

SLEEP APNOEA AND TYPE 2 DIABETES

The IDF
Consensus
Statement on

**SLEEP APNOEA AND
TYPE 2 DIABETES**



International Diabetes Federation

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IDF Communications

Avenue Emile De Mot 19

B-1000 Brussels, Belgium

By fax at +322 – 5385114 or

By e-mail at communications@idf.org

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The working group members included:

Paul Zimmet, co-chair, Melbourne, Australia
Sir George Alberti, co-chair, London, UK

Stephanie Amiel, London, UK
Matthew Cohen, Melbourne, Australia
Joachim Ficker, Nürnberg, Germany
Greg Fulcher, Sydney, Australia
Lee R Goldberg, Philadelphia, USA
Leif Groop, Lund, Sweden
David Hillman, Perth, Australia
Mary Ip, Hong Kong, China
Markku Laakso, Kuopio, Finland
Pierre Lefèbvre, Liège, Belgium
Yuji Matsuzawa, Osaka, Japan
Jean-Claude Mbanya, Yaounde, Cameroon
Naresh Punjabi, Baltimore, USA
Stephan Rossner, Stockholm, Sweden
Shaukat Sadikot, Mumbai, India
Jonathan Shaw, Melbourne, Australia
Martin Silink, Sydney, Australia
Eberhard Standl, Munich-Schwabing, Germany.
Colin Sullivan, Sydney, Australia
John Wilding, Liverpool, UK

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This booklet has been developed by IDF based on the manuscript.

IDF Executive Office: Anne Pierson



| Introduction

Recent research demonstrates the likelihood of a relationship between sleep-disordered breathing (SDB) and type 2 diabetes. Whilst the exact nature of the relationship between the two conditions remains uncertain, the association between them has important implications for public health and for individuals. Additionally, both type 2 diabetes and SDB are strongly associated with cardiovascular disease (CVD). SDB is increasingly considered as a condition to be treated for the prevention of CVD. When type 2 diabetes is already present, the treatment of SDB is even more relevant, because people with diabetes are already at high risk of CVD.

Today, while the enormity of the type 2 diabetes epidemic is well recognized, disorders of breathing during sleep are not. However, they make a significant contribution to the burden of disease in individuals and the financial burden on communities. In 2007, the International Diabetes Federation (IDF) Task Force on Epidemiology

and Prevention convened a working group on SDB and type 2 diabetes, with the intention of reviewing and evaluating the current information on these two topics and to make recommendations for both therapy and further research. The group recognized that there was a need for a global, multidisciplinary approach to raise awareness, improve clinical practice and coordinate research efforts to better understand the links between SDB and type 2 diabetes.

Discussions resulted in the production of a statement focusing on obstructive sleep apnoea (OSA), the most common form of SDB, and its possible links with type 2 diabetes and CVD. In addition to highlighting the need for further research into these links, the statement is meant to assist healthcare professionals in their approaches to prevention, diagnosis and treatment of OSA and diabetes and should be the basis for an educational programme for all healthcare workers involved in the care of people presenting either of the conditions.

| Extent of the problem

Today type 2 diabetes is certainly well recognized as a rampant global epidemic. The number of people with type 2 diabetes worldwide is set to increase from its present level of over 250 million to 380 million by 2025.² Approximately seven million people develop it every year and almost four million die of its consequences every year².

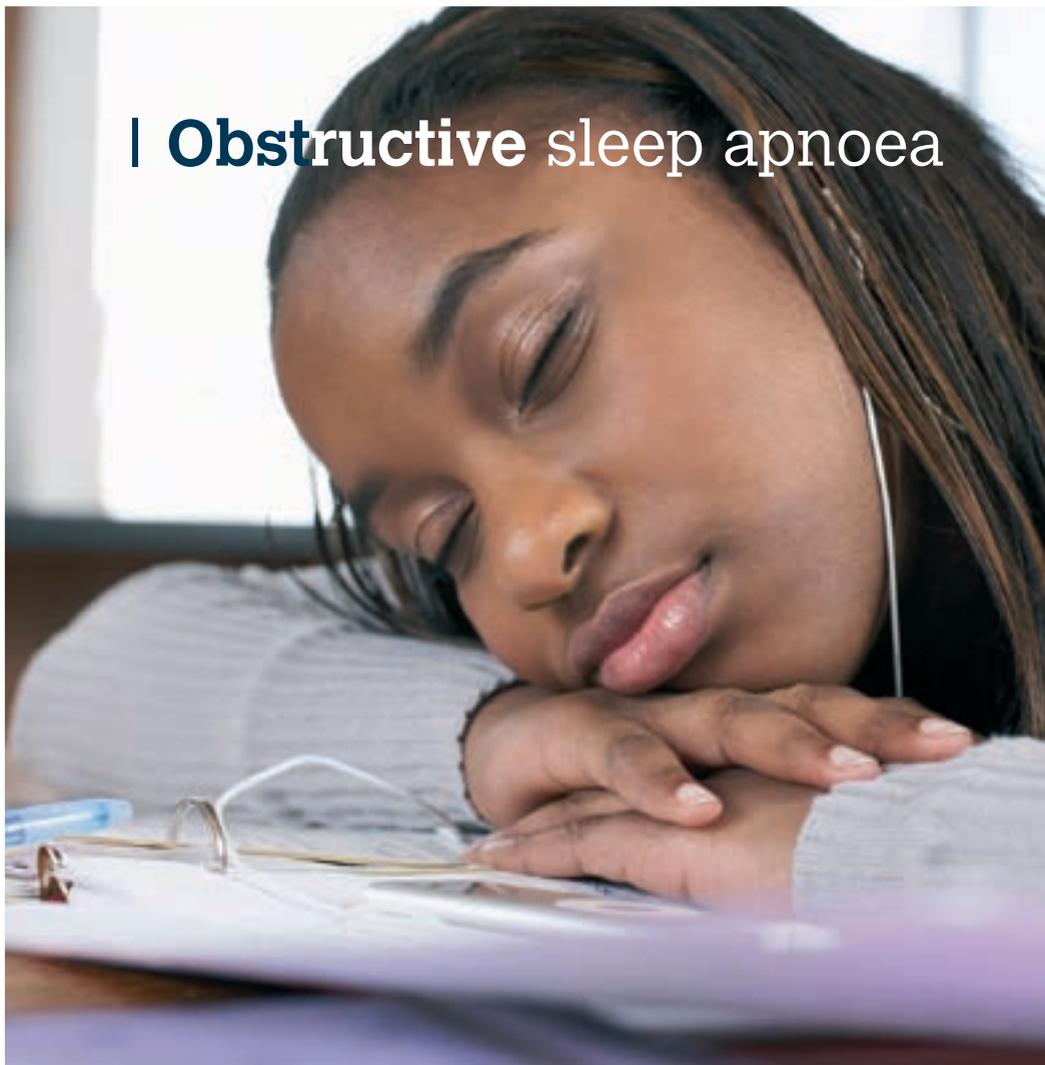
CVD is the major cause of death in diabetes, accounting for some 50% of all diabetes fatalities, and much disability. People with type 2 diabetes are over twice as likely to have a heart attack or stroke as people who do not have diabetes².

OSA is the most common form of SDB. It is often present among people with type 2 diabetes, CVD or obesity. OSA has been noted in up to 9% of women and 24% of men³. Risk factors include being male, overweight, and over the age of forty⁴, but sleep apnoea can strike anyone at any age, even children. Yet because of the lack of awareness by the public and healthcare professionals, the vast majority remain undiagnosed and therefore untreated, despite the fact that this serious disorder can have significant consequences.

Untreated, sleep apnoea can cause high blood pressure⁵ and other cardiovascular diseases, memory problems, weight gain, impotence and headaches. Moreover, untreated sleep apnoea may be responsible for workplace problems and car accidents. The medical costs of untreated OSA in the United States are estimated at USD 3.4 billion/year⁶, but the total economic impact of OSA is far greater due to indirect costs such as loss of productivity, accidents and disability.⁷

There is increasing evidence that OSA is associated with type 2 diabetes and with CVD. It is likely that more than half of the people with type 2 diabetes suffer from some form of sleep disturbances⁸ and that up to a third have OSA at a level where treatment would be recommended. Conversely, estimates suggest that up to 40% of people with OSA will have diabetes.^{9,10} OSA is known to be a risk factor for the development of hypertension⁵: it has been shown that people with mild to moderate OSA are twice as likely to develop hypertension as are people without OSA. Additionally, OSA has been shown to increase the risks of heart attacks.¹¹

| Obstructive sleep apnoea



What is obstructive sleep apnoea?

Sleep apnoea is a sleep disorder characterized by pauses in breathing during sleep. There are several forms of sleep apnoea, but the obstructive is the most common form. In OSA, pauses in breathing are caused by a physical block to airflow. OSA is usually defined by interruptions in airflow of at least 10 seconds (apnoeas), or by a decrease in airflow of at least 10 seconds (hypopnoeas) associated with either an arousal (the brain briefly arouses people in order for them to resume breathing) or a blood oxygen desaturation¹². OSA occurs two to three times more often in older adults and is twice as common in men as in women.

Table 1: Symptoms of sleep apnoea

Cardinal features of sleep apnoea	<ul style="list-style-type: none"> • A history of habitual snoring • A record of witnessed apnoeas • Excessive daytime sleepiness
Associated symptoms of sleep apnoea	<ul style="list-style-type: none"> • Fatigue, sleepiness during the day, loss of energy • Irritability • Poor memory • Depression • Mood changes • Morning headaches • Sexual dysfunction • Nocturia

1. Symptoms

The person with sleep apnoea is rarely aware of having difficulty breathing, even upon awakening, therefore sleep apnoea often goes undiagnosed. Sleep apnoea is often first noticed by others who witness the person during episodes or is suspected because of a history of habitual snoring and/or its daytime effects, such as sleepiness and fatigue. The latter are the consequences of sleep that is extremely fragmented and/or of poor quality. There are other common symptoms associated with sleep apnoea (see table 1).

2. Diagnosis

Sleep apnoea is often diagnosed with an overnight sleep test called polysomnography, although other

simpler methods are available. Two measurements of sleep disturbance can be used:

- the apnoea-hypopnoea index (AHI) (defined as the mean number of apnoea and hypopnoea episodes per hour of sleep)
- the blood oxygen desaturation index (ODI) (the mean number of blood oxygen desaturations per hour of sleep).

For each of these scores, the following categories apply^{13,14}:

< 5 / hour	Normal
5-15	Mild
15-30	Moderate
≥30	Severe

3. OSA, excess weight and type 2 diabetes

It is now well recognized that excess weight is associated with a higher risk of developing hypertension, hyperlipidemia, impaired glucose tolerance and insulin resistance. Excess weight, in particular central obesity, is also the strongest risk factor for the development of OSA. OSA affects about 4% of men and 2% of women in the general population, but the prevalence rate is significantly higher in the obese population.³

An increasing number of studies also show that OSA is independently associated with insulin resistance and type 2 diabetes. It has been reported that the prevalence of some form of sleep disturbance among people with diabetes is very high and can reach 58%.⁸ Similarly, both impaired glucose tolerance and diabetes have a high prevalence among people with sleep apnoea. Additionally, increasing insulin resistance has been correlated with increasing severity of OSA.

4. Treatment of sleep apnoea

There are several options for the treatment of sleep apnoea.

Lifestyle changes. Weight loss should be recommended for all overweight or obese people with

sleep apnoea. Avoiding alcohol and sleeping pills is likely to be beneficial.

Continuous Positive Airway Pressure (CPAP) is a treatment in which a mask is worn over the nose and/or mouth whilst sleeping. The mask is linked up to a machine that delivers a continuous stream of compressed air. The positive pressure helps keep the airways open so that breathing is not impaired.

Oral Devices such as dental appliances can be made that help keep the airway open during sleep. Such devices can be specifically designed by dentists with special expertise in treating sleep apnoea.

Surgery may be considered in some cases, particularly when people have enlarged tonsils and adenoids or nasal polyps or if people have facial deformities such as a small jaw or a deviated nasal septum.

| Type 2 diabetes



Type 2 diabetes is primarily characterized by insulin resistance and relative insulin deficiency. Type 2 diabetes can remain undetected for many years, as it is often asymptomatic. Its diagnosis is often made from associated complications or incidentally through an abnormal blood or urine glucose test.

Type 2 diabetes is often, but not always, associated with excess weight and is most common in people older than 45 who are overweight. However, as a consequence of increased obesity among the young, it is becoming more common in children and young adults. Although the onset of type 2

diabetes is also linked to genetic factors, obesity, physical inactivity and unhealthy diet increase the risks. Ethnicity, family history and intrauterine environment are further risk factors for the development of type 2 diabetes.

Type 2 diabetes is the most common form of diabetes accounting for 85 to 95% of all diabetes in developed countries, and for an even higher percentage in developing countries. If people with type 2 diabetes are not diagnosed and treated, they can develop serious complications, which can result in severe disability and early death.

The IDF consensus statement on sleep apnoea & type 2 diabetes

The working group analyzed the links between OSA and disorders of glucose metabolism and the links between OSA and CVD. The latter are particularly relevant in the case of people who have both diabetes and OSA, because people with diabetes are already at higher risk of CVD. The group developed recommendations for treatment and care aimed at healthcare professionals working in both type 2 diabetes and SDB.

1. LINKS between OSA and disorders of glucose metabolism

Although there is a recognized association between type 2 diabetes and OSA, the question of its exact nature has not yet been fully answered. The additional question is if central obesity, which is a known risk factor for both sleep apnoea and type 2 diabetes, could be the main cause in

the association of these two conditions. There is now emerging evidence that the association between type 2 diabetes, insulin resistance, metabolic syndrome and OSA does not totally depend on obesity^{15,16,17} however there is not yet enough evidence to fully exclude obesity from being the main driver.

Estimates suggest that up to 40% of people with OSA will have diabetes,^{9,10} but the incidence of new

diabetes in people with OSA is not known. In people who have diabetes, the prevalence of OSA may be up to 23%¹⁶, and the prevalence of some form of SDB may be as high as 58%.⁸

Does OSA play a role in the development of type 2 diabetes?

Some early studies suggested that the presence of OSA could possibly lead to the development of type 2 diabetes, but these studies showed significant limitations. To date, two types of studies have looked into the issue:

1. Studies using self-report sleep parameters and type 2 diabetes: two large studies^{17,18} found snoring to be a risk factor for the development of type 2 diabetes over 10 years, independent of other factors. However these studies used data reported by the patient, which assumed the presence of sleep-breathing disturbance without objective measurement.
2. Studies using the polysomnograph to define OSA: Several studies such as the Sleep Heart Health Study¹⁹ and the Wisconsin Sleep Study²⁰ reported a correlation between OSA and changes in glucose metabolism. Additionally, a study of French men showed

that those with mild OSA were significantly more likely to have impaired glucose tolerance and diabetes than those without OSA.⁹ However longitudinal data from the same Wisconsin study showed that after adjusting for obesity, OSA was not a significant predictor of the development of diabetes over four years.

Further studies are required before definitive conclusions can be reached about the fact that OSA does or does not play a role in the development of type 2 diabetes.

Does OSA have effects on glycaemic control in people with existing type 2 diabetes?

Studies have reported that among people with diabetes, sleep duration and quality were significantly linked with glycaemic control (HbA_{1c}).²¹ Some studies analyzed whether OSA had effects on glycaemic control by evaluating the impact of CPAP treatment of OSA on insulin resistance, glycaemic control and HbA_{1c}. However, these studies have had confusing and conflicting results. More research is needed before it can be concluded that OSA has effects on glycaemic control in people with type 2 diabetes.

Does OSA have effects on components of the metabolic syndrome?

A relationship has been suggested between the presence of the metabolic syndrome and OSA. People with OSA are more likely to have the metabolic syndrome²² and conversely, people with metabolic syndrome have been shown to have an increased risk of OSA.²³

How can OSA affect glucose metabolism?

There is evidence that the intermittent shortage of oxygen in the body (hypoxia)^{24,25,26} and/or the sleep fragmentation^{27,28} that result from OSA cause a physiologic stress which can have an impact on glucose metabolism and can play an important role in the development of insulin resistance. This impact can be explained by one or several biological mechanisms (see appendix 1).

2. LINKS between OSA and CVD

OSA is associated with a variety of cardiovascular conditions ranging from hypertension to heart failure^{29,30} and doctors increasingly consider treating OSA in order to prevent CVD.

OSA has been definitively shown to be an independent risk factor for the development of hypertension⁵. The study showed that people with mild to moderate OSA were twice as likely to develop hypertension, and people with severe OSA were almost three times as likely to develop hypertension as were those without OSA.

Other studies showed that OSA was associated with a range of CVD such as stroke, heart failure and ischaemic heart disease³¹. The prevalence of CVD increased progressively with the increasing severity of OSA. OSA was also associated with myocardial infarction³². Studies reported that people with known coronary disease and OSA had an increased risk of cardiovascular events and death³³ and that people with OSA were more likely to face sudden cardiac death.^{34,35,36,37}

How can OSA lead to CVD?

Similar to the mechanisms that link OSA with impaired glucose metabolism and type 2 diabetes, there is evidence that a variety of mechanisms and pathways may promote the development of CVD in people with OSA.

Recommendations for treatment

Even if the positive impact of treatment of OSA on glucose control, obesity and other risk factors has yet to be consistently demonstrated, the treatment has beneficial effects on quality of life and blood pressure control. It has been established that treatment of OSA improves sleep and consequently reduces fatigue and daytime sleepiness. As it reduces daytime sleepiness, it also reduces risks of car accidents and job impairment.

Available therapies include weight reduction in the overweight and obese, reduction in alcohol intake, use of CPAP treatment and/or dental appliances.

Weight loss

Although very few data exist from controlled trials, weight loss should be the primary treatment strategy for OSA in people who are overweight or obese. Losing weight may improve energy, social interaction, cognition and work performance, reduce accidents and erectile dysfunction. Additionally, reduction of daytime fatigue may lead to increased physical activity, which in turn will have positive effects

on glucose metabolism and on achieving and maintaining a healthy body weight.

Continuous Positive Airway Pressure (CPAP) treatment

While CPAP treatment of OSA has been shown to have mixed results on glucose metabolism, it has been shown to have an impact on CVD.

In people without diabetes, the impact of CPAP treatment on the improvement in insulin sensitivity was not clearly demonstrated. In people with diabetes, the impact of CPAP treatment on the improvement in insulin sensitivity also had confusing results but some studies have shown a significant reduction of HbA_{1c} in people who had less than optimal control.^{38,39}

In people who have CVD, CPAP treatment of OSA has been shown to have an impact on their condition. In resistant hypertension, guidelines recommend the investigation for and treatment of any existing OSA⁴⁰. Finally, CPAP treatment of OSA may improve cardiovascular outcomes in people with heart failure.⁴¹

Recommendations for screening



Screening people with OSA for metabolic disorders

IDF recommends that healthcare professionals monitor people with OSA for any metabolic disease, including type 2 diabetes: screening tests for diabetes and the metabolic syndrome are inexpensive and easy to conduct. The screening tests include waist measurement, blood

pressure measurement and fasting lipids and glucose (followed with a glucose tolerance test (OGTT), where appropriate). Treatment is available that is likely to reduce the risk of micro- and macrovascular diabetic complications. The monitoring of metabolic parameters is an essential part of the care of people with OSA.

Screening people with type 2 diabetes for OSA

To date, there is not enough evidence to support screening of OSA in all people with diabetes since there is no conclusive evidence that treatment of OSA will improve metabolic parameters. Additionally, screening questionnaires for OSA are not well adapted for people with diabetes, who may experience fatigue and daytime sleepiness even in the absence of OSA⁴². However, since people with symptomatic daytime sleepiness are likely to benefit most from treatment of OSA (as well as the most likely to comply with treatment in the long-term), it may be considered worthwhile to target these people specifically.

Until more research information is available, IDF recommends a practical approach which is to investigate those people with classical symptoms such as witnessed apnoeas, heavy snoring or daytime sleepiness, despite the fact that some people with OSA will not be identified this way. People with diabetes with refractory hypertension should also be considered for screening since treating OSA may improve blood pressure.⁴⁰

The identification of OSA has long relied on the use of an in-laboratory sleep test called a polysomnogram.

However diagnostic testing is expensive and may not be accessible in all clinical settings. One screening strategy uses a two-stage approach in which a structured questionnaire (eg the Berlin questionnaire⁴³) is used in the first stage to assess the probability of sleep apnoea. Those at high risk undergo a second stage, with an overnight evaluation at home with pulse oximetry or portable monitoring (PM). People with a high pretest probability of OSA but a negative test on PM may require further investigation by polysomnogram, as a negative test with PM does not necessarily rule out OSA.³

People with evidence of some form of sleep apnoea on PM should be referred, if possible, to a sleep specialist. In the absence of such clinical expertise, an empirical trial of CPAP therapy with an auto-titrating device can be considered with involvement of a primary care physician and a trained respiratory therapist.

There is no doubt that further research is needed given the countless barriers in identifying undiagnosed people with OSA. Until diagnostic strategies are adjusted, a detailed history or a structured assessment followed by a simple night-time evaluation will identify those in urgent need for treatment.

Recommendations for care

There is an evident need for healthcare professionals to be aware, educated and trained in the area of OSA and type 2 diabetes.

IDF recommends that healthcare professionals working in both type 2 diabetes and OSA should adopt clinical practices to ensure that a person presenting with one condition is considered for the other. Healthcare professionals should aim to develop routine interventions that are locally appropriate for both type 2 diabetes and sleep services.

Sleep services: People with OSA should be routinely screened for markers of metabolic disturbance and cardiovascular risk. Minimum testing should include measurement of:

- waist circumference
- blood pressure
- fasting lipids
- fasting glucose

Diabetes services: The possibility of OSA should be considered in the assessment of all people with type 2 diabetes and the metabolic syndrome.

- People should be assessed for symptoms of OSA: snoring, observed apnoea during sleep and daytime sleepiness.
- People should be referred to a specialist in an early stage in order to establish a diagnosis, because of the confirmed benefits of therapy on hypertension and quality of life.
- Management of OSA should focus initially on weight reduction for the overweight and obese. CPAP is the current best treatment for moderate to severe OSA and should be considered where appropriate.

Recommendations for research



Because of the direct impact of OSA on the individual's life and its financial consequences on society, IDF recommends further research in the following areas:

• **Epidemiological studies of prevalence of OSA in**

- people with type 2 diabetes and metabolic syndrome
- children with obesity, especially those with type 2 diabetes
- different ethnic groups
- gestational diabetes and pre-eclampsia

• **Studies of the effects of OSA on**

- insulin secretion, insulin resistance, mitochondrial function and inflammatory markers
- complications of type 2 diabetes

• **Intervention studies**

- Appropriately powered randomised controlled trials of CPAP and other therapies in people with type 2 diabetes with emphasis on cardiovascular risk factors and outcomes, and glycaemic control. Additional outcomes should also include oxidative stress, inflammatory markers and adipokines/lipid metabolism.
- Trials of weight loss in people with OSA and diabetes (including use of anti-obesity medication)

• **Resource development**

- A reliable but inexpensive diagnostic strategy for OSA to be used in a primary care setting
- Treatments for OSA that are easier to use and cheaper than CPAP

| Conclusion

Type 2 diabetes and OSA are common disorders that often coexist. There is a high prevalence of OSA in people with type 2 diabetes and abnormal glucose metabolism and, conversely, there is a high prevalence of type 2 diabetes and related metabolic disorders in people with OSA. Additionally, there is a link between OSA and hypertension and CVD. One explanation for this overlap is the presence of shared risk factors such as obesity but an increasing number of studies show that these two conditions can be associated independently of obesity.

Because both diabetes and OSA are associated with increased cardiovascular morbidity and mortality and other important adverse consequences, IDF calls to action to raise awareness, improve clinical practice and support scientific research in the links between type 2 diabetes and OSA.

IDF recommendations for treatment of OSA include weight reduction in the overweight and obese, reduction in alcohol intake, use of CPAP treatment and/or dental appliances. Beneficial effects on glucose control, obesity and other cardiovascular risk factors have been suggested but have yet to be consistently demonstrated.

However, the benefits of treatment of OSA have been established, particularly as they improve quality of life and blood pressure control.

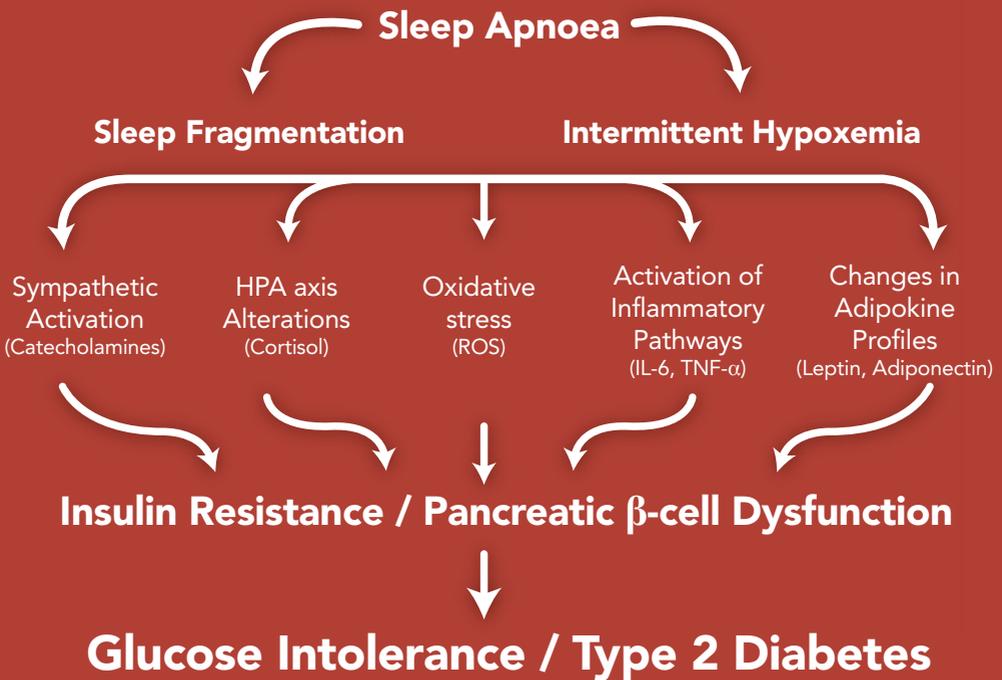
When people have type 2 diabetes or OSA, IDF recommends screening for the other condition. People with OSA should be routinely screened for metabolic disease and type 2 diabetes as screening tests are inexpensive and easy to conduct. People with diabetes should be screened for OSA particularly when they present classical symptoms such as witnessed apnoeas, heavy snoring or daytime sleepiness. Diagnosis can be confirmed by appropriate testing, but where facilities are limited, simpler home monitoring devices can help in the diagnosis of OSA.

IDF recommends that all healthcare professionals involved with diabetes or OSA should be educated about the links between the two conditions and trained in their care. Further research is needed to better understand the links between the two conditions and improve treatment and care. Finally, health policy makers and the general public must also be made more aware of OSA and the significant financial and disability burden that it places on both individuals and societies.

Appendix 1:

Sleep apnoea is characterized by sleep fragmentation and/or intermittent hypoxemia. Both impose a physiologic stress which may be involved in the pathogenesis of insulin resistance via one or several biological mechanisms (see fig 1).

Fig 1: Potential mechanisms linking sleep apnoea to glucose intolerance⁴⁵



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International Diabetes Federation

International Diabetes Federation (IDF)
Avenue Emile de Mot 19 • B-1000 Brussels • Belgium
Phone: +32-2-5385511 • Fax: +32-2-5385114
www.idf.org • communications@idf.org