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TREATMENT OF SNORING AND OBSTRUCTIVE SLEEP APNOEA USING A MANDIBULAR ADVANCEMENT SPLINT

A thesis submitted in partial requirement for the degree of Master of Dental Science (Orthodontics)

by

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1998
DEDICATION

This thesis is dedicated to my family. Especially to my wife, Roopa, who I love and admire. She has been an eternal source of encouragement and inspiration and has supported me untiringly during the preparation of my thesis and during the Masters Program.

To our parents for their love and support. They have opened the doors and given us the opportunities to become what we are today.
ABSTRACT

There has been a growing interest in the use of oral appliances (OA) in the treatment of snoring and obstructive sleep apnoea (OSA) in the last decade. However, nasal continuous positive airway pressure (CPAP) remains the treatment of choice. While treatment of OSA with CPAP is highly effective, it is poorly tolerated. Therefore, effective and acceptable alternative treatments for both snoring and OSA are required. Oral appliances provide a viable alternative, but there is a paucity of robust research investigating their effectiveness.

The aim of this prospective, randomised, placebo-controlled, cross-over study was to evaluate the effectiveness of a newly designed mandibular advancement splint (MAS) in patients with mild to severe OSA, and to identify predictors of response to MAS therapy.

The MAS consisted of an upper and lower removable appliance. Mechanical protrusion of the mandible was obtained by bilateral posterior palatal flanges of the upper plate locking into slots on the lower plate. Incremental advancement of the mandible was obtained by means of screws on the lower plate.

The patient sample consisted of 30 patients who met the eligibility criteria. Twenty-four patients (19 males, 5 females) completed the study protocol, and had a mean age of 48.0 ± 9.2 years (range 35.0 – 73.0 years). Baseline investigations included standard dental, anthropometric and radiographic measurements and completion of a validated questionnaire. Mean baseline apnoea hypopnoea index (AHI) and minimum arterial oxygen saturation (MinSaO₂), based on initial polysomnography, were 26.8 ± 16.5 /hr (range 10.0 – 68.0 /hr) and 84.7 ± 8.4% (range 61.0 – 96.0%) respectively. A MAS was then constructed for each patient for use during sleep. Over the acclimatisation period of 19.7 ± 8.8 weeks (mean ± sd) (range 5.0 – 40.0 weeks) the mandible was incrementally advanced until symptoms resolved or the maximum comfortable limit was reached.

The mean actual advancement with the MAS was 7.5 ± 1.8 mm (range 5.0 – 11.5 mm). This represented 78.2 ± 8.4% of maximum jaw protrusion. Following the acclimatisation period, there was a one week washout period where the MAS was not worn. Patients were then randomised into either the ABB or BAA sequence and underwent 3 polysomnograms one week apart (A refers to treatment with placebo; B
refers to treatment with MAS). The study cross-over design was unique compared to other OA studies in that it included an extra period which allowed simultaneous assessment of carry-over, period and sequence effects.

Outcomes were measured by subjective (questionnaires) and objective (standard polysomnographic) variables. Treatment Success was defined as a resolution of symptoms and a reduction in AHI to < 5/hr. Partial Success was defined as improved symptoms and ≥ 50% reduction in AHI, but AHI ≥ 5.

Subjective improvements were reported by 96% of the sample in relation to snoring, 91% for sleep quality and 96% for excessive daytime sleepiness.

The MAS resulted in a significant reduction in mean (± SEM) AHI (14.4 ± 1.8 /hr vs 29.9 ± 1.8 /hr), total time spent in apnoea in non-rapid eye movement (NREM) sleep (10.9 ± 4.3 min vs 23.3 ± 4.4 min), total time spent in apnoea and hypopnoea in NREM sleep (23.9 ± 4.4 min vs 65.8 ± 4.5 min), arousal index (27.5 ± 1.7 /hr vs 40.9 ± 1.7 /hr), NREM sleep (79.4 ± 0.8% vs 83.6 ± 0.9%), snoring frequency (223.0 ± 25.6 /hr vs 421.9 ± 27.0 /hr) and snoring intensity (49.2 ± 0.4 dB vs 52.5 ± 0.4 dB) compared to the placebo. There was also a significant increase in MinSaO₂ (90.7 ± 0.6% vs 86.7 ± 0.6%) and rapid eye movement (REM) sleep (20.6 ± 1.0% vs 16.4 ± 1.0%) with the MAS. There was no difference in total sleep time, time spent supine and sleep efficiency.

Treatment Success was achieved in 9 patients (37.5%), Partial Success in 6 patients (25%) and Treatment Failure in 9 patients (37.5%).

The compliance rate with the MAS over the acclimatisation period was 87.5%. During this period, the side-effects experienced with the MAS were minimal and did not prevent use of the appliance. Overall, 96% of the sample expressed their desire to continue use of the MAS.

A model to predict treatment response was derived using stepwise multiple regression analysis which identified neck circumference (NC), pre-treatment AHI, and 2 cephalometric parameters (Phw-spt distance and SN-Mp angle) as significant variables. The mathematical equation is:

$$\text{AHI (MAS)} = 19.4 + 1.3\text{NC} - 2.7\text{Phw-spt} + 0.4\text{BaseAHI} - 1.0\text{SN-Mp}$$

$$r^2 = 0.82, s = 8.06$$
ACKNOWLEDGMENTS

Deep gratitude is expressed to the following people:

Dr Peter Cistulli, Director of the Sleep Disorder Centre, St. George Hospital, for his supervision, expertise, guidance and encouragement. Peter not only gave time to supervise the project, but was available to engage in stimulating discussions, which have broadened my knowledge.

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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>A</td>
<td>treatment with placebo</td>
</tr>
<tr>
<td>AHI</td>
<td>Apnoea Hypopnoea Index</td>
</tr>
<tr>
<td>AI</td>
<td>Apnoeic Index</td>
</tr>
<tr>
<td>AMP</td>
<td>Anterior Mandibular Positioner</td>
</tr>
<tr>
<td>ANOVA</td>
<td>ANalysis Of VARIance</td>
</tr>
<tr>
<td>ASDA</td>
<td>American Sleep Disorders Association</td>
</tr>
<tr>
<td>B</td>
<td>treatment with mandibular advancement splint</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>CTX</td>
<td>Clinical Trial eXemption scheme</td>
</tr>
<tr>
<td>CPAP</td>
<td>Continuous Positive Airway Pressure</td>
</tr>
<tr>
<td>CPITN</td>
<td>Community Periodontal Index of Treatment Needs</td>
</tr>
<tr>
<td>dB</td>
<td>DeciBels</td>
</tr>
<tr>
<td>ECG</td>
<td>ElectroCardioGram</td>
</tr>
<tr>
<td>EEG</td>
<td>ElectroEncephaloGram</td>
</tr>
<tr>
<td>EMG</td>
<td>ElectroMyoGram</td>
</tr>
<tr>
<td>EOG</td>
<td>Electro-OculoGram</td>
</tr>
<tr>
<td>ESS</td>
<td>Epworth Sleepiness Scale</td>
</tr>
<tr>
<td>GLM</td>
<td>General Linear Model</td>
</tr>
<tr>
<td>kg/m²</td>
<td>KiloGrams per square Metre</td>
</tr>
<tr>
<td>MAD</td>
<td>Mandibular Advancement Device</td>
</tr>
<tr>
<td>MAS</td>
<td>Mandibular Advancement Splint</td>
</tr>
<tr>
<td>min</td>
<td>MINutes</td>
</tr>
<tr>
<td>MinSaO₂</td>
<td>MINimum arterial Oxygen SAturation level</td>
</tr>
<tr>
<td>mm</td>
<td>MilliMetres</td>
</tr>
<tr>
<td>NREM</td>
<td>Non-Rapid Eye Movement</td>
</tr>
<tr>
<td>ns</td>
<td>Non-Significant</td>
</tr>
<tr>
<td>OA</td>
<td>Oral Appliance</td>
</tr>
<tr>
<td>Acronym</td>
<td>Definition</td>
</tr>
<tr>
<td>---------</td>
<td>------------</td>
</tr>
<tr>
<td>OSA</td>
<td>Obstructive Sleep Apnoea</td>
</tr>
<tr>
<td>p</td>
<td>level of significance (Probability value)</td>
</tr>
<tr>
<td>r²</td>
<td>correlation coefficient</td>
</tr>
<tr>
<td>REM</td>
<td>Rapid Eye Movement</td>
</tr>
<tr>
<td>RDI</td>
<td>Respiratory Disturbance Index</td>
</tr>
<tr>
<td>sd</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SE</td>
<td>Standard Error</td>
</tr>
<tr>
<td>SEM</td>
<td>Standard Error of the Mean</td>
</tr>
<tr>
<td>TMJ</td>
<td>TemporoMandibular Joint</td>
</tr>
<tr>
<td>TST</td>
<td>Total Sleep Time</td>
</tr>
<tr>
<td>TRD</td>
<td>Tongue Retaining Device</td>
</tr>
<tr>
<td>UPPP</td>
<td>UvuloPalatoPharyngoPlasty</td>
</tr>
<tr>
<td>%</td>
<td>percent</td>
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*Note: The letters of words used to make up the acronym are capitalised.*
LIST OF DEFINITIONS

Acclimatisation Period refers to the period between the date when the appliance was first fitted and when the patient was instructed to stop wearing the appliance for the one week washout period.

Carry-over Effect refers to the fact that an effect of treatment given in one period might still be present at the start of the following period.

Epoch is a time period; it means the sleep study was studied with each page representing 30 seconds.

Oral Appliance is used as a generic term for devices inserted into the mouth in order to modify the position of the mandible, tongue and other structures in the upper airway for the purpose of relieving snoring and sleep apnoea.

Period Effect refers to the effect that the length of time between treatments has on the outcome.

Placebo is defined as an inactive treatment or administered substance used in the course of a trial.

Sequence Effect refers to the effect that a particular treatment sequence has on the outcome.

Sleep Efficiency is the proportion of sleep in the episode potentially filled by sleep ie the ratio of total sleep time to sleep study duration.

Washout Period is to avoid any carry-over effect, which could have affected the result of the first sleep study.
1. INTRODUCTION

In recent years, increasing interest has developed in sleep related breathing disorders such as snoring and obstructive sleep apnoea (OSA). It is unclear whether the interest is due to greater awareness or to a real increase in prevalence of these disorders.

A quotation from Charcot in 1850 about Duchenne’s dystrophy is applicable: “How come that a disease so common, so widespread, and so recognisable at a glance - a disease which has doubtless always existed - how come that it is only recognised now?” (Stradling, 1988).

A survey (Loube and Strauss, 1997) of oral appliance (OA)1 practice in the USA, found that over the preceding year, dentists evaluated or treated 5% of their patients for either snoring or sleep apnoea. At present, there are at least twenty five different OAs in use for the treatment of snoring or OSA with the efficacy of individual OAs varying widely (Lowe, 1994). It has been speculated that therapy for OSA will occupy more dental office time in the 1990’s than treatment for temporomandibular joint (TMJ) disorders required in the 1980’s (Lowe, 1989; George, 1993).

The literature review details the current knowledge on snoring and OSA. The prevalence, pathophysiology, clinical features, consequences and diagnosis of OSA are discussed.

The review will focus on the management, in particular, the use of Mandibular Advancement Splints (MAS) in the treatment of snoring and OSA.

1.1 Background

Sleep apnoea was described as early as 360 BC (Aelianus, 1666). It was later highlighted by a number of writers. In 1837, Charles Dickens in his novel “The Posthumous Papers of the Pickwick Club” referring to one of his characters (Joe) wrote, “and on the box sat a fat and red-faced boy, in a state of somnolency”.

1 The term ‘oral appliance’ is used as a generic term for devices inserted into the mouth in order to modify the position of the mandible, tongue and other structures in the upper airway for the purpose of relieving snoring and sleep apnoea (Schmidt-Nowara et al., 1995).
Other references in Dicken’s book suggest Joe had severe sleep apnoea, “Joe-darn that boy, he’s gone to sleep again....In response to the firing of enormous guns at a military exercise, everybody was excited except the fat boy, and he slept soundly as if the roaring of cannon were his ordinary lullaby....Be good enough to pinch him, sir-in the leg, if you please; nothing else wakes him....(Joe) snores as he waits at the table....the snoring of the fat boy penetrated in a low and monotonous sound from the distant kitchen” (Dickens, 1837).

In 1889, William Hill wrote “The stupid looking lazy kid who frequently suffers from headaches at school, breathes through his mouth instead of his nose, snores and is restless at night, wakes up with a dry mouth in the morning, is well worthy of the attention of the school medical officer”.

In 1901 Sir William Osler coined the term “Pickwickian” to refer to obese, hypersononolent patients (Kryger, 1983; Lavie, 1984). In 1956, Dr Burwell and colleagues in describing several obese, hypersononolent patients with respiratory and cardiac failure used the term “Pickwickian Syndrome” (Kryger, 1983).

Gastault and his French colleagues (Gastault et al., 1965) made the important observation that “Pickwickian” patients had repetitive apnoea events while asleep. Guilleminault and colleagues (Guilleminault et al., 1973) were the first to describe sleep apnoea as a syndrome. They were one of the first to describe the interaction between sleep, the respiratory muscles of the chest, and the muscles of the upper airway. This 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) thus initiating the most common and successful treatment, currently known, for this disorder. Prior to this, tracheostomy was the only effective treatment (Westbrook and Millman, 1994). Sullivan’s landmark paper prompted a vast amount of research elucidating why sleep apnoea occurs, the incidence of this condition and what type of treatments are most successful.
1.2 Snoring

1.2.1 Definition

Snoring is an inspiratory noise caused by vibration of the elements of the airway, predominantly the soft palate and posterior faucial pillars (Lugaresi and Partinen, 1994).

Snoring, a sign of a partially obstructed upper airway during sleep, affects people of all ages but is most common in overweight, middle-aged and elderly adults (American Sleep Disorders Association and Sleep Research Society (ASDA), 1995). It affects about 10% of the population, being more common in men than in women (Guilleminault and Dement, 1978). Although not all snorers have sleep apnoea, snoring is a cardinal symptom of OSA.

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 and sleepiness. This is known as “upper airway resistance syndrome” (Guilleminault et al., 1992) and is characterised by repeated arousals related to increased upper airway resistance without recognisable hypopnoea or apnoea.

1.2.2 Pathophysiology

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

During sleep, the muscles and soft tissues in the throat and mouth relax narrowing the airway. Flow limitation is a prerequisite for snoring. This decrease in the airway space increases the velocity of air flowing through the airway during breathing. As the velocity of air is increased in the constricted space, soft tissues like the soft palate and the uvula vibrate. These vibrations of the soft tissues in the mouth and throat result in “noisy breathing” or snoring (Isono and Remmers, 1994).

1.2.3 Clinical Consequences

Snoring has been identified as 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 the apparent association between snoring and cardiovascular disease could be confounded by variables such as age and obesity. However, the increased risk of these conditions is still demonstrated after adjusting for age, body mass index and other factors (Koskenvuo et al., 1987; D'Alessandro et al., 1990).

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

1.3 Sleep Apnoea

1.3.1 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 for sleep apnoea to be diagnosed, at least 5 such episodes must occur per hour (Guilleminault and Dement, 1978).

A hypopnoea, or reduction in airflow, 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) or the Respiratory Disturbance Index (RDI). AHI$^2$ 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 term 'sleep apnoea syndrome', in which cessation of breathing occurs repeatedly during sleep for long enough periods to cause measurable blood deoxygenation (Berkow Robert, 1992), 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:

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$^2$ For the purposes of this thesis, the term AHI is used.
excessive daytime sleepiness, loud snoring, witnessed apnoeas\textsuperscript{3}, unrefreshing sleep or underlying cardiopulmonary disease (Naughton, 1997).

1.3.2 Classification

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

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

Obstructive sleep apnoea, the most common of the three types of apnoea, is related to upper airway blockage despite airflow drive 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). For sleep apnoea to be diagnosed, at least five such episodes must occur per hour (Guilleminault and Dement, 1978).

Mixed apnoeas occur 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 which, although initially useful for research in the field, 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 OSA than a healthy, asymptomatic 75 year old with 15 apnoeas per hour (Guilleminault et al., 1977).

This thesis will focus on snoring and obstructive sleep apnoea.

\textsuperscript{3} An apnoeic event witnessed by the bed partner.
1.3.3 Prevalence

OSA is more common in middle-aged (greater than 40 years) and overweight, men (Guilleminault and Dement, 1978). However, cases also occur among infants, children (Brouillette et al., 1982) and women (Wilholt and Suratt, 1987; Guilleminault et al., 1988).

Estimates of the prevalence 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 at a conservative estimate, 2% of females and 4% of males in the USA, have a degree of sleep apnoea which is severe enough to warrant treatment. This makes OSA one of the most common medical disorders within the adult population.

The wide range in prevalence of OSA reported in the general population, by various epidemiological studies, could be attributed to differences in the diagnostic criteria employed, patient groups studied or methodologies used. For example, the percentage of the population with heavy snoring, doubles when the bed partner contributes to the questionnaire (Stradling et al., 1991). Also, population differences in obesity, alcohol consumption and genetic variability could have a bearing on prevalence figures.

Although there is conjecture in the literature about the incidence of OSA, there is general agreement that there is a higher incidence of the disorder in males compared to females and the likelihood of acquiring the condition increases with age and obesity.

1.3.4 Pathophysiology

The upper airway in humans is a complex structure composed of the nasal cavity, nasopharynx and oropharynx (Figure 1). The nasal cavity is situated between the bony palate below and the floor of the anterior cranial fossa above. The nasopharynx lies behind the nasal cavity and above the soft palate. The oropharynx extends from the soft palate to the level of the epiglottis (Johnson and Moore, 1983). Each segment has been considered as a possible site of obstruction in OSA (Solow, 1992).
Although the precise mechanism of OSA is not fully understood, current evidence (Anch \textit{et al.}, 1982; Lowe \textit{et al.}, 1986; Rodenstein \textit{et al.}, 1990; Hudgel, 1992; Cistulli and Sullivan, 1994) suggests that the aetiology is related to an interplay between:

- \textit{Predisposing factors}

- \textit{Anatomical structures} which may affect upper airway size and/or

- \textit{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 occlusion during sleep.

An overview of the aetiology of OSA is presented to allow an understanding of the rationale for OSA treatment.

\subsection{1.3.4.1 Predisposing Factors}

A number of factors may contribute to the severity of OSA. Pre-existing heart or lung disease makes breathing more difficult, thereby favouring decreased blood oxygen tensions. Central nervous system depressants such as alcohol, sedatives and
sleeping pills induce relaxation of the pharyngeal musculature, and therefore airway occlusion (Battagel, 1996).

Obesity and excess fat in both peripharyngeal and subcutaneous regions will also diminish the airway. Fatty deposits both subcutaneously and in the pharyngeal wall lead to narrowing of the oropharynx, encouraging its occlusion once the subject is supine (Battagel, 1996).

Other factors associated are male gender; increasing age; sleeping supine; familial tendency; metabolic and endocrine disorders, in particular hypothyroidism (McNamara et al., 1994).

1.3.4.2 Anatomical Structures Affecting Upper Airway Size

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

These studies, despite limitations, such as studying patients in the awake state and often in the erect posture, have implicated various skeletal and soft tissue craniofacial structures in the narrowing of the upper airway in patients with OSA. The sites of this 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).

The 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

A more acute cranial base angle (Na-S-Ba) was reported in OSA subjects by Jamieson et al. (1986) and Battagel and L'Estrange (1996). A reduction in the
anterior cranial base length has also been reported in OSA subjects by Bacon et al. (1990); Tangugsorn et al. (1995a); and Battagel and L’Estrange (1996).

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). However, other studies have found no evidence of mandibular retrognathia in OSA subjects (DeBerry-Borowiecki et al., 1988; Zucconi et al., 1992). Tsuchiya et al. (1992), categorising OSA patients by cluster analysis,

found mandibular retrognathia in patients with a high Apnoeic Index (AI) and low Body Mass Index (BMI). This suggests that in non-obese patients with a high AI, skeletal abnormalities may be an important aetiological factor in OSA.

Whilst a reduction in length of the body of the mandible in OSA patients was reported by Rivlin et al. (1984) and Battagel and L’Estrange (1996); Bacon et al. (1990) and Tangugsorn et al. (1995a) did not find any such reduction.

Hence, in the antero-posterior 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., 1995a).

Head Posture And Hyoid Bone

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

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Cluster analysis is a set of techniques for grouping objects or persons in terms of similarity.
Hyoid bone position has been found to be more inferior than normal in relation to the mandibular plane for OSA subjects (Jamieson et al., 1986; DeBerry-Borowiecki et al., 1988; Tsuchiya et al., 1992). During normal growth, the position of the hyoid bone becomes more inferior, and at adulthood is at the level of C4 (Durzon and Brodie, 1962). In OSA patients it has been found between C4-C6 (Tangugsorn et al., 1995a).

However the position of the hyoid bone is subject to a high degree of variation because of physiological adaptations and changes of head position. 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 inferiorly positioned hyoid bones and extended head posture. 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

The current literature 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) have reported a larger tongue length and area in OSA patients. Other studies (Pracharktam et al., 1994; Battagel and L’Estrange, 1996) have 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 airspace at this level.
Soft Palate

The soft palate in OSA patients is longer and thicker, with an area approximately 20% greater than the average individual, further reducing the effective airway (Jamieson et al., 1986; Lyberg et al., 1989; Battagel and L’Estrange, 1996).

Pharyngeal Dimensions

The dimensions of the pharynx are consistently reported to be reduced in the literature, 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.

Although some authors (Strelzow et al., 1988; Djupesland et al., 1987) 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.

In summary, 3 categories of OSA have been proposed based on the anatomical site of obstruction (Riley et al., 1990):

Type I (oropharynx): includes those 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): includes those patients who are retrognathic with a concurrent reduced posterior airway space\(^5\) 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).

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\(^5\) Posterior airway space is the linear measurement between the base of the tongue and the posterior pharyngeal wall.
1.3.4.3 Functional Processes Related To Upper Airway Muscle Activity

It has been postulated that the functional processes implicated in the aetiology of OSA are due to a normal physiological loss of muscle tone in the upper airway with the onset of sleep.

Breathing

Breathing normally occurs when the intercostal muscles and the diaphragm receive electrical impulses from the brain, causing them to contract. When these muscles contract they expand the thorax and create 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 be sucked closed. This is prevented by "activation" and contraction of the upper airway dilator muscles (e.g. genioglossus and tensor palatini).

Hence 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 the airway. This "balance of forces" concept (Cistulli and Sullivan, 1994) is illustrated in Figure 2.

*Figure 2. Balance Of Forces That Sustain Upper Airway Patency*

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).

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

**Breathing And Sleeping**

When a person changes from the standing or sitting position to the supine position, there is a natural tendency for the upper airway to become narrower (Brown et al., 1987). This is mainly due to the effect of gravity on the tongue causing it to fall back. 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. When a person falls asleep their muscles start to relax, the degree of relaxation depending on their stage of sleep. With sleep onset, a normal physiologic loss of muscle tone can therefore lead to upper airway obstruction. This can result in snoring (Cistulli and Sullivan, 1994).

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 an apnoea results. This results in 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.

The apnoea is terminated by a brief arousal from sleep. During this arousal the partially awake brain increases the stimulus to the upper airway muscles causing them to contract harder and thus open the upper airway. As this occurs the sleep apnoea patient is able to take several large breaths and quickly correct the oxygen and carbon dioxide levels.

Normally, the OSA subject will very 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.
Patients with OSA also have increased activation of their upper airway muscles when awake (Mezzanotte et al., 1992) which may reflect the need to keep their narrowed upper airway patent. This is clearly demonstrated in OSA patients during wakefulness where genioglossus electromyographic (EMG) activity is reduced significantly following the application of 5cm H₂O of continuous positive airway pressure. In normal controls, there is only a small reduction in EMG activity (White and Mezzanotte, 1993). Similarly, White and Ballard (1990) 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.

In summary, these studies support the theory that the underlying cause of sleep apnoea is airway narrowing due to relaxation of the upper airway muscles. When awake, OSA subjects have more activation of the upper airway dilator muscles simply to keep the airway open. Hence, the occurrence of upper airway obstruction during sleep is the result of a normal physiological loss of muscle tone with sleep onset and the dominant pathological element is a mechanical narrowing of the upper airway.

1.3.5 Clinical Features

1.3.5.1 Symptoms Of OSA

Clinically, patients describe a number of symptoms which may be considered typical of OSA. These symptoms are outlined in Table 1. Many of these symptoms are observed and reported by the spouse or partner.
Table 1. Symptoms Of Obstructive Sleep Apnoea

<table>
<thead>
<tr>
<th>Major symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Snoring</td>
</tr>
<tr>
<td>* Excessive daytime somnolence (sleepiness)</td>
</tr>
<tr>
<td>* Witnessed apnoeas</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other symptoms</th>
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</thead>
<tbody>
<tr>
<td>* Nocturnal choking episodes</td>
</tr>
<tr>
<td>* Nocturnal arousals</td>
</tr>
<tr>
<td>* Sleep disruption/insomnia</td>
</tr>
<tr>
<td>* Abnormal motor activity in sleep</td>
</tr>
<tr>
<td>* Nocturia/nocturnal enuresis</td>
</tr>
<tr>
<td>* Gastroesophageal reflux</td>
</tr>
<tr>
<td>* Headaches (morning; nocturnal)</td>
</tr>
<tr>
<td>* Atypical chest pain</td>
</tr>
<tr>
<td>* Nocturnal sweating</td>
</tr>
<tr>
<td>* Diminished libido/impotence</td>
</tr>
<tr>
<td>* Concentration and memory deficit</td>
</tr>
<tr>
<td>* Personality changes/depression</td>
</tr>
</tbody>
</table>

Source: Clinical Aspects of Sleep Apnoea by McNamara et al., 1994 In: Sleep and Breathing, Second Edition, Edited by Saunders NA and Sullivan CE.

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

Nocturnal Symptoms

The most obvious night-time problem is loud snoring. In OSA, 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, he⁶ may wake up or the event be accompanied by a bout of choking. Some patients 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).

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⁶ All references made to “he” pertain to either gender.
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 an additional strain on the respiratory muscles and diaphragm.

An increased frequency of nocturia (voiding during the night) is a further symptom, waking the subject.

OSA subjects and their partners complain of restlessness that is manifested by involuntary kicking movements of the legs.

**Daytime Symptoms**

Complaints of tiredness and sleepiness during the day are the most common daytime symptoms from OSA patients. This is due to the frequent arousals from sleep which interfere with the amount and quality of sleep the subject gets. 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 I*).

Nasal obstruction and headaches are common during the day for patients who suffer from OSA.

If the day time hypersomnolence (excessive sleepiness) is extreme, the subject may fall asleep at unexpected and inappropriate moments. Driving a car or operating machinery therefore presents a danger. 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. Another study (Aldrich, 1989) found that 31% of drivers with OSA had been involved in a road traffic accident within the last 5 years. Further, 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).
Neuropsychological Symptoms
Poor memory and difficulty concentrating are further consequences of patients suffering from OSA, leading to an inability to remember everyday items such as appointments and telephone numbers. 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 and some of the symptoms of sleep apnoea described above (Kales et al., 1985; Bedard et al., 1991).

1.3.5.2 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 has been associated with.

Nocturnal hypoxaemia (inadequate blood and tissue oxygenation) occurs with sleep apnoea. If this is prolonged, then hypertension and cardiac abnormalities may develop (Klitzman and Miller, 1994; Rapoport, 1994) or be exacerbated, if these conditions already exist. 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, recent data implicate sleep apnoea as an independent contributor to the development of hypertension (Carlson, 1994; Hoffstein, 1991).

Decreased cerebral blood flow is a further complication and there is an increased risk of suffering a cerebrovascular accident. However, there is less evidence for this condition (Hedner et al., 1994).

In summary, in severe cases of 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 problems underline the importance of studying OSA and the rationale for adequate management of this condition, through effective preventative and treatment measures.
1.3.6 Diagnosis

Detailed clinical testing is required to diagnose sleep apnoea. 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).

Overnight polysomnography, an objective measure of respiration during sleep, is the most accepted diagnostic investigation distinguishing between simple snoring and true obstructive sleep apnoea (Aboussouan et al., 1997).

Polysomnography monitors a wide range of parameters while the subject is asleep, including assessment of respiratory and cardiac function. These include:

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

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

There are limitations to the use of polysomnography. Firstly, the studies are carried out in a sleep laboratory and not in the patient's home. Portable monitoring devices are available. However, these systems have not been validated as yet (Flemons, 1996). Secondly, there is significant night-to-night variability in the apnoea index. Studies have however 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).

1.4 Management Of OSA

The management options for OSA are diverse because the aetiology is not precisely understood. In addition, a number of different treatment approaches may be required as a result of multiple possible 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 major cardiovascular illness and hypoxic complications.

The desired treatment outcomes set 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 15 years after its use was first reported (Sullivan et al., 1981). Although CPAP is an effective therapy, there are questions about compliance, tolerance and acceptance by patients.

OAs and surgery provide other treatment approaches to the management of OSA.

Current management strategies for OSA are summarised in Figure 3. A stepwise approach is recommended to guide therapy and depends on the response at each step of the algorithm.
Figure 3. Overview Of Treatment Of Obstructive Sleep Apnoea

Step 1

Diagnosis of OSA

Elimination of aggravating factors and weight reduction, if appropriate

Step 2

CPAP (moderate to severe OSA)

Not tolerated or refuses treatment

Tolerated

Continue

Improved

OA

Not improved

Surgery

Improved

Not improved

Step 3

Surgery

Improved

Not improved

Step 4

Continue

Improved

Surgery

Not improved

Follow up

CPAP or further surgery

Step 5

Follow up

CPAP or further surgery

Improved

Not improved

Modified using ASDA 1995; ASDA, 1996; and Hudgel, 1996.
The following section briefly reviews the management strategies in the treatment of OSA. A separate section will follow, where the major emphasis will be on the treatment of OSA using OAs, in particular MAS. It should be noted that the majority of treatments outlined below offer only symptomatic relief rather than curative therapy.

1.4.1 Conservative Measures

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

The earliest therapy for snoring and sleep apnoea may have been an elbow nudge to the ribs of the snorer in an effort to stop the snoring or to induce a change of sleep position, usually from a supine to a sideways posture.

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 is also important (Battagel, 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). However, 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 seem to benefit by sleeping in a more upright position at a 60° angle to the horizontal plane (McEvoy et al., 1986).

Obesity is a well recognised aggravating factor of upper airway obstruction during sleep and is present in the majority of patients with sleep apnoea (Peiser et al., 1984). Weight loss may improve breathing during sleep both 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 between weight loss and improvement in the number of apnoeas is not
linear (Browman et al., 1984). The number of apnoeas will decrease by approximately 50% with a 10% weight loss, suggesting that weight loss should receive a major focus in the management of OSA (Hudgel, 1996).

The intake of alcohol produces various effects. 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 noted that alcohol evoked obstructive apnoea in heavy snorers who did not otherwise manifest apnoeas. 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. Therefore, such patients should be advised to reduce their alcohol intake.

### 1.4.2 Medical Treatment

The most widely prescribed treatment for OSA is CPAP (Hudgel, 1996). CPAP 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. The positive pressure produced within the upper airway counteracts the subatmospheric pressure occurring during an obstructive apnoea (Hudgel, 1996).

Because CPAP provides a pneumatic splint to open the airway, it is 100% successful in keeping the airway open at night. The success of CPAP is however dependent on the patient’s compliance with wearing the device. Hans and colleagues 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 <10/hour with relief of symptoms.
Disadvantages Of CPAP

A major limitation of CPAP is tolerance. To be effective, CPAP 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). Recent studies have shown that as many as 24% of patients discontinue therapy with CPAP (Reeves-Hoche et al., 1994; Waldhorn et al., 1990). Reported long-term use of CPAP is 50% to 80%, and covert monitoring has shown that the average usage is < 50% of the night. Also, less symptomatic patients are 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) as listed below:

- Noise
- Cumbersome nature of CPAP (to both patient and partner)
- Nasal or oral dryness
- Nasal congestion
- Sneezing
- Sinusitis
- Nose bleeds and/or rhinorrhoa
- Skin reactions from facemask
- Nasal bridge abrasions
- Red eyes
- Aerophagia (swallowing of air)

1.4.3 Dental Treatment

The role of OAs in the management of OSA is discussed in detail in Section 1.5.

Randomized, 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 < 10/hr in these studies. 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 recently reported (Palmisano et al., 1996). However, this study was a case report and further research is recommended to validate the use of this procedure in the treatment of OSA.

1.4.4 Surgical Treatment

Surgery is indicated to treat OSA in patients who have an anatomical abnormality that is causing the sleep apnoea, 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 presence and severity of OSA must be determined before initiating surgical therapy (ASDA, 1996).

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 (Guilleminault and Rosekind, 1981). However, it is not favourably accepted by most patients because of both cosmetic defects and the morbidity associated with the procedure. Its use is therefore limited to emergency situations (ASDA, 1996).

The most widely used surgical technique is uvulopalatopharyngoplasty (UPPP). UPPP 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. Although it does improve 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).
More than half of the published papers addressing UPPP made no reference to the occurrence of complications with UPPP. Of those that have, none have reported significant or long-term complications. The incidence of complications appears to be low, with the most common complication reported as velopharyngeal insufficiency (VPI) for greater than one month (Sher et al., 1996).

Maxillo-facial surgery is another surgical treatment option (Powell et al., 1990). In theory, 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 was based on AHI of ≤ 20 in addition to a 50% or greater reduction in AHI.

When maxillary-mandibular advancement was carried out with no adjunctive procedure(s), 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).

Other surgical procedures are the inferior sagittal mandibular osteotomy and genioglossal advancement with or without hyoid myotomy and suspension (ASDA, 1996).

Studies which use surgical procedures in the treatment of OSA have limitations. These studies present Sackett’s Level III or Level IV evidence (Sackett, 1986), that is either non-randomised comparisons between patients who did or did not have therapy or case series without controls. The studies also presented biases related to small sample size, patient selection, and have limited follow up (Sher et al., 1996).
1.5 The Role Of Oral Appliances In The Management Of OSA

1.5.1 Background

The first reported use of any oral appliance as treatment for upper airway obstruction and mandibular deficiency was as early as 1902 by Pierre Robin (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.

In 1982, Cartwright and Samelson 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). In 1985, Soll and George published a case report on the effectiveness of a modified one piece activator advancement device which resulted in a marked improvement in the apnoea index and oxygen saturation following insertion of the device.

Since then, there has been a growing interest in the use of OAs in the treatment of snoring and OSA. At present, there are at least twenty five different OAs currently used in the treatment of snoring or OSA with the efficacy of individual OAs varying widely (Lowe, 1994).

There is no consensus in the literature regarding the suitability of OA therapy in mild, moderate or severe OSA. According to ASDA (1995), OA therapy is indicated as a primary treatment for patients with mild OSA and 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 sleep disorder physicians there are no accepted criteria for classifying OSA severity. A recent 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.

OAs are divided into 2 types:

- Those that hold the tongue forward during sleep called tongue retaining devices (TRD) (Cartwright and Samelson, 1982), and

- Those that advance the mandible. This group makes up 93% of OA currently in use (Loube and Strauss, 1997), and has a variety of names, including: mandibular
advancement devices (MAD) (Schmidt-Nowara et al., 1995); mandibular advancement splints (MAS)\(^7\) (O'Sullivan et al., 1995); and anterior mandibular positioning devices (AMP) (Clark et al., 1996).

1.5.2 **Tongue Retaining Devices**

The following section discusses the mechanism of action and efficacy of the tongue retaining device (TRD) in the treatment of OSA.

1.5.2.1 **Mechanism Of Action**

The mechanism of action of the TRD is to 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. This presupposes that backward motion of the tongue plays the major role in airway occlusion.

1.5.2.2 **Evaluation Of Efficacy**

Studies show that TRD is an effective appliance in causing a reduction of the mean AHI (Table 2).

The TRD is 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

\(^7\) For the purpose of this thesis, MAS is a term used synonymously with mandibular advancement devices (MAD).
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 effectiveness of this treatment with behaviour modification.

Table 2. Comparison Of TRD For The Treatment Of OSA

<table>
<thead>
<tr>
<th>First Author (reference)</th>
<th>Number of Patients</th>
<th>Study Design</th>
<th>Mean AHI</th>
<th>SaO₂ minimum</th>
<th>AHI with treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>without/with appliance</td>
<td>without/with appliance</td>
<td>&lt;50% initial AHI</td>
</tr>
<tr>
<td>Cartwright &amp; Samelson, 1982</td>
<td>14</td>
<td>Case series</td>
<td>56/27</td>
<td>-</td>
<td>71</td>
</tr>
<tr>
<td>Cartwright, 1985</td>
<td>16</td>
<td>Case series</td>
<td>54/33</td>
<td>73/79</td>
<td>50</td>
</tr>
<tr>
<td>Cartwright et al., 1988</td>
<td>12</td>
<td>Case series</td>
<td>37/17</td>
<td>-</td>
<td>75</td>
</tr>
<tr>
<td>Cartwright et al., 1991</td>
<td>15</td>
<td>Case series</td>
<td>27/11</td>
<td>-</td>
<td>73</td>
</tr>
<tr>
<td>Cartwright et al., 1991 (TRD plus posture alarm)</td>
<td>15</td>
<td>Case series</td>
<td>31/8</td>
<td>-</td>
<td>80</td>
</tr>
</tbody>
</table>

⁰Percent of all patients
⁵Percent of patients with initial AHI>20

However, none of the studies in Table 2 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 are that these studies have all used a small sample size, are retrospective case series and have provided no data about relief of snoring, sleepiness or long-term usage patterns. Thus, at the present time, the efficacy of TRD in the successful treatment of OSA has not been proved objectively.

1.5.3 Mandibular Advancement Splints

1.5.3.1 Mechanism Of Action

MAS are thought to function in the treatment of OSA in the following ways (Bonham et al., 1988; Lowe, 1990; Lowe, 1994):
• an increase in the airway space;
• the provision of a stable anterior position of the mandible;
• the advancement of the tongue and soft palate;
• a possible change in genioglossus muscle activity.

Possible 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).

The exact mechanism of action of MAS in improving snoring and OSA during sleep is as yet undetermined. Cephalometric (Schmidt-Nowara et al., 1991; Johnson et al., 1992) and computerised tomography (Lowe et al., 1990) studies which have sought to determine the action of the OAs have done so with the patient in the awake state. Hence, each of these studies has external validity as a limitation since observations were made with the patient in the awake state, whereas oral appliances are intended to be used in sleeping patients.

1.5.3.2 Appliance Design

Various 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 one or 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 recent survey (Loube and Strauss, 1997), these designs represent 14% of OAs used by dentists to treat patients with OSA (Figure 4).

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1 External validity is the applicability of experimental results to situations external to the actual experimental context.
Figure 4. Types Of Oral Appliances Used To Treat OSA Patients

Source: Loube and Strauss (1997)

The important aspects of the MAS design (Battagel, 1996) are:

- **Good retention to both the upper and lower teeth**
  This is important to ensure that the lower jaw does not drop out of the appliance during sleep. In addition, without good maxillary retention the entire appliance will be dislodged.

- **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 from subject to subject. 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 amount of protrusion must be tolerated by the individual. Since tolerance increases with time, splints capable of incremental advancement (such as Herbst and AMP used by Ferguson et al., 1997) would seem to have clear practical advantages.

- **Minimal vertical opening**
  Excess opening will diminish the benefits to the airway from protrusion (Battagel, 1996). All oral appliances produce some downward rotation of the mandible and this effect varies from subject to subject. There are many appliances that fail to meet this criteria of minimal vertical opening (Esmarch device used by Mayer and
Meier-Ewert, 1995; MAS used by O'Sullivan et al., 1995; Snore guard used by Schmidt-Nowara et al., 1991; Ferguson et al., 1996).

- *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. To date, it is also unclear whether custom-fitted or serially adjusted appliances are more effective than prefitted appliances in the treatment of snoring and OSA. In addition, there are no well designed studies that directly compare the efficacy of specific appliances to each other.

1.5.3.3 Evaluation Of Efficacy

The clinical utility of a 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).

Efficacy of oral appliances includes 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 discussion reviews the scientific evidence regarding the efficacy of the MAS on snoring and OSA.
Efficacy Of MAS In Snoring

All published literature in which snoring was assessed, representing a variety of devices, has shown that snoring improved in a high proportion of patients (Table 3).

Table 3. Efficacy Of Oral Appliances In Snoring

<table>
<thead>
<tr>
<th>First Author (reference)</th>
<th>Number Of Patients</th>
<th>Device</th>
<th>Snoring Improved (%)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kloss et al., 1986</td>
<td>7</td>
<td>Esmarch</td>
<td>100</td>
<td>Patient report</td>
</tr>
<tr>
<td>Bonham et al., 1988</td>
<td>12</td>
<td>MAS</td>
<td>73</td>
<td>Spouse report</td>
</tr>
<tr>
<td>Lyon et al., 1990</td>
<td>15</td>
<td>Elastomeric</td>
<td>100</td>
<td>Method not specified</td>
</tr>
<tr>
<td>Ichiooka et al., 1991</td>
<td>14</td>
<td>MAS</td>
<td>100</td>
<td>Subjective score</td>
</tr>
<tr>
<td>Schmidt-Nowara, et al., 1991</td>
<td>68</td>
<td>Snore-Guard</td>
<td>98</td>
<td>Patient report</td>
</tr>
<tr>
<td>Nakazawa et al., 1992</td>
<td>12</td>
<td>MAS</td>
<td>100</td>
<td>Patient report</td>
</tr>
<tr>
<td>Clark et al., 1993</td>
<td>24</td>
<td>Herbst</td>
<td>Yes</td>
<td>Subjective scale</td>
</tr>
<tr>
<td>O’Sullivan et al., 1995</td>
<td>51</td>
<td>MAS</td>
<td>100</td>
<td>Patient report and laboratory measurement</td>
</tr>
<tr>
<td>Ferguson et al., 1996</td>
<td>27</td>
<td>Snore-Guard</td>
<td>76</td>
<td>Patient report</td>
</tr>
<tr>
<td>Ferguson et al., 1997</td>
<td>24</td>
<td>AMP *</td>
<td>55</td>
<td>Patient report</td>
</tr>
</tbody>
</table>

*Anterior Mandibular Positioner
Adapted from: Schmidt-Nowara et al., (1995)

However, in a majority of these studies, 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. To date, only one study (O’Sullivan et al., 1995) has objectively measured snoring frequency as well as sound intensity. This study found that snores per sleep minute, corrected for time in apnoea, decreased with the MAS from 11.0 ± 5.8 to 9.0 ± 6.0 (p<0.01). Sound intensity of snores (% snores ≥ 50 dB) also decreased with the MAS from 42.0 ± 25.0% to 26.2 ± 25.2% (p<0.01).
Efficacy Of MAS In OSA

1. Effect On AHI

Schmidt-Nowara and colleagues (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 the results of a Herbst appliance in 19 patients with OSA. Their success rate was 53%; treatment success defined as patients having an AHI less than 10/h with the oral appliance.

O’Sullivan and colleagues (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.

All reports (Table 4) have therefore shown a significant improvement in the average AHI with patients who use an appliance. A recent review of publications reporting the effects of OAs on OSA carried out by Schmidt-Nowara et al. (1995), showed that the mean AHIs before and with treatment were 42.6 and 18.8 respectively, an average reduction of 56%. The degree of improvement varied. 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 normal breathing, defined as an AHI<10, with treatment. Conversely, 39% of patients with an initial AHI of >20 remained above that level with treatment.
Table 4. Peer Reviewed Literature On The Efficacy Of Oral Appliances On OSA

<table>
<thead>
<tr>
<th>First Author (reference)</th>
<th>Number of Patients</th>
<th>Study Design</th>
<th>Device</th>
<th>Mean AHI (^a)</th>
<th>Minimum SnO (^b)</th>
<th>AHI with treatment</th>
<th>Sleep</th>
<th>Sleepiness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meier-Ewert, 1987</td>
<td>44</td>
<td>Case series</td>
<td>Esmand</td>
<td>50/23</td>
<td>-</td>
<td>59</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bonham, 1988</td>
<td>12</td>
<td>Case series</td>
<td>MAS</td>
<td>54/36</td>
<td>75/80</td>
<td>58</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lyon, 1990</td>
<td>15</td>
<td>Case series</td>
<td>MAS</td>
<td>47% decrease</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ichioaka, 1991</td>
<td>14</td>
<td>Case series</td>
<td>MAS</td>
<td>32/9</td>
<td>Improved</td>
<td>100</td>
<td>71</td>
<td>9</td>
</tr>
<tr>
<td>Schmidt-Nowara, 1991</td>
<td>20</td>
<td>Case series</td>
<td>Snore-Guard</td>
<td>47/20</td>
<td>75/80</td>
<td>75</td>
<td>40</td>
<td>31</td>
</tr>
<tr>
<td>Nakazawa, 1992</td>
<td>12</td>
<td>Case series</td>
<td>MAS</td>
<td>50/19</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Clark, 1993</td>
<td>15</td>
<td>Case series</td>
<td>Herbst</td>
<td>48/12</td>
<td>Improved</td>
<td>87</td>
<td>46</td>
<td>20</td>
</tr>
<tr>
<td>Eveloff, 1994</td>
<td>19</td>
<td>Case series</td>
<td>Herbst</td>
<td>35/13</td>
<td>84/88</td>
<td>53</td>
<td>33</td>
<td>-</td>
</tr>
<tr>
<td>O'Sullivan, 1995</td>
<td>51</td>
<td>Case series</td>
<td>MAS</td>
<td>32/18</td>
<td>84/87</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Clark, 1996</td>
<td>21</td>
<td>Crossover</td>
<td>AMP</td>
<td>34/20</td>
<td>84/90</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ferguson, 1996</td>
<td>19</td>
<td>Crossover</td>
<td>Snore-Guard</td>
<td>20/10</td>
<td>83/84</td>
<td>-</td>
<td>48</td>
<td>-</td>
</tr>
<tr>
<td>Ferguson, 1997</td>
<td>19</td>
<td>Crossover</td>
<td>AMP</td>
<td>25/14</td>
<td>79/76</td>
<td>-</td>
<td>55</td>
<td>-</td>
</tr>
</tbody>
</table>

\(^a\)Percent of all patients  \(^b\)Percent of patients with initial AHI>20

Adapted from: Schmidt-Nowara et al., (1995)
In summary, OAs have been shown to be an effective method of treatment in 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. This is because the definition of success varies in each of the studies.

2. **Effect On Arterial Blood Oxygenation**

Most studies (Table 4) have reported an improvement in oxygenation assessed by the minimum arterial oxygen saturation (MinSaO2), although the changes were modest. 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 <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.

1.5.3.4 **Compliance**

The data on long-term compliance of OAs (Table 5) are limited and 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. 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). Covert monitoring to objectively evaluate the true compliance rate of OAs is required.

1.5.3.5 **Side-Effects And Complications**

The side-effects and complications with the use of OAs as reported in the literature are outlined in Table 5. 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. To date, no clinical study has evaluated long-term
dental, skeletal or TMJ changes with the use of OAs, and this requires further
investigation.

Table 5. Peer Reviewed Literature On The Side-Effects, Complications And Patient
Compliance Using OAs

<table>
<thead>
<tr>
<th>First Author (reference)</th>
<th>Number of Patients</th>
<th>Device</th>
<th>Side-effect Or Complication</th>
<th>Rate Of Occurrence</th>
<th>Compliance</th>
<th>Length Of Follow-up (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ichiooka, 1991</td>
<td>14</td>
<td>MAS</td>
<td>Discomfort</td>
<td>14%</td>
<td>100%</td>
<td>0.4-1.75</td>
</tr>
<tr>
<td>Schmidt-Nowara, 1991</td>
<td>68</td>
<td>Snore-Guard</td>
<td>Discomfort</td>
<td>48%</td>
<td>75%</td>
<td>Mean 0.6</td>
</tr>
<tr>
<td>Nakazawa, 1992</td>
<td>12</td>
<td>MAS</td>
<td>Discomfort, Occlusal changes, &quot;TMJ dullness&quot;</td>
<td>10%</td>
<td>67%</td>
<td>Mean 0.6</td>
</tr>
<tr>
<td>Clark, 1993</td>
<td>24</td>
<td>Herbst</td>
<td>TMJ pain</td>
<td>15%</td>
<td>50%</td>
<td>3</td>
</tr>
<tr>
<td>Eveloff, 1994</td>
<td>19</td>
<td>Herbst</td>
<td>No Pain</td>
<td>-</td>
<td>93%</td>
<td>1-3.5 (mean, 2)</td>
</tr>
<tr>
<td>O’Sullivan, 1995</td>
<td>51</td>
<td>MAS</td>
<td>“Jaw discomfort”, Dryness Of Mouth, Excessive Salivation, Gum Irritation, Bruxing</td>
<td>67%</td>
<td>79%</td>
<td>-</td>
</tr>
<tr>
<td>Clark, 1996</td>
<td>21</td>
<td>AMP</td>
<td>Did not evaluate side effects</td>
<td>-</td>
<td>81%</td>
<td>0.25-0.85</td>
</tr>
<tr>
<td>Ferguson, 1996</td>
<td>19</td>
<td>Snore-Guard</td>
<td>Sore Teeth, Sore Jaw Muscles, Excess Salivation,</td>
<td>-</td>
<td>60%</td>
<td>0.33</td>
</tr>
<tr>
<td>Ferguson, 1997</td>
<td>19</td>
<td>AMP</td>
<td>Sore Teeth, Sore Jaw Muscles, Excess Salivation, Difficulty In Chewing</td>
<td>-</td>
<td>70%</td>
<td>0.33</td>
</tr>
</tbody>
</table>

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

1.5.3.6 Predictors Of Treatment Response

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

Cephalometric parameters have also been considered to predict post treatment AHI (Eveloff et al., 1994; Mayer and Meier-Ewert, 1995). However, these observations are based on small sample sizes and have not been validated to formulate any recommendations.
2. RESEARCH OBJECTIVES

Studies of OAs for the treatment of snoring and OSA, have found that they are effective to varying degrees (Lowe, 1994). However, these studies lack the discipline of randomised controlled trials. Most of the reports (Table 4 in Section 1.5.3.3) are case series, using a small sample size. There is little description of patient demographics and of the study methods used. In addition, the effectiveness of the OAs on snoring has been based on subjective (patient reports) rather than objective assessment.

The clinical impetus for this study rests on the fact that OSA has a high incidence and, in severe cases, is life-threatening. In the published literature, there has been no clinical trial comparing the methods under consideration in this project.

The aims and objectives of this study are:

1. To design a new MAS which meets the design criteria outlined by Battagel, 1996
2. To evaluate the effectiveness of this new MAS, using a prospective, randomised, placebo-controlled cross-over study
3. To compare efficacy, both subjectively and objectively
4. To identify predictors of response to MAS therapy
3. MATERIALS AND METHODS

3.1 Sample Selection

The patient sample consisted of 30 patients (24 males and 6 females) recruited from the Centre of Sleep Disorders and Respiratory Failure, St. George Hospital, Sydney. This is a tertiary teaching hospital (University of New South Wales).

Patients evaluated at this Centre were referred for assessment and management of snoring and/or OSA. All patients had undergone an initial laboratory polysomnography to confirm a diagnosis of OSA. The respiratory/sleep physician explained the treatment alternatives to all patients, allowing the patients to make an informed choice regarding their preferred treatment. One of the options offered was the use of a MAS. In offering treatment with the MAS, the respiratory/sleep physician stated that similar devices had been used to treat snoring and OSA in other centres and a positive response to treatment was not always achieved. In addition, patients were advised that follow-up clinical review and polysomnography would be required. Subject selection was based on the agreement of the first 30 patients to participate in the study who fitted the eligibility criteria listed below.

3.2 Inclusion And Exclusion Criteria

The criteria for inclusion in the study were selected to ensure that patients had a definitive diagnosis of OSA. Inclusion and exclusion criteria are listed in Table 6.

Table 6. Inclusion And Exclusion Criteria

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• At least two of the following symptoms: snoring, fragmented sleep, witnessed apnoeas and/or daytime sleepiness</td>
</tr>
<tr>
<td>• Evidence of obstructive sleep apnoea on polysomnography with AHI ≥ 10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Exhibit predominantly central sleep apnoea</td>
</tr>
<tr>
<td>• Substantial clinical evidence of periodontal disease (CPITN⁹ code 4 in any one sextant) or dental caries (&gt; 3 teeth)</td>
</tr>
<tr>
<td>• Edentulous patients</td>
</tr>
<tr>
<td>• Use of narcotic or psychoactive medications</td>
</tr>
<tr>
<td>• Previous failure of a dental device as treatment for OSA</td>
</tr>
<tr>
<td>• Exaggerated gag reflex</td>
</tr>
</tbody>
</table>

⁹ Community Periodontal Index of Treatment Needs
3.3 Ethics Approval And Consent

The research protocol was approved by both the Central Sydney Area Health Service Ethics Review Committee and the South Eastern Sydney Area Health Service Ethics Committee.

All patients recruited into the study gave written informed consent prior to participation in the study (Appendix 2). A general information sheet, providing details of the study, was given to each patient (Appendix 3).

The patients were seen at St. George Hospital, Sydney between March 1997 and March 1998.

3.4 Experimental Protocol

The patients accepted into the study were initially assessed by a series of baseline investigations as listed below:

- Medical and Dental History
- Clinical Examination
- Radiographs: Lateral Cephalogram and Orthopantomogram
- Validated Sleep Questionnaire (Questionnaire 1)

Patients were asked to stop using any other forms of treatment for OSA. They were then issued with a custom made MAS which had to be worn every night for the duration of the acclimatisation period. During this period, the length of which varied depending on individual adaptation, adjustments were carried out if the MAS was ill-fitting. In addition, the mandible was serially advanced as far as was comfortably possible, by turning specially designed screws in the lower appliance.

A second validated sleep questionnaire (Questionnaire 2) was completed for each patient at the end of the acclimatisation period, to ascertain any changes in snoring (frequency and intensity), sleep quality and side effects experienced with the MAS.
3.5 Overview Of Study

Patient referred by family physician or clinical specialist

Patient reviewed by Respiratory Sleep Physician, St. George

32 patients consent and willing to participate in the study

Patient reviewed by author

30 patients chosen for inclusion in the study

24 patients undergo acclimatisation period with MAS

For assessment and management of snoring and/or OSA

Patient given informed choice of treatment alternatives

Patient referred to author

Eligibility criteria applied to patients

MAS fabricated and fitted

Patient undergoes
- medical & dental history
- clinical examination
- impressions & casts
- radiographs
- questionnaire 1

2 patients did not meet the eligibility criteria for the study because they had an exaggerated gag reflex

2 patients fail to return for follow up following fitting of MAS; 4 patients drop out of study during acclimatisation period
3.6 Study Design

A prospective, randomised, placebo-controlled, cross-over study, with an extra period (ABB-BAA), was used to evaluate the effectiveness of the MAS (Figure 5).

Following the acclimatisation period, each patient was randomised, and grouped for gender, into either Group I or Group II. They then underwent a washout period for one week, where no appliance was worn, in order to minimise any carry-over effect\(^{10}\). This was followed by three sleep studies at St. George Hospital at one week intervals with each sleep study performed one week after treatment with MAS or placebo as shown in Figure 5.

\begin{center}
\textit{Figure 5. Protocol For Patient Groups}
\end{center}

\begin{center}
\begin{tikzpicture}
    \node (A1) at (0,0) {A};
    \node (B1) at (1,0) {B};
    \node (B2) at (2,0) {B};
    \node (A2) at (1,-1) {A};
    \node (B3) at (2,-1) {A};
    \node (Ac) at (-1,0) {Acclimatisation Period};
    \node (W) at (-1,-1) {1 Week Washout};
    \node (G1) at (0,1.5) {	extit{Group 1}};
    \node (G2) at (0,-1.5) {	extit{Group 2}};
    \draw[->] (A1) -- (B1);
    \draw[->] (B1) -- (B2);
    \draw[->] (B2) -- (B3);
    \draw[->] (B3) -- (A2);
    \draw[->] (A2) -- (B1);
    \draw[->] (Ac) -- (A1);
    \draw[->] (Ac) -- (B1);
    \draw[->] (W) -- (Ac);
    \draw[->] (W) -- (B2);
    \draw[->] (W) -- (A2);
\end{tikzpicture}
\end{center}

\textbf{Note:}

The two treatments were labelled:

- A - treatment with placebo (inactive lower appliance)
- B - treatment with MAS

Half the subjects (12 patients) received A first, and then after a week, crossed-over to B until the end of their protocol. That is, their first sleep study was recorded with the placebo and their second and third sleep studies were recorded with the MAS. This sequence was classified as the ABB sequence with the period between each treatment being one week.

\(^{10}\) Carry-over effect refers to the fact that an effect of treatment given in one period might still be present at the start of the following period.
The remaining subjects (12 patients) received B first and then after a period of one week crossed-over to A until the end of their protocol. In their case, their first sleep study was recorded with the MAS and their second and third sleep studies were recorded with the placebo. This sequence was classified as the BAA sequence with the period between each treatment being one week.

3.7 Orthodontic Clinical Assessment

After consultation with the respiratory/sleep physician at the Centre of Sleep Disorders and Respiratory Failure, St. George Hospital and consenting to participate in the research program, subjects were referred to the author at the Dental Clinic to undergo a clinical examination and further check their eligibility.

A medical and dental history was taken from the patients including a history of any pain or joint sounds from the temporomandibular joints. This was followed by an orthodontic examination (Appendix 4).

Extra-orally, a full frontal and profile facial analysis was carried out with the patient seated upright and in centric occlusion with the lips relaxed. Palpation of the temporomandibular joints, masseter and temporalis muscles was carried out to ascertain any signs of temporomandibular dysfunction. This palpation involved using the index finger tip to apply pressure to the muscles and joints for a 2-3 second period. An assessment for centric occlusion to centric relation discrepancy and the full range of jaw function in all excursive movements and on maximum opening was recorded.

Intra-orally, soft and hard tissue analysis was undertaken.

3.8 Questionnaire

Questionnaires (Appendices 5 and 6) were completed by the author interviewing patients on their first visit and at the end of the acclimatisation period, prior to the first of the three sleep studies. The patient’s bed partner was also consulted when answering the questions.

Using a small sample, the questionnaires were pre-tested for omissions and ambiguity.
The aim of Questionnaire 1 was to ascertain snoring frequency and intensity, daytime sleepiness and quality of sleep. The Epworth Sleepiness Scale (ESS), which has been validated, was used to assign a score for the degree of daytime sleepiness (Johns, 1992).

The ESS asks the subject to rate on a scale of 0-3 the chances that, over "recent times", he/she would have dozed in eight specific situations that are commonly met in daily life (0=would never doze; 3=high chance of dozing). The ESS scores range between 0 and 24, with the lower scores indicating decreased daytime sleepiness and higher scores increased daytime sleepiness. The mean score for subjects with a history of normal sleep habits without apnoea is 6, whereas those with mild to severe sleep apnoea score between 10 and 16 (Johns, 1991).

The second questionnaire, asked at the end of the acclimatisation period, was used to ascertain the reported use of the oral appliance and its effectiveness on snoring frequency and intensity, daytime sleepiness and quality of sleep. Change in sleeping habit due to the MAS together with any side effects experienced with the use of the appliance were also recorded. Side effects were noted in terms of frequency (never, rarely, sometimes, often), severity (absent, mild, moderate, severe) and duration (< 2 weeks, 2-3 weeks, > 3 weeks). At the end of the research study each patient was asked to rate their satisfaction with the MAS (very satisfied, satisfied, dissatisfied, very dissatisfied) and whether they would prefer to use the MAS as a long-term treatment. The questions were administered to subjects and partners without variation in format or order.

The sleep questionnaire was designed to be simple to administer, brief and effective. This was in accordance with the finding that predictive ability is not significantly improved with multiple questions or a separate spouse/partner questionnaire (Kump, 1994).

3.9 Radiographs

A lateral cephalogram radiograph was taken for each of the subjects before treatment, in the standing natural head position. OSA subjects were recorded with the head in natural head position (Rivlin et al., 1984; Guilleminault et al., 1984; Davies and
Stradling, 1990). This posture was obtained by having the subject look into his own pupils reflected in a mirror located at eye level (Moorrees and Kean, 1958).

To clarify the outline of the oropharyngeal soft tissues, each subject was asked to take a tablespoon of Barium Sulphate Esophageal Cream (Liquid "C", Field Diagnostics, Rosebery, NSW) prior to radiography. Each patient was instructed to distribute the cream within the mouth using the tongue for 10 seconds and then swallow the remaining cream, lightly contact the posterior teeth with the lips relaxed. To ensure that the subject did not swallow when radiographs were taken, the subject had to respond to the investigator's directions by raising his/her finger and the exposure was made as the finger was being raised, at the end of the expiratory phase.

The distance from the focus of the cephalostat (Philips, Orthoralix L.D.) to the midsagittal plane of the subject's head was 135 cm, while the distance from the midsagittal plane of the subject's head to the film was 15 cm. Exposures were made at 76 Kvp and 14 mA at 0.6 s exposure time.

An orthopantomogram was also taken for each patient to exclude dental pathology.

3.9.1 Cephalogram Measurements

All lateral head radiographs were hand traced by the author, blinded to the subject's apnoeic status, on 0.03 inch matte acetate paper over a light-viewing box with a 0.5mm 2H lead pencil. Where bilateral landmarks presented as two images, the average of the two was used. The mean enlargement factor of the cephalometric radiographs was 11%. Angular measurements are not affected by the enlargement. All values for distances were transformed by this factor.

The landmarks and planes used for the lateral cephalograms are detailed in Table 7.

To quantify the level of random errors, twelve lateral cephalograms were randomly chosen from the main series, and the tracings were replicated and measured by the author under the same conditions a month later.
Table 7. Definitions Of Anatomical Landmarks

<table>
<thead>
<tr>
<th>Point</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Point</td>
<td>The deepest midline point on the maxillary alveolus between the anterior nasal spine (ANS) and the maxillary alveolar crest</td>
</tr>
<tr>
<td>ANS</td>
<td>Anterior nasal spine - the tip of the median sharp bony process of the palatine bone in the hard palate</td>
</tr>
<tr>
<td>B Point</td>
<td>The deepest midline point between the mandibular alveolar crest and pogonion (Pg)</td>
</tr>
<tr>
<td>Ba (Basion)</td>
<td>The most inferior point on the anterior margin of the foramen magnum in the median plane</td>
</tr>
<tr>
<td>C2</td>
<td>The tangent point on the dorsal surface of the second cervical vertebra to a line from C4</td>
</tr>
<tr>
<td>C4</td>
<td>Postero-inferior point of the fourth cervical vertebra</td>
</tr>
<tr>
<td>Co</td>
<td>Condylion: The highest point on the bony outline of the mandibular condyle</td>
</tr>
<tr>
<td>Eb</td>
<td>Base of epiglottis: The deepest point of the epiglottis</td>
</tr>
<tr>
<td>Go (Gonion)</td>
<td>The most lateral external point at the junction of the horizontal and ascending rami of the mandible. It is found by bisecting the angle formed by tangents to the posterior and inferior borders of the mandible</td>
</tr>
<tr>
<td>Gn</td>
<td>Gnathion: The most antero-inferior point on the bony mandibular symphysis</td>
</tr>
<tr>
<td>H</td>
<td>Hyoidale: The most superior-anterior point on the body of the hyoid bone</td>
</tr>
<tr>
<td>Ht</td>
<td>The most superior point of the tongue in relation to the line from Eb to T</td>
</tr>
<tr>
<td>Me (Menton)</td>
<td>The lowest point on the bony outline of the mandibular symphysis</td>
</tr>
<tr>
<td>Mp</td>
<td>Mandibular plane: Line joining menton and gonion</td>
</tr>
<tr>
<td>N (Nasion)</td>
<td>The most anterior point of the fronto-nasal suture, as seen in the lateral skull radiograph</td>
</tr>
<tr>
<td>P</td>
<td>Tip of the soft palate</td>
</tr>
<tr>
<td>PNS</td>
<td>Posterior nasal spine: Tip of the posterior spine of the palatine bone in the hard palate</td>
</tr>
<tr>
<td>Phw</td>
<td>Posterior pharyngeal wall. A point on the posterior pharyngeal wall at the same horizontal level as spt</td>
</tr>
<tr>
<td>pm</td>
<td>Pterygomaxillare: The intersection between the nasal floor and the posterior contour of the maxilla</td>
</tr>
<tr>
<td>spt</td>
<td>The tangent point on a line parallel to pm-P on the dorsal surface of the soft palate at the maximum width</td>
</tr>
<tr>
<td>S (Sella)</td>
<td>The centre of the sella turcica, determined by inspection</td>
</tr>
<tr>
<td>T</td>
<td>Tongue tip: The most anterior point of the tongue which touches the lingual surface of the mandibular incisor</td>
</tr>
</tbody>
</table>
The lateral cephalograms were analysed and linear measurements detailed in Table 8 were taken.

*Table 8. Lateral Cephalometric Measurements*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cranial Base</strong></td>
<td></td>
</tr>
<tr>
<td>1 BaSN (degrees)</td>
<td>Cranial base angulation in mid sagittal plane</td>
</tr>
<tr>
<td>2 SN (mm)</td>
<td>Anterior cranial base length measured in the mid sagittal plane between points S and N</td>
</tr>
<tr>
<td><strong>Maxilla</strong></td>
<td></td>
</tr>
<tr>
<td>3 ANS-pm (mm)</td>
<td>Length of the nasal cavity</td>
</tr>
<tr>
<td>4 Co-A (mm)</td>
<td>Distance from condyion to A Point (effective midfacial length)</td>
</tr>
<tr>
<td><strong>Mandible</strong></td>
<td></td>
</tr>
<tr>
<td>5 Go-Gn (mm)</td>
<td>Distance from Gonion to Gnathion</td>
</tr>
<tr>
<td><strong>Anteroposterior measurements</strong></td>
<td></td>
</tr>
<tr>
<td>6 SNA (degrees)</td>
<td>Angle from sella to nasion to A Point</td>
</tr>
<tr>
<td>7 SNB (degrees)</td>
<td>Angle from sella to nasion to B Point</td>
</tr>
<tr>
<td>8 ANB (degrees)</td>
<td>Angle from A Point to nasion to B Point</td>
</tr>
<tr>
<td><strong>Vertical measurements</strong></td>
<td></td>
</tr>
<tr>
<td>9 LAFH (mm)</td>
<td>Lower Anterior Face Height: distance from ANS to Me</td>
</tr>
<tr>
<td>10 TPFH (mm)</td>
<td>Total Posterior Face Height (measured from S to Go)</td>
</tr>
<tr>
<td>11 SN-Mp (degrees)</td>
<td>Angulation of the mandibular plane with the SN line</td>
</tr>
<tr>
<td><strong>Hyoid</strong></td>
<td></td>
</tr>
<tr>
<td>12 H-Mp (mm)</td>
<td>Perpendicular distance from the mandibular plane to Hyoidale (vertical position of the hyoid bone relative to the mandibular plane)</td>
</tr>
<tr>
<td><strong>Neck</strong></td>
<td></td>
</tr>
<tr>
<td>13 C2C4-SN (degrees)</td>
<td>A craniocervical angle formed by a line from C2 to C4 and S-N plane</td>
</tr>
<tr>
<td><strong>Soft Tissues</strong></td>
<td></td>
</tr>
<tr>
<td>14 Phw-spt (mm)</td>
<td>Measurement of width of the pharynx where soft palate thickest</td>
</tr>
<tr>
<td>15 pm-P (mm)</td>
<td>Soft palate length measured from pm to tip of soft palate</td>
</tr>
<tr>
<td>16 PAS (mm)</td>
<td>The 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</td>
</tr>
<tr>
<td>17 SPT (mm)</td>
<td>Soft palate thickness: maximal thickness of the soft palate measured on a line perpendicular to the pm-P</td>
</tr>
<tr>
<td>18 TI (mm)</td>
<td>Tongue length measured from tongue tip (T) to base of epiglottis (Eb)</td>
</tr>
<tr>
<td>19 THt (mm)</td>
<td>Tongue height: perpendicular distance from Ht to the line connecting Eb and T</td>
</tr>
</tbody>
</table>

46
3.10 MAS Appliance Construction

Once patients were accepted into the study, a specific MAS was custom made for each patient. This removable, two piece intra-oral appliance, constructed of a methyl methacrylate material (Orthocryl®, Dentaurum, Australia Pty Ltd, Rydalmere, NSW 2116) advanced the mandible during sleep. It is a unique design with several novel features.

The fabrication procedure involved the following stages:

3.10.1 Impressions And Casts

Alginate impression material (Unijel-II, Type I fast setting, Unitek/3M, 9-15 Chilver Road, Thornleigh, NSW 2120) was mixed according to the manufacturer’s instructions. Upper and lower impressions were taken and orthodontic stone poured within 30 minutes. Orthodontic stone (Whip mix, ADA type III, 361 Farmington Avenue, PO Box 17183, Louisville, Kentucky 40217) weighing 900 g was added to 250 ml of water and vacuum mixed for 30 seconds for pouring up a set of upper and lower models.

Casts were used to customise the MAS to fit the patient’s mouth dimensions.

3.10.2 Protrusive Wax Record

A protrusive position wax (Moyco®, MOYCO Industries, Inc, York, PA) interocclusal record using “Projet” (Cat No: 150-001/150-002, Oradec Ortho Supplies, McGrath Hill, NSW 2756) was taken in the following manner. The patient was instructed to open and protrude the mandible to the most protrusive position on the “Projet” bite record and remain in this position for 3 minutes. If the patient was comfortable in this position and could repeat this manoeuvre and arrive at the same position a number of times, then a wax bite was obtained in this comfortable protrusive position, with a softened wax wafer over the “Projet”. In those patients who could not tolerate the most protrusive position on the “Projet”, the middle protrusive position was selected, as this was comfortable and reproducible.

The vertical opening was dictated by the thickness of the “Projet” on the incisor edge region 4mm.
The orthodontic casts and protrusive wax record was sent to a certified orthodontic/prosthodontic laboratory for construction of the MAS. All appliances were made by the same technician and fitted by the author, two weeks from the date of the initial impressions.

3.10.3 MAS Design Features

The typical appliance design is shown in Figures 7 to 9. This removable device for intra-oral use was exempt according to Schedule I, Item 5 of the Therapeutic Goods Regulations under the clinical trial exemption scheme (CTX).

*Figure 7. Photograph Of The MAS*
Figure 8. Photograph Of The Upper Appliance

Figure 9. Photograph Of The Lower Appliance
The MAS included the following features:

1. Two separate, full-occlusal coverage, clear acrylic appliances that fitted onto the dental arches. All anterior teeth were capped on the incisal, lingual and labial surfaces by acrylic. An opening was cut through the acrylic to allow an anterior gap between the two appliances, enabling respiration if the subject developed nasal congestion.

2. The upper appliance had two acrylic flanges, one on either side of the palatal aspect of the molars, which fitted into slots cut into the acrylic on the lingual sides of the lower appliance in the molar region. The length and angle of the flanges on the upper appliance were extended to guide the mandible. This allowed the upper and lower appliances to fit together and prevented the mandible from sliding back if the mouth was opened.

3. Two, 10mm “Lewa” screw devices (code 1009, LG Rocky Mountain Orthodontics, Hurstville, NSW 2220) to enable anterior advancement of the slots. The patient would now have to advance the mandible until the slot and flange fitted. In this way, the mandible was advanced in serial adjustments, as far forward as was comfortably possible.

4. Interproximal ball clasps were used to retain each appliance firmly to the teeth.

5. The vertical height of the appliance was kept to a minimum (the average thickness of each upper and lower appliance was between 1.5-2.0 mm).

6. Each appliance had the patient’s name tag inserted into the clear acrylic for identification purposes.

3.10.4 Placebo

The aim of using a placebo was to show that advancement of the mandible was critical for reducing AHI and improving MinSaO2. The lower appliance worn at night, acted as the placebo because it had no protrusive (active) effect on the mandible. To ensure patients were blind to the MAS and placebo, they were informed that the lower appliance may also benefit their condition by stimulating reflex pathways.
3.11 Acclimatisation Period

This was defined as the period between the date when the appliance was first fitted and when the patient was instructed to stop wearing the appliance for the one week washout period, prior to the laboratory sleep studies. This period varied in length for each patient.

During this period the following activities were carried out:

- Telephone monitoring of each patient every two weeks. The patient was assessed for subjective change in snoring frequency and intensity, daytime sleepiness and quality of sleep and were asked whether they could further advance the mandible with the MAS. The patients were advised to contact the author if they experienced any problems.

- Adjustments were made to the appliances, if they were causing any irritation.

- The mandible was then progressively advanced until subjectively snoring ceased and OSA symptoms improved or until the patient could not tolerate further advancement. The most protrusive, comfortable position was considered optimal for each individual patient. If fatigue or soreness developed and/or snoring and OSA symptoms deteriorated, then the screw was wound back until a less protrusive position was obtained consistent with maximum improvement in subjective symptoms. The actual protrusion, maximum protrusion and overjet were each measured twice using a stainless steel ruler and the mean of each variable was recorded.

  ➢ Actual protrusion was measured as the distance between the U1 edge and the labial surface of the L1 with the lower jaw in the most protrusive comfortable position. This distance (in mm) when added to the overjet (in mm) was equivalent to Actual (absolute) advancement. The value was also recorded as a percentage of maximum jaw protrusion.

  ➢ Maximum protrusion was recorded at the final appointment of MAS adjustment. It was measured as the distance between the U1 edge and the labial surface of the L1 with the lower jaw in maximum protrusion. This distance (in mm) when added to the overjet (in mm) was equivalent to Maximum jaw protrusion.
In situations with an alignment discrepancy between the upper and/or lower central incisors, the most prominent central incisor was used in the measurement analysis.

- Each patient was then randomised (using a random number generator) into either Group I (ABB) or Group II (BAA) grouped by gender. Written instructions were given to each patient, pertaining to their group allocation, which explained the protocol for the period up to the end of the three sleep studies (Appendices 7 and 8).
- Sleep Questionnaire 2 was completed.

3.12 Post Acclimatisation

Following the acclimatisation period, there was a one week washout when the MAS was not worn. The subsequent week the patient wore either the lower appliance only as a placebo (Group I) or the full appliance (Group II).

3.13 Anthropometric Measurements

Each subject was weighed and their height was measured on the night of the first sleep study as standard aspects of the sleep laboratory examination. This data was then used to determine the individual’s body mass index (BMI)\(^\text{11}\). The neck circumference (NC) was measured (in cm) at the level of the cricothyroid cartilage, using a measurement tape. This measurement reflects obesity in the region of the upper airway (Ferguson et al 1995).

3.14 Sleep Studies

Each patient then underwent 3 separate sleep studies (a week apart) performed one week after treatment with MAS or placebo.

Polysomnography was performed at the Sleep Laboratory at St. George Hospital between 9 pm and 7 am. A number of variables were recorded continuously on a 20-channel computerised polygraph (Grass Instrument, Quincey, Mass). The sleep data were relayed and displayed on monitor screens in the monitoring room next to the sleeping room.

\(^{11}\) Body mass index is an index for measuring obesity and is equal to weight in kilograms / (height in metres)\(^2\). The normal range for BMI is considered to be between 20 and 25 kg/m\(^2\) (Battagel, 1996).
Figure 10. Patient Set Up For Sleep Study

(a) Electroencephalogram leads  
(b) Nasal airflow cannula  
(c) Electro-oculogram leads  
(d) Electromyogram leads  
(e) Thoracic band  
(f) Abdominal band  
(g) Pulse oximeter  
(h) Junction box circuit
The polysomnographic variables recorded were:

1) **Electroencephalogram (EEG)**

   The four points used were C3, A1, A2 and O2. Surface electrodes were attached to the scalp with the aid of a special skin glue. The EEG provided information on the different stages of sleep and their duration throughout the night. It also recorded the total awake and sleep time. The latter included recording of rapid eye movement sleep and non-rapid eye movement sleep times.

2) **Electromyogram (EMG)**

   Surface electrodes were attached to the chin, legs and chest. The electrodes monitored the electrical activity of the mentalis muscle, the supra-hyoid muscles, the anterior tibialis muscle of the leg and the diaphragm. Three electrodes were used for the mentalis and supra-hyoid muscles. Two electrodes were used for the leg muscle and one electrode was positioned between the 7th and 8th intercostal space to monitor the movement of the diaphragm.

3) **Electrocardiogram (ECG)**

   A modified electrocardiogram using two leads was used to monitor the electrical activity of the heart to detect cardiac arrythmias.

4) **Electro-oculogram (EOG)**

   A right and left oculogram was set up to monitor the eye movements. One electrode was placed on the right outer canthus approximately 1 cm above the eye. The other was placed 1 cm below the left outer canthus. Movements were identified by a shift in electric polarity between the retina and skin surface.

5) **Oronasal Airflow**

   Oronasal airflow was evaluated by continuous measurement of pressure change in nasal prongs/thermistors (Grass volumetric unit, Grass Instrument, Quincy, Mass).

6) **Arterial Oxygen Saturation**

   Arterial oxygen saturation was monitored continuously with a pulse oximeter (Ohmeda Biox 3700e, Louisville, CO) attached to the middle finger.
7) *Abdominal and Thoracic Movements*

Breathing variables included chest wall and abdominal motion monitored by a respiratory inductance plethysmograph (Respirtrace, Ambulatory Monitoring Inc., Ardsley, New York). Special bands were strapped across the chest and abdomen to monitor movements over these areas.

8) *Body Position Monitor*

An electronic position monitor (mercury switch transducer) was attached to the front of the chest.

10) *Sound*

Sound intensity was measured using a calibrated sound level meter and a perpendicular response microphone positioned at 1 m and directed at the sound source.

*No patient was using any sedating medications or consumed alcohol prior to the study. Also, no attempt was made to control sleeping posture.*

3.14.1 *Scoring Of Sleep Studies*

Sleep recordings were scored in 30-second epochs and staged according to standard criteria (Rechtschaffen and Kales, 1968), by an experienced polysomnographer, who was blinded to the patients’ clinical status and mode of treatment (placebo versus MAS). The sleep data were recorded using 3 categories: sleep architecture, snoring variables and respiratory function.

3.14.1.1 *Sleep Architecture*

The following variables were calculated:

(a) Total Sleep Time (TST) in minutes beginning from onset of sleep
(b) % of Total Sleep Time Spent Supine
(c) Sleep stage distribution- NREM and REM in minutes and as % of TST
(d) Arousal index (Number of awakenings per hour)
(e) Sleep Efficiency (%) (ratio of TST to sleep study duration)
3.14.1.2 Snoring Variables

The following indices were calculated:

(a) Snoring Frequency- number of snores per total sleep time
(b) Snoring Intensity- maximal dB levels were recorded for each snore as well as the mean intensity (in dB) over the duration of the sleep. Snores were scored as inspiratory noise greater than 5dB above background noise. Background noise ranged from 32-37dB on the nights of measurement.

3.14.1.3 Respiratory Function

The calculated respiratory variables were:

(a) Minimum arterial oxygen saturation, MinSaO₂
(b) Apnoea Hypopnoea index, AHI
(c) Total time spent in apnoea in REM and NREM sleep
(d) Total time spent in hypopnoea in REM and NREM sleep
(e) Total time spent in apnoea and hypopnoea in REM and NREM sleep

3.15 Definitions Set For This Study

3.15.1 Apnoea And Hypopnoea

**Apnoea**

Cessation of airflow for at least 10 seconds with oxygen desaturation undefined, or cessation of airflow for less than 10 seconds (but at least one respiratory cycle) if associated with an oxygen desaturation of more than 4%.

**Hypopnoea**

Reduction in amplitude of airflow or thoraco-abdominal wall movement of greater than 50% of the baseline measurement for more than 10 seconds (oxygen desaturation need not occur), or the same reduction with an accompanying oxygen desaturation of at least 4% (no time limit), and associated with arousal.

The AHI was calculated by dividing the total number of events by the sleep duration (in hours). These events were considered obstructive if they occurred in association with continued diaphragm EMG activity and thoraco-abdominal wall movement.
Central events were defined as those accompanied by absence of diaphragm EMG activity and thoraco-abdominal wall movement. Mixed apnoeas were defined as a combination of an obstructive and central apnoea. OSA was defined as an AHI $\geq 5$/hour.

All of these sleep studies were manually scored for sleep stage, apnoea type and duration.

3.15.2 Severity Of OSA

- **Mild OSA**
  - Baseline AHI $< 20$ events/hour

- **Moderate OSA**
  - Baseline AHI 20 - 40 events/hour

- **Severe OSA**
  - Baseline AHI $> 40$ events/hour

3.15.3 Treatment Outcome

- **Treatment Success**
  - was defined as a resolution of symptoms plus reduction in AHI to $< 5$/hour.

- **Partial Success**
  - was defined as improved symptoms plus $\geq 50\%$ reduction in AHI, but AHI $\geq 5$

- **Treatment Failure**
  - was defined as ongoing clinical symptoms and/or a $< 50\%$ reduction in AHI

- **Compliance Failure**
  - was defined as an inability or unwillingness of the patient to continue to use the treatment.