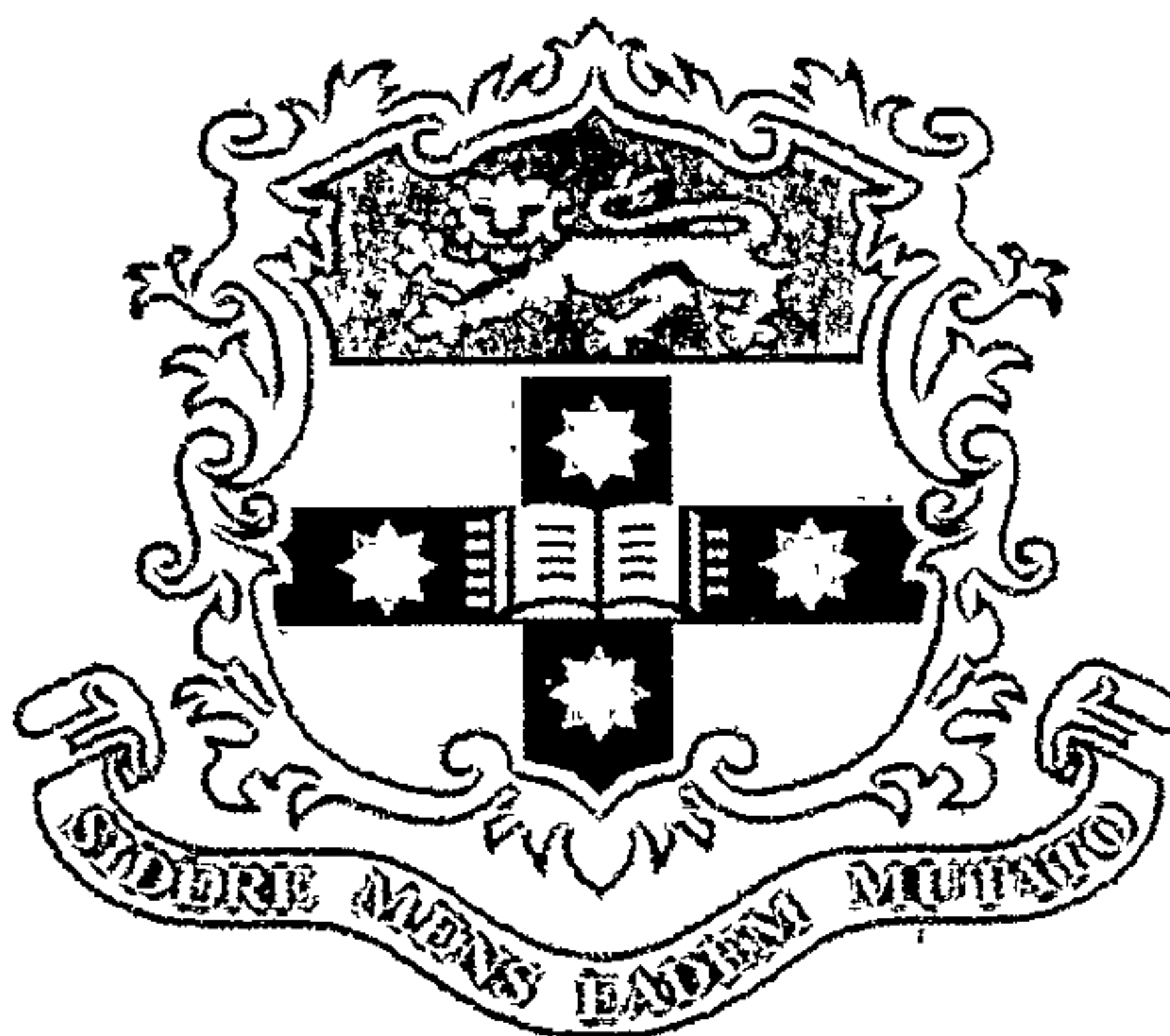


**THE EFFECT OF VERTICAL DIMENSION IN A MANDIBULAR
ADVANCEMENT SPLINT FOR OBSTRUCTIVE SLEEP APNOEA**



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DEDICATION

To my fiancée, Zenna, for her total devotion, patience and everlasting love. Thank you for your help and for your complete confidence in my abilities. You are outstanding.

To my mother, Antonia, who has given me everything – her strength, her love and her extraordinary faith. Thank you for being the best mother I could ever have. I am forever grateful.

To my father, Christopher, for his continual support, love and generosity and to my brother, George, for his endless love, support and friendship.

DECLARATION OF AUTHORSHIP

I, Andrew John Pitsis, postgraduate candidate for the Master of Dental Science degree, Discipline of Orthodontics, Faculty of Dentistry, University of Sydney, declare that this work has not been submitted to any other university or institution for a higher degree.

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ABBREVIATIONS

AHI	Apnoea Hypopnoea Index
AI	Apnoeic Index
AMP	Anterior Mandibular Positioner
BMI	Body Mass Index
CPAP	Continuous Positive Airway Pressure
CPITN	Community Periodontal Index of Treatment Needs
dB	Decibels
ECG	Electrocardiogram
EEG	Electroencephalogram
EMG	Electromyogram
EOG	Electro-oculogram
ESS	Epworth Sleepiness Scale
GLM	General Linear Model
kg/m ²	Kilograms per square metre
MAD	Mandibular Advancement Device
MAS	Mandibular Advancement Splint
min	Minutes
MinSaO ₂	Minimum arterial oxygen saturation level
mm	Millimetres
NREM	Non-Rapid Eye Movement
nCPAP	Nasal Continuous Positive Airway Pressure
OA	Oral Appliance
OSA	Obstructive Sleep Apnoea
REM	Rapid Eye Movement
RDI	Respiratory Disturbance Index
TMJ	Temperomandibular Joint
TST	Total Sleep Time
TRD	Tongue Retaining Device
UPPP	Uvulopalatopharyngoplasty

ABSTRACT

There has been no systematic comparison to determine the effect of vertical mandibular opening of Mandibular Advancement Splints (MAS) on the efficacy and side effects of obstructive sleep apnea (OSA), which was our aim. Twenty-three patients underwent a randomized, 2 period (AB/BA) crossover study with either MAS-1 or MAS-2 (additional 10mm opening) for 2-week periods. Data from the baseline polysomnograph, lateral cephalometric radiograph and questionnaire were compared to those of the treatment periods. MAS-1 was preferred by 78% of patients. One hundred percent and 91% of patients using MAS-1 and MAS-2 reported subjective improvements in snoring with 91% and 78% reporting every night use, respectively. There were significant improvements in AHI ($21 \pm 2/\text{hr}$ vs MAS-1: $8 \pm 1/\text{hr}$ and MAS-2: $10 \pm 2/\text{hr}$, $p < 0.001$), arousal index ($36 \pm 4/\text{hr}$ vs MAS-1: $26 \pm 4/\text{hr}$ and MAS-2: $24 \pm 4/\text{hr}$, $p < 0.001$) and for the longest apnea ($31 \pm 5\text{s}$ vs MAS-1: $16 \pm 3\text{s}$, $p < 0.02$ and MAS-2: $18 \pm 4\text{s}$, $p < 0.04$). Polysomnographic variables did not differ significantly between MAS's. Complete or partial success was achieved in 74% and 61% of patients using MAS-1 and MAS-2 respectively, which were not significantly different. Three cephalometric predictors for AHI were identified when using either MAS: narrowest posterior airway space, cranio-cervical angle and tongue length. In conclusion, the increased vertical opening in MAS-2 does not significantly effect treatment outcome and was not preferred by the majority of patients.

LITERATURE REVIEW

1. INTRODUCTION

The literature review details the current knowledge on snoring and obstructive sleep apnoea (OSA). The prevalence, pathophysiology, clinical features, consequences, diagnosis and management of OSA are discussed. It will focus on the design and use of Mandibular Advancement Splints (MAS) in the treatment of snoring and OSA.

Obstructive sleep apnoea (OSA) is caused by partial or complete collapse of the pharyngeal airway during sleep (McNamara *et al.*, 1994). 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, 1993). Decreased muscle tone during sleep and upper airway narrowing are aetiological factors (Cistulli and Sullivan, 1994). It affects approximately 4% of men and 2% of women in the middle-aged workforce (Young *et al.*, 1983). Continuous positive airway pressure (CPAP) was first reported in 1981 and is a highly effective and safe treatment (Sullivan *et al.*, 1981). Some patients poorly tolerate it, which makes compliance less than optimal (Kribbs *et al.*, 1993; Engleman *et al.*, 1996; Weaver, 1997). Thus there is a need for an alternative treatment which is safe, cheap, silent and less obtrusive.

Extensive research into treatment of OSA has developed since, including numerous oral appliance designs that primarily act by advancing the mandible during sleep. The postulated mechanism of action is to increase the anteroposterior dimension of the retroglossal space and thereby reduce the degree of pharyngeal airway collapse (Schmidt-Nowara *et al.*, 1995). Oral appliances are an effective form of treatment, including patients with moderate or severe OSA (Mehta *et al.*, 2001). At present it is uncertain which patients do best with such treatment. Similarly, it is not certain how appliance design influences treatment outcome, particularly vertical mandibular opening.

2. BACKGROUND

Guilleminault and colleagues (Guilleminault *et al.*, 1973) were the first to describe sleep apnoea as a syndrome. They described the interaction between sleep and the respiratory muscles of the chest and upper airway, which partially explained why the upper airway collapses during sleep, leading to OSA.

Sullivan (Sullivan *et al.*, 1981) from Australia published the first account of treating sleep apnoea patients with continuous positive airway pressure (CPAP). This initiated the most common and successful treatment currently known for OSA. Prior to this, tracheostomy was the only effective treatment (Westbrook and Millman, 1994). Sullivan's landmark paper prompted increasing research into the pathophysiology, incidence and treatment for sleep apnoea.

3. SNORING

3.1 Definition

Snoring is the noise emanating from the soft tissue portion of the oropharyngeal walls that occurs during inspiration (Bailey, 1997). It results from a partially obstructed upper airway during sleep and affects people of all ages. It is most common in overweight, middle-aged and elderly adults (American Sleep Disorders Association and Sleep Research Society {ASDA}, 1995). According to different studies, 20% of the adult population (60% men, 40% women) snore (Bailey, 1997); 44% men, 28% women (Young *et al.*, 1993) and 50% men, 19% women (Katsantonis *et al.*, 1990). Not all snorers have sleep apnoea but snoring is a cardinal symptom of almost all OSA patients (Chaudhary and Smith, 1991; Ryan *et al.*, 1991; Stradling and Crosby, 1991; Boudewyns and Van de Heyning, 1995).

The term "primary snoring" refers to snoring that is not accompanied by apnoea, hypoventilation or excessive sleepiness. However, snoring in some patients without apnoea has been associated with significant sleep disturbance, which leads to excessive daytime sleepiness. This is known as "upper airway resistance syndrome" (Guilleminault *et al.*, 1992) and is characterised by repeated arousals without recognisable hypopnoea or apnoea.

3.2 Pathophysiology

Snoring is an example of a flutter valve in which elements of the upper pharyngeal airway vibrate under the force of inspiratory pressure (Cistulli and Sullivan, 1994). The soft palate is the structure most important for the fluttering to occur.

During sleep, the muscles and soft tissues in the throat and mouth relax which causes narrowing of the airway. This decrease in the airway space increases the velocity of air flowing through during breathing. This causes the soft palate and uvula to vibrate resulting in snoring (Isono and Remmers, 1994).

3.3 Clinical Consequences

Snoring is a possible risk factor for hypertension, ischaemic heart disease and stroke, although its aetiological role in these conditions is not clear (Waller and Bhopal, 1989). It has been argued that age and obesity could confound the association between snoring and cardiovascular disease. However, the increased risk of these conditions is still demonstrated after adjusting for age and body mass index (Koskenvuo *et al.*, 1987; D'Alessandro *et al.*, 1990).

Snoring is recognised as a symptom that may be related to clinical conditions with significant morbidity. It is for this reason that treatment may be necessary, in addition to the fact that snoring is a social embarrassment and can be disturbing to family members.

4. SLEEP APNOEA

4.1 Definition

An *apnoea* is defined as a cessation of breathing during sleep that lasts for 10 seconds or more. The average number of episodes of apnoea per hour of sleep is termed the Apnoeic Index and at least 5 episodes must occur per hour for OSA to be diagnosed (Guilleminault and Dement, 1978).

A *hypopnoea* is when a 50% or greater reduction in tidal volume occurs, simultaneously with a 4% or greater reduction in blood oxygen saturation, lasting 10 seconds or more

(Wynne *et al.*, 1979; Guilleminault *et al.*, 1980). The average number of episodes of apnoea plus hypopnoea per hour during sleep is called the Apnoea Hypopnoea Index (AHI). AHI is used to quantify the degree of severity of OSA and to evaluate the efficacy of treatment by measuring the change in this index before and after therapy (Parisi *et al.*, 1988). The Respiratory Disturbance Index (RDI) is the same as AHI but also includes the average number of arousal per hour of sleep (Loubé *et al.*, 1999).

The term 'sleep apnoea syndrome', is when cessation of breathing occurs repeatedly during sleep for long enough periods to cause measurable blood deoxygenation (Berkow Robert, 1992). It refers to the occurrence of at least 5 apnoeas or hypopnoeas per hour of sleep when combined with two or more of the following features: excessive daytime sleepiness, loud snoring, witnessed apnoeas by the bed partner or unrefreshing sleep (Naughton, 1997).

4.2 Classification

Apnoeas and hypopnoeas can be classified into 3 types: central, obstructive or mixed.

1. *Central sleep apnoea* is characterised by the cessation of airflow and respiratory movements. It occurs when the brain fails to send impulses to the respiratory muscles so that breathing is not initiated.

2. *Obstructive sleep apnoea*, the most common of the three types of apnoea, is related to upper airway blockage despite impulses sent from the brain. It is a progressive and potentially life-threatening disorder in which breathing stops repeatedly for at least 10 seconds for each apnoeic event, during 7 hours of nocturnal sleep in both rapid eye movement (REM) stage and non-rapid eye movement (NREM) stage (*see Appendix I for definition of sleep stages*).

3. *Mixed apnoea* occurs when initially there is no inspiratory effort but subsequently when efforts are initiated the apnoea persists because the upper airway is collapsed (Guilleminault and Dement, 1978). Mixed apnoea occurs more often than central but less often than the obstructive type (Berkow Robert, 1992).

Current opinion has moved away from the early rigid definitions that, although useful for research, excluded many patients with disabling symptoms (Royal College of Physicians of London, 1993). For example, the individual with one or two apnoeas per hour, oxygen desaturation to 60-70% and impaired arousal reflexes due to autonomic neuropathy, can be far more vulnerable to the consequences of OSA than a healthy, asymptomatic 75 year old with 15 apnoeas per hour (Guilleminault *et al.*, 1977).

4.3 Prevalence

Prevalence studies vary widely, ranging from 1 to 24%, for groups of middle aged adults (Gisalon *et al.*, 1988; Cirignotta *et al.*, 1989; Young *et al.*, 1993). These studies have concluded that 2% of females and 4% of males in the USA, have a degree of sleep apnoea severe enough to warrant treatment. This makes OSA one of the most common medical disorders within the adult population and the second most common respiratory disorder to asthma (McNicholas, 2000).

The wide range in prevalence of OSA reported could be attributed to differences in the diagnostic criteria employed, patient groups studied or methodologies used. For instance, the percentage of the population with heavy snoring doubles when the bed partner contributes to the questionnaire (Stradling *et al.*, 1991). Population differences in age, obesity, alcohol consumption and genetic variability could also have a bearing on prevalence figures. OSA prevalence has been found to increase with age (Roehrs *et al.*, 1983) and obesity (Battagel, 1996).

Middle-aged (greater than 40 years) and overweight men (Guilleminault and Dement, 1978) are most prevalent to OSA but it can occur among infants, children (Brouillette *et al.*, 1982) and women (Wilholt and Suratt, 1987; Guilleminault *et al.*, 1988).

4.4 Pathophysiology

The upper airway includes the structures of the *nasopharynx, oropharynx and hypopharynx* (Worsnop *et al.*, 1998). The upper airway is a soft tissue structure with minimal bony support (Figures 1, 2). Each structural segment has been considered as a possible site of obstruction in OSA (Solow, 1992).

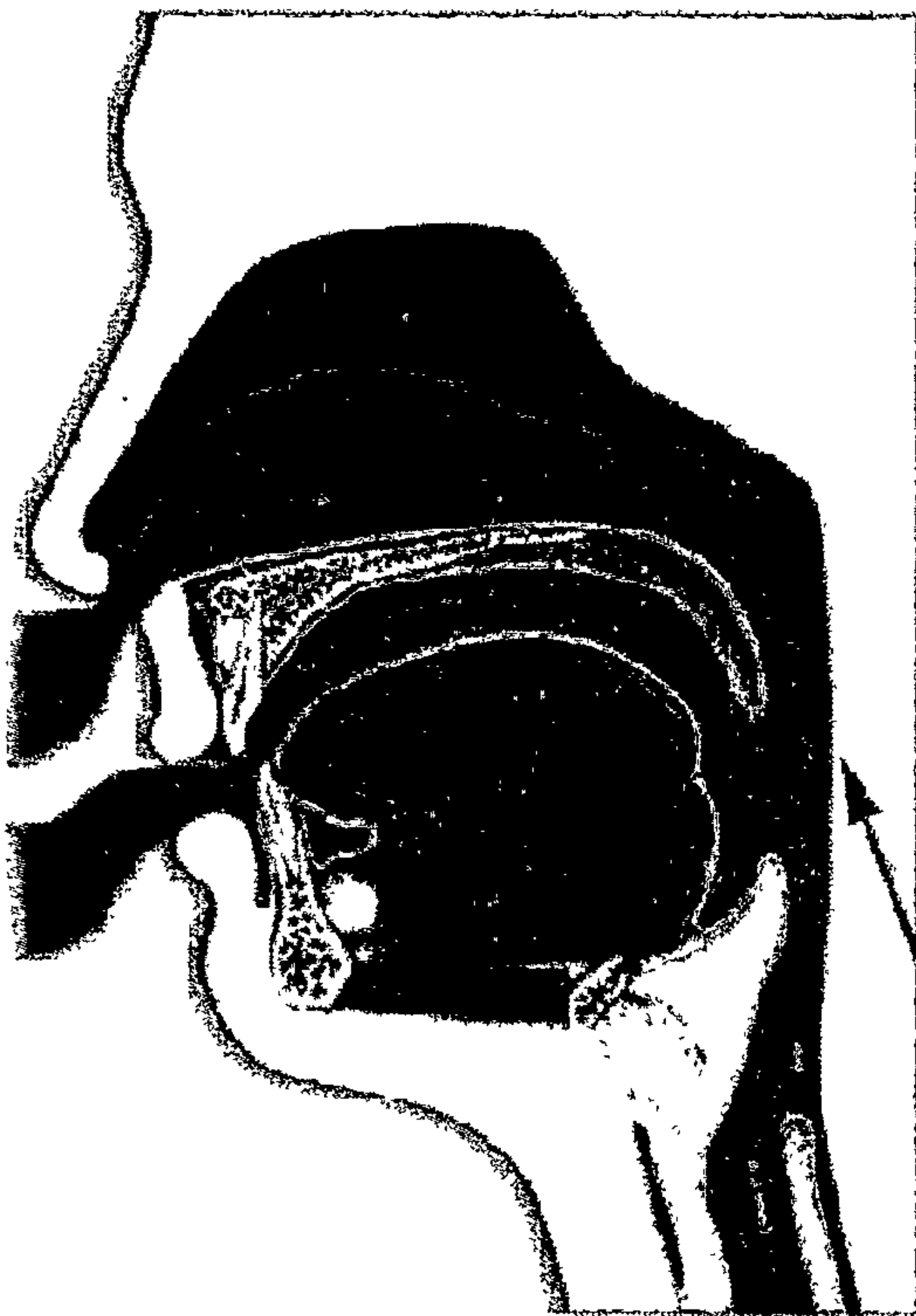


Figure 1. Anatomy of a normal airway



Figure 2. Anatomy of an OSA patient during an apnoea

Source: Ivanhoe, 1999

The precise mechanism of OSA is complex and not fully understood. Current evidence (Anch *et al.*, 1982; Lowe *et al.*, 1986; Rodenstein *et al.*, 1990; Hudgel, 1992; Cistulli and Sullivan, 1994) suggests that the aetiology is multifactorial due to:

- *Predisposing factors*
- *Anatomical structures* which may affect upper airway size

- *Functional processes* related to upper airway muscle activity

These aetiological factors in combination are thought to lead to a narrowing of the airway with repetitive closure during sleep. The aetiology of OSA is presented to allow an understanding of the rationale for OSA treatment.

4.4.1 Predisposing Factors

Numerous factors in combination may contribute to the severity of OSA. Pre-existing heart or lung disease makes breathing more difficult which leads to decreased blood oxygen tensions. Central nervous system depressants such as alcohol, sedatives and sleeping pills induce relaxation of the pharyngeal airway musculature, which can result in airway occlusion (Dolly and Block, 1982; Issa and Sullivan, 1982; Chaudhary and Smith, 1991; Battagel, 1996).

Increasing age has also been shown to predispose to OSA (Prinz, 1995; Strohl and Redline, 1996). Other factors associated are metabolic and endocrine disorders, in particular hypothyroidism, male gender, sleeping supine and familial tendency (McNamara *et al.*, 1994).

Obesity and excess fat in peripharyngeal and subcutaneous regions will also narrow the airway, encouraging its occlusion once the subject is supine (Homer *et al.*, 1989; Battagel, 1996). Obesity and neck circumference may be a significant predictor of OSA (Davies and Stradling, 1990; Katz *et al.*, 1990; Millman *et al.*, 1995). One study found that men and women were at greater risk for OSA if they had neck circumferences of 17 and 16 inches or greater, respectively (Davies and Stradling, 1990).

4.4.2 Anatomical Structures Affecting Upper Airway Size

A direct causal relationship between craniofacial structure and OSA has not been established (Miles *et al.*, 1996). However, studies using fluoroscopy (Suratt *et al.*, 1983), acoustic reflection (Katz *et al.*, 1990), fiberoptic endoscopy (Borowiecki *et al.*, 1978), cephalometric radiographs (DeBerry-Borowiecki *et al.*, 1988), computerised tomography (Lowe and Fleetham, 1991; Bhattacharyya *et al.*, 2000), cinematographic computerised tomography (Shepard *et al.*, 1990a) and magnetic resonance imaging (Abbey *et al.*, 1989) have demonstrated that OSA patients have narrower airways than control subjects.

These studies have limitations, such as studying patients are awake and are often in the erect posture. Despite this, they have implicated various skeletal and soft tissue craniofacial structures in the narrowing of the upper airway in patients with OSA. The sites of minimum cross-sectional area during wakefulness can vary between individual patients but the majority demonstrate maximum narrowing in the velopharyngeal (retropalatal) segment (Shepard *et al.*, 1991).

Anatomical structures affecting upper airway size can be divided into skeletal and soft tissue structures. Skeletal structures implicated are *the cranial base, maxilla, mandible, hyoid bone and head posture*.

Cranial Base

Bacon *et al.* (1990); Tangugsorn *et al.* (1995); Battagel and L'Estrange (1996) and Liu *et al.* (2000) have reported a reduction in the anterior cranial base length in OSA subjects. A more acute cranial base angle (Ba-SN) has been reported in OSA subjects by Jamieson *et al.* (1986), Battagel and L'Estrange (1996) and Battagel *et al.* (2000).

Maxilla and Mandible

Bimaxillary retrusion (Lowe *et al.*, 1986) or retrognathia of the mandible alone has been reported in OSA subjects (Jamieson *et al.*, 1986; Series *et al.*, 1992; Hochban and Bradenburg, 1994). Other studies however, have found no evidence of mandibular retrognathia in OSA subjects (DeBerry-Borowiecki *et al.*, 1988; Zucconi *et al.*, 1992). Tsuchiya *et al.* (1992) found mandibular retrognathia in patients with a high Apnoeic Index (AI) and low Body Mass Index (BMI). This suggests that skeletal abnormality may be an important aetiological factor in OSA in non-obese patients with a high AI.

Although a reduction in the length of the body of the mandible in OSA patients was reported by Rivlin *et al.* (1984), Battagel and L'Estrange (1996) and Battagel *et al.* (2000); Bacon *et al.* (1990), Tangugsorn *et al.* (1995) and Trenouth and Timms (1999) did not find any such reduction.

Therefore, in the anteroposterior dimension the cranial base, maxilla and mandible have been implicated as being shorter or retropositioned (Battagel and L'Estrange, 1996).

In the vertical dimension most studies have reported an increase in the lower anterior facial height with a concomitant increase in the maxillo-mandibular plane angle (Lowe *et al.*, 1986; Bacon *et al.*, 1990; Tsuchiya *et al.*, 1992; Tangugsorn *et al.*, 1995; Liu *et al.*, 2000).

Head Posture and Hyoid Bone

Flexion or extension of the head has been postulated by some authors to influence the dimensions of the oropharyngeal airway (Hellsing, 1989; Davies and Stradling, 1990). Solow *et al.* (1993) found that the average craniocervical angulation of OSA patients in the standing position was significantly greater than in controls. This was mainly mediated by a forward inclination of the cervical column and confirmed by Petri *et al.* (1994) and Solow *et al.* (1996).

Hyoid bone position has been found to be more inferior in relation to the mandibular plane for OSA subjects (Jamieson *et al.*, 1986; DeBerry-Borowiecki *et al.*, 1988; Tsuchiya *et al.*, 1992). The position of the hyoid bone becomes more inferior during growth and at adulthood it is at the level of C4 in normal subjects (Durzon and Brodie, 1962). In OSA patients it has been found between C4-C6 (Tangugsorn *et al.*, 1995).

The position of the hyoid bone however is subject to a high degree of variation because of physiological adaptations and changes of head position. During normal growth Winnberg *et al.* (1988) demonstrated that a more extended head posture dropped the hyoid apparatus inferiorly and anteriorly. Pae (1989) investigated the relationship between airway size and body position and suggested that patients with OSA had an inferiorly positioned hyoid bone and extended head postures. He concluded that a smaller than optimal airway induced an extended head posture for better airway patency and that an extended head posture elicited an inferiorly positioned hyoid bone. The contemporary view regarding an inferiorly positioned hyoid bone and an extended head position suggests that, rather than predisposing factors, these are physiological adaptations to lift away the base of the tongue and the soft palate from the posterior pharyngeal wall in order to alleviate the obstructive condition.

Soft tissue factors implicated as possible aetiological factors for OSA are *the tongue, soft palate and pharyngeal dimensions*.

Tongue

It is unclear on exactly what role the tongue plays in the aetiology of OSA. Some authors (Lowe *et al.*, 1986; DeBerry-Borowiecki *et al.*, 1988; Strelzow *et al.*, 1988; Battagel *et al.*, 2000) have reported a larger tongue length and area in OSA patients. Prachartam *et al.* (1994) found tongue size and area is normal but the functional space of the tongue is reduced, forcing the tongue backwards into the pharynx and diminishing the airway space at this level. Ryan *et al.* (1991) found that obese OSA patients have larger tongues and smaller airways. Do *et al.* (2000) found that tongue volume only positively correlated with BMI and neck circumference but there was no correlation with age or AHI.

Soft Palate

OSA patients have longer and thicker soft palates, with an area approximately 20% greater than normal subjects which results in further reduction of the airway (Jamieson *et al.*, 1986; Lyberg *et al.*, 1989; Battagel and L'Estrange, 1996; Battagel *et al.*, 2000). Pae *et al.* (1994) also showed that the thickness of the soft palate increases and the oropharyngeal cross sectional area decreases when a patient changes from an upright to supine position. Johnston and Richardson (1999) studied the longitudinal changes of the airway in 16 adults with a mean age of 20 years. A lateral cephalometric radiograph was taken at this age and 32 years later. It was found that the soft palate became longer and thicker and the oropharynx became narrower, which may explain the increased prevalence of OSA in later life.

Pharyngeal Dimensions

The dimensions of the pharynx are reduced (Battagel *et al.*, 2000), whether the subjects are investigated in the upright or supine position (Yildirim *et al.*, 1991) and independent of the assessment technique (Lowe *et al.*, 1986; DeBerry-Borowiecki *et al.*, 1988). The narrowest pharyngeal diameter is located behind the soft palate (Borowiecki *et al.*, 1978; Rojewski *et al.*, 1984) with about a 50% reduction of the pharyngeal diameter in OSA patients compared to controls.

Some authors (Djupestrand *et al.*, 1987; Strelzow *et al.*, 1988) have suggested that soft tissue abnormalities are more important than skeletal factors in patients with OSA. It has not yet been established whether the soft tissue abnormalities are in fact a consequence of the vibratory trauma associated with OSA, rather than the cause.

Three categories of OSA have been proposed based on the anatomical site of obstruction (Riley *et al.*, 1990):

- Type I (oropharynx): patients with larger soft palates and related factors, such as a longer hard palate with the resultant reduction of this region of the airway.
- Type III (hypopharynx): patients who are retrognathic with a concurrent reduced posterior airway space due to the posterior positioning of the tongue and/or macroglossia.
- Type II: is a combination of oro- and hypopharyngeal obstruction (Types I and III).

(Posterior airway space is the linear measurement between the base of the tongue and the posterior pharyngeal wall.)

4.4.3 Functional Processes Related to Upper Airway Muscle Activity

Breathing

Breathing occurs when the intercostal muscles and the diaphragm receive electrical impulses from the brain, causing them to contract. This leads to expansion of the thorax and creates a negative pressure inside the chest, drawing air into the lungs. This negative intraluminal pressure is transmitted to the upper airway creating the tendency for it to occlude. Activation and contraction of the upper airway dilator muscles such as the genioglossus and tensor palatini prevent this. The patency of the airway at any time is influenced by the balance of forces generated by the dilator muscles of the airway and the forces of inspiration that tend to occlude it. Normally the upper airway remains patent

during breathing because the dilating force exerted by the upper airway muscles exceeds the subatmospheric intraluminal pressure generated during inspiration (Remmers *et al.*, 1978; Suratt *et al.*, 1985; Howell *et al.*, 1989).

There is greater predisposition to closure in a narrower airway and a greater dependence on the dilator muscle activity to maintain patency. This is due to a greater subatmospheric inspiratory pressure that is generated in an attempt to achieve adequate airflow through the narrow airway (Cistulli and Sullivan, 1994).

Breathing And Sleeping

The awake person is capable of making the upper airway muscles contract sufficiently so that the upper airway does not collapse when they are lying down. Studies (Mezzanotte *et al.*, 1992, 1996) have indicated that the genioglossus and tensor veli muscles may have increased activity in the awake OSA patients and thus help maintain the shape of the upper airway. This is clearly demonstrated in OSA patients during wakefulness where genioglossus electromyographic (EMG) activity is reduced significantly following the application of continuous positive airway pressure. In normal controls, there is only a small reduction in EMG activity (White and Mezzanotte, 1993). White and Ballard (1990) also found that patients with sleep apnoea had considerable phasic inspiratory-linked electromyographic activity in the genioglossus, both awake and asleep, whereas little or no activity could be found in normal subjects.

However, when the patient assumes a supine position and goes to sleep, there is a decrease in the activity of the genioglossus and tensor veli palatini muscles that result in a decreased airway space (Adachi *et al.*, 1993). This decreased airway space may result in an increase in the velocity of the air passing through the airway, increasing the degree of subatmospheric pressure. The combination of decreased negative pressure and decrease in muscle activity allows the tongue and soft palate to move toward and often contact the posterior wall of the oropharynx, resulting in a decreased airway space. If the blockage is not complete, the increase in airflow velocity during inspirataton and expiration may cause the soft tissues, particularly the uvula, to vibrate. For others, this combination of negative pressure, decreased muscle activity and movement of the tongue and soft palate toward the

posterior wall of the pharynx results in a complete blockage of the airway. The resulting conditions may be snoring and/or OSA (Surrat *et al.*, 1983; Cartwright, 1984)

When there is a 50% or greater reduction in resting tidal volume a hypopnoea occurs and if the airway closes completely for 10 seconds or more then apnoea results. This leads to a drop in the body's blood oxygen level (hypoxaemia), an increase in the blood carbon dioxide concentration (hypercapnia) as well as an increase in blood pressure and heart rate (Ivanhoe *et al.*, 1999).

An apnoea is terminated by a brief arousal from sleep. During this arousal the subject partially awakes and the brain increases the stimulus to the upper airway muscles causing them to contract harder and thus open the upper airway. This enables the subject to take several large breaths and quickly corrects the oxygen and carbon dioxide levels. Normally the subject will quickly return to sleep without any recollection of arousal. This cycle of apnoea and arousal repeats itself for part or all of the sleep period.

In summary, these studies support the theory that the main underlying cause of sleep apnoea is airway narrowing due to relaxation of the upper airway muscles.

4.5 Clinical Features

4.5.1 Symptoms of OSA

Patients describe a number of symptoms that may be considered typical of OSA. Many of these symptoms are observed and reported by the spouse or partner and include (McNamara *et al.*, 1994):

- Snoring
- Excessive daytime somnolence (sleepiness)
- Witnessed apnoeas
- Nocturnal choking episodes
- Nocturnal arousals
- Sleep disruption/insomnia
- Abnormal motor activity in sleep

- Nocturia
- Gastroesophageal reflux
- Headaches (morning; nocturnal)
- Atypical chest pain
- Nocturnal sweating
- Diminished libido/impotence
- Concentration and memory deficit
- Personality changes/depression

Snoring and daytime sleepiness are the most likely reasons for a patient to consult a clinician. The symptoms of OSA can be divided into *nocturnal*, *daytime* and *neuropsychological*.

Nocturnal Symptoms

The most obvious problem is loud snoring (Schwab, 1996). The snoring typically crescendos whilst futile respiratory movements occur and then breaks off suddenly, as air finally enters the lungs. At this point the subject's sleep becomes lighter, they may wake up or the event may be accompanied by a period of choking. Some subjects complain that they wake up with a very sore and/or dry throat (Battagel, 1996).

It is not uncommon for patients to wake up numerous times per night as a consequence of apnoeic events, however most patients do not remember these events when they finally awaken in the morning (Flemons, 1996). An increased frequency of nocturia is a further symptom, waking the subject. OSA subjects and their partners also complain of restlessness that is manifested by involuntary kicking movements of the legs.

The chemical changes resulting from an apnoeic event (hypoxaemia and hypercapnia) are partially responsible for an increased cardiac workload together with an increase in blood pressure. The body's attempts to continue to breathe with an obstructed upper airway, places strain on the respiratory muscles and diaphragm. Severe medical conditions can result, including tachycardia, systmeic hypertension, pulmonary hypertension, acute pulmonary oedema, reversible high grade protein-urea and possibly Sudden Infant Death

Syndrome (Chaudhary and Smith, 1991; Boudewyns and Van de Heyning, 1995; Fletcher, 1995; Rappaport *et al.*, 1986)

Daytime Symptoms

Daytime somnolence is the most common daytime symptom of OSA patients. This is due to the frequent arousals from sleep, which interferes with the amount and quality of sleep (Ivanhoe *et al.*, 1999). Sleep apnoea also interferes with the normal architecture and stages of sleep (Flemons, 1996). Many OSA patients spend an inordinate amount of time in Stages 1 and 2 NREM sleep and much less time in Stages 3 and 4 NREM and REM sleep (*Appendix 1*). Nasal obstruction and headaches are common during the day for patients who suffer from OSA (Ferguson *et al.*, 1995)

Daytime hypersomnolence can be extreme and the subject may fall asleep at unexpected and inappropriate moments. Driving a car or operating machinery therefore presents a danger. Epidemiological studies have shown an increased motor vehicle accident rate in OSA patients including those with mild disease (Young *et al.*, 1997). In a study by Findley *et al.* (1988), 24% of a sample of OSA sufferers reported falling asleep whilst driving, at least once per week. Aldrich (1989) found that 31% of drivers with OSA had been involved in a road traffic accident within the last 5 years. Drivers suffering from excessive sleepiness were up to seven times as likely to be implicated in an accident than normal individuals (Findley *et al.*, 1988; Aldrich, 1989; Haraldsson *et al.*, 1990). Findley *et al.* (2000) studied 50 OSA patients, of which 36 were using CPAP. Using traffic records, the CPAP treated patients had no motor vehicle accidents in the 2-year study period compared with a significant 0.07 amount of accidents with those not using CPAP.

Driving simulator data suggest that sleepiness due to OSA is associated with a marked driving impairment comparable to that produced by a blood alcohol level above the legal limit for driving in the United Kingdom. This impairment was shown to respond to CPAP therapy in a controlled study by Hack *et al.* (2001).

Neuropsychological Symptoms

Poor memory and difficulty concentrating are further consequences of patients suffering from OSA, leading to an inability to remember everyday items. Some OSA subjects have

been described as short-tempered or as having undergone a personality change. OSA patients may even experience depression. These symptoms are thought to be the result of the change in sleep quality (Kales *et al.*, 1985; Bedard *et al.*, 1991).

4.5.2 Clinical Consequences of OSA

Many patients with sleep apnoea are overweight and therefore it is unclear to what extent the medical problems are a direct result of obesity or the effects of sleep apnoea itself. The following section details the medical conditions that sleep apnoea have been associated with.

Nocturnal hypoxaemia (inadequate blood and tissue oxygenation during sleep) occurs with sleep apnoea and if this is prolonged, hypertension and cardiac abnormalities may develop or be exacerbated, if these conditions already exist (Klitzman and Miller, 1994; Rapoport, 1994).

Cardiac arrhythmia, nocturnal angina and myocardial ischaemia may result, with the possibility of the latter culminating in a myocardial infarction (Guilleminault *et al.*, 1994). Although hypertension in patients with OSA is often confounded by the presence of obesity and increased age, some studies implicate sleep apnoea as an independent contributor to the development of hypertension (Carlson, 1994; Hoffstein, 1991).

Cerebral blood flow reduction is a further complication and there is an increased risk of suffering a cerebrovascular accident. An increase in the frequency of OSA in patients with recent stroke has been reported (Dyken, 1996), however, there is less evidence for this condition (Hedner *et al.*, 1994).

In summary, OSA patients are at increased risk of injury and cardiovascular disease compared to normal subjects, as well as a poorer quality of life (AHTAC, 1993). These consequences highlight the importance of OSA research and the rationale for adequate management of this condition.

4.6 Diagnosis

A careful history and clinical examination are the essential first steps in diagnosing OSA. This includes taking a history from the patient's spouse or partner. However, clinical evaluation has significant limitations and does not identify all OSA patients. One study identified only 52% of OSA patients based on history and physical examination (Viner *et al.*, 1991).

Polysomnography is an objective measure of respiration during sleep and is the most accepted diagnostic investigation distinguishing between simple snoring and true obstructive sleep apnoea (Aboussouan *et al.*, 1997). It monitors a wide range of parameters while the subject is asleep, including the assessment of respiratory and cardiac function. These include:

Electroencephalogram (EEG)	<i>to monitor brain wave activity</i>
Electro-oculogram (EOG)	<i>to monitor eye movements</i>
Electromyogram (EMG)	<i>attached below the chin and to each leg, to monitor throat muscle and leg muscle activity respectively</i>
Electrocardiogram (ECG)	<i>to monitor the heart's electrical activity, in particular arrhythmia</i>
Pulse oximetry	<i>to monitor the peripheral arterial oxygen saturation</i>
Respiratory thermistors	<i>to indicate whether the subject is breathing, by detecting the temperature of expired air</i>
Measurement of respiratory effort	<i>by measuring chest and abdominal wall movement</i>
Snore microphone	<i>snoring and choking sounds are charted</i>

The data is recorded, allowing the number of apnoeas and hypopnoeas to be quantified. This allows a definitive diagnosis to be made and permits an evaluation of the severity of the OSA (Battagel, 1996). The severity is established in order to make an appropriate treatment decision (ASDA, 1995).

There are limitations of polysomnography. The studies are carried out in a sleep laboratory and not in the patient's home. Portable monitoring devices are available, however these systems do not record all data (Flemons, 1996). Secondly, there is significant night-to-night variability in the apnoea index. Studies however have demonstrated that one overnight polysomnograph is sufficient and identifies OSA in 94% of subjects that would be detected by two consecutive overnight studies (Mendelson, 1994).

5. MANAGEMENT OF OSA

Management options for OSA are diverse because the aetiology is not precisely understood. Also, a number of different treatment approaches may be required as a result of possible multiple sites of airway obstruction in any one patient. The rationale for treatment of OSA is primarily based on two aspects: consequences of excessive daytime sleepiness and susceptibility to cardiovascular illness.

The treatment outcomes desired by the American Sleep Disorders Association (ASDA) include resolution of clinical signs and symptoms of OSA, normalisation of sleep quality, normalisation of the AHI and arterial oxygen saturation levels (ASDA, 1996).

CPAP remains the treatment of choice for OSA more than 20 years after its use was first reported (Sullivan *et al.*, 1981). Although CPAP is the most effective therapy, there are questions about compliance, tolerance and acceptance by patients. OAs and surgery provide alternative treatment approaches to the management of OSA.

The following section reviews the management strategies in treating OSA. A separate section will follow where the major focus will be on the treatment of OSA using OAs. It should be noted that the majority of treatments outlined below offer symptomatic relief rather than curative therapy.

5.1 Conservative Measures

Management of predisposing factors associated with sleep apnoea is an important aspect in the treatment of OSA. Predisposing risk factors include obesity, adenotonsillar hypertrophy, hypothyroidism, nasal obstruction and evening alcohol ingestion.

Conservative measures include advice on sleep posture, weight loss, avoidance of alcohol consumption and cessation of sedative drugs. Therapeutic control of co-existing medical conditions such as chronic obstructive airways disease, asthma and hypothyroidism are also important (Battagel, 1996).

Patients with known OSA are observed to have an increased frequency and duration of apnoeic episodes as well as a low haemoglobin oxygen saturation during sleep after alcohol ingestion (Guilleminault and Rosekind, 1981; Issa and Sullivan, 1982). These authors found that alcohol induced obstructive apnoea in heavy snorers who did not otherwise suffer from OSA. Alcohol ingestion decreases genioglossus activity in normal individuals (Krol *et al.*, 1984) and increases upper airway collapsibility (Issa and Sullivan, 1982) in both non-snorers and snorers. Such patients should be advised to reduce their alcohol intake.

The majority of patients with sleep apnoea present with obesity. It is a well recognised aggravating factor of upper airway obstruction during sleep (Peiser *et al.*, 1984). Weight loss may improve breathing during sleep by increasing lung volumes and resting arterial blood gas tensions (Thomas *et al.*, 1989) and by decreasing nasopharyngeal collapsibility (Suratt *et al.*, 1987; Rubinstein *et al.*, 1988). Weight loss has been shown to decrease the number of apnoeic events, although the relationship is not linear (Browman *et al.*, 1984). The number of apnoeas will decrease by approximately 50% with weight loss of 10%, suggesting that weight loss should receive a major focus in the management of OSA (Hudgel, 1996).

Many studies have investigated the effect of sleep posture and sleep apnoea severity (Cartwright, 1984; Cartwright *et al.*, 1985; Cartwright *et al.*, 1991; George *et al.*, 1988). The beneficial effects of a lateral sleeping position appear to be limited to patients with mild obesity and mild forms of sleep apnoea syndrome (Cartwright, 1984; George *et al.*, 1988). Patients with marked obesity and hypoxaemia benefit by sleeping in a more upright position at a 60 degree angle to the horizontal plane (McEvoy *et al.*, 1986).

5.2 Medical Treatment

CPAP is the most widely prescribed treatment for OSA (Hudgel, 1996) and can provide dramatic relief of symptoms by keeping the airway patent during sleep (Sullivan *et al.*, 1981). A continuous stream of air under pressure generated by an electrically driven pump is delivered to the pharynx via a nasal mask which counteracts the subatmospheric pressure occurring during an obstructive apnoea (Hudgel, 1996). It is 100% successful in keeping the airway open but the success of CPAP is dependent on the patient's compliance with wearing the device. One study found a compliance failure rate of approximately 35% in subjects who use CPAP (Hans *et al.*, 1997). Other studies have found treatment success using CPAP ranges from 62% (Ferguson *et al.*, 1996) to 70% (Ferguson *et al.*, 1997). Success was measured by a reduction in the AHI to less than 10 per hour with relief of symptoms.

Disadvantages Of CPAP

Compliance is a major limitation of CPAP therapy. To be effective it should be in place for 6 hours per night, 7 days a week (Battagel, 1996). Only 46% of users meet these strict criteria of regular use (Barone Kribbs *et al.*, 1993) and recent studies have shown that as many as 24% of patients discontinue therapy with CPAP (Reeves-Hoche *et al.*, 1994; Waldhom *et al.*, 1990). Reported long-term use of CPAP is 50% to 80%, and covert monitoring has shown that the average usage is less than 50% of the night. Less symptomatic patients are also more likely to discontinue treatment (Ferguson, 1996).

There are also a number of problems associated with the use of CPAP (Hudgel, 1992; Battagel, 1996; Naughton, 1997) including:

- Noise
- Cumbersome nature of CPAP (to both patient and partner)
- Nasal or oral dryness
- Nasal congestion
- Sneezing
- Sinusitis
- Nose bleeds and/or rhinorrhoea
- Skin reactions from facemask

- Nasal bridge abrasions
- Red eyes
- Aerophagia (swallowing of air)
- Electronically fed
- Cost

5.3 Dental Treatment

The role of OAs in the management of OSA is discussed in Section 6.

Randomised, cross-over studies using OAs and CPAP by Ferguson *et al.* (1996, 1997) and Clark *et al.* (1996) have demonstrated that OAs are less effective than CPAP for treating OSA. Efficacy of OAs verses CPAP ranged from 48% verses 62% (Ferguson *et al.*, 1996) to 55% verses 70% (Ferguson *et al.*, 1997). Treatment success was defined as a reduction in post-treatment AHI to less than 10 per hour. These studies have also demonstrated that patients prefer treatment with OAs over CPAP (Loube and Strauss, 1997).

Ferguson and colleagues (1996) reported that side effects were more common and the patients were less satisfied with CPAP when compared to use of OAs. In a more recent study, the same authors have reported no difference in side effects or compliance between CPAP and OAs (Ferguson *et al.*, 1997).

Rapid maxillary expansion for OSA patients with maxillary constriction has also been reported (Palmisano *et al.*, 1996). The study was a case report and further research is recommended to validate the use of this procedure in the treatment of OSA.

5.4 Surgical Treatment

Historically, tracheostomy was the surgical procedure undertaken for patients with OSA. It is the only operation shown to be consistently effective as a sole procedure in successfully treating obstructive sleep apnoea (Guilleniinault and Rosekind, 1981). Due to the cosmetic defects and the associated morbidity, patients do not favourably accept it and its use is limited to emergency situations (ASDA, 1996).

Surgery is indicated in patients who have an anatomical abnormality, such as nasal polyps, deviated nasal septa, enlarged tonsils or severe craniofacial abnormalities. Surgery is also indicated for those patients in whom conservative or medical treatments have been unsuccessful or have been unacceptable, who desire surgery and who have stable cardiopulmonary function (ASDA, 1996). The severity of OSA must be determined before initiating surgical therapy (ASDA, 1996).

Uvulopalatopharyngoplasty (UPPP) is the most widely used surgical technique. It is a procedure in which the uvula, part of the soft palate and tonsillar pillars are excised, with or without tonsillectomy. The process by which this surgical procedure works is unclear and although it does improve the symptoms of OSA, minimal improvement is observed in the apnoea pattern (Miljeteig *et al.*, 1994). The success rate of UPPP in treating OSA patients as reported by retrospective studies is only 50%. Criteria for success was defined in these studies as a reduction in AHI by 50% (Shepard and Olsen, 1990; Sher *et al.*, 1996). The incidence of complications with UPPP appear to be low, with the most common complication reported as velopharyngeal insufficiency for greater than one month (Sher *et al.*, 1996).

Maxillo-facial surgery is another surgical treatment option (Powell *et al.*, 1990). Advancement of the maxilla will increase the airway patency at the level of the soft palate and advancement of the mandible will increase the airway posterior to the tongue base. Mandibular advancement is thought to be effective in patients with mandibular retrognathia, however, more commonly bimaxillary surgery is undertaken. Advancement and repositioning of the hyoid bone are also recommended (Riley *et al.*, 1987; Riley *et al.*, 1990). Riley and colleagues (1993) reported a success rate of 97% in patients undergoing maxillary-mandibular advancement osteotomy with hyoid advancement. Criteria for success were based on AHI of less than 20 in addition to a 50% or greater reduction in AHI. When maxillary-mandibular advancement was carried out with no adjunctive procedures, the response rate was much lower at 20%. The response rate was defined as post-operative AHI of less than 10 (Waite *et al.*, 1989).

Distraction osteogenesis has shown a high success rate as shown by Molina *et al.*, (1998) with maxillary distraction and Cohen *et al.*, (1998) with mandibular distraction. Other surgical procedures include genioglossal advancement with or without hyoid myotomy and suspension and inferior sagittal mandibular osteotomy (ASDA, 1996).

6. THE ROLE OF ORAL APPLIANCES IN THE MANAGEMENT OF OSA

6.1 Background

Pierre Robin in 1902 was the first to report the use of any oral appliance for treatment of upper airway obstruction and mandibular deficiency (Robin, 1934). No further articles were published in the English literature on the use of OAs as a therapeutic method for snoring and OSA until the mid 1980's.

Cartwright and Samelson (1982) published the first description of the tongue retaining device (TRD), which was followed 2 years later by an abstract from Meier-Ewert and co-workers (1984) describing the use of a mandibular advancement device (MAD). Soll and George (1985) published a case report on the effectiveness of a modified one-piece activator advancement device, which resulted in improvement of the apnoea index and oxygen saturation.

Since then there has been a growing interest in the use of OAs in the treatment of snoring and OSA. In 1998, there were at least twenty-five different OAs being used in the treatment of snoring or OSA with the efficacy of individual OAs varying widely (Lowe, 1994). Since then, hundreds of different OAs have been made with varying designs and efficacy.

There is no consensus in the literature regarding the suitability of OA therapy for mild, moderate or severe cases of OSA. According to ASDA (1995), OA therapy is indicated as a primary treatment for patients with mild OSA and as a secondary treatment for patients with moderate and severe OSA who cannot tolerate treatment with CPAP. However, the definition of mild OSA is not specified in these practice parameters and even among

respiratory physicians there are no accepted criteria for classifying OSA severity. A report by Loube and Strauss (1997) suggests that the role of OAs in the treatment of OSA may be broader than that envisaged in the ASDA practice parameters. Recently, Mehta *et al.*, (2001) found that MAS therapy was an effective treatment even in patients with moderate or severe OSA.

OAs are divided into 2 types:

- Those that hold the tongue forward during sleep which are called tongue retaining devices (TRD) (Cartwright and Samelson, 1982)
- Those that advance the mandible. This group made up 93% of OA used in 1997 (Loube and Strauss, 1997) and has a variety of names, including: mandibular advancement devices (MAD) (Schmidt-Nowara *et al.*, 1995); mandibular advancement splints (MAS) (O'Sullivan *et al.*, 1995); and anterior mandibular positioning devices (AMP) (Clark *et al.*, 1996).

6.2 Tongue-Retaining Devices

6.2.1 Mechanism of Action

TRD hold the tongue forward during sleep. The tongue is placed into a cup or a bubble positioned between the front teeth and is held there by surface adhesion (Pack, 1994). The aim is to prevent backward motion of the tongue during sleep that could otherwise occlude the airway.

6.2.2 Evaluation of Efficacy

Studies show that TRD is an effective appliance in causing a reduction of the mean AHI (Cartwright and Samelson, 1982; Cartwright *et al.*, 1985; Cartwright *et al.*, 1988; Cartwright *et al.*, 1991). TRD are believed to be most successful in patients who are less than 50% above ideal weight and in whom their OSA is worse when they sleep in the supine position (Cartwright *et al.*, 1985). In another study, TRD was shown to be more effective when used in conjunction with behaviour modification (Cartwright *et al.*, 1991). In this study, a sample of 60 adult men with AHI values greater than 12.5 who had two or

more times the apnoea rate during supine sleep, in comparison with their lateral sleep rate, were assigned to four treatment groups:

- TRD only
- posture alarm
- TRD plus posture alarm
- health habit instruction

Using a 50% reduction in AHI as the index of successful treatment, 73% of the TRD group and 80% of the TRD plus posture alarm group were successful. The 15 subjects treated with the TRD alone had a reduction in mean AHI from 27 to 11. For the 15 subjects in the TRD plus posture alarm group, a mean AHI reduction from 31 to 8 was achieved, therefore demonstrating the effectiveness of this treatment.

However, none of the studies have shown that the TRD is successful at eliminating OSA by reducing the mean AHI to below 5, the level at which sleep apnoea is diagnosed. Other criticisms include a small sample size (12 to 15 patients), are retrospective case series and have provided no data about relief of snoring, sleepiness or long-term usage patterns. Therefore the efficacy of TRD in the successful treatment of OSA has not been proven objectively.

6.3 Mandibular Advancement Splints

6.3.1 Mechanism of Action

MAS are thought to treat OSA in the following ways (Bonham *et al.*, 1988; Lowe, 1990; Lowe, 1994; Ayas and Epstein, 1998):

- increase the airway space
- provide of a stable anterior position of the mandible
- advance the tongue and soft palate
- change the genioglossus and pharyngeal muscle activity

Mechanisms for the improvement in snoring include an increase in oropharyngeal and hypopharyngeal dimensions with associated reduction in turbulent airflow in the region

and/or an increase in passive tension within the pharyngeal wall. These events serve to reduce the vibration of these structures which is the source of the noise (Lugaresi *et al.*, 1984).

Woodson *et al.* (1997) used video endoscopy during sleep and found that the area of the retroglossal airway increased when using a MAS, however hypopharyngeal airway size decreased. Schwab *et al.* (1996) used magnetic resonance imaging to show that MAS's increase the lateral dimension of the airway space due to thinning of the pharyngeal walls. Masumi *et al.* (1996) demonstrated the functional consequence of increasing airway size. They found increases in flow during a forced inspiration with a MAS in place in subjects with and without OSA. The variability in the location of the airway changes in the various studies may be due to differences in appliance design, patient characteristics or imaging technique.

Several studies have evaluated the effect of oral appliances on pharyngeal muscle activity. Downward rotation of the mandible increases the baseline electromyogram activity of the genioglossus, an upper airway dilator muscle (Lowe *et al.*, 1990). Because oral appliances also cause downward rotations of the mandible, it has been postulated that some of the improvement in the AHI after treatment with an oral appliance may be due to an augmentation in genioglossus tone. Two studies cast doubt on this hypothesis. First, Ono *et al.* (1996) determined the effect of a tongue-retaining device on genioglossus muscle activity (assessed by surface electrodes) in 10 awake subjects with OSA and 6 control subjects. In non-OSA subjects, tongue protrusion resulted in increases in peak genioglossus electromyogram activity compared with baseline. In those with OSA however, decreases in electromyogram activity were noted after use of a tongue-retaining device. These data are consistent with a study by Mezzanotte *et al.* (1992) in which individuals with OSA had increased awake genioglossus tone compared with control subjects. The increased genioglossus activity was thought to represent neuromuscular compensation to prevent airway collapse.

Therefore, in Ono *et al.*'s study, the decrease in genioglossus muscle tone seen in those with OSA after use of an oral appliance may represent a decrease in the need for this compensation due to enlargement of the upper airway by the oral appliance. Also, a study

by Oshima *et al.* (1998) demonstrated that genioglossus electromyogram activity, as measured with subcutaneous electrodes, decreased with progressive mandibular advancement with an oral appliance in sleeping subjects with OSA. In conclusion therefore, the improvements in AHI after oral appliance treatment are likely due to changes in upper airway anatomy rather than augmentation of genioglossus activity.

Liu *et al.* (2000) found that the cross sectional area of the soft palate and the vertical distance of the hyoid bone to the mandibular plane decreased significantly with the use of an MAS. Thus the soft palate and hyoid bone are implicated in the mechanism of action of MAS.

Lowe *et al.* (2000) used fiber optic video endoscopy on 9 OSA patients with and without an MAS. They found no significant differences in hypopharynx or oropharynx cross sectional areas, but at the level of the velopharynx, the airway size was significantly increased.

6.3.2 Appliance Design

Numerous designs have been described for the treatment of snoring or sleep apnoea, but essentially they resemble a functional appliance. Most of these appliances use traditional dental techniques to attach the device to both dental arches and vary in design from relatively simple acrylic mouldings (Nakazawa *et al.*, 1992) to appliances incorporating metallic rod and tube fittings (Herbst attachments) and interarch elastics (Clark *et al.*, 1993; Clark *et al.*, 1996). Construction requires dental impressions, a protrusive bite registration and fabrication by a dental laboratory. Prefabricated forms are also available and according to a survey by Loube and Strauss (1997), these designs represent 14% of OAs used by dentists to treat patients with OSA. 45% are custom made while 34% are adjustable and 7% are TRD.

Important aspects of MAS design include (Battagel, 1996):

- *Good retention to both the upper and lower teeth*

This is important to ensure that the maxilla or mandible does not dislodge out of the appliance during sleep.

- *Sufficient protrusion to prevent pharyngeal collapse in the supine position*

Some studies have proposed sufficient protrusion to be 75% of maximal protrusion (Clark *et al.*, 1993; O'Sullivan *et al.*, 1995). However, the degree of forward protrusion required may vary and some subjects show no alteration in airway dimensions even with maximal protrusion (L'Estrange *et al.*, 1995). Hence, there is no scientific basis in proposing 75% of maximal protrusion as the ideal advancement. Furthermore, the individual must tolerate the amount of protrusion. Since tolerance increases with time, splints capable of incremental advancement (such as Herbst and AMP used by Ferguson *et al.*, 1997) may have practical advantages although cost of fabrication will increase. Also, the side effects such as TMJ discomfort and occlusal changes may increase.

- *Vertical opening*

There are no randomized clinical crossover trials in the literature that systematically assess the effect of vertical mandibular opening on OSA. The amount of vertical mandibular opening varies greatly in the literature. There are many appliances that do not cause vertical mandibular opening (Snore guard used by Schmidt-Nowara *et al.*, 1991; Esmarch device used by Mayer and Meier-Ewert, 1995; MAS used by O'Sullivan *et al.*, 1995; Ferguson *et al.*, 1996). However, there are many appliances that do cause vertical mandibular opening (O'Sullivan *et al.*, 1995; Lamont *et al.*, 1998; Bloch *et al.*, 2000; Mehta *et al.*, 2001) even up to an interincisal space of 15mm (Lowe *et al.*, 1994).

O'Sullivan *et al.* (1995) used a MAS with 10mm of mandibular vertical opening to aid the retention during sleep by inducing passive tension in the jaw musculature. They also used a suggestion by Lowe (1993) for their design justification, who suggested that the displacement of the mandible anteriorly moves the tongue away from the posterior wall of the pharynx while displacement of it inferiorly moves the tongue away from the soft palate.

However, excess opening is thought to diminish the benefits to the airway from protrusion according to Battagel (1996). L' Estrange *et al.* (1996), used fluoroscopy on 6 subjects with OSA for assessing the upper airway dimension changes. They found that vertical mandibular opening resulted in synchronous posterior movement of both

the tongue and soft palate, with a consequent narrowing of the oropharyngeal airway space.

Lamont *et al.* (1998) compared two MAS's for 24 patients. Type A-MAS had maximal mandibular protrusion and 3-4mm interincisal opening whereas Type B-MAS had up to 70% maximal protrusion and 6-9mm of interincisal opening. Type A-MAS had no significant effect on AHI whereas Type B did, reducing AHI from 7.1 to 0.8. They concluded that splint design might have a considerable bearing on efficacy including the amount of vertical mandibular opening. Unfortunately the subjects could open their mouths during sleep so it is unsure whether the amount of vertical mandibular opening remained constant during polysomnography. Also, the amount of sagittal protrusion varied between each appliance, which may have had an effect on AHI reduction.

Bloch *et al.* (2000) also compared two MAS's for 24 patients. They compared a Herbst with 4-6mm of interincisal opening to that of a Monobloc with 5-10mm of interincisal opening. The initial AHI of 22.6 decreased significantly with both appliances to 8.7 and 7.9 respectively. They suspected that the difference in the vertical mandibular opening between the two MAS's may have had an effect on their efficacy. They thought it conceivable that a downward rotation of the mandible with jaw opening may result in a retrusive motion of the tongue base. Unfortunately the subjects could open their mouths during sleep so it is unsure whether the amount of vertical mandibular opening remained constant during polysomnography.

Bucca *et al.* (1999) reported that the number of apnoeas/hypopnoeas increased significantly when 6 edentulous male patients did not wear their full dentures at night. Supine lateral cephalometry showed that removal of dentures led to a striking decrease in the anteroposterior oropharyngeal wall distance from 1.5cm to 0.6mm.

It has also been reported that the vertical mandibular posture during sleep in patients with OSA is more open than in normal subjects, that it increases during apnoeic episodes and decreases at the termination of those episodes (Miyamoto *et al.*, 1999). This increase in vertical mandibular opening may be causing a collapse of the airway; however, it may also be the consequence of a stronger effort to breathe.

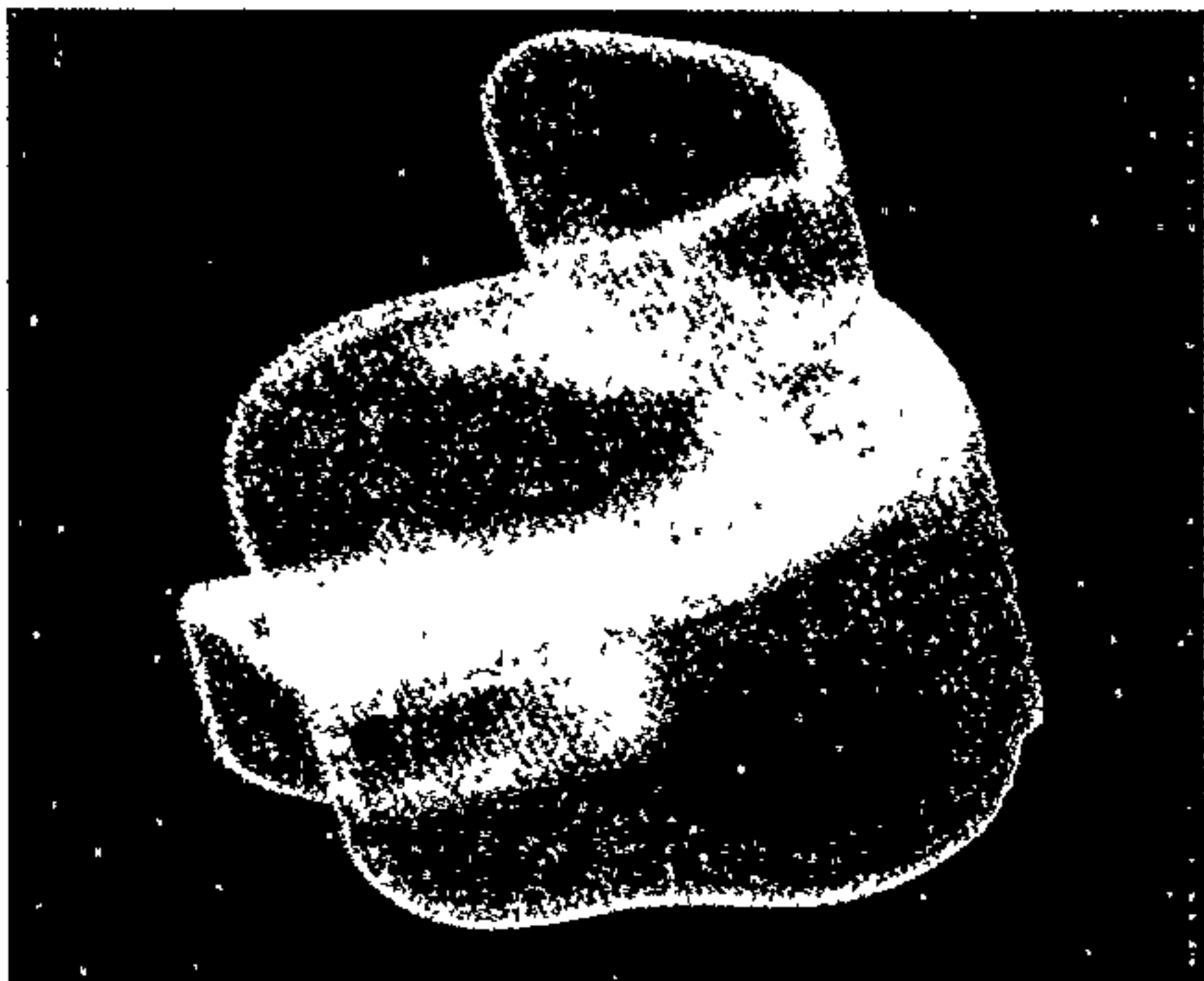
- *An anterior space between upper and lower segments of the splint*

This is helpful for those patients who are mouth breathers.

- *Full occlusal coverage*

This is to prevent long term vertical dental changes from eruption of teeth.

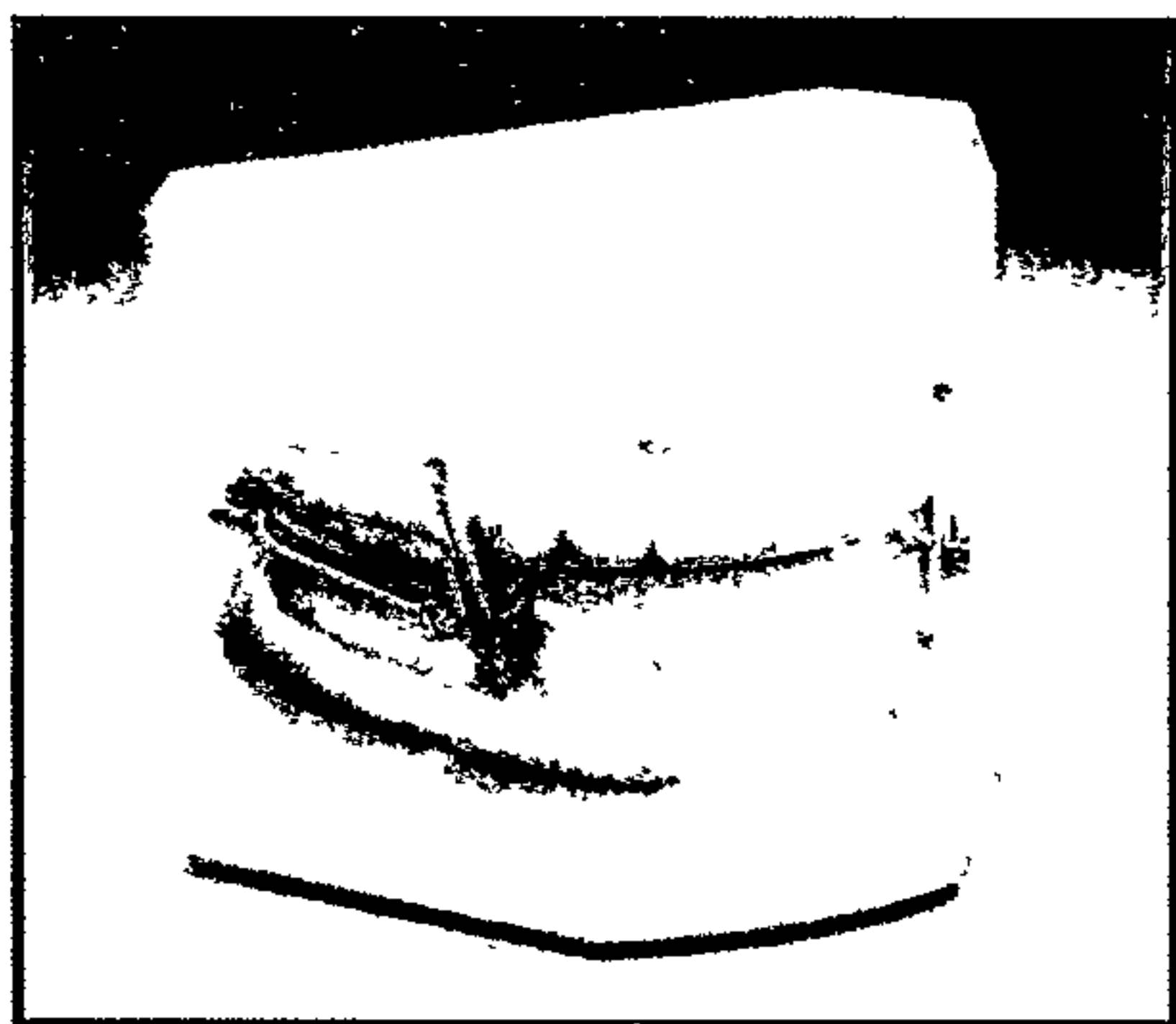
Apart from fulfilling the above criteria the ideal MAS should be inexpensive, easy to fabricate and well accepted by patients. It is evident from the literature that most splints do not meet these design criteria. In addition, there are no well-designed studies that directly compare the efficacy of specific appliances to each other.



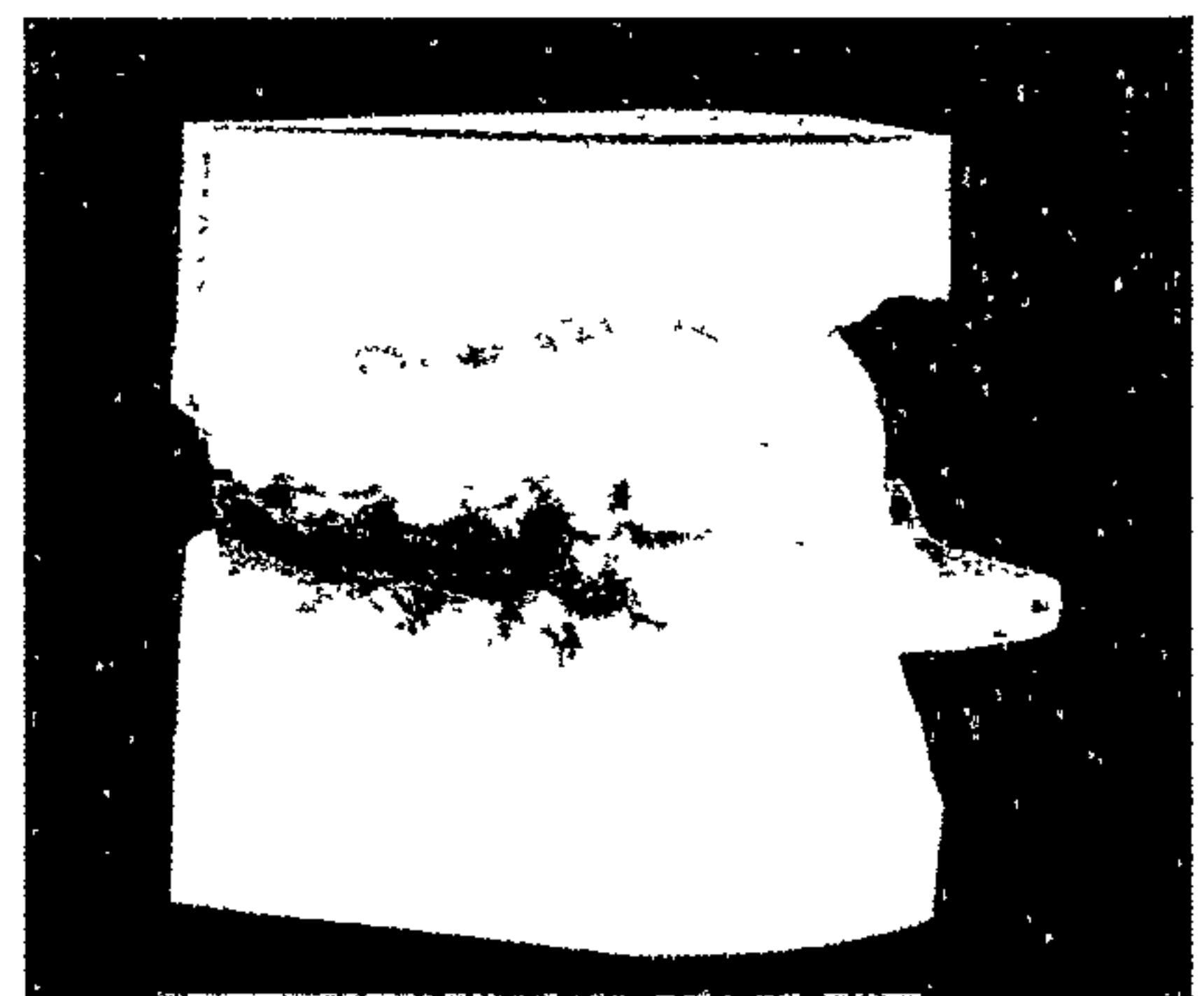
Herbst



NAPA



Snore-Eze



Klearway



Silent Nite

Figure 3. Examples of oral appliances used to treat Obstructive Sleep Apnoea.

Source: Mehta, 2001

6.3.3 Evaluation of Efficacy

Treatment consists of the *benefit*, including efficacy and patient compliance, and the *cost*, including side effects, complications and the financial cost of treatment (Schmidt-Nowara *et al.*, 1995). Efficacies of oral appliances include their effects on snoring and sleep apnoea as well as their secondary consequences, including sleep disturbance, daytime sleepiness and any long-term sequelae.

The following section reviews the scientific evidence regarding the efficacy of the MAS on snoring and OSA.

Efficacy of MAS in Snoring

Numerous studies (Schmidt-Nowara *et al.*, 1991; Clark *et al.*, 1993; O'Sullivan *et al.*, 1995; Ferguson *et al.*, 1996) in which snoring was assessed, representing a variety of devices, has shown that snoring improved in 76% to 100% of patients. However the improvement in snoring has been inferred from reports of patients or bed partners (Schmidt-Nowara *et al.*, 1995) and not measured objectively in relation to the sound intensity or snoring frequency. O'Sullivan *et al.*, (1995) has objectively measured snoring frequency as well as sound intensity. This study found that snore frequency significantly decreased by 18% and that sound intensity of snores (% snores ≥ 50 dB) also significantly decreased by 38% with MAS use. Bloch *et al.* (2000) showed a 36% reduction in snoring frequency with a Herbst type MAS and a 58% reduction with a monobloc type MAS. Mehta *et al.* (2001) found that the mean snoring frequency decreased by 47% and the mean intensity by 3 dB with MAS use as compared to the control plate.

Efficacy of MAS in OSA

1. Effect on AHI

All reports show a significant improvement in the average AHI with patients who use an appliance. Table 1 (pg. 44) outlines some of the studies performed for the efficacy of oral appliances. Examples include:

- Schmidt-Nowara *et al.*, (1991) evaluated 68 patients with snoring and/or OSA. In the 20 patients with follow-up polysomnography the Snore-Guard reduced the AHI by more than 50% and also significantly improved arterial oxygen saturation and sleep quality.
- Clark *et al.* (1993) reported their experience with a Herbst appliance in 24 patients with OSA. In the 15 patients who had polysomnography before and after treatment, 12 had a reduction in AHI to less than 15/h. Several of the patients who had a poor response to treatment did not have follow-up polysomnography, so the precise success rate is not known.
- Eveloff *et al.* (1994) reported a 53% success rate with a Herbst appliance in 19 patients with OSA. Success was defined as patients having an AHI less than 10/h with the MAS.
- O'Sullivan *et al.* (1995) showed that a MAS decreases AHI to less than 20/h in 12 of 17 patients in whom untreated AHI was between 20 to 60/h, and in 2 of 9 patients in whom untreated AHI was more than 60/h.
- Liu *et al.* (2000) showed a significant decrease in RDI in 21 of 22 patients from 40.3 to 11.7. The mandible was advanced 75% and the vertical opening was 7mm.
- Lowe *et al.* (2000) found a significant reduction in RDI from 32.6 to 12.1 in 38 patients using an MAS.
- Bloch *et al.* (2000) showed a reduction in AHI from 22.6 to 8.7 with a Herbst type MAS and to 7.9 with a monobloc type MAS.
- Mehta *et al.* (2001) showed a reduction in AHI from 30 to 14 with a MAS. This is the first prospective randomized placebo controlled crossover study of a MAS.

A review of publications reporting the effects of OAs on OSA carried out by Schmidt-Nowara *et al.* (1995), showed that the mean AHI before and with treatment were 42.6 and

18.8 respectively, an average reduction of 56%. Although 70% of the patients in these studies had at least a 50% reduction in AHI, many did not correct to normal levels and some patients did not improve or became worse. 51% of patients achieved success, defined as an AHI less than 10 with treatment. 39% of patients with an initial AHI of greater than 20 remained above that level with treatment.

In summary, OAs have been shown to be an effective method of treatment for OSA when AHI is used as a measure of effectiveness. However, whether it can be regarded as providing a successful treatment has yet to be established because the definition of success varies in each of the studies.

2. Effect on Arterial Blood Oxygenation

Numerous studies (Schmidt-Nowara *et al.*, 1991; Clark *et al.*, 1993; Ferguson *et al.*, 1996; Mehta *et al.*, 2001) have reported an improvement in oxygenation assessed by the minimum arterial oxygen saturation (MinSaO₂). In one study (O'Sullivan *et al.*, 1995), the median oxygen saturation during sleep remained unchanged, but the time in sleep with oxygen saturation of less than 90% was reduced from 4.4% to 3.1 % ($p>0.01$).

3. Effect on Sleep and Sleepiness

Polygraphic assessments of sleep before and during oral appliance treatment have shown a reduction in stage 1 sleep, an increase in slow wave (NREM) and REM sleep and a reduction in sleep fragmentation, mid-sleep wake time and arousals (Schmidt-Nowara *et al.*, 1995). Most patients reported a reduction in daytime sleepiness. This was a subjective evaluation based on patient reports.

6.3.4 Compliance

The data on long-term compliance of OAs vary from 100% (Ichioka *et al.*, 1991) to 52% (Clark *et al.*, 1993). This variation may be related to the length of follow up. In the first study, patients were queried after 3 to 21 months; in the latter study the follow up period was 3 years. Pantin *et al.*, (1999) had a 5-year follow up where 76% of patients reported regular use of their MAS. Another drawback of the reported compliance rates is they are based on patient reports, which may significantly over-estimate actual use (Reeves-Hoche *et al.*, 1994).

Table 1. Peer Reviewed Literature on the Efficacy of Oral Appliances on OSA

Authors	Sample Size	Study Design	Device	Mean AHI	Minimum SaO2	AHI with treatment			Sleep	Sleepiness
				without/with appliance	without/with appliance	<50% ^a	<10 ^b	>20 ^b		
Meier-Ewert et al., 1987	44	Case Series	Esmarch	50/23	-	59%	-	-	-	Improved, vigilance test
Bonham et al., 1988	12	Case Series	MAS	54/36	75/80	58%	-	-	-	9/12 improved, patient report
Lyon et al., 1990	15	Case Series	MAS	47% decrease	-	-	-	-	-	-
Ichioika et al., 1991	14	Case Series	MAS	32/9	Improved	100%	71%	9%	-	Improved, symptom score
Schmidt-Nowara et al., 1991	20	Case Series	Snore-guard	47/20	75/80	75%	40%	31%	Significantly less sleep fragmentation	18/35 improved, subjective scale
Nakazawa et al., 1992	12	Case Series	MAS	50/19	-	-	-	-	Significantly more delta and REM and less mid-sleep wake time	10/12 improved, patient report
Clark et al., 1993	15	Case Series	Herbst	48/12	Improved	87%	46%	20%	Less stage 1, more REM	Improved, subjective scale
Eveloff et al., 1994	19	Case Series	Herbst	35/13	84/88	-	53%	33%	-	-
O'Sullivan et al., 1995	51	Case Series	MAS	32/18	84/87	-	-	-	Decreased mean arousals from 31 to 19 per hour	24/39 improved, patient report
Clark et al., 1996	21	Cross-over	AMP	34/20	84/90	-	-	-	Less stage 1 and 2, more REM	Improved, patient report
Ferguson et al., 1996	19	Cross-over	Snore-guard	20/10	83/84	-	48%	-	Less stage 1, more REM	-
Ferguson et al., 1997	19	Cross-over	AMP	25/14	79/76	-	55%	-	More NREM, less REM	65% improved, subjective scale
Mehta et al., 2001	24	Cross-over	MAS	30/14	87/91	63%	-	-	More REM, less NREM	91% improved, subjective scale

6.3.5 Side Effects

Tables 2 (pg. 46) outlines the literature of the side effects with the use of OAs including:

- discomfort
- occlusal changes
- sore teeth
- TMJ pain
- dryness of mouth
- salivation
- gum irritation
- bruxism

Excess salivation and transient discomfort after waking are commonly reported, but with regular use these symptoms subside (Schmidt-Nowara *et al.*, 1995). The published reports suggest that TMJ pain and occlusal changes are relatively uncommon occurrences.

Pantin *et al.*, (1999) showed that 14% (15) of 106 patients using MAS over a 5-year period had occlusal changes. 13 patients had a 1mm decrease in overjet while the other 2 patients had a 1.5mm and 3mm decrease in overjet. The proportion of patients with occlusal change increased with the length of use of the MAS up to 2 years. Beyond 2 years the proportion remained relatively the stable. Other side effects included excess salivation (38%), xerostomia (28%), TMJ pain (33%) and dental discomfort (33%).

Bondemark *et al.* (1999) studied 30 patients after 2 years of use with a MAS giving 70% mean protrusion and 5mm vertical opening. A small but statistically significant forward (0.4mm) and downward (0.3mm) change in mandibular position were found.

Bondemark and Lindman (2000) studied 32 patients after 2 years of use with an MAS giving 70% mean protrusion and 5mm vertical opening. The patients TMJ's were studied clinically and none of the patients showed more than five symptoms of dysfunction.

In conclusion, the side effects of MAS's vary greatly. This is most probably due to patient selection/population and the fact that all MAS's vary in design.

Table 2. Peer Reviewed Literature on the Side Effects, Complications and patient Compliance using OA's

Authors	Sample Size	Device	Side Effects or Complications	Rate of Occurrence	Compliance	Length of Follow-up (years)
Ichioaka et al., 1991	14	MAS	Discomfort	14%	100%	0.4-1.75
Schmidt-Nowara et al., 1991	68	Snore-Guard	Discomfort	48%	75%	Mean 0.6
Nakazawa et al., 1992	12	MAS	Discomfort. Occlusal changes. TMJ dullness.	10% 21% 7%	67%	Mean 0.6
Clark et al., 1993	24	Herbst	TMJ pain	15%	50%	3
Eveloff et al., 1994	19	Herbst	No pain	-	93%	1-3.5 (mean, 2)
O'Sullivan et al., 1995	51	MAS	Jaw discomfort. Dryness of mouth. Excessive Salivation. Gum irritation, Bruxing	67% 39% 22% 8% 6%	79%	-
Clark et al., 1996	21	AMP	Did not evaluate side effects	-	81%	0.25-.0.85
Ferguson et al., 1996	19	Snore-Guard	Sore teeth, sore jaw muscles, excess salivation	-	60%	0.33
Ferguson et al., 1997	19	AMP	Sore teeth, sore jaw muscles, excess salivation, difficulty in chewing	-	70%	0.33

Adapted from: Schmidt-Nowra *et al.*, (1995)

6.3.6 Predictors of Treatment Response

Attempts have been made to predict treatment success with OAs. In 3 studies (Schmidt-Nowara *et al.*, 1991; Eveloff *et al.*, 1994; O'Sullivan *et al.*, 1995; Schmidt-Nowara *et al.*, 1991) success was related to the initial AHI. Two studies (Schmidt-Nowara *et al.*, 1991; O'Sullivan *et al.*, 1995) suggested success would be unlikely with an AHI of less than 60, but substantial improvement has been reported in patients with AHI greater than 60 (George, 1987; Lowe *et al.*, 1990; Clark *et al.*, 1993; Eveloff *et al.*, 1994).

Cephalometric parameters have also been considered to predict post treatment AHI (Eveloff *et al.*, 1994; Mayer and Meier-Ewert, 1995). Mehta *et al.* (2001) used a multiple regression analysis to identify neck circumference, baseline AHI, mandibular plane angle and posterior airway space as predictors of treatment outcome.

7. FUTURE DIRECTIONS

Electrical pacing

Electrical pacing using the submental approach was initially attempted by Miki *et al.* (1989) who showed favourable results in a small number of OSA patients. Guillemineault *et al.* (1995) attempted electrical stimulation using the submental and sublingual approaches in 7 patients and found that both approaches did not produce any significant change in AHI, obstructive duration, or the lowest oxygen saturation level. In addition, alpha-electroencephalography arousals were seen secondary to electrical stimulation when breaks of apnoea occurred. Schwartz *et al.* (1996) attempted pacing of the soft palate via a dental plate with a lower voltage and managed to abolish snoring, but they were unable to consistently stop apnoea. Hence, there is currently no convincing support for the use of electrical stimulation to treat OSA but may be an area of future research.

Radio-frequency ablation

Radio-frequency ablation has been used experimentally for cranial nerve problems, cancer, the Wolff-Parkinson-White syndrome and prostate hypertrophy for the past two decades. Using a radio-frequency generator, low-level energy is generated producing temperatures around 80 degrees celcius. Because human protein denatures at approximately 46 degrees celcius, the radio-frequency energy produces tissue necrosis, scar formation and a

reduction in tissue volume. Using this approach, Powell *et al.* (1997) were able to achieve a volume reduction of 26% in a pig's tongue. Radio-frequency ablation of the soft palate has been attempted in a small group of humans with simple snoring, upper-airway resistance syndrome, or mild OSA. The participants showed significant reduction in soft palate size, subjective snoring, scores on the Epworth sleepiness scale and excessive daytime sleepiness. However, there was worsening of AHI two and three days post-operatively due to oedema, which subsequently subsided and caused the AHI to return to the baseline value (Powell *et al.*, 1998). More research is needed before any conclusion can be drawn from this procedure.

Combination Treatment

Several studies suggest that oral appliances may be useful in combination with other interventions. For instance, Cartwright *et al.* (1991) found that the use of sleep position therapy combined with an oral appliance was slightly more effective than either used alone. Also, Millman *et al.* (1998) added oral appliance therapy to patients in whom uvulopalatopharyngoplasty had failed and found that a significant proportion (10 of 24 subjects) experienced a reduction in the AHI to less than 10 per hour with the appliance. Further prospective studies are needed to determine whether the combination of an oral appliance and uvulopalatopharyngoplasty is better than either one alone.

The combination of available treatments as well as those that require validation may provide more efficacious treatment of patients with OSA.

On the horizon for the field of oral appliance therapy is the introduction of a compliance monitor that will allow an objective determination of appliance usage. In addition, several investigators are developing systems that would allow overnight titration of oral appliances in the sleep laboratory.

8. CONCLUSION

Although CPAP provides the most efficacious treatment for OSA, it is poorly tolerated. Mandibular Advancement Splints provide a treatment alternative for those in whom conservative management measures fail and/or who cannot tolerate CPAP. At present, the exact mechanism of action of MAS's is unclear.

Long-term studies with MAS therapy are still required to objectively measure performance and sleepiness as well as complications that may not emerge for several years. Perhaps previous authors will continue to follow their patients and report later on the long-term outcome.

There is a lack of randomized clinical trials on oral appliance therapy for OSA in the literature. Most of the published studies have several deficiencies including small sample size, with no control or comparison group and are usually retrospective in design. Also, treatment outcome criteria are usually poorly defined and subjective. Not all patients have polysomnography at baseline and during treatment and some studies exclude patients with severe OSA. The frequency, severity and duration of side effects are rarely reported and predictors of outcome are not known. Few studies have reported subjective compliance and there is a lack of description for appliance design, including the optimal amount of mandibular protrusion. Only one recent study by Mehta *et al.* (2001) does not have the deficiencies mentioned and proves the efficacy of MAS in even moderate to severe OSA patients. There are however, no randomized clinical crossover trials in the literature that systematically assess the effect of vertical mandibular opening on OSA.

BIBLIOGRAPHY

AHTAC, The Australian Health Technology Advisory Committee: Treatment of Obstructive Sleep Apnoea. National Health and Medical Research Council, 1993.

ASDA, An American Sleep Disorders Association Report: Practice Parameters for the Treatment of Snoring and Obstructive Sleep Apnea with Oral Appliances. *Sleep*, 1995; 18: 511-513.

ASDA, An American Sleep Disorders Association Report: Practice Parameters for the Treatment of Obstructive Sleep Apnea in Adults: The Efficacy of Surgical Modifications of the Upper Airway. *Sleep*, 1996; 19: 152-155.

Abbey NC, Block AJ, Green D, Mancuso A, Hellard DW. Measurement of pharyngeal volume by digitized magnetic resonance imaging. Effect of nasal continuous positive airway pressure. *Am Rev Respir Dis*, 1989; 140: 717-723.

Aboussouan LS, Golish JA, Dinner DS, Strome M, Mendelson WB. Limitations and promise in the diagnosis and treatment of obstructive sleep apnoea. *Respiratory Medicine*, 1997; 91: 181-191.

Adachi S, Lowe AA, Tsuchiya M, Ryan CF, Fleetham JA. Genioglossus muscle activity and inspiratory timing in obstructive sleep apnea. *Am J Orthod Dentofacial Orthop*, 1993; 104: 138-145.

Aldrich MS. Automobile accidents in patients with sleep disorders. *Sleep*, 1989; 12: 487-494.

Anch AM, Remmers JE, Bunce H. Supraglottic airway resistance in normal subjects and patients with occlusive sleep apnea. *Journal of Applied Physiology*, 1982; 53: 1158-1163.

Ayas NT, Epstein LJ. Oral appliances in the treatment of obstructive sleep apnea and snoring. *Current Opinion In Pulmonary Medicine*, 1998; 4: 355-360.

Bacon WH, Turlot JC, Krieger J, Stierle J. Cephalometric evaluation of pharyngeal obstructive factors in patients with sleep apneas syndrome. *Angle Ortho*, 1990; 60: 115-122.

Bailey DR. Sleep disorders: Overview and relationship to orofacial pain. *Dent Clin North Am*, 1977; 41: 189-209.

Barone Kribbs N, Pack AI, Kline LR, *et al*. Objective measurements of patterns of nasal CPAP use by patients with obstructive sleep apnea. *Am Rev Respir Dis*, 1993; 147: 887-895.

Battagel JM. Obstructive Sleep Apnoea: Fact not Fiction*. *Br J Orthod*, 1996; 23: 315-324.

Battagel JM, L'Estrange PR. The cephalometric morphology of patients with obstructive sleep apnoea (OSA). *Eur J Orthod*, 1996; 18: 557-569.

Battagel JM, Johal A, Kotecha B. The cephalometric comparison of subjects with snoring and obstructive sleep apnoea. *Eur J Orthod*, 2000; 22: 353-365.

Bedard MA, Montplaisir J, Richer F, Rouleau 1, Malo J. Obstructive sleep apnea syndrome: pathogenesis of neuropsychological deficits. *J Clin Exp, Neuropsychol*, 1991; 13: 950-964.

Berkow Robert, Editor-in-Chief. *The Merck Manual of Diagnosis and Therapy*. 1992: Merck Research Laboratories.

Bhattacharyya N, Blake SP, Fried MP. Assessment of the airway in obstructive sleep apnoea syndrome with 3-dimensional airway computed tomography. *Otolaryngology & Head & Neck Surgery*, 2000; 123: 444-449.

Bloch KE, Iseli A, Zhang JN, Xie X, Kaplan V, Stoeckli PW, Russi EW. A Randomized, Controlled Crossover Trial of Two Oral Appliances for Sleep Apnea Treatment. *Am J Respir Crit Care Med*, 2000; 162: 246-251.

Bondemark L. Does 2 years nocturnal treatment with mandibular advancement splint in adult patients with snoring and OSAS cause a change in the posture of the mandible? *Am J Orthod Dentofacial Orthop*, 1999; 116: 621-628.

Bondemark L, Lindman R. Craniomandibular status and function in patients with habitual snoring and obstructive sleep apnoea after nocturnal treatment with mandibular advancement splint: a 2-year follow-up. *Eur J Orthod*, 2000; 22: 53-60.

Bonham PE, Currier GF, Orr WC, Othman J, Nanda RS. The effect of a modified functional appliance on obstructive sleep apnea. *Am J Orthod*, 1988; 94: 384-392.

Borowiecki B, Pollak CP, Weitzman ED, Rakoff S, Imperato J. Fibro-optic study of pharyngeal airway during sleep in patients with hypersomnia obstructive sleep-apnea syndrome. *Laryngoscope*, 1978; 88: 1310-1313.

Boudewyns AN, Van de Heyning PH. Obstructive sleep apnea syndrome in children: an overview. *Acta Otorhinolaryngol Belg*, 1995; 49: 275-279.

Brouillette RT, Fernbach SK, Hunt CE. Obstructive sleep apnea in infants and children. *Journal of Pediatrics*, 1982; 100: 31-40.

- Browman CP, Sampson MG, Yolles SF, *et al.* Obstructive sleep apnea and body weight. *Chest*, 1984; 85: 435-436.
- Bucca C, Carossa S, Pivetti S, Gai V, Rolla G, Preti G. Edentulism and worsening of obstructive sleep apnea. *Lancet*, 1999; 353: 121-122.
- Carlson JT, Hedner JA, Ejnell H, Peterson LE. High prevalence of hypertension in sleep apnea patients independent of obesity. *Am J Respir Crit Care Med*, 1994; 150: 72-77.
- Cartwright RD, Samelson C. The effects of a nonsurgical treatment for obstructive sleep apnea: the tongue retaining device. *J Am Med Assoc*, 1982; 248: 705-709.
- Cartwright RD. Effect of position on sleep apnoea severity. *Sleep*, 1984; 7: 110-114.
- Cartwright RD, Lloyd S, Lilic J, Kravitz H. Sleep position training as treatment for sleep apnea syndrome: a preliminary study. *Sleep*, 1985; 8: 87-94.
- Cartwright RD. Predicting response to the tongue retaining device for sleep apnea syndrome. *Arch Otolaryngol*, 1985; 111: 385-8.
- Cartwright RD, Stefoski D, Calderelli D, *et al.* Toward a treatment logic for sleep apnea: the place of the tongue retaining device. *Behav Res Ther*, 1988; 26: 121-126.
- Cartwright RD, Diaz F, Lloyd S. The effects of sleep posture and sleep stage on apnea frequency. *Sleep*, 1991; 14: 351-353.
- Cartwright RD, Ristanovic R, Diaz F, *et al.* A comparative study of treatments for positional sleep apnea. *Sleep*, 1991; 14: 546-552.
- Chaudhary BA, Smith JK. Obstructive sleep apnea syndrome. *J Med Assoc*, 1991; 80: 541-545.

Cirignotta F, D'Alessandro R, Partinen M, Zucconi M, Christina E, Geradi R, Cacciatore FM, Lugaresi E. Prevalence of every night snoring and obstructive sleep apnea among 30-60-yearold men in Bologna, Italy. *Acta Neurologica Scandinavica*, 1989; 79: 366-372.

Cistulli PA, Sullivan CE. Pathophysiology of sleep apnea. In: *Sleep and Breathing*. 1994, New York: Marcel Dekker Inc. 405-488.

Clark GT, Arand D, Chung E, Tong D. Effect of anterior mandibular positioning on obstructive sleep apnea. *Am Rev Respir Dis*, 1993; 147: 624-629.

Clark GT, Blumenfeld I, Yoffe N, Peled E, Lavie P. A Crossover Study Comparing the Efficacy of Continuous Positive Airway Pressure With Anterior Mandibular Positioning Devices on Patients With Obstructive Sleep Apnea. *Chest*, 1996; 109: 1477-1483.

Cohen SR, Simms C, Burstern FD. Mandibular distraction osteogenesis in the treatment of upper airway obstruction in children with craniofacial deformities. *Plastic and Reconstructive Surgery*, 1998; 101: 312-318.

D'Alessandro R, Magelli C, Gamberini G, *et al.* Snoring every night as a risk factor for myocardial infarction: A case-control study. *BMJ*, 1990; 300: 1557-1558.

Davies RJO, Stradling JR. The relationship between neck circumference, radiographic pharyngeal anatomy, and the obstructive sleep apnea syndrome. *European Respiratory Journal*, 1990; 3: 509-514.

DeBerry-Borowiecki B, Kukwa A, Blanks RH. Cephalometric Analysis For Diagnosis and Treatment of Obstructive Sleep Apnea. *Laryngoscope*, 1988; 98: 226-234.

Djupestrand G, Lyberg T, Krogstad O. Cephalometric analysis and surgical treatment of patients with obstructive sleep apnea. *Acta Otolaryngol*, 1987; 103: 551-557.

Do KL, Ferreyra H, Henly JF, Davidson TM. Does tongue size differ between patients with and without sleep-disordered breathing? *Laryngoscope*, 2000; 110: 1552-1555.

Dolly FR, Block AJ. Effect of flurazepam on sleep-disordered breathing and nocturnal oxygen desaturation in asymptomatic subjects. *Am J Med*, 1982; 73: 239-243.

Douglas NJ, Jan MA, Yildirim N, Warren PM, Drummond GB. Effect of posture and breathing route on genioglossal electromyogram activity in normal subjects and in patients with the sleep apnoea/hypopnea syndrome. *Am J Respir Crit Care Med*, 1993; 148: 1341-1345.

Durzon C, Brodie A. Growth behaviour of the hyoid. *Angle Orthod*, 1962; 32: 193-204.

Dyken ME, Somers VK, Yamada T, Ren Z, Zimmerman B. Investigating the relationship between stroke and obstructive sleep apnea. *Stroke and obstructive sleep apnea. Stroke*, 1996; 27: 40-47.

Engleman, HM, Asgari-Jirhandeh N, McLeod AL, Ramsay CF, Deary IJ, Douglas NJ. Self reported use of CPAP and benefits of CPAP therapy: a patient survey. *Chest*, 1996; 109: 1470-1476.

Eveloff SC, Rosenberg CL, Carlisle CC, Millman RP. Efficacy of a Herbst Mandibular Advancement Device in Obstructive Sleep Apnea. *Am J Respir Crit Care Med*, 1994; 149: 905-909.

Ferguson KA, Ono T, Lowe AA, Ryan CF, Fleetham JA. The Relationship Between Obesity and Craniofacial Structure in Obstructive Sleep Apnea*. *Chest*, 1995; 108: 375-381.

Ferguson KA, Ono T, Lowe AA, Keenan SP, Fleetham JA. A Randomized Crossover Study of an Oral Appliance vs Nasal-Continuous Positive Airway Pressure in the Treatment of Mild to Moderate Obstructive Sleep Apnea*. *Chest*, 1996; 109: 1269-1275.

Ferguson KA, Ono T, Lowe AA, Al-Majed S, Love LL, Fleetham JA. A short term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnoea. *Thorax*, 1997; 52: 362-368.

Findley LJ, Unverzagt ME, Suratt PM. Automobile accidents involving patients with obstructive sleep apnea. *Laryngoscope*, 1988; 98: 337-340.

Findley L, Smith C, Hooper J, Dineen M, Suratt PM. Treatment with nasal CPAP decreases automobile accidents in patients with sleep apnoea. *Am J Respir Crit Care Med*, 2000; 161: 857-859.

Fleetham JA, Ferguson KA, Lowe AA, Ryan CF. Oral Appliance Therapy for the Treatment of Obstructive Sleep Apnea. *Sleep*, 1996; 19: S288-S290.

Flemons WW. Sleep Apnea: Internet Article - Sleep Apnea Society of Alberta. 1996.

Fletcher EC. The relationship between systemic hypertension and obstructive sleep apnea: facts and theory. *Am J Med*, 1995; 98: 118-128.

George PT. A modified functional appliance for treatment of obstructive sleep apnea. *J Clin Orthod*, 1987; 21: 171-175.

George CF, Miller TW, Kryger MH. Sleep apnea and body position during sleep. *Sleep*, 1988; 11: 9099.

Gisalon T, Almqvist M, Eriksson G, Taube A, Boman G. Prevalence of sleep apnoea syndrome among Swedish men- an epidemiological study. *Journal of Clinical Epidemiology*, 1988; 41: 571-576.

Guilleminault C, Eldridge FL, Dement WC. Insomnia with sleep apnoea: A new syndrome. *Science*, 1973; 181: 856-858.

Guilleminault C, Tilkian A, Lehrman K, Forno L, Dement WC. Sleep apnoea syndrome: states of sleep and autonomic dysfunction. *J Neurol Neurosurg Psychiatry*, 1977; 40: 718-724.

Guilleminault C, Dement WC. *Sleep Apnea Syndromes*. 1978, New York: Liss, A.R.

Guilleminault C, Cumiskey J, Motta J. Chronic obstructive airflow disease and sleep studies. *Am Rev Respir Dis*, 1980; 122: 397-406.

Guilleminault C, Rosekind M. The arousal threshold: sleep deprivation, sleep fragmentation, and obstructive sleep apnea syndrome. *Bull Physiopathol Respir*, 1981; 17: 341-349.

Guilleminault C, Quera-Salva MA, Partinen M, Jamieson A. Women and the obstructive sleep apnea syndrome. *Chest*, 1988; 93: 104-109.

Guilleminault C, Stoohs R, Clerk A, Simmons J, Labonowski M. From obstructive sleep apnoea syndrome to upper airway resistance syndrome: consistency of daytime sleepiness. *Sleep*, 1992; 15: S13-S16.

Guilleminault C, Stoohs R, Partinen M, Kryger M. Mortality and Morbidity of Obstructive Sleep Apnea Syndrome. In: *Sleep and Breathing*. 1994, New York: Marcel Dekker, Inc. 557-574.

Guilleminault C, Powell N, Bowman B, Stoohs R. The effect of electrical stimulation on obstructive sleep apnoea syndrome. *Chest*, 1995; 107: 67-73.

Hack MA, Choi SJ, Vijayapalan P, Davies RJ, Stradling JR. Comparison of the effects of sleep deprivation, alcohol and obstructive sleep apnoea (OSA) on simulated steering performance. *Respiratory Medicine*, 2001; 95: 594-601.

Hans MG, Nelson S, Luks VG, Lorkovich P, Back S. Comparison of two dental devices for treatment of obstructive sleep apnea syndrome (OSAS). *Am J Orthod*, 1997; 111: 562-570.

Hedner JA, Wilcox 1, Sullivan CE. Speculations on the Interaction Between Vascular Disease and Obstructive Sleep Apnea. In: *Sleep and Breathing*. 1994, New York: Marcel Dekker, Inc. 823-846.

Hochban W, Bradenburg U. Morphology of the viscerocranium in obstructive sleep apnea syndromecephalometric evaluation of 400 patients. *Journal of Cranio-Maxillo-facial Surgery*, 1994; 22: 205-213.

Hoffstein V, Chan CK, Slutsky AS. Sleep apnea and systemic hypertension: a causal association review. *Am J Med*, 1991; 91: 190-196.

Homer RL, Mohiaddin RH, Lowell DG, Shea SA, Burman ED, Longmore DB. Sites and sizes of fat deposits around the pharynx in obese patients with obstructive sleep apnea and weight matched controls. *Eur Respir J*, 1989; 2: 613-622.

Howell DE, Jensen P, Funsten AW, Suratt PM. Activation of masseter muscles during sleep in obstructive sleep apnea. *Am Rev Respir Dis*, 1989; 139: 448.

Hudgel DW. The role of upper airway anatomy and physiology in obstructive sleep apnea. *Clin Chest Med*, 1992; 13: 383-398.

Hudgel DW. Treatment of Obstructive Sleep Apnea: A Review. *Chest*, 1996; 109: 1346-1358.

- Ichioaka M, Tojo N, Yoshizawa M, *et al.* A dental device for the treatment of obstructive sleep apnea: a preliminary study. *Otolaryngol Head Neck Surg*, 1991; 104: 555-558.
- Isono S, Remmers JE. Anatomy and physiology of upper airway obstruction. In: *Principles and Practice of Sleep Medicine*. 1994, Philadelphia: WB Saunders and Co. 642-656.
- Issa FG, Sullivan CE. Alcohol, snoring and sleep apnoea. *J Neurol Neurosurg Psychiatry*, 1982; 45: 353-359.
- Ivanhoe JR, Cibirka RM, Lefebvre CA, Parr G. Dental considerations in upper airway sleep disorders: A review of the literature. *J Prosthet Dent*, 1999; 82: 685-698.
- Jamieson A, Guilleminault C, Partinen M, Quera-Salva MA. Obstructive Sleep Apneic Patients Have Craniomandibular Abnormalities. *Sleep*, 1986; 9: 469-477.
- Johnston CD, Richardson A. Cephalometric changes in adult pharyngeal morphology. *Eur J Orthod*, 1999; 21: 357-362.
- Kales A, Caldwell AB, Cadieux RJ, Vela-Bueno A, Ruch LG, Mayes SD. Severe obstructive sleep apnea II. Associated psychopathology and psychosocial consequences. *J Chronic Dis*, 1985; 38: 427-434.
- Katsantonis GP, Freidman WH, Rosenblum BN, Walsh JK. The surgical treatment of snoring: a patient's perspective. *Laryngoscope*, 1990; 100: 138-140.
- Katz I, Stradling J, Slutsky AS, Zamel N, Hoffstein V. Do patients with obstructive sleep apnea have thick necks? *Am Rev Respir Dis*, 1990; 141: 1228-1231.
- Klitzman D, Miller A. Obstructive sleep apnea syndrome: complications and sequelae. *Mount Sinai Journal of Medicine*, 1994; 61: 113-121.
- Koskenvuo M, Kaprio J, Telakivi T, *et al.* Snoring as a risk factor for ischaemic heart disease and stroke in men. *BMJ*, 1987; 294: 16-19.

Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. *Am Rev Respir Dis*, 1993; 147: 887-895.

Krol RC, Knuth SL, Bartlett DJ. Selective reduction of genioglossal muscle activity by alcohol in normal human subjects. *Am Rev Respir Dis*, 1984; 129: 247-250.

Lamont J, Baldwin DR, Hay KD, Veale AG. Effect of two types of mandibular advancement splints on snoring and obstructive sleep apnoea. *Eur J Ortho*, 1998; 20: 293-297.

L'Estrange PR, Battagel JM, Nolan PJ, Harkness B, Jorgensen GI. The importance of a multidisciplinary approach to the assessment of patients with obstructive sleep apnoea. *Journal of Oral Rehabilitation*, 1995; 23: 72-77.

L'Estrange PR, Battagel JM, Harkness B, Spratley MH. A method of studying adaptive changes of the oropharynx to variation in mandibular position in patients with obstructive sleep apnoea. *Journal of Oral Rehabilitation*, 1996; 23: 72-77.

Liu Y, Zeng X, Fu M, Huans X, Lowe AA. Effects of mandibular repositioner on obstructive sleep apnoea. *Am J Orthod Dentofacial Orthop*, 2000; 118: 248-256.

Loube DI, Strauss AM. Survey of Oral Appliance Practice Among Dentists Treating Obstructive Sleep Apnea Patients*. *Chest*, 1997; 111: 382-386.

Loube DI, Gay PC, Strohl KP, Pack AJ, White DP, Collop NA. Indications for positive airway pressure treatment of adult obstructive sleep apnea patients: a consensus statement. *Chest*, 1999; 115: 863-836.

Lowe AA, Santamaria JD, Fleetham JA, Price C. Facial morphology and obstructive sleep apnea. *Am J Orthod*, 1986; 90: 484-491.

Lowe A. In: Neurophysiology of the jaws and teeth. 1990, London: McMillan Press Ltd. 322-368.

Lowe A, The tongue and airway. In: Otolaryngol Clin North Am. Vol. 23. 1990. 677-698.

Lowe A, Fleetham J, Ryan F, Mathews B. Effects of a mandibular repositioning appliance used in the treatment of obstructive sleep apnea on tongue muscle activity. In: Sleep and Respiration. 1990, New York: Wiley-Liss. 395-405.

Lowe AA, Fleetham JA. Two-and Three-Dimensional Analyses of Tongue, Airway and Soft Palate Size. Atlas of the Difficult Airway. 1991: Mosby Year Book. Chapter 8: 74-82.

Lowe AA. Dental appliances for the Treatment of Snoring and Obstructive Sleep Apnea. 2nd ed. In: Kryder MH, Dement WC, Editors. Principles and Practice of Sleep Medicine. 1993, Philadelphia: W.B. Saunders Co. 722-735.

Lowe AA, Sjolhm TT, Ryan CF, Fleetham JA, Ferguson KA, Remmers JF. Treatment, airway and compliance effects of a titratable oral appliance. Sleep, 2000; 23: S172-S8.

Lugaresi E, Cirignotta F, Coccagna G, Montagna P. Clinical significance of snoring. In Sleep and Breathing. 1984, New York: Marcel Dekker. 283-298.

Lyon HE, Phillips B, Theiss BL. Treatment of snoring and obstructive sleep apnea. Compend Contin Educ Dent, 1990; XIII: 416-420.

Masumi S, Nishigawa K, Williams A, Yan-Go FL, Clark GT. Effect of jaw position and posture on forced inspiratory airflow in normal subjects and patients with obstructive sleep apnea. Chest, 1996; 109: 1484-1489.

Mayer G, Meier-Ewert K. Cephalometric predictors for orthopaedic mandibular advancement in obstructive sleep apnoea. Eur J Orthod, 1995; 17: 35-43.

McEvoy RD, Sharp DJ, Thornton AT. The effects of posture on obstructive sleep apnea. *Am Rev Respir Dis*, 1986; 133: 662-666.

McNamara S, Cistulli PA, Sullivan CE, Strohl KP. Clinical Aspects of Sleep Apnea. In: *Sleep and Breathing*. 1994, New York: Marcel Dekker Inc. 493-528.

McNicholas WT. Obstructive Sleep Apnea Syndrome: Who Should be Treated? *Sleep*, 2000; 4: S187-S190.

Mehta A, Qian J, Petocz P, Darendeliler MA, Cistulli PA. A Randomized, Controlled Study of a Mandibular Advancement Splint for Obstructive Sleep Apnea. *Am J Respir Care Med*, 2001; 163: 1457-1461.

Meier-Ewert K, Schafer H, Kloss W. Treatment of sleep apnea by a protracting device. In: *Seventh European Congress on Sleep Research*. 1984.

Meier-Ewert K, Brosig B. Treatment of sleep apnea by prosthetic mandibular advancement. In: *Sleep related disorders and internal medicine*. 1987: Berlin: Springer-Verlag. 341-345.

Mendelson WB. Use of the sleep laboratory in suspected sleep apnea syndrome: Is one night enough? *Cleve Clin J Med*, 1994; 61: 299-303.

Mezzanotte WS, Tangel DJ, White DP. Waking genioglossus electromyogram in sleep apnea patients versus normal controls (a neurocompensatory mechanism). *J Clin Invest*, 1992; 89: 1571-1579.

Mezzanotte WS, Tangel DJ, White DP. Influence of sleep onset on upper-airway muscle activity in apnea patients versus normal controls. *Am J Respir Crit Care Med*, 1996; 153: 1880-1887.

Miki H, Hida W, Chonan T, Kikuchi Y, Takishima T. Effects of submental electrical stimulation during sleep on upper airway patency in patients with OSA. *Am Rev Respir Dis*, 1989; 140: 1285-1289.

Miles PG, Vig PS, Weyant RJ, Forrest TD, Rockette Jr HE. Craniofacial structure and obstructive sleep apnea syndrome- a qualitative analysis and meta-analysis of the literature. *Am J Orthod*, 1996; 109: 163-172.

Miljeteig H, Haight J, *et al.* Subjective and objective assessment of uvulopalatopharyngoplasty for the treatment of snoring and obstructive sleep apnea. *Am J Respir Crit Care Med*, 1994; 150: 1286-1290.

Millman RP, Carlisle CC, McGarvey ST, Eveloff SE, Levinson PD. Body fat distribution and sleep apnea severity in women. *Chest*, 1995; 107: 362-366.

Miyamoto K, Ozbek MM, Lowe AA, Sjolhm TT, Love LL, Fleetham JA, Ryan CF. Mandibular posture during sleep in patients with obstructive sleep apnoea. *Archives of Oral Biology*, 1999; 657-664.

Molina F, Ortiz Monasterio F, de la Paz Aguilar M, Burrera J. Maxillary Distraction: aesthetic and functional benefits in cleft lip-palate and prognathic patients during mixed dentition. *Plastic and Reconstructive Surgery*, 1998; 101: 951-963.

Nakazawa Y, Sakamoto T, Yasutake R, Yamaga K, Kotorii T, *et al.* Treatment of sleep apnoea with prosthetic mandibular advancement. *Sleep*, 1992; 15: 499-504.

Naughton M. Sleep apnoea- from social to medical consequences. *Modern Medicine of Australia*, 1997; 36-44.

O'Sullivan RA, Hillman DR, Mateljan R, Pantin C, Finucane KE. Mandibular Advancement Splint: An Appliance to Treat Snoring and Obstructive Sleep Apnea. *Am J Respir Crit Care Med*, 1995; 151: 194-198.

Ono T, Lowe AA, Ferguson KA, Fleetham JA. The effect of the tongue retaining device on awake genioglossus muscle activity in patients with obstructive sleep apnea. *Am J Orthod Dentofacial Orthop*, 1996; 110: 28-35.

Oshima T, Tsai WH, Hajduk EA, Remmers JE. Mandibular protrusion decreases genioglossus EMG during sleep in patients with obstructive sleep apnea. *Am J Respir Crit Care Med*, 1998; 157: 655.

Pack, Al. Obstructive sleep apnea. *Adv Intern Med*, 1994; 39: 517-566.

Pae E-K. A comparative study of the relationship between airway size, tongue activity and body position. 1989, University of British Columbia.

Pae EK, Lowe AA, Sasaki K, Price C, Tsuchiya M, Fleetham JA. A cephalometric and electromyographic study of upper airway structures in the upright and supine positions. *Am J Orthod Dentofacial Orthop*, 1994; 106: 52-59.

Palmisano RG, Wilcox I, Sullivan CE, Cistulli PA. Treatment of snoring and obstructive sleep apnoea by rapid maxillary expansion. *Aust NZ J Med*, 1996; 26: 428-429.

Pantin, CC, Hillman DR, Tennant M. Dental side effects of an oral device to treat snoring and obstructive sleep apnea. *Sleep*, 1999; 22: 237-240.

Parisi RA, Santiago TV, Edelman NH. Genioglossal and diaphragmatic EMG responses to hypoxia during sleep. *Am Rev Respir Dis*, 1988; 138: 610-616.

Peiser J, Lavie P, Ovnat A, Charuzi I. Sleep apnea syndrome in the morbidly obese as an indication for weight reduction surgery. *Ann Surg*, 1984; 199: 112-115.

Petri N, Suadican P, Wildschiodtz G, Bjorn-Jorgensen J. Predictive value of Muller maneuver, cephalometry and clinical features for the outcome of uvulopalatopharyngoplasty. *Acta Otolaryngologica*, 1994; 114: 565-571.

Powell NB, Riley RW, Guilleminault C. Maxillofacial surgery for obstructive sleep apnoea. In: Obstructive sleep apnoea syndrome. 1990, Raven Press: New York. 153-182.

Powell NB, Riley RW, Troell RJ, Blumen MB, Guilleminault C. Radiofrequency volumetric reduction of the tongue: a porcine pilot study for the treatment of sleep apnea syndrome. *Chest*, 1997; 111: 348-355.

Powell NB, Riley RW, Troell RJ, Li K, Blumen MB, Guilleminault C. Radiofrequency volumetric tissue reduction of the palate in subjects with sleep-disordered breathing. *Chest*, 1998; 113: 1163-1174.

Prachartam N, Hans MG, Strohi KP, Redline S. Upright and supine cephalometric evaluation of obstructive sleep apnea syndrome and snoring subjects. *Angle Orthod*, 1994; 64: 63-74.

Prinz PN. Sleep and sleep disorders in older adults. *J Clin Neurophysiol*, 1995; 12: 139-146.

Rapoport DM, Garay SM, Epstein H, Goldring RM. Hypercapnia in the obstructive sleep apnea syndrome. A reevaluation of the "Pickwickian Syndrome." *Chest*, 1986; 627-635.

Rapoport DM. Treatment of sleep apnea syndromes. *Mount Sinai Journal of Medicine*, 1994; 61: 123-130.

Reeves-Hoche MK, Meck R, Zwillich CW. Nasal CPAP: an objective evaluation of patient compliance. *Am J Respir Crit Care Med*, 1994; 149: 149-154.

Remmers JE, DeGroot WJ, Sauerland EK. Pathogenesis of upper airway occlusion during sleep. *J Appl Physiol Respirat Environ Exercise Physiol*, 1978; 44: 931-938.

Riley RW, Powell NB, Guilleminault C. Current surgical concepts for treating obstructive sleep apnoea syndrome. *J Oral and Maxillofac Surg*, 1987; 45: 149-157.

Riley RW, Powell NB, Guilleminault C. Maxillary, mandibular and hyoid advancement for treatment of obstructive sleep apnea: A review of 40 patients. *J Oral Maxillofac Surg*, 1990; 48: 20-26.

Riley RW, Powell NB, Guilleminault C. Obstructive sleep apnea syndrome: a review of 306 consecutively treated surgical patients. *Otolaryngol Head Neck Surg*, 1993; 108: 117-125.

Rivlin J, Hoffstein V, Kalbfleisch J, McNicholas W, Zamel N, Bryan C. Upper airway morphology in patients with idiopathic obstructive sleep apnea. *Am Rev Respir Dis*, 1984; 129: 355-360.

Robin P. Glossoptosis due to atresia and hypertrophy of the mandible. *Am J Dis Child*, 1934; 48: 541-547.

Rodenstein DO, Doms G, Thomas Y, Liistro G, Stanescu DC, Culee C, Aubert-Tulkens G. Pharyngeal shape and dimensions in healthy subjects, snorers and patients with obstructive sleep apnoea. *Thorax*, 1990; 45: 722-727.

Roehrs T, Zorick F, Sicklesteel J, Witting R, Roth T. Age-related sleep-wake disorder at a sleep disorders center. *J Am Geriatr Soc*, 1983; 31: 364-370.

Rojewski TE, Schuller DE, Clark RW, Schmidt HS, Potts RE. Videoscopic determination of the mechanism of obstruction in obstructive sleep apnea. *Otolaryngology Head and Neck Surgery*, 1984; 92: 127-131.

Royal College of Physicians. Sleep apnoea and related conditions. A report of working party with recommendations for service provision. 1993, London: Royal College of Physicians.

Rubinstein I, Colapinto N, Rotstein LE, Brown G, Hoffstein V. Improvement in upper airway function after weight loss in patients with obstructive sleep apnea. *Am Rev Respir Dis*, 1988; 138: 1192-1195.

Ryan CF, Lowe AA, Li D, Fleetham JA. Magnetic resonance imaging of the upper airway in obstructive sleep apnea before and after chronic nasal continuous positive airway pressure therapy. *Am Rev Respir Dis*, 1991; 144: 939-44.

Schmidt-Nowara WW, Mead TE, Hays MB. Treatment of snoring and obstructive sleep apnea with a dental orthosis. *Chest*, 1991; 99: 1378-1385.

Schmidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F, Menn S. Oral Appliances for the Treatment of Snoring and Obstructive Sleep Apnea: A Review. *Sleep*, 1995; 18: 501-510.

Schwab RJ, Gupta D, Duaong D, Schmidt-Nowara WW, Pack AJ, Geftter WB. Upper airway soft tissue structural changes with dental appliances in apnaics. *Am J Respir Crit Care Med*, 1996; 153: 719.

Schwartz R, Salome N, Ingmundon PT, Rugh JD. Effects of electrical stimulation to the soft palate on snoring and obstructive sleep apnoea. *J Prosthet Dent*, 1996; 76: 273-281.

Series F, St Pierre S, Carrier G. Surgical correction of nasal obstruction in the treatment of obstructive sleep apnea. *Am Rev Respir Dis*, 1992; 146: 1261-1265.

Shepard JW, Olsen KD. Uvulopalatopharyngoplasty for the treatment of obstructive sleep apnea. *Mayo Clin Proc*, 1990; 65: 1260-1267.

Shepard JWJ, Stanson AW, Sheedy PF, Westbrook PR. Fast-CT evaluation of the upper airway during wakefulness in patients with obstructive sleep apnea. *Prog Clin Biol Res*, 1990a; 345: 273-279.

Shepard JWJ, Geftter WB, Guilleminault C, Hoffman EA, Hoffstein V, Hudgel DW, Suratt PM, White DW. Evaluation of the upper airway in patients with obstructive sleep apnea. *Sleep*, 1991; 14: 361-371.

Sher AE. Obstructive sleep apnoea syndrome: A complex disorder of the upper airway. *Otolaryngologic Clin North Am*, 1990; 23: 593-608.

Sher AE, Schechtman KB, Piccirillo JF. The Efficacy of Surgical Modifications of the Upper Airway in Adults with Obstructive Sleep Apnea Syndrome. *Sleep*, 1996; 19: 156-177.

Soll BA, George PT. Treatment of obstructive sleep apnea with a nocturnal airway-patency appliance. *N Engl J Med*, 1985; 313: 386-387.

Solow B. Upper airway obstruction and facial development. In: *The Biological Mechanisms of Tooth Movement and Craniofacial Adaptation*. 1992, Columbus, Ohio, USA: The Ohio State University College of Dentistry. 571-579.

Solow B, Ovesen J, Wurtzen Nielsen P, Wildschiodtz G, Tallgren A. Head posture in obstructive sleep apnoea. *Eur J Orthod*, 1993; 15: 107-114.

Solow B, Skov S, Ovesen J, Norup PW, Wildschiodtz G. Airway dimensions and head posture in obstructive sleep apnoea. *Eur J Orthod*, 1996; 18: 571-579.

Stradling JR, Crosby JH, Payne CD. Self-reported snoring and daytime sleepiness in men aged 35-65 years. *Thorax*, 1991; 46: 807-810.

Strelzow VV, Blanks RH, Basile A, Strelzow AE. Cephalometric Airway Analysis in Obstructive Sleep Apnea Syndrome. *Laryngoscope*, 1988; 98: 1149-1158.

Strohl KP, Redline S. Recognition of obstructive sleep apnea. *Am J Respir Crit Care Med*, 1996; 154: 279-289.

Sullivan CE, Berthon-Jones M, Issa FG, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nose. *Lancet*, 1981; 1: 862-865.

Suratt PM, Dee P, Atkinson RL, Armstrong P, Wilhoit SC. Fluoroscopic and computed tomographic features of the pharyngeal airway in obstructive sleep apnea. *Am Rev Respir Dis*, 1983; 127: 487-492.

Suratt PM, McTier RF, Wilhoit SC. Collapsibility of the nasopharyngeal airway in obstructive sleep apnoea. *Am Rev Respir Dis*, 1985; 132: 967-971.

Suratt PM, McTier R, Findley LJ, Pohl SL, Wilhoit SC. Changes in breathing and the pharynx after weight loss in obstructive sleep apnea. *Chest*, 1987; 92: 631-637.

Tangugsorn V, Skatvedt O, Krogstad O, Lyberg T. Obstructive sleep apnoea: a cephalometric study. Part 1. Cervico craniofacial skeletal morphology. *Eur J Orthod*, 1995; 17: 45-56.

Thomas PS, Cowen ERT, Hudlands G, Milledge JS. Respiratory function in the morbidly obese before and after weight loss. *Thorax*, 1989; 44: 382-386.

Trenouth MJ, Timms DJ. Relationship of the functional oropharynx to craniofacial morphology. *Angle Orthod*, 1999; 69: 419-423.

Tsuchiya M, Lowe AA, Pae E-K, Fleetham JA. Obstructive sleep apnea subtypes by cluster analysis. *Am J Orthod*, 1992; 101: 533-542.

Viner S, Szalai JP, Hoffstein V. Are history and physical examination a good screening test for sleep apnoea? *Ann Intern Med*, 1991; 115: 356-359.

Waite PD, Wooten V, Lachner J, Guyette RF. Maxillomandibular advancement surgery in 23 patients with obstructive sleep apnea syndrome. *J Oral Maxillofac Surg*, 1989; 47: 1256-1261.

Waldhorn RE, Her-rick TW, Nguyen MC, O'Donnell AE, Dodero J, Potolicchio SJ. Long-term compliance with nasal continuous positive airway pressure therapy of obstructive sleep apnea. *Chest*, 1990; 97: 33-38.

Waller PC, Bhopal RS. Is snoring a cause of vascular disease? An epidemiological review. *Lancet*, 1989; 1: 143-146.

Weaver TE, Kribbs NB, Pack AI, Kline LR, Chugh DK, Maislin G, Smith PL, Schwartz AR, Schubert NM, Gillen KA, Dinges DF. Night-to-night variability in CPAP use over the first three months of treatment. *Sleep*, 1997; 20: 278-283.

Westbrook PR, Millman RP. Pathophysiology of sleep apnea. In: *Sleep and Breathing*. 1994, New York: Marcel Dekker Inc. 529-555.

White DP, Ballard RD. Pharyngeal muscle activity and upper airway resistance in obstructive apnoea patients versus controls. In: *Sleep and Respiration*. 1990, New York: Wiley-Liss. 243-251.

White DP, Mezzanotte WS. Neuromuscular compensation in the human upper airway. *Sleep*, 1993; 16: S90-92.

Winnberg A, Pancherz H, Westesson P-L. Head posture and hyomandibular function in man: a synchronized electromyographic and videofluorographic study of the open-close-clench cycle. *Am J Orthod*, 1988; 94: 393-404.

Woodson BT, Feroah T, Connolly LA, Toohill RJ. A method to evaluate upper airway mechanics following intervention in snorers. *Am J Otolaryngol*, 1997; 18: 308-314.

Worsnop C, Pierce R, McEvoy RD. Obstructive sleep apnoea. *Aust NZ J Med*, 1998; 28: 421-427.

Wynne JW, Block AJ, Hemenway J, Hunt LA, Flick MR. Disordered breathing and oxygen desaturation during sleep in patients with chronic obstructive lung disease (COPD). *Am J Med*, 1979; 66: 573-579.

Yildirim M, Fitzpatrick MF, Whyte K.F, Jalleh R, Wightman AJA, Douglas NJ. The effect of posture on upper airway dimensions in normal subjects and in patients with the sleep apnea/hypopnea syndrome. *Am Rev Respir Dis*, 1991; 144: 845-847.

Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep disordered breathing among middle-aged adults. *New England Journal of Medicine*, 1993; 328: 1230-1235.

Young T, Blustein J, Finn L, Palta M. Sleep-disordered breathing and motor vehicle accidents in a population-based sample of employed adults. *Sleep*, 1997; 20: 603-613.

Zucconi M, Ferini-Strambi L, Palazzo S, Orena C, Zonta S, Smirne S. Habitual snoring with and without obstructive sleep apnoea: the importance of cephalometric variables. *Thorax*, 1992; 47: 157-161.

MANUSCRIPT

**The Effect of Vertical Dimension in a Mandibular Advancement Splint
for Obstructive Sleep Apnea**

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Abstract

There has been no systematic comparison to determine the effect of vertical mandibular opening of Mandibular Advancement Splints (MAS) on the efficacy and side effects of obstructive sleep apnea (OSA), which was the aim of the study. Twenty-three patients underwent a randomized, 2 period (AB/BA) crossover study with either MAS-1 or MAS-2 (additional 10mm opening) for 2-week periods. Data from the baseline polysomnograph, lateral cephalometric radiograph and questionnaire were compared to those of the treatment periods. MAS-1 was preferred by 78% of patients. One-hundred percent and 91% of patients using MAS-1 and MAS-2 reported subjective improvements in snoring with 91% and 78% reporting every night use, respectively. There were significant improvements in AHI ($21 \pm 2/\text{hr}$ versus MAS-1: $8 \pm 1/\text{hr}$ and MAS-2: $10 \pm 2/\text{hr}$, $p < 0.001$), arousal index ($36 \pm 4/\text{hr}$ versus MAS-1: $26 \pm 4/\text{hr}$ and MAS-2: $24 \pm 4/\text{hr}$, $p < 0.001$) and for the longest apnea ($31 \pm 5\text{s}$ versus MAS-1: $16 \pm 3\text{s}$, $p < 0.02$ and MAS-2: $18 \pm 4\text{s}$, $p < 0.04$). Polysomnographic variables did not differ significantly between MAS's. Complete or partial success was achieved in 74% and 61% of patients using MAS-1 and MAS-2 respectively, which were not significantly different. Three cephalometric predictors for AHI were identified when using either MAS: narrowest posterior airway space, cranio-cervical angle and tongue length. In conclusion, the increased vertical opening in MAS-2 does not significantly effect treatment outcome and was not preferred by the majority of patients.

Key Words: Obstructive sleep apnea, vertical splint dimension, mandibular advancement splint

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Introduction

Obstructive sleep apnea (OSA) is one of the most common medical disorders within the adult population and the second most common respiratory disorder to asthma (1). It is characterized by repetitive partial or complete collapse of the pharyngeal airway during sleep resulting in oxygen desaturation and arousals from sleep (2). This can lead to snoring, excessive daytime sleepiness, cardiovascular sequelae, decreased cognitive functioning (3) and an increased risk of road accidents (4). OSA is thought to result from upper airway narrowing and the normal physiological decrease in muscle tone during sleep (5). Obesity (6) is a major risk factor for the disorder, and anatomical factors such as tonsillar hypertrophy (7), macroglossia (8), retrognathia and a low hyoid bone (9, 10) may also contribute to its development. Treatment of OSA with nasal continuous positive airway pressure (nCPAP) during sleep is highly effective; however, some patients tolerate it poorly (11), making compliance less than optimal (12-14).

Several studies have reported successful treatment of OSA by Mandibular Advancement Splints (MAS) (15-22). These removable oral appliances are an alternative form of treatment to nCPAP and are thought to act primarily by advancing the mandible during sleep. This results in an increase of the anteroposterior dimension of the retroglossal space with a consequent reduction in the degree of pharyngeal collapse (15). Whilst these devices are effective in treating a significant proportion of patients with OSA (15-22), including those that are moderate and severe (22), they are not effective in all patients and it is uncertain as to which patients are likely to benefit from such treatment. Although MAS therapy has been shown to be less effective than nCPAP (23-25) it is preferred by patients because they are less costly, easy to transport, silent, less obtrusive and do not require a power supply (6, 26). Thus an optimization in MAS design so as to increase efficacy and decrease side effects would be beneficial to such patients.

There are no randomized crossover clinical trials in the literature that systematically assess the effect of vertical mandibular opening on OSA. The amount of vertical mandibular opening in MAS design varies greatly between studies including those that do not cause significant vertical mandibular opening (16, 23, 27) as well as those that do (19, 22, 28, 29).

O'Sullivan and colleagues (19) justified 10mm of mandibular vertical opening by claiming that it aided retention during sleep by the jaw musculature tension. Moreover, they referred to Lowe's proposal that the displacement of the mandible anteriorly moves the tongue away from the posterior wall of the pharynx while displacement of it inferiorly moves the tongue away from the soft palate (30). Bucca and colleagues (31) reported that the number of apneas/hypopneas increased significantly when 6 edentulous male patients did not wear their full dentures at night. Supine lateral cephalometry showed that removal of full dentures led to a striking decrease in the anteroposterior oropharyngeal wall distance from 1.5cm to 0.6cm. This decrease in vertical mandibular opening was extreme and no option for MAS therapy exists for edentulous patients with OSA due to retention and stability problems.

However, according to Battagel (6), excess opening is thought to diminish the benefits to the airway from protrusion. In a fluoroscopic study carried out on 6 subjects with OSA, L' Estrange and colleagues (32) found that vertical mandibular opening resulted in synchronous posterior movement of both the tongue and soft palate, with a consequent narrowing of the oropharyngeal airway space. Lamont and colleagues (28) compared a MAS with maximal mandibular protrusion and 3-4mm interincisal opening to a MAS which had up to 70% maximal protrusion and 6-9mm of interincisal opening. Only the latter MAS had a significant effect on AHI reducing it from 7.1 to 0.8 per hour. They concluded that splint design, including the amount of vertical mandibular opening might have a considerable bearing on efficacy. A limitation of the study was that the subjects could open their mouths during sleep and hence it is uncertain whether the amount of vertical mandibular opening remained constant during polysomnography. In addition, the amount of sagittal protrusion varied between appliances, which may have had an effect on AHI reduction.

In a randomized study, Bloch and colleagues (29) compared a Herbst appliance with 4-6mm of interincisal opening to that of a Monobloc appliance with 5-10mm of interincisal opening in 24 patients. The initial AHI of 22.6 ± 3.1 /hr decreased significantly with both appliances to 8.7 ± 1.5 /hr and 7.9 ± 1.6 /hr respectively. They suspected that the difference in the vertical mandibular opening between the two MAS's might have had an effect on their efficacy. They suggested that a downward rotation of the mandible with jaw opening

may result in a retrusive motion of the tongue base. These subjects could also open their mouths during sleep, hence limiting the interpretation of the results. Miyamoto and colleagues (33) reported that the vertical mandibular posture during sleep in patients with OSA is more open than in normal subjects, which increases during apnea and decreases at the termination of apnea. They suggested that collapse of the airway may occur as a consequence of an increase in vertical mandibular opening or a stronger effort to breathe.

Hence the primary aim of this study was to systematically compare the efficacy and side effects of a MAS with a predetermined increase in vertical mandibular opening, to that of a similar one previously tested (22). In addition, the study aimed to predict treatment outcome for individual patients with each appliance by using BMI and cephalometric variables.

Methods

Study population: Twenty-four patients (21 men, 3 women) with a mean age of 51 ± 10 years were recruited from St. George Hospital, Sydney, Australia. Inclusion criteria were at least two symptoms of OSA (snoring, fragmented sleep, witnessed apneas, daytime sleepiness) and evidence of OSA on polysomnography, with an Apnea/Hypopnea Index (AHI) $> 5/\text{hr}$. Patients were excluded if there was evidence of central sleep apnea, periodontal disease or edentulism. The institutional ethics committee approved the study and written informed consent was obtained from all patients (*Appendices 2, 3, 4*).

Mandibular Advancement Splint Design: A dental examination (*Appendix 5*) was carried out on all patients by the author (A.J.P). Dental impressions and an interocclusal record with the mandible in the most comfortable protrusive position were used to fabricate each MAS (Figures 1 and 2).



Figure. 1 Photograph of the Mandibular Advancement Splint with minimal mandibular opening (MAS-1). The design features included: (1) upper and lower removable acrylic appliances utilising tooth undercuts for retention. (2) Buccal flanges angled at 80 degrees on the lower appliance, which fitted against buccal blocks on the upper appliance to prevent posterior movement of the mandible. (3) Ball clasps embedded in the anterior aspect of the appliances to ensure that they were kept together during sleep, by use of an orthodontic elastic band. (4) The average thickness of each upper and lower appliance in the incisor region was 2.0 mm.



Figure. 2 Photograph of the Mandibular Advancement Splint with an additional 10mm of mandibular opening (MAS-2). MAS-2 was exactly the same as MAS-1 except that it had a removable acrylic overlay 10mm thick at its most anterior aspect, which fitted between the upper and lower appliances. It was retained by acrylic protrusions fitting against two retentive grooves in the lower appliance.

Study Design: A randomized crossover design (AB/BA) was used. Following an acclimatization period with MAS-1, patients were randomized into either Group I (sequence-AB) or Group II (sequence-BA). After a 1-week washout period during which no appliance was worn, patients were treated with either MAS-1 (A) or MAS-2 (B) for 2 weeks and the alternate treatment for another 2 weeks with an intervening washout period of 1-week. Polysomnography was performed on the last night of each treatment period.

Outcome Measures

A self-administered *questionnaire* was completed by patients at baseline and at the end of each treatment period (*Appendix 6*). These were used to assess the frequency, severity and duration of side effects as well as treatment compliance and satisfaction with each MAS. Daytime sleepiness was assessed by using the Epworth Sleepiness Scale (ESS), a validated self-administered questionnaire (34). *Polysomnography* was performed as previously described (22). Body Mass Index (BMI) was calculated using height and weight measurements.

Treatment Outcome: Complete success was defined as a resolution of symptoms and reduction in AHI to < 5/hour and with a > 50% reduction from baseline AHI. Partial

success was defined as improved symptoms and $\geq 50\%$ reduction in AHI but remaining $\geq 5/\text{hr}$. Treatment failure was defined as ongoing clinical symptoms and/or a $< 50\%$ reduction in AHI.

Radiographs: A lateral cephalometric radiograph was taken at baseline and with each MAS in place, as previously described (22). All radiographs were hand traced by the author (A.J.P) who was blinded to the patients' polysomnographic results. Cephalometric landmarks and measurements made are detailed in Figure 3. Seven radiographs were randomly chosen from all radiographs and were re-traced and re-measured under the same conditions a month later by the same author to quantify the percentage of absolute error.

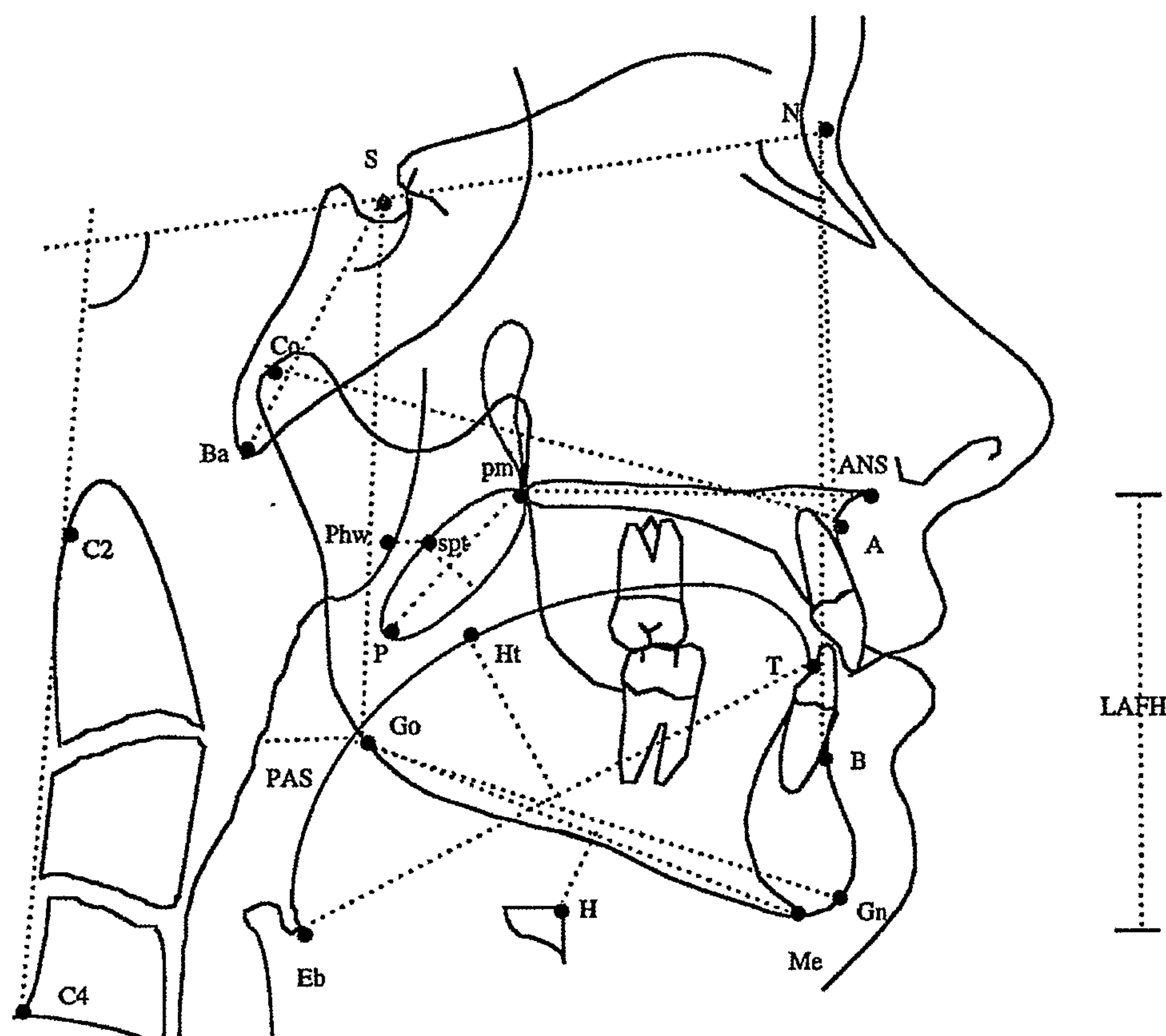


Figure. 3 Definitions of cephalometric landmarks and measurements. Anatomical landmarks: ANS = Anterior nasal spine, tip of the median sharp bony process of the palatine bone in the hard palate. A Point = deepest midline point on the maxillary alveolus between ANS and the maxillary alveolar crest. B Point = deepest midline point between the mandibular alveolar crest and gnathion. Ba = Basion, most inferior point on the anterior margin of foramen magnum in the median plane. Go = Gonion, most lateral external point

at the junction of the horizontal and ascending rami of the mandible. Gn = Gnathion, most antero-inferior point on the bony mandibular symphysis. H = Hyoidale, most superior-anterior point on the body of the hyoid bone. Me = Menton, lowest point on the bony outline of the mandibular symphysis. MP = Mandibular plane, line joining Me and Go. N = Nasion, most anterior point of the fronto-nasal suture. PNS = Posterior nasal spine, tip of the posterior spine of the palatine bone. Spt = tangent point on a line parallel to the long axis of the soft palate at the maximum width. Phw = Posterior pharyngeal wall, point on the posterior pharyngeal wall at the same horizontal level as Spt, S = Sella, centre of the sella turcica. *Measurement angles (degrees)*: BaSN = cranial base angulation in mid sagittal plane, SNB = angle from S to N to B Point. ANB = angle from A Point to N to B Point. SN-MP = angulation of the mandibular plane with the SN line. CC = craniocervical angle formed by a line from C2 to C4 and the SN line. *Measurement lengths (mm)*: H-MP = perpendicular distance from the MP to H. S-H = distance between sella and hyoidale. LAFH = lower anterior face height measured from ANS to Me. TAFH = total anterior face height measured from N to Me. Overbite = vertical overlap of incisors measured from the incisal tips. Overjet = horizontal distance between upper incisor tip and labial surface of the lower incisor. SPL = soft palate length measured from PNS to the end of the soft palate. SPT = maximum soft palate thickness measured perpendicular to the SPL line. RPAS = width of nasopharynx from Phw to Spt. PAS = distance between the posterior pharyngeal wall and the dorsal surface of the base of the tongue, measured on the line that intersects Go and B point. NPAS = narrowest distance between the posterior pharyngeal wall and the dorsal surface of the base of the tongue or soft palate. TL = tongue length measured from tongue tip to the base of the epiglottis.

Statistics: Data were analysed using SPSS software (Version 10.0, SPSS Inc, Chicago IL). A General Linear Model (UNIANOVA) was used to analyse polysomnographic, BMI and questionnaire data and to assess for carryover and sequence effect. A multiple regression model was constructed incorporating BMI and cephalometric variables to predict AHI with each MAS. All descriptive statistics are presented as mean $\pm$ SD, while estimated means are presented as mean $\pm$ SEM.

Methods word count: 481

Results

Study Population: Of the 24 patients recruited, 23 finished the protocol with one male patient withdrawing after initial dental examination, due to time constraints. The initial BMI did not change significantly during the treatment periods ($31.5 \pm 1.1 \text{ kg/m}^2$ versus MAS-1: $32.0 \pm 1.1 \text{ kg/m}^2$ and MAS-2: $31.9 \pm 1.1 \text{ kg/m}^2$, $p=0.06$). The mean baseline AHI was $21.0 \pm 2.4/\text{hr}$ and the average MinSaO_2 was $87 \pm 1\%$. The mean mandibular advancement of maximal protrusion was significantly greater ($p=0$) with MAS-1 ($87 \pm 4\%$) compared to MAS-2 ($60 \pm 6\%$) as measured by overjet change radiographically. The amount of protrusion with MAS-2 was less due to a reduction in overjet with increased opening of the mandible. The average acclimatization period was 2.6 ± 0.9 weeks.

Subjective Outcomes: The MAS was well tolerated by all patients who completed the protocol. Side effects for MAS-1 and MAS-2 respectively, did not differ significantly and included jaw discomfort (48% vs 70%; $p=0.13$), excessive salivation (48% vs 57%; $p=0.55$), mouth dryness (26% vs 22%; $p=0.73$), tooth grinding (22% vs 13%; $p=0.43$) and gum irritation (22% vs 13%; $p=0.43$). These were described as mild, moderate or severe in intensity with the frequency recorded as rare, sometimes or often. The duration of side effects were described as < 1-week, 1-2 weeks or > 2weeks (Table 1). There was no significant difference in the severity or duration of side effects between appliances. There was no significant difference in the proportion of patients who reported an improvement in snoring between MAS-1 and MAS-2 (100% vs 95%, $p=0.31$). The average daytime sleepiness improved similarly with both MAS's, with an initial ESS of 17.9 ± 1.0 versus 12.4 ± 0.8 with MAS-1 and MAS-2 ($p < 0.0001$). Sleep quality improved in 87% of patients with MAS-1 and in 78% of patients with MAS-2, which did not differ significantly between appliances ($p=0.43$). Ninety one percent and 78% of patients reported every night use of MAS-1 and MAS-2 respectively, which was not significantly different between appliances ($p=0.21$). Ninety six per cent of patients stated they would like to continue to use either MAS due to a perceived improvement in symptoms. A significantly higher proportion of patients preferred to use MAS-1 than MAS-2 (78% vs 22%, $p=0.007$).

Table. 1 Side Effects of MAS-1 and MAS-2

Side Effect	Total	Severity			Frequency				Duration		
		Mild	Moderate	Severe	Rarely	Sometimes	Often		<1week	1-2 weeks	>2weeks
Jaw Discomfort											
MAS 1	11 (48%)	8	3	0	3	3	5		7	1	3
MAS 2	16 (70%)	12	3	1	4	5	7		6	3	7
Salivation											
MAS 1	11 (48%)	9	2	0	3	4	4		2	3	6
MAS 2	13 (57%)	7	4	2	1	3	9		2	2	9
Dryness of Mouth											
MAS 1	6 (26%)	4	2	0	2	3	1		1	1	4
MAS 2	5 (22%)	2	3	0	0	3	2		1	0	4
Grinding of Teeth											
MAS 1	5 (22%)	5	0	0	1	3	1		0	1	4
MAS 2	3 (13%)	3	0	0	0	3	0		1	1	1
Gum Irritation											
MAS 1	5 (22%)	4	1	0	1	3	1		1	1	3
MAS 2	3 (13%)	1	2	0	0	1	2		0	0	3

Objective Outcomes: Polysomnographic outcomes are outlined in Table 2. Initial AHI significantly improved with both MAS-1 (by 62%) and MAS-2 (by 52%). Arousal index decreased significantly with both MAS-1 (by 28%) and MAS-2 (by 33%). The duration of the longest apnea significantly decreased with both MAS-1 (by 48%) and MAS-2 (by 42%). Of the remaining polysomnographic variables examined, none were found differ significantly either treatment in comparison to baseline. No significant difference, carryover or sequence effect was found for any polysomnographic variable between MAS-1 and MAS-2.

Table. 2 Effect of Each MAS on Polysomnographic Variables

Variable	Baseline	MAS 1	MAS 2
Sleep Variables			
TST (min)	334 ± 12	363 ± 13*	361 ± 12*
REM Sleep (min)	58 ± 6	69 ± 6*	70 ± 6*
REM (%)	17 ± 2	19 ± 2*	19 ± 2*
NREM Sleep (min)	273 ± 9	294 ± 10*	291 ± 10*
NREM (%)	82 ± 1	81 ± 1*	81 ± 1*
Arousal Index (/hr)	36 ± 4	26 ± 4§	24 ± 4§
Sleep Efficiency (%)	79 ± 1	84 ± 2*	84 ± 3*
Respiratory Variables			
AHI (/hr)	21 ± 2	8 ± 1§	10 ± 2§
MinSaO ₂	87 ± 1	89 ± 1*	88 ± 1*
Longest Apnea (s)	31 ± 5	16 ± 3‡	18 ± 4†
Longest Hypopnea	63 ± 6	55 ± 4*	61 ± 5*

Definition of abbreviations: TST=total sleep time, REM%=time in REM sleeps as % of TST, NREM%=time in NREM sleep as a % of TST.

All values represent mean ± SEM.

* Not significant

† p < 0.04

‡ p < 0.02

§ p < 0.001

Treatment Outcome: Figure 4 shows treatment outcome for each MAS and combined. Treatment resulted in either partial or complete success in 74% of patients with MAS-1, in 61% of patients with MAS-2 (not significantly different, $p=0.34$) and in 83% patients with either MAS (taking the best result of either MAS 1 or 2). Complete success was achieved in 52% of patients with MAS-1, 35% of patients with MAS-2 (not significantly different, $p=0.23$) and in 57% of patients with either MAS. Partial success was achieved in 22% of patients with MAS-1, 26% of patients with MAS-2 (not significantly different, $p=0.73$) and in 26% of patients with either MAS.

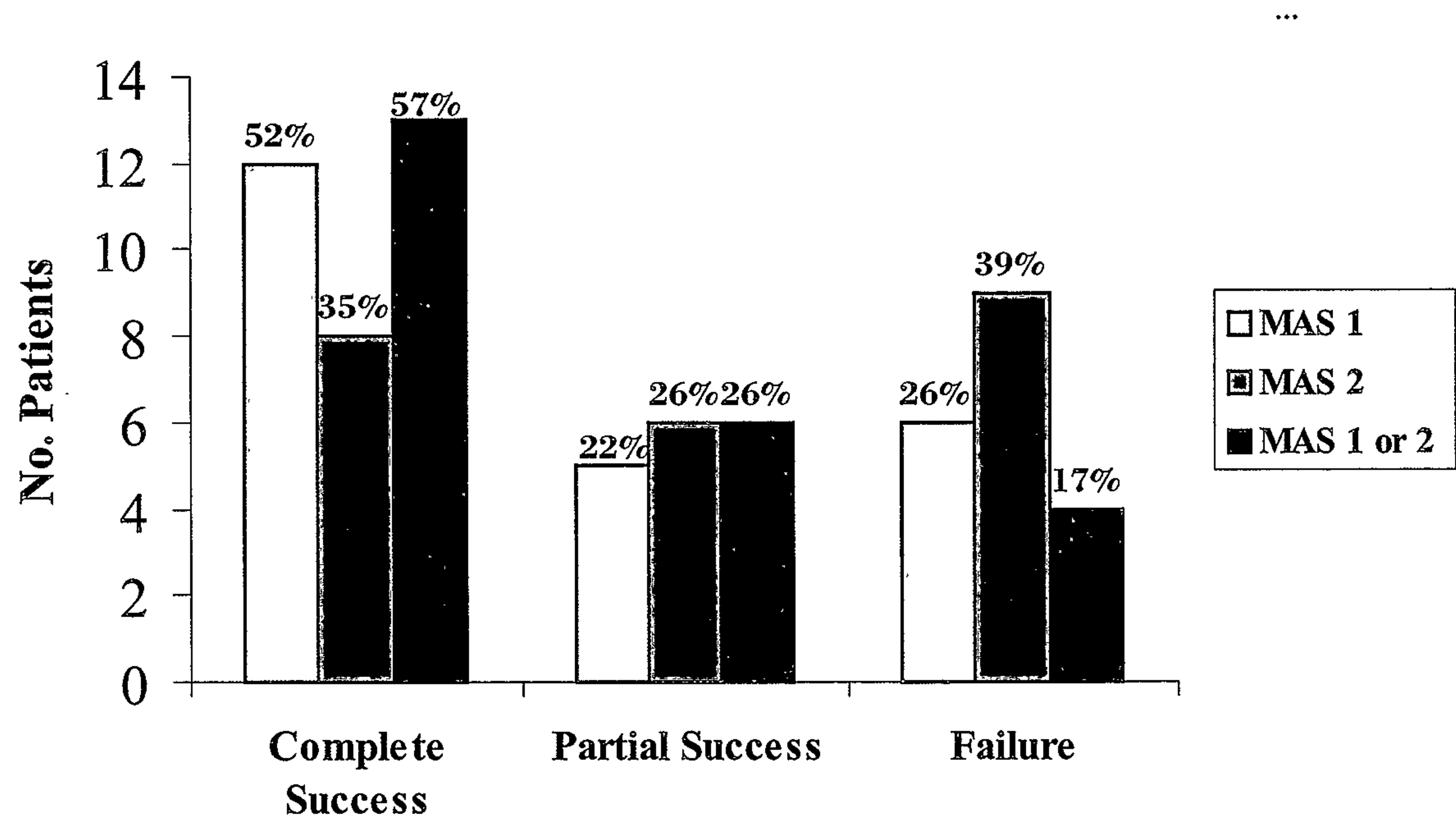


Figure. 4 Treatment outcome for MAS-1, MAS-2, and MAS-1 or MAS-2 combined.

Model for outcome prediction: A multiple regression analysis using all cephalometric measurements (at baseline, with MAS-1 in place and with MAS-2 in place) as well as BMI were used to predict AHI when using either MAS (*Appendices 7, 8*). Three independent predictors were identified: narrowest posterior airway space (NPAS), cranio-cervical angle (CC), and tongue length (TL). The derived equation was:

$$\text{AHI (MAS)} = 81.4 - 0.7 \text{ NPAS} - 0.4 \text{ CC} - 0.3 \text{ TL} \text{ (R}^2 = 30\%, \text{ S} = 7.85)$$

A multiple regression analysis was also performed to try and predict which MAS would reduce AHI more but no independent predictors were found.

The percentage of absolute error of the repeated cephalometric radiographs was 0.16%, indicating a high degree of reproducibility.

The power to distinguish a difference in AHI of 5 per hour between MAS-1 and MAS-2 was 0.9.

Discussion

There is a lack of randomized clinical trials on oral appliance therapy for OSA in the literature. As stated by Ferguson (35) most of the published studies have several deficiencies including small sample size, with no control or comparison group and are usually retrospective in design. Also, treatment outcome criteria are usually poorly defined and subjective. Not all patients have polysomnography at baseline and during treatment and some studies exclude patients with severe OSA. The frequency, severity and duration of side effects are rarely reported and predictors of outcome are not known. Few studies have reported subjective compliance and there is a lack of description for appliance design, including the optimal amount of mandibular protrusion. Only one recent study does not have the deficiencies mentioned and proves the efficacy of MAS in even moderate to severe OSA patients (22, 35). There are however, no randomized clinical crossover trials in the literature that systematically assess the effect of vertical mandibular opening on OSA. This was our primary aim while trying to find predictors for treatment outcome was our secondary aim.

The selected patients were typical of the OSA population- most being male and middle aged. They were randomly assigned to the AB or BA sequence for subjective and objective comparison. No control group was required because the baseline data allowed direct comparisons to be made to either MAS. Since a crossover study design was used, the sample achieved was considered appropriate and the treatment periods long enough to compare short term side effects. The only difference between each MAS used was the amount of vertical mandibular opening. The same clinical procedure as described by Mehta and colleagues (22) was used to dictate the vertical dimension of MAS-1. The efficacy of this type of MAS had thus already been proven, even in patients with severe OSA (22). Our study also did not exclude severe OSA patients. Their study showed a lack of carryover when using a 1-week washout period after acclimatization and between treatment periods, which justifies the 1-week washout period that was used in our study. We also used similar robust definitions of treatment outcome, a weakness of almost all previous studies (Schmidt-Nowara *et al.*, 1995).

The vertical dimension of MAS-2 was increased by 10mm at the most anterior region of the MAS, which was considered substantially greater, clinically. Also, other studies have

used similar amounts of vertical mandibular opening (19, 28, 29). Overjet was measured on the cephalometric radiographs from the most labial surface of the most protrusive mandibular incisor to the most protrusive maxillary incisal edge. Overjet decreased from MAS-1 to MAS-2 because as the mandible opened, it moved on the same trajectory-inferiorly and posteriorly guided by the 80-degree buccal flanges.

Subjectively, side effects did not differ significantly between MAS-1 and MAS-2 for frequency, severity or duration. However, there was a significant difference in the reported preference of each MAS, with the majority of patients preferring MAS-1 because it was perceived as being more effective, comfortable and less bulky. As in other studies (15, 22), the majority of our patients experienced a significant subjective benefit from MAS therapy. All patients had a substantial improvement in subjective snoring with MAS-1 and all but one patient with MAS-2. The proportion of patients who reported an improvement in sleep quality was not significantly higher with MAS-1 (87%) compared with MAS-2 (78%). There was no significant difference in the degree of improvement in subjective daytime sleepiness between the two appliances.

The short-term side effects reported in this study were mainly of mild to moderate intensity. These included jaw discomfort, salivation, dryness of the mouth and grinding of the teeth, also reported in other studies (15, 22, 36). Both MAS's clearly improved subjective snoring, ranging from slight improvement to complete cessation as assessed by the patient or bed partner. The self-reported short-term compliance rate with the MAS was high hence comparing favourably with compliance rates reported by other studies (15, 22). Twenty-two out of 23 patients wished to continue using the MAS because of a perceived health benefit.

There may have been an element of response bias for the questionnaires, which leaves some uncertainty of the subjective results reported. Objective measures of daytime sleepiness and performance are required in future studies to verify the subjective improvements. Also, development of objective monitoring of MAS compliance in the future is required to verify the subjective response.

The impressive subjective responses corresponded with the objective polysomnographic outcomes, with 74% of patients having complete or partial success with MAS-1 and 61% with MAS-2. Both MAS's were found to be effective in significantly reducing AHI, arousal index and the longest apnea, however no significant polysomnographic difference existed between each MAS. The increased success of MAS-1 compared to a similar type previously used by Mehta and colleagues (22) may be attributed to the increased mean mandibular advancement of 87% compared with their 78%. Also, our mean baseline AHI was $21 \pm 2/\text{hr}$, being less than their AHI of $30 \pm 2/\text{hr}$. Also, the incorporation of advancement flanges in our MAS on the buccal rather than on the lingual surfaces may have increased the airway and tongue space. Our MAS had no incremental advancement screws incorporated, which decreased the cost of appliance fabrication and reduced the acclimatization period (3 weeks compared to their 20 weeks).

Treatment success with oral appliances is not achievable in all patients and it would be advantageous to be able to predict which MAS would reduce AHI more. This would result in a more optimal MAS design for patients with less wastage of resources. From our data, we were unable to derive any independent BMI or cephalometric variables to make such a prediction. This led to a further analysis so as to predict AHI with either MAS. Three independent baseline predictors were identified: narrowest posterior airway space, cranio-cervical angle and tongue length. This contrasts to the predictors previously found (22), which were posterior airway space, SN-MP angle, baseline AHI and neck circumference. A prospective study is required to validate the predictors found in both studies.

Conclusions

1. Both MAS's were shown to be effective in reducing AHI, arousal index and the longest apnea.
2. The 10mm of increased vertical opening at the incisal region of the MAS did not significantly affect treatment outcome.
3. Patients preferred the minimal mandibular opening MAS because they perceived it to be more effective, comfortable and less bulky.
4. Narrowest posterior airway space, cranio-cervical angle and tongue length, seem to be independent baseline predictors for treatment outcome.

Acknowledgements

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References

1. McNicholas WT. Obstructive Sleep Apnea Syndrome: Who Should be Treated? *Sleep* 2000;4:S187-190.
2. McNamara SG, Grunstein RR, Sullivan CE. Obstructive sleep apnoea. *Thorax* 1993;48: 754-764.
3. Epstein LJ, Weiss JW: Clinical consequences of obstructive sleep apnea. *Semin Respir Crit Care Med* 1998;19:132-132.
4. Findley LJ, Unverzagt ME, Suratt PM. Automobile accidents involving patients with obstructive sleep apnea. *Laryngoscope* 1988;98: 337-340.
5. Cistulli PA, Sullivan CE. In: Sullivan CE, Saunders NA, editors. *Sleep and Breathing*, 2nd Ed. New York: Marcel Dekker; 1994, p. 405-488.
6. Battagel JM. Obstructive Sleep Apnoea: Fact not Fiction. *Br J Orthod* 1996;23: 315-324.
7. Battagel JM, L'Estrange PR. The cephalometric morphology of patients with obstructive sleep apnoea (OSA). *Eur J Orthod* 1996;18:557-569.
8. Lowe AA, Santamaria JD, Fleetham JA, Price C. Facial morphology and obstructive sleep apnea. *Am J Orthod* 1986;90:484-491.
9. Riley R, Guilleminault C, Herran J, Powell N. Cephalometric analyses and flow volume loops in obstructive sleep apnea patients. *Sleep* 1983;6:304-317.
10. Jamieson A, Guilleminault C, Partinen M, Quera-Salva MA. Obstructive Sleep Apneic Patients Have Craniomandibular Abnormalities. *Sleep* 1986;9: 469-477.
11. Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnea by continuous positive pressure applied through the nares. *Lancet* 1981;1:862-865.
12. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. *Am Rev Respir Dis* 1993;147:887-895.
13. Engleman, HM, Asgari-Jirhandeh N, McLeod AL, Ramsay CF, Deary IJ, Douglas NJ. Self reported use of CPAP and benefits of CPAP therapy: a patient survey. *Chest* 1996;109: 1470-1476.
14. Weaver TE, Kribbs NB, Pack AI, Kline LR, Chugh DK, Maislin G, Smith PL, Schwartz AR, Schubert NM, Gillen KA, Dinges DF. Night-to-night variability in CPAP use over the first three months of treatment. *Sleep* 1997;20:278-283.

15. Schmidt-Nowara, W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F, Menn S. Oral Appliances for the Treatment of Snoring and Obstructive Sleep Apnea: A Review. *Sleep* 1995;18:501-510.
16. Schmidt-Nowara WW, Mead TE, Hays MB. Treatment of snoring and obstructive sleep apnea with a dental orthosis. *Chest* 1991;99:1378-1375.
17. Clark GT, Arand D, Chung E, Tong D. Effect of anterior mandibular positioning on obstructive sleep apnea. *Am Rev Respir Dis* 1993;147:624-629.
18. Eveloff SC, Rosenberg CL, Carlisle CC, Millman RP. Efficacy of a Herbst Mandibular Advancement Device in Obstructive Sleep Apnea. *Am J Respir Crit Care Med* 1994;149:905-909.
19. O'Sullivan RA, Hillman DR, Mateljan R, Pantin C, Finucane KE. Mandibular Advancement Splint: An Appliance to Treat Snoring and Obstructive Sleep Apnea. *Am J Respir Crit Care Med* 1995;151:194-198.
20. Pancer JS, Al-Faifi S, Al-Faifi M, Hoffstein V. Evaluation of variable mandibular advancement appliance for treatment of snoring and sleep apnea. *Chest* 1999;116:1511-1518.
21. Henke E, Frantz DE, Kuna ST. An oral elastic mandibular advancement device for obstructive sleep apnea. *Am J Respir Crit. Care Med* 2000;161:420-425.
22. Mehta A, Qian J, Petocz P, Darendeliler MA, Cistulli PA. A Randomized, Controlled Study of a Mandibular Advancement Splint for Obstructive Sleep Apnea. *Am J Respir Care Med* 2001;163:1457-1461.
23. Ferguson KA, Ono T, Lowe AA, Keenan SP, Fleetham JA. A randomized crossover study of an oral appliance vs nasal-continuous positive airway pressure in the treatment of mild-moderate obstructive sleep apnea. *Chest* 1996;109:1269-1275.
24. Ferguson KA, Ono T, Lowe AA, Al-Majed S, Love LL, Fleetham JA. A short term controlled trial of an adjustable oral appliance for the treatment of mild- moderate obstructive sleep apnoea. *Thorax* 1997;52:362-368.
25. Naughton M. Sleep apnoea - from social to medical consequences. *Modern Medicine of Australia* 1997;36-44.
26. Clark GT, Blumenfeld I, Yoffe N, Peled E, Lavie P. A Crossover Study Comparing the Efficacy of Continuous Positive Airway Pressure with Anterior Mandibular Positioning Devices on Patients with Obstructive Sleep Apnea. *Chest* 1996;109:1477-1483.

27. Mayer G, Meier-Ewert K. Cephalometric predictors for orthopaedic mandibular advancement in obstructive sleep apnoea. *Eur J Orthod* 1995;17:35-43.
28. Lamont J, Baldwin DR, Hay KD, Veale AG. Effect of two types of mandibular advancement splints on snoring and obstructive sleep apnoea. *Eur J Ortho* 1998;20:293-297.
29. Bloch KE, Iseli A, Zhang JN, Xie X, Kaplan V, Stoeckli PW, Russi EW. A Randomized, Controlled Crossover Trial of Two Oral Appliances for Sleep Apnea Treatment. *Am J Respir Care Med* 2000;162:246-251.
30. Lowe AA. Dental appliances for the Treatment of Snoring and Obstructive Sleep Apnea. 2nd ed. In: Kryder MH, Dement WC, Editors. *Principles and Practice of Sleep Medicine*. Philadelphia: WB Saunders Co; 1993, p. 722-735.
31. Bucca C, Carossa S, Pivetti S, Gai V, Rolla G, Preti G. Edentulism and worsening of obstructive sleep apnea. *The Lancet* 1999;353:121-122.
32. L'Estrange PR, Battagel JM, Harkness B, Spratley MH. A method of studying adaptive changes of the oropharynx to variation in mandibular position in patients with obstructive sleep apnoea. *Journal of Oral Rehabilitation* 1996;23:2-77.
33. Miyamoto K, Ozbek MM, Lowe AA, Sjolhm TT, Love LL, Fleetham JA, Ryan CF. Mandibular posture during sleep in patients with obstructive sleep apnoea. *Archives of Oral Biology* 1999;657-664.
34. Johns, MW. A New Method for Measuring Daytime Sleepiness: The Epworth Sleepiness Scale. *Sleep* 1991;14:540-545.
35. Ferguson K. Oral appliance Therapy for Obstructive Sleep Apnea. *Am J Respir Crit Care Med* 2001;163:1294-1295.
36. Pantin CC, Hillman DR, Tennant M. Dental side effects of an oral device to treat snoring and obstructive sleep apnea. *Sleep* 1999;22:237-240.

FUTURE DIRECTIONS

Future research recommendations are as follows:

1. Patients who derived a benefit from MAS therapy need long term follow up to confirm the improvement, investigate the side effects, and to objectively measure daytime performance and sleepiness.
2. The multiple regression model derived to predict indicators for treatment outcome should be clinically validated with a larger sample size using a prospective study design.
3. The exact mechanism of action of MAS therapy is unknown. Computerised tomography and magnetic resonance imaging techniques might resolve this question.
4. Overnight titration of sagittal advancement and vertical mandibular opening so as to design the most effective MAS for individual patients.
5. Objective assessment of daytime sleepiness and performance is required for MAS therapy.
6. Covert compliance monitoring is required to confirm subjective compliance results.
7. Combination treatment.

APPENDICES

- APPENDIX 1. DEFINITION OF SLEEP STAGES
- APPENDIX 2. COVER LETTER FOR CONSENT FORM
- APPENDIX 3 SUBJECT INFORMATION STATEMENT AND
 CONSENT FORM
- APPENDIX 4. LETTER OF REQUEST
- APPENDIX 5. ORTHODONTIC HISTORY AND EXMANINATION
 FORM
- APPENDIX 6. SLEEP QUESTIONNAIRES
- APPENDIX 7. INDIVIDUAL PATIENT CHARACTERISTIC DATA
- APPENDIX 8. INDIVIDUAL PATIENT CEPHALOMETRIC
 MEASUREMENTS

APPENDIX 1. DEFINITION OF SLEEP STAGES (McNamara et al., 1994)

Sleep consists of two different states known as rapid-eye movement (REM) sleep and non-REM (NREM) sleep. EEG patterns distinguish between the two sleep states.

REM sleep is characterised by “desynchronised” or “activated” EEG patterns. Sleep is characterised by recurrent, typically periodic episodes of relative motor inactivity with raised thresholds of sensory response. By most parameters, the brain is in a state like that seen in waking. There are intermittent twitches in fine distal muscles, including the extraocular eye muscles that produce the rapid eye movements. Sleep episodes are rapidly reversible by arousal.

It is the slow-wave “synchronised” EEG patterns that characterise the NREM state (also known as slow-wave sleep). NREM sleep is divided into stages 1, 2, 3 and 4 based on details of the EEG patterns. Stages 3 and 4 are considered to be “deeper” sleep.

When apneas are present, they appear more frequently during light NREM sleep (stages 1 and 2) and REM sleep, than in NREM 3 and 4 sleep, when breathing is in general, more regular.

APPENDIX 2. COVER LETTER FOR CONSENT FORM



Faculty of Dentistry
The University of Sydney

United Dental Hospital
Level 8, 2 Chalmers Street
Surry Hills 2010, Australia
Telephone: (61-2) 9351 8329
Facsimile: (61-2) 9351 8336

Dr. Andrew J Pitsis B.D.S. Hons.(Syd.)
Orthodontic Department

May, 2000

Dear Patient,

Thank you for considering participation in our clinical trial investigating the effect of Mandibular Advancement Splint design on the treatment of Obstructive Sleep Apnoea. Enclosed, please find an information statement and consent form providing details of all treatment and testing procedures to be undergone should you choose to participate. The study is being conducted by the Sleep Disorders Centre, at St. George Hospital, The University of New South Wales and by the United Dental Hospital, University of Sydney.

Your decision to participate or otherwise should be made following careful consideration of the enclosed information and its discussion with members of the research team from the Sleep Disorders Centre at St. George Hospital. If you elect to consent, a dental appointment at the United Dental Hospital finally determines whether you meet certain dental criteria for inclusion in the study and subsequent commencement of treatment.

I will contact you in the near future regarding an appointment at the United Dental Hospital, Surry Hills. At your first appointment you will need to bring with you, your plastic bite device and a cheque for \$400.00 as outlined in the subject information statement and consent form.

If you require any further information, please contact Dr. Andrew Pitsis, Orthodontic Registrar (Ph: 9293 3389) or Dr. Peter Cistulli, Director of the Centre for Sleep Disorders & Respiratory Failure, St. George Hospital (Ph: 9350 2696).

Yours Sincerely,

Dr. Andrew J. Pitsis

APPENDIX 3. SUBJECT INFORMATION STATEMENT AND CONSENT FORM

CENTRE FOR SLEEP DISORDERS AND RESPIRATORY FAILURE

Ground Floor

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Ph: (02) 9350 2696

Fax: 9350 2570

Ethics Approval No. 99/90

**ST. GEORGE HOSPITAL, THE UNIVERSITY OF NEW SOUTH WALES
AND THE UNITED DENTAL HOSPITAL, UNIVERSITY OF SYDNEY**

Subject Information Statement and Consent Form

EFFECT OF MANDIBULAR ADVANCEMENT SPLINT DESIGN ON TREATMENT OUTCOME IN OBSTRUCTIVE SLEEP APNOEA

- You are invited to participate in a study of an orthodontic treatment for obstructive sleep apnoea, a common condition associated with snoring and collapse of the throat during sleep. The most commonly used treatment for sleep apnoea is continuous positive airway pressure (CPAP), whereby pressurised air is pumped into the throat passage via the nose, and prevents the throat from collapsing. Some patients with sleep apnoea prefer using Mandibular Advancement Splints (MAS), specially designed dental plates that hold the lower jaw forward during sleep. This is a more simple form of treatment, but is not always effective. In this study we aim to assess the effectiveness of two specially designed splints:
 - MAS 1: will keep your jaw relatively closed
 - MAS 2: will keep your jaw relatively open

You were selected as a possible participant because you have obstructive sleep apnoea. If you decide to participate:

- (a) You will have already undergone a number of investigations as part of your routine clinical workup for sleep apnoea, including a sleep study.
- (b) You will be required to use a plastic device to help you get used to the splint before your orthodontic examination. You must bring this device to your first appointment at the United Dental Hospital (UDH) as it will be used as a record required for the construction of your splint .
- (c) You will be required to undergo an orthodontic examination at the United Dental Hospital (Level 8, 2 Chalmers Street, Surry Hills 2010) at which time dental impressions will be taken so that the appliance can be constructed. Two standard orthodontic x-rays will also be taken.
- (d) You will then have the splint issued to you at the UDH. You will also undergo a standard orthodontic x-ray with each of the 2 splints.
- (e) You will then have a period to get used to the splint (approximately 4-6 weeks), during which any adjustment to fit will be made at the United Dental Hospital.
- (f) Once you are used to the splint, you will be randomly assigned to one of two groups, I or II.

Group I: After 1 week of NOT wearing a splint, you will be required to wear MAS 1 for 2 weeks, at the end of which you will undergo testing, as outlined below. This is followed by a week of NO MAS, and subsequently 2 weeks of MAS 2, again ending with tests. *Group II:* This is identical to Group I except that MAS 2 is used for the first 2 week treatment period, and MAS 1 for the second.

- (g) You will be required to keep a diary of MAS use during sleep (hours worn each night) for each of the two 2-week treatment periods.

Signature of subject: Date:

(Print name)

Signature of witness: Date:

(Print name)

Signature of investigator: Date:

(Print name)

Ethics Approval No. 99/90

ST. GEORGE HOSPITAL, THE UNIVERSITY OF NEW SOUTH WALES
AND THE UNITED DENTAL HOSPITAL, UNIVERSITY OF SYDNEY

Subject Information Statement and Consent Form (Cont'd)

**EFFECT OF MANDIBULAR ADVANCEMENT SPLINT DESIGN ON
TREATMENT OUTCOME IN OBSTRUCTIVE SLEEP APNOEA**

The tests performed at the end of each 2-week treatment period, regardless of whether you are in group I or II, are as follows:

- 1) A questionnaire to assess your response to the splint.
- 2) An overnight sleep study with the MAS that you have been wearing during the particular treatment period to determine whether it effectively treats your snoring and sleep apnoea. This is identical to the sleep study you previously had to diagnose sleep apnoea.

It is important that you understand that part or all of the appliance will be given to you or taken away from you at specific times during the study to ensure strict adherence to the study protocol. All these procedures are safe and carry minimal risk to you. The research study involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 to 3 millisieverts (mSv) each year. The effective dose from this study is about 0.05 mSv. At this dose level, no harmful effects of radiation have been demonstrated and the risk is minimal.

The MAS appliance: This consists of custom-made upper and lower plastic plates, which fit over the teeth. There are grooves in the plates to hold the lower jaw forward. They are similar to small upper and lower mouth guards, and are relatively comfortable. The appliance is worn only during sleep. Patients commonly report excessive salivation and discomfort for a brief time after awakening when they start using these appliances. However, with regular use and adjustment of fit, these symptoms usually subside. Pain in the temporomandibular joint (the jaw joint located just in front of the ear) is relatively uncommon with short term use and usually subsides upon discontinuation of the appliance.

Cost: You will be required to pay a deposit of \$400 for the cost price of the splint charged to us by the dental laboratory. A cheque brought to the United Dental Hospital will be necessary before the orthodontic examination can commence on that day. This deposit is fully refundable to you at the completion of the study and by the return of the mandibular advancement splints. However, if you would like to continue using the device to treat your sleep apnoea, you are able to purchase it at cost price by leaving us with the original deposit. This will be entirely your decision, and will not affect your relationship with us. Please note that any future splint repair and/or replacement will be your own responsibility. It is important that you receive regular dental check-ups while using the appliance for continual monitoring of the splint and the health of your teeth, gums and jaw joints. Should any sleep apnoea symptoms return, please consult with your sleep specialist.

Your decision whether or not to participate will not affect your future relationship with St. George Hospital or United Dental Hospital. If you do decide to participate, you are free to withdraw your consent and to discontinue participation at any time without prejudice. If you have any questions at a later time, Dr. Andrew Pitsis, Orthodontic Registrar, United Dental Hospital (Ph. 9293 3388) will be happy to answer them. Any person who has any concerns or complaints about the conduct of this research can contact the Ethics Secretariat on (02) 9350 2986.

You are making a decision whether or not to participate in this study. Your signature indicates that you have decided to participate, having read the information provided.

Signature of subject: Date:
(Print name)

Signature of witness: Date:
(Print name)

Signature of investigator: Date:
(Print name)

APPENDIX 4. LETTER OF REQUEST



Faculty of Dentistry
The University of Sydney

United Dental Hospital
Level 8, 2 Chalmers Street
Surry Hills 2010, Australia
Telephone: (61-2) 929 33 388/389
Facsimile: (61-2) 9351 8336

Dr. Andrew J. Pitsis B.D.S. Hons.(Syd.)
Orthodontic Registrar

1st December, 2000

Dr. S. Buchanan
Director of Dental Services
United Dental Hospital
2 Chalmers Street
SURRY HILLS NSW 2010

Dear Dr. Buchanan,

Re: Thesis MDS Sc (Orthodontics): Effect of MAS design in OSA

I am requesting that
be admitted as a patient to the UDH as a professorial patient involved in the above
mentioned study.

Yours sincerely,

Dr. Andrew J. Pitsis

APPENDIX 5. ORTHODONTIC HISTORY AND EXAMINATION

Date	:		Reason for referral	:	
Name	:		Weight	:	
Date of Birth	:		Height	:	
Patient Number	:		BMI	:	

Medical History

Asthma	:	
Medication	:	
Respiratory Mode	:	Mouth ☐ Nose ☐
Previous / Current OSA Tx	:	

Dental History

Any previous dental device Tx before	:	No ☐	Yes ☐
If yes, then has it failed	:	No ☐	Yes ☐
Jaw Surgery	:	No ☐	Yes ☐
Bruxism	:	No ☐	Yes ☐
Last Dental Visit	:		

Extra-Oral Examination

FRONTAL

Symmetry and shape	:	
Vertical thirds	:	
Lips	:	
Nose	:	

PROFILE

Skeletal base	:	
Vertical thirds	:	
Lips	:	
Nose	:	

Intra-Oral Hygiene

Oral Hygiene	:	Teeth Present	:	<u>87654321 / 12345678</u>
CPITN	:	Caries	:	<u>87654321 / 12345678</u>

Intra-Oral Examination (cont'd)

Soft tissue abnormalities	:	Restorations	:	
Periodontium	:	RHS	LHS	
Pocketing	:	Molars	:	
Overbite	:	Canines	:	
Crossbites	:	Overjet	:	
Inter canine width	:	Interpremolar / Intermolar width	:	

Functional

Evaluation

Jaw function / TMJ complaint now	:	No	☐	Yes	☐
If yes, specify	:				
History of pain	:	No	☐	Yes	☐
If yes, duration	:				
History of joint sounds	:	No	☐	Yes	☐
TM Joint tenderness to palpation	:	No	☐	Yes	☐
If yes, which joint	:	Right	☐	Left	☐
Muscle tenderness to palpation	:	No	☐	Yes	☐
If yes, where	:				

Range of motion: Maximum opening : _____ mm

Right excursion : _____ mm

Left excursion : _____ mm

Protrusion : _____ mm

CR/CO discrepancy :

Exaggerated GAG reflex : Yes ☐ No ☐

Final Advancement : _____ mm

APPENDIX 6. SLEEP QUESTIONNAIRES

SLEEP QUESTIONNAIRE: 1

Name:

Age:

Patient Number:

Date:

1. Do you snore?
- ☐ Yes
- ☐ No (please proceed to question 4.)
-
2. On average, how many days/nights during the last month have you snored or been told that you snore? (Tick one only).
- ☐ Rarely (once a week)
- ☐ Sometimes (1-2 times per week)
- ☐ Frequently (3-4 times per week)
- ☐ Almost always (5-7 times per week)
- ☐ Do not know
-
3. Please describe your snoring over the last month (Tick one only):
- ☐ Only slightly louder than heavy breathing
- ☐ As loud as mumbling or talking
- ☐ Louder than talking
- ☐ So loud that it can be heard through a closed door
- ☐ Do not know

4. Who has provided information on questions 1, 2 and 3?

- ☐ You
- ☐ Your partner
- ☐ Both

5. Please pick a number from the scale below to show the extent of your daytime sleepiness / fatigue in the last month, when undertaking each of the activities listed below. Mark your selection in the space to the right of each item.

Scale

- 1 = Would **never** doze
- 2 = **Slight** chance of dozing
- 3 = **Moderate** chance of dozing
- 4 = **High chance** of dozing

Sitting and reading	_____
Watching TV	_____
Sitting, inactive in a public pace (e.g. theatre, meetings)	_____
A passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after lunch without alcohol	_____
In a car while stopped for a few minutes in the traffic	_____

6. How would you describe the quality of your sleep (tick one only)?

- ☐ Refreshing
- ☐ Slightly unrefreshing
- ☐ Moderately unrefreshing
- ☐ Very unrefreshing

7. How tired are you when waking?

- ☐ Not tired
- ☐ Slightly tired
- ☐ Moderately tired
- ☐ Very tired

8. Do you live with a partner?

- ☐ Yes (**please proceed to question 9**)
- ☐ No

9. If you live with a partner do you:

- ☐ share the same bedroom
- ☐ sleep in different rooms because of the snoring
- ☐ sleep in different rooms for reasons other than snoring

Any further comments:

Thank you for your cooperation

SLEEP QUESTIONNAIRE: 2

This questionnaire pertains to the period of Appliance Use

Name:

Age:

Patient Number:

Date:

1. How often did you use your oral appliance in the last 2 weeks? (Tick one only)

- ☐ Regularly: everyday of the week
- ☐ Occasionally: 3-4 times per week
- ☐ Rarely: 1-2 times per week
- ☐ Not at all

2. Did you snore while wearing the appliance:

- ☐ Yes
- ☐ No (please proceed to question 5)

3. On average, how many days / nights during the last 2 weeks have you snored or been told that you snored? (Tick one only)

- ☐ Never
- ☐ Rarely: once a week
- ☐ Sometimes: 1-2 times per week
- ☐ Frequently: 3-4 times per week
- ☐ Almost always: 5-7 times per week
- ☐ Do not know

4. Please describe your snoring over the last 2 weeks (Tick one only):

- ☐ Only slightly louder than heavy breathing
- ☐ As loud as mumbling or talking
- ☐ Louder than talking
- ☐ So loud that it can be heard through a closed door
- ☐ Do not know

5. How much has your snoring improved since using the Oral Appliance? (Tick one only)

- ☐ Snoring cured
- ☐ Snoring greatly improved
- ☐ Snoring improved
- ☐ Snoring slightly improved
- ☐ No improvement

6. Did you involuntarily remove the Oral Appliance on any night:

- ☐ Yes
- ☐ No

If yes, why?

7. Did the Oral Appliance loosen with time?

- ☐ Yes
- ☐ No

8. Did you stop using the Oral Appliance over the last 2 weeks?

- ☐ Yes **(please answer below and proceed to question 9)**
- ☐ No

If yes, why?

9. When did you stop using the Oral Appliance?

- ☐ After 1-3 days
- ☐ After 4-6 days
- ☐ After 7-9 days
- ☐ After 10-13 days

10. Please pick a number from the scale below to show the extent of your daytime sleepiness / fatigue in the last month (whilst using the Oral Appliance at night), when undertaking each of the activities listed below. Mark your selection in the space to the right of each item.

Scale

- 1 = Would **never** doze
- 2 = **Slight** chance of dozing
- 3 = **Moderate** chance of dozing
- 4 = **High** chance of dozing

Sitting and reading	_____
Watching TV	_____
Sitting, inactive in a public pace (e.g. theatre, meetings)	_____
A passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after lunch without alcohol	_____
In a car while stopped for a few minutes in the traffic	_____

How has the Oral Appliance affected the degree of your daytime sleepiness/fatigue:

- ☐ Cured
- ☐ Improved
- ☐ Same
- ☐ Unsure

11. How would you rate the quality of your sleep with the appliance?

- ☐ Refreshing
- ☐ Slightly unrefreshing
- ☐ Moderately unrefreshing
- ☐ Very unrefreshing

12. How has the Oral Appliance improved the quality of your sleep?

- ☐ Huge improvement
- ☐ Improvement
- ☐ Same
- ☐ Unsure

13. How tired were you when waking whilst using the Oral Appliance in the last 2 weeks?

- ☐ Not tired
- ☐ Slightly tired
- ☐ Moderately tired
- ☐ Very tired

14. How has the Oral Appliance affected your level of tiredness when waking?

- ☐ Huge improvement
- ☐ Improvement
- ☐ Same
- ☐ Unsure

15. Since obtaining the Oral Appliance has your sleeping habit changed?

- ☐ Yes. Now sleep in the same room as partner.
- ☐ No change. Sleep in different rooms because of snoring.
- ☐ No change. Sleep in different rooms for reasons other than snoring.
- ☐ No change. Sleep in the same room as partner.

16. Have you encountered difficulties with the appliance?

- ☐ Yes (**please proceed to question 18**)
- ☐ No (**please proceed to question 21**)

17. Which of the following side effects did you experience with the Oral Appliance?

Please mark your selections below.

<u>SIDE EFFECT</u>	<u>SEVERITY</u>	<u>FREQUENCY</u>	<u>DURATION</u>
A. Jaw Discomfort ☐ Yes ☐ No (If No, go to B)	If yes, specify severity ☐ Mild ☐ Moderate ☐ Severe	If yes, specify frequency ☐ Rarely ☐ Sometimes ☐ Often	If yes, specify duration ☐ < 1 week ☐ 1 week ☐ 2 weeks ☐ 3 weeks ☐ > 3 weeks
B. Excess Salivation ☐ Yes ☐ No (If No, go to C)	If yes, specify severity ☐ Mild ☐ Moderate ☐ Severe	If yes, specify frequency ☐ Rarely ☐ Sometimes ☐ Often	If yes, specify duration ☐ < 1 week ☐ 1 week ☐ 2 weeks ☐ 3 weeks ☐ > 3 weeks
C. Dry mouth ☐ Yes ☐ No (If No go to D)	If yes, specify severity ☐ Mild ☐ Moderate ☐ Severe	If yes, specify frequency ☐ Rarely ☐ Sometimes ☐ Often	If yes, specify duration ☐ < 1 week ☐ 1 week ☐ 2 weeks ☐ 3 weeks ☐ > 3 weeks
D. Grinding of Teeth at night ☐ Yes ☐ No (If No, go to E)	If yes, specify severity ☐ Mild ☐ Moderate ☐ Severe	If yes, specify frequency ☐ Rarely ☐ Sometimes ☐ Often	If yes, specify duration ☐ < 1 week ☐ 1 week ☐ 2 weeks ☐ 3 weeks ☐ > 3 weeks
E. Gum Irritation ☐ Yes ☐ No (If No go to Q. 19)	If yes, specify severity ☐ Mild ☐ Moderate ☐ Severe	If yes, specify frequency ☐ Rarely ☐ Sometimes ☐ Often	If yes, specify duration ☐ < 1 week ☐ 1 week ☐ 2 weeks ☐ 3 weeks ☐ > 3 weeks

18. Please list any other side effects (if any) not mentioned above:

19. Did the side effects prevent you from using the Oral Appliance

☐ Yes

☐ No

20. How would you rate your satisfaction with the appliance?

☐ Very satisfied

☐ Satisfied

☐ Dissatisfied

☐ Very dissatisfied

21. Would you like to continue using the Oral Appliance?

☐ Yes

☐ No

Any further comments:

Thank you for your cooperation

SLEEP QUESTIONNAIRE: 3

This questionnaire pertains to the comparison of the appliances.

Name:

Age:

Patient Number:

Date:

1. How often did you use your oral appliance in the last 2 weeks? (Tick one only)

- ☐ Regularly: everyday of the week
- ☐ Occasionally: 3-4 times per week
- ☐ Rarely: 1-2 times per week
- ☐ Not at all

2. Did you snore while wearing the appliance:

- ☐ Yes
- ☐ No (please proceed to question 5)

3. On average, how many days / nights during the last 2 weeks have you snored or been told that you snored? (Tick one only)

- ☐ Never
- ☐ Rarely: once a week
- ☐ Sometimes: 1-2 times per week
- ☐ Frequently: 3-4 times per week
- ☐ Almost always: 5-7 times per week
- ☐ Do not know

4. Please describe your snoring over the last 2 weeks (Tick one only):

- ☐ Only slightly louder than heavy breathing
- ☐ As loud as mumbling or talking
- ☐ Louder than talking
- ☐ So loud that it can be heard through a closed door
- ☐ Do not know

5. How much has your snoring improved since using the Oral Appliance? (Tick one only)

- ☐ Snoring cured
- ☐ Snoring greatly improved
- ☐ Snoring improved
- ☐ Snoring slightly improved
- ☐ No improvement

6. Did you involuntarily remove the Oral Appliance on any night:

- ☐ Yes
- ☐ No

If yes, why?

7. Did the Oral Appliance loosen with time?

- ☐ Yes
- ☐ No

8. Did you stop using the Oral Appliance over the last 2 weeks?

- ☐ Yes **(please answer below and proceed to question 9)**
- ☐ No

If yes, why?

9. When did you stop using the Oral Appliance?

- ☐ After 1-3 days
- ☐ After 4-6 days
- ☐ After 7-9 days
- ☐ After 10-13 days

10. Please pick a number from the scale below to show the extent of your daytime sleepiness / fatigue in the last month (whilst using the Oral Appliance at night), when undertaking each of the activities listed below. Mark your selection in the space to the right of each item.

Scale

- 1 = Would **never** doze
- 2 = **Slight** chance of dozing
- 3 = **Moderate** chance of dozing
- 4 = **High** chance of dozing

Sitting and reading	_____
Watching TV	_____
Sitting, inactive in a public place (e.g. theatre, meetings)	_____
A passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after lunch without alcohol	_____
In a car while stopped for a few minutes in the traffic	_____

11. How has the Oral Appliance affected the degree of your daytime sleepiness/fatigue:

- ☐ Cured
- ☐ Improved
- ☐ Same
- ☐ Unsure

12. How would you rate the quality of your sleep with the appliance?

- ☐ Refreshing
- ☐ Slightly unrefreshing
- ☐ Moderately unrefreshing
- ☐ Very unrefreshing

13. How has the Oral Appliance improved the quality of your sleep?

- ☐ Huge improvement
- ☐ Improvement
- ☐ Same
- ☐ Unsure

14. How tired were you when waking whilst using the Oral Appliance in the last 2 weeks?

- ☐ Not tired
- ☐ Slightly tired
- ☐ Moderately tired
- ☐ Very tired

15. How has the Oral Appliance affected your level of tiredness when waking?

- ☐ Huge improvement
- ☐ Improvement
- ☐ Same
- ☐ Unsure

16. Since obtaining the Oral Appliance has your sleeping habit changed?

- ☐ Yes. Now sleep in the same room as partner.
- ☐ No change. Sleep in different rooms because of snoring.
- ☐ No change. Sleep in different rooms for reasons other than snoring.
- ☐ No change. Sleep in the same room as partner.

17. Have you encountered difficulties with the appliance?

- ☐ Yes (**please proceed to question 18**)
- ☐ No (**please proceed to question 21**)

18. Which of the following side effects did you experience with the Oral Appliance?
Please mark your selections below.

SIDE EFFECT	SEVERITY	FREQUENCY	DURATION
A. Jaw Discomfort ☐ Yes ☐ No (If No, go to B)	If yes, specify severity ☐ Mild ☐ Moderate ☐ Severe	If yes, specify frequency ☐ Rarely ☐ Sometimes ☐ Often	If yes, specify duration ☐ < 1 week ☐ 1 week ☐ 2 weeks ☐ 3 weeks ☐ > 3 weeks
B. Excess Salivation ☐ Yes ☐ No (If No, go to C)	If yes, specify severity ☐ Mild ☐ Moderate ☐ Severe	If yes, specify frequency ☐ Rarely ☐ Sometimes ☐ Often	If yes, specify duration ☐ < 1 week ☐ 1 week ☐ 2 weeks ☐ 3 weeks ☐ > 3 weeks
C. Dry mouth ☐ Yes ☐ No (If No go to D)	If yes, specify severity ☐ Mild ☐ Moderate ☐ Severe	If yes, specify frequency ☐ Rarely ☐ Sometimes ☐ Often	If yes, specify duration ☐ < 1 week ☐ 1 week ☐ 2 weeks ☐ 3 weeks ☐ > 3 weeks
D. Grinding of Teeth at night ☐ Yes ☐ No (If No, go to E)	If yes, specify severity ☐ Mild ☐ Moderate ☐ Severe	If yes, specify frequency ☐ Rarely ☐ Sometimes ☐ Often	If yes, specify duration ☐ < 1 week ☐ 1 week ☐ 2 weeks ☐ 3 weeks ☐ > 3 weeks
E. Gum Irritation ☐ Yes ☐ No (If No go to Q. 19)	If yes, specify severity ☐ Mild ☐ Moderate ☐ Severe	If yes, specify frequency ☐ Rarely ☐ Sometimes ☐ Often	If yes, specify duration ☐ < 1 week ☐ 1 week ☐ 2 weeks ☐ 3 weeks ☐ > 3 weeks

19. Please list any other side effects (if any) not mentioned above:

20. Did the side effects prevent you from using the Oral Appliance

☐ Yes

☐ No

21. How would you rate your satisfaction with the appliance?

☐ Very satisfied

☐ Satisfied

☐ Dissatisfied

☐ Very dissatisfied

22. Would you like to continue using the Oral Appliance?

☐ Yes

☐ No

23. Which appliance was more comfortable?

☐ MAS 1 (which keeps your jaw relatively closed)

☐ MAS 2 (which keeps your jaw relatively open)

Why?

24. Which appliance do you prefer?

- ☐ MAS 1 (which keeps your jaw relatively closed)
- ☐ MAS 2 (which keeps your jaw relatively open)

Why?

Any further comments:

Thank you for your cooperation

APPENDIX 7. INDIVIDUAL PATIENT CHARACTERISTIC DATA

Patient No.	Patient Group AB=1 BA=2	Sex 1=M 2=F	Age (yr)	Weight (kg)	Height (m)	BMI (kg/m ²)	AHI (per hr)	AHI-A (per hr)	AHI-B (per hr)	Arousal Index (per hr)	Arousal-A Index (per hr)	Arousal-B Index (per hr)	Longap (s)	Longap-A (s)	Longap-B (s)	MINSO (%)	MINSO-A (%)	MINSO-B (%)
1	1	2	60	84.72	1.64	31.5	18.5	10.2	9.2	21.1	25.8	22.9	80	22	24	84	92	92
2	2	1	50	88.9	1.7	30.76	19.8	1.3	1	32.2	13	14.5	48	0	0	87	91	93
3	2	1	54	71.5	1.82	21.59	15.2	9.8	2.5	22.2	16.8	8.8	54	0	33	87	93	93
4	1	1	53	92	1.7	31.83	35.1	10.9	13.6	45.4	31.3	21.3	37.3	30	68	84	86	81
5	1	2	41	62.7	1.62	23.89	10.8	1.4	1	31.8	19.8	25.1	0	16	0	94	91	93
6	2	1	63	85.6	1.63	32.22	30.3	25.8	19.7	49.7	41.8	32.4	23	35	18	85	85	87
7	2	1	64	107	1.67	38.37	22.9	20.2	13	19.1	25.3	15	28	47	22	94	82	85
8	1	1	41	93.3	1.67	33.45	43.8	5.7	9.3	42.5	14	12.4	50	0	0	80	91	88
9	2	1	39	90.7	1.72	30.66	25.6	10	17.3	22.9	17.7	10.5	22	12	22	87	88	88
10	1	2	54	90	1.62	34.29	6.3	9.1	8.3	77.7	98.5	97	0	13	0	88	87	86
11	2	1	43	73.6	1.66	26.71	7.6	3.1	2.3	27.8	20.5	13.9	45	34	20	91	93	94
12	1	1	58	82	1.65	30.12	10.7	2.8	13	20.2	14.3	10.9	0	0	44	86	90	84
13	1	1	64	99	1.77	31.6	29.9	18.7	19.7	90.5	53.9	50.1	43	28	49	85	85	87
14	1	1	41	98	1.81	29.91	13.6	3.6	1.9	22	9.4	13.4	24	0	40	88	89	88
15	2	1	52	75	1.7	25.96	10	2.8	6.8	10.7	13.9	17.2	0	35	0	90	90	89
16	1	1	48	110.3	1.76	35.61	9.8	3.5	30.9	37.5	21.1	31.5	24	26	32	83	81	87
17	2	1	46	130	1.73	43.44	6.4	0.2	1.5	23.8	34.4	28.8	19	0	0	93	93	92
18	2	1	62	100	1.77	31.92	19	3.9	14.6	36	27.2	27.9	19	0	0	84	79	73
19	1	1	45	114.4	1.84	33.79	47	17.2	17.6	38	14.5	30.2	65	37	39	84	87	81
20	2	1	47	96.4	1.74	31.84	17.5	4.5	5.8	35.4	32.8	28.5	23.3	0	0	82	92	88
21	1	1	64	93.6	1.81	28.57	29	11.6	12.7	29.8	20.2	24.2	62	33	0	85	90	83
22	1	1	29	127.4	1.73	42.57	32.8	2.5	3.5	49.5	15.8	12.4	12	0	0	86	91	91
23	2	1	43	72	1.76	23.24	21.2	2.2	0.6	42.6	12	13	29	0	0	88	92	95

APPENDIX 8. INDIVIDUAL PATIENT CEPHALOMETRIC MEASUREMENTS

Patient No.	PH-ST (mm)	PH-ST-A (mm)	PH-ST-B (mm)	PPAS (mm)	PASA (mm)	PASB (mm)	PM-P (mm)	PM-P-A (mm)	PM-P-B (mm)	SPT (mm)	SPT-A (mm)	SPT-B (mm)	TL-A (mm)	TL-B (mm)	PPAS (mm)	PPAS-A (mm)	PPAS-B (mm)	SNB (°)	SNB-A (°)	SNB-B (°)	ANB-A (°)	ANB-B (°)
1	15	12	16	7	11	11	45	47	44	7	9	9	71	65	4	7	8	78	78	75	4	7
2	11	10	14	8	15	14	39	46	47	13	13	11	86	87	6	7	6	77	77	73	4	6
3	7	8	11	14	15	15	50	45	45	12	11	9	72	73	4	3	5	78	79	77	3	4
4	10	8	7	9	7	7	51	42	47	10	9	11	74	74	4	3	4	70	71	69	1	2
5	10	10	11	3	5	7	32	40	39	9	9	8	69	66	3	4	6	69	70	67	5	6
6	13	13	12	8	8	12	35	36	38	11	11	11	76	71	4	4	4	80	81	77	2	4
7	8	10	11	10	10	10	41	36	41	12	12	10	83	78	4	6	6	77	80	76	1	1
8	8	9	9	9	10	8	43	41	43	9	9	9	85	79	5	6	5	80	86	82	-1	-2
9	13	12	14	9	9	6	44	41	42	11	11	11	80	84	6	7	6	80	81	78	1	-2
10	8	9	9	8	7	8	41	40	40	10	10	10	71	67	3	3	4	80	83	78	5	7
11	9	12	15	9	10	8	48	46	40	14	12	9	78	79	4	5	5	77	79	83	4	3
12	24	18	20	19	20	18	37	40	49	9	11	9	77	73	19	15	13	78	78	75	0	4
13	10	12	8	8	11	9	46	44	51	10	10	10	72	67	7	8	4	71	81	76	4	10
14	14	13	14	9	11	12	40	38	36	7	10	10	86	78	8	8	6	80	82	81	5	4
15	13	15	14	16	15	12	44	41	44	10	10	10	76	80	10	13	11	88	89	87	-3	-2
16	6	11	8	12	12	12	47	43	45	15	12	13	78	74	3	6	4	85	87	82	0	2
17	11	14	13	7	7	9	56	55	53	10	10	9	92	92	4	6	6	80	83	79	3	3
18	5	8	5	7	8	7	50	49	49	13	13	14	88	82	1	5	2	81	87	84	3	-1
19	9	13	12	3	4	3	61	57	56	11	9	10	87	80	3	3	3	74	77	75	-1	0
20	13	17	17	13	14	19	46	49	49	11	9	12	88	74	9	10	12	82	84	88	3	-4
21	6	7	7	9	7	9	54	47	54	14	12	12	78	77	3	2	2	80	82	80	3	4
22	12	13	11	14	14	13	46	46	46	15	11	12	88	83	6	8	7	90	92	90	-3	-2
23	7	10	13	9	11	9	46	41	44	12	12	10	79	80	5	10	8	76	77	75	1	2

APPENDIX 8. INDIVIDUAL PATIENT CEPHALOMETRIC MEASUREMENTS

Patient No.	PAFH (mm)	PAHHA (mm)	PAHFB (mm)	LABH (mm)	LABHA (mm)	LABHB (mm)	OB (mm)	OBHA (mm)	OBHB (mm)	OU (mm)	QUB (mm)	SN-C24 (°)	SNB2 (°)	SNMP (°)	SNMPA (°)	SNMPB (°)	SH (mm)	SHA (mm)	SHB (mm)	HEMP (mm)	HEMPA (mm)	HEMPB (mm)
1	126	138	148	72	84	94	3	-9	-19	1	-4	-1	103	33	38	45	107	102	107	16	6	5
2	127	138	148	78	89	98	3	-8	-18	1	-1	3	104	24	25	34	130	126	125	25	16	16
3	131	142	151	74	85	94	4	-8	-18	3	-4	-2	112	23	28	35	114	116	118	9	0	0
4	134	142	156	79	86	102	0	-11	-21	0	-6	-3	111	34	36	44	127	123	130	28	13	14
5	138	149	156	81	91	100	3	-8	-18	3	-6	-5	110	59	65	72	104	99	102	8	4	2
6	149	157	168	86	93	102	0	-9	-19	-1	-4	-3	95	25	28	35	148	143	143	20	8	5
7	122	134	145	75	84	91	4	-9	-19	3	-4	-3	115	25	32	38	112	108	111	17	6	6
8	109	117	126	62	71	82	5	-5	-15	2	-6	-3	104	25	23	30	123	116	119	30	21	19
9	134	147	159	74	86	102	6	-8	-18	3	-7	-5	107	27	31	38	124	123	126	17	3	1
10	115	125	133	70	79	86	5	-6	-16	3	-1	-1	110	24	28	33	108	105	104	15	3	1
11	144	154	163	84	91	100	2	-7	-17	2	-8	-6	115	31	33	42	131	127	135	16	3	10
12	134	145	154	80	90	100	4	-6	-16	2	-5	-3	113	34	39	46	121	120	122	22	10	12
13	130	150	157	73	94	102	15	-7	-17	2	-4	-3	105	32	44	51	140	138	138	33	21	16
14	133	144	153	74	86	95	3	-8	-18	4	-5	-3	107	27	33	39	145	137	137	34	22	19
15	127	139	147	71	81	92	2	-9	-19	1	-6	-4	112	24	29	37	134	135	137	33	22	24
16	126	137	149	75	89	100	4	-8	-18	4	-2	1	97	21	24	33	135	132	129	27	16	11
17	137	146	154	80	87	97	5	-5	-15	2	-4	-3	111	31	34	40	129	131	136	27	22	24
18	132	142	150	80	90	100	2	-8	-20	1	-12	-9	109	32	31	38	138	131	133	30	15	14
19	153	144	154	71	80	90	3	-7	-17	3	-6	-5	100	31	35	43	133	133	134	31	23	18
20	127	138	142	77	86	96	3	-6	-16	4	-4	-2	100	23	26	28	121	123	121	17	14	13
21	136	148	155	78	87	95	7	-6	-16	2	-6	-4	103	22	25	31	135	135	135	21	9	8
22	132	139	148	80	86	92	0	-8	-18	0	-6	-3	101	20	22	25	130	129	128	16	12	8
23	147	157	167	86	94	105	1	-9	-22	2	-10	-4	108	39	43	52	138	136	141	22	16	19