OBSTRUCTIVE SLEEP APNEA: THE KILLER IN THE BEDROOM?

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Executive Summary *Sleep-related disordered breathing is probably more common than any one of us realizes. Starting with snoring and ending with obstructive sleep apnea, it has a considerable effect on many people's lives, and is a significant cause of increased mortality and morbidity.*

This review focuses on obstructive sleep apnea, its epidemiology, treatment and impact on both mortality and morbidity.

Introduction

Sleep apnea is a common, chronic condition in which the affected individual repeatedly stops breathing. Each episode of breathing cessation is called an apnea and usually sufficiently long that more than one breath is missed. Episodes are repeated throughout the night, although the affected individual is usually unaware of them[1,2].

The accepted definition of an apneic episode states that there must be a minimum 10 second interval between breaths, with either blood oxygen desaturation of at least 3-4% or a neurological arousal (>3 second shift in electroencephalogram [EEG] frequency), or with both desaturation and arousal[2,3].

The most common form is obstructive sleep apnea, caused by recurrent episodes of upper airway collapse during sleep. Central sleep apnea or Cheyne-Stokes respiration is rare and is associated with significant mortality and morbidity[2-4].

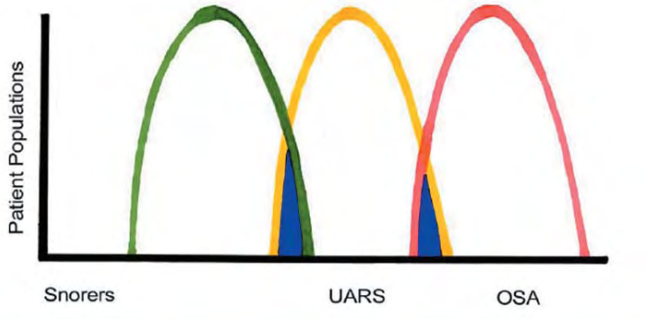
A continuum of sleep disordered breathing suggests that the initial presentation is with snoring, which increases in severity over time and with associated medical disorders such as obesity. Once upper airways resistance develops, symptoms of sleepiness due to increased levels of arousal occur. This is known as upper airways resistance syndrome (UARS). Patients with UARS are thought to eventually progress to obstructive sleep apnea if left untreated. See Figure 1[3].

Obstructive sleep apnea (OSA) is defined by the American Academy of Sleep Medicine (AASM) as repetitive episodes of complete (apnea) or partial (hypopnea) upper airways obstruction occurring during sleep. By definition, apneic and hypopneic events last a minimum of 10 seconds. At least five apnea events must occur per hour of sleep time in association with clinical symptoms, or at least 15 apneic events must occur per hour of sleep time with or without clinical symptoms[5].

Obstruction of the airways causes sudden increase in inspiratory effort, disruption of normal sleep patterns, and a reduction in gaseous exchange causing hypoxia and hypercapnia (an increased level of carbon dioxide in the blood)[3,6].

Risk factors for OSA include male gender, obesity, rounded head and short neck, a neck circumference >43 cm (approx. 17 in), alcohol, sedative use, smoking, postmenopausal status and aging. There is a positive family history in 25-40% of cases, which may

Figure 1: Sleep-related disordered breathing continuum ranging from simple snoring to obstructive sleep apnea (OSA). Upper airway resistance syndrome (UARS) occupies an intermediate position between these extremes. *Source*: http://emedicine.medscape.com/article/295807-overview



be a reflection of pharyngeal structure or intrinsic ventilatory drive[6].

OSA is commonly associated with disorders such as cardiac arrhythmias, hypertension, stroke, gastro-esophageal reflux, angina, heart failure and hypothyroidism.

Epidemiology

Sleep disordered breathing and apnea are generally more common in men, occurring in 1 of 25 middle-aged men compared with 1 in 50 middle-aged women, although postmenopausal women are three times more likely to have moderate to severe OSA than those who are premenopausal[3,6].

Over half of cases are overweight or obese. Prevalence increases with age, with OSA being 2-3 times more common above age 65, compared with age 30-64 [3,6].

Signs and Symptoms

The cardinal symptoms of OSA are snoring, excessive daytime sleepiness, apnea and impaired concentration[7].

The most widely reported symptom is loud, chronic and disruptive snoring, sometimes with pauses followed by gasping or choking. The affected individual may not be aware of these symptoms and they are commonly reported by the partner or roommate. Sleep is usually restless and unrefreshing, leading to excessive daytime sleepiness, impaired concentration and fatigue. Other common symptoms include:[3,6,8]

- Dry throat on awakening
- Morning headache
- Irritability, depression, mood swings
- Nighttime urination
- Reduced libido
- Gastro-esophageal reflux disorder

Investigations and Diagnosis

The initial investigation usually takes the form of history taking and a physical examination. If sleep apnea is suspected, polysomnography (PSG) may be performed. This is a multi-channel recording of sleep and breathing, usually performed in a sleep laboratory. It commonly includes measurement of sleep architecture, an electroencephalogram (EEG), eye and chin movements, respiratory effort and airflow, oximetry (measuring the amount of oxygen in the blood), resting electrocardiogram, body position and leg movement, as well as level or frequency of snoring[3,5].

Severity is commonly measured using the Apneic/Hypopneic Index or Respiratory Disturbance Index (AHI or RDI):

- <5 – no sleep apnea
- 5-14 mild sleep apnea
- 15-30 moderate sleep apnea
- >30 severe sleep apnea

The AHI or RDI score is calculated by dividing the number of apneas + hypopneas + respiratory event related arousals by the number of hours sleep[5].

For a definitive diagnosis of OSA to be given, the *International Classification of Sleep Disorders: Diagnostic and Coding Manual 2nd Edition* states that at least one of the following criteria must be fulfilled:[3]

- Daytime sleepiness, unrefreshing sleep, fatigue, insomnia and/or unintentional sleep episodes during waking hours. Awaking with breath holding, gasping or choking. Loud snoring and/or interrupted breathing reported by partner.
- PSG shows more than five scoreable respiratory events (e.g., apneas, hypopneas or respiratory event-related arousals [RERAs]) per hour of sleep and/or evidence of respiratory effort during all or a portion of each respiratory event in association with clinical symptoms.
- PSG shows more than 15 scoreable respiratory events (e.g., apneas, hypopneas, RERAs) per hour of sleep and/or evidence of respiratory effort during all or a portion of each respiratory event.

Treatment

Treatment usually consists of the control of risk factors and lifestyle changes, and where OSA exists with at least moderate daytime sleepiness, the application of continuous positive airway pressure (CPAP). Surgical options are also available.

Control of risk factor and lifestyle changes

For the overweight or obese, even modest weight loss can reduce frequency of apnea and hypopnea episodes. However, losing weight takes time, even following bariatric surgery, and only a small percentage of individuals are able to maintain a lower weight[3,9].

Other lifestyle changes include restriction of sedatives and alcohol, particularly before bedtime; stopping smoking is also encouraged[8,9].

Breathing devices

For moderate to severe OSA, continuous positive airway pressure (CPAP) is the most common form of treatment. The soft mask covers the nose and provides a pneumatic stent for the upper airway, thus preventing collapse during inhalation[9].

The amount of pressure required is usually deter-

mined from the PSG results; the average starting level is 8-10 cmH2O, which is tolerable to most individuals once they become accustomed to it. Levels above 15 cmH2O are rarely tolerated[9].

CPAP is highly effective, often with improvements in daytime symptoms after a single night of treatment. Sleep patterns tend to normalize within weeks, with significant improvement in quality of life for both patient and their bed partner[9].

CPAP can improve scores on the Epworth Sleepiness Scale (ESS). This asks the likelihood of dozing in eight everyday situations, e.g., watching television, driving, reading etc.; 0 – unlikely to fall asleep; 1 – slight risk of falling asleep; 2 – moderate risk of falling asleep; 3 – high risk of falling asleep. A score of 11-14 = mild daytime sleepiness, 15-18 = moderate daytime sleepiness and >18 = severe daytime sleepiness[9].

As well as improving sleep, CPAP improves depression, concentration and insulin sensitivity. Other positive effects include lower blood pressure, increased cardiac output and stroke volume, reduced systemic vascular resistance and the risk of cardiovascular mortality[9].

Treatment compliance is a major issue as it can be difficult to tolerate the CPAP mask. Problems include claustrophobia, dry mouth and nasal passages, skin irritation, mask leaks causing eye problems, chest discomfort and lack of tolerance by bed partner[9].

Surgery
In some cases surgery may be considered. The most common procedures are:[10]

- Uvulectomy – beneficial in those with large uvulas who snore but have no or few symptoms of OSA.
- Pillar system – palatal implants or the pillar system is used to treat habitual snorers and those who have mild to moderate OSA. Here, three tiny woven inserts are placed in the soft palate to help reduce the vibration that causes snoring and collapse that can obstruct the airway. This procedure is relatively successful, with up to 70% of bed partners reporting an improvement in snoring, but the cure rate depends on preoperative apnea severity.
- Nasal reconstruction – this is rarely a cure for OSA, but the relief of nasal obstruction can improve both patient tolerance of and response to CPAP. Common procedures are septoplasty, septorhinoplasty and turbinate reduction.
- Adenotonsillectomy – commonly used as a relief of restless sleep and snoring in children, rarely performed in adults.
- Palatal surgery – uvulopalatopharyngoplasty (UPPP) is the most common surgical treatment for OSA. It consists of tonsillectomy, reorientation of the anterior and posterior tonsillar pillars, and excision of the uvula and posterior rim of the soft palate.
- Permanent tracheostomy – nowadays this treatment is usually reserved for severe apnea associated with life-threatening cardiac arrhythmias. It can also be performed for morbid obesity, significant obstruction-causing hypoxia or disabling daytime somnolence[8].

Other treatments
Other forms of treatment include:

- Positional therapy, whereby the affected individual should be encouraged to avoid sleeping on his back. This can be facilitated by attaching a tennis ball to the back of the pajamas, which makes lying on the back uncomfortable; special pillows can also help[11].
- Oral or dental appliances which work by pushing the jaw forwards, or preventing the tongue falling back, or a combination of both. They are generally most effective in those who have mild forms of apnea[11].
- Antidepressants, which have been shown to have beneficial effects on OSA, but this is likely to be as a result of the suppression of REM sleep, when most apneas occur, rather than from any direct alleviating action.
- Other drugs such as naloxone, baclofen, bromocriptine and prochlorperazine have all been investigated, but none have been shown to be consistently effective for OSA[9].

Prognosis

Obstructive sleep apnea has a significant effect not only on quality of life, but also on general health and mortality. It is also a concern for public health because of the increased risk of accident due to daytime somnolence[3].

Accidents
Around 23% of women and 16% of men with OSA report excessive daytime sleepiness significantly increasing the risk of motor vehicle accidents, e.g., in the United States in 2000 more than 800,000 drivers were involved in OSA-related accidents, resulting in 1400 deaths[12].

Sleepiness whilst driving is estimated to cause 20% of motorway accidents in the UK. Drivers with OSA who participated in a study carried out on a driving simulator showed a significant improvement in performance following CPAP treatment[7].

Cognitive performance
Excessive daytime sleepiness also reduces cognitive performance. Around two-thirds of participants in recent studies report difficulties with performing new tasks, reduction in work efficiency and memory problems, and three-quarters reported concentration problems[13].

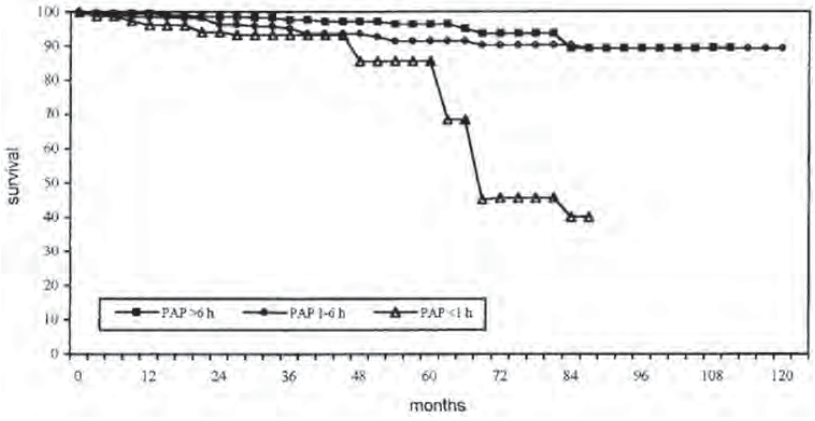
Cardiovascular disease
Cardiovascular conditions associated with OSA include:[14]

- Hypertension
- Cardiac arrhythmias
  - o Sinus bradycardia
  - o Atrioventricular block
- Tachydysrhythmias
  - o Supraventricular tachycardia
  - o Atrial fibrillation
  - o Ventricular tachycardia
- Left ventricular systolic dysfunction
- Left ventricular diastolic dysfunction
- Congestive heart failure
- Stroke
- Coronary heart disease
- Pulmonary heart disease

Table 1: Causes of death.
Source: Campos-Rodriguez et al. Chest 2005

Causes	PAP Compliance			
	> 6 h/d (n = 322)	1–6 h/d (n = 342)	< 1 h/d (n = 85)	Ignored (n = 122)
Cardiovascular diseases	5	7	4	3
Myocardial infarction	4	5	2	2
Sudden death		2	1	
Congestive heart failure	1		1	1
Neoplasia	3	7	1	5
Lung	2	3		1
Head and neck		1	1	
GI	1			3
Urogenital		2		
Others		1		1
Acute respiratory failure	1		1	1
Others	1	2	1	2
Unknown	1		1	

Figure 2: Kaplan-Meier cumulative survival rates according to categories of PAP compliance. Cumulative survival rates in the PAP >6h group were significantly higher than in the PAP <1 h group (p <0.00005). Cumulative survival rates in the PAP 1–6 h group were significantly higher than in the PAP <1 h group (p <0.01). Cumulative survival rates were not different in the PAP >6 h group and the PAP 1–6 h group (p <0.11). *Source*: Campos-Rodriguez et al. *Chest* 2005



Mortality Risk
Several studies report increased risk of mortality due to OSA, with one reporting around 40% mortality in severe OSA during an 8-year follow-up period. Other studies suggest an age-adjusted odds ratio for mortality arising from cardiovascular disease of 4.9 for those receiving no treatment, compared with those who had undergone tracheostomy, and an actual:expected mortality ratio of 3.3 below age 70[14].

Poor compliance with treatment increases mortality risk. Campos-Rodgriguez et al. found survival rates were directly linked to compliance with CPAP treatment. See Table 1 and Figure 2[15].

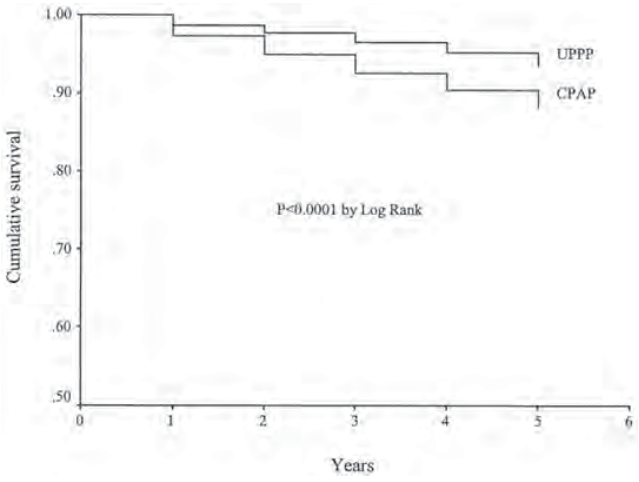
Weaver et al. found more CPAP than UPPP patients died during the course of their study (see Figure 3, next page)[16]. They concluded surgical intervention appears to be associated with an improved survival rate and suggest this may be due to poor compliance with, or adherence to, CPAP therapy over lengthy periods of time. Therefore, they advise surgical intervention for CPAP intolerant or noncompliant patients.

Even after adjustment for a variety of variables, including age and comorbidities, CPAP treatment incurred a 31% greater chance of dying compared to UPPP (see Table 2, next page)[16].

Summary and Considerations for Underwriting

- Sleep apnea is a common chronic condition affecting 2-4% of all adults.
- The most common form is obstructive sleep apnea (OSA), where there are recurrent episodes of collapse in the upper airways during sleep. Primary central sleep apnea is rare.
- The cardinal symptoms of OSA are snoring, excessive daytime sleepiness and impaired concentration.
- Obstructive sleep apnea is associated with in-

Figure 3: Survival curves for uvulopalatopharyngoplasty (UPPP) and continuous positive airway pressure (CPAP). [N.B. Curves are unadjusted for either age or comorbidities.] *Source*: Weaver et al. *Otolaryngol Head Neck Surg* 2004.



creased mortality and morbidity risk.

- Assessment is by a comprehensive evaluation of symptoms including a measure of sleepiness severity and an overnight sleep study (polysomnography [PSG]) to establish severity according to the Apneic/Hypopneic Index (AHI).
- There is strong evidence of an increased all-cause mortality risk, the level of which is associated with the severity of symptoms.
- Untreated OSA is a significant risk factor for disability cover, mainly due to daytime sleepiness, resulting in an increased accident risk and causing concentration and memory problems. Associated psychological issues such as depression should not be ignored.
- Treatment with CPAP is effective in relieving symptoms and reducing mortality and morbidity. Compliance is necessary over long periods.

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Table 2: Mortality hazard
Source: Weaver et al. *Otolaryngol Head Neck Surg* 2004.

Variable	Reference group	Unadjusted HR (95% CI)	Adjusted* HR (95% CI)	*P* value (adjusted model)
Therapy (CPAP)	UPPP	2.11 (1.66-2.68)	1.31 (1.03-1.67)	0.03
Age at treatment (yr)	One year prior	1.07 (1.07-1.08)	1.06 (1.06-1.07)	<0.001
Sex (male)	Female	2.76 (1.52-4.99)	1.82 (1.01-3.30)	0.048
Race (white)	Nonwhite	1.16 (1.00-1.35)	0.98 (0.84-1.13)	0.77
Date of treatment (yr)	One year prior	0.93 (0.88-0.98)	0.92 (0.87-0.97)	0.001
Comorbidity Index	One less index score	1.11 (1.10-1.12)	1.09 (1.08-1.10)	<0.001

UPPP, Uvulopalatopharyngoplasty; *CPAP*, continuous positive airway pressure; *HR*, hazard ratio, the hazard of being dead at any time relative to the reference group; *CI*, confidence interval.
*Adjusted for age at treatment, sex, race, date treatment initiated, and comorbidity.

About the Author

Nicky Virgo is a senior underwriting consultant at RGA, specialising in medical research. Her key role is the development of evidence-based underwriting guidelines for RGA's global underwriting manual, *GUM*. With over 25 years in insurance, Nicky has worked in all aspects of life and disability underwriting, focusing on manual development, training and auditing in recent years.

Before joining RGA in 2009, Nicky worked at Aviva and Swiss Re. She has a degree in human biology and completed a post-graduate course on the neurobiology of addiction and risk-taking. Her areas of special interest are neurological and mental disorders. She enjoys writing articles and giving presentations on both topics.