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Inadequate sleep & obesity: Breaking the vicious cycle

Poor sleep negatively affects hormones that govern the food reward system and can interfere with weight-loss programs. Obesity in turn restricts sleep. Which treatments have shown promise?

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PRACTICE RECOMMENDATIONS

› *Consider cognitive behaviorial therapy for insomnia (CBT-I) first-line treatment for insomnia.* (A)

› *Carefully review patients' medication lists, as many pharmaceuticals can affect weight and sleep.* (C)

Strength of recommendation (SOR)

(A) Good-quality patient-oriented evidence

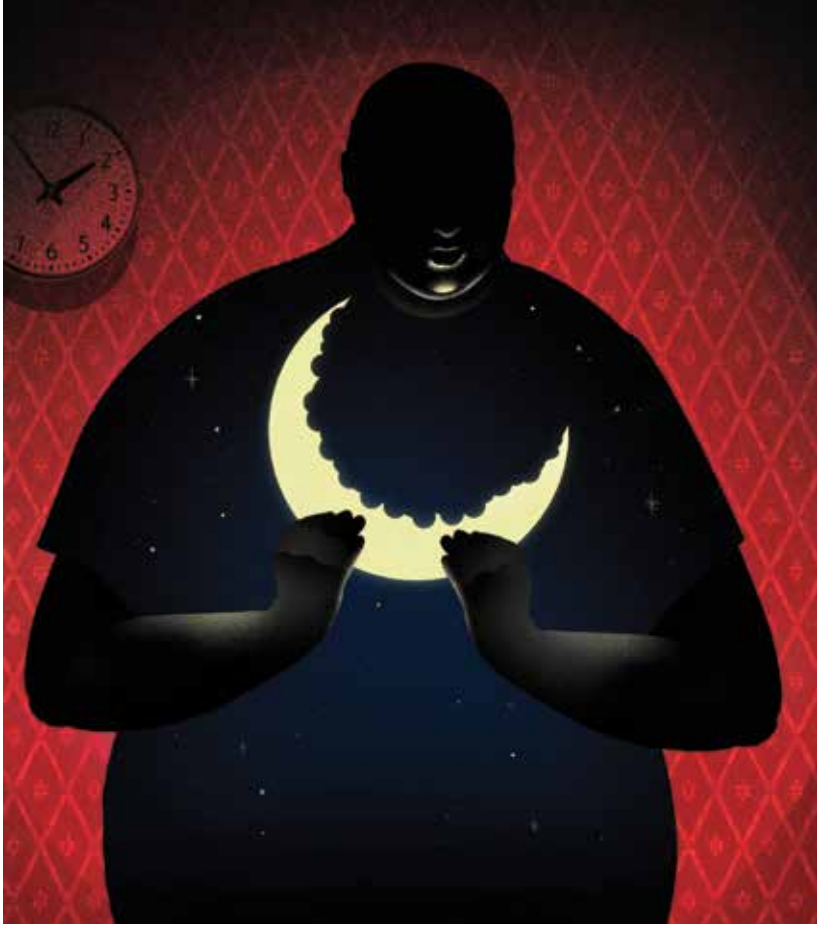
(B) Inconsistent or limited-quality patient-oriented evidence

(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

Sleep is fundamental to overall health and longevity, with the average person spending about one-third of their life sleeping.[1] Adequate sleep is critical for optimal cognition, memory consolidation, mood regulation, metabolism, appetite regulation, and immune and hormone functioning. According to the American Academy of Sleep Medicine and the Sleep Research Society, adults should sleep at least 7 hours per night on a regular basis "to promote optimal health."[2] Yet, between 2013 and 2020, only about 65% of adults in the United States were meeting this amount.[3] Insufficient sleep is associated with an increased risk for chronic health conditions, including obesity, diabetes, cardiovascular diseases, and even premature death.[4]

In a population-based longitudinal study of sleep disorders, short sleep duration was associated with increased body mass index (BMI), low blood levels of leptin, and high ghrelin levels.[5] In addition to physical impairments, poor sleep can impair cognitive performance and lead to vehicular accidents and increased accidents at work.[4] The potential economic impact that this may have is significant, and includes increased costs and loss of productivity in the workplace.[6]

Many factors may contribute to short sleep duration: environment, mental and physical condition, and social influences such as occupation, family responsibilities, travel, group activities, and personal care. Furthermore, the rapidly evolving and developing media, communication, and entertainment industries are already strongly implicated in poor sleep quality and quantity, both contributing to excessive daytime sleepiness.[7] Poor sleep quality is most notable in modern societies, and it correlates with the increasing prevalence of obesity, likely due to sleep's effect on food consumption and physical activity.[8] Optimizing a person's sleep will improve overall health and longevity by inhibiting the development of chronic disease.



Poor sleep will increase the risk for obesity and hinder its treatment. Therefore, sleep quality and duration are vital components of obesity management.

How insufficient sleep raises the risk for obesity

Not only is sleep beneficial for brain health, memory, learning, and growth, its effect on food consumption and physical activity likely correlates with the increased prevalence of obesity in modern society. Yet the optimal amount of sleep is controversial, and current recommendations of 7 or more hours of sleep per night for adults are derived from expert panels only.[2] The recommended sleep duration for children is longer, and it varies by age.[9] The quality of sleep and its impact on neuroendocrine hormones, not just the quantity of sleep, needs to be factored into these recommendations.

Sleep restriction activates the orexigenic system via the hormones leptin and ghrelin. These hormones control the food reward system, essentially increasing hunger and food intake. Leptin, created by white adipose tissue, is responsible for satiety and decreased food consumption.[10] Ghrelin, made by oxyntic glands in the stomach, is responsible for the sensation of hunger.

In a 2004 study by Spiegel et al,[11] leptin and ghrelin levels were measured during 2 days of sleep restriction (4 hours in bed) and sleep extension (10 hours in bed). Sleep restriction was associated with a decrease in leptin levels and an increase in ghrelin levels. The researchers reported that participants experienced an increase in hunger and appetite—especially for calorie-dense foods with high carbohydrate content.

Although research design has limitations with predominantly self-reported sleep data, studies have shown that short sleep time leads to increased food intake by increasing hunger signals and craving of unhealthy foods, and by providing more opportunities to eat while awake. It also may lead to decreased physical activity, creating a sedentary lifestyle that further encourages obesity.[8] Reduced sleep is even correlated to decreased efficacy of weight-loss treatments.[12]

Other sleep characteristics weakly correlated with obesity are sleep variability, timing, efficiency, quality, and daytime napping.[8] Sleep variability causes dysregulation of eating patterns, leading to increased food intake. A shift to later sleep and waking times often results in higher consumption of calories after 8 PM[13]; late-night snacks are a part of this sleep–obesity equation.[14]

Poor sleep efficiency and quality decreases N3-stage (deep non-REM) sleep, affects the autonomic nervous system, and has

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It is a cycle of poor sleep causing obesity and obesity causing poor sleep.

been associated with increased abdominal obesity. Daytime napping, which can cause irregular circadian rhythms and sleep schedules, is associated with increased obesity.[15] Thus, each component of sleep needs to be assessed to promote optimal regulation of the orexigenic system.

Another study showed that inadequate sleep not only promotes unhealthy lifestyle habits that can lead to obesity but also decreases the ability to lose weight.[16] This small study with 10 overweight patients provided its subjects with a controlled caloric intake over 2 weeks. Patients spent two 14-day periods 3 months apart in the laboratory, divided into 2 time-in-bed arms of 8.5 and 5.5 hours per night. Neuroendocrine changes caused by decreased sleep were associated with a significant lean body mass loss while conserving energy-dense fat.[16] This study highlights the importance of sleep hygiene counseling when developing a weight-management plan with patients.

Sleep, and its many components, play an integral role in the prevention and treatment of obesity.[17] Poor sleep will increase the risk for obesity and hinder its treatment. Therefore, sleep quality and duration are vital components of obesity management.

The sleep–obesity link in children and the elderly

Childhood obesity is linked to several chronic diseases in adulthood, including type 2 diabetes, cardiovascular disease, nonalcoholic fatty liver disease, asthma, and obstructive sleep apnea (OSA).[18] According to 2017-2018 NHANES (National Health and Nutrition Examination Surveys) data, obesity (BMI ≥ 95th percentile) prevalence among children and adolescents was reported at 19.3% and severe obesity (BMI ≥ 120% of the 95th percentile) at 6.1%. Pediatric overweight prevalence (≥ 85th percentile and < 95th percentile) was 16.1%.[19]

Although poor sleep is associated with increased risk for obesity, there is no proven cause-effect relationship.[20] Nutrition and physical activity have been identified as 2 critical factors in childhood obesity, but sleep health also needs to be investigated. Shorter sleep duration is strongly associated with the development of obesity. Furthermore, children with obesity are more likely to have shorter sleep duration.[21] A short sleep duration alters plasma levels of insulin, low-density lipoprotein, and high-sensitivity C-reactive protein. It is associated with lower diet quality, an increased intake of nutrient-poor foods, and a lower intake of vegetables and fruits.[22] Recent studies have shown that interventions to promote earlier bedtimes can improve sleep duration in children.

Older adults have many sleeping issues, including insomnia, circadian rhythm sleep-wake disorders, sleep-related movement disorders, and sleep-breathing disorders. Additionally, the older population has increased sleep latency, decreased sleep efficiency and total sleep time, decreased REM sleep, more frequent nighttime awakenings, and more daytime napping.[23] The increased sleep disturbance with age is mainly related to higher risk factors for sleep disorders than the aging process itself. Sleeping 5 or fewer hours is associated with an increased risk for obesity and central abdominal fat compared with those who sleep 7 to 8 hours per night.[24] Similar to children and youth, older adults also show a strong correlation between inadequate sleep and obesity.[24]

The consequence: A vicious cycle

Obesity in turn leads to shorter sleep duration and more disruptions. This negatively affects the orexigenic system, and the resulting hormonal derangement promotes worsening obesity. It is a cycle of poor sleep causing obesity and obesity causing poor sleep. Insomnia, in combination with shorter (and longer) sleep times, also has been linked with obesity.[25] These patients experience more daytime sleepiness, fatigue, and nighttime sleep disturbances, all correlated with decreased quality of life and higher prevalence of medical comorbidities.[8,26] Additional comorbidities secondary to obesity, including gastroesophageal reflux, depression, and asthma, also have been linked to sleep disturbances.[8]

OSA is a common sleep complication associated with obesity. With the increasing prevalence of obesity, the prevalence of OSA

is rising.[8,27] Factors that heighten the risk for OSA are male sex, age 40 to 70 years, postmenopausal status, elevated BMI, and craniofacial and upper airway abnormality.[28] However, the US Preventive Services Task Force found insufficient evidence to screen for or treat OSA in asymptomatic adults.[28] Signs and symptoms of OSA include nighttime awakenings with choking, loud snoring, and feeling unrefreshed after sleep.[29]

OSA is caused by the intermittent narrowing and obstruction of the pharyngeal airway due to anatomical and structural irregularities or neuromuscular impairments. Untreated OSA is associated with cardiovascular disease and cardiac arrhythmias such as atrial fibrillation. Even with this correlation between obesity and sleep, it is estimated that 80% of OSA remains undiagnosed.[30] Approximately half of primary care clinicians do not screen at-risk patients for OSA, and 90% do not use validated OSA screening tools.[31] Screening tools that have been validated are the STOP, STOP-BANG, Epworth Sleepiness Scale, and 4-Variable Screening Tool. However, the US Department of Veterans Affairs and the US Department of Defense have a more recent guideline recommending STOP as an easier-to-administer screen for OSA.[32] A positive result with a screening tool should be confirmed with polysomnography.[32]

Intervention for OSA. The longest randomized controlled study to date, Sleep AHEAD, evaluated over a period of 10 years the effect of weight loss on OSA severity achieved with either an intensive lifestyle intervention (ILI) or with diabetes support and education (DSE).[33] OSA severity is rated on an Apnea-Hypopnea Index (AHI), with scores reflecting the number of sleep apnea events per hour. This study demonstrated that weight loss was associated with decreased OSA severity. At 4-year follow-up, the greater the weight loss with ILI intervention, the lower the patients' OSA severity scores. The study found an average decrease in AHI of 0.68 events per hour for every kilogram of weight loss in the ILI group ($P < .0001$).[33,34] Over the follow-up visits, the ILI participants had 7.4 events per hour, a more significantly reduced AHI than the DSE participants ($P < .0001$).[33,34]

Additionally, a small cohort of study participants achieved OSA remission (ILI, 34.4%; DSE, 22.2%), indicated by a low AHI score (< 5 events per hour). At the conclusion of the study, OSA severity decreased to a greater degree with ILI intervention.[33,34]

Alcohol and drug use can negatively influence sleep patterns and obesity. Higher alcohol consumption is associated with poorer sleep quality and higher chances of developing short sleep duration and snoring.[35] Alcohol, a muscle relaxant, causes upper airway narrowing and reduced tongue muscle tone, thereby increasing snoring and OSA as demonstrated by increased AHI on polysomnography after alcohol intake. Alcohol also changes sleep architecture by increasing slow-wave sleep, decreasing REM sleep duration, and increasing sleep arousal in the second half of the night.[36] Disrupted circadian rhythm after alcohol consumption was correlated with increased adenosine neurotransmitters derived from ethanol metabolism.[37] Alcohol dependence may be related to other psychiatric symptoms, and chronic alcohol use eventually alters sleep mechanisms leading to persistent insomnia, further perpetuating adverse outcomes such as suicidal ideation.[36] There are positive associations between beer drinking and measures of abdominal adiposity in men, and "the combination of short sleep duration [and] disinhibited eating ... is associated with greater alcohol intake and excess weight."[38]

Therefore, counsel patients to avoid alcohol since it is a modifiable risk factor with pervasive adverse health effects.

Many drugs have a profound effect on sleep patterns. Illicit drug use in particular can affect the brain's neurotransmitter serotonin system. For example, ecstasy users have an increased risk for OSA.[39] People with cocaine and heroin use disorder tend to have more sleep-maintenance insomnia.[40]

In contrast, those with alcohol or cannabis use disorder tend to have more sleep-onset insomnia.[40] Not only do illicit drugs interrupt sleep, but daily tobacco use also has been correlated with increased insomnia and shorter sleep duration since nicotine is a stimulant.[41]

Insomnia is commonly treated with

Approximately half of primary care clinicians do not screen at-risk patients for OSA, and 90% do not use validated OSA screening tools.

TABLE 1

Accuracy of questionnaires for assessing obstructive sleep apnea-hypopnea syndrome (OSAHS)[44]

OSAHS severity	ESS	Berlin	STOP	STOP BANG	4-Variable ≥ 11	4-Variable ≥ 14
Mild (AHI 5-14)						
Sensitivity	50%	84.4%	95%	96.2%	78%	50.7%
Specificity	67%	35.3%	15.7%	14%	40.8%	78%
Moderate and severe (AHI ≥ 15)						
Sensitivity	54%	87%	96%	97.6%	79%	55%
Specificity	67%	32.6%	13%	12.7%	36%	74.4%

AHI, apnea-hypopnea index; ESS, Epworth Sleepiness Scale.
Adapted from: Pataka et al. *Sleep Med*. 2014.[44]

sedative antidepressants and hypnotics—eg, mirtazapine and olanzapine—that contribute to weight gain.[42] In addition, other common pharmaceuticals used for sleep disorders, such as diphenhydramine, have sedative properties and tend to lead to weight gain.[43] Because so many medications affect sleep and weight, carefully review patients' medication lists and switch offending agents to weight-neutral drugs if possible.

Treatment and tools to improve sleep in patients with obesity

Given the strong correlation between obesity and sleep disorders, validated screening tools should be used to assess sleep quality, including onset and potential symptoms associated with poor sleep (**TABLE 1**[44]). For weight management to succeed in patients with obesity, it is crucial to address sleep in addition to nutrition and physical activity.[17,45]

Physical activity has many benefits to overall health, especially for chronic diseases such as type 2 diabetes and hypertension. The Centers for Disease Control and Prevention recommends at least 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous-intensity aerobic exercise per week in addition to muscle-strengthening activities 2 or more days per week.[46] However, approximately 300 minutes of moderate-intensity activity per week is suggested for successful weight loss with exercise alone.[47]

Physical activity and diet in combination are vital, but diet restriction has a more substantial effect on weight loss than physical activity alone.[48] Still, physical activity is essential in helping maintain and prevent weight regain.

Nonpharmacologic interventions include promoting greater sleep quality and quantity by emphasizing good sleep hygiene practices. Developing a practical and effective bedtime routine, creating a quiet sleep environment, and practicing healthy daily habits are essential components to sleep hygiene (**TABLE 2**[49,50]). Relaxation techniques and cognitive behavioral therapy (CBT) also can help. CBT for insomnia (CBT-I) is the first-line intervention for chronic insomnia.[51] Sleep restriction is a type of CBT used to treat insomnia, encouraging short-term sleep loss in the hopes of improving insomnia. A trial by Logue et al showed that patients with overweight and obesity randomized to undergo CBT with better sleep hygiene (nonpharmacologic) interventions had a greater mean weight loss percentage (5% vs 2%; $P = .04$) than did those who received CBT alone.[52]

Eastern medicine including herbal interventions lack evidence of efficacy and safety. Further studies need to be done on the effects that chamomile, kava, valerian root (*Valeriana officinalis),* tryptophan, and Wu Ling (from mycelia Xylaria nigripes) might have on sleep.[53]

Proceed cautiously with medication. The American College of Physicians recommends a shared decision-making approach when considering pharmacologic therapy

TABLE 2

Patient tips for improving sleep pattern[49,50]

Bedtime routine	• Create a consistent sleep schedule with fixed sleep and wake-up times, including weekends. • Create a bedtime routine that follows the same steps each night. • Practice relaxation and stress management, including meditation, mindfulness, and breathing exercises. • Unplug from electronics 30-60 min before bedtime and dim lights to promote the production of melatonin, an essential hormone in the body that facilitates the sleep cycle.
Sleep environment	• Choose a comfortable mattress and pillow. • Make sure your bedroom is quiet. Consider ear plugs, a white noise machine, or a fan to reduce noise. • Remove all electronics from the bedroom. • Set the bedroom thermostat to a comfortable temperature. Consider setting it to a cooler temperature, around 68° or less.
Daily healthy habits	• Avoid large meals, caffeine, alcohol, or nicotine before bedtime. • Engage in regular daily physical activity. Avoid at least 3-4 h before bedtime. • Get daily sunlight exposure.

for chronic insomnia and the American Academy of Sleep Medicine (AASM) offers guidance on options.[51,54] However, the evidence behind AASM sleep pharmacologic recommendations is weak, implying a lesser degree of confidence in the outcome and, therefore, in its appropriateness. Thus, it falls upon the clinician and patient to weigh the benefits and burdens of the pharmacologic treatments of insomnia. If indicated, medications suggested to treat sleep onset and sleep maintenance insomnia are eszopiclone, zolpidem, and temazepam. Zaleplon, triazolam, and ramelteon may improve sleep initiation. Suvorexant and doxepin are used for sleep-maintenance insomnia.[54] Exploring patient preferences, cost of treatment, health care options, and available resources should all be considered. JFP

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