Review


Obstructive sleep apnea: personal, societal, public health, and legal implications

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Abstract

Introduction: Obstructive sleep apnea (OSA) is a widely prevalent sleep-related breathing disorder, which leads to several life-threatening diseases. OSA has systemic effects on various organ systems. Untreated OSA is associated with long-term health consequences including hypertension, heart disease, diabetes, depression, metabolic disorders, and stroke. In addition, untreated OSA is reported to be associated with cognitive dysfunction, impaired productivity at the workplace and in an increased risk of motor vehicle accidents (MVAs) resulting in injury and fatality. Other consequences of OSA include, but are not limited to, impaired vigilance, daytime somnolence, performance deficits, morning headaches, mood disturbances, neurobehavioral impairments, and general malaise. Additionally, OSA has become an economic burden on most health systems all over the world. Many driving license regulations have been developed to reduce MVAs among OSA patients.

Methods: Studies of the personal, societal, public health, and legal aspects of OSA are reviewed. Data were collected through the following databases: MEDLINE, Google Scholar, Scopus, SAGE Research Methods, and ScienceDirect.

Conclusion: OSA leads to worsening of patients' personal relationships, decreasing work productivity, and increasing occupational accidents as well as MVAs. The costs of undiagnosed and untreated OSA to healthcare organizations are excessive. Thus, proper management of OSA will benefit not only the patient but will also provide widespread benefits to the society as a whole.

Keywords: economic cost; legal; obstructive sleep apnea; OSA; road traffic accidents; society.

Introduction

Obstructive sleep apnea (OSA) in the third edition of International Classification of Sleep Disorders (ICSD-3) (1) is defined as a clinical syndrome characterized by repetitive episodes of partial or complete airway obstructions which during sleep, these obstructions result in desaturation of the blood’s normal oxygen levels and are usually terminated by brief arousals from sleep (1). These breathing gaps result in reductions in the oxygen supply to the brain and an accumulation of carbon dioxide (2), which briefly activates the brain’s arousal system to reopen the airways. This process is frequently repeated, the consequence of which is to deprive patients of normal restorative sleep, the resulting sequelae includes daytime sleepiness, headaches and cognitive deficits such as reduced ability to concentrate (3). Additionally, sympathetic overstimulation, systemic inflammation, and deoxygenation take place (4).
Polysomnography (PSG) has been traditionally used as the gold standard for the diagnosis of OSA (5); it records several sleep variables which are monitored overnight in a sleep laboratory, a procedure that is time-consuming and expensive (6). Recently with advances in technology, several portable devices have been developed which allow patients themselves to measure sleep variables at home (7). Recently the American Academy of Sleep Medicine (AASM) issued clinical practice guidelines for the diagnostic testing for adult OSA (8). Clinical examination, rating scales, and estimated algorithms should not be the cornerstone of OSA diagnosis in adults. On the contrary, PSG and/or home sleep apnea testing should accompany the former subjective tests. Further, the guidelines recommended that full PSG, i.e. that which is monitored overnight by sleep technicians in a sleep clinic, should be performed for the diagnosis of OSA only when the home sleep apnea test is negative, inconclusive, or technically inadequate. The guidelines also identify certain specific medical conditions might additionally require full PSG testing in a sleep clinic. Full PSG testing is superior to home sleep apnea testing for the diagnosis of OSA in patients with evident cardiorespiratory disease, potential neuromuscular conditions causing respiratory muscle weakness, hypoventilation during wakefulness or where there is suspected sleep-related hypoventilation, opioid use and abuse, a history of cerebrovascular insufficiency, or chronic insomnia. The apnea-hypopnea index (AHI) (9) is a variable that is usually used to diagnose and assess the severity of OSA (10, 11). According to the ICSD-3: “an AHI of 15 or higher per h or 5 or higher per h, and the presence of one or more obstructive sleep apnea symptoms or signs and associated medical or psychiatric disorders is required to diagnose sleep apnea” (12).

OSA is a widely prevalent problem in the general population (13). Although the condition is not acutely life-threatening in itself, if left untreated, it is associated with many complications such as high blood pressure and metabolic and cardiovascular disease. The high-risk groups for OSA include patients with ischemic heart disease (IHD), heart failure, arrhythmias, cerebrovascular diseases, and type II diabetes (14).

The adverse effects of OSA extend beyond the margin of the patient’s life and can influence his family, workplace performance and the community as a whole (14–17). The symptoms of OSA symptoms may disrupt the sleep quality of the patient’s and this may negatively affect their personal relationship (18, 19). Also, the problem may affect a patient’s work due to daytime sleepiness. Being sleepy while on duty can cause many occupational accidents and injuries (20). Moreover, the economic impact of OSA on the health system is substantial due to the high prevalence of associated morbidities and complications which can represent a significant financial burden to healthcare services (21, 22). Additionally, in a study by Ronald et al. (23), health care services (as defined by physician claims and overnight stays in hospital) were used twice as frequently by OSA patients in the 10 years preceding their preliminary diagnostic assessment for apnea. Physician dues for the OSA patients added up to $686,365 ($3972 per patient), compared to $356,376 ($1969 per patient) for the controls for the 10-year period scanned in this study. Additionally use of health services by OSA patients was noticeably greater in 7 out of 10 years following their initial diagnosis. OSA patients also had additional overnight hospitalizations: they spent 1118 nights (6.2 per patient) in hospital vs. 676 nights (3.7 per patient) for controls in the period preceding the diagnosis (23, 24). In view of these widespread effects, we have sought in this article to critically review studies that addressed the impact of OSA in terms of its personal, societal, public health, and legal impact.

Methods

This is a narrative review aimed at highlighting the impact of OSA on the society starting from the patient’s personal relationships, broader effects on to the community at large. Data were collected from relevant articles in the following databases: MEDLINE, Google Scholar, Scopus, SAGE Research Methods, and ScienceDirect. Data were also collected from official national reports and relevant websites such as the Federal Motor Carrier Safety Administration and the AASM. We systematically searched the databases using appropriate medical subject headings (25) and text words. The following key terms were used (Obstructive sleep apnea), (disordered breathing), (Obstructive sleep apnea and accidents), (Obstructive sleep apnea AND partner), (Obstructive sleep apnea) AND relationship), (Obstructive sleep apnea) AND workplace). Data were collected from April 2017 to April 2018. We mainly screened studies with the following criteria: 1) studies discussing the impact of OSA on the individual and family life of adult patients; 2) detection of OSA either subjectively by questionnaires or objectively using PSG; 3) studies reporting the societal and

<table>
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<th>Box 1: Framing the research question.</th>
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<td><strong>Planned research query</strong></td>
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<td><strong>Population:</strong> adults</td>
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<td><strong>Exposure:</strong> the presence of obstructive sleep apnea and/or medical comorbidities</td>
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<td><strong>Outcomes:</strong> cardiovascular diseases, pulmonary hypertension, hypertension not responding to treatment, COPD, morbidity and mortality, quality of life, hospitalization frequency</td>
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<tr>
<td><strong>Study design:</strong> observational and comparative studies of any prevalence design which investigated the clinical consequences in patients with severe OSA</td>
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The magnitude of the problem

The problem OSA has gained public health importance over the last few decades (26). The prevalence of OSA is high and increasing especially with the current epidemic of obesity, which is one of the most important risk factors of OSA (27, 28). In terms of OSA’s prevalence, patients who are actually diagnosed with the disorder represent the tip of an iceberg. Young et al. found that, with no barriers to healthcare, 82% of men and 93% of women with moderate-to-severe OSA were never diagnosed as having the condition (29). A study from the USA estimated the prevalence of moderate-to-severe OSA among a random sample of employed adults to be 13% among 30–70-year-old men and 6% among 30–70-year-old women (30). The same study estimated the relative increase in the prevalence to range from 14% to 55% in the period from 1988 to 1994 and 2007 to 2010 depending on the age group and sex. This dramatic increase means millions of affected individuals and consequently a higher incidence of comorbidities (30). In Saudi Arabia, in a research by Wali et al. (31), a total of 235 (67.9%) subjects had OSA with an AHI of ≥5; 22 had OSA syndrome (OSAS), defined by an AHI of ≥15 plus daytime sleepiness; and 65.6% had clinically diagnosed OSA syndrome (COSAS), as defined by the AASM. A conservative estimate of at least 8.8% (12.8% in men and 5.1% in women) was calculated as the overall prevalence of OSA. Similarly, the overall estimated prevalence of OSAS and COSAS was 2.8% (4.0% in men and 1.8% in women) and 8.5% (12.4% in men and 4.8% in women), respectively. Multivariate analysis revealed that age, gender, obesity, and hypertension were independent risk factors for OSA. Another recent study from Switzerland estimated the prevalence of moderate-to-severe OSA (≥15 events per hour) to be 23.4% in adult females and 49.7% in adult males. The study reported further that the very high prevalence of the problem among the general population was related to the high sensitivity of the techniques used for diagnosis; the study recommended revision of the definitions of these disorders (32). Additionally, a review study that included 11 population-based studies in the USA, China, Spain, India, Korea, Japan, and Sweden published between 1993 and 2013 estimated the prevalence of OSA to be 17% (range, 4–50%) in women and 22% (range, 9–37%) in men. The review indicated that the prevalence of the problem was lower in women than in men but that it increased with obesity and older age, which are major risk factors of OSA (13). Another study conducted in Saudi Arabia among male attendants of primary healthcare (PHC) clinics reported that 39% of males (n = 578, mean age: 45 ± 9.3 years) were at high risk of OSA based on the Berlin Questionnaire (33). Using the same methodology as the previous study, another study among 400 women (mean age: 45 ± 9.3 years) reported that 39% of female attendants of PHC clinics were at high risk of OSA (33).

The prevalence of OSA is much greater among certain high-risk groups. OSA with chronic obstructive pulmonary disease (COPD) is defined as an overlap syndrome (34). Overlap syndrome is uncommon in the general population (range: 1.0–3.6%), but is common among patients diagnosed with OSA (range: 7.6–55.7%) (35), 70.5% among hypertensive patients (36), and 56.7% among patients with thromboembolic pulmonary hypertension (37). This is because OSA affects the coagulation system and results in a hypercoagulable state due to hypoxic vasconstriction and vascular remodeling (9, 38). Additionally, OSA is significantly associated with insulin resistance, impaired glucose tolerance, and dyslipidemia which are the criteria for the “metabolic syndrome” (39). Moreover, evidence is being accumulated on the association between OSA and liver steatosis and non-alcoholic fatty liver (40). Higher morbidity-mortality rates are consequences of untreated OSA (41). Furthermore, the risk of developing cardiovascular diseases is greater in untreated OSA (42) including heart failure (43), arrhythmias (two- to four-fold increase) (43–45), and hypertension (10-fold increase) (46) and stroke (47) in addition to ocular complications (48). In a large observational cohort study, untreated OSA significantly and independently increased the risk of stroke or death from any cause (49).

Apart from its effect at the individual level, OSA has detrimental effects on society as described in this review and summarized in Figure 1.

Effects on interpersonal relationships

In studying the effect of any disease on health, researchers mainly focus on the effect of that disease on the patient’s physical functioning, complications, and to some extent on the quality of his life (50). But some diseases have broader effects on the family of the patients especially on their bed partners and caregivers (17). OSA is a typical example in which the family may be the main trigger for the patient to seek help. Several studies have measured the
Effects of OSA particularly on bed partners, whose sleep quality and quality of life are negatively affected (51–53). Subjects suffering from OSA often complain of having poor personal relationships (54). The patient’s excessive daytime sleepiness (EDS) may be manifested as irritability or mood swings that harm the relationships between couples (17). OSA can also cause decreased libido, abnormal sexual behavior, and erectile dysfunction (55–57). Moreover, the affected patient’s stress over personal relationships may be exacerbated by misconceptions which family and friends may have about OSA, in as much as they may attribute sleepiness to dullness, sluggishness, or psychological problems (58). This usually leaves most patients feeling lonely and unsupported by those who are closest in their social network (58, 59).

In a healthy relationship, a partner acts as a successful stress barrier that counteracts health behaviors that could have a negative impact on sleep. Conversely, stressful relationships are known to elevate the risk for sleep disturbance (58–60). Several studies have investigated the effect of bed sharing on the sleep quality among the sharing couples. In a cross-sectional study, nearly 50% of the bed partners of 37 consecutive snoring men suffered decreased sleep quality and increased sleep fragmentation (61). In another study conducted by Ulfbberg et al. (62, 63), it was found that spouses of snorers reported more frequently than normal the presence of sleep problems, including insomnia, daytime fatigue, and sleepiness. Additionally, the data showed evidence of a “dose/response relationship” between the assessed sound exposure and the stated complaints, regardless of whether the female partner snored. Attempting to sleep in a separate bedroom did not seem to give the women any relief (62, 63). Additionally, a case-control study by Smith et al. of 17 wives of patients with OSA and 17 wives of healthy subjects reported that wives of OSA patients showed increases in their pain threshold as measured by several variables, including tender point (TP) count and algometric index, distress, and poor sleep quality in comparison to controls, regardless of age and menopausal status (64). A prospective study was conducted on three groups of wives whose husbands had severe OSA (n = 26), mild OSA (n = 19), and controls (n = 19) from attendants of primary health care clinics. The study showed that spouses in the apneic groups were prone to sleep in different rooms 2.9 times more often than the control group. However, marital satisfaction did not vary significantly among the three groups (65).

On the other hand, it was found that objective sleep quality did not improve considerably in non-snoring partners when they slept alone for one night (66). Consistent with these findings, was a study of a population-based sample of 110 bed partners of OSA patients which showed further evidence of impaired sleep quality among the sleep partners. Twelve of the studied couples slept in the same bed but were monitored. All other couples were studied on the same night. The couples were divided into three groups as follows: 1) neither person had sleep-disordered breathing (SDB) (NoSDB-NoSDB, 46 couples); 2) one person with SDB and one person without SDB (NoSDB-SDB, 42 couples); and 3) both persons with SDB (SDB-SDB, 22 couples).

SDB was defined as “a respiratory disturbance index (RDI) >10 events/h” with ≥4% associated oxygen desaturation. No SDB was defined as having an RDI 4% of <5 events/h (vide infra). An additional 67 couples with at least one bed partner having an RDI >5, but less than 10 were excluded to minimize the likelihood of misclassifying a couple’s SDB (67). A summary of the interpersonal relationship effects are presented in Figure 2.

The association between OSA and sleep quality of bed partners is further substantiated by several studies confirming the effect of OSA treatment on the sleep quality of partners. McArdle et al. (18) stated that 69% of the partners of sleep apnea or hypopnea patients had moderate-to-severe sleep disturbances compared to the normal population; they reported a reduced level of sleep quality, which was assessed using the Pittsburgh Sleep Quality Inventory (PSQI) (p < 0.001) (18). Moreover, in a study
by Engleman et al. (51) showed that therapeutic reductions in OSA symptoms could benefit the sleep quality of bed partners. The study utilized a randomized, placebo-controlled crossover design, in which all patients spent 4 weeks on continuous positive airway pressure (CPAP) and 4 weeks on an oral placebo therapy, with no washout period. Compared to the normal UK population, the bed partners of OSA patients had poor physical (p < 0.002), social (p < 0.02), and mental (p < 0.02) functioning as quantified by the Short Form (36) Health Survey (SF36), and the study concluded through its crossover design that treatment with CPAP positively correlated with sleep quality among the bed partners (r = 0.6, p < 0.001) (51). The previous results are in line with the results by Parish et al., who used the Epworth Sleepiness Scale (ESS), the Calgary Sleep Apnea Quality of Life Index (SAQLI), and the SF-36, for the assessment of quality of life and sleep, respectively, in patients with OSA and their partners (53). Parish et al. also stated that both quality of sleep and quality of life were poor in partners but significantly changed after the OSA patients received treatment with CPAP (53). Also, Doherty et al. (68) reported the change in the ESS scores of bed partners of OSA patients in a prospective study among 45 couples after 8 weeks of starting CPAP therapy. Bed partners reported significant improvements in ESS scores [median, 4 (interquartile range [IQR], 1–8.5) before CPAP; median, 2 (IQR, 1–5) during CPAP] as well as improvements in measures of anxiety, social functioning, mental health, and role limitation due to physical problems or emotional problems (all p < 0.05) (67). Consistent with the results of previous studies, Lai et al. found that adherence to CPAP treatment improved the intimate relationship of patients, both directly by improving sleep quality and indirectly through reducing daytime sleepiness and increasing the activity level of men (69).

A somewhat different perspective on the issue was provided by another study which focused on the behavior of bed partners. The study investigated the association between reports that bed partners poked or elbowed the OSA patient when they snored and whether this activity was related to a later diagnosis. The study was conducted in 128 patients and found that a positive response to being elbowed/poked for apneic spells significantly improved the pretest prediction of OSA (69). Moreover, there is evidence that by having a healthy relationship and being a motivating co-sleeper, wives can even have a supportive effect on the use of CPAP. A study conducted by Cartwright (54) found that adherence by OSA patients to CPAP treatment was strongly related to sharing the bed, i.e. the number of nights both couples shared their beds during the 2 weeks of the study (54). On the other hand, it has been suggested that if relationship problems are
presumed to be a major factor in causing or maintaining a sleep disorder, couples’ counseling should be considered an adjunct to treatment (70).

Of note, not only CPAP therapy was found to affect the perception of partners of patients with SDB, Armstrong et al. also found that laser-assisted uvulopalatoplasty (LAUP), which was successfully done for 24 snoring patients, had positive effects on their marital state (p < 0.01) and quality of life (p < 0.05) (71). There is evidence that this effect was sustained over the intermediate term. Prasad et al. investigated the effect of LAUP and uvulopalatopharyngoplasty (UVPP) done for snorers on their partners after 1 year. The investigators found that partners experienced a reduction in sleep disturbances and the need to wake up after surgery (p < 0.001) (72).

Additionally, Izci et al. found that marital satisfaction among partners of individuals with snoring and OSA did not change significantly after the OSA patient’s use of a mandibular repositioning splint although partners positively reported changes in the patients’ quality of sleep and reduction of snoring. They also found that patients and their partners reported that sharing the same room improved after MRS usage. This may be connected with our other finding that improvement in patients’ snoring could be a positive reinforcement from their partners. However, when partners do not see benefits this may discourage patients from using their device (73).

Scott et al. tried to explore if there was a difference between snorers’ and otolaryngologists’ comprehensive perception of the problem of snoring (74). They found that both groups agreed that sleep-related disturbance was the main problem – but that doctors reported more relationship problems in the snorers’ marriages than the snorers themselves and speculated that this might be due to the association between snoring and possible presence of sleep apnea. Additionally, Scott et al. assessed the quality of marital relationship in a group of snorers and a group of controls and they found that snorers were more depressed than the controls and further, that they were more concerned about the sleep of others (74).

Wives of patients suffering from OSA perceive their marriages as being more stressful, and this perception is not reduced by social activities. The investigators thus concluded that wives should be integrated into the treatment of their husbands who were suffering from sleep apnea. The aim of this strategy was to improve not only the patients’ health but to enhance the relationship satisfaction and quality of life of the partner (60, 75).

The studies reviewed above clearly show that OSA is not just a personal problem but has larger social consequences which merit attention, especially when it is realized that family concerns may be in some occasions the main trigger for seeking medical help and for adhering to the therapy. It is for this reason Ashtyani and Hutter, after reviewing these broader effects, concluded that OSA is a “community health problem” (52).

Comorbidity of OSA and depression

In some prevalence studies rates of depression as high as 7% to 63% have been shown in both the clinical populations and the community, samples. Nevertheless, prevalence rates for depressive symptoms are considerably higher among samples of OSA patients. In a recent meta-analysis, it was found that the pooled prevalence of depressive and anxious symptoms in OSA patients was 35.0% and 32.0%, respectively (76). Moreover, a considerable number of studies have shown that patients complaining of OSA comorbid with severe depression have the lowest quality of life and suffer most from EDS and fatigue (77). Daytime sleepiness, loss of energy, lack of concentration, irritability psychomotor retardation, and weight gain are all symptoms that are shared between depression and OSA, and thus might lead to confusion in the diagnosis of both. Efforts to determine the prevalence of depression in OSA patients, various prevalence studies have included widely used instruments such as the Beck Depression Inventory (BDI), the Zung Self-rating Depression Scale (SDS), and the Hospital Anxiety and Depression Scale (HADS), while only a very few studies involved clinical diagnosis. Some studies used a structured clinical interview, while others relied on telephone interview data or data extracted from OSA study reports. A psychiatrist was involved in the minority of investigations with no diagnoses being reported (78). Among these instruments, only the Center for Epidemiological Studies Depression Scale (CES-D) and Mini International Neuropsychiatric Interview 6.0 (MINI) were designed specifically to assist in the rating of symptom severity of depression. Each of these listed scales has its own limitations. For instance, they cannot exclude other illnesses that may mimic depression, such as fibromyalgia and chronic fatigue syndrome (79).

Sleep fragmentation and oxygen desaturation are the two main factors which are suspected to underlie the depressive symptoms in OSA. Figure 3 summarizes the shared pathophysiology. Sleep fragmentation is a direct result of the recurring micro-arousals which occur in OSA patients. The associated hypopneas and apneas, produce deficits in oxygen saturation and ultimately to nocturnal hypoxemia (80). These deficits have further adverse effects on daytime wakefulness, mood, and
cognitive function (81). Intermittent hypoxemia leads to dose-dependent cell loss in brain areas rich in noradrenergic and dopaminergic pathways both of which are important for both sleep/wakefulness regulation and maintenance of normal mood and mood regulation (82). While these linkages have received both direct and indirect empirical support, the association between OSA and depression has not been confirmed in some studies. In view of this inconsistency a recent metaanalysis concluded that AHI and other respiratory events are not the most appropriate polysomnographic measures of the clinical impact of OSA; the reviewers concluded that, sleep disruption, fatigue, or other objective indices of OSA severity could be better predictors of depression in OSA patients (76). Furthermore, it is known that serotonin is also involved in the etiology of depression. Also, the hypoglossal nucleus which affects the upper airway dilator motor neurons uses serotonin as its principal neurotransmitters, which is further reduced during various sleep stages. Abnormalities in neurotransmission of serotonin (central and peripheral) have thus been hypothesized to underlie the development of depression (83); pro-inflammatory markers such as tumor necrosis factor (TNF) and interleukin 6 (IL6) seem to be significant mediators between OSA and depression (84). Furthermore, an elevation in these cytokines is detected in obesity, particularly visceral obesity, which could be a manifestation of atypical depression that would deteriorate the severity of OSA (81). Certain polysomnographic have been shown to occur in both OSA and depression. Depressed patients show changes in their sleep architecture and usually complain of light sleep. More specifically, the commonest PSG features found in depressed subjects 1) early morning awakenings, prolongation of sleep latency (SL), reduced total sleep time (TST), and disruption of sleep maintenance, which includes increased waking after sleep onset (WASO) and decreased sleep efficiency (SE); 2) rapid eye movement (REM) sleep abnormalities, which presents as shortened REM latency, increased REM density (frequency of REMs), and an increased proportion of REM sleep; 3) slow-wave sleep (SWS) disruption, manifested as decreased stage 3 (N3) of non-REM sleep and reduced delta power (especially in the first 100 min of sleep) (85).

Over time OSA can lead to treatment-resistant depression (TRD) (a term often used in clinical psychiatry to describe the refractory form of depression). In a study by Khazai et al. it was demonstrated that 64% of patients with TRD were at high risk of OSA. Additionally, comorbid hypertension, diabetes mellitus, and obesity lead to a higher risk of associated OSA in TRD patients (86).

Previous studies have shown inconstant outcomes regarding CPAP efficiency in alleviating depressive symptoms among OSA patients (87). This variability could be due to several factors such as the total duration of the studies, the rating of depression severity, or the coexistence of other comorbidities (medical or psychiatric).

Figure 3: Summary of the shared pathophysiology between depression and OSA.
associated with depression in OSA patients. Generally, it seems that depression may persist in some patients despite good adherence to CPAP therapy (79).

**Workplace effects**

Changes in personality and reductions in quality of work are widespread in people with sleep disorders (88). Nevertheless, in the present working environment, these features are frequently misjudged by co-workers or supervisors and the person is often mistakenly viewed as being lazy and apathetic (89, 90). The most widely reported work performance impairments in individuals with untreated OSA include reduced productivity (presentism) and the practice or habit of being absent from work (absenteeism) behaviours which frequently cause affected individuals to become unemployed (88). Problems with concentration and learning are commonly reported in individuals with OSA, together with higher rates of injuries and work accidents when compared to non-snoring controls (88–91).

Workers with SDB who complain of EDS often feel sleepy and take naps at work, even at important business meetings or during driving. A small percentage of them are easily provoked due to lack of patience and impulsivity, which are additional symptoms of impairments in the quality of their nocturnal sleep (90). Supervisors and colleagues are frequently unable to distinguish these symptoms from the personality traits of the sufferers. Thus, workers with SDB tend to have disputes at work and thus may earn lower evaluation grades from their supervisors (92).

Being major symptoms of OSA, daytime sleepiness and snoring were assessed in a retrospective study by Lindberg et al. that examined the association between these symptoms and workplace accidents (93). The study found that workers who experienced these symptoms had 2.2 times the risk of having occupational accidents [95% confidence interval (CI) 1.3–3.8] more than workers who did not have such symptoms. Lindberg et al. did not confirm the diagnosis of OSA in the assessed workers and they relied on symptoms only (93). In another retrospective study, Ulfberg et al. used the 10-year statistics of the Occupational Injury Division of the Swedish National Board and reported that work accidents were two-fold higher in heavy male snorers than in normal, but that this risk increased by 50% among patients with OSA. They suggested that reduced vigilance and attention were behind these accidents (62, 63). Furthermore, Omachi and colleagues found that patients with OSA and EDS have a very high risk of occupational disability [odds ratio (OR), 13.7; 95% CI, 3.9–48]. However, patients diagnosed with OSA without EDS had twice as great a risk of work-related disability (OR, 2.6; 95% CI, 1.2–5.8) (94).

On the other hand, Jurado-Gámez et al. found in a case-control study that there was less risk of work accidents among patients with OSA (27.4% vs. 25.4%; p > 0.050). But they reported that the prevalence of long sick leaves (longer than 30 days) was greater among OSA patients than in healthy controls (16.6% vs. 7%, p = 0.049) and further, that the productivity was lower among the patients than in healthy individuals (63.80% vs. 83.20%, p = 0.000) (95).

In a meta-analysis of seven studies, the investigators found that the odds of work accidents were nearly doubled in workers with OSA (OR, 2.18; 95% CI, 1.53–3.10) when compared to controls especially among those involved in occupational driving which was associated with a higher effect size (20).

In addition, Mulgrew et al. showed that the severity of OSA is not significantly related to work limitation [assessed by the Work Limitations Questionnaire (WLQ)] in the whole assessed study group but the difference was significant among blue-collar workers in terms of time management (p = 0.05) and mental/personal interactions (p = 0.05). On the other hand, the severity of subjective sleepiness (as assessed by the ESS) was significantly associated with three of the four scales of work limitation, namely time management (p < 0.001), mental-interpersonal relationships (p < 0.001), and work output (p < 0.001). These domains significantly improved after treatment with CPAP (96). This conclusion was supported by the work of Aral et al. who revealed that treatment of OSA using dental appliance therapy significantly decreases dysfunction of task performances, such as mean error and mean performance time, and improves work performance (97).

**Road Traffic Accidents (RTA)**

During the past two decades, the relationship between OSA and RTA has become increasingly obvious, with the increase in RTA risk fluctuating between two- and sevenfold in different studies (97–100). The augmented risk could be detected for single or multiple accidents and near-miss accidents. The strength of the association between OSA and accidents was inconsistent between studies however. A recent meta-analysis of the OSA-related risk of crashes in commercial motor vehicle (CMV) drivers, sought to determine whether individuals with OSA were at an increased risk for having a motor vehicle crash when compared to comparable individuals who did not have the disorder. It
was concluded that the accident risk among OSA patients is 2.4 times higher than that of the general population (101). Another meta-analysis reviewed the health-related factors and mandatory medical examinations required for driver's license and license renewal in countries participating in the EU IMMORTAL project. The reviewers compared the risks for RTA for all medical situations reported in the literature (102). It was concluded that most medical conditions such as vision impairment, hearing impairment, arthritis, diabetes, and even alcoholism increased the risk of RTA by 20–100% with respect to the healthy population. Out of all of these, OSA was associated with nearly the highest risk of RTA – second only to age and gender as general risk factors for RTA – with a relative risk of 3.71.

It was found that driving risk in OSAS is more strictly related to the extent of EDS more than the actual objective severity of SDB as measured by AHI (102–105). Karimi et al. found that EDS based on an ESS >15 was significantly related to RTA rate, and was a better predictor of RTA risk among OSA patients than the AHI (106). Nevertheless, Terán-Santos et al. found that AHI was more closely related to accident risk than subjective sleepiness based on ESS among a group of 102 OSA patients presenting to a hospital following RTAs (107). Moreover, the recent report from the European Sleep Apnea Database (ESADA) cohort study (106) found that OSA severity based on AHI was superior to subjective sleepiness based on ESS in predicting accident risk, a finding that was also published in an earlier Canadian study by Mulgrew et al. (96).

Of note, accidents in which fatigue was a major contributing factor could be inferred from some indicators such as the occurrence of a head-on or rear-end collision, and accidents occurring late at night, early morning, or mid-afternoon. Among other associated factors were accident outcomes involving a higher than expected crash severity, involve a single vehicle leaving the roadway, occurs on a high-speed road, and where driver was the sole occupant in the vehicle and where no attempt was made to avoid the crash as indicated by the absence of brake marks. Figure 4 summarizes fatigue-related accidents (108).

The adverse effects of fatigue-related inattentiveness is of course not restricted to highway driving. OSA was found to be the cause of major railway accidents among which was the collision of two Canadian National/Illinois central railway trains near Clarkston, Michigan on November 15, 2001. The accident led to the death of two crewmen and spilled about 3000 gallons of diesel fuel. The accident report published by the National Transportation Safety Board (2002) revealed that fatigue of two crewmen on a Canadian National freight train was the cause of the accident (109). The investigation also found that both of the crewmen were suffering from severe OSA, but that their medical conditions were not included in the company records (109). Various studies have found that driving while fatigued has adverse effects on critical behaviors including decision making ability (108) and psychomotor vigilance (110). There is evidence that a patient’s AHI can be an important predictor of skills that affect driving performance. In one study a multivariate linear regression analysis with adjustment for age, sex, body mass index, and the AHI, AHI during NREM (AHINREM) compared to AHI during REM (AHIREM) was found to be considerably more closely linked to psychomotor vigilance test lapses than AHI during REM.

Several studies have assessed the effect of therapeutic treatments, generally CPAP, of OSA with effective therapy, generally CPAP on RTA or near-miss accidents. These studies used a before/after comparative approach, with some including a discrete group of healthy controls or the general population. In nearly all studies concerned, effective treatment resulted in considerable decreases, or even normalization, of the risk of RTA (108, 111, 112). These studies are summarized in Table 1.

Karimi et al. reported that CPAP use for more than 4 h per night was linked to a decreased risk of RTA (7.6–2.5 accidents/1000 drivers/year) (122). Also, the RTA rate of OSA patients was investigated by the researchers in Ontario, Canada. In this study the accident rate of OSA patients for the 3-year period prior to diagnosis and the 3-year period after commencing CPAP therapy were compared (123). They also compared the accident rate of OSA patients with the accident rate of the general population during the same study period. A three-fold higher accident rate was found in OSA patients for the 3-year period prior to diagnosis, but no significant difference was found in the accident rate between OSA and the general population.
These outcomes underscore the importance of identifying OSA patients and the consequent application of effective therapy. Nevertheless, despite the decrease in accident rates with CPAP therapy in OSA, there is evidence that the driving performance in OSA patients remains poorer than that of matched controls even after CPAP therapy, a finding also from experiments using the driving simulator (123).

Impact on academic performance

The poor academic performance among school and university students is a common problem among OSA patients in comparison to their healthy peers (124–127). A recent meta-analysis of 16 articles from 12 countries conducted by Galland et al. (128), the authors concluded that OSA can lead to poorer academic performance for core academic domains related to language arts, math and science (the effect size [ES] of each respective study was $-0.31$, $p<0.001$; $F=55$; $ES=-0.29$, $p=0.001$; $F=0.5$), but general school performance was not affected. Cognitive and executive functions are strongly impaired in OSA especially memory, attention, executive function, psychomotor function, and language function. In OSA patients, short-term sleep disruption leads to deficits in attention and language function. In OSA patients, psychomotor function and sleepiness were reported in OSA patients included impairments in psychology, memory, executive function, psychomotor function, and language function. In OSA patients, psychomotor function and sleepiness were reported (129, 130).

Table 1: Studies of RTA before and after CPAP use in OSA patients.

<table>
<thead>
<tr>
<th>Study name and year</th>
<th>Study country</th>
<th>No. of participants who continued CPAP therapy</th>
<th>Mean age</th>
<th>Mean duration of CPAP use (minimum 4 h/night)</th>
<th>RTA rate before and after CPAP use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cassel et al. (113)</td>
<td>Sweden</td>
<td>567</td>
<td>53.6</td>
<td>3.5 years</td>
<td>7.6 accidents/1000 drivers/year</td>
</tr>
<tr>
<td>Krieger et al. (114)</td>
<td>Germany</td>
<td>78</td>
<td>48±1.1</td>
<td>1 year</td>
<td>0.8 per 100,000 km</td>
</tr>
<tr>
<td>Yamamoto et al. (115)</td>
<td>Japan</td>
<td>46</td>
<td>44.1±9.9</td>
<td>2 years</td>
<td>33% had RTA; 82% had near-miss accidents</td>
</tr>
<tr>
<td>Findley et al. (116)</td>
<td>USA</td>
<td>36</td>
<td>56±2</td>
<td>2 years</td>
<td>0.07 RTA/driver/year</td>
</tr>
<tr>
<td>Horstmann et al. (117)</td>
<td>Switzerland</td>
<td>85</td>
<td>56.5±10</td>
<td>Not reported</td>
<td>10.6 per million km</td>
</tr>
<tr>
<td>Schaff et al. (118)</td>
<td>USA</td>
<td>316</td>
<td>48.79±6.7</td>
<td>6 months</td>
<td>Not reported</td>
</tr>
<tr>
<td>Engelman et al. (119)</td>
<td>UK</td>
<td>204</td>
<td>53±10</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Mineura et al. (120)</td>
<td>Japan</td>
<td>14</td>
<td>46±7</td>
<td>11±9 months</td>
<td>RMA in 42% and near-miss accidents in 64%</td>
</tr>
<tr>
<td>George (111)</td>
<td>Canada</td>
<td>210</td>
<td>52±11</td>
<td>3 years</td>
<td>RMA/driver/year 0.18 (0.29)</td>
</tr>
<tr>
<td>Barbé et al. (121)</td>
<td>Spain</td>
<td>80</td>
<td>49±1</td>
<td>2 years</td>
<td>RMA rate ratio (RR) = 2.57</td>
</tr>
</tbody>
</table>

RTA, road traffic accidents; CPAP, continuous positive airway pressure; OSA, obstructive sleep apnea.
such as somatic complaints, oppositional or aggressive behaviors, and social problems (134). Snoring and OSA were more common among male university students and was associated with poor academic work (135). There is an improvement in academic functioning after proper use of CPAP and adherence to it (136, 137).

**Legal implications**

The previous data obviously point to OSA as a significant independent causative factor of RTA. This association has important implications for public safety, mainly because accidents which involve patients with OSA are more likely to be accompanied by serious injuries (138). These concerns raise the question of the appropriateness of OSA patients being allowed to hold a valid driving license before their illness is satisfactorily treated. This inquiry has been addressed by the American Thoracic Society in their previous report (99), which highlighted the difficulty in conveying firm criteria to define the fitness of OSA patients to hold a valid driver’s license. These problems are emphasized by the broadly accepted opinion that the diagnosis of OSA should not be governed by a precise level of AHI alone, but ought to take into consideration the degree of sleepiness that can lead to functional impairment (139). The objective assessment of EDS by multiple sleep latency testing (MSLT) or maintenance of wakefulness testing (MWT) is burdensome and not applicable for widespread use, challenges which further complicate the task of how to effectively assess the public safety risk of allowing OSA patients to drive (140).

However, the Oxford Sleep Resistance Test (OSLER), an abridged objective test of EDS, may be beneficial in some situations (141) especially when valid normative data are available. Validated subjective screening tools of sleepiness, such as the ESS (142), are easy to administer, but at the same time, they are liable to manipulation by patients who do not desire to have their driving license sanctioned (143). Of note, is the fact that sleepiness is not the exclusive contributor to impaired cognitive function, nor executive functions, and is thus not only factor involved in compromised (driving) performance in OSA patients. As a consequence, simple tests of alertness or vigilance alone may not accurately reflect the full extent OSA-related impairment. The multiple constituents of driving capability suggest that driving simulators, which measure broader range of driving skills, and which, presumably, test many underlying psychomotor skills, may be more suitable for the estimation of driving capacity than simple vigilance tests (144). Although the predictability of true-life accidents from driving simulator performance is weakly reliable, calibration of driving simulators against real driving situations is still required (145).

It should be noted that 50% of OSA patients perform as well as controls on driving simulators (144). As the prevalence of OSA and other breathing-related sleep disorders is high in the general population, and due to the large amount of evidence stating that treatment decreases the risk of accidents in treated patients, it seems reasonable to take preventive measures to reduce to sleepiness-related RTA in affected OSA subjects by qualifying their access to a driving license in those patients (102).

In the USA, the Federal Motor Carrier Safety Administration (FMCSA) studied 4826 commercial truck drivers and found that 17.6% had mild OSA, 5.8% had moderate OSA, and 4.7% had severe OSA (146). Consequently they recommended in February 2012 that changes to be made in the medical examination reporting form before licenses were issued. More specifically, they recommended that all drivers should be subjected to sleep assessment by a qualified sleep physician. Thus, patients with OSA would have their driving licenses temporarily suspended until adherence to treatment with an elimination of all symptoms of sleepiness were objectively shown (147).

In Europe, a revision of Annex III of the European Union (EU) Directive on Driving Licenses has been implemented following the widespread recognition that while OSA represents an important risk factor for motor vehicle accidents (MVAs), this risk can be reversed by successful therapy with CPAP, has led to a revision of Annex III of the European Union (EU) Directive on Driving Licenses (148). The European Respiratory Society has issued a new directive regarding the issuance of driving licenses to OSA patients, which is subject to obligatory execution by all Member States from 31st December 2015. The directive states that:

- Drivers with suspected moderate or severe OSAS shall be referred for further approved medical check-up before a driving license is dispensed or renewed.
- Drivers with moderate or severe OSAS under treatment shall be exposed to an episodic medical examination, at durations not exceeding 3 years for drivers in group 1 (i.e. non-commercial drivers) and 1 year for drivers of group 2 (i.e. commercial drivers) with the aim of detecting and establishing the level of compliance with the treatment, the need for continuing the treatment and continued good vigilance ensuring non-risky driving behaviors (149).

In some developing countries, neither EDS nor SDB are cited in the traffic legislation, despite numerous recent
studies that have shown the medical fitness assessment of driving in the interest of public safety (150). Implicit in the driving legislation of many countries is a general attitude that the driver should always be able to control the motor vehicle, but with no specific mention of conditions such as OSA which might interfere with this capability. The failure of legislation in many countries to incorporate scientifically-based recommendations regarding the importance of medical examinations for drivers’ license applicants, especially those with suspected OSA, is clearly a public safety issue which continues to merit attention.

**Economic cost**

Although the precise costs are difficult to measure, OSA appears to represent a vast economic burden (billions of dollars per year) and is analogous to other chronic diseases (22). The presence of OSA-related accidents, absenteeism, and general inefficiencies account for numerous costs in any workforce. Among these are workers’ reimbursement costs, healthcare costs, safety- and insurance-related costs, productivity costs, and brand protection costs (151–153).

Each year, an OSA victim has additional costs resulting from more than twice the number of physician dues. Several studies have found that OSA patients are heavy consumers of healthcare services, even before the diagnosis of OSA is made (151–153). The cost of healthcare utilization have been shown to be significantly associated with the severity of OSA (152). In addition, excess costs of OSA result from 1.9 times more cardiovascular medication, 2.7 times more hypertension medication (154), 50% more hospital stays (155), 2.63 times the amount of nonattendance to work (156), 20% reductions in performance efficiency (62, 63), elevated costs for accidents, injuries, absenteeism, and overtime, workers’ compensation, property damage, scrap and rework, etc.

Nevertheless there is evidence that these costs can be reduced. The difference in healthcare utilization between OSA patients and their matched controls has been shown to decrease after diagnosis and effective treatment (24).

In a 5-year follow-up study which included 342 men with OSA and a group of matched controls, Albarak et al. found that the mean total physician fees in the year before diagnosis ($148.65) was greater than in the fifth year before diagnosis and further, that these fees decreased over the next 5 years after treatment ($p = 0.0009). These findings supported the conclusion that the increasing pattern of healthcare utilization before a diagnosis is reversed after treatment (157).

Watson referred to two recent white papers commissioned by the AASM (1). They conducted an in-depth analysis of the hidden costs of undiagnosed and untreated OSA among American adults (138). The papers estimated that the cost of undiagnosed OSA in American adults included $86.9 billion due to lost productivity and absenteeism, $30 billion because of associated comorbidities, $26.2 billion due to RTA, $6.5 billion due to occupational accidents with a total cost of $149.6 billion in 2015. And although diagnosing and treating every case of OSA patients would cost the healthcare system additional $49.5 billion, there would be saving of $100.1 billion. Watson concluded that effective treatment of OSA would provide astounding healthcare saving for payer and large employers (138).

In addition to the cost of healthcare of medical conditions related to OSA, some researchers have tried to evaluate the costs attributable to RTA related to OSA depending on data from the US official foundations for the year 2000. They included that costs are not only limited to medical costs but also include salaries and productivity losses, administrative costs, vehicle damages, and employer costs for damages to the working drivers. They also added missing financial values due to mortalities and lost financial values due to a decreased quality of life after an RTA. The summary of the findings was that OSA-related RTA represented a financial burden of about US $16 billion per year. Treating all drivers with CPAP would decrease the cost by about US $11 billion per year. An annual savings of US $79 billion was obtained because the cost of screening, diagnosing, and treating all drivers was calculated at US $3.2 billion only. These quantities come from an estimated 810,000 crashes per year and 1400 fatalities attributable to OSA-related RTA. Some 567,000 crashes and 980 mortalities could be evaded with CPAP treatment every year (158). The incidence of traffic accidents among people with untreated daytime sleepiness remains high and the estimated cost to the society of just a single fatal road accident in the UK is £1.25 million (159, 160). UK research elucidated how prevention of sleep-related accidents can attain significant cost-savings related to accident prevention. Treating 500 OSA patients for 5 years could be expected to prevent one fatal road accident, 75 accidents that cause injury, and 224 accidents that involve damage to assets, which means £5.3 million savings against an expected treatment cost of £0.4 million (159).

**Conclusion**

Although OSA is a well-recognized disease that affects patients physically and psychologically, its negative impact...
on the different levels of society may be even higher. OSA leads to worsening patients’ personal relationships especially with bed partners who are already under stress, and due to poor quality, in addition to the negative impact of the disorder on the marriage itself and decreased libido. Depression and OSA are inter-related and both disorders tend to exist in the same patient (79); they also share the same symptoms and polysomnographic features, which lead to masking and missing of the diagnosis of OSA. OSA can lead to TRD. Additionally, OSA may result in decreasing work productivity mainly due to EDS, which is frequently misperceived by work authorities as laziness. More attention should be directed toward the risks associated with OSA not only in RTA but also train collisions and aircraft safety. At a higher level, more broadly, OSA results in an excessive increase in healthcare costs due to over-utilization of medical services by this patient group especially before the diagnosis and the treatment of the disease. Therefore, proper management of OSA will not only benefit the patient but also improve many aspects of society.

Healthcare service providers are usually keen to control diseases at the individual level to prevent complications. Treating OSA will provide the patient with several health benefits including increased energy and attentiveness during the day, increased productivity, less waking during the night to go to the bathroom, better mood, improved overall quality of life, fewer morning headache episodes, lower blood pressure, and decreased risk of stroke and cardiovascular diseases. On the other hand, if minimal attention is directed toward the psychosocial impact of OSA on the lives of its sufferers, these benefits would be significantly reduced. Physicians should always remember that they are treating humans, not diseases.

It is strongly advised that sleep physicians should adopt the biopsychosocial treatment model in the management of OSA. This approach incorporates biological, psychological, and sociocultural factors. We do not mean that doctors should be physicians, psychiatrists, and sociologists at the same time; we think that paying attention to these factors collectively is crucial for the success of the medical treatment itself. Taking these factors into consideration will also improve the patient’s quality of life and benefit also the society, the family, caregivers, and partners of patients who will be a part of the successful treatment plan. Additionally, negative impacts and consequences on the lives of people other than the patient will be alleviated, in addition to the decrease in unnecessary medical cost.

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