# Sleep Apnoea, Obesity, Diabetes and the Metabolic Syndrome

*a report by*

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Obstructive sleep apnoea (OSA) is a common and disabling medical condition that is part of the broad spectrum of breathing disorders associated with abnormal sleep. Many epidemiological studies have shown a clear association between type 2 diabetes, various components of the metabolic syndrome and the presence of sleep apnoea. There is clear evidence that sleep apnoea treatment both improves the symptoms of sleep apnoea, particularly excessive daytime sleepiness, and lowers blood pressure. There is some evidence that treatment also reduces cardiovascular disease risk and may sometimes improve diabetes control. This article will review the clinical features of OSA and its association with metabolic risk factors and cardiovascular disease, and outline briefly a practical approach for sleep specialists and diabetes specialists given the known associations between these two common conditions.

## What Is Sleep Apnoea?

Sleep apnoea is defined by more than five episodes per hour of cessation of breathing for at least 10 seconds. It is part of the spectrum of disorders characterised by abnormal breathing during sleep, which range from intermittent snoring to persistent snoring, upper airway resistance syndrome, OSA syndrome and obesity hypoventilation syndrome (see *Figure 1*). The overall population prevalence of sleep apnoea in adults is between 2 and 4%,[1,2] with the condition being about twice as common in men.[3] Sleep-related breathing disorders are associated with obesity, and epidemiological studies show that the majority of patients with sleep apnoea are obese and that up to 30% of people with clinical obesity with a body mass index over 30 will have OSA if formally investigated for the presence of the condition.[4] The strongest association is with upper body obesity, particularly increased girth around the neck and upper airways. In those patients who are not obese, abnormalities in the soft palette and uvula may cause obstruction to breathing during sleep, as may craniofacial abnormalities characterised by a small or receding jaw, which reduces the diameter of the upper airway.

OSA may be associated with such symptoms as excessive daytime sleepiness, loud snoring reported by the patient and/or his or her partner, a feeling of choking or suffocating at night, unrefreshing or restless sleep, changes in mood and personality and cognitive changes.[5] These symptoms can be readily detected using simple questionnaires such as the Epworth and Berlin questionnaires, which can be used as screening tools to find people who are likely to suffer from, respectively, excessive sleepiness and sleep-related breathing disorders[6,7] (see *Tables 1a* and *1b*).

Sleep apnoea syndrome is characterised by disordered breathing in sleep and is associated with daytime sleepiness or other symptoms of sleep deprivation, whereas obesity hypoventilation syndrome is characterised by ventilatory failure during wakefulness and sleep, frequently leading to pulmonary hypertension and, eventually, cardiac failure. The diagnosis of sleep apnoea can be made using full polysomnography, which records changes in oxygen saturation, air flow and respiratory effort, together with sleep stage as assessed by electroencephalogram (EEG) (see *Figures 2a* and *2b*).[8] However, sleep specialists are now adopting simpler screening studies that can even be conducted at home; these tests simply measure oxygen saturation, nasal air flow and/or respiratory effort.[9] The purpose of these tests is to evaluate how many episodes of oxygen desaturation (defined as a fall of >4% from baseline lasting >10 seconds) occur per hour slept, and to associate these episodes with changes in respiratory effort to distinguish them from central sleep apnoea syndromes, which will not be discussed further here.

Severe cases of sleep apnoea may be associated with more than 15, and often as many as 40 or 50, episodes of oxygen desaturation per hour slept. The severity of sleep apnoea is defined using the apnoea–hypopnoea index (AHI) or the respiratory disturbance index (RDI), which record the number of apnoeas and episodes of oxygen desaturation per hour slept. These lead to disrupted sleep and daytime sleepiness, which can affect performance in common tasks, such as work performance and driving. Given these effects, it is not surprising that sleep apnoea can impair quality of life, have adverse effects on relationships with family and spouse and negatively influence work and leisure activities due to the severe daytime sleepiness.

## Associations of Sleep Apnoea with Metabolic Disease

Research over the last 10 years has begun to highlight the important associations that occur between sleep apnoea, hypertension and

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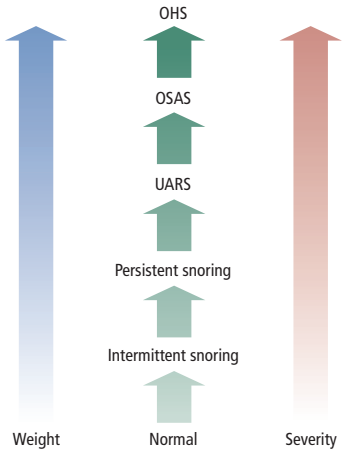
**Figure 1: The Spectrum of Sleep-disordered Breathing**




*OHS = obesity hypoventilation syndrome; OSAS = obstructive sleep apnoea syndrome; UARS = upper airways resistance syndrome.*

**Table 1a: Epworth Sleepiness Scale**

How likely are you to doze off or to fall asleep in the following situations, in contrast to just feeling tired? This refers to your usual way of life in recent times. Use the following scale to choose the most appropriate number for each situation:

0 – Would never doze
1 – Slight chance of dozing
2 – Moderate chance of dozing
3 – High chance of dozing

| Situation | Chance of dozing |
|---|---|
| Sitting and reading | |
| Watching TV | |
| Sitting inactive in a public place | |
| Being a passenger in a car for an hour | |
| Lying down to rest in the afternoon | |
| Sitting and talking to someone | |
| Sitting quietly after a lunch without alcohol | |
| Being in a car while stopped for a few minutes | |
| Total | /24 |

*A score >10 indicates significant daytime sleepiness.*

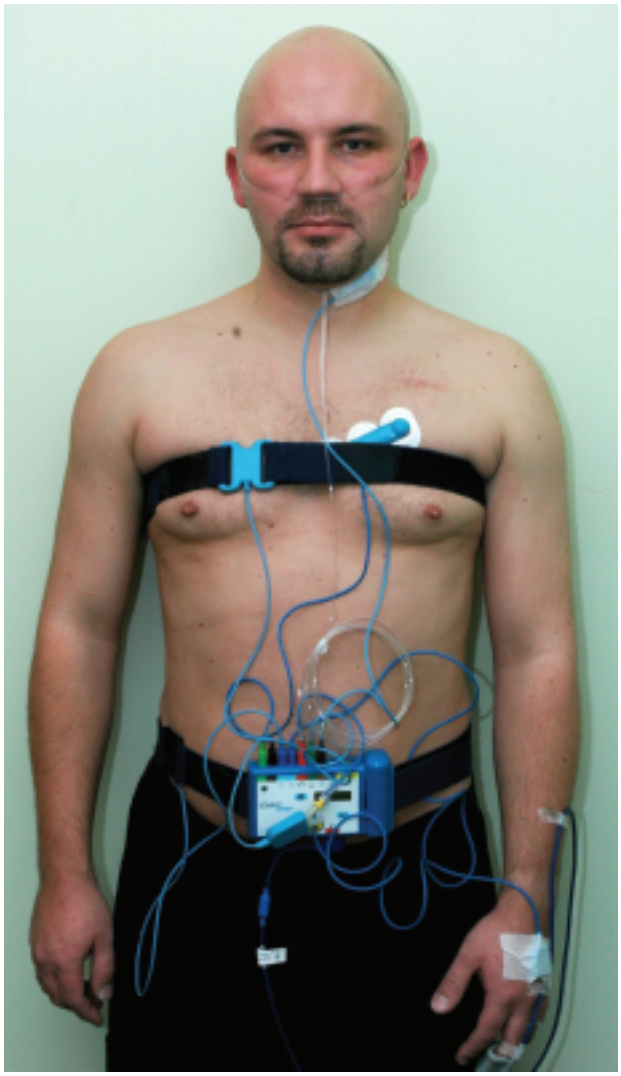
**Table 1b: Classification of Severity of Sleep-disordered Breathing Using the Respiratory Disturbance Index**

| Score | Severity |
|---|---|
| <5 | Normal |
| 5–10 | Mild |
| 10–15 | Moderate |
| >15 | Severe |

metabolic conditions, which together make up the metabolic syndrome.[10] The most powerful relationship is with blood pressure, and there is now ample evidence that the presence of sleep apnoea is associated with hypertension independent of the known association between hypertension and obesity.[11,12] Furthermore, the risk of being hypertensive increases as the severity of sleep apnoea increases.

More recent research has shown associations with insulin resistance, dyslipidaemia, impaired glucose intolerance and features of the metabolic syndrome.[4,13–16] Many of these epidemiological studies have

**Figure 2a: Making the Diagnosis of Obstructive Sleep Apnoea – Polysomnography**



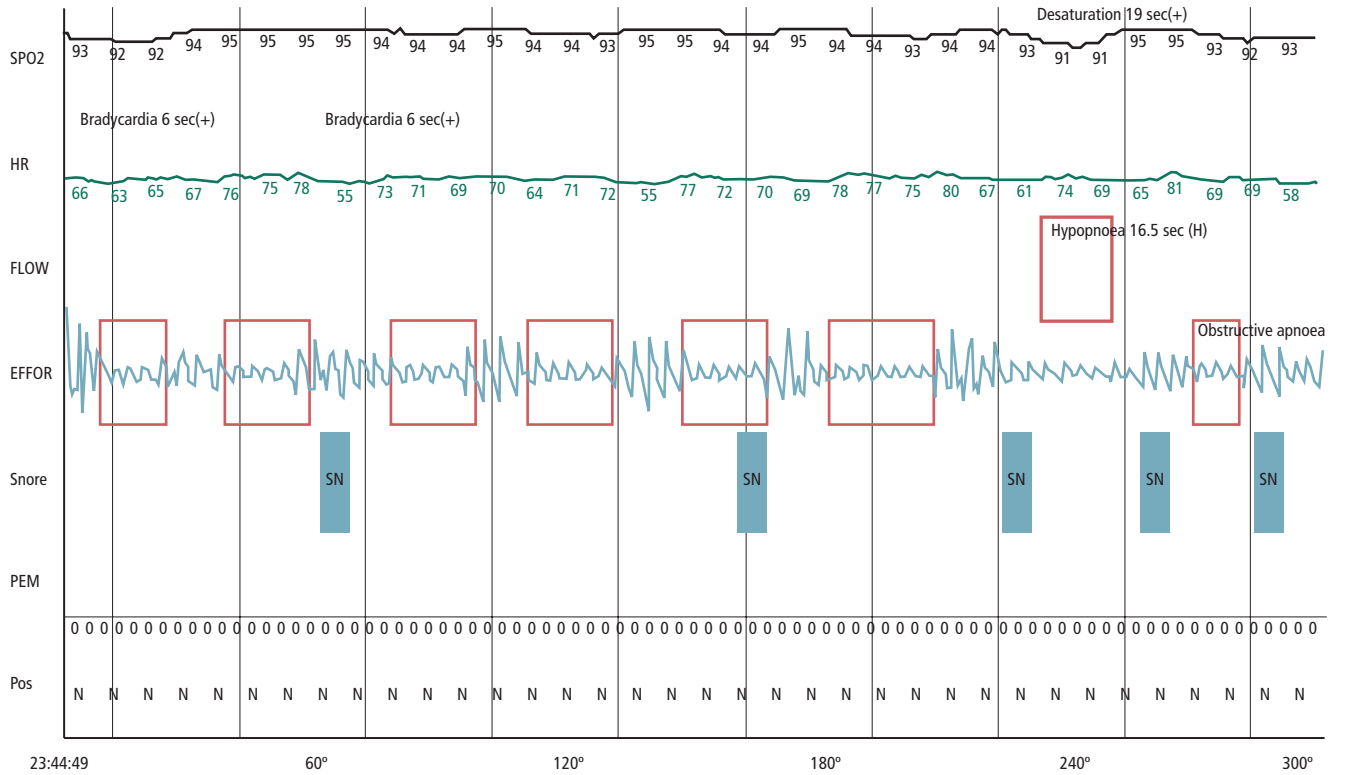
not controlled adequately for obesity, but where this has been done or in studies that have matched patients carefully for body fat, there is an increased risk of all of the metabolic syndrome components: 79% of patients with sleep apnoea may have metabolic syndrome compared with only 41% of age-, gender- and weight-matched controls.[17]

In the Wisconsin sleep cohort, diabetes was present in 15% of patients with an AHI above 15 compared with only 3% of patients with an AHI less than 5.[18] A community and clinic study in Oxford demonstrated a four-fold increase in diabetes prevalence in sleep apnoea in male patients with diabetes compared with the community studies. This study suggested that up to 23% of men with type 2 diabetes may have obstructive sleep apnoea[19] (see *Figure 3*).

## Treatment of Sleep Apnoea

Given its association with obesity, it is important that patients with sleep apnoea make every effort to lose weight. In those with severe (morbid) obesity, bariatric surgery can be helpful; this may also be the case for those patients who have co-existing diabetes, but this will not be an option for most patients. There are reports that modest weight loss, for example 10% of bodyweight, can improve symptoms of sleep apnoea,[20,21] but this has never been subjected to a

**Figure 2b: Making the Diagnosis of Obstructive Sleep Apnoea – Graph Showing Dips in Oxygen Levels**




formal randomised controlled trial.[22] Patients who have specific abnormalities of the palate or jaw may benefit from specific surgery, but the majority of patients will require treatment with nasal continuous positive airway pressure (CPAP) ventilation (see *Figure 4*), which has been shown to improve symptoms of sleep apnoea and blood pressure in a range of studies.[15,23,24]

> Reduced physical activity is a feature of patients with daytime sleepiness, and could contribute to low levels of high-density lipoprotein cholesterol and insulin resistance.

## Why Is Sleep Apnoea Associated with the Metabolic Syndrome and Diabetes?

Though both sleep apnoea and OSA are associated with obesity, which explains much of the association between the two conditions, the studies described above clearly show that this increased risk is partly independent of adiposity. Possible mechanisms that have been investigated include increased sympathetic nervous system activity, which may contribute to insulin resistance, hypertension and increased fatty acids.[25] Reduced physical activity is a feature of patients with daytime sleepiness, and could contribute to low levels of high-density lipoprotein (HDL) cholesterol and insulin resistance. More recently, it has been suggested that adipose tissue hypoxia may drive metabolic abnormalities in obesity via the secretion of inflammatory cytokines, although there is currently no direct evidence to support this mechanism in sleep apnoea.[26] These are clearly areas that will be important areas for future research.

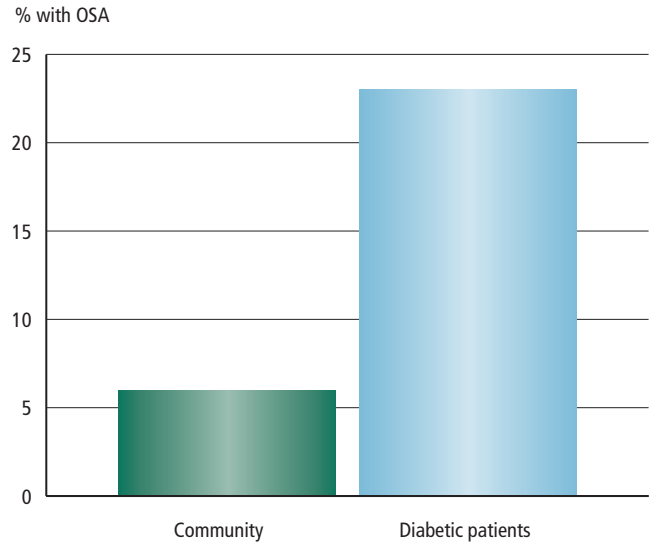
## Effects of Continuous Positive Airway Pressure Treatment on Symptoms and Associated Features of Sleep Apnoea

There is no doubt that CPAP treatment improves daytime sleepiness and quality of life and lowers blood pressure, partly through improvements in baroreflex sensitivity,[15,27] but it is currently unproven whether CPAP improves insulin resistance, features of the metabolic syndrome or diabetes control. One small uncontrolled study suggested that insulin resistance can improve with CPAP, but this effect appears to be confined to lean patients with a body mass index less than 30kg/m$^2$.[28]

Three small controlled studies have recently been reported. These include a study in patients with type 2 diabetes, where there was no change in glycated haemoglobin ($HbA_{1c}$) or indices of insulin resistance during a cross-over study of three months of CPAP and three months of sham CPAP.[29] A further study in 29 obese patients with severe OSA showed no change in insulin resistance as measured by the euglycaemic clamp after three months of CPAP treatment,[30] and a study in patients – most of whom had the metabolic syndrome – again using a cross-over design with sham CPAP also showed no effect, despite CPAP improving blood pressure and baroreflex sensitivity.[15]

One large epidemiological study did suggest that patients who chose to be treated with CPAP for sleep apnoea had lower rates of fatal and non-fatal cardiovascular events after 10 years, but as this was an epidemiological follow-up study it is unclear whether the improvement was related to changes in metabolic syndrome status, blood pressure or other factors, including the possibility of selection bias.[31]

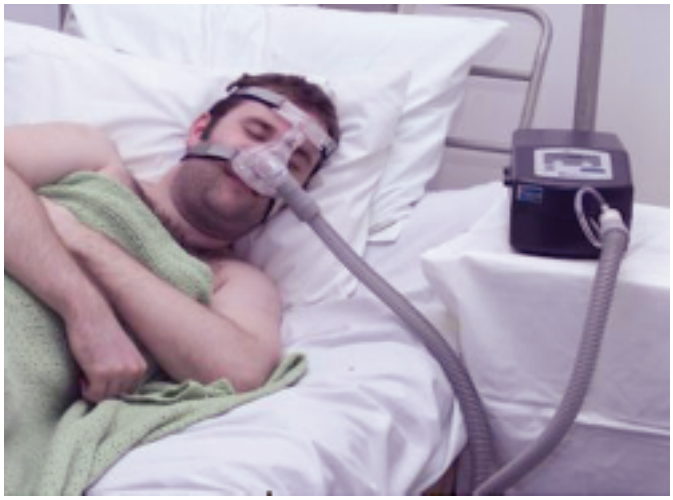
**Figure 3: Proportion of Diabetes Patients with a Diagnosis of Obstructive Sleep Apnoea Compared with a Non-diabetic Community Sample**




*OSA = obstructive sleep apnoea.*
*Source: West et al., 2006.*[19]

Despite these provisos, it is important that clinicians are aware of the relationships between sleep apnoea and metabolic disease and that specialists and generalists seeing patients with diabetes, metabolic disease or sleep apnoea are equipped to initiate appropriate investigation and referral. In a sleep clinic, it would seem sensible to investigate all patients for components of the metabolic syndrome, including measurements of neck and waist circumference, blood pressure, fasting glucose and lipids, and to monitor changes in these parameters during treatment. In clinics looking after patients with diabetes or other metabolic diseases, it is important to consider the possibility of sleep apnoea in patients who have complained of daytime sleepiness or troublesome snoring or who have resistant hypertension. Use of the Epworth or the Berlin questionnaire could be used to identify such high-risk patients. Where these cardinal symptoms are present, it is important to have a low threshold for referral, investigation and treatment by sleep specialists, and to consider offering bariatric surgery for the most severely obese patients, who are likely to benefit in terms of both weight loss and improvement in diabetes and sleep apnoea symptoms. ■

**Figure 4: Continuous Positive Airway Pressure Treatment**

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