowski RJ et al., The direct and indirect costs of untreated insomnia in adults in the United States *Sleep* 2007 Vol. 30, No.3
- ³⁶ Germain A, et al., Effects of a brief behavioral treatment for late-life insomnia: preliminary findings *Clinical Sleep Medicine* 2006 Vol. 15, No. 2
- ³⁷ Morin CM, et al. Nonpharmacologic treatment of chronic insomnia: an American Academy of Sleep Medicine Review *Sleep* 1999 Vol. 22
- ³⁸ National Institutes of Health State of the Science Conference Statement on Manifestations and Management of Chronic Insomnia in Adults June 13-15, 2005 *Sleep* 2005 Vol. 28
- ³⁹ National Institutes of Health State of the Science Conference Statement on Manifestations and Management of Chronic Insomnia in Adults June 13-15, 2005 *Sleep* 2005 Vol. 28
- ⁴⁰ Polo-Kantola P and Erkkola R, Sleep and the menopause *British Menopause Society* 2004 Vol. 10, No. 4
- ⁴¹ Polo-Kantola P and Erkkola R, Sleep and the menopause *British Menopause Society* 2004 Vol. 10, No. 4
- ⁴² Ohayon MM, Severe hot flashes are associated with chronic insomnia *Archives of Internal Medicine* 2006 Vol. 166, No. 12