

Jauhar, Sachin (2010) *Sleep medicine and dentistry*. MSc(R) thesis.

http://theses.gla.ac.uk/2252/

Copyright and moral rights for this thesis are retained by the author

A copy can be downloaded for personal non-commercial research or study, without prior permission or charge

This thesis cannot be reproduced or quoted extensively from without first obtaining permission in writing from the Author

The content must not be changed in any way or sold commercially in any format or medium without the formal permission of the Author

When referring to this work, full bibliographic details including the author, title, awarding institution and date of the thesis must be given

Glasgow Theses Service http://theses.gla.ac.uk/ theses@gla.ac.uk **Sleep Medicine and Dentistry**

Sachin Jauhar BDS MFDS (Edin) FDS Rest Dent (Glas)

Submitted in fulfilment of the requirements for the Degree of Master of Science

Department of Restorative Dentistry Faculty of Medicine University of Glasgow

June 2010

Abstract

Many health care professionals and patients are unclear of the role that dentists may play in the management of Obstructive Sleep Apnoea-Hypopnoea Syndrome (OSAHS.) The dentists' role is primarily in the construction of appliances for OSAHS but in the United States of America some dentists have practices limited to "Sleep dentistry". However, in the United Kingdom there is limited training for dentists in this field.

This thesis aims to review the relevant literature that pertains to OSAHS and dentistry and then, through three studies, to look at the past, present and future involvement of dentists in OSAHS. Assessing outcome is clearly important and this thesis firstly presents patient-based findings of the long term success of mandibular advancement appliances. Secondly, the experience and views of dentists and sleep specialists, assessed by questionnaire, is presented. Finally, a prospective study of a promising screening tool (the Kushida Index) for the diagnosis of sleep apnoea is carried out.

Table of contents

1.1 Sle	Review of the literature	
	ер	
1.2 Sno	oring	
1.2.1	Snoring overview	
1.2.2	Examination of snorers	
1.2.3	Clinical significance of snoring	
1.2.4	Treatment of snoring	
	structive sleep apnoea-hypopnoea syndrome (OSAHS)	
1.3.1	Overview of OSAHS	
1.3.2	Epidemiology of OSAHS	
1.3.3	Risk Factors for OSAHS	
1.3.4	Pathogenesis of OSAHS	
1.3.5	Other causes of excessive daytime sleepiness	
1.3.6	Diagnosis of OSAHS	
1.3.7	Sleep apnoea - screening	
1.3.8	Treatment of sleep apnoea	30
1.4 Up	per Airways resistance syndrome	34
1.5 Ora	al Appliances	34
1.5.1	Oral appliance types and features	34
1.5.2	Soft palate lifters	
1.5.3	Tongue retaining devices	35
1.5.4	Mandibular advancement appliances	36
1.5.5	Side effects of oral appliances	39
1.5.6	Compliance with oral appliances	40
1.6 Sur	nmary	
	٠ 	
Chapter 2 -	Long term follow-up of mandibular advancement appliances for	the
•	t of energing and close appear	
managemen	t of snoring and sleep apnoea	41
-	roduction	
2.1 Int		41
2.1 Int 2.2 Hy	roduction	41 41
2.1 Int 2.2 Hy 2.3 Ma	roduction	41 41 41
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res	roduction	41 41 41 42
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis	roduction pothesis terial and Methods sults	41 41 41 42 54
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Co	roduction bothesis terial and Methods sults cussion nclusions	41 41 41 42 54
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 -	roduction bothesis terial and Methods sults cussion nclusions Dentists' and doctors' attitudes to the provision of intra-oral	41 41 41 42 54 56
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances f	roduction pothesis terial and Methods sults cussion nclusions Dentists' and doctors' attitudes to the provision of intra-oral or the management of snoring and sleep apnoea	41 41 42 54 56 57
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances f 3.1 Int	roduction bothesis. terial and Methods. sults cussion nclusions. Dentists' and doctors' attitudes to the provision of intra-oral or the management of snoring and sleep apnoea roduction.	41 41 42 54 56 57 57
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Cor Chapter 3 - appliances 1 3.1 Int 3.2 Ain	roduction pothesis terial and Methods sults cussion nclusions Dentists' and doctors' attitudes to the provision of intra-oral or the management of snoring and sleep apnoea	41 41 42 54 56 57 57 57
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances 1 3.1 Int 3.2 Ain 3.3 Ma	roduction bothesis. terial and Methods. sults cussion nclusions. Dentists' and doctors' attitudes to the provision of intra-oral for the management of snoring and sleep apnoea roduction.	41 41 42 54 56 57 57 57 57
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Cor Chapter 3 - appliances 1 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res	roduction bothesis. terial and Methods. sults cussion nclusions. Dentists' and doctors' attitudes to the provision of intra-oral for the management of snoring and sleep apnoea roduction. hs terials and Methods.	41 41 42 54 56 57 57 57 57 58
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Col Chapter 3 - appliances f 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res 3.5 Dis	roduction bothesis. terial and Methods. sults cussion nclusions. Dentists' and doctors' attitudes to the provision of intra-oral for the management of snoring and sleep apnoea roduction. ns terials and Methods. sults cussion	41 41 42 54 56 57 57 57 57 58 60
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances 1 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res 3.5 Dis 4 Chapter	roduction bothesis. terial and Methods sults cussion cussion Dentists' and doctors' attitudes to the provision of intra-oral for the management of snoring and sleep apnoea roduction sults terials and Methods. sults cussion r 4 - The Kushida Index as a screening tool for Obstructive Sleep	41 41 42 54 56 57 57 57 57 58 60
 2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Condition Chapter 3 - appliances 1 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res 3.5 Dis 4 Chapter 	roduction bothesis. terial and Methods. sults cussion cussion cussions. Dentists' and doctors' attitudes to the provision of intra-oral for the management of snoring and sleep apnoea coduction coduction cussion cussion r 4 - The Kushida Index as a screening tool for Obstructive Sleep opnoea Syndrome.	41 41 42 54 56 57 57 57 57 58 60
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances f 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res 3.5 Dis 4 Chapter Apnoea-Hyp 4.1 Int	roduction	41 41 42 54 56 57 57 57 57 57 58 60 68 68
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances f 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res 3.5 Dis 4 Chapter Apnoea-Hyp 4.1 Int 4.2 Ain	roduction	41 41 42 54 56 57 57 57 57 57 58 60 68 68 68
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances f 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res 3.5 Dis 4 Chapter Apnoea-Hyp 4.1 Int 4.2 Ain	roduction	41 41 42 54 56 57 57 57 57 57 57 58 60 68 68 68 69
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances f 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res 3.5 Dis 4 Chapter Apnoea-Hyp 4.1 Int 4.2 Ain 4.3 Ma 4.3.1	roduction	41 41 42 54 56 57 57 57 57 57 57 58 60 68 68 68 68 69 71
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances f 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res 3.5 Dis 4 Chapter Apnoea-Hyp 4.1 Int 4.2 Ain 4.3 Ma 4.3.1 4.4 Res	roduction	41 41 42 54 56 57 57 57 57 57 57 58 60 68 68 68 68 69 71 71
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances f 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res 3.5 Dis 4 Chapter Apnoea-Hyp 4.1 Int 4.2 Ain 4.3 Ma 4.3.1 4.4 Res 4.5 Dis	roduction	$\begin{array}{c} \dots & 41 \\ \dots & 41 \\ \dots & 41 \\ \dots & 54 \\ \dots & 56 \\ \dots & 57 \\ \dots & 58 \\ \dots & 68 \\ \dots & 69 \\ \dots & 71 \\ \dots & 71 \\ \dots & 73 \end{array}$
2.1 Int 2.2 Hy 2.3 Ma 2.4 Res 2.5 Dis 2.6 Con Chapter 3 - appliances f 3.1 Int 3.2 Ain 3.3 Ma 3.4 Res 3.5 Dis 4 Chapter Apnoea-Hyp 4.1 Int 4.2 Ain 4.3 Ma 4.3.1 4.4 Res 4.5 Dis 4.6 Con	roduction	$\begin{array}{c} \dots & 41 \\ \dots & 41 \\ \dots & 41 \\ \dots & 42 \\ \dots & 54 \\ \dots & 56 \\ \dots & 57 \\ \dots & 5$

Table 2.1 Comfort tabled against satisfaction.	45
Table 2.2 Side effects of the appliance.	46
Table 2.3 Success tabled against BMI.	51
Table 2.4 Success tabled against smoking.	51
Table 2.5 Success tabled against alcohol consumption.	52
Table 2.6 Success tabled against sleep duration.	52
Table 2.7 Success tabled against sleep quality.	53
Table 3.1 A list of the services offered by GDP's to patients with	
possible OSA or problem snoring.	63
Table 3.2 Referral patterns of the 29 dentists who included	
"referral" in their management.	64
Table 3.3 Possible issues and side effects of appliances that	
dentists discussed with patients.	65
Table 3.4 Additional comments made by dentists.	66
Table 4.1 Comparison of demographics of patients included	
and excluded from the analysis.	80
Table 4.2 Incisal relationship of patients.	81
Table 4.3 Pooled intra-oral measurements of all patients.	82
Table 4.4 Results for the 71 patients included in the study.	83
Table 4.5 Relationship between the diagnosis obtained from respiratory	
polysomnography and the results of the Kushida Screening test.	84
Table 4.6 Diagnostic category of the 71 patients included in the study.	85

Page

List of figures

Figure 1.1 Normal adult hypnogram.	11
Figure 1.2.CPAP Mask	31
Figure 1.3 Soft palate lifter appliance	35
Figure 1.4 Tongue retaining device.	35
Figure 1.5 Mandibular advancement appliance.	37
Figure 2.1 Number of nights appliance used.	43
Figure 2.2 Number of hours a night appliance worn.	43
Figure 2.3 Comfort of appliance.	44
Figure 2.4 Effectiveness of appliance on snoring.	44
Figure 2.5 Number of hours of sleep per night.	47
Figure 2.6 Position whilst snoring.	48
Figure 2.7 Sleep apnoea severity.	48
Figure 2.8 BMI.	49
Figure 2.9 Number of units of alcohol per week.	50
Figure 4.1 Jenny Callipers.	76
Figure 4.2 Goniometer.	77
Figure 4.3 Measurement of mandibular intermolar distance.	78
Figure 4.4 Modified Mallampati Score.	79
Figure 4.5 The Receiver Operator Curve for the Kushida Index in	
the diagnosis of OSAHS.	86

Appendices

	Page
Epworth Sleepiness Scale	88
Stanford Sleepiness Scale	89
Patient Questionnaire	90

Publications and Presentations

Posters presented to Learned Societies:

Dentists' and doctors' attitudes to the provision of intra-oral appliances for the management of snoring and sleep apnoea.

S. Jauhar, M. F. Lyons, S. W. Banham, R. Orchardson, E. Livingston. European Sleep Research Society September 2008.

Prospective study assessing the validity of the Kushida Index for screening for sleep apnoea in a west of Scotland population.

S. Jauhar, M. F. Lyons, R. Orchardson, E. Livingston, D. MacFarlane, S.W Banham. European Sleep Research Society September 2008.

Abstracts published:

S. Jauhar, M.F. Lyons, R. Orchardson, E. Livingston, D. MacFarlane, S. Banham. Prospective study to assess the validity of the Kushida Index in the screening of sleep apnoea in a West of Scotland population. Journal of Sleep Research. Volume 17, Supplement 1, December 2008

S. Jauhar, M.F. Lyons, S.W. Banham, R. Orchardson, E. Livingston Dentists' and doctors' attitudes to the provision of intra-oral appliances for the management of snoring and sleep apnoea.

Journal of Sleep Research. Volume 17, Supplement 1, December 2008

Published papers:

S. Jauhar, M.F. Lyons, S.W. Banham, R. Orchardson, E. Livingston, Dentists' and doctors' attitudes to the provision of intra-oral appliances for the management of snoring and sleep apnoea. Br Dent J. 2008 Dec 20;205(12):653-7; discussion 647. Epub 2008 Nov 21.

Sachin Jauhar, Mervyn F Lyons, Stephen W Banham, Donald A Cameron, Robin Orchardson

Ten-year follow-up of mandibular advancement devices for the management of snoring and sleep apnea.

J Prosthet Dent. 2008 Apr ;99 (4):314-21

In Press: S Jauhar *et al*. Sleep apnoea, snoring and their relationship to dentistry. Commissioned by Dental Update - accepted awaiting publication.

Under Review:

Sachin Jauhar Robin Orchardson Stephen W. Banham Eric Livingston Andrea Sherriff Mervyn F. Lyons.

The Kushida Index as a screening tool for Obstructive Sleep Apnoea-Hypopnoea Syndrome. Under review BDJ

Acknowledgements

I would like to thank the following individuals for their help:

Dr M Lyons for his time, and supervision in the preparation of this thesis and the published papers that arose from the studies.

Dr S Banham, for his help in the study protocols and his support with participant recruitment.

Dr R Orchardson kindly stepped in as supervisor to my thesis and provided me with help in writing of the publications and this thesis.

Dr A Sheriff for her help with the statistical analysis.

Dr E Livingston helped with the patient recruitment at Gartnavel General Hospital.

The BACS research group partially funded the presentations to the ERSS Conference in Glasgow.

My parents supported me though-out this project, and my wife, Ingrid has been a constant aid without whom this thesis would not be possible, thank you.

Author's declaration

This thesis is the original work of the author.

Sachin Jauhar

June 2010

Definitions and abbreviations

OSAHS - Obstructive Sleep Apnoea-Hypopnoea Syndrome.

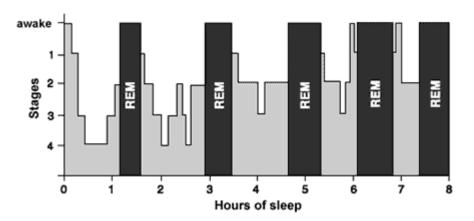
- REM Rapid eye movement (sleep).
- NREM Non-rapid eye movement (sleep).
- CPAP Continuous Positive Airway Pressure.
- AHI Apnoea Hypopnoea Index.
- RDI Respiratory Disturbance Index.
- BMI Body Mass Index (weight (kg) / height (m) 2).
- CT Computed Tomography.
- MRI Magnetic Resonance Imaging.
- EMG Electromyogram.
- ESS Epworth Sleepiness Scale.
- MSLT Multiple Sleep Latency Test.
- SIGN Scottish Intercollegiate Guidelines Network.
- SSS Stanford Sleepiness Scale.
- UPPP Uvulopalatopharyngoplasty.
- LAUP Laser-assisted uvulopalatopharyngoplasty.
- NICE National Institute for Health and Clinical Excellence.
- UARS Upper airways resistance syndrome.
- ICSD International classification of sleep disorders.
- MAA Mandibular advancement appliances.
- STARD Standards for reporting of diagnostic accuracy.
- ODI Oxygen Desaturation Index.
- ROC Receiver Operator Curve.
- ARTP Association of Respiratory Technology and Physiology.

Chapter 1- Review of the literature

1.1 Sleep

Sleep is something that we are all very familiar with, but a suitably precise definition might be "A reversible behavioural state of perpetual disengagement from and unresponsiveness to the environment." (Carskadon, Dement 2005) The functions of sleep are uncertain but can be categorized into biochemical, physiological, neurological, psychological and social. (Shneerson 2005)

Physiological studies have shown there are two main types of sleep which are distinct from one another: (a) rapid eye movement (REM) sleep and (b) non-rapid eye movement (NREM) sleep. In addition to episodic bursts of rapid eye movement, REM sleep is characterized by muscle atonia and increased electroencephalogram (EEG) activity. The mental activity of REM sleep is associated with dreaming in 80% of cases. (Dement, Kleitman 1957) In contrast, NREM sleep usually is subdivided into four stages, and is associated with minimal mental activity. Sleep usually begins with an NREM stage, and REM sleep does not occur until 80 minutes or longer thereafter. NREM and REM sleep then alternate through the night with an approximately 90 minute cycle. (Carskadon, Dement 2005) A normal adult hypnogram is shown in Figure 1.1.





NREM sleep can be called orthodox sleep, synchronized sleep or quiet sleep (infants). Stages 1 and 2 of NREM sleep are light sleep. Stages 3 and 4 are deep sleep, slow-wave sleep and Delta sleep. REM sleep can be called paradoxical sleep, desynchronised sleep or active sleep (infants).

The majority (60%) of the adult population in the UK obtain 7-8 hours sleep a night, but some (~8%) sleep less than 5 hours per day and few (2%) sleep more than 10 hours per day. (Groeger, Zijlstra et al. 2004) Loss of NREM sleep in stages 3 and 4 particularly, probably causes more daytime sleepiness than loss of REM sleep. (Shneerson 2005)

Most studies of the function of sleep are based upon sleep deprivation, which show that the long term consequences of inadequate sleep are severely reduced performance, bizarre behaviour, and (in animal experiments) eventual death. (Shneerson 2005, Rechtschaffen, Bergmann et al. 1989) Research into sleep restriction in humans found that sleeping 6 hours or less per night produced cognitive performance deficits equivalent to up to 2 nights of total sleep deprivation. (Van Dongen, Maislin et al. 2003)

Sleep may have a function in wound healing as this, and the immune response, was impaired in sleep-deprived rats. (Gumustekin, Seven et al. 2004, Zager, Andersen et al. 2007) Sleep may also have an effect on anabolic activity and memory processing. (Turner, Drummond et al. 2007) There are beliefs that sleep has a function in preservation and protection, and that dreaming is an important process, but this is based on subjective opinion rather than objective data. Despite the lack of outcomes from sleep research into the reasons why we sleep, we know that people need to sleep in order to function successfully. (Shneerson 2005)

1.2 Snoring

Sleep apnoea and snoring are often confused; snoring is simply the abnormal noise made whilst sleeping, whereas sleep apnoea is a disorder where the individual commonly snores, but also has cessation of breathing.

1.2.1 Snoring overview

Snoring is defined by the International Classification of Sleep Disorders as "Loud upper airway breathing sounds in sleep, without episodes of apnea or hypoventilation". (Thorpy 1990, revised 1997 and 2005, Guilleminault, Stoohs et al. 1991a). It is an inspiratory noise caused by the vibration of the soft tissues of the pharynx, soft palate, and sometimes the uvula, although it is recognised that

there can be expiratory noises also. It has a distinct sound unlike that of other respiratory sounds, such as wheezes and coughs. (Perez-Padilla, Slawinski et al. 1993)

The social disturbance caused by the snorer can result in marital disharmony. In a Scottish study it was found that 85% of snorers were sleeping in a separate room from their partner due to their snoring noise. (Armstrong, Wallace et al. 1999) According to the Guinness Book of World Records, the loudest recorded snore measured 93 decibels in 1993 by Kare Walkert, equivalent to the sound of a lawnmower or chain-saw. (Guinness World Records 1994)

Snoring is more common in males than females, and in overweight people of both sexes. Its prevalence rises markedly after the age of 40 yrs, with 63% of males and 44 % of females being habitual snorers.(Lugaresi, Cirignotta et al. 1980) In the UK, a telephone questionnaire study of 4972 people aged between 15 and 100 years old, found the prevalence of regular snoring to be 40%. (Ohayon, Guilleminault et al. 1997)

1.2.2 Examination of snorers

Uncomplicated snorers (snorers who do not have sleep apnoea) make up the majority of the patients that dentists will see for construction of oral appliances. However, as many snorers are unaware of the extent of their snoring (Hoffstein, Mateika et al. 1994) it would seem appropriate to ask the patient's bed partner about the problem. This presents a challenge, as many patients will attend either without their bed partner or they may live alone. In addition, there is variability in snoring intensity and frequency from night to night. Comparison between self-reported snoring and objective measurement reveals that snorers cannot reliably assess their own snoring level. A study where a sleep technician and a snorer both evaluated the snoring noise following a recording of the previous night's polysomnography, revealed a poor correlation.(Hoffstein, Mateika et al. 1994)

In an examination of a chronic snorer, it is good practice to ask the bed partner questions on the duration of snoring, loudness, degree of social disruption it has caused, if the sleep position has an effect and if there are any signs of cessation of breathing whilst sleeping. The most common risk factors for snoring are

patients who are male, obese, smokers, drink alcohol, and those who take tranquilizers or muscle relaxants. (Hoffstein 1996b) If a patient has recent awareness of snoring, analysis of the onset of snoring and possible associated risk factors is recommended.

An examination of the nasal passages for signs of obstruction, rhinitis, sinusitis or allergies is also considered advisable. (Hoffstein 1996b) Sleep nasendoscopy may be carried out to determine the site of vibration, however the results in this sedative-induced sleep may not accurately reflect natural sleep. (Agrawal, Stone et al. 2002) The use of overnight polysomnography for patients with only snoring as a symptom and with no signs of obesity, hypertension, observed apnoeas, or daytime dysfunction is not cost effective, as most would have a normal sleep study. (Hoffstein 1996b)

1.2.3 Clinical significance of snoring

Many studies show an association between sleep apnoea and impaired general health (Wright, Johns et al. 1997, Redline, Strohl 1998), but fewer studies have compared uncomplicated snoring and health. (Hoffstein 1996a) In addition to the obvious social problems with snoring, it has been associated with vascular disease, and other conditions such as, daytime dysfunction, asthma and hearing loss. There are contradictory results from the few studies and the current thinking is snoring alone has no implications on systemic health. (Guilleminault, Stoohs et al. 1991b, Fitzpatrick, Martin et al. 1993, Lu, Peat et al. 2003, Prazic 1973, Hoffstein, Haight et al. 1999, Sardesai, Tan et al. 2003)The main problems with the studies that found an association were the lack of standardised assessments of individuals and the presence of confounding factors, mainly obesity.

1.2.4 Treatment of snoring

If a patient has simple snoring, with no social implications, they may be managed by lifestyle advice and made aware of the signs and risk factors for sleep apnoea. If the patient has daytime dysfunction due to un-refreshing sleep or social issues due to the snoring, the management is similar to that of sleep apnoea. The first step is usually lifestyle advice, then possibly nasal medication or more commonly oral appliance treatment, followed by continuous positive airway pressure (CPAP) and, finally, surgery may be considered. (Hoffstein

1996b, Kushida, Morgenthaler et al. 2006, Hassid, Afrapoli et al. 2002, Littlefield, Mair 1999, Nakano, Ikeda et al. 2003)

All patients, particularly if obese, should be advised to lose weight. (Dixon, Schachter et al. 2001) Patients should be advised to limit alcohol intake before sleep. (Kara, Zencir et al. 2005) and adopt a lateral sleeping position. A retrospective study has shown that lateral sleeping positions decrease snoring in patients without sleep apnoea. (Nakano, Ikeda et al. 2003)

Nasal congestion and increased airway resistance can be related to snoring.(Young, Finn et al. 2001) Nasal decongestants, lubricants and nasal steroids have been used in patients with nasal symptoms; however there is little evidence that these are successful. (Kiely, Nolan et al. 2004) Nasal dilators are no better than placebos and controls in randomised clinical trials. (Djupesland, Skatvedt et al. 2001)

CPAP has been shown to stop snoring, with a significant reduction in the mean number of snoring episodes per night from 1,015 to 23. (Berry, Block 1984) However, compliance with CPAP is the major problem with its use as it is estimated that only 50-60% of patients will comply. (Kribbs, Pack et al. 1993, McArdle, Devereux et al. 1999, Janson, Noges et al. 2000) Compliance in snorers without sleep apnoea, measured by an Apnoea Hypopnoea Index (AHI) <5, was poor with only 11 out of 118 patients accepting it. Also, those 11 patients used it for only 2.8 +/- 1.5 h per night over six months. (Rauscher, Formanek et al. 1995)

Uvulopalatopharyngoplasty was recommended for snoring after it was first used to treat sleep apnoea. (Fujita 1984) A tonsillectomy, followed by a partial removal of the soft palate, uvula, and pharyngeal arches is carried out under general anaesthetic. (Littlefield, Mair 1999) The long term success rates ranged from 45% - 53% and patient satisfaction was generally poor. (Hassid, Afrapoli et al. 2002, Hicklin, Tostevin et al. 2000)

For snoring, soft palate implants can be used. This is a procedure, carried out under local anaesthetic, in which a hollow introducer needle containing the implant is used to pierce the soft palate close to the junction with the hard

palate, into the muscle. The needle is then withdrawn, leaving the implant in position. The aim of the procedure is to stiffen the soft palate over subsequent weeks as a result of fibrosis. The evidence for these implants is limited to small case series and therefore a recent NICE guideline recommended further research before widespread clinical use. (National Institute for Health and Clinical Excellence (NICE) 2007b)

The current evidence indicates that oral appliances are suitable for patients with snoring, mild-moderate sleep apnoea or where CPAP or surgery has failed. (Kushida, Morgenthaler et al. 2006, Scottish Intercollegiate Guidelines Network 2003)

1.3 Obstructive sleep apnoea-hypopnoea syndrome (OSAHS)

1.3.1 Overview of OSAHS

The major health risk associated with snoring is OSAHS and it is important that dentists are aware of this syndrome, particularly its pathogenesis and treatment. Dentists will treat patients who suffer from OSAHS, and increasingly are asked to provide oral appliances for these patients.

OSAHS is characterised by abnormal breathing during sleep and this causes recurrent arousals, sleep fragmentation, and nocturnal hypoxaemia. The syndrome includes daytime sleepiness, impaired vigilance and cognitive functioning, mood and personality changes, and reduced quality of life. (Gastaut, Tassarini et al. 1965, Bassari, Guilleminault 2000)

OSAHS has also been associated with impaired relationships between spouses and partners, decreased alertness and an increased risk of accidents whilst driving. (Cartwright, Knight 1987, Horne, Reyner 1995, Maycock 1996, Teran-Santos, Jimenez-Gomez et al. 1999, George, Smiley 1999) There is an increased incidence of cardiovascular disease proven during a 7 year follow up period in previously healthy middle aged men with incompletely treated obstructive sleep apnoea. (Peker, Hedner et al. 2002)

The sleep deprivation caused by OSAHS has significant effects. If children are sleep deprived, they may exhibit hyperactive behaviour and perform worse at school. Adults may suffer from decreased academic and occupational performance. (Landrigan, Rothschild et al. 2004, Lockley, Cronin et al. 2004) It is likely that more than 100,000 motor vehicle accidents annually in the United States are caused by driving while drowsy. In the UK, research has shown that heavy-goods vehicle drivers are more liable to have accidents if they have signs of sleep apnoea. (Maycock 1997) A systematic review of motor vehicle crash risk in persons with sleep apnoea demonstrated that people suffering from sleep apnoea have a 2-3 times increased risk of a motor vehicle accident. The majority of the studies are on men, so the same figure cannot necessarily be applied to women. (Ellen, Marshall et al. 2006)A review of major disasters, including the "Challenger Disaster", were officially attributed to sleepiness-related impaired judgement in the workplace. (Moss, Sills 1981, United States. Presidential Commission on the Space Shuttle Challenger Accident 1986, National Commission on Sleep Disorders Research 1992)

In the late 19th century, there were clinical descriptions of cases of obesity with extreme excessive sleepiness. (Peretz 2003) These were similar to the description of the fat boy in the Pickwick Papers (Dickens 1835). This led to the use of the term "Pickwickian syndrome" to describe the combination of obesity and marked excessive sleepiness. However, the meaning of the term Pickwickian syndrome became more specific and was restricted to those obese individuals who also had hypoventilation during wakefulness. (Burwell, Robin et al. 1956) Further studies of individuals with Pickwickian symptoms revealed that they had nocturnal cessation of respiration (apnoea). This was found to be due to obstruction of the upper airway and thus OSAHS was first recognised. (Gastaut, Tassarini et al. 1965)

Cessation of breathing, or apnoea, is defined as the absence of airflow at the nose and mouth for at least 10 seconds, and hypopnoea is a major reduction (> 50%) in airflow, also for at least 10 seconds. Apnoeas may be "central", in which there is cessation of inspiratory drive, or "obstructive", in which inspiratory efforts continue but are ineffective because of upper airway obstruction.

Apnoeas, hypopnoeas, or increased upper airways resistance all result in a brief awakening from sleep caused by the increased respiratory effort, sometimes termed "arousals". (Kimoff, Cheong et al. 1994) This arousal restores upper airway dilating muscle tone and the patient gasps, takes a few deep breaths, and falls back to sleep, at which point the upper airway dilating muscles relax again and the cycle starts off once more. These episodes of upper airway narrowing, terminated by arousal, may recur many hundred times in a night; and the recurrent sleep disruption accounts for the daytime symptoms and clinical features of the condition. (Douglas, Polo 1994) Essentially the airway narrowing leads to increased inspiratory effort, which leads to an arousal (brief awakening).

Of interest was Gould's work reporting that hypopnoeas can have the same consequences as apnoeas. (Gould, Whyte et al. 1988)

1.3.2 Epidemiology of OSAHS

The epidemiology of OSAHS has been examined in large cohort studies on middle-aged adults in the USA and Australia. (Young, Palta et al. 1993, Bearpark, Elliott et al. 1995, Bixler, Vgontzas et al. 1998, Bixler, Vgontzas et al. 2001) The studies give similar estimates of the prevalence of the disorder at different degrees of severity. For mild OSAHS the prevalence ranges from 17-25.9%, moderate OSAHS ranges from 3.1-9.1%, and severe OSAHS ranges from 3.1-4%. Prevalence in the middle aged workforce is higher in men (4%) than women (2%), but the prevalence in women can increase after menopause. (Young, Palta et al. 1993) The peak prevalence is in men between 40-65 years old (4.7%). (Young, Palta et al. 1993, Bixler, Vgontzas et al. 1998) OSAHS may increase with age, with 62% of people aged 65 and over, having a respiratory disturbance index (RDI) of 10 or more. (Ancoli-Israel, Kripke et al. 1991)

Sleep apnoea is responsible for the majority of referrals to sleep clinics, with one study showing that 67.8% of individuals referred to a sleep centre had a primary diagnosis of sleep apnoea. (Punjabi, Welch et al. 2000)

1.3.3 Risk Factors for OSAHS

The strongest risk factors for OSAHS are obesity and age greater than 65 years. (Bloom, Kaltenborn et al. 1988, Phillips, Cook et al. 1989, Rajala, Partinen et al. 1991, Levinson, McGarvey et al. 1993, Grunstein, Wilcox et al. 1993, Dealberto, Ferber et al. 1994, Strohl, Redline 1996) The body mass index {BMI = (weight in kg)/(height in m²)}is commonly used to quantify obesity and a BMI of more than 25kg/m2 has been shown to have a sensitivity of 93% and a specificity of 74% for OSAHS. (Grunstein, Wilcox et al. 1993) Men who are obese tend to have fat deposits predominantly in the neck and abdomen, in contrast to women, where fat deposition is mainly on the hips and legs. The former distribution may be related to OSAHS, due to a narrowing of the upper airway, and could explain the greater prevalence in males. (Millman, Carlisle et al. 1995, Legato 1997) The male to female ratio of patients with OSAHS in community based studies is 2-3:1, whereas the ratio for patients attending a clinic is 10-90:1. (Strohl, Redline 1996)The risk of OSAHS for women increases with obesity and postmenopausal status.

Young et al. reviewed the risk factors for OSAHS and found that in the middleaged (30-60 years old) population, obesity was the main factor. (Young, Palta et al. 1993, Young, Skatrud et al. 2004) Obesity increases the rate of progression of the disease and this is accelerated by further weight gain. (Peppard, Young et al. 2000) In the elderly, this may not be as closely associated as screening for obesity does not identify sleep apnoea in elderly people. Indeed there is a need for further research into the risk factors for OSAHS in the elderly. (Young, Shahar et al. 2002)

There may be a genetic component to sleep apnoea, and studies in a Scottish population provided evidence of a familial component to OSAHS, even with obesity excluded as a factor. (Mathur, Douglas 1995) There is also evidence that obesity itself can be familial. (Stunkard, Sorensen et al. 1986)

Some studies have found that neck circumference, especially when adjusted for height, is a good prospective indicator for OSAHS in adults, with values less than 37 cm and greater than 48 cm being strong predictors for low and high risk respectively. (Stradling, Crosby 1990, Davies, Stradling 1990, Stradling, Crosby

1991, Davies, Ali et al. 1992, Hoffstein, Mateika 1992) In children, the major risk factor for OSAHS is adenoidal-tonsillar hypertrophy. (Marcus 2001)

Racial origin may be a factor, with African Americans, Mexican Americans, Pacific Islanders, and East Asians having an increased incidence of OSAHS. (Schmidt-Nowara, Coultas et al. 1990, Redline, Kump et al. 1994, Li, Kushida et al. 2000) Several studies have shown that sleep disordered breathing is exacerbated by alcohol ingestion, especially around bedtime. (Taasan, Block et al. 1981, Scrima, Broudy et al. 1982, Krol, Knuth et al. 1984) Alcohol reduces the activity of the genioglossus muscle and can therefore predispose to upper airway collapse and apnoeas. (Krol, Knuth et al. 1984) It is not clear from the literature how much alcohol is required to reduce the activity of the muscles of the tongue and soft palate which are the main structures relevant to OSAHS.

OSAHS may be exacerbated by sedatives, sleep deprivation, and a supine posture. (Mendelson, Garnett et al. 1981, Dolly, Block 1982, Roth, Roehrs et al. 1985) Respiratory allergies and nasal congestion may also increase OSAHS.

In addition, disorders that impair sensory function and delay adjustment to abnormal airway narrowing (such as type 1 diabetes, chronic uraemia, dysautonomia) can cause and even worsen OSAHS. (Guilleminault, Mondini et al. 1984, Mondini, Guilleminault 1985, Resnick, Redline et al. 2003)

Of particular interest to dentists is the association between a number of craniofacial features and an increased risk of OSAHS. Jamieson et al (1986) investigated cephalometric values in 155 patients with sleep apnoea and compared them to 41 normal control patients. (Jamieson, Guilleminault et al. 1986) They found a number of characteristics in patients with OSAHS including: retro position of the mandible, an acute nasion-sella-basion angle, and a displacement of the hyoid bone to a lower position than expected. These combined changes reduced the space occupied by soft tissues anchored on the skull and mandible, and the length of the soft palate was increased. (Jamieson, Guilleminault et al. 1986) This investigation led to numerous studies which, in general, have found that the following characteristics are more prevalent in patients with OSAHS:

- a high and narrow hard palate,
- an elongated soft palate,
- retrognathia with associated increased overjet. (Seto, Gotsopoulos et al. 2001)

A recent case control study corroborated the above findings with statistically significant differences between OSAHS patients and case matched controls for: maxillary and mandibular reduction in length, a significant (3.1mm) reduction in inter-maxillary space, a narrower nasopharyngeal airway and increased tongue size, and soft palate length and thickness. (Johal, Patel et al. 2007)

There are reports in the literature of syndromic patients suffering from OSAHS more than normal individuals. These include patients with Treacher Collins Syndrome and clefts of the lip and palate. (Colmenero, Esteban et al. 1991)

If a patient has a narrowed airway they are more likely to be at risk of OSAHS. It has been shown that patients with OSAHS have narrowed upper airways, even during wakefulness, as revealed by multiple imaging modalities, including computed tomography (CT) and magnetic resonance imaging (MRI). (Ahmed, Schwab 2006) The upper airway is not only smaller in patients with OSAHS but also more collapsible. (Horner, Shea et al. 1989, Gleadhill, Schwartz et al. 1991) The airway narrowing is more commonly found in the retro-palatal and retro-glossal regions of the pharynx. It has also been shown that the volume of upper airway soft tissue structures (tongue, lateral pharyngeal walls, soft palate, and para-pharyngeal fat pads) was significantly greater in patients with OSAHS than in normal subjects, even when other confounding factors were taken into account. (Schwab, Pasirstein et al. 2003, Schwab 2003)

1.3.4 Pathogenesis of OSAHS

Sleep apnoea is a slowly progressive disorder. (Peppard, Young et al. 2000) Most, if not all, apnoeas are caused by collapse of the pharyngeal airway. Pharyngeal patency depends critically on the action of upper airway dilator muscles, which contract during each inspiration to prevent the upper airway being closed by suction. These muscles include the palatal muscles (levator veli, palatoglossus,

tensor veli palatini), supra-hyoid muscles (genioglossus, geniohyoid) infra hyoid muscles (sternohyoid, sternothyroid) and laryngeal muscles (cricothyroid, and posterior cricoarytenoid.) (Lee-Chiong, Sateia et al. 2008) During sleep there is a reduction of activity of the upper airway dilator muscles, as well as a decrease in electromyogram (EMG) activity of genioglossus and tensor palatine, therefore predisposing to collapse. (Tangel, Mezzanotte et al. 1991, Tangel, Mezzanotte et al. 1992, Pack 2006) Muscle tone throughout the body decreases during sleep, with relaxation of the upper airway dilating muscles. In many individuals, this effect results in considerable upper airway narrowing during inspiration, which causes the turbulent flow and vibration of snoring. There are also changes in the upper airway that are likely to be secondary to the vibration produced by snoring and/or the large swings in intraluminal pressure during sleep. (Pack 2006) These include denervation of soft palatal tissue in subjects with OSAHS and an inflammatory cell infiltrate in both the mucosal and muscle layers. (Friberg, Ansved et al. 1998, Boyd, Petrof et al. 2004) This has led to the concept of OSAHS being the progressive snorer's disorder. (Friberg, Ansved et al. 1998)

In some individuals this upper airway narrowing may progress to produce clinically significant airway narrowing or occlusion which causes OSAHS. (Douglas, Polo 1994)

1.3.5 Other causes of excessive daytime sleepiness

The three main causes of excessive daytime sleepiness are insufficient duration of sleep, impaired quality of sleep, or hypersomnia. Sleep deprivation is the most common cause of excessive daytime sleepiness and is usually due to work or social pressures. (Shneerson 2005)

Shift work can significantly disrupt sleep-wake patterns. Most individuals who present with this will be advised on sleep hygiene. (Shneerson 2005) Sleep hygiene can be defined as "all behavioural and environmental factors that precede sleep and may interfere with sleep."(van der Heijden, Smits et al. 2006) The main issues involved are sleep scheduling, use of stimulants, stimulating or upsetting activities too close to bedtime and an uncomfortable sleeping environment.

The prevalence of excessive daytime somnolence is difficult to quantify due to the different criteria used and populations studied. The largest objective study included 740 day workers in Israel. The Epworth scale was used to assess sleepiness and it was found that 23% of the respondents had a score greater than 10, indicating excessive sleepiness. (Melamed, Oksenberg 2002) The two main predictive factors associated with excessive sleepiness are full time employment and being single. Excessive sleepiness has also been correlated with severe depression and snoring episodes on more than 3 nights per week. (Hublin, Kaprio et al. 1996)

The Epworth Sleepiness Scale (ESS) is a self-administered questionnaire, which reflects the person's general level of daytime sleepiness. (Johns 1991) It was designed to measure and quantify sleep inclination rather than fatigue, as manifested by the tendency to fall asleep in a variety of conditions. The maximum score is 24. The higher the score, the sleepier the patient, generally with scores up to 6-7 considered normal, 8-12 mild sleepiness, 13-17 moderate sleepiness, and 18 and above severe sleepiness. It is considered to be independent of short-term variations in sleepiness and the time of the day, and is consistent from day to day. It has been shown to be consistently higher in conditions associated with daytime somnolence (such as sleep apnoea, narcolepsy, idiopathic hypersomnolence), and normal in other sleep disturbances such as insomnia. However, again it reflects subjective assessment of sleepiness, without objective documentation. The ESS results correlate reasonably well with patient's self ratings for overall sleepiness, but not well with Multiple Sleep Latency Test (MSLT) results. (Johns 1991, Johns 1994, Chervin, Aldrich et al. 1997, Chervin, Aldrich 1999) For objective measurement of sleepiness, the Multiple Sleep Latency Test has been developed, with the working hypothesis that the drowsier the person, the more rapidly he or she should fall asleep under favourable conditions. (Lavie, Pillar et al. 2002)

Impaired quality of sleep is the failure to sustain sleep or a stage of sleep because of frequent transitions to a lighter stage of sleep or to wakefulness. (Shneerson 2005) This can be due to external factors such as a noisy, light or uncomfortable temperature area in which to sleep. It can also be due to medical disorders including OSAHS, a motor disorder during sleep, gastro-oesophageal reflux, asthma, nocturnal angina, pain due to arthritis, neurological disorders

and drugs. Stimulant drugs such as caffeine and amphetamines can cause arousals, tricyclic antidepressants may increase the frequency of limb movements, dopamine agonists can cause awakenings due to vivid dreams and alcohol and short acting hypnotics cause rebound insomnia at the end of the night. (Shneerson 2005)

Other causes of excessive daytime sleepiness are circadian rhythm disorders, neurological disorders, systemic disorders and psychiatric disorders.

1.3.6 Diagnosis of OSAHS

Obstructive sleep apnoea is the most prevalent sleep disorder seen in diagnostic sleep laboratories world-wide, accounting for some 75-80% of the diagnoses. Central sleep apnoea is considerably less prevalent, except for specific patient populations, such as patients with chronic heart failure or patients with neurological disorders. Telephone based research in the UK of non-institutionalised people found that sleep disordered breathing was under-diagnosed. (Ohayon, Guilleminault et al. 1997)

The diagnosis of OSAHS is ideally made when a person with daytime symptoms has significant sleep disordered breathing as shown by polysomnography (study of sleep state, breathing, and oxygenation). Subjective clinical impressions of OSAHS tend to have inadequate sensitivity and specificity. (Viner, Szalai et al. 1991, Hoffstein, Szalai 1993)Nocturnal pulse oximetry is widely used to screen for OSAHS, but polysomnography is the gold standard. The criteria for the diagnosis of significant sleep disordered breathing have not been rigorously assessed, but they have been set by a combination of consensus and convention. (Ross, Sheinhait et al. 2000) Diagnostic criteria for OSAHS have variable sensitivity and specificity. For example, an apnoea/hypopnoea index (AHI) of less than five is considered normal; however, people with upper airway resistance syndrome may have an AHI below five episodes per hour, and many healthy elderly people have an AHI greater than five. (National Commission on Sleep Disorders Research 1992, Guilleminault, Stoohs et al. 1993) In an effort to achieve international consensus, criteria have been proposed by The Report of an American Academy of Sleep Medicine Task Force (1999). (American Academy of Sleep Medicine Task Force 1999) and these criteria are becoming more widely used.

The severity of OSAHS can be classified according to two factors: daytime sleepiness and AHI. Severe OSAHS is defined as severe sleep disordered breathing (AHI > 35 episodes per hour) plus symptoms of excessive daytime sleepiness (such as Epworth Sleepiness Scale > 10.) In Scotland, the SIGN guidelines classify OSAHS by AHI: 5-14/hr is mild, 15-30/hr is moderate, and >30/hr is severe. (Scottish Intercollegiate Guidelines Network 2003) It is emphasised that these arbitrary units act as a guide only and each case must be evaluated on its own merits taking into account signs and symptoms as well as other related factors such as age. (Scottish Intercollegiate Guidelines Network 2003)

The main features of OSAHS are excessive daytime sleepiness, impaired concentration, snoring, un-refreshing sleep, choking episodes during sleep, witnessed apnoeas, restless sleep, irritability/personality change, nocturia, and decreased libido. (Scottish Intercollegiate Guidelines Network 2003) Patients who have clinically significant sleep apnoea classically have an AHI in the moderate range, excessive daytime sleepiness and at least two other symptoms, some of which may need to be elicited from the partner of the patient. Certain ENT problems can cause some of the symptoms of OSAHS, and if this is suspected, early evaluation of these is recommended, especially if the patient's symptoms are of rapid onset.

Subjective assessment of OSAHS involves questioning both the patient and patient's partner to evaluate their symptoms. Several questionnaires have been proposed to evaluate the likelihood of a patient suffering from OSAHS with varying accuracy. (Stradling, Crosby 1991, Partinen, Telakivi et al. 1988, Douglass, Bornstein et al. 1994, Sweere, Kerkhof et al. 1998, Netzer, Stoohs et al. 1999, Hersberger, Renggli et al. 2006)

Other questionnaires are used to assess sleepiness, the two main ones are the Stanford Sleepiness Scale (SSS) and the Epworth Sleepiness Scale (ESS). (Johns 1991, Johns 1994, Hoddes, Zarcone et al. 1973, Richardson, Carskadon et al. 1978) The Epworth is the most commonly used questionnaire in UK sleep clinics and for research purposes. The Stanford Sleepiness Scale represents the sleepiness at a given moment, and changes on a moment-by-moment basis according to the circumstances. The scale ranges between 1 and 7, and participants are asked to record on the scale the statement that best describes

their state of sleepiness. The SSS is good for monitoring an individual patient's progress, but is less suitable for comparing between patients.

There are also some home monitoring systems suggested for the diagnosis of OSAHS. Ambulatory devices have initially included oximetry alone, but other methods of home monitoring, including a variety of recorded channels such as breathing effort and airflow, body movements and peripheral arterial tone, are also used. Some centres use split night studies, with CPAP titration for the second half of the night, the authors state these can be beneficial in some cases. (McArdle, Grove et al. 2000) Studies have also reported that limited sleep studies may be useful to reduce costs and technician's time. (Johnson, Carter et al. 2004)

1.3.7 Sleep apnoea – screening

It is estimated that 93% of women and 82% of men with moderate to severe sleep apnoea are undiagnosed and there is recognition that sleep services cannot, at present, arrange sleep studies for each patient, therefore there is a justifiable need for a valid screening tool. (Scottish Intercollegiate Guidelines Network 2003, Young, Evans et al. 1997, Harding 2001) In addition, elderly or infirm patients may find overnight studies in a hospital environment distressing and the equipment uncomfortable.

Some studies have found Epworth sleep scores to be higher in patients with sleep apnoea (mean 13.2) than chronic snorers (mean 7.5.) (Chung 2000/11) Others have found no correlation between Epworth scores and AHI. (Osman, Osborne et al. 1999) Therefore excessive sleepiness is very sensitive for sleep apnoea but not specific, as sleep deprivation from other causes can also give high Epworth scores.

One clinical study found a statistically significant correlation between the modified Mallampati score and the Respiratory Disturbance Index (RDI). The Mallampati score was devised by anaesthetists to estimate the size of the upper airway and therefore the ease of intubation. (Mallampati, Gatt et al. 1985a) The RDI is similar to the AHI, however, it also includes respiratory events which are not apnoeas or hypopnoeas but do disrupt sleep. The same group also found that tonsil size and BMI were statistically significantly correlated with RDI.

(Friedman, Tanyeri et al. 1999) Another study found that the Mallampati score was only statistically significantly associated with OSAHS if the patient also has nasal obstruction. (Liistro, Rombaux et al. 2003)

As was previously mentioned a BMI of at least 25kg/m² has been shown to have a sensitivity of 93% and a specificity of 74% for OSAHS. (Grunstein, Wilcox et al. 1993) Although clinicians can use questionnaires, BMI, and neck circumference to help distinguish if a patient has OSAHS, the evidence suggests that clinical impressions alone are not sufficient for the screening of OSAHS. (Viner, Szalai et al. 1991)

Different surveys and formulae have been used to distinguish patients with sleep apnoea from either patients with another sleep disorder or normal patients. The results range from 40% to 99% sensitivity and 28% to 100% specificity. (Viner, Szalai et al. 1991, Netzer, Stoohs et al. 1999, Maislin, Pack et al. 1995, Kushida, Efron et al. 1997, Kirby, Eng et al. 1999, Dixon, Schachter et al. 2003) Recent reviews of the literature highlight the need for further validation of these methods before widespread use is implemented. (Pang, Terris 2006)

The Kushida Index is one of the above-mentioned screening methods and is potentially of interest to dentists. (Kushida, Efron et al. 1997) This index was not the first to attempt to predict whether a patient has OSAHS, but it was the first to take into account the craniofacial characteristics which are related to OSAHS. (Rojewski, Schuller et al. 1982, Rivlin, Hoffstein et al. 1984, Lowe, Santamaria et al. 1986, Ferguson, Ono et al. 1995) The test was formulated on 30 subjects, 15 with a diagnosis of OSAHS and 15 without. In Kushida's study, patient's BMI, neck circumference, and some oral cavity measurements were used. Oral cavity measurements included palatal height, maxillary inter-molar distance, mandibular inter-molar distance, and overjet in millimetres.

Kushida's equation was established as follows:

Equation 1- Kushida Index {P + (Mx - Mn) + 3 x OJ} + 3 x [Max (BMI - 25,0)] x (NC / BMI)

P is palatal height (in millimetres), or the distance from the dorsum of the tongue at the median lingual sulcus to the highest point of the palate, measured with the tongue in a relaxed position and the maxillary and mandibular incisor tips subtending an angle of 20 degrees from the mandibular condyle.

Mx is the maxillary inter-molar distance (in millimetres) between the mesial surfaces of the crowns of the maxillary second molars.

Mn is the mandibular inter-molar distance (in millimetres) between the mesial surfaces of the crowns of the mandibular second molars.

OJ is the overjet (in millimetres), or the horizontal overlap of the crowns of the maxillary and mandibular right central incisors.

BMI is the body mass index (in kg/m^2)

NC is neck circumference (in centimetres) measured at the level of the cricothyroid membrane.

The area of the formula in bold reflects the contribution of craniofacial dysmorphism, as measured from the oral cavity, to the prediction of OSAHS. The normal area reflects the contribution of obesity, as measured by BMI and neck circumference, to the prediction of OSAHS. The fraction NC \div BMI was selected to scale neck circumference relative to body size. The segment of the model enclosed within square brackets is limited to the larger of the two quantities: BMI -25, or zero. For example, if BMI is 25 or less, then [Max (BMI -25, 0)] is zero: That is, if BMI is 23, then (23 -25) = -2 and, because 0 is greater than -2, the maximum is zero. Therefore, if a patient is not obese (BMI \leq 25), the contribution of the second part of the model to the final index value is nil; the final index value reflects only the degree of craniofacial dysmorphism.

Kushida et al (1997) conducted a prospective study of 423 patients, 300 of whom underwent polysomnography. Using their cut off value of 70 for the Kushida index, they found the means (\pm SD) for the OSAHS and non-OSAHS groups were 95.3 \pm 21.2 and 61.6 \pm 6.2, respectively. The sensitivity (248 of 254) was 97.6% (95% CI, 95% to 98.9%), the specificity (46 of 46) was 100% (CI, 92% to 100%), the

positive predictive value (248 of 248) was 100% (CI, 98.5% to 100%), and the negative predictive value (46 of 52) was 88.5% (CI, 77% to 96%). The test also had good inter-examiner reliability of 99.2% and the estimated degree of error was a maximum of 4%.

This morphometric model missed cases of OSAS in only six patients; that is, it gave six false-negative results. However, the mean calculated result was 67.3 ± 3.3 for these six patients, which was close to the separation value of 70. In addition, the mean RDI for the six patients was low at 7.4 ± 3.1 (range: 5.3 to 13.5). Thus, Kushida et al advised that values below but near the cut-off of 70 (for example, between 65 and 70) should be interpreted with caution.

The criteria for a diagnosis of OSAHS used by Kushida in 1997 was excessive sleepiness measured by Epworth >10, excessive daytime sleepiness, witnessed apnoeas and a RDI of 5 or more. As previously mentioned, current guidelines would classify a patient with an RDI of less than 10 as normal. (Scottish Intercollegiate Guidelines Network 2003)

In 2004, Soares et al evaluated the Kushida index to assess its clinical acceptability and whether it was possible to distinguish OSAHS severity. (Soares, de Azeredo Bittencourt et al. 2006) They recruited 80 patients, but there was no randomisation in the selection process, instead they selected 20 mild OSAHS, 20 with moderate OSAHS, 20 with severe OSAHS and 20 normal patients. All patients had undergone polysomnography. There was a higher percentage of men than women (approximately 2:1) which would account for more patients with OSAHS. They concluded that it was not possible to classify patients with OSAHS according to severity. However, this conclusion is not valid as the cut off value of 70 suggested by Kushida et al would not have identified the mean value for those patients with mild, moderate or severe OSAHS.

One other group has used the Kushida Index. (Jung, Cho et al. 2004) They compared it to acoustic pharyngometry for the evaluation of the upper airway in patients with and without OSAHS. This group reported that the Kushida Index had a sensitivity of 89% (48 of 54) and a specificity of 94% (15 of 16) for the diagnosis of OSAHS. The authors reported that acoustic pharyngometry had a better sensitivity and specificity in their study (93% and 94%) than the Kushida

Index (89% and 94%). They also used the cut off value of 70 for the Kushida Index. This study had a significant difference in the number of subjects recruited without OSHAS (16) in comparison to those with OSAHS (54). In addition, there was no evidence of a power calculation to determine sample size or of blinding of the assessors.

It is apparent that further analysis of the Kushida Index is required before it could be recommended as a useful clinical screening tool.

1.3.8 Treatment of sleep apnoea

There are various approaches to the treatment of OSAHS and these can be categorised into behavioural, mechanical, pharmacological, and surgical.

Behaviour change is difficult to achieve but can be very effective. Weight loss can be curative and even modest weight loss (10%) can relieve mild sleep apnoea. (Peppard, Young et al. 2000, Schwartz, Gold et al. 1991) All obese patients should be counselled about weight loss, but unfortunately this takes time and compliance may be low.

Smokers have a higher incidence of respiratory problems than non-smokers and nicotine disturbs sleep patterns, so smoking cessation advice should be given to all smokers. (Phillips, Danner 1995)

Airway tone can be reduced if patients take muscle relaxants, including alcohol and sedatives. This reduction in airway tone can prolong apnoeas and increase the arousal threshold. Patients should be advised of this and encouraged to reduce alcohol consumption. (Young, Skatrud et al. 2004)

Patients of a normal weight and with mild disease may benefit from lying on their side rather than in a supine position. Studies have shown that upper airway dimensions, airflow resistance and airway collapsibility, all deteriorate in the supine posture, and have shown that change in sleeping posture is effective for the treatment of mild sleep apnoea. (Oksenberg, Silverberg 1998)

Continuous positive airway pressure (CPAP) is a mechanical therapy developed by Sullivan et al (1981), pressure typically being applied in the range of 5-15cm

 H_2O through a nasal or oro-nasal mask. (Figure 1.2) CPAP pneumatically splints the entire airway and increases the functional residual capacity, may increase pharyngeal dilator activity, and reduces after-load on the heart. (Patel, White et al. 2003) During sleep, the tongue and soft palate lie against the posterior oropharyngeal wall and CPAP prevents this, keeping the airway open. (Strohl, Redline 1986)



Figure 1.2 CPAP Mask

In 2002 the benefit of CPAP in patients with hypertension was shown in a randomised trial. (Pepperell, Ramdassingh-Dow et al. 2002) In that study, 118 OSAHS patients with an average oxygen desaturation index (ODI) of 37 per hour were randomized to either CPAP, or sub-therapeutic CPAP for 4 weeks. The mean ambulatory arterial blood pressure dropped by 2.4mmHg during sleep and 3.4 mmHg whilst awake in the CPAP group, and an increase of 0.8mmHg for the control group. The most severe OSAHS patient had the largest decrease in blood pressure. The significance of this finding may be seen when it is pointed out that small blood pressure decreases, in the region of 5mmHg, have been shown in a prospective long term study of 420,000 people to lessen the incidence of stroke by 34% and coronary heart disease by 21%. (MacMahon, Peto et al. 1990)

After a diagnosis of sleep apnoea has been made during the first half of a sleep study, the titration of the CPAP air flow can be carried out in the second half. Auto-titration machines are now available which respond to the vibration of

upper airway tissues or measure airflow and modify air pressure appropriately. (Littner, Hirshkowitz et al. 2002, Massie, McArdle et al. 2003)

Compliance with CPAP is the major problem with its use. It is estimated that only 50-60% of patients will use the machine on a regular basis. (Kribbs, Pack et al. 1993, McArdle, Devereux et al. 1999, Janson, Noges et al. 2000)

The adverse effects of CPAP are frequent, with some studies reporting 96% of patients having at least one side effect, although many of these are minor. (Kalan, Kenyon et al. 1999) The side-effects can be due to the nasal mask, to local intra-nasal adverse effects, or to problems due to the noise and bulk of the machine. Major side effects of CPAP are rare (such as significant epistaxis, paranasal sinusitis), but minor side effects (including, rhinitis, nasal bridge sores, discomfort and noise) have been frequently reported. (Kalan, Kenyon et al. 1999, Pepin, Leger et al. 1995) Some patients may suffer from rhinitis and intranasal corticosteroid therapy may improve their sleep apnoea, but not necessarily their sleep quality or snoring. (Kiely, Nolan et al. 2004) A financial disadvantage of CPAP is the high cost of the machine and maintenance. (NHS Quality Improvement Scotland 2008)

The benefits of CPAP are that it can reduce mortality, frequency of automobile accidents, hypertension and other cardiovascular diseases, cognitive impairment, sleepiness, healthcare costs, impaired quality of life, depression and impotence. (Wright, Johns et al. 1997, Peker, Hedner et al. 2002, Pepperell, Ramdassingh-Dow et al. 2002, He, Kryger et al. 1988, Engleman, Martin et al. 1994, Karacan, Karatas 1995, Whittle, Finch et al. 1997, Jenkinson, Davies et al. 1999, Bahammam, Delaive et al. 1999, Hack, Davies et al. 2000, Bardwell, Ancoli-Israel et al. 2001, Means, Lichstein et al. 2003, Becker, Jerrentrup et al. 2003)

Supplemental oxygen improves overall oxygenation during sleep in patients with OSAHS but increases apnoea duration while reducing apnoea frequency only slightly. (Martin, Sanders et al. 1982, Gold, Schwartz et al. 1986) Daytime sleepiness is not reduced. Therefore, in most instances supplemental oxygen alone is not sufficient for treating OSAHS. (Ryan 2005)

A number of surgical procedures have been used in the treatment of OSAHS including: Tracheotomy, Uvulopalatopharyngoplasty (UPPP), Laser-assisted Uvulopalatopharyngoplasty (LAUP), septoplasty, maxillofacial surgery, radiofrequency volumetric tissue reduction (somnoplasty), and recently soft palate implants.

Uvulopalatopharyngoplasty (UPPP) is the most commonly used and researched form of surgical treatment for OSAHS. It involves enlargement of the retropalatal airway by excision of any enlarged tonsils, trimming and reorientation of the posterior and anterior tonsillar pillars, and excision of the uvula and posterior portion of the palate. Sher's review (2002) concluded that UPPP results in a mean decrease of 55% in the AHI and a mean decrease of RDI of 38% and the success rate of UPPP is about 50%. (Sher 2002) Complications include velopharyngeal insufficiency (2%), post-operative bleeding (1%), nasopharyngeal stenosis (1%), voice changes (1%), foreign body sensation (0.2%) and in rare circumstances death can occur. The incidence of complications is difficult to accurately calculate as many studies do not report the complications. (Sher, Schechtman et al. 1996/2)

Dramatic improvements have been reported with surgical weight loss, although on long-term follow-up of patients undergoing gastric reduction surgery, a recurrence of substantial apnoea has been observed in some, despite only minimal weight gain. A systematic review and meta analysis found that following bariatric surgery, OSAHS had resolved in 85.7% of patients. (Buchwald, Avidor et al. 2004)

Soft palate implants for snoring were not recommended for clinical use until further research was carried out, and in a separate NICE guidance document, they are not currently used for sleep apnoea due to inadequate evidence and the serious nature of sleep apnoea. (National Institute for Health and Clinical Excellence (NICE) 2007a)

1.4 Upper Airways resistance syndrome

The term "upper airways resistance syndrome" (UARS) was first introduced in 1992, and applies to people who have impaired respiration during sleep but do not fit the typical diagnosis of OSAHS. (Guilleminault, Stoohs et al. 1992) The patients typically snore, have daytime sleepiness but no clear signs of apnoeas, hypopnoeas, or oxygen desaturations. It is a controversial term, not used by all, and the second edition of the International Classification of Sleep Disorders (ICSD-2) incorporated it under OSAHS as it was felt that the pathophysiology does not differ significantly from that of OSAHS. (Duchna 2006)

1.5 Oral Appliances

Pierre Robin (1902) first published his work on the "monobloc" device for the treatment of glossoptosis, and then later used this type of appliance to reposition the mandible. (Robin 1902, Robin 1934) The first report of the use of surgical mandibular advancement for a sleep disorder was in 1980. (Bear, Priest 1980) This work was taken forward for non-surgical management by using tongue retaining devices. (Cartwright, Samelson 1982)

1.5.1 Oral appliance types and features

Three types of oral appliance can be used for treating snoring and sleep apnoea; these are soft palate lifters, tongue retaining devices, and mandibular advancement appliances.

1.5.2 Soft palate lifters

Soft palate lifters (Figure 1.3) have been used for treating snoring, however due to gagging problems and their ineffectiveness, they are no longer used for sleep disorders. In addition, they could only work if the site of snoring was the soft palate.(Paskow 1987, Wagner, Price 1987, Paskow, Paskow 1993, Marklund, Franklin 1996, Barthlen, Brown et al. 2000) Currently they are only used for patients with soft palate incompetence after referral from a speech therapist. (La Velle, Hardy 1979)



Figure 1.3 Soft Palate Lifter Appliance

1.5.3 Tongue retaining devices

Tongue retaining devices reposition the tongue in an anterior position by securing it with suction in a soft plastic bulb or with a resin depressor that comes into direct contact with the base of the tongue. (Figure 1.4 This was the first type of oral appliance described for treating sleep disorders. In a study of 20 patients, 3 could not tolerate the appliance, but for the remainder there was a reduction in apnoeas. (Cartwright, Samelson 1982) The one credible advantage of these appliances over mandibular advancement appliances is that they can be used for edentulous patients. However, they are unsightly, require nasal breathing, can cause tongue irritation and are less effective than mandibular advancement appliances. (Barthlen, Brown et al. 2000)



Figure 1.4 Tongue Retaining Device.

1.5.4 Mandibular advancement appliances

Mandibular advancement appliances (also called mandibular advancement devices) are now the most widely used oral appliances for sleep disordered breathing. (Figure 1.5)

The mandibular advancement appliances are either a one-piece, or a two-piece design and can be either prefabricated or custom-made (Eckhart 1998) The prefabricated appliances generally are constructed of a thermolabile material which is warmed and moulded by the individual, a so called "boil and bite" appliance. The custom made appliances are generally constructed by a dentist via impression making, jaw registration and then fabrication in a dental laboratory. (Lindman, Bondemark 2001) It has been suggested that the thermolabile preformed appliances could reduce costs and predict success with a custommade appliance. (Schonhofer, Hochban et al. 2000, Maurer, Huber et al. 2007) The suggestions are based only on opinion and a recent randomized controlled cross-over trial has shown that the custom-made appliances are superior to the pre-formed appliances in terms of reduction in snoring and apnoeas. (Vanderveken, Devolder et al. 2008) Also, it is clear that failure with a pre-formed appliance does not mean that failure will occur with a custom made appliance, simply because retention is considerably better in a custom-made device.

The appliances can have partial or full occlusal coverage. They may be constructed using a soft or hard material and some permit jaw movement. It is also possible to provide adjustment of protrusion to provide maximum relief of symptoms with minimal side effects.

In bruxists, it is advised that a flexible two piece design is used to permit lateral movement. (Henke, Frantz et al. 2000, Sjoholm, Lowe et al. 2000)

There is no robust evidence that a two-piece design appliance is better than a one piece designed appliance for the treatment of OSAHS. (George 2001)

There is some debate over the amount of jaw opening provided by the appliance, as too much opening increases the chance of posterior displacement of the tongue and soft palate, although it also may improve upper-airway

36

patency by stretching palatoglossus and the superior pharyngeal constrictor muscles. (George 2001) One randomized controlled crossover study (Pitsis, Darendeliler et al. 2002) compared appliances which provided 4mm and 14mm of jaw opening. Although there was no difference in efficacy in the short term of the study, 78 % of patients preferred the appliance with less increase in vertical dimension.



Figure 1.5 Mandibular Advancement Appliance

The obstruction of the airway in sleep apnoea is most likely due to a combination of abnormal anatomy and abnormal physiology. (Schwab 2003, Strohl 2003) Cephalometric studies on awake patients, in both upright and supine positions, have demonstrated that anterior repositioning of the mandible increases the posterior airway space and sagittal cross sectional area of the pharynx. (Schmidt-Nowara, Meade et al. 1991a, Ishida, Inoue et al. 1998, Liu, Park et al. 2000) Computerised tomography and videoendoscopy studies on awake supine patients have also shown an increase in the pharyngeal cross sectional airway size and velopharynx size when using a mandibular advancement appliance. (Ryan, Love et al. 1999, Gale, Sawyer et al. 2000) Magnetic resonance imaging studies both in the asleep and awake patient in a supine position have shown increased area in the nasopharnyx, oropharynx, and hypopharynx with a mandibular advancement appliance. (Ishida, Inoue et al. 1998, Gao, Zeng et al. 1999)Therefore there is a large body of evidence that has shown that advancing the mandible can enlarge the airway and reduce collapsibility. (Ryan, Love et al. 1999, Gale, Sawyer et al. 2000, Kato, Isono et al. 2000, Hiyama, Tsuiki et al. 2003, Ng, Gotsopoulos et al. 2003, Battagel, Johal et al. 2005, Ng, Qian et al. 2006)

Mandibular advancement appliances are reported to reduce snoring by 73% to 100%. (Schmidt-Nowara, Lowe et al. 1995) It is also clear that these appliances improve snoring according to bed partners and this is probably the most relevant outcome measure. (Bonham, Currier et al. 1988, Cameron, Lyons et al. 1998, Lyons, Cameron et al. 2001) A recent review, which included 18 studies and 529 patients, found that no matter what outcome measure was used, mandibular advancement appliances were successful in reducing snoring. (Hoffstein 2006)

Hoffstein (2006) reviewed the evidence on the efficacy of oral appliances for the treatment of sleep apnoea. He classified success as an AHI less than 10 with the appliance in place. He classified response rates as the percentage of patients in whom the AHI, with the appliance in place, was greater than 10 but less than 50% of the baseline value. Using these definitions, he found that 21% of 1577 patients from 51 studies had a 50% reduction in AHI (response rate) and 54% of 2087 patients from 59 studies had an AHI less than 10 (success rate.) (Hoffstein 2006) Only five randomised, crossover, controlled studies of the efficacy of oral appliances have been reported. (Hoffstein 2006, Mehta, Qian et al. 2001, Johnston, Gleadhill et al. 2002, Gotsopoulos, Chen et al. 2002, Barnes, McEvoy et al. 2004, Naismith, Winter et al. 2005) Four used a control (non active) appliance and one used a drug placebo. In 270 patients with mild to moderate sleep apnoea, the success rate was 50% and response rate was 14%.

A recent Cochrane review highlighted six studies that compared a control appliance which did not advance the mandible to oral appliances which did advance the mandible for the treatment of sleep apnoea. (Johnston, Gleadhill et al. 2002, Gotsopoulos, Chen et al. 2002, Hans, Nelson et al. 1997, Duran, Esnaola et al. 2002, Engleman, McDonald et al. 2002, Blanco, Zamarron et al. 2005, Lim, Lasserson et al. 2006) This review showed that when the results were pooled, a 15.5 point decrease in AHI was observed with the active appliance. (Lim, Lasserson et al. 2006)

The same review reported that CPAP was more effective than oral appliance therapy. Nine studies compared an oral appliance to CPAP. Contacting authors allowed additional data to be obtained for seven of these studies. A 7.97 AHI difference between CPAP and oral appliances in favour of CPAP was observed. (Barnes, McEvoy et al. 2004, Engleman, McDonald et al. 2002, Lim, Lasserson et

al. 2006, Ferguson, Ono et al. 1996, Ferguson, Ono et al. 1997, Olson, Ambrogetti et al. 2002, Tan, L'Estrange et al. 2002, Randerath, Heise et al. 2002)

In Hoffstein's meta-analysis (Hoffstein 2006), 232 patients from seven studies compared CPAP and oral appliances, and found that AHI with an oral appliance remained at 14, whereas AHI with CPAP was 6. However, patients in general preferred the oral appliance to CPAP.

It would be beneficial if clinicians were able to predict who would respond favourably to an oral appliance, yet despite ongoing research there are no robust criteria. As there is a biological plausibility that patients with retroglossal collapse, as opposed to velopharyngeal collapse, would have a greater chance of success with a mandibular advancement appliance it would seem sensible to recommend oral appliances for this group of patients. The only study which has investigated the success of mandibular advancement appliances in both types of patients found that those with retro-glossal collapse benefited more than those with velopharngeal collapse. However, the study only included four patients with retro-glossal collapse and eight with velopharyngeal collapse. (Ng, Qian et al. 2006)

1.5.5 Side effects of oral appliances

The side effects most commonly reported are dry mouth, excessive salivation, discomfort, occlusal changes, headaches and temporomandibular joint discomfort. (Schmidt-Nowara, Meade et al. 1991a, Cameron, Lyons et al. 1998, Clark, Arand et al. 1993, Eveloff, Rosenberg et al. 1994, O'Sullivan, Hillman et al. 1995, Shadaba, Battagel et al. 2000, Fritsch, Iseli et al. 2001, McGown, Makker et al. 2001, Walker-Engstrom, Ringqvist et al. 2003, Marklund, Stenlund et al. 2004, Dort, Hussein 2004)

Occlusal changes involving a 2-4mm reduction in overbite and overjet following use of the appliance have been reported. If data from studies which analysed tooth movement are amalgamated, there are 389 patients with a mean follow up of 39 months that showed a mean overbite reduction from 3.8 to 2.4 mm and a mean overjet reduction from 4.0 to 2.7mm. (Hoffstein 2006, Almeida, Lowe et al. 2006a, Almeida, Lowe et al. 2006b, Marklund 2006)

1.5.6 Compliance with oral appliances

As most patients receive an appliance for mild sleep apnoea or chronic snoring, they may be less motivated to wear the appliance, even if the side effects are minimal, as the main complaint may be from the patient's bed partner. If the bed partner was no longer present, or no longer complained of the snoring, the patient is unlikely to wear the appliance. (Hoffstein 2006)

Compliance with mandibular advancement appliances has been reported to range from 4-76% at the end of one year. (Jauhar, Lyons et al. 2008a) Hoffstein (2006), who reviewed 21 studies with 3107 patients using mandibular advancement appliances, with longer term follow up of 33 months found compliance rates of 56-68%. (Hoffstein 2006)

1.6 Summary

Oral appliances have a good evidence base for treatment; however there is a need for long term follow up studies with patient centred outcomes. The role of the dentist in their management needs clarification.

1.7 Aims

The aim of this project is to examine the role of dentists in the management of snoring and sleep apnoea. The specific aims are three-fold:

- To assess the long-term success of mandibular advancement devices.
- To determine the views of dentists and sleep specialists on the involvement of dentists in these medical problems.
- To assess the value of a screening tool which shows potential for use by dentists to evaluate patients with snoring or OSAHS.

Chapter 2 - Long term follow-up of mandibular advancement appliances for the management of snoring and sleep apnoea

2.1 Introduction

Although oral appliances have been shown to be an effective treatment option, long term evidence of their tolerance is limited. Marklund et al 2004 carried out a prospective study on 619 patients who received mandibular advancement appliances from 1989 until 2000. (Marklund et al. 2004) The results show 76% of subjects complied with oral appliance treatment but there was limited information on patient based outcomes. One of the earlier UK studies involving mandibular advancement appliances was that of Cameron et al in 1998. (Cameron, Lyons et al. 1998, Lyons, Cameron et al. 2001, D. Sword, W. T. N. Lee et al. 2004) In this study, patients were seen by a consultant respiratory physician, provided with a mandibular advancement appliance and reviewed over a number of months. It was evident that the majority of patients that snored and that wore the appliance responded favourably. The results of the study indicated that 96.7% of patients had their snoring reduced or eliminated. What was unknown was how useful patients found these appliances over a longer period of time.

2.2 Hypothesis

The hypothesis was that Mandibular Advancement Appliances (MAA) are an acceptable form of treatment in the long term for patients with problem snoring and mild to moderate obstructive sleep apnoea.

2.3 Material and Methods

A questionnaire study was designed to follow up 180 patients who had been provided with appliances 10 years previously. Ethics Committee approval was obtained for the original trial in 1996 but was not required for this present service evaluation. (Personal communication from West of Scotland Ethics Committee)

The questionnaire was first piloted on current patients attending the clinic for construction of an MAA, then reviewed and finalised. (See Appendix) There were 18 questions relating to the appliance, patients sleep quality and lifestyle. Patients were asked to give their weight and height (in either imperial or metric units) and whether they smoked and if so, the quantity. They were also asked how much alcohol they consumed, in units per week. A UK unit of alcohol is 10ml or 8 grams of pure alcohol (ethanol). As a guide, half a pint of 3.5% beer is 1 unit and 1 small glass (125 ml) of 9% wine is 1 unit. Sleep duration was simply recorded as hours per night on average and sleep quality as either "good", "average" or "poor". The effects of body mass index, alcohol consumption, sleep duration, and sleep quality on success were analyzed using chi-squared tests (α =.05).

2.4 Results

The 180 patients who were sent a questionnaire consisted of 150 males (83%) and 30 females (17%). The response rate was 40% with 72 replies, 56 males (78%) and females 16 (22%). There was a varying degree of completion of data in each questionnaire returned. Two questionnaires were returned unopened as the patients had died. One other was returned as the patient had since moved and left no forwarding address.

Section 1. The appliance.

When asked "how many days/nights do you wear the appliance?", the results showed that 47% of patients wear their appliance every night (Figure 2.1). 24 patients indicated that they had abandoned wearing the device.

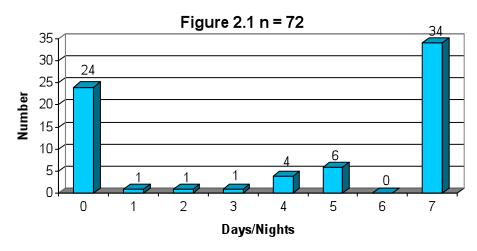


Figure 2.1 Number of nights appliance used.

Of the 24 who had abandoned wearing the device, 12 found it 'Very Uncomfortable', 3 found it 'Slightly Uncomfortable', 2 found it 'Comfortable', and no data were available on the remaining 7.

We asked the patients "How many hours per night/day do you wear it?" 56 patients responded to this question. 60.7% stated that they wore the appliance for 7 hours or more. If those who wore the appliance for 6 hours are included, the percentage goes up to 75.0%.

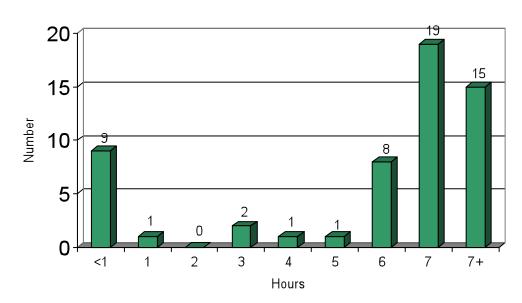


Figure 2.2 n = 56

Figure 2.2 Number of hours a night appliance worn.

As it is important that patients find the appliance comfortable we asked "How comfortable do you find it?" 71 patients responded to this question (Figure 2.3).

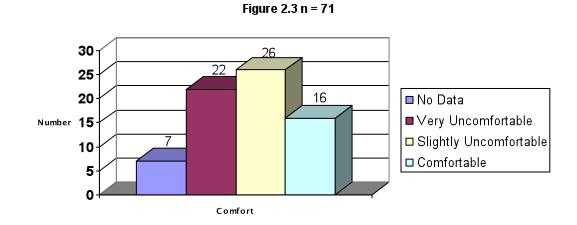


Figure 2.3 Comfort of the appliance.

The main outcome measure is whether the appliance helps their snoring so the patients were asked "Does the appliance affect your snoring?" The results are depicted in Figure 2.4.

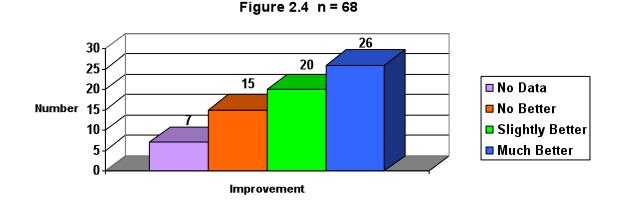


Figure 2.4 Effectiveness of appliance on snoring.

There were 68 responses to this question. 7 gave no data and 15 stated that there was no improvement. 20 respondents indicated that there was a slight improvement and 26 stated that it was much better.

Patients were also asked to assess their opinion of the appliance, "How satisfied are you with the appliance?" 39 out of 68 respondents indicated that they were

very satisfied/ satisfied with the appliance, a satisfaction rate of 57.4%. There were 23 who were not satisfied with the appliance and no data on 6 replies.

The results from Question 3 have been cross-tabulated (Table 2.1) with the results from Question 5. Those who found the device uncomfortable were not satisfied and vice versa.

Table 2.1 Comfort tabled against satisfaction.

	No	Very	Slightly	Comfortable	Total
	Data	Uncomfortable	Uncomfortable		
No Data	6	0	0	0	6
Very Satisfied	0	3	4	8	15
Satisfied	0	2	16	6	24
Not Satisfied	0	16	5	2	23
Total	6	21	25	16	68

The patients were also asked "Have you noticed any side effects?" 32 out of 68 respondents stated that they had noticed a side effect (47%). Those who indicated a side effect were asked to give details, these are summarised as follows (Table 2.2):-

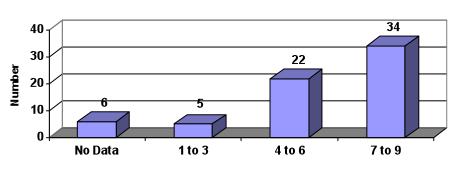
Table 2.2 Side effects of the appliance.

Side effect	Number
Pain/discomfort	9
Excessive salivation	2
Dry mouth/ difficulty breathing if nose blocked	2
Loose	2
Teeth more stained by bacteria.	1
Lower jaw displaced. Caused problems when chewing food.	1
Repositioned jaw	1
Excessive "wind"	1

Section 2. Sleep Quality.

Patients were asked "On average, how many hours do you sleep per night?" The results are shown in Figure 5. Slightly over 50% of respondents stated that they slept 7-9 hours per night.

Figure 2.5 Number of hours of sleep per night.





68 patients replied to the next question "Do you feel more refreshed on waking when you wear the appliance than if you do not wear it?" 31 respondents stated that felt more refreshed, 45.6%. 28 said 'No' and 3 'Don't know', 45.6%. Data was not provided from a further 6 responses.

Patients were also asked "Does wearing the appliance affect your level of sleepiness following sleep?" 65 responded, 30 (46.2%) were less sleepy; and 24 (36.9%) said there was no effect; Data was not provided for 11(16.9%) patients.

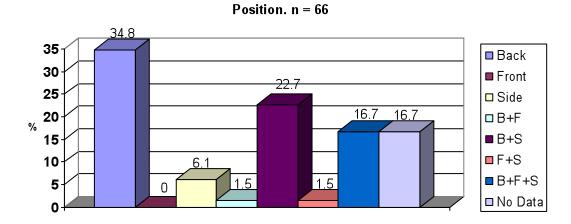
Patients were asked "Do you feel refreshed following your sleep?" Of the 65 that responded, 22 (33.8%) said Yes; 26 (40%) said Sometimes; and 11 (16.9%) said No; No data was provided for 6 (9.2%) patients.

Taking the two positive responses together gives a total of 73.8%.

Another question on sleep quality was "Do you feel sleepy during the day?" 66 responded, of those 15 (22.7%) said Yes; 13 (19.7%) said No; 32 (48.5%) said Sometimes. There was no data provided for 6(9.1%).

Patients were asked "Which position are you in when you snore? Tick all that apply." The results of the 66 replies are shown in Figure 2.6. Supine was the most common position for snoring.

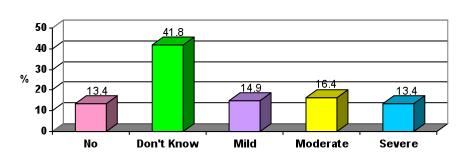




Patients were also asked "How would you rate your quality of sleep?" There were 66 responses, 12 (18.2%) said their sleep quality was good, 34 (51.5%) said it was average, 14 (21.2%) said it was poor and there was no data provided for 6 (9.1%).

Patients were asked "Do you suffer from sleep apnoea and if so what is your category?" the results are shown in figure 2.7.

Figure 2.7 Sleep apnoea severity.



Sleep Apnoea. n = 67

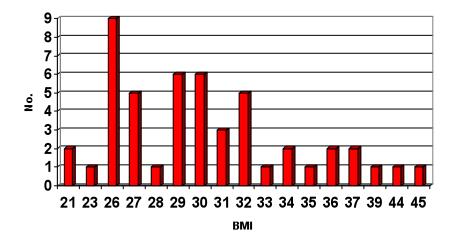
56.2% of respondents denied sleep apnoea or did not know. Over 1 in 8 (13.4%) claimed to suffer from severe sleep apnoea.

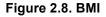
Section 3 of the questionnaire was about the patients themselves.

Patients were asked to submit details of height and weight in either imperial or metric units. 49 responded with both height and weight measurements. From this, the Body Mass Index (BMI) was recorded.

Height varied from 5 feet to 6 feet four inches. Weight ranged from 8 stone to 21 stone.

BMI ranged from 21 to 45 with the mean at 30.18. The range of values for the 49 responses are shown in Figure 2.8.





Patients were asked if they smoked, 66 replied with 8 smokers and 55 nonsmokers.

Of the 8 that smoked, 3 smoked cigars/cheroots, and 5 smoked cigarettes. Two smoked 1-5 per day, one smoked 6-15 per day, and four smoked 15+ per day. No data from 1 respondent regarding type and number per day.

There were 66 replies to the question on alcohol consumption, 53 (80.3%) drank alcohol and 10 (15.2%) did not. There was no information given for 3 patients. (Fig 2.9)

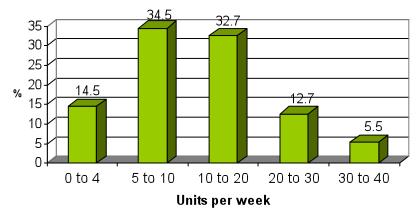


Figure 2.9 Number of units of alcohol per week.

Patients were then asked, "How motivated are you to stop or reduce your snoring?" There were 63 responses to this question. A minority, 3 (2.4%) said 'Not at all'; 19 (29.4%) said their 'Partner was more concerned'; and 42 (66.6%) were 'Very motivated'. There was no data provided for 1 patient (1.6%).

The final question asked, "Overall, how would you rate the success of the appliance?" There were 64 responses, with 29 (45.3%) stating the appliance was good, 15 (23.4%) stating it was fair, 19 (29.7%) stating it was poor, and 1 (1.6%) did not provide data.

The following tables outline data examined for any links between success and the following factors: BMI (Table 2.3), smoking (Table 2.4), alcohol consumption (Table 2.5), sleep duration (Table 2.6) and sleep quality (Table 2.7). The only factor that showed a significant association with success was sleep quality (P=.027).

Table 2.3 Success tabled against BMI.

BMI	21	23	26	27	28	29	30	31	32	33	34	35	36	37	39	44	45	Total
Poor	0	0	4	1	0	3	0	1	1	1	1	1	1	1	0	0	1	16
Fair	0	0	1	1	1	1	3	2	2	0	0	0	0	0	0	1	0	12
Good	2	1	4	3	0	2	2	0	2	0	1	0	1	1	1	0	0	20
Total	2	1	9	5	1	6	5	3	5	1	2	1	2	2	1	1	1	48

Green shaded area = normal

Orange shaded area = overweight

Red shaded area = obese

There is no apparent relationship.

 Table 2.4. Success tabled against Smoking.

	Smoker	Non-Smoker	Total
Poor	4	14	18
Fair	0	15	15
Good	4	25	29
Total	8	54	63

There are not enough smokers in the sample to provide significant conclusions.

Table 2.5. Success tabled against Alcohol Consumption.

	0-4 units	5-10 units	10 - 20	20 - 30	30 - 40	Total
Poor	1	7	6	1	0	15
Fair	2	3	4	2	3	14
Good	4	9	7	4	0	24
Total	7	19	17	7	3	53

There does not appear to be a significant variation detected.

Table 2.6. Success tabled against sleep duration.

	0	1-3 hours	4-6 hours	7-9 hours	Total
0	1	0	0	0	1
Poor	1	3	7	7	18
Fair	0	1	6	8	15
Good	0	1	9	18	28
Total	2	5	22	33	62

 Table 2.7 Success tabled against sleep quality.

	0	Poor	Average	Good	Total
0	1	0	0	0	1
Poor	1	6	8	1	16
Fair	0	3	11	1	15
Good	0	5	14	10	29
Total	2	14	33	12	61

Patients were then given the opportunity to make any other comment.

A total of 59 comments were received, some more relevant than others. Generally speaking, 27 comments were positive, 10 were neutral and 18 were negative with frequencies in brackets where appropriate.

Comments:

Negative

Loose (11)

Discomfort (4)

"His snoring is a COMPLETE NIGHTMARE and that is with us sleeping in separate rooms and I have earplugs." (wife)

<u>Neutral</u>

Now using CPAP (10)

Lost appliance (1)

"No difference" (1)

<u>Positive</u>

"Device is marvellous. A marriage saver"

"I make less noise when I use the appliance"

I only wear it when I am on holiday/staying with relatives/ have guests. My relatives tell me it works."

"It has made a big difference."

"My wife said it was good."

"The device is a life-saver. It needs to be replaced. It has made life bearable."

2.5 Discussion

The response rate of 40% is in line with other previously published questionnaire studies on compliance with oral appliances for sleep disorders. (Almeida, Lowe et al. 2005) A response rate of 40% may be considered good, considering that the patients attended 10 years ago and were not followed up specifically for their MAA. Other studies of patients' satisfaction with dental treatment have found returns of questionnaires to vary between 30 and 40%. (Chapko, Bergner et al. 1985)The fact that 69% of respondents categorized the appliance as "fair" or "good" after 10 years is a remarkably high level of success.

The use of these appliances is 67% (48), with 47.2% (34) wearing the appliance nightly (Figure 2.1). This is similar to the findings of McGowan, who found that 68% used the appliance nightly. (McGowan, Makker et al. 2001) Of those that had stopped wearing the appliance, 24, 50% (12) had stated that it was very uncomfortable, which is the most likely reason for it not being worn.

As the disturbance to the partner has usually prompted the referral for treatment, then it can be assumed that patients would not wear the appliance if it was not effective. It is also unlikely that the patient would wear the appliance if they no longer have a partner or if the partner no longer complains about the snoring even if it was comfortable and effective. (Hoffstein 2006)

In this present study, 75% reported wearing the appliance for 6 hours or more per night (Figure 2.2), which also is comparable to previously published data of an average usage of 6.6 hours per night. (McGown, Makker et al. 2001)

The total number of patients that indicated some improvement in this study was 67.6%. This is very good for a 10 year follow up and for limited expense to the health service and compares favourably with other studies, but is a reduction in efficacy from the initial published pilot study results (Schmidt-Nowara, Lowe et al. 1995, Cameron, Lyons et al. 1998).

The reported side effects (Table 2.2) are broadly in agreement with published data and appear to be minor in nature. (Cameron, Lyons et al. 1998, Clark, Arand et al. 1993, Eveloff, Rosenberg et al. 1994, O'Sullivan, Hillman et al. 1995, McGown, Makker et al. 2001, Marklund, Stenlund et al. 2004) However, the reported discomfort of 9 out of 32 (28%) was lower than other published data, which ranged from 44.4%-52%. (McGown, Makker et al. 2001, Almeida, Lowe et al. 2005)

Respondents self professed motivation to reduce or stop their snoring revealed 22 out of 63 (35%) of patients stated they were not at all motivated or that their partner was more motivated than themselves. Clinical experience has shown that these individuals are less likely to succeed as they will give up on a treatment sooner than the more motivated patients.

The majority of the comments (27 out of 59 comments (46%)) were positive, with some making qualitative statements about improvement in quality of life for both the patient and their partner.

A high proportion of the patients were overweight (mean BMI over 30). A BMI of at least 25kg/m^2 has been shown to have a sensitivity of 93% and a specificity of

74% for OSAHS. (Grunstein, Wilcox et al. 1993) Obesity increases the rate of progression of the disease and weight gain further accelerates this process. (Peppard, Young et al. 2000) It is possible that some patient's weight will have changed over the 10 years and this may explain the difference between the diagnosis at first presentation and the diagnosis 10 years later.

There is some evidence that in the absence of other factors, mild to moderate sleep apnoea may worsen over time, therefore some of these patients may have a higher AHI now than when originally studied. However, another long term study looked at the AHI over time and found that those treated with a MAA did not have an increase in AHI and they hypothesised that this could be a direct result of wearing the appliance. (Marklund, Sahlin et al. 2001, Pendlebury, Pepin et al. 1997)

It is a limitation of this present study that there was no specific follow-up of these patients after the first year of the study period and therefore there was no information on the number of appliances that had been replaced during that time. A further limitation is the lack of follow-up sleep study data, as it is possible that some patients' AHI may have become higher during the 10 year study period. Further prospective long-term studies are required which include data from periodic sleep studies and regular (typically annual) review and replacement of appliances as required.

2.6 Conclusions

The results of this study tend to support the original hypothesis that the MAA is an acceptable form of treatment in the long term for patients with problem snoring and mild to moderate obstructive sleep apnoea based on patient based outcomes. It is clear that some patients will use this form of treatment for a long period of time even though they may not have received the motivation of regular review of their appliance.

Chapter 3 - Dentists' and doctors' attitudes to the provision of intra-oral appliances for the management of snoring and sleep apnoea

3.1 Introduction

Intra-oral appliances were first used for the control of snoring and OSA in Canada and the USA in the late 1980's and in the UK in the mid 1990's. (Cameron, Lyons et al. 1998, Clark, Nakano 1989, Schmidt-Nowara, Meade et al. 1991b, Stradling, Negus et al. 1998) The increased availability of intra-oral appliances, almost exclusively mandibular advancement appliances (MAA), has undoubtedly contributed to the increased public awareness of the possibility of controlling snoring and sleep apnoea with a dental device. However, in the UK there is no agreement as to how the provision of these appliances should be organised or funded. Therefore, in order to make progress on these issues it was considered that the opinions of hospital doctors and dental practitioners should be sought on various questions related to this treatment.

3.2 Aims

The primary aim was to identify current practice of dentists in Scotland in the management of patients with sleep apnoea or disruptive snoring. The secondary aim was to obtain the views of doctors with an interest in sleep medicine on the potential involvement of dentists.

3.3 Materials and Methods

Draft questionnaires were piloted amongst dentists based in hospital, community and general dental practice. These were then amended following feedback. A list of dentists in Scotland was obtained from the Dentists Register of the General Dental Council and entered into a database. A random number generator was then used to select 210 dentists from this database. Questionnaires, together with reply-paid envelopes, were sent to these 210 dentists and a covering letter pledged a donation of £1 to charity for each questionnaire returned.

Seventeen doctors with an interest and expertise in sleep medicine were identified. The questionnaire to the doctors simply consisted of 5 questions relating to whom they considered should provide an MAA and what screening tests should be performed in a primary care setting prior to referral. The questionnaire to the dentists consisted of 10 questions to obtain general information on the respondents and also their attitude to the provision of MAAs'.

3.4 Results

There were 14 replies (82%) from the doctors and 105 (50%) from the dentists.

There were 12 doctors whose specialty was Respiratory Medicine and 2 from other specialities (not specified.) All 14 thought that dentists had a role in helping patients with OSAHS or socially disruptive snoring. Twelve doctors (86%) felt that dentists could be involved in the screening and referral of patients as well as the provision of appliances, with 8 (57%) believing that dentists could give lifestyle advice to patients.

There were 105 replies from the dentists, a response rate of 50%. The returns were relatively evenly split between genders with 53 (50.5%) male and 51 (48.6%) female, with 1 (1%) not stated. The average age of respondents was 40 years (females) and 46 years (males). The questions asked and details of the responses are as follows (it should be noted that some respondents did not answer every question):

1. What is your current area of practice?

The areas of activity of the dentists were Community Dental Service (10), Hospital practitioners (9), mixed private and NHS general dental practice (36), NHS general dental practice (33), private general dental practice (7), specialist practice (3).

2. How often do you see patients with possible sleep apnoea or chronic snoring?

There were 101 replies: frequently (1), occasionally (5), infrequently or never (95).

3. What do you offer patients with possible sleep apnoea or chronic snoring?

There were 60 responses (Tables 3.1 and 3.2). 10% did not offer anything, 40% would make an appliance, 25% would refer to a sleep clinic and 25% would refer to other specialist services.

4. Would you discuss any side effects of oral appliances with patients?

There were 58 replies. Yes - 27 (45%), No - 29 (48%). Details of the side effects discussed may be seen in Table 3.3.

5. Do you currently provide patients with appliances?

There were 60 replies. 19 (32%) currently provide patients with appliances while 41 (68%) do not.

6. What criteria do you use to refer patients to a sleep specialist?

There were 45 replies. Excessive tiredness was cited by 6 respondents, patient's request by 10 and a high Epworth score by 2. A variety of other factors were listed, including severity of symptoms, effect on lifestyle and failure of an appliance.

7. Have you attended any course on the management of sleep apnoea or socially disruptive snoring?

Of the total of 105 returns, 77 (73%) responded "no", 25 (24%) responded "yes" and 3 (3%) did not respond.

8. With your current level of training, would you be comfortable providing patients with oral appliances for sleep apnoea or disruptive snoring?

From the total of 105 returns, 76 (72.4%) responded that they were not comfortable and 25 (23.8%) responded that they were and 4 (3.8%) did not respond to this particular question.

9. Would you be interested in attending a course on the dentists' role in the management of sleep disorders?

From the 76 respondents to this question, 60 (79%) were interested in attending a course and 16 (21%) indicated that they would not be interested in attending. From the 25 who responded that they were comfortable providing patients with oral appliances, 18 (72%) were interested in attending further training and 7 (28%) were not.

10. Do you think that any of your patients would be interested in these appliances if you were to offer them?

82 (78%) thought that they would be, 6 (6%) thought that they might possibly be interested, 10 (9%) thought that they would not and 7 (7%) did not respond.

Finally, dentists were given the opportunity to make any further comments and these are listed in Table 3.4.

3.5 Discussion

As was mentioned already, there have been no previous studies on the current practice of dentists in relation to patients with sleep apnoea or disruptive snoring, or the views of doctors as to what they believe dentists could offer. While this was not a large scale study, the number of responses from both doctors and dentists was considered to be sufficient to give an indication of current practice in Scotland. Methods have been used to try and increase the response rate to questionnaires and it has been suggested that achieving the best response rate involves using a monetary incentive, making the questionnaire interesting or, as in this study, stating an organisation will benefit from their response. (Edwards, Roberts et al. 2002, Edwards, Roberts et al. 2007) The authors of this study attempted to maximise the response rate by promising money to a charity, Oxfam, for all responses received.

The results of this study indicate that doctors in this field are keen for dentists to be involved in the management of these patients however there is no consensus who the patient should be referred to. Dentists, on the other hand, are not aware of the current patient demand and lack training in this field.

Most dentists stated patients would be interested in these appliances if offered, but only 30% currently provided appliances. The side effects of mandibular advancement appliances have been reported by others, but fewer than 50% of dentists in this current survey discussed side effects of the appliances with their patients. (Battagel, Kotecha 2005)

It might be of interest to dentists to note a Position Statement provided by Dental Protection Limited in December 2005 on the provision of appliances by dentists. In summary, they will assist dentists with any claim provided that: 1) the dentist has been trained to provide these appliances, 2) the patient has been appropriately assessed for OSA, 3) they have a medical referral if OSA is suspected, 4) patients have been warned of possible risks and 5) an appliance is part of an integrated treatment plan if OSA is present.

The role of mandibular advancement appliances was clarified and confirmed by the Scottish Intercollegiate Guidelines Network (SIGN) in 2003 and this Guideline was endorsed by the British Thoracic Society. (Scottish Intercollegiate Guidelines Network 2003)Their recommendations are that intra-oral devices are appropriate for:

snorers and patients with mild OSA with normal daytime alertness.

an alternative therapy for patients who are unable to tolerate CPAP (continuous positive airway pressure)

They also recommend that intra-oral devices should be monitored in order to assess the control of OSA and associated symptoms.

It will also be of interest to dentists to know that the dental team at Practitioner Services, a Division of NHS National Services Scotland (responsible for the verification and payment for treatment and services provided by NHS primary care dentists in Scotland) have indicated that an NHS fee may be available for the provision of an intra-oral appliance for the treatment of OSA if full details are provided and prior approval is sought.

The British Society for Dental Sleep Medicine recently published a draft protocol for the management of these patients which has an algorithm that practitioners can use which will develop with increased use. There is no evidence the algorithm will prove useful or is the most effective method of management and is based on expert opinion. (Stradling, Dookun 2009)

In summary, the current practice of dentists and doctors in relation to dental involvement in the management of obstructive sleep apnoea and socially disruptive snoring in Scotland is varied. Whilst doctors appear to be happy for dentists to be involved, dentists need further training in the provision of these appliances, in the use of appropriate screening tests and the possible side effects of wearing appliances. Professionals are unclear of the funding available under the National Health Service and it is suggested that familiarity with the available clinical guidelines on patient management and the involvement of dentists could clarify the treatment options for this group of patients.

Table 3.1 A list of the services offered by GDPs' to patients with possible OSA or problem snoring.

Services offered	Number of responses
No treatment or no data:	7
Construct appliance:	
Appliance only	12
Appliance and lifestyle advice	5
Appliance and referral	4
Appliance, advice and referral	4
Lifestyle advice:	
Advice only	7
Advice and referral	8
Referral only:	13

Table 3.2. Referral patterns of the 29 dentists who included "referral" in their management.

Refer to:	Number
Sleep clinic	14
Dental hospital, oral surgery or oral	7
General medical practitioner	4
GDP who provides appliances	2
Orthodontist	1
ENT surgery	1

Table 3.3 Possible issues and side effects of appliances that dentists discussed with patients.

Number	Side effect
13	Poor compliance
7	TMJ pain
5	Oral hygiene
4	Lack of effectiveness
2	Hyper-salivation
2	Caries
2	Periodontal issues
1	Appliance hygiene
1	Social issues
1	Movement of upper anterior
1	Occlusal disruption
1	Gagging
1	Dry mouth

Table 3.4. Additional comments made by dentists.

Generally favourable comments or suggestions

A list of local sleep clinics for referral would be useful

Appliances could be offered to a limited number of patients if it is felt that this would be of benefit.

I am happy to make appliances.

I believe this is more common than is currently acknowledged.

I do not treat these cases because they do not present at my practice. However, I would be interested in learning about them and how to treat.

I don't think that patients are generally aware that these disorders can be treated by dentists. I have never been asked - but I have not offered treatment either.

I've made one appliance which worked very well. Would do it again.

Not a topic that has come up as yet. However, I would like more information on the management of such cases.

Patients have enquired about 'gum shields'. They were referred to an orthodontist who provided an appliance which proved difficult to wear.

The anti-snoring devices that we have provided have received good feedback. Device works well.

Very interested. This is an under diagnosed and under treated condition.

Less favourable or uncertain

The idea of a tool that could reduce the problem is good, but as I find with biteraising appliances for TMJ problems, compliance rate is very low. Patients try it for a week then give up.

Currently working as NHS community dental officer. Are we able to offer this service?

I think most patients would go to their GP first.

I'd prefer to refer patients to a specialist - hospital or private.

Difficulty getting onto courses

Cost aspects

Appliance provided after sleep clinic consultant. Cost is an issue. Lots would like to try it but can't afford it. Good success with careful patient selection.

Appliances have to be cost effective. Remember it is the partners who are disturbed. Sleep apnoea is different.

Cost could be a problem as NHS do not provide a fee.

I have offered an appliance to 2 patients but both declined as they considered it too expensive.

Main problem is cost. If this is perceived as a medical problem would the cost be borne by NHS?

4 Chapter 4 - The Kushida Index as a screening tool for Obstructive Sleep Apnoea-Hypopnoea Syndrome.

4.1 Introduction

The current gold standard for the investigation of OSAHS includes clinical examination, assessment of daytime somnolence and an overnight sleep study (polysomnography). Many different screening methods have been used to attempt to reduce the cost and inconvenience of overnight sleep studies, but Pang et al concluded that there needed to be further validation of these methods before widespread use could be recommended. (Pang, Terris 2006/0) However, one screening method that showed potential, with a sensitivity of 97.6% and a specificity of 100%, was published by Kushida et al in 1997. (Kushida, Efron et al. 1997) The Kushida Index is calculated as previously mentioned.

There have been several recent articles highlighting the possible role of dentists in the management of patients with OSAHS. (Lyons, Cameron et al. 2001, Jauhar, Lyons et al. 2008a, D. Sword, W. T. N. Lee et al. 2004, Stradling, Dookun 2009, Lyons 1999, Jauhar, Lyons et al. 2008b)

The Kushida test appears to be a simple screening test, with good sensitivity and specificity, and could be carried out by dentists in general dental practice.

4.2 Aims

The aim of this study was to assess the validity and reliability of the Kushida Index as a screening tool for OSAHS in a West of Scotland population. A secondary aim was to assess whether other factors (Mallampati score, Epworth sleepiness score, enlarged tongue, enlarged soft palate, or obstruction due to tonsil enlargement) were correlated to the diagnosis of OSAHS.

4.3 Materials and Methods

The Standards for Reporting of Diagnostic Accuracy (STARD) checklist was used in this study. (Bossuyt, Reitsma et al. 2003) The study protocol was approved by the Glasgow West Local Research Ethics Committee 2. (see Appendix) A power calculation was carried out based on data from Kushida's study, with the assumption of finding 95% sensitivity and 95% specificity, and this indicated that a sample size of 73 patients would be appropriate. 85 participants were recruited to allow for any drop-outs. A history and clinical examination was conducted by a consultant respiratory physician and a specialist registrar. Patients were recruited in a consecutive series and informed consent was obtained. The inclusion criteria were that subjects should be over 18 years of age and who were judged to require a sleep study. Patients were excluded if they were involved in other research studies or did not require a sleep study. The examiner carrying out the morphological measurements was blinded to the clinical history, the provisional diagnosis of the participants and to their sleep study results. The following data were obtained:

1) Height (m) and weight (kg) to allow calculation of Body Mass Index (BMI)

2) Neck circumference at crico-thyroid region in centimetres (cm).

3) Palatal height (mm), measured by Jenny Callipers which had the sharp points modified. The advantage of these callipers is that there is an adjustable screw on one arm so the depth of the palate could be accurately measured (Figure 4.1). The callipers were sterilized before use and disposable plastic coverings were used for each patient. The measurement was taken from the midline of the dorsal surface of the tongue at the median lingual sulcus to the highest point in the palate, measured with the tongue in a relaxed position. The measurement was taken at 20 degrees of mouth opening which was established by a plastic goniometer. (Figure 4.2)

4) Maxillary and mandibular inter-molar distance (mm), measured from the mesial surface of the second molars with jenny callipers. If these teeth were missing, an estimate was made of the position of the mesial surface of second molars using associated anatomy and teeth present. If patients wore dentures at night, measurements were taken of the denture teeth. (Figure 4.3)

5) Overjet (mm).

6

These measurements were then used in the Kushida formula to calculate the Kushida Index.

Additional non-interventional measurements collected were:

- 1) Unit number
- 2) Sex
- 3) Age
- 4) Date of examination
- 5) Epworth score (at a later date from patient's notes)
- 6) Teeth present
- 7) Incisal relationship
- 8) Visual inspection of the tongue.
- 9) Visual airway evaluation and assignment of Mallampati score (see below)
- 10) Visual inspection of nasal passage to assess patency.

The Mallampati score is a scoring method to assess the ease of intubation of a patient, graded on a scale of 1-4. (Figure 4.5) The use of the Mallampati score was based on studies of the use of this score as a clinical predictor for OSAHS. (Friedman, Tanyeri et al. 1999, Liistro, Rombaux et al. 2003, Nuckton, Glidden et al. 2006) This scoring method is used in anaesthetics to assess the ease with which the upper airway may be visualised during tracheal intubation. (Mallampati, Gatt et al. 1985b, Samsoon, Young 1987)

Participants all had limited sleep studies (respiratory polysomnography) carried out using the Somnoscreen system (S-Med, UK) and manually analysed by a sleep technician (DM). The diagnosis of OSAHS was based on the daytime somnolence (an Epworth Sleepiness score \geq 10) and an Oxygen De-saturation Index (ODI) \geq 10/hr. The criteria for the diagnosis of OSAHS were based on the recommendations in SIGN Guideline Number 73 and on local protocols and were as follows: ODI less than 10 was considered normal, 11-15 inconclusive/borderline, 16-20 mild, 21-30 moderate, and 31 or greater was considered severe. (Scottish Intercollegiate Guidelines Network 2003)

4.3.1 Statistical Methods

Statistical calculations were carried out using Minitab and SPSS. Differences between means and 95% confidence intervals for each variable in OSAHS and normal patients, were calculated. P-values were calculated using an Independent T Test if the data were normally distributed. Where data were not normally distributed, Mann Whitney tests were used as the sample size was not sufficiently large for large sample assumptions of normality. Correlations were calculated using a Pearsons Correlation Coefficient for normally distributed data and a Spearmans Rank Correlation Coefficient for non-parametric data. When comparing categorical data, a Chi Square test was used. If the expected count was less than 5, a Fishers exact test was used.

Sensitivity is the proportion of true positives (respiratory PSG confirmed OSAHS) that are correctly identified by the screening test (Kushida). Specificity is the proportion of true negatives (respiratory PSG confirmed not OSHAS) that are correctly identified by the screening test (Kushida). (Altman, Bland 1994b)

Positive predictive value is the proportion of patients with positive test results (Kushida positive) who are correctly diagnosed. Negative predictive value is the proportion of patients with negative test results (Kushida negative) who are correctly diagnosed. (Altman, Bland 1994a)

4.4 Results

85 participants were recruited from Gartnavel General Hospital Sleep Clinic, in Glasgow, Scotland, between May and November 2007. However, of these 10 failed to attend for the sleep study and 4 were edentulous and did not wear their dentures at night.

Of the 71 patients subsequently included in the study, 49 (69%) were fully dentate, 8 (11%) were partially dentate with enough teeth to estimate the intraoral distances but missing one or more second molar teeth, 10 (14%) were partially dentate but had all the teeth required for calculation of the Kushida index present, and 4 (6%) were edentulous but slept with their dentures in at night.

The demographics of the patients initially recruited and those finally included in the study are summarised in Table 4.1. There were no statistically significant differences between these two groups in the variables listed in Table 4.1. The occlusal pattern and morphological measurements of the subjects are summarised in Tables 4.2 and 4.3.

In some patients when the AHI was not available, the ODI was used, as is often done in clinical practice. There was a highly significant correlation between the ODI and AHI (r = 0.77; p<0.001, n= 52). Compared to patients without OSAHS, patients with OSAHS were older (50 ± 10.2 years vs 42.85 ± 11.1, p = 0.006), had a higher BMI (35.8 ± 9.4 vs 28.9 ± 6.1, p < 0.001) and a larger collar size (43.2 ± 4.1 vs 39.2 ± 2.9, p < 0.001) (Table 4.4).

The cut-off used for a positive Kushida Index was 70, based on previously published data. (Kushida, Efron et al. 1997) The sensitivity of the Kushida Index in this present study was 68%. (95% CI 50 - 81) and the specificity was 71% (95% CI 52 - 84). The positive predictive value was 71%; the negative predictive value was 67%. (Table 4.5)

The receiver operator curve (ROC) for the Kushida Index and a diagnosis of OSAHS is presented in Figure 4.3 and consists of a plot of the true positive rate (sensitivity) against the false positive rate (specificity) for different subjects. A test with perfect discrimination (no overlap in the two distributions) has a ROC plot that passes through the upper left corner (100% sensitivity, 100% specificity). Therefore the closer the ROC plot is to the upper left corner, the higher the overall accuracy of the test. (Zweig, Campbell 1993) The diagnostic category of the patients achieved by using our criteria may be seen in Table 4.6. The Mallampati score, Epworth sleepiness score and enlargement of the tongue, soft palate or tonsils were not significantly related to a diagnosis of sleep apnoea (p > 0.05).

4.5 Discussion

The sensitivity and specificity of the Kushida Index for the prediction of OSAHS were found to be rather lower in this present study compared to Kushida's original results. Kushida's formula was originally based on data from 30 subjects and then prospectively tested on a further 300 subjects. (Kushida, Efron et al. 1997) This formula has been further tested in Brazil by Soares et al on 80 subjects and in Korea by Jung et al on 54 subjects. (Soares, de Azeredo Bittencourt et al. 2006, Jung, Cho et al. 2004) The inclusion of 71 subjects in this present study has been calculated to give 80-90% adequate power at the 5% significance level. In Kushida's study, the sensitivity of the index was found to be 97.6% and the specificity was 100%, rather higher than the 68% and 71% of this present study. Jung (2004) also reported higher figures, with sensitivity of 89% and a specificity of 94%. All of these figures are based on a cut-off value of 70 in the Kushida Index.

One possible reason for the difference in the sensitivity and specificity in our study was that we used a higher threshold level for sleep apnoea (>11) than the original study by Kushida (>5). The reason for using a higher level was that an AHI of >5 is no longer considered to represent clinically significant sleep apnoea, which was not the case when Kushida published his data in 1997. (Scottish Intercollegiate Guidelines Network 2003) However, when we calculated the results using Kushida's definition of OSAHS, we obtained a sensitivity of 60% and a specificity of 76%. These values are too low to validate the Kushida Index in our population.

The gender and age distributions are similar in previous studies to this present study. (Kushida, Efron et al. 1997, Soares, de Azeredo Bittencourt et al. 2006, Jung, Cho et al. 2004) However, Kushida et al was the only other group to publish the Epworth score; they found a larger difference (mean difference 4) between those with OSAHS and those without compared to the findings of this present study (mean difference 0.1). However, the range of Epworth scores in both studies, for those with and without OSAHS, was 5 - 6. Therefore it is

7

unlikely that this is the reason for the difference in the sensitivity or specificity between this present study and Kushida's study.

There were similar neck circumferences found in all studies cited, but perhaps the largest difference between these studies was in the intra-oral measurements. In comparison to Kushida, Jung and our own results, Soares et al found smaller maxillary and mandibular intermolar distances and lower palatal heights. This may be due to differences in craniofacial characteristics in that demographic area.

This present study was prospective in design, with sufficient participants to achieve a power of 80%. Although the sensitivity and specificity are considerably lower than those found by others, we are confident that these results are valid for the population studied. All patients were recruited in a consecutive order and the number of those diagnosed with OSAHS was similar to the number of healthy controls. The intra-oral measurements were carried out by one calibrated operator (SJ) who was also blinded to the history and presenting complaint of the patients. A test of the reproducibility of the measurements was carried out on volunteers prior to the study. The sleep technician (DM) is employed in a large sleep department and has been trained to ARTP (Association of Respiratory Technology and Physiology) standards and complies with ARTP Standards of Care for Sleep Apnoea Services.

It could be argued that all subjects without second molar teeth and anterior maxillary and mandibular incisor teeth perhaps should have been excluded from the study as it was not possible to make the intra-oral measurement in the way that Kushida intended. However, this would have distorted the applicability of the test in the West of Scotland area where a significant proportion of patients are partially dentate or edentulous. Therefore these patients were included if there was sufficient detail to reliably estimate the required intra-oral measurements.

In previous studies, if a subject had a nasal obstruction and a high Mallampati score this was correlated to a diagnosis of OSAHS.(Liistro, Rombaux et al. 2003) However, even without nasal obstruction, those with a Mallampati score of 3 or 4 have been reported to have a 1.95 relative risk of having OSAHS.(Nuckton, Glidden et al. 2006) The Mallampati score could be easily carried out by dentists

as part of a screening procedure, but in our study a high Mallampati score was not correlated to a diagnosis of OSAHS.

4.6 Conclusions

The Kushida test is quick, simple and non-invasive to perform and could easily be applied in the dental surgery. However, with the limited sensitivity and specificity demonstrated in this study, it cannot be recommended as a screening test. A primary care based large scale study would be required before it could be recommended as a routine screening test for those with a high suspicion of OSAHS prior to referral to a sleep clinic.



Figure 4.1 Jenny Callipers

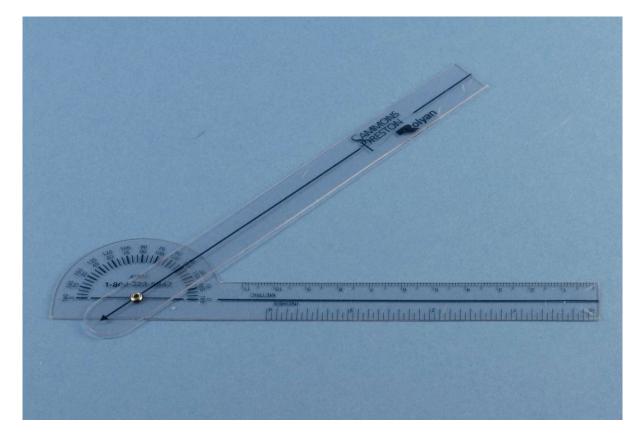
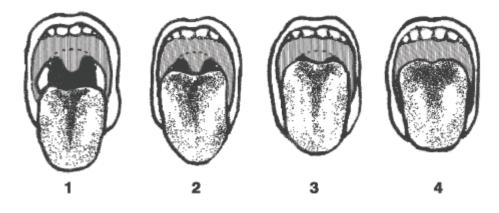


Figure 4.2 Goniometer



Figure 4.3 Measurement of mandibular intermolar distance





Class 1: Full visibility of tonsils, uvula and soft palate

Class 2: Visibility of hard and soft palate, upper portion of tonsils and uvula

Class 3: Soft and hard palate and base of the uvula are visible

Class 4: Only Hard Palate visible

Variable	Number	Mean (SD)	Range of	Number of	Mean (SD)	Range of
	Recruited	values for	values for	patients	values for	values for
		those	those	included in	those	those
		recruited	recruited	study	included	included
Age	85	47.6 (11.2)	21-78	71	46.6 (11.2)	21-78
Gender	85	63 Males		71	53 males	
Neck	84	42 (4.8)	33-58.4	71	41.3 (4.1)	33-57.15
circumference						
(cm)						
BMI	85	33.7 (8.8)	19.4-64.3	71	32.5 (8.7)	19.4-64.3
Kushida Index	84	74.2 (21.9)	31-142.6	71	71.3 (21.3)	31-142.6
Modified	85	3.3 (0.96)	1-4	71	3.2 (0.99)	1-4
Mallampati						
Score						
Epworth	85	11.8 (5.5)	0-24	71	11.1 (5.4)	0-21
Sleepiness						
Score						

Table 4.1 Comparison of demographics of patients included and excluded from the analysis.

Incisal	relationship	Frequency (%)			
Class I		39 (55)			
Class	ll div l	14 (20)			
Class	ll div ll	7 (10)			
Class III		11 (15)			
Total		71 (100)			

Table 4.2 Incisal relationship of patients

Г

				Maxillary	Mandibular
	Overbite	Overjet	Palatal	inter-molar	inter-molar
	(mm)	(mm)	height (mm)	distance (mm)	distance (mm)
Ν	71	71	71	71	71
Mean	1.9	2.2	40.1	40	41.5
SD	1.6	2	7	3.7	4.6
Minimum	0	-1	26	34	31
Maximum	6	11	55	50	52

Table 4.3 Pooled intra-oral measurements of all patients.

٦

Sex M:F	30:7	23:11		
Age (years), mean				
(SD)	50 (10.2)	42.85 (11.1)	-7.1 (-12.2, -2)	0.006
BMI, kg/m ²) mean				
(SD)	35.8 (9.4)	28.9 (6.1)	-6.8 (-10.6, -3.1)	<0.001
Neck				
circumference				
(cm)				
mean (SD)	43.2 (4.1)	39.2 (2.9)	-4 (-5.7, -2.3)	<0.001
Maxillary inter-				
molar distance				
(mm) mean (SD)	40.8 (3.7)	39.1 (3.5)	-1.7 (-3.4, 0.3)	0.54
Mandibular inter-				
molar distance				
(mm) mean (SD)	42.5 (4)	40.4 (4.8)	-2.1 (-4.2, -0.2)	0.048
Palatal height				
(cm) mean (SD)	39.2 (7.3)	41 (6.5)	1.86 (-1.4, 5.1)	0.264
Overjet Median				
(Range) {IQR}	2 (-1,8) {.5,3}	2 (0,11) {1.38,3}		0.467
ODI Median	24 (11,68)			
(Range) {IQR}	{16.3,38}	3 (0,9) {1,6}		<.001
	(1000,000)			
Kushida Index			-16.5 (-25.9, -	
mean (SD)	79.2 (21.7)	62.8 (17.5)	7.1)	<0.001
. ,	, , , , , , , , , , , , , , , , , , ,		,	
Epworth				
Sleepiness Score				
mean (SD)	10.4 (5.5)	10.3 (5.6)	-1.4 (-3.96, 1.15)	0.27

Table 4.4 Results for the 71 patients included in the study

* P values are from Independent t-tests or Mann Whitney tests

	OSAHS Present	OSAHS Absent	Total
Kushida Positive	25	10	35
Kushida Negative	12	24	36
Total	37	34	71

Table 4.5 Relationship between the diagnosis obtained from respiratory polysomnography and the results of the Kushida Screening test.

	Number
Diagnosis from Sleep Study	of patients
Normal	34
Inconclusive/borderline OSAHS	8
Mild OSAHS	9
Moderate OSAHS	7
Severe OSAHS	13

Table 4.6 The diagnostic category of the 71 patients included in the study.

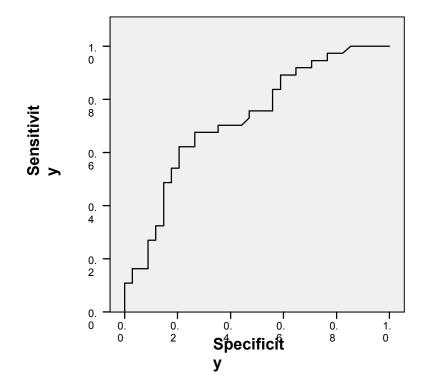


Figure 4.5 The Receiver Operator curve for the Kushida Index in the diagnosis of OSAHS.

5 Chapter 5 - Summary and recommendations for future research.

From the studies presented in this thesis, it is clear that doctors involved in sleep medicine see a role for dentists in treating patients with chronic snoring and mild OSAHS, the oral appliances made can work well for patients over a long period of time, but the methods dentists should use to screen for sleep apnoea before construction of an appliance and the clear need for training in this field is still to be addressed.

I suggest that the profile of sleep medicine and its relationship to dentistry needs to be raised. It would be beneficial to conduct a primary care based study that could analyse if screening tests such as the Kushida Index and Epworth Sleepiness Score are appropriate screening tools to rule out sleep apnoea so dentists could construct an appliance for patients with snoring alone without being concerned that the patient has underlying OSAHS with subsequent medical complications.

One very interesting future study would be to investigate the effect of denture wearing at night on OSAHS in edentulous patients as previous reports highlight this may help, however these studies are underpowered and have not been validated.

Appendices

EPWORTH SLEEPINESS SCALE

How likely are you to doze off in the following situations (in contrast to just feeling tired)? Even if you have not done some of these things, try to work out how these situations would affect you. Use the following scale:

0	=	would never doze								
1	=	slight chance of d	slight chance of dozing							
2	=	moderate chance	moderate chance of dozing							
3	=	high chance of do	high chance of dozing							
Situ	lation		Chance of dozing							
1. 9	Sitting a	and reading								
2. \	Watchin	g TV								
3. Sitting, inactive in a public place (e.g., a theatre or a meeting)										
4. /	As a pas	senger in a car for a	n hour without a break							
		own to rest in the aft ces permit	ternoon when							
6. 9	Sitting a	and talking to someo	ne							
7. 9	Sitting o	juietly after a lunch	without alcohol							
8.	In a car,	, while stopped for a	few minutes in traffic							

Total

Epworth sleepiness Scale. Johns MW (1991). "A new method for measuring daytime sleepiness: the Epworth sleepiness scale". Sleep 14 (6): 540-5. Scores greater than 10 merit referral to a sleep physician.

Stanford Sleepiness Scale (SSS)

Degree of Sleepiness Scale					
Feeling active, vital, alert, or wide awake	1				
Functioning at high levels, but not at peak; able to concentrate	2				
Awake, but relaxed; responsive but not fully alert	3				
Somewhat foggy, let down	4				
Foggy; losing interest in remaining awake; slowed down					
Sleepy, woozy, fighting sleep; prefer to lie down	6				
No longer fighting sleep, sleep onset soon; having dream-like thoughts	7				
Asleep	Х				

Patient que Name		[Date:	(re	ef no: office use)-
		e appropriate	. Please ask	your partne	er if appropriate to
help fill in s					
A. How	many days of	the week do	you wear the	e appliance?	
1 🗆 2	□ 3 □	4 🗆 5 🗆	□ 6 □ 7 □]	
B. How	comfortable i	is the applian	ice to wear?		
Very und	comfortable [∃Slightly und	comfortable	Comfort	able 🗆
C. Did t	he appliance	make a diffe	rence to you	snoring?	
No 🗆	Slightly bet	ter 🗆	Much bette	er 🗆	
D. How	satisfied are y	you with the	appliance?		
Not satis	sfied 🗆 Satisf	ied □ Very s	atisfied 🗆		
E. Were	there any sic	le effects fro	m wearing th	ne appliance	:
4		f al a a a a initia			_
I. HOW	many hours o	r steep a nigi	it do you get	<u>{</u>	
1-3 🗆	4-6 🗆	7-9			
2. Do yo	ou wake up fe	eling refresh	ed?		
No 🗆	Sometimes		Yes 🗆		
3. Do yo	ou feel sleepy	during the d	ay?		
No 🗆	Sometimes		Yes 🗆		
4. What applicab		you sleep in v	when you sno	ore? (can tic	k more than one if
On back		On front	On side	Don't kno)W
5. Prese	ent body weig	htst	lbs		

Height (Office use)									
6. Do you smok	e?	Yes		No					
Cigarettes		Cigar		Pipe					
1-4 per day 🗆	6-15 j	per day		>15 p	er day 🗆]			
7. Do you drink	alcoho	ol: Yes		No					
Alcohol consum	ption:	In unit	:s (1 ur	nit is a	a glass o	f wine	e or a spi	rit, a	a pint of
beer is 2 units)	0 🗆	5-10 🗆	10-20		20-30 [30-40 🗆		>40 🗆
8. How would y	/ou rat	e the q	Juality	of you	r sleep?				
Poor	Avera	ge 🗆		Good					
9. Do you knov in?	v if you	ı suffei	from	sleep	apnoea,	if so v	what cate	gory	' are you
Don't know 🛛	Mild [Mode	rate 🗆	Severe				
10. How motivate	ed are y	ou to st	op or re	duce ye	our snorin	ıg?			
Not really \Box	Partne	er more	than me			Very n	notivated		
11. In summary	please	rate tł	ne over	all suc	cess of t	he ap	pliance		
Poor 🗆	ок Г		Good						
COMMENTS									
								-	
								-	

Thank you for taking the time to fill out this questionnaire.

List of references

AGRAWAL, S., STONE, P., MCGUINNESS, K., MORRIS, J. and CAMILLERI, A.E., 2002. Sound frequency analysis and the site of snoring in natural and induced sleep. *Clinical otolaryngology and allied sciences*, 27(3), 162-166.

AHMED, M.M. and SCHWAB, R.J., 2006. Upper airway imaging in obstructive sleep apnea. *Current opinion in pulmonary medicine*, 12(6), 397-401.

ALMEIDA, F.R., LOWE, A.A., OTSUKA, R., FASTLICHT, S., FARBOOD, M. and TSUIKI, S., 2006a. Long-term sequellae of oral appliance therapy in obstructive sleep apnea patients: Part 2. Study-model analysis. *American Journal of Orthodontics and Dentofacial Orthopedics : Official Publication of the American Association of Orthodontists, its Constituent Societies, and the American Board of Orthodontics,* 129(2), 205-213.

ALMEIDA, F.R., LOWE, A.A., SUNG, J.O., TSUIKI, S. and OTSUKA, R., 2006b. Long-term sequellae of oral appliance therapy in obstructive sleep apnea patients: Part 1. Cephalometric analysis. *American Journal of Orthodontics and Dentofacial Orthopedics : Official Publication of the American Association of Orthodontists, its Constituent Societies, and the American Board of Orthodontics*, 129(2), 195-204.

ALMEIDA, F.R., LOWE, A.A., TSUIKI, S., OTSUKA, R., WONG, M., FASTLICHT, S. and RYAN, C.F., 2005. Long-Term Compliance and Side effects of Oral Appliances Used for the Treatment of Snoring and Obstructive Sleep Apnea Syndrome. *Journal of Clinical Sleep Medicine*, 01(02), 143-152.

ALTMAN, D.G. and BLAND, J.M., 1994a. Diagnostic tests 2: Predictive values. British Medical Journal (Clinical research ed.), 309(6947), 102.

ALTMAN, D.G. and BLAND, J.M., 1994b. Diagnostic tests. 1: Sensitivity and specificity. *British Medical Journal (Clinical research ed.)*, 308(6943), 1552.

AMERICAN ACADEMY OF SLEEP MEDICINE TASK FORCE, 1999. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. *Sleep*, 22(5), 667-689.

ANCOLI-ISRAEL, S., KRIPKE, D.F., KLAUBER, M.R., MASON, W.J., FELL, R. and KAPLAN, O., 1991. Sleep-disordered breathing in community-dwelling elderly. *Sleep*, 14(6), 486-495.

ARMSTRONG, M.W., WALLACE, C.L. and MARAIS, J., 1999. The effect of surgery upon the quality of life in snoring patients and their partners: a between-subjects case-controlled trial. *Clinical otolaryngology and allied sciences*, 24(6), 510-522.

BAHAMMAM, A., DELAIVE, K., RONALD, J., MANFREDA, J., ROOS, L. and KRYGER, M.H., 1999. Health care utilization in males with obstructive sleep apnea syndrome two years after diagnosis and treatment. *Sleep*, 22(6), 740-747.

BARDWELL, W.A., ANCOLI-ISRAEL, S., BERRY, C.C. and DIMSDALE, J.E., 2001. Neuropsychological effects of one-week continuous positive airway pressure treatment in patients with obstructive sleep apnea: a placebo-controlled study. *Psychosomatic medicine*, 63(4), 579-584.

BARNES, M., MCEVOY, R.D., BANKS, S., TARQUINIO, N., MURRAY, C.G., VOWLES, N. and PIERCE, R.J., 2004. Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. *American journal of respiratory and critical care medicine*, 170(6), 656-664.

BARTHLEN, G.M., BROWN, L.K., WILAND, M.R., SADEH, J.S., PATWARI, J. and ZIMMERMAN, M., 2000. Comparison of three oral appliances for treatment of severe obstructive sleep apnea syndrome. *Sleep medicine*, 1(4), 299-305.

BASSARI, A.G. and GUILLEMINAULT, C., 2000. Clinical features and evaluation of obstructive sleep apnea hypopnea syndrome. In: T. ROTH, W.C. DEMENT and M. KRYGER, eds, *Principles and practice of sleep medicine*. Philadelphia: WB Saunders, pp. 869-87.

BATTAGEL, J.M., JOHAL, A. and KOTECHA, B.T., 2005. Sleep nasendoscopy as a predictor of treatment success in snorers using mandibular advancement splints. *The Journal of laryngology and otology*, 119(2), 106-112.

BATTAGEL, J.M. and KOTECHA, B., 2005. Dental side-effects of mandibular advancement splint wear in patients who snore. *Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery*, 30(2), 149-156.

BEAR, S.E. and PRIEST, J.H., 1980. Sleep apnea syndrome: correction with surgical advancement of the mandible. *Journal of oral surgery (American Dental Association* : 1965), 38(7), 543-549.

BEARPARK, H., ELLIOTT, L., GRUNSTEIN, R., CULLEN, S., SCHNEIDER, H., ALTHAUS, W. and SULLIVAN, C., 1995. Snoring and sleep apnea. A population study in Australian men. *American journal of respiratory and critical care medicine*, 151(5), 1459-1465.

BECKER, H.F., JERRENTRUP, A., PLOCH, T., GROTE, L., PENZEL, T., SULLIVAN, C.E. and PETER, J.H., 2003. Effect of nasal continuous positive airway pressure treatment on blood pressure in patients with obstructive sleep apnea. *Circulation*, 107(1), 68-73.

BERRY, R.B. and BLOCK, A.J., 1984. Positive nasal airway pressure eliminates snoring as well as obstructive sleep apnea. *Chest*, 85(1), 15-20.

BIXLER, E.O., VGONTZAS, A.N., LIN, H.M., TEN HAVE, T., REIN, J., VELA-BUENO, A. and KALES, A., 2001. Prevalence of sleep-disordered breathing in women: effects of gender. *American journal of respiratory and critical care medicine*, 163(3 Pt 1), 608-613.

BIXLER, E.O., VGONTZAS, A.N., TEN HAVE, T., TYSON, K. and KALES, A., 1998. Effects of age on sleep apnea in men: I. Prevalence and severity. *American journal of respiratory and critical care medicine*, 157(1), 144-148.

BLANCO, J., ZAMARRON, C., ABELEIRA PAZOS, M.T., LAMELA, C. and SUAREZ QUINTANILLA, D., 2005. Prospective evaluation of an oral appliance in the treatment of obstructive sleep apnea syndrome. *Sleep & breathing = Schlaf & Atmung*, 9(1), 20-25.

BLOOM, J.W., KALTENBORN, W.T. and QUAN, S.F., 1988. Risk factors in a general population for snoring. Importance of cigarette smoking and obesity. *Chest*, 93(4), 678-683.

BONHAM, P.E., CURRIER, G.F., ORR, W.C., OTHMAN, J. and NANDA, R.S., 1988. The effect of a modified functional appliance on obstructive sleep apnea. American Journal of Orthodontics and Dentofacial Orthopedics : Official Publication of the American Association of Orthodontists, its Constituent Societies, and the American Board of Orthodontics, 94(5), 384-392.

BOSSUYT, P.M., REITSMA, J.B., BRUNS, D.E., GATSONIS, C.A., GLASZIOU, P.P., IRWIG, L.M., LIJMER, J.G., MOHER, D., RENNIE, D., DE VET, H.C. and STANDARDS FOR REPORTING OF DIAGNOSTIC ACCURACY, 2003. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. *BMJ* (*Clinical research ed.*), 326(7379), 41-44.

BOYD, J.H., PETROF, B.J., HAMID, Q., FRASER, R. and KIMOFF, R.J., 2004. Upper airway muscle inflammation and denervation changes in obstructive sleep apnea. *American journal of respiratory and critical care medicine*, 170(5), 541-546.

BUCHWALD, H., AVIDOR, Y., BRAUNWALD, E., JENSEN, M.D., PORIES, W., FAHRBACH, K. and SCHOELLES, K., 2004. Bariatric surgery: a systematic review and meta-analysis. *JAMA* : the Journal of the American Medical Association, 292(14), 1724-1737.

BURWELL, C.S., ROBIN, E.D., WHALEY, R.D. and BICKELMANN, A.G., 1956. Extreme obesity associated with alveolar hypoventilation: a pickwickian syndrome. *American Journal Medicine*, 21, 811-818.

CAMERON, D.A., LYONS, M.F., FOX, D.L. and BANHAM, S.W., 1998. Pilot study of a semi-flexible intra-oral appliance for the control of snoring. *British Dental Journal*, 185(6), 304-307.

CARSKADON, M.A. and DEMENT, W.C., 2005. Normal Human Sleep: An overview. In: M. KRYGER, T. ROTH and W.C. DEMENT, eds, fourth edn. Elsevier Saunders, pp. 13.

CARTWRIGHT, R.D. and KNIGHT, S., 1987. Silent partners: the wives of sleep apneic patients. *Sleep*, 10(3), 244-248.

CARTWRIGHT, R.D. and SAMELSON, C.F., 1982. The effects of a nonsurgical treatment for obstructive sleep apnea. The tongue-retaining device. *JAMA* : *the Journal of the American Medical Association*, 248(6), 705-709.

CHAPKO, M.K., BERGNER, M., GREEN, K., BEACH, B., MILGROM, P. and SKALABRIN, N., 1985. Development and validation of a measure of dental patient satisfaction. *Medical care*, 23(1), 39-49.

CHERVIN, R.D. and ALDRICH, M.S., 1999. The Epworth Sleepiness Scale may not reflect objective measures of sleepiness or sleep apnea. *Neurology*, 52(1), 125-131.

CHERVIN, R.D., ALDRICH, M.S., PICKETT, R. and GUILLEMINAULT, C., 1997. Comparison of the results of the Epworth Sleepiness Scale and the Multiple Sleep Latency Test. *Journal of Psychosomatic research*, 42(2), 145-155.

CHUNG, K.F., 2000/11. Use of the Epworth Sleepiness Scale in Chinese patients with obstructive sleep apnea and normal hospital employees. *Journal of Psychosomatic Research*, 49(5), 367-372.

CLARK, G.T., ARAND, D., CHUNG, E. and TONG, D., 1993. Effect of anterior mandibular positioning on obstructive sleep apnea. *The American Review of Respiratory Disease*, 147(3), 624-629.

CLARK, G.T. and NAKANO, M., 1989. Dental appliances for the treatment of obstructive sleep apnea. *Journal of the American Dental Association (1939)*, 118(5), 611-5, 617-9.

COLMENERO, C., ESTEBAN, R., ALBARINO, A.R. and COLMENERO, B., 1991. Sleep apnoea syndrome associated with maxillofacial abnormalities. *The Journal of laryngology and otology*, 105(2), 94-100.

D. SWORD, W. T. N. LEE, D. A. CAMERON, M. F. LYONS, A. NICOL and S. W. BANHAM, 2004. Longterm [7 year] follow-up of patients fitted with a nonadjustable intra-oral device (IOD) for snoring/obstructive sleep apnoea (OSAS). *European Respiratory Journal*, 24(28), 477.

DAVIES, R.J. and STRADLING, J.R., 1990. The relationship between neck circumference, radiographic pharyngeal anatomy, and the obstructive sleep apnoea syndrome. The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology, 3(5), 509-514.

DAVIES, R., ALI, N. and STRADLING, J., 1992. Neck circumference and other clinical features in the diagnosis of the obstructive sleep apnoea syndrome. *Thorax*, 47(2), 101-105.

DEALBERTO, M.J., FERBER, C., GARMA, L., LEMOINE, P. and ALPEROVITCH, A., 1994. Factors related to sleep apnea syndrome in sleep clinic patients. *Chest*, 105(6), 1753-1758.

DEMENT, W. and KLEITMAN, N., 1957. The relation of eye movements during sleep to dream activity: an objective method for the study of dreaming. *Journal of experimental psychology*, 53(5), 339-346.

DICKENS, C., 1835. Pickwick Papers.

DIXON, J.B., SCHACHTER, L.M. and O'BRIEN, P.E., 2001. Sleep disturbance and obesity: changes following surgically induced weight loss. *Archives of Internal Medicine*, 161(1), 102-106.

DIXON, J.B., SCHACHTER, L.M. and O'BRIEN, P.E., 2003. Predicting Sleep Apnea and Excessive Day Sleepiness in the Severely Obese: Indicators for Polysomnography. *Chest*, 123(4), 1134-1141.

DJUPESLAND, P.G., SKATVEDT, O. and BORGERSEN, A.K., 2001. Dichotomous physiological effects of nocturnal external nasal dilation in heavy snorers: the answer to a rhinologic controversy? *American Journal of Rhinology*, 15(2), 95-103.

DOLLY, F.R. and BLOCK, A.J., 1982. Effect of flurazepam on sleep-disordered breathing and nocturnal oxygen desaturation in asymptomatic subjects. *The American Journal of Medicine*, 73(2), 239-243.

DORT, L.C. and HUSSEIN, J., 2004. Snoring and obstructive sleep apnea: compliance with oral appliance therapy. *The Journal of otolaryngology*, 33(3), 172-176.

DOUGLAS, N.J. and POLO, O., 1994. Pathogenesis of obstructive sleep apnoea/hypopnoea syndrome. *Lancet*, 344(8923), 653-655.

DOUGLASS, A.B., BORNSTEIN, R., NINO-MURCIA, G., KEENAN, S., MILES, L., ZARCONE, V.P., JR, GUILLEMINAULT, C. and DEMENT, W.C., 1994. The Sleep Disorders Questionnaire. I: Creation and multivariate structure of SDQ. *Sleep*, 17(2), 160-167.

DUCHNA, H.W., 2006. Sleep-related breathing disorders--a second edition of the International Classification of Sleep Disorders (ICSD-2) of the American Academy of Sleep Medicine (AASM). *Pneumologie (Stuttgart, Germany)*, 60(9), 568-575.

DURAN, J.J., ESNAOLA, S., RUBIO, R., DE LATORRE, G., ANITUA, E. and ZUBIA, S., 2002. A randomised, double blind, crossover, placebo-controlled trial of mandibular advancement device for the treatment of snoring and mild obstructive sleep apnoe-hypopnoea syndrome. *European Respiratory Journal* 2002, 20(Suppl 38), 102.

ECKHART, J.E., 1998. Comparisons of oral devices for snoring. *Journal of the California Dental Association*, 26(8), 611-623.

EDWARDS, P., ROBERTS, I., CLARKE, M., DIGUISEPPI, C., PRATAP, S., WENTZ, R. and KWAN, I., 2002. Increasing response rates to postal questionnaires: systematic review. *British Medical Journal (Clinical research ed.)*, 324(7347), 1183.

EDWARDS, P., ROBERTS, I., CLARKE, M., DIGUISEPPI, C., PRATAP, S., WENTZ, R., KWAN, I. and COOPER, R., 2007. Methods to increase response rates to postal questionnaires. *Cochrane database of systematic reviews (Online)*, (2)(2), MR000008.

ELLEN, R.L., MARSHALL, S.C., PALAYEW, M., MOLNAR, F.J., WILSON, K.G. and MAN-SON-HING, M., 2006. Systematic review of motor vehicle crash risk in persons with sleep apnea. *Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine*, 2(2), 193-200.

ENGLEMAN, H.M., MARTIN, S.E., DEARY, I.J. and DOUGLAS, N.J., 1994. Effect of continuous positive airway pressure treatment on daytime function in sleep apnoea/hypopnoea syndrome. *Lancet*, 343(8897), 572-575.

ENGLEMAN, H.M., MCDONALD, J.P., GRAHAM, D., LELLO, G.E., KINGSHOTT, R.N., COLEMAN, E.L., MACKAY, T.W. and DOUGLAS, N.J., 2002. Randomized crossover trial of two treatments for sleep apnea/hypopnea syndrome: continuous positive airway pressure and mandibular repositioning splint. *American journal of respiratory and critical care medicine*, 166(6), 855-859.

EVELOFF, S.E., ROSENBERG, C.L., CARLISLE, C.C. and MILLMAN, R.P., 1994. Efficacy of a Herbst mandibular advancement device in obstructive sleep apnea. *American journal of respiratory and critical care medicine*, 149(4 Pt 1), 905-909.

FERGUSON, K.A., ONO, T., LOWE, A.A., AL-MAJED, S., LOVE, L.L. and FLEETHAM, J.A., 1997. A short-term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnoea. *Thorax*, 52(4), 362-368.

FERGUSON, K.A., ONO, T., LOWE, A.A., KEENAN, S.P. and FLEETHAM, J.A., 1996. A randomized crossover study of an oral appliance vs nasal-continuous positive airway pressure in the treatment of mild-moderate obstructive sleep apnea. *Chest*, 109(5), 1269-1275.

FERGUSON, K.A., ONO, T., LOWE, A.A., RYAN, C.F. and FLEETHAM, J.A., 1995. The relationship between obesity and craniofacial structure in obstructive sleep apnea. *Chest*, 108(2), 375-381.

FITZPATRICK, M.F., MARTIN, K., FOSSEY, E., SHAPIRO, C.M., ELTON, R.A. and DOUGLAS, N.J., 1993. Snoring, asthma and sleep disturbance in Britain: a community-based survey. The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology, 6(4), 531-535.

FRIBERG, D., ANSVED, T., BORG, K., CARLSSON-NORDLANDER, B., LARSSON, H. and SVANBORG, E., 1998. Histological indications of a progressive snorers disease in an upper airway muscle. *American journal of respiratory and critical care medicine*, 157(2), 586-593.

FRIEDMAN, M., TANYERI, H., LA ROSA, M., LANDSBERG, R., VAIDYANATHAN, K., PIERI, S. and CALDARELLI, D., 1999. Clinical predictors of obstructive sleep apnea. *The Laryngoscope*, 109(12), 1901-1907.

FRITSCH, K.M., ISELI, A., RUSSI, E.W. and BLOCH, K.E., 2001. Side effects of mandibular advancement devices for sleep apnea treatment. *American journal of respiratory and critical care medicine*, 164(5), 813-818.

FUJITA, S., 1984. UPPP for sleep apnea and snoring. *Ear, nose, & throat journal,* 63(5), 227-235.

GALE, D.J., SAWYER, R.H., WOODCOCK, A., STONE, P., THOMPSON, R. and O'BRIEN, K., 2000. Do oral appliances enlarge the airway in patients with obstructive sleep apnoea? A prospective computerized tomographic study. *European journal of orthodontics*, 22(2), 159-168.

GAO, X.M., ZENG, X.L., FU, M.K. and HUANG, X.Z., 1999. Magnetic resonance imaging of the upper airway in obstructive sleep apnea before and after oral appliance therapy. *The Chinese journal of dental research : the official journal of the Scientific Section of the Chinese Stomatological Association (CSA)*, 2(2), 27-35.

GASTAUT, H., TASSARINI, C.A. and DURON, B., 1965. Polygraphic study of the episodic diurnal and nocturnal (hypnic and respiratory) manifestations of the Pickwick syndrome. *Brain Res*, 2, 167-186.

GEORGE, C.F. and SMILEY, A., 1999. Sleep apnea & automobile crashes. Sleep, 22(6), 790-795.

GEORGE, P.T., 2001. Selecting sleep-disordered-breathing appliances. Biomechanical considerations. *Journal of the American Dental Association* (1939), 132(3), 339-347.

GLEADHILL, I.C., SCHWARTZ, A.R., SCHUBERT, N., WISE, R.A., PERMUTT, S. and SMITH, P.L., 1991. Upper airway collapsibility in snorers and in patients with obstructive hypopnea and apnea. *The American Review of Respiratory Disease*, 143(6), 1300-1303.

GOLD, A.R., SCHWARTZ, A.R., BLEECKER, E.R. and SMITH, P.L., 1986. The effect of chronic nocturnal oxygen administration upon sleep apnea. *The American Review of Respiratory Disease*, 134(5), 925-929.

GOTSOPOULOS, H., CHEN, C., QIAN, J. and CISTULLI, P.A., 2002. Oral appliance therapy improves symptoms in obstructive sleep apnea: a randomized, controlled trial. *American journal of respiratory and critical care medicine*, 166(5), 743-748.

GOULD, G.A., WHYTE, K.F., RHIND, G.B., AIRLIE, M.A., CATTERALL, J.R., SHAPIRO, C.M. and DOUGLAS, N.J., 1988. The sleep hypopnea syndrome. *The American Review of Respiratory Disease*, 137(4), 895-898.

GROEGER, J.A., ZIJLSTRA, F.R. and DIJK, D.J., 2004. Sleep quantity, sleep difficulties and their perceived consequences in a representative sample of some 2000 British adults. *Journal of sleep research*, 13(4), 359-371.

GRUNSTEIN, R., WILCOX, I., YANG, T.S., GOULD, Y. and HEDNER, J., 1993. Snoring and sleep apnoea in men: association with central obesity and hypertension. International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity, 17(9), 533-540.

GUILLEMINAULT, C., MONDINI, S. and GREENFIELD, M., 1984. Abnormal respiratory pattern generation during sleep in patients with autonomic dysfunction. *The American Review of Respiratory Disease*, 129(3), 512-513.

GUILLEMINAULT, C., STOOHS, R., CLERK, A., CETEL, M. and MAISTROS, P., 1993. A cause of excessive daytime sleepiness. The upper airway resistance syndrome. *Chest*, 104(3), 781-787.

GUILLEMINAULT, C., STOOHS, R., CLERK, A., SIMMONS, J. and LABANOWSKI, M., 1992. From obstructive sleep apnea syndrome to upper airway resistance syndrome: consistency of daytime sleepiness. *Sleep*, 15(6 Suppl), S13-6.

GUILLEMINAULT, C., STOOHS, R. and DUNCAN, S., 1991a. Snoring (I). Daytime sleepiness in regular heavy snorers. *Chest*, 99(1), 40-48.

GUILLEMINAULT, C., STOOHS, R. and DUNCAN, S., 1991b. Snoring (I). Daytime sleepiness in regular heavy snorers. *Chest*, 99(1), 40-48.

GUINNESS WORLD RECORDS 2004, Body Extremes (Humans), Edition April 2004, Editor Claire Folkard, Published by Random House. (Guinness Book of Records)

GUMUSTEKIN, K., SEVEN, B., KARABULUT, N., AKTAS, O., GURSAN, N., ASLAN, S., KELES, M., VAROGLU, E. and DANE, S., 2004. Effects of sleep deprivation, nicotine, and selenium on wound healing in rats. *The International journal of neuroscience*, 114(11), 1433-1442.

HACK, M., DAVIES, R.J., MULLINS, R., CHOI, S.J., RAMDASSINGH-DOW, S., JENKINSON, C. and STRADLING, J.R., 2000. Randomised prospective parallel trial of therapeutic versus subtherapeutic nasal continuous positive airway pressure on simulated steering performance in patients with obstructive sleep apnoea. *Thorax*, 55(3), 224-231.

HANS, M.G., NELSON, S., LUKS, V.G., LORKOVICH, P. and BAEK, S.J., 1997. Comparison of two dental devices for treatment of obstructive sleep apnea syndrome (OSAS). American Journal of Orthodontics and Dentofacial Orthopedics : Official Publication of the American Association of Orthodontists, its Constituent Societies, and the American Board of Orthodontics, 111(5), 562-570.

HARDING, S.M., 2001. Prediction formulae for sleep-disordered breathing. *Current opinion in pulmonary medicine*, 7(6), 381-385.

HASSID, S., AFRAPOLI, A.H., DECAESTECKER, C. and CHOUFANI, G., 2002. UPPP for snoring: long-term results and patient satisfaction. *Acta Oto-Rhino-Laryngologica Belgica*, 56(2), 157-162.

HE, J., KRYGER, M.H., ZORICK, F.J., CONWAY, W. and ROTH, T., 1988. Mortality and apnea index in obstructive sleep apnea. Experience in 385 male patients. *Chest*, 94(1), 9-14.

HENKE, K.G., FRANTZ, D.E. and KUNA, S.T., 2000. An oral elastic mandibular advancement device for obstructive sleep apnea. *American journal of respiratory and critical care medicine*, 161(2 Pt 1), 420-425.

HERSBERGER, K.E., RENGGLI, V.P., NIRKKO, A.C., MATHIS, J., SCHWEGLER, K. and BLOCH, K.E., 2006. Screening for sleep disorders in community pharmacies-evaluation of a campaign in Switzerland. *Journal of clinical pharmacy and therapeutics*, 31(1), 35-41.

HICKLIN, L.A., TOSTEVIN, P. and DASAN, S., 2000. Retrospective survey of long-term results and patient satisfaction with uvulopalatopharyngoplasty for snoring. *The Journal of laryngology and otology*, 114(9), 675-681.

HIYAMA, S., TSUIKI, S., ONO, T., KURODA, T. and OHYAMA, K., 2003. Effects of mandibular advancement on supine airway size in normal subjects during sleep. *Sleep*, 26(4), 440-445.

HODDES, E., ZARCONE, V., SMYTHE, H., PHILLIPS, R. and DEMENT, W.C., 1973. Quantification of sleepiness: a new approach. *Psychophysiology*, 10(4), 431-436.

HOFFSTEIN, V., 2006. Review of oral appliances for treatment of sleepdisordered breathing. *Sleep Breath*.

HOFFSTEIN, V., 1996a. Is snoring dangerous to your health? *Sleep*, 19(6), 506-516.

HOFFSTEIN, V., 1996b. Snoring. Chest, 109(1), 201-222.

HOFFSTEIN, V., HAIGHT, J., COLE, P. and ZAMEL, N., 1999. Does snoring contribute to presbycusis? *American journal of respiratory and critical care medicine*, 159(4 Pt 1), 1351-1354.

HOFFSTEIN, V. and MATEIKA, S., 1992. Differences in abdominal and neck circumferences in patients with and without obstructive sleep apnoea. *The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology*, 5(4), 377-381.

HOFFSTEIN, V., MATEIKA, S. and ANDERSON, D., 1994. Snoring: is it in the ear of the beholder? *Sleep*, 17(6), 522-526.

HOFFSTEIN, V. and SZALAI, J.P., 1993. Predictive value of clinical features in diagnosing obstructive sleep apnea. *Sleep*, 16(2), 118-122.

HORNE, J.A. and REYNER, L.A., 1995. Sleep related vehicle accidents. *British Medical Journal (Clinical research ed.)*, 310(6979), 565-567.

HORNER, R.L., SHEA, S.A., MCIVOR, J. and GUZ, A., 1989. Pharyngeal size and shape during wakefulness and sleep in patients with obstructive sleep apnoea. *The Quarterly journal of medicine*, 72(268), 719-735.

HUBLIN, C., KAPRIO, J., PARTINEN, M., HEIKKILA, K. and KOSKENVUO, M., 1996. Daytime sleepiness in an adult, Finnish population. *Journal of internal medicine*, 239(5), 417-423.

ISHIDA, M., INOUE, Y., SUTO, Y., OKAMOTO, K., RYOKE, K., HIGAMI, S., SUZUKI, T. and KAWAHARA, R., 1998. Mechanism of action and therapeutic indication of prosthetic mandibular advancement in obstructive sleep apnea syndrome. *Psychiatry and clinical neurosciences*, 52(2), 227-229.

JAMIESON, A., GUILLEMINAULT, C., PARTINEN, M. and QUERA-SALVA, M.A., 1986. Obstructive sleep apneic patients have craniomandibular abnormalities. *Sleep*, 9(4), 469-477. JANSON, C., NOGES, E., SVEDBERG-RANDT, S. and LINDBERG, E., 2000. What characterizes patients who are unable to tolerate continuous positive airway pressure (CPAP) treatment? *Respiratory medicine*, 94(2), 145-149.

JAUHAR, S., LYONS, M.F., BANHAM, S.W., CAMERON, D.A. and ORCHARDSON, R., 2008a. Ten-year follow-up of mandibular advancement devices for the management of snoring and sleep apnea. *The Journal of prosthetic dentistry*, 99(4), 314-321.

JAUHAR, S., LYONS, M.F., BANHAM, S.W., ORCHARDSON, R. and LIVINGSTON, E., 2008b. The attitudes of general dental practitioners and medical specialists to the provision of intra-oral appliances for the management of snoring and sleep apnoea. *British Dental Journal*.

JENKINSON, C., DAVIES, R.J., MULLINS, R. and STRADLING, J.R., 1999. Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. *Lancet*, 353(9170), 2100-2105.

JOHAL, A., PATEL, S.I. and BATTAGEL, J.M., 2007. The relationship between craniofacial anatomy and obstructive sleep apnoea: a case-controlled study. *Journal of sleep research*, 16(3), 319-326.

JOHNS, M.W., 1994. Sleepiness in different situations measured by the Epworth Sleepiness Scale. *Sleep*, 17(8), 703-710.

JOHNS, M.W., 1991. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*, 14(6), 540-545.

JOHNSON, M.K., CARTER, R., NICOL, A., PATON, R. and BANHAM, S.W., 2004. Long-term continuous positive airway pressure (CPAP) outcomes from a sleep service using limited sleep studies and daycase CPAP titration in the management of obstructive sleep apnoea/hypopnoea syndrome. *Chronic respiratory disease*, 1(2), 83-88.

JOHNSTON, C.D., GLEADHILL, I.C., CINNAMOND, M.J., GABBEY, J. and BURDEN, D.J., 2002. Mandibular advancement appliances and obstructive sleep apnoea: a randomized clinical trial. *European journal of orthodontics*, 24(3), 251-262.

JUNG, D.G., CHO, H.Y., GRUNSTEIN, R.R. and YEE, B., 2004. Predictive value of Kushida index and acoustic pharyngometry for the evaluation of upper airway in subjects with or without obstructive sleep apnea. *Journal of Korean medical science*, 19(5), 662-667.

KALAN, A., KENYON, G.S., SEEMUNGAL, T.A. and WEDZICHA, J.A., 1999. Adverse effects of nasal continuous positive airway pressure therapy in sleep apnoea syndrome. *The Journal of laryngology and otology*, 113(10), 888-892.

KARA, C.O., ZENCIR, M., TOPUZ, B., ARDIC, N. and KOCAGOZOGLU, B., 2005. The prevalence of snoring in adult population. *Kulak burun bogaz ihtisas dergisi* : *KBB* = Journal of ear, nose, and throat, 14(1-2), 18-24. KARACAN, I. and KARATAS, M., 1995. Erectile dysfunction in sleep apnea and response to CPAP. Journal of sex & marital therapy, 21(4), 239-247.

KATO, J., ISONO, S., TANAKA, A., WATANABE, T., ARAKI, D., TANZAWA, H. and NISHINO, T., 2000. Dose-dependent effects of mandibular advancement on pharyngeal mechanics and nocturnal oxygenation in patients with sleep-disordered breathing. *Chest*, 117(4), 1065-1072.

KIELY, J.L., NOLAN, P. and MCNICHOLAS, W.T., 2004. Intranasal corticosteroid therapy for obstructive sleep apnoea in patients with co-existing rhinitis. *Thorax*, 59(1), 50-55.

KIMOFF, R.J., CHEONG, T.H., OLHA, A.E., CHARBONNEAU, M., LEVY, R.D., COSIO, M.G. and GOTTFRIED, S.B., 1994. Mechanisms of apnea termination in obstructive sleep apnea. Role of chemoreceptor and mechanoreceptor stimuli. *American journal of respiratory and critical care medicine*, 149(3 Pt 1), 707-714.

KIRBY, S.D., ENG, P., DANTER, W., GEORGE, C.F.P., FRANCOVIC, T., RUBY, R.R.F. and FERGUSON, K.A., 1999. Neural Network Prediction of Obstructive Sleep Apnea From Clinical Criteria. *Chest*, 116(2), 409-415.

KRIBBS, N.B., PACK, A.I., KLINE, L.R., SMITH, P.L., SCHWARTZ, A.R., SCHUBERT, N.M., REDLINE, S., HENRY, J.N., GETSY, J.E. and DINGES, D.F., 1993. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. *The American Review of Respiratory Disease*, 147(4), 887-895.

KROL, R.C., KNUTH, S.L. and BARTLETT, D., JR, 1984. Selective reduction of genioglossal muscle activity by alcohol in normal human subjects. *The American Review of Respiratory Disease*, 129(2), 247-250.

KUSHIDA, C.A., EFRON, B. and GUILLEMINAULT, C., 1997. A predictive morphometric model for the obstructive sleep apnea syndrome. *Annals of Internal Medicine*, 127(8 Pt 1), 581-587.

KUSHIDA, C.A., MORGENTHALER, T.I., LITTNER, M.R., ALESSI, C.A., BAILEY, D., COLEMAN, J., JR, FRIEDMAN, L., HIRSHKOWITZ, M., KAPEN, S., KRAMER, M., LEE-CHIONG, T., OWENS, J., PANCER, J.P. and AMERICAN ACADEMY OF SLEEP, 2006. Practice parameters for the treatment of snoring and Obstructive Sleep Apnea with oral appliances: an update for 2005. *Sleep*, 29(2), 240-243.

LA VELLE, W.E. and HARDY, J.C., 1979. Palatal lift prostheses for treatment of palatopharyngeal incompetence. *The Journal of prosthetic dentistry*, 42(3), 308-315.

LANDRIGAN, C.P., ROTHSCHILD, J.M., CRONIN, J.W., KAUSHAL, R., BURDICK, E., KATZ, J.T., LILLY, C.M., STONE, P.H., LOCKLEY, S.W., BATES, D.W. and CZEISLER, C.A., 2004. Effect of reducing interns' work hours on serious medical errors in intensive care units. *The New England journal of medicine*, 351(18), 1838-1848.

LAVIE, P., PILLAR, G. and MALHOTRA, A., 2002. Sleep Disorders: Diagnosis, Management and Treatment A handbook for clinicians.

LEE-CHIONG, T., SATEIA, M. and CARSKADON, M.A., 2008. Sleep Medicine.

LEGATO, M.J., 1997. Gender-specific aspects of obesity. *International journal of fertility and women's medicine*, 42(3), 184-197.

LEVINSON, P.D., MCGARVEY, S.T., CARLISLE, C.C., EVELOFF, S.E., HERBERT, P.N. and MILLMAN, R.P., 1993. Adiposity and cardiovascular risk factors in men with obstructive sleep apnea. *Chest*, 103(5), 1336-1342.

LI, K.K., KUSHIDA, C., POWELL, N.B., RILEY, R.W. and GUILLEMINAULT, C., 2000. Obstructive sleep apnea syndrome: a comparison between Far-East Asian and white men. *The Laryngoscope*, 110(10 Pt 1), 1689-1693.

LIISTRO, G., ROMBAUX, P., BELGE, C., DURY, M., AUBERT, G. and RODENSTEIN, D.O., 2003. High Mallampati score and nasal obstruction are associated risk factors for obstructive sleep apnoea. *European Respiratory Journal*, 21(2), 248-252.

LIM, J., LASSERSON, T.J., FLEETHAM, J. and WRIGHT, J., 2006. Oral appliances for obstructive sleep apnoea. *Cochrane database of systematic reviews (Online)*, (1)(1), CD004435.

LINDMAN, R. and BONDEMARK, L., 2001. A review of oral devices in the treatment of habitual snoring and obstructive sleep apnoea. *Swedish dental journal*, 25(1), 39-51.

LITTLEFIELD, P.D. and MAIR, E.A., 1999. Snoring surgery: which one is best for you? *Ear, nose, & throat journal,* 78(11), 861-5, 868-70.

LITTNER, M., HIRSHKOWITZ, M., DAVILA, D., ANDERSON, W.M., KUSHIDA, C.A., WOODSON, B.T., JOHNSON, S.F., MERRILL, S.W. and STANDARDS OF PRACTICE COMMITTEE OF THE AMERICAN ACADEMY OF SLEEP MEDICINE, 2002. Practice parameters for the use of auto-titrating continuous positive airway pressure devices for titrating pressures and treating adult patients with obstructive sleep apnea syndrome. An American Academy of Sleep Medicine report. *Sleep*, 25(2), 143-147.

LIU, Y., PARK, Y.C., LOWE, A.A. and FLEETHAM, J.A., 2000. Supine Cephalometric Analyses of an Adjustable Oral Appliance Used in the Treatment of Obstructive Sleep Apnea. *Sleep Breath*, 4(2), 59-66.

LOCKLEY, S.W., CRONIN, J.W., EVANS, E.E., CADE, B.E., LEE, C.J., LANDRIGAN, C.P., ROTHSCHILD, J.M., KATZ, J.T., LILLY, C.M., STONE, P.H., AESCHBACH, D., CZEISLER, C.A. and HARVARD WORK HOURS, HEALTH AND SAFETY GROUP, 2004. Effect of reducing interns' weekly work hours on sleep and attentional failures. *The New England journal of medicine*, 351(18), 1829-1837.

LOWE, A.A., SANTAMARIA, J.D., FLEETHAM, J.A. and PRICE, C., 1986. Facial morphology and obstructive sleep apnea. American Journal of Orthodontics and Dentofacial Orthopedics : Official Publication of the American Association of Orthodontists, its Constituent Societies, and the American Board of Orthodontics, 90(6), 484-491.

LU, L.R., PEAT, J.K. and SULLIVAN, C.E., 2003. Snoring in preschool children: prevalence and association with nocturnal cough and asthma. *Chest*, 124(2), 587-593.

LUGARESI, E., CIRIGNOTTA, F., COCCAGNA, G. and PIANA, C., 1980. Some epidemiological data on snoring and cardiocirculatory disturbances. *Sleep*, 3(3-4), 221-224.

LYONS, M.F., 1999. The role of dental appliances in the control of snoring. *ENT News*, 8(17),.

LYONS, M.F., CAMERON, D.A. and BANHAM, S.W., 2001. Snoring, sleep apnoea and the role of dental appliances. *Dental Update*, 28(5), 254-256.

MACMAHON, S., PETO, R., CUTLER, J., COLLINS, R., SORLIE, P., NEATON, J., ABBOTT, R., GODWIN, J., DYER, A. and STAMLER, J., 1990. Blood pressure, stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. *Lancet*, 335(8692), 765-774.

MAISLIN, G., PACK, A.I., KRIBBS, N.B., SMITH, P.L., SCHWARTZ, A.R., KLINE, L.R., SCHWAB, R.J. and DINGES, D.F., 1995. A survey screen for prediction of apnea. *Sleep*, 18(3), 158-166.

MALLAMPATI, S.R., GATT, S.P., GUGINO, L.D., DESAI, S.P., WARAKSA, B., FREIBERGER, D. and LIU, P.L., 1985a. A clinical sign to predict difficult tracheal intubation: a prospective study. *Canadian Anaesthetists' Society journal*, 32(4), 429-434.

MALLAMPATI, S.R., GATT, S.P., GUGINO, L.D., DESAI, S.P., WARAKSA, B., FREIBERGER, D. and LIU, P.L., 1985b. A clinical sign to predict difficult tracheal intubation: a prospective study. *Canadian Anaesthetists' Society journal*, 32(4), 429-434.

MARCUS, C.L., 2001. Sleep-disordered breathing in children. *American journal of respiratory and critical care medicine*, 164(1), 16-30.

MARKLUND, M., 2006. Predictors of long-term orthodontic side effects from mandibular advancement devices in patients with snoring and obstructive sleep apnea. American Journal of Orthodontics and Dentofacial Orthopedics : Official Publication of the American Association of Orthodontists, its Constituent Societies, and the American Board of Orthodontics, 129(2), 214-221.

MARKLUND, M. and FRANKLIN, K.A., 1996. Dental appliances in the treatment of snoring. A comparison between an activator, a soft-palate lifter, and a mouth-shield. *Swedish dental journal*, 20(5), 183-188.

MARKLUND, M., SAHLIN, C., STENLUND, H., PERSSON, M. and FRANKLIN, K.A., 2001. Mandibular advancement device in patients with obstructive sleep apnea : long-term effects on apnea and sleep. *Chest*, 120(1), 162-169.

MARKLUND, M., STENLUND, H. and FRANKLIN, K.A., 2004. Mandibular advancement devices in 630 men and women with obstructive sleep apnea and

snoring: tolerability and predictors of treatment success. *Chest*, 125(4), 1270-1278.

MARTIN, R.J., SANDERS, M.H., GRAY, B.A. and PENNOCK, B.E., 1982. Acute and long-term ventilatory effects of hyperoxia in the adult sleep apnea syndrome. *The American Review of Respiratory Disease*, 125(2), 175-180.

MASSIE, C.A., MCARDLE, N., HART, R.W., SCHMIDT-NOWARA, W.W., LANKFORD, A., HUDGEL, D.W., GORDON, N. and DOUGLAS, N.J., 2003. Comparison between automatic and fixed positive airway pressure therapy in the home. *American journal of respiratory and critical care medicine*, 167(1), 20-23.

MATHUR, R. and DOUGLAS, N.J., 1995. Family studies in patients with the sleep apnea-hypopnea syndrome. *Annals of Internal Medicine*, 122(3), 174-178.

MAURER, J.T., HUBER, K., VERSE, T., HORMANN, K. and STUCK, B., 2007. A mandibular advancement device for the ENT office to treat obstructive sleep apnea. Otolaryngology-head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery, 136(2), 231-235.

MAYCOCK, G., 1997. Sleepiness and driving: the experience of heavy goods vehicle drivers in the UK. *Journal of sleep research*, 6(4), 238-244.

MAYCOCK, G., 1996. Sleepiness and driving: the experience of UK car drivers. *Journal of sleep research*, 5(4), 229-237.

MCARDLE, N., DEVEREUX, G., HEIDARNEJAD, H., ENGLEMAN, H.M., MACKAY, T.W. and DOUGLAS, N.J., 1999. Long-term use of CPAP therapy for sleep apnea/hypopnea syndrome. *American journal of respiratory and critical care medicine*, 159(4 Pt 1), 1108-1114.

MCARDLE, N., GROVE, A., DEVEREUX, G., MACKAY-BROWN, L., MACKAY, T. and DOUGLAS, N.J., 2000. Split-night versus full-night studies for sleep apnoea/hypopnoea syndrome. *The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology*, 15(4), 670-675.

MCGOWN, A.D., MAKKER, H.K., BATTAGEL, J.M., L'ESTRANGE, P.R., GRANT, H.R. and SPIRO, S.G., 2001. Long-term use of mandibular advancement splints for snoring and obstructive sleep apnoea: a questionnaire survey. *European Respiratory Journal*, 17(3), 462-466.

MEANS, M.K., LICHSTEIN, K.L., EDINGER, J.D., TAYLOR, D.J., DURRENCE, H.H., HUSAIN, A.M., AGUILLARD, R.N. and RADTKE, R.A., 2003. Changes in depressive symptoms after continuous positive airway pressure treatment for obstructive sleep apnea. *Sleep & breathing* = *Schlaf & Atmung*, 7(1), 31-42.

MEHTA, A., QIAN, J., PETOCZ, P., DARENDELILER, M.A. and CISTULLI, P.A., 2001. A randomized, controlled study of a mandibular advancement splint for obstructive sleep apnea. *American journal of respiratory and critical care medicine*, 163(6), 1457-1461. MELAMED, S. and OKSENBERG, A., 2002. Excessive daytime sleepiness and risk of occupational injuries in non-shift daytime workers. *Sleep*, 25(3), 315-322.

MENDELSON, W.B., GARNETT, D. and GILLIN, J.C., 1981. Flurazepam-induced sleep apnea syndrome in a patient with insomnia and mild sleep-related respiratory changes. *The Journal of nervous and mental disease*, 169(4), 261-264.

MILLMAN, R.P., CARLISLE, C.C., MCGARVEY, S.T., EVELOFF, S.E. and LEVINSON, P.D., 1995. Body fat distribution and sleep apnea severity in women. *Chest*, 107(2), 362-366.

MONDINI, S. and GUILLEMINAULT, C., 1985. Abnormal breathing patterns during sleep in diabetes. *Annals of Neurology*, 17(4), 391-395.

MOSS, T.H. and SILLS, D.L., 1981. The Three Mile Island nuclear accident : lessons and implications. New York, N.Y.: New York Academy of Sciences.

NAISMITH, S.L., WINTER, V.R., HICKIE, I.B. and CISTULLI, P.A., 2005. Effect of oral appliance therapy on neurobehavioral functioning in obstructive sleep apnea: a randomized controlled trial. *J Clin Sleep Med*, 1, 374-380.

NAKANO, H., IKEDA, T., HAYASHI, M., OHSHIMA, E. and ONIZUKA, A., 2003. Effects of body position on snoring in apneic and nonapneic snorers. *Sleep*, 26(2), 169-172.

NATIONAL COMMISSION ON SLEEP DISORDERS RESEARCH, 1992. Report of the National Commission on Sleep Disorders Research Washington, DC: .

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE (NICE), 28 November 2007, 2007a-last update, IPG241 Soft-palate implants for obstructive sleep apnoea : Guidance

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE (NICE), 28 November 2007, 2007b-last update, IPG240 Soft-palate implants for simple snoring: Guidance.

NETZER, N.C., STOOHS, R.A., NETZER, C.M., CLARK, K. and STROHL, K.P., 1999. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Annals of Internal Medicine*, 131(7), 485-491.

NG, A.T., GOTSOPOULOS, H., QIAN, J. and CISTULLI, P.A., 2003. Effect of oral appliance therapy on upper airway collapsibility in obstructive sleep apnea. *American journal of respiratory and critical care medicine*, 168(2), 238-241.

NG, A.T., QIAN, J. and CISTULLI, P.A., 2006. Oropharyngeal collapse predicts treatment response with oral appliance therapy in obstructive sleep apnea. *Sleep*, 29(5), 666-671.

NHS QUALITY IMPROVEMENT SCOTLAND, 2008. Continuous Positive Airway Pressure (CPAP) for the treatment of obstructive sleep apnoea / hypopnoea syndrome - Resource & Cost Impact Report. NUCKTON, T.J., GLIDDEN, D.V., BROWNER, W.S. and CLAMAN, D.M., 2006. Physical examination: Mallampati score as an independent predictor of obstructive sleep apnea. *Sleep*, 29(7), 903-908.

OHAYON, M.M., GUILLEMINAULT, C., PRIEST, R.G. and CAULET, M., 1997. Snoring and breathing pauses during sleep: telephone interview survey of a United Kingdom population sample. *British Medical Journal (Clinical research ed.)*, 314(7084), 860-863.

OKSENBERG, A. and SILVERBERG, D.S., 1998. The effect of body posture on sleep-related breathing disorders: facts and therapeutic implications. *Sleep medicine reviews*, 2(3), 139-162.

OLSON, L.G., AMBROGETTI, A. and TREVILLIAN, Z., 2002. A randomised crossover comparison of nasal CPAP and a mandibular advancement splint in mild obstructive sleep apnea. *Personal communication to Cochrane reviewers*.

OSMAN, E.Z., OSBORNE, J., HILL, P.D. and LEE, B.W.V., 1999. The Epworth Sleepiness Scale: can it be used for sleep apnoea screening among snorers? *Clinical Otolaryngology*, 24, 239-241.

O'SULLIVAN, R.A., HILLMAN, D.R., MATELJAN, R., PANTIN, C. and FINUCANE, K.E., 1995. Mandibular advancement splint: an appliance to treat snoring and obstructive sleep apnea. *American journal of respiratory and critical care medicine*, 151(1), 194-198.

PACK, A.I., 2006. Advances in sleep-disordered breathing. *American journal of respiratory and critical care medicine*, 173(1), 7-15.

PANG, K.P. and TERRIS, D.J., 2006/0. Screening for obstructive sleep apnea: an evidence-based analysis. *American Journal of Otolaryngology*, 27(2), 112-118.

PARTINEN, M., TELAKIVI, T., KOSKENVUO, M. and KARPIO, J., 1988. Do people know about their snoring? In: C.H. CHOUARD, ed, London: John Libbey, Eurotex Ltd, pp. 93-96.

PASKOW, H., 1987. We can control snoring! *Journal of the New Jersey Dental Association*, 59(1), 18-19.

PASKOW, H. and PASKOW, S., 1993. The adjustable soft palate lifter. *The Alpha Omegan*, 86(2), 33-4, 36.

PATEL, S.R., WHITE, D.P., MALHOTRA, A., STANCHINA, M.L. and AYAS, N.T., 2003. Continuous positive airway pressure therapy for treating sleepiness in a diverse population with obstructive sleep apnea: results of a meta-analysis. *Archives of Internal Medicine*, 163(5), 565-571.

PEKER, Y., HEDNER, J., NORUM, J., KRAICZI, H. and CARLSON, J., 2002. Increased incidence of cardiovascular disease in middle-aged men with obstructive sleep apnea: a 7-year follow-up. *American journal of respiratory and critical care medicine*, 166(2), 159-165. PENDLEBURY, S.T., PEPIN, J.L., VEALE, D. and LEVY, P., 1997. Natural evolution of moderate sleep apnoea syndrome: significant progression over a mean of 17 months. *Thorax*, 52(10), 872-878.

PEPIN, J.L., LEGER, P., VEALE, D., LANGEVIN, B., ROBERT, D. and LEVY, P., 1995. Side effects of nasal continuous positive airway pressure in sleep apnea syndrome. Study of 193 patients in two French sleep centers. *Chest*, 107(2), 375-381.

PEPPARD, P.E., YOUNG, T., PALTA, M., DEMPSEY, J. and SKATRUD, J., 2000. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA : the journal of the American Medical Association, 284(23), 3015-3021.

PEPPERELL, J.C., RAMDASSINGH-DOW, S., CROSTHWAITE, N., MULLINS, R., JENKINSON, C., STRADLING, J.R. and DAVIES, R.J., 2002. Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised parallel trial. *Lancet*, 359(9302), 204-210.

PERETZ, L., 2003. Restless Nights: Understanding Snoring and Sleep Apnea. New Haven, CT: Yale University Press.

PEREZ-PADILLA, J.R., SLAWINSKI, E., DIFRANCESCO, L.M., FEIGE, R.R., REMMERS, J.E. and WHITELAW, W.A., 1993. Characteristics of the snoring noise in patients with and without occlusive sleep apnea. *The American Review of Respiratory Disease*, 147(3), 635-644.

PHILLIPS, B., COOK, Y., SCHMITT, F. and BERRY, D., 1989. Sleep apnea: prevalence of risk factors in a general population. *Southern medical journal*, 82(9), 1090-1092.

PHILLIPS, B.A. and DANNER, F.J., 1995. Cigarette smoking and sleep disturbance. Archives of Internal Medicine, 155(7), 734-737.

PITSIS, A.J., DARENDELILER, M.A., GOTSOPOULOS, H., PETOCZ, P. and CISTULLI, P.A., 2002. Effect of vertical dimension on efficacy of oral appliance therapy in obstructive sleep apnea. *American journal of respiratory and critical care medicine*, 166(6), 860-864.

PRAZIC, M., 1973. Snoring and presbyacusis. *Acta Oto-Laryngologica*, 75(2), 216-219.

PUNJABI, N.M., WELCH, D. and STROHL, K., 2000. Sleep disorders in regional sleep centers: a national cooperative study. Coleman II Study Investigators. *Sleep*, 23(4), 471-480.

RAJALA, R., PARTINEN, M., SANE, T., PELKONEN, R., HUIKURI, K. and SEPPALAINEN, A.M., 1991. Obstructive sleep apnoea syndrome in morbidly obese patients. *Journal of internal medicine*, 230(2), 125-129.

RANDERATH, W.J., HEISE, M., HINZ, R. and RUEHLE, K.H., 2002. An individually adjustable oral appliance vs continuous positive airway pressure in mild-to-moderate obstructive sleep apnea syndrome. *Chest*, 122(2), 569-575.

RAUSCHER, H., FORMANEK, D. and ZWICK, H., 1995. Nasal continuous positive airway pressure for nonapneic snoring? *Chest*, 107(1), 58-61.

RECHTSCHAFFEN, A., BERGMANN, B.M., EVERSON, C.A., KUSHIDA, C.A. and GILLILAND, M.A., 1989. Sleep deprivation in the rat: X. Integration and discussion of the findings. *Sleep*, 12(1), 68-87.

REDLINE, S., KUMP, K., TISHLER, P.V., BROWNER, I. and FERRETTE, V., 1994. Gender differences in sleep disordered breathing in a community-based sample. *American journal of respiratory and critical care medicine*, 149(3 Pt 1), 722-726.

REDLINE, S. and STROHL, K.P., 1998. Recognition and consequences of obstructive sleep apnea hypopnea syndrome. *Clinics in chest medicine*, 19(1), 1-19.

RESNICK, H.E., REDLINE, S., SHAHAR, E., GILPIN, A., NEWMAN, A., WALTER, R., EWY, G.A., HOWARD, B.V., PUNJABI, N.M. and SLEEP HEART HEALTH STUDY, 2003. Diabetes and sleep disturbances: findings from the Sleep Heart Health Study. *Diabetes care*, 26(3), 702-709.

RICHARDSON, G.S., CARSKADON, M.A., FLAGG, W., VAN DEN HOED, J., DEMENT, W.C. and MITLER, M.M., 1978. Excessive daytime sleepiness in man: multiple sleep latency measurement in narcoleptic and control subjects. *Electroencephalography and clinical neurophysiology*, 45(5), 621-627.

RIVLIN, J., HOFFSTEIN, V., KALBFLEISCH, J., MCNICHOLAS, W., ZAMEL, N. and BRYAN, A.C., 1984. Upper airway morphology in patients with idiopathic obstructive sleep apnea. *The American Review of Respiratory Disease*, 129(3), 355-360.

ROBIN, P., 1934. Glossoptosis due to atresia and hypotrophy of the mandible. *Am J Dis Child*, 48, 541-547.

ROBIN, P., 1902. Demonstration pratique sur la construction et la mise enbouche d'un Nouvelle appareil de redressement. *Revue de Stomatologie*, 9, 561-590.

ROJEWSKI, T.E., SCHULLER, D.E., CLARK, R.W., SCHMIDT, H.S. and POTTS, R.E., 1982. Synchronous video recording of the pharyngeal airway and polysomnograph in patients with obstructive sleep apnea. *The Laryngoscope*, 92(3), 246-250.

ROSS, S.D., SHEINHAIT, I.A., HARRISON, K.J., KVASZ, M., CONNELLY, J.E., SHEA, S.A. and ALLEN, I.E., 2000. Systematic review and meta-analysis of the literature regarding the diagnosis of sleep apnea. *Sleep*, 23(4), 519-532.

ROTH, T., ROEHRS, T., ZORICK, F. and CONWAY, W., 1985. Pharmacological effects of sedative-hypnotics, narcotic analgesics, and alcohol during sleep. *The Medical clinics of North America*, 69(6), 1281-1288.

RYAN, C.F., 2005. Sleep x 9: an approach to treatment of obstructive sleep apnoea/hypopnoea syndrome including upper airway surgery. *Thorax*, 60(7), 595-604.

RYAN, C.F., LOVE, L.L., PEAT, D., FLEETHAM, J.A. and LOWE, A.A., 1999. Mandibular advancement oral appliance therapy for obstructive sleep apnoea: effect on awake calibre of the velopharynx. *Thorax*, 54(11), 972-977.

SAMSOON, G.L. and YOUNG, J.R., 1987. Difficult tracheal intubation: a retrospective study. *Anaesthesia*, 42(5), 487-490.

SARDESAI, M.G., TAN, A.K. and FITZPATRICK, M., 2003. Noise-induced hearing loss in snorers and their bed partners. *The Journal of otolaryngology*, 32(3), 141-145.

SCHMIDT-NOWARA, W., LOWE, A., WIEGAND, L., CARTWRIGHT, R., PEREZ-GUERRA, F. and MENN, S., 1995. Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. *Sleep*, 18(6), 501-510.

SCHMIDT-NOWARA, W.W., COULTAS, D.B., WIGGINS, C., SKIPPER, B.E. and SAMET, J.M., 1990. Snoring in a Hispanic-American population. Risk factors and association with hypertension and other morbidity. *Archives of Internal Medicine*, 150(3), 597-601.

SCHMIDT-NOWARA, W.W., MEADE, T.E. and HAYS, M.B., 1991a. Treatment of snoring and obstructive sleep apnea with a dental orthosis. *Chest*, 99(6), 1378-1385.

SCHMIDT-NOWARA, W.W., MEADE, T.E. and HAYS, M.B., 1991b. Treatment of snoring and obstructive sleep apnea with a dental orthosis. *Chest*, 99(6), 1378-1385.

SCHONHOFER, B., HOCHBAN, W., VIEREGGE, H.J., BRUNIG, H. and KOHLER, D., 2000. Immediate intraoral adaptation of mandibular advancing appliances of thermoplastic material for the treatment of obstructive sleep apnea. *Respiration; international review of thoracic diseases*, 67(1), 83-88.

SCHWAB, R.J., 2003. Pro: sleep apnea is an anatomic disorder. *American journal of respiratory and critical care medicine*, 168(3), 270-1; discussion 273.

SCHWAB, R.J., PASIRSTEIN, M., PIERSON, R., MACKLEY, A., HACHADOORIAN, R., ARENS, R., MAISLIN, G. and PACK, A.I., 2003. Identification of upper airway anatomic risk factors for obstructive sleep apnea with volumetric magnetic resonance imaging. *American journal of respiratory and critical care medicine*, 168(5), 522-530.

SCHWARTZ, A.R., GOLD, A.R., SCHUBERT, N., STRYZAK, A., WISE, R.A., PERMUTT, S. and SMITH, P.L., 1991. Effect of weight loss on upper airway collapsibility in obstructive sleep apnea. *The American Review of Respiratory Disease*, 144(3 Pt 1), 494-498.

SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK, 2003. Management of Obstructive Sleep Apnoea/Hypopnoea Syndrome in adults.

SCRIMA, L., BROUDY, M., NAY, K.N. and COHN, M.A., 1982. Increased severity of obstructive sleep apnea after bedtime alcohol ingestion: diagnostic potential and proposed mechanism of action. *Sleep*, 5(4), 318-328.

SETO, B.H., GOTSOPOULOS, H., SIMS, M.R. and CISTULLI, P.A., 2001. Maxillary morphology in obstructive sleep apnoea syndrome. *The European Journal of Orthodontics*, 23(6), 703-714.

SHADABA, A., BATTAGEL, J.M., OWA, A., CROFT, C.B. and KOTECHA, B.T., 2000. Evaluation of the Herbst Mandibular Advancement Splint in the management of patients with sleep-related breathing disorders. *Clinical otolaryngology and allied sciences*, 25(5), 404-412.

SHER, A.E., SCHECHTMAN, K.B. and PICCIRILLO, J.F., 1996/2. The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnea syndrome. *Sleep*, 19(2), 156-177.

SHER, A.E., 2002. Upper airway surgery for obstructive sleep apnea. *Sleep medicine reviews*, 6(3), 195-212.

SHNEERSON, J.M., 2005. Sleep Medicine - a guide to sleep and its disorders. Second edn. Blackwell Publishing.

SJOHOLM, T.T., LOWE, A.A., MIYAMOTO, K., FLEETHAM, J.A. and RYAN, C.F., 2000. Sleep bruxism in patients with sleep-disordered breathing. *Archives of Oral Biology*, 45(10), 889-896.

SOARES, M.C., DE AZEREDO BITTENCOURT, L.R., ZONATO, A.I. and GREGORIO, L.C., 2006. Application of the Kushida morphometric model in patients with sleep-disordered breathing. *Revista brasileira de otorrinolaringologia (English ed.)*, 72(4), 541-548.

STRADLING, J. and DOOKUN, R., 2009. Snoring and the role of the GDP: British Society of Dental Sleep Medicine (BSDSM) pre-treatment screening protocol. *British Dental Journal*, 206(6), 307-312.

STRADLING, J.R. and CROSBY, J.H., 1991. Predictors and prevalence of obstructive sleep apnoea and snoring in 1001 middle aged men. *Thorax*, 46(2), 85-90.

STRADLING, J.R. and CROSBY, J.H., 1990. Relation between systemic hypertension and sleep hypoxaemia or snoring: analysis in 748 men drawn from general practice. *British Medical Journal (Clinical research ed.)*, 300(6717), 75-78.

STRADLING, J.R., NEGUS, T.W., SMITH, D. and LANGFORD, B., 1998. Mandibular advancement devices for the control of snoring. *The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology*, 11(2), 447-450.

STROHL, K.P., 2003. Con: sleep apnea is not an anatomic disorder. *American journal of respiratory and critical care medicine*, 168(3), 271-2; discussion 272-3.

STROHL, K.P. and REDLINE, S., 1996. Recognition of obstructive sleep apnea. *American journal of respiratory and critical care medicine*, 154(2 Pt 1), 279-289.

STROHL, K.P. and REDLINE, S., 1986. Nasal CPAP therapy, upper airway muscle activation, and obstructive sleep apnea. *The American Review of Respiratory Disease*, 134(3), 555-558.

STUNKARD, A.J., SORENSEN, T.I., HANIS, C., TEASDALE, T.W., CHAKRABORTY, R., SCHULL, W.J. and SCHULSINGER, F., 1986. An adoption study of human obesity. *The New England journal of medicine*, 314(4), 193-198.

SWEERE, Y., KERKHOF, G.A., DE WEERD, A.W., KAMPHUISEN, H.A., KEMP, B. and SCHIMSHEIMER, R.J., 1998. The validity of the Dutch Sleep Disorders Questionnaire (SDQ). *Journal of psychosomatic research*, 45(6), 549-555.

TAASAN, V.C., BLOCK, A.J., BOYSEN, P.G. and WYNNE, J.W., 1981. Alcohol increases sleep apnea and oxygen desaturation in asymptomatic men. *The American Journal of Medicine*, 71(2), 240-245.

TAN, Y.K., L'ESTRANGE, P.R., LUO, Y.M., SMITH, C., GRANT, H.R., SIMONDS, A.K., SPIRO, S.G. and BATTAGEL, J.M., 2002. Mandibular advancement splints and continuous positive airway pressure in patients with obstructive sleep apnoea: a randomized cross-over trial. *European journal of orthodontics*, 24(3), 239-249.

TANGEL, D.J., MEZZANOTTE, W.S., SANDBERG, E.J. and WHITE, D.P., 1992. Influences of NREM sleep on the activity of tonic vs. inspiratory phasic muscles in normal men. *Journal of applied physiology (Bethesda, Md.: 1985)*, 73(3), 1058-1066.

TANGEL, D.J., MEZZANOTTE, W.S. and WHITE, D.P., 1991. Influence of sleep on tensor palatini EMG and upper airway resistance in normal men. *Journal of applied physiology (Bethesda, Md.: 1985), 70*(6), 2574-2581.

TERAN-SANTOS, J., JIMENEZ-GOMEZ, A. and CORDERO-GUEVARA, J., 1999. The association between sleep apnea and the risk of traffic accidents. Cooperative Group Burgos-Santander. *The New England journal of medicine*, 340(11), 847-851.

THORPY, M.J., 1990, revised 1997 and 2005. International classification of sleep disorders: Diagnostic and coding manual. Diagnostic Classification Steering Committee.

TURNER, T.H., DRUMMOND, S.P., SALAMAT, J.S. and BROWN, G.G., 2007. Effects of 42 hr of total sleep deprivation on component processes of verbal working memory. *Neuropsychology*, 21(6), 787-795.

UNITED STATES. PRESIDENTIAL COMMISSION ON THE SPACE SHUTTLE CHALLENGER ACCIDENT, 1986. Report to the President. Washington, D.C.: The Commission.

VAN DER HEIJDEN, K.B., SMITS, M.G. and GUNNING, W.B., 2006. Sleep hygiene and actigraphically evaluated sleep characteristics in children with ADHD and chronic sleep onset insomnia. *Journal of sleep research*, 15(1), 55-62.

VAN DONGEN, H.P., MAISLIN, G., MULLINGTON, J.M. and DINGES, D.F., 2003. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep*, 26(2), 117-126.

VANDERVEKEN, O.M., DEVOLDER, A., MARKLUND, M., BOUDEWYNS, A.N., BRAEM, M.J., OKKERSE, W., VERBRAECKEN, J.A., FRANKLIN, K.A., DE BACKER, W.A. and VAN DE HEYNING, P.H., 2008. Comparison of a custom-made and a thermoplastic oral appliance for the treatment of mild sleep apnea. *American journal of respiratory and critical care medicine*, 178(2), 197-202.

VINER, S., SZALAI, J.P. and HOFFSTEIN, V., 1991. Are history and physical examination a good screening test for sleep apnea? *Annals of Internal Medicine*, 115(5), 356-359.

WAGNER, A.G. and PRICE, R.R., 1987. An intraoral device to prevent snoring. *General dentistry*, 35(3), 212-213.

WALKER-ENGSTROM, M.L., RINGQVIST, I., VESTLING, O., WILHELMSSON, B. and TEGELBERG, A., 2003. A prospective randomized study comparing two different degrees of mandibular advancement with a dental appliance in treatment of severe obstructive sleep apnea. *Sleep & breathing* = *Schlaf & Atmung*, 7(3), 119-130.

WHITTLE, A.T., FINCH, S.P., MORTIMORE, I.L., MACKAY, T.W. and DOUGLAS, N.J., 1997. Use of home sleep studies for diagnosis of the sleep apnoea/hypopnoea syndrome. *Thorax*, 52(12), 1068-1073.

WRIGHT, J., JOHNS, R., WATT, I., MELVILLE, A. and SHELDON, T., 1997. Health effects of obstructive sleep apnoea and the effectiveness of continuous positive airways pressure: a systematic review of the research evidence. *British Medical Journal (Clinical research ed.)*, 314(7084), 851-860.

YOUNG, T., EVANS, L., FINN, L. and PALTA, M., 1997. Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. *Sleep*, 20(9), 705-706.

YOUNG, T., FINN, L. and PALTA, M., 2001. Chronic nasal congestion at night is a risk factor for snoring in a population-based cohort study. *Archives of Internal Medicine*, 161(12), 1514-1519.

YOUNG, T., PALTA, M., DEMPSEY, J., SKATRUD, J., WEBER, S. and BADR, S., 1993. The occurrence of sleep-disordered breathing among middle-aged adults. *The New England journal of medicine*, 328(17), 1230-1235.

YOUNG, T., SHAHAR, E., NIETO, F.J., REDLINE, S., NEWMAN, A.B., GOTTLIEB, D.J., WALSLEBEN, J.A., FINN, L., ENRIGHT, P., SAMET, J.M. and SLEEP HEART HEALTH STUDY RESEARCH GROUP, 2002. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. *Archives of Internal Medicine*, 162(8), 893-900.

YOUNG, T., SKATRUD, J. and PEPPARD, P.E., 2004. Risk factors for obstructive sleep apnea in adults. *JAMA* : *the journal of the American Medical Association*, 291(16), 2013-2016.

ZAGER, A., ANDERSEN, M.L., RUIZ, F.S., ANTUNES, I.B. and TUFIK, S., 2007. Effects of acute and chronic sleep loss on immune modulation of rats. *American journal of physiology.Regulatory, integrative and comparative physiology,* 293(1), R504-9.

ZWEIG, M.H. and CAMPBELL, G., 1993. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clinical chemistry*, 39(4), 561-577.