Screening for Sleep Apnea in Morbidly Obese Pilots

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BACKGROUND: Debate regarding the merits of screening pilots for sleep apnea has been stimulated by recently issued guidance from the Federal Aviation Administration. It has long been appreciated that sleep apnea results in poor quality sleep, and that poor quality sleep is associated with daytime fatigue and decrements in performance. However, the relationship between sleep apnea and poor performance, including risk for accidents is not as well understood. Good quality data are available for commercial truck drivers and have helped influence transportation policy, but there is a lack of pilot specific data. The purpose of this article is to review the basic epidemiology, pathophysiology, and treatment of sleep apnea, including major risk factors for apnea, such as body mass index (BMI), and to look at what is known about the impact of sleep apnea on performance in transportation related occupations. While pilot specific data may be lacking, good quality data for commercial truckers are available and can be used to formulate rational public policy with the goal of improving aviation safety. This article was reviewed by the Council of the Aerospace Medical Association and approved as a position paper of the Association.

KEYWORDS: obesity, obstructive sleep apnea, safety, sleep deprivation.

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Obese commercial truck drivers[19,33,45] and recreational and commercial pilots may be at risk for obstructive sleep apnea (OSA), which may pose a risk to public safety. Recommendations for OSA screening in these groups are therefore currently a topic of debate. Obesity is the most important modifiable risk factor for developing obstructive sleep apnea, and its incidence is rising rapidly.[55] Links between OSA and impaired daytime functioning are well established,[28] making screening for sleep apnea an urgent flight safety issue.

Body weight in the general population has been rising at a rapid rate since the 1980s.[55] Worldwide, the prevalence of being overweight (body mass index or BMI $\geq 25\ kg \cdot m^{-2}$) increased from 25 to 34%, and of being obese (BMI $\geq 30\ kg \cdot m^{-2}$) increased from 6 to 12% between 1980 and 2008.[55] In the United States nearly one-third of the adult population is overweight (BMI between 25 and 29.9 $kg \cdot m^{-2}$) and an additional one-third is obese (BMI $\geq 30\ kg \cdot m^{-2}$). Furthermore, the rate of increase has been accelerating in the population segments with the highest BMI.[56]

There is a very strong relationship between elevated BMI and presence of sleep apnea.[22] An increase of 1 SD in any body habitus measure is associated with a threefold increase in risk of sleep apnea,[68] and it is estimated that 98% of individuals with a BMI over 40 have sleep apnea.[60] The relationship between sleep deprivation and impairment of daytime functioning is well established.[31,40] For example, individuals with sleep apnea, which can result in sleep disruption, have higher rates of motor vehicle accidents.[6,57] Treatment with continuous positive airway pressure (CPAP) substantially decreases this risk.[58] Untreated OSA, especially when severe, is also associated with comorbidities that include coronary artery disease, stroke, and diabetes mellitus.[14,30,37] While there is little disagreement that untreated sleep apnea is associated with poor daytime performance and increases in cardiovascular disease and death, the extent of this impact on pilot performance is unknown. Furthermore, although there are protocols for screening pilots, the best way to identify those individuals who are at the highest risk for impairment in the aviation environment is being debated. This is in large part due to a lack of pilot-specific data on this issue.

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EPIDEMIOLOGY

OSA is characterized by repeated episodes of upper airway obstruction during sleep (**Fig. 1**). It is highly prevalent in the United States, affecting approximately 10% of the general population,[14] with some studies suggesting that in men aged 50-70 yr the prevalence is as high as 17%.[46] As discussed previously, OSA is strongly associated with obesity,[22] and is nearly universal in people with a BMI of 40 $kg \cdot m^{-2}$, which corresponds to a 180 cm (71 inches) person who weighs 134 kg (295 pounds).[67] This relationship is nonlinear and is observed irrespective of the measure used. Increasing body weight by 10 kg (22 lb) nearly doubles the risk of OSA, while a fourfold increase in risk is associated with a 6 $kg \cdot m^{-2}$ increase in BMI or an increase in waist or hip circumference by 13 to 15 cm (5 to 6 inches).[50] Likewise, a neck circumference of greater than 43 cm (17 inches) in men or greater than 41 cm (16 inches) in women is also a risk factor for OSA because adipose and muscle tissue around the neck can compress the airway. Macroglossia (a large tongue) may be a predisposing factor for OSA. The Mallampati classification is used as a predictor for difficult endotracheal intubation, and American Academy of Sleep Medicine guidelines recommend assessing the Mallampati score as part of diagnostic workup for OSA.[27] Although the Mallampati score is easy to assess, it is dependent on patient effort, and more precise predictive methods are needed.[10]

PHYSIOLOGY

Airway obstruction in OSA is caused by occlusion of the nasopharynx and oropharynx that occurs when the tongue and palate move posteriorly during sleep and come to rest against the posterior pharyngeal wall. Narrower airways are more easily collapsible and prone to airway occlusion. People who are obese have extrinsic narrowing of the area surrounding the collapsible region of the pharynx that is caused by excess soft tissue in the area. Obesity is associated with deposition of fatty tissue and submucosal edema in the lateral walls of the pharynx.[47] Obesity is also associated with increased amounts of peripharyngeal fat, and in turn larger neck circumference. These pharyngeal fat deposits cause narrowing of the lumen and increased upper airway collapsibility, and may predispose the patient to obstruction when neuromuscular tone decreases during sleep. Obesity may also increase upper airway collapsibility by reducing lung volumes, particularly functional residual capacity.

Fig. 1. Upper airway obstruction in sleep apnea.

OSA causes significant stress on the cardiovascular system. During normal sleep, blood pressure and heart rate fall by approximately 25%. During OSA, abrupt inspiratory efforts occur during pharyngeal collapse, in turn causing a sudden, large increase in negative intrathoracic pressure. This increases left ventricular transmural pressure, left atrial wall tension, and venous return to the right ventricle. The ultimate result is decreased preload and stroke volume. As arterial oxygen saturation decreases, myocardial oxygen supply becomes insufficient to meet demand while peripheral and central sympathetic excitatory reflexes are stimulated. The patient then abruptly arouses from sleep, further increasing sympathetic nerve discharge and decreasing vagal tone. The net effect is an increase in heart rate and a surge in blood pressure that subside as the patient goes back to sleep.[14] This may ultimately result in hypertension, congestive heart failure, and other cardiovascular complications.

OSA causes significant sleep disruption.[41] Normal sleep is characterized by an alternate cycling between non-rapid-eye-movement (NREM) sleep and rapid-eye-movement (REM) sleep.[17] NREM sleep consists of three stages that range from "light" Stages 1 (N1) and 2 (N2) sleep, to "deep" Stage 3 (N3) sleep. A period of REM sleep typically follows each episode of NREM sleep. This alternating cyclic pattern of NREM and REM sleep occurs throughout the night, and each cycle lasts about 90 min. In the earlier part of the night, slow-wave or deep sleep predominates, and in the last third of the night, REM sleep (or "dream sleep") predominates. A typical young adult will spend 70–75% of sleep in NREM and 20–25% of sleep in REM. Wakefulness within the sleep period typically occurs during less than 5% of the night. Although the precise functional role of each type of sleep and the cyclical pattern of sleep stages is not yet fully understood, it is generally accepted that disruptions to the continuity of sleep will affect the restorative value of sleep as well as next-day functioning and/or alertness.[54] OSA results in sleep fragmentation due to the numerous apnea-related asphyxias that persist throughout the night.[38] The severity of apnea is determined by the Apnea-Hypopnea Index (AHI), which is the number of times per hour an individual has a decrease in airflow by ≥90% (apnea) or ≥70–90% with either an arousal or an oxygen desaturation ≥3% (hypopnea), as measured by either an oronasal thermal sensor or positive airway pressure device flow.[9] Fewer than 5 events per hour are considered to be within normal limits, 5-15 events per hour are classified as mild, 15-30 per hour are classified as moderate, and greater than 30 per hour are classified as severe. These events are accompanied by oxygen desaturations and arousals that interfere with sleep quality.[27] Since respiratory rate varies according to the state of consciousness, there is a particularly pronounced deprivation in the deepest stages of sleep (often

thought to be the most restorative stages) as well as in REM sleep (which is thought to play a role in memory consolidation). Because of these changes, the sleep of OSA sufferers is disrupted and therefore inadequate.[15]

OSA AND HUMAN PERFORMANCE

Effects of Sleep Curtailment/Disruption on Performance

Multiple well-designed studies have shown unequivocally that inadequate sleep adversely impacts neurocognitive functioning and performance.[31,40,63] All cognitive performance measures are negatively affected, including attention, judgment, reaction time, and accuracy.[4,5,43] Sleep loss produces decrements in vigilance, cognitive slowing, short-term memory failures, deficits in frontal lobe function, and rapid, involuntary episodes of "dozing off".[12,35,36] The severity of these disturbances is closely related to the degree of sleep disruption. For example, total sleep deprivation will cause an immediate and drastic disruption to overall functioning,[40] whereas milder sleep restriction or sleep fragmentation may exert a less-pronounced impact, at least in the near-term.[5] Several nights of this type of disrupted sleep have the same effects as acute sleep restriction; alertness and performance are degraded to the same extent.

General Types of Sleep Disturbances

The majority of sleep and performance studies have historically focused on the effects of total acute sleep deprivation, but more recently the effects of partial sleep restriction have received increased attention.[48] This shift in focus may be due to the greater societal prevalence of partial sleep loss as a result of medical conditions and sleep disorders, as well as lifestyle factors (e.g., shiftwork, jet lag, prolonged work hours).[5] Partial sleep deprivation results from sleep restriction, which can occur due to work-scheduling factors and/or poor sleep habits; sleep fragmentation, which occurs with certain sleep disorders (e.g., untreated obstructive sleep apnea); or selective sleep stage deprivation, which can occur if sleep fragmentation is isolated to a specific sleep stage (e.g., when apneic episodes disrupt primarily one stage of sleep such as REM sleep).

Total sleep deprivation. A meta-analysis conducted by Lim and Dinges[40] showed that sleep deprivation produces relatively rapid and significant decrements in most cognitive domains, with simple attention and vigilance tasks showing the largest effect, while complex attention and working memory tasks are affected to a lesser extent. Durmer and Dinges concluded that the homeostatic sleep pressure that rapidly builds during periods of prolonged wakefulness leads to uncontrollable lapses into sleep, or micro sleeps.[24] These prolonged periods of wakefulness affect not only neurocognitive states, but also cause changes in mood and increase levels of subjective fatigue. Years of research support the serious negative effects of total sleep deprivation across a range of people involved in diverse endeavors and occupations.

Sleep restriction. Total sleep deprivation is clearly a concern in safety-sensitive scenarios, but chronic sleep restriction is more common, and scientific interest in its effects has grown in recent years.[7] The impact of sleep restriction is generally similar to that of total deprivation, but is somewhat less pronounced, at least in the near-term. Sleep restriction of the type often faced by personnel who work nonstandard schedules, cross multiple time zones, or practice inadequate sleep hygiene, produces serious decrements in cognition and performance. Two classic studies in which the effects of chronic sleep restriction were assessed indicated that chronic sleep loss produced a "dose response" effect, with performance decrements progressively increasing as time in bed (and thus time asleep) is systematically reduced.[8,61] Sleep duration under 6 h per night produced the greatest decrements in both investigations – a finding confirmed by other reports.[5,32,52] Of further interest is the fact that when sleep is restricted to 4 – 6 h per night, cognitive performance declines are similar to the deficits seen during 24 – 48 h of continuous wakefulness.[61] Moreover, recovery from chronic sleep restriction across consecutive days is not rapid; return to well-rested baseline performance can take from several days up to a week after the sleep restriction has ended.[3,8] Research participants who were restricted to 7 or fewer hours of sleep for several days did not experience a full recovery in performance even after 3 d of 8 h of sleep per night.[8] Although extended postsleep-restriction recovery-sleep opportunities had beneficial effects, even people who were offered a 10-h night in bed following several days of sleep restriction were not fully recovered after one night.[5] Thus, personnel who are chronically sleep restricted due to work-related scheduling factors (i.e., pilots, truck drivers, traveling executives, etc.) are at risk not only during the sleep-restriction periods themselves, but for several days afterwards as well.

Sleep fragmentation and selective sleep stage deprivation. Sleep disruptions of the sort that occur with untreated sleep disorders, particularly sleep apnea, likewise cause performance deficits and excessive on-the-job sleepiness or fatigue.[11,15] Although there is a lack of complete scientific consensus on the extent of these effects,[13,51] it is generally accepted that sleep fragmentation adversely affects cognitive functioning and performance.[15,39,54] A meta-analysis conducted by Bucks et al. indicated that the sleep alterations associated with obstructive sleep apnea (i.e., significant reductions in REM sleep and deep sleep) slow cognitive processes, produce deficits in attention and vigilance, impair long-term visual and verbal memory, and disrupt visual-spatial/constructional abilities.[15] OSA-induced sleep alterations also degrade the executive functions essential for volition, planning, purposeful action, and the monitoring of effective performance. There is indirect evidence that obstructive sleep apnea leads to structural damage to the brain over time.[39] This damage forms the foundation for cognitive impairments that include decrements in reasoning abilities, vigilance, learning, and memory.

Sleep apnea linked to increased risk of accidents. OSA has been associated with an increased risk of accidents in both commercial and noncommercial drivers. A systematic review of 40 studies found that noncommercial drivers who had been diagnosed with OSA were at increased risk for a traffic accident; however, in part due to methodological issues, no consistent statistically significant relationship was found between the severity of OSA and accident risk.[57] Other studies which examined the efficacy of treatment of OSA with CPAP found improvement in driver performance.[26] Xie et al. studied the effectiveness of screening criteria for OSA in commercial drivers. These criteria included a history of snoring, excessive daytime sleepiness, or witnessed apnea events; an Epworth Sleepiness Scale (ESS) score of greater than 10; body mass index of 35 $kg \cdot m^{-2}$ or greater, and a neck circumference of greater than 17 inches in men or greater than 16 inches in women; uncontrolled hypertension; and sleeping in the examination or waiting rooms. They found that these criteria had a positive predictive value of 78%.[65] A systematic review by Treager et al. found that there was a significant association between OSA and motor vehicle accidents in commercial drivers; drivers with OSA had a risk that was up to four times greater than a driver without OSA.[57]

Although OSA has not been implicated as a direct causal factor in an aviation accident, fatigue has been associated with both incidents and accidents. The National Transportation Safety Board determined that fatigue was the probable cause of an incident in which both the captain and first officer of a Part 121 flight fell asleep and overflew their destination. Undiagnosed OSA was listed as a contributing factor based on the fact that 3 mo after the incident, the captain was diagnosed with severe OSA.[34] A study using electroencephalography to measure brain activity found 10 episodes of sleep or reduced alertness in 400 person-hours of flight.[64] In 2008, the Federal Motor Carrier Safety Administration recommended that all commercial driver license candidates with a BMI over 30 $kg \cdot m^{-2}$ undergo screening for OSA. Because of its potential impact on flight safety, the Federal Aviation Administration requires that airmen diagnosed with OSA obtain a special issuance medical certificate. An airman undergoing treatment for OSA must submit a polysomnogram and information regarding the elimination of symptoms such as daytime sleepiness. OSA may also be an additional risk factor for developing significant arterial hypoxia during flight, therefore when a minimum overnight SpO_2 of less than 65% is seen during polysomnography, further assessment may be required.[1]

Sleep apnea associated with serious comorbidities. OSA is associated with a number of comorbidities that could cause sudden incapacitation. Sleep apnea has been demonstrated to increase risk of stroke and death by any cause,[66] and may predispose patients to cardiovascular disease through a number of mechanisms, including sleep fragmentation, intermittent hypoxia, chronic activation of the sympathetic nervous system, and inflammation. OSA increases the risk of Type 2 diabetes mellitus, and may also exacerbate the vascular complications of diabetes. The latter may be caused by chronic hypoxia and oxidative stress-induced injury of endothelium and peripheral nerves.[44] One longitudinal study of adults referred for polysomnography found that both the presence of OSA and nocturnal hypoxemia were independent risk factors for sudden cardiac death.[30] Another study linked total time spent during sleep with an oxygen saturation less than 90% to a 50% increase in the risk of a cardiovascular event or death.[37]

Additive impact of sleep-disruptive factors. The two primary determinants of on-the-job alertness are the sleep regulatory process or the degree to which the minimum routine physiological sleep requirement is being met (i.e., the homeostatic component of the fatigue equation); and the circadian rhythm or the timing of the work/sleep period in relationship to the body's biological clock (i.e., the circadian component of the fatigue equation).[31] Although sleep regulation is an important consideration, failure to obtain sufficient high-quality sleep causes an accumulation of homeostatic sleep pressure. This in turn can be expected to impair both cognition and performance.[31] This failure in sleep regulation is not affected by its cause; poor personal choices, work-related scheduling factors, sleep disorders, or other factors produce the same effects. Insufficient sleep from any cause will ultimately decrease performance and alertness, with possible catastrophic consequences in safety-sensitive occupations. It is therefore imperative that operational personnel obtain the requisite amount of high-quality sleep on a day-to-day basis. Although regulatory bodies such as the Federal Aviation Administration (FAA) dictate duty and rest schedules in an attempt to meet this objective and safeguard personnel from unwanted sleep reductions (and a consequent increase in the homeostatic drive toward dangerous on-the-job sleepiness), unpredictable schedule changes from weather or maintenance delays; requirements for late-night or early-morning duty times; and/or rapid and constant time-zone changes often create sleep-related difficulties. Unfortunately, when work-related sleep curtailments are exacerbated by medically related sleep disruptions or fragmentations, the resulting additive effects can seriously undermine even the best fatigue-risk-management systems.

APPROACH TO SCREENING FOR SLEEP APNEA

Screening for sleep apnea is most frequently initiated during a general history and physical examination, with questioning about the presence of loud snoring, poorly refreshing sleep, and daytime sleepiness, and collection of objective measures such as body mass index (BMI). Increasingly, brief questionnaires such as the eight-item STOP-BANG,[18] designed to facilitate the identification of important risk factors such as loud snoring, witnessed apneas, presence of hypertension, morning headaches, and elevated BMI, are being used to identify those at highest risk for sleep apnea. High-risk individuals require further specialized evaluation. Clinical evaluation by a sleep specialist includes a review of sleep habits, daily sleep duration, environmental, social, and medical factors influencing sleep quality, and identification of poorly controlled hypertension,

cardiovascular disease, and type II diabetes mellitus, all of which have been associated with untreated apnea.[14,30,37] The clinical exam is also used to screen for other common sleep disorders such as insomnia, and Restless Leg Syndrome (RLS) that can contribute to poor quality rest. The latter is important because over 30% of patients with a primary diagnosis of sleep apnea have additional sleep problems,[53] which may require treatment to ensure optimal sleep quality and daytime performance. There should also be a detailed discussion of lifestyle issues, including optimal sleep hygiene and weight management. Screening for alcohol use is especially important because alcohol can disrupt sleep quality, worsen sleep apnea, and work synergistically with sleep deprivation to worsen performance.[23,25,59] After clinical evaluation, if apnea or other disorders requiring polysomnographic evaluation are suspected, then a sleep study is ordered.

The gold standard for evaluation of sleep apnea is in-laboratory overnight polysomnography (PSG), which involves measurement of airflow at the oropharynx as well as chest and abdominal movements, pulse oximetry, electrocardiography (EKG), electroencephalography (EEG, for sleep staging), and electromyography (EMG, for movements). In many cases, especially if severe sleep apnea is identified early in the night, the second half of the study is used to initiate treatment with continuous positive airway pressure (CPAP), using a single study for diagnosis and treatment. Studies performed in a sleep laboratory provide a high degree of diagnostic accuracy and reproducibility, but the associated time and expense have placed an increasing focus on the use of at-home testing. Currently available at-home sleep testing devices measure airflow, respiratory effort, and blood oxygenation.[20] Single channel devices measuring both oxygen saturation and photoplethysmography are under investigation. At-home tests reduce cost by a factor of two-thirds, but are not suitable for all individuals, require specialized expertise to interpret, and most importantly can only be used to rule in sleep apnea. The latter is a critical and often overlooked point because a negative home test means that the patient must start the process again in the laboratory.[20] If significant sleep apnea is found on home sleep testing, then in many cases, an auto-titrating CPAP machine can be prescribed for treatment. While other methods such as overnight oximetry have been advocated as screening methods, currently these techniques lack sufficient sensitivity and specificity to make them effective tools for diagnosis.[21]

Although CPAP remains the gold-standard for therapy, two other treatment options are available, surgical intervention with uvulopalatopharyngoplasty (UPPP),[2] and therapy with oral appliances.[42] The former intervention is most successful in patients with mild to moderate sleep apnea.[2] UPPP is invasive, requires considerable recovery time, and it is often hard to predict presurgically whether an individual's apnea will be significantly treated. After recovery from surgery, it is necessary to repeat overnight polysomnography to determine response, and some patients may still require CPAP after surgery. Complications of UPPP include voice changes, difficulty swallowing, nasal regurgitation, and disturbances in taste.[29] Maxillofacial advancement surgery produces a significant decrease in the apnea-hypopnea index,[16] but is a long and technically challenging procedure. Complications can include facial sensory deficits and dental malocclusion. A number of different oral appliances have been studied and may be useful for treating mild to moderate sleep apnea. However, they require individualized fabrication by a dentist with specialized training, and initially require multiple adjustments. After the adjustment of an oral appliance has been optimized, repeat sleep study testing with the device in place is needed to ensure that the OSA has been treated. This process is almost always more expensive than standard CPAP therapy.

Once a diagnosis is made and appropriate treatment has been initiated, response to therapy must be periodically evaluated to ensure compliance. Six percent of individuals have significant residual daytime sleepiness even after they have been optimally treated,[49] so patients must be clinically evaluated to confirm that both respiratory events and daytime sleepiness have resolved.[62] Modern CPAP devices incorporate technology that allows monitoring of daily usage, including hours used, mask leak, and residual sleep disordered breathing. This technology is already used to help monitor response to therapy, provides an objective measure of response to treatment, and helps individuals demonstrate adherence to therapy for occupational considerations. At this time, there are insufficient data to support the use of standard overnight oximetry for the routine monitoring of response to therapy. Additionally, even after successful therapy has been initiated, periodic follow-up is required to insure continued benefit. Factors such as aging, weight gain, and in women the onset of menopause can result in worsening apnea severity,[47] which requires adjustment in therapy.

ASMA POSITION STATEMENT

Sleep apnea is highly prevalent in the general population, and is nearly universally present in individuals with a BMI greater than 40 $kg \cdot m^{-2}$. It is strongly associated with impaired cognitive performance and daytime performance, and linked with increased motor vehicle accident rates. Although there is a paucity of pilot-specific data, extrapolation from the motor vehicle data (a setting likely to be less cognitively demanding), strongly suggests that screening and treatment for OSA should be considered in this population. While the approach to the optimal screening of the general pilot population is being debated and refined, individuals who are morbidly obese and in whom OSA is highly likely should undergo screening.

Although many real-world constraints may prevent every person in a safety-sensitive occupation from receiving consistent, high-quality sleep in all situations, ensuring that these personnel are free from treatable disorders that prevent high quality sleep is an achievable objective. Sleep disorders, such as obstructive sleep apnea, present serious health and performance risks. With proper screening and follow-up, however, the risks associated with sleep apnea can be reasonably managed in the modern occupational environment. The Aerospace Medical Association encourages any initiatives which enhance

awareness and lead to treatment of this condition as it affects flight safety and pilot performance.

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REFERENCES

1. Ali M, Smith IE, Gulati A, Shneerson JM. Hypoxic challenge assessment in individuals with obstructive sleep apnea. Sleep Med. 2011; 12(2): 158–162.
2. Aurora RN, Casey KR, Kristo D, Auerbach S, Bista SR, et al. Practice parameters for the surgical modifications of the upper airway for obstructive sleep apnea in adults. Sleep. 2010; 33(10):1408–1413.
3. Axelsson J, Kecklund G, Akerstedt T, Donofrio P, Lekander M, Ingre M. Sleepiness and performance in response to repeated sleep restriction and subsequent recovery during semi-laboratory conditions. Chronobiol Int. 2008; 25(2):297–308.
4. Balkin TJ, Rupp T, Picchioni D, Wesensten NJ. Sleep loss and sleepiness: current issues. Chest. 2008; 134(3):653–660.
5. Banks S, Dinges DF. Behavioral and physiological consequences of sleep restriction. J Clin Sleep Med. 2007; 3(5):519–528.
6. Barbé Pericás J, Muñoz A, Findley L, Antó JM, Agustí AG. Automobile accidents in patients with sleep apnea syndrome. An epidemiological and mechanistic study. Am J Respir Crit Care Med. 1998; 158(1):18–22.
7. Basner M, Rao H, Goel N, Dinges DF. Sleep deprivation and neurobehavioral dynamics. Curr Opin Neurobiol. 2013; 23(5):854–863.
8. Belenky G, Wesensten NJ, Thorne DR, Thomas ML, Sing HC, et al. Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose-response study. J Sleep Res. 2003; 12(1):1–12.
9. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012; 8(5):597–619.
10. Bins S, Koster TD, de Heij AH, de Vries AC, van Pelt AB, et al. No evidence for diagnostic value of Mallampati score in patients suspected of having obstructive sleep apnea syndrome. Otolaryngol Head Neck Surg. 2011; 145(2):199–203.
11. Bittencourt LR, Lucchesi LM, Rueda AD, Garbuio SA, Palombini LO, et al. Placebo and modafinil effect on sleepiness in obstructive sleep apnea. Prog Neuropsychopharmacol Biol Psychiatry. 2008; 32(2): 552–559.
12. Bonnet MH. Sleep deprivation. In: Kryger MH, Roth T, Dement WC, ed. Principles and Practice of Sleep Medicine, 2 ed. Philadelphia (PA): W. B. Saunders Company; 1994:50–67.
13. Bonnet MH, Arand DL. Clinical effects of sleep fragmentation versus sleep deprivation. Sleep Med Rev. 2003; 7(4):297–310.
14. Bradley TD, Floras JS. Obstructive sleep apnoea and its cardiovascular consequences. Lancet. 2009; 373(9657):82–93.
15. Bucks RS, Olaithe M, Eastwood P. Neurocognitive function in obstructive sleep apnoea: a meta-review. Respirology. 2013; 18(1):61–70.
16. Caples SM, Rowley JA, Prinsell JR, Pallanch JF, Elamin MB, et al. Surgical modifications of the upper airway for obstructive sleep apnea in adults: a systematic review and meta-analysis. Sleep. 2010; 33(10): 1396–1407.
17. Carskadon MA, Dement W. C. Normal human sleep: an overview. In: Kryger MH, Roth T, Dement WC, ed. Principles and Practice of Sleep Medicine, 2 ed. Philadelphia (PA): W.B. Saunders Company 1994:16–25.
18. Chung F, Subramanyam R, Liao P, Sasaki E, Shapiro C, Sun Y. High STOP-BANG score indicates a high probability of obstructive sleep apnoea. Br J Anaesth. 2012; 108(5):768–775.
19. Collop N, Hartenbaum N, Rosen I, Phillips B. Paying attention to at-risk commercial vehicle operators. Chest. 2006; 130(3):637–639.
20. Collop NA, Anderson WM, Boehlecke B, Claman D, Goldberg R, et al. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. Portable Monitoring Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2007; 3(7):737–747.
21. Collop NA, Tracy SL, Kapur V, Mehra R, Kuhlmann D, et al. Obstructive sleep apnea devices for out-of-center (OOC) testing: technology evaluation. J Clin Sleep Med. 2011; 7(5):531–548.
22. Daltro C, Gregorio PB, Alves E, Abreu M, Bomfim D, et al. Prevalence and severity of sleep apnea in a group of morbidly obese patients. Obes Surg. 2007; 17(6):809–814.
23. Dawson A, Bigby BG, Poceta JS, Mitler MM. Effect of bedtime alcohol on inspiratory resistance and respiratory drive in snoring and nonsnoring men. Alcohol Clin Exp Res. 1997; 21(2):183–190.
24. Durmer JS, Dinges DF. Neurocognitive consequences of sleep deprivation. Semin Neurol. 2005; 25(1):117–129.
25. Ebrahim IO, Shapiro CM, Williams AJ, Fenwick PB. Alcohol and sleep I: effects on normal sleep. Alcohol Clin Exp Res. 2013; 37(4):539–549.
26. Ellen RL, Marshall SC, Palayew M, Molnar FJ, Wilson KG, Man-Son-Hing M. Systematic review of motor vehicle crash risk in persons with sleep apnea. J Clin Sleep Med. 2006; 2(2):193–200.
27. Epstein LJ, Kristo D, Strollo PJ, Friedman N, Malhotra A, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009; 5(3):263–276.
28. Ferguson KA, Fleetham JA. Sleep-related breathing disorders. 4. Consequences of sleep disordered breathing. Thorax. 1995; 50(9): 998–1004.
29. Franklin KA, Anttila H, Axelsson S, Gislason T, Maasilta P, et al. Effects and side-effects of surgery for snoring and obstructive sleep apnea–a systematic review. Sleep. 2009; 32(1):27–36.
30. Gami AS, Olson EJ, Shen WK, Wright RS, Ballman KV, et al. Obstructive sleep apnea and the risk of sudden cardiac death: a longitudinal study of 10,701 adults. J Am Coll Cardiol. 2013; 62(7):610–616.
31. Goel N, Basner M, Rao H, Dinges DF. Circadian rhythms, sleep deprivation, and human performance. Prog Mol Biol Transl Sci. 2013; 119: 155–190.
32. Haavisto ML, Porkka-Heiskanen T, Hublin C, Härmä M, Mutanen P, et al. Sleep restriction for the duration of a work week impairs multitasking performance. J Sleep Res. 2010; 19(3):444–454.
33. Hartenbaum N, Collop N, Rosen IM, Phillips B, George CF, et al. Sleep apnea and commercial motor vehicle operators: Statement from the joint task force of the American College of Chest Physicians, the American College of Occupational and Environmental Medicine, and the National Sleep Foundation. Chest. 2006; 130(3):902–905.
34. Hersman D. Safety Recommendation. Washington (DC): National Transportation Safety Board; 2009:A-09-61 - A-09-66.
35. Horne JA. Sleep loss and "divergent" thinking ability. Sleep. 1988; 11(6): 528–536.
36. Horne JA. Human sleep, sleep loss and behaviour. Implications for the prefrontal cortex and psychiatric disorder. Br J Psychiatry. 1993; 162:413–419.

37. Kendzerska T, Gershon AS, Hawker G, Leung RS, Tomlinson G. Obstructive sleep apnea and risk of cardiovascular events and all-cause mortality: a decade-long historical cohort study. PLoS Med. 2014; 11(2):e1001599.
38. Kryger MH, Roth T, Dement WC. Principles and practice of sleep medicine, 5th ed. Philadelphia (PA): Saunders/Elsevier; 2011.
39. Lal C, Strange C, Bachman D. Neurocognitive impairment in obstructive sleep apnea. Chest. 2012; 141(6):1601–1610.
40. Lim J, Dinges D. A meta-analysis of the impact of short-term sleep deprivation on cognitive variables. Psychol Bull. 2010; 136(3):375–389.
41. Naismith S, Winter V, Gotsopoulos H, Hickie I, Cistulli P. Neurobehavioral functioning in obstructive sleep apnea: differential effects of sleep quality, hypoxemia and subjective sleepiness. J Clin Exp Neuropsychol. 2004; 26(1):43–54.
42. Ngiam J, Balasubramaniam R, Darendeliler MA, Cheng AT, Waters K, Sullivan CE. Clinical guidelines for oral appliance therapy in the treatment of snoring and obstructive sleep apnoea. Aust Dent J. 2013; 58(4):408–419.
43. Olson EA, Weber M, Rauch SL, Killgore WD. Daytime sleepiness is associated with reduced integration of temporally distant outcomes on the Iowa Gambling Task. Behav Sleep Med. 2014; (Nov):1–12 (epub ahead of print.).
44. Pallayova M, Banerjee D, Taheri S. Novel insights into metabolic sequelae of obstructive sleep apnoea: A link between hypoxic stress and chronic diabetes complications. Diabetes Res Clin Pract. 2014; 104(2):197-205.
45. Parks P, Durand G, Tsismenakis AJ, Vela-Bueno A, Kales S. Screening for obstructive sleep apnea during commercial driver medical examinations. J Occup Environ Med. 2009; 51(3):275–282.
46. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol. 2013; 177(9):1006–1014.
47. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA. 2000; 284(23):3015–3021.
48. Philip P, Sagaspe P, Prague M, Tassi P, Capelli A, et al. Acute versus chronic partial sleep deprivation in middle-aged people: differential effect on performance and sleepiness. Sleep. 2012; 35(7):997–1002.
49. Pépin JL, Viot-Blanc V, Escourrou P, Racineux JL, Sapene M, et al. Prevalence of residual excessive sleepiness in CPAP-treated sleep apnoea patients: the French multicentre study. Eur Respir J. 2009; 33(5):1062–1067.
50. Redline S, Young T. Epidemiology and natural history of obstructive sleep apnea. Ear Nose Throat J. 1993; 72(1):20–1, 24–6.
51. Reynolds L, Beckmann J, Kurz A. Perioperative complications of hypothermia. Best Pract Res Clin Anaesthesiol. 2008; 22(4):645–657.
52. Rupp TL, Wesensten NJ, Balkin TJ. Sleep history affects task acquisition during subsequent sleep restriction and recovery. J Sleep Res. 2010; 19(2):289–297.
53. Scharf SM, Tubman A, Smale P. Prevalence of concomitant sleep disorders in patients with obstructive sleep apnea. Sleep Breath. 2005; 9(2):50–56.
54. Stepanski EJ. The effect of sleep fragmentation on daytime function. Sleep. 2002; 25(3):268–276.
55. Stevens GA, Singh GM, Lu Y, Danaei G, Lin JK, et al. National, regional, and global trends in adult overweight and obesity prevalences. Popul Health Metr. 2012; 10(1):22.
56. Sturm R, Hattori A. Morbid obesity rates continue to rise rapidly in the United States. Int J Obes (Lond.) 2013; 37(6):889–891.
57. Tregear S, Reston J, Schoelles K, Phillips B. Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. J Clin Sleep Med. 2009; 5(6):573–581.
58. Tregear S, Reston J, Schoelles K, Phillips B. Continuous positive airway pressure reduces risk of motor vehicle crash among drivers with obstructive sleep apnea: systematic review and meta-analysis. Sleep. 2010; 33(10):1373–1380.
59. Vakulin A, Baulk SD, Catcheside PG, Antic NA, van den Heuvel CJ, et al. Effects of alcohol and sleep restriction on simulated driving performance in untreated patients with obstructive sleep apnea. Ann Intern Med. 2009; 151(7):447–455.
60. Valencia-Flores M, Orea A, Castaño VA, Resendiz M, Rosales M, et al. Prevalence of sleep apnea and electrocardiographic disturbances in morbidly obese patients. Obes Res. 2000; 8(3):262–269.
61. Van Dongen HP, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep. 2003; 26(2):117–126.
62. Wolkove N, Baltzan M, Kamel H, Dabrusin R, Palayew M. Long-term compliance with continuous positive airway pressure in patients with obstructive sleep apnea. Can Respir J. 2008; 15(7):365–369.
63. Wright N, McGown A. Vigilance on the civil flight deck: incidence of sleepiness and sleep during long-haul flights and associated changes in physiological parameters. Ergonomics. 2001; 44(1):82–106.
64. Wright N, Powell D, McGown A, Broadbent E, Loft P. Avoiding involuntary sleep during civil air operations: validation of a wrist-worn alertness device. Aviat Space Environ Med. 2005; 76(9):847–856.
65. Xie W, Chakrabarty S, Levine R, Johnson R, Talmage JB. Factors associated with obstructive sleep apnea among commercial motor vehicle drivers. J Occup Environ Med. 2011; 53(2):169–173.
66. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. N Engl J Med. 2005; 353(19):2034–2041.
67. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med. 2002; 165(9):1217–1239.
68. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med. 1993; 328(17):1230–1235.