4. **STATISTICAL ANALYSIS**

4.1 **Data Storage And Statistical Software**

Data were stored and analysed on a computerised spreadsheet/graphic statistics software package (SPSS Version 8.0; SPSS Inc, 444 North Michigan Avenue, Chicago IL 60614).

4.2 **Preparing The Data For Analysis**

The raw data obtained from the questionnaires and sleep studies were edited by identifying omissions, ambiguities and errors in responses and coding them appropriately. The questionnaire and sleep study data were coded to allow the statistical software programme to be employed.

4.3 **Statistics**

4.3.1 **Tests For Normality**

The author performed normal probability plots to test for normality of the data.

4.3.2 **Group Analysis**

A two-tailed student t-test was performed to compare physical characteristics and baseline data between Groups I and II. Studies have shown the two-tailed student t-test is robust down to sample sizes of 5 (Kitchens, 1987).

4.3.3 **OSA Severity**

A one-way Analysis of Variance (ANOVA) was used to identify whether a difference existed in the means of the baseline variables (age, BMI, neck circumference and baseline MinSaO₂) and OSA severity (mild, moderate, severe). Where a significant difference existed between OSA severity groups, multiple comparisons with Bonferroni Adjustment, were used to identify the significant differences between pairs of means.

4.3.4 **Cephalometric Analysis**

A z-test was performed to identify any difference in the means of the cephalometric measurements between the OSA sample and the published normative data. A z-score
is the number of standard deviations that a variable is above or below the mean. This was calculated as:

\[ z = (\text{OSA sample mean} - \text{Normative mean})/\text{Normative S.D.} \]

If \( z > 2 \) or \( z < -2 \) than a significant difference was present. The corresponding \( p \) value was recorded using statistical tables\(^{12}\).

An analysis of errors of cephalometric measurements was undertaken by calculating the mean differences between the initial set and the repeated set of measurements. This mean difference was recorded for each variable, and the standard deviation of the difference calculated. The measurement error was derived using a formula, according to Houston (1983):

\[ se = \sqrt{sd^2}/2 \]

\( se \) = Error of a single series of measurement

\( sd \) = Standard deviation of the differences between replicates

4.3.5 Questionnaire Analysis

A two-tailed paired student t-test was performed to identify any significant difference in the Epworth Sleepiness Score before and with the use of the MAS at the end of the acclimatisation period.

4.3.6 Sleep Study Analysis

Each patient received the treatment in one of two possible orders: Sequence ABB (placebo, followed by MAS, followed by MAS) or Sequence BAA (MAS, followed by placebo, followed by placebo).

A General Linear Model (GLM) was used to estimate the treatment effect using the differences of the three observations from each patient. In order to rule out a treatment-by-period and a treatment-by-sequence interaction, tests for carry-over, period and sequence effects were performed (Jones and Kenward, 1989).

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A two-tailed paired student t-test was carried out to determine whether there was a significant treatment effect of the placebo when compared with baseline AHI.

4.3.7 Treatment Outcome

A one-way ANOVA was used to indicate a difference among the means of various variables (age, BMI, neck circumference, baseline AHI and MinSaO₂, acclimatisation period, percentage of actual mandibular advancement, absolute mandibular advancement and cephalometric variables) and treatment outcome (Treatment Success, Partial Success or Treatment Failure). Where a significant difference existed between the treatment outcome groups, multiple comparisons with Bonferroni Adjustment were used to identify significant differences between pairs of means.

4.3.8 Identifying Predictors Of Response With The MAS

A multiple regression model was constructed to examine the relationship between several independent numeric variables and a numeric dependant variable (AHI with MAS) (Dawson-Sanders and Trapp, 1994). A step-wise method (combining forward and backward selection) was used to select the significant variables. Normal probability plots were used as a check for normality of the residuals.

4.3.9 Presentation Of Descriptive Statistics And Level Of Significance

All descriptive statistics in this thesis are presented as mean ± standard deviation (sd). Estimated means are presented as mean ± standard error of the mean (SEM).

A p-value of less than 0.05 was considered significant. This significance level is the probability of rejecting the null hypothesis, assuming that the null hypothesis is true.

4.4 Power Calculation

A power calculation indicated that a sample size of 30 using the ABB-BAA design would have an 80% chance of showing a reduction in AHI using a significance of 0.05.
5. RESULTS

5.1 Study Population

From the sample of thirty patients who met the entry criteria, twenty-four (80%) completed the research protocol. Two patients who claimed intolerance to the MAS and refused to proceed with the study were classified as compliance failures. One patient developed severe asthma and did not wish to continue and another patient cited family commitments for dropping out. Two patients have failed to return for follow-up and have been uncontactable by telephone or letter.

*Figure 11. Sample Population*

30 patients selected for research study  
4 dropped out  
24 patients completed protocol  
2 yet to complete

The resulting data, unless otherwise indicated, are presented on the 24 subjects who completed the research protocol.

5.2 Sample Characteristics

*Table 9. Sample Characteristics By Group*

<table>
<thead>
<tr>
<th>Sample Variables</th>
<th>All Group</th>
<th>Group I</th>
<th>Group II</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 24</td>
<td>n = 12</td>
<td>n = 12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.0±9.2</td>
<td>47.8±6.8</td>
<td>48.2±11.4</td>
<td>0.92</td>
</tr>
<tr>
<td>Range</td>
<td>35.0-73.0</td>
<td>36.0-57.0</td>
<td>35.0-73.0</td>
<td></td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.75±0.1</td>
<td>1.8±0.1</td>
<td>1.7±0.1</td>
<td>0.80</td>
</tr>
<tr>
<td>Range</td>
<td>1.6-2.0</td>
<td>1.6-2.0</td>
<td>1.6-1.9</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>90.2±14.1</td>
<td>92.4±16.9</td>
<td>87.9±10.9</td>
<td>0.45</td>
</tr>
<tr>
<td>Range</td>
<td>72.0-127.0</td>
<td>72.0-127.0</td>
<td>72.0-107.0</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29.4±3.1</td>
<td>28.9±3.5</td>
<td>30.0±2.7</td>
<td>0.39</td>
</tr>
<tr>
<td>Range</td>
<td>24.8-36.3</td>
<td>24.8-36.3</td>
<td>25.8-35.8</td>
<td></td>
</tr>
<tr>
<td>Neck circumference (cm)</td>
<td>40.4±3.9</td>
<td>41.4±4.9</td>
<td>39.3±2.4</td>
<td>0.20</td>
</tr>
<tr>
<td>Range</td>
<td>34.0-53.0</td>
<td>34.0-53.0</td>
<td>35.0-42.0</td>
<td></td>
</tr>
<tr>
<td>Baseline AHI (/hr)</td>
<td>26.8±16.5</td>
<td>26.0±15.1</td>
<td>27.7±18.6</td>
<td>0.81</td>
</tr>
<tr>
<td>Range</td>
<td>10.0-68.0</td>
<td>10.0-68.0</td>
<td>10.0-54.0</td>
<td></td>
</tr>
<tr>
<td>Baseline MinSaO₂ (%)</td>
<td>84.7±8.4</td>
<td>87.7±6.9</td>
<td>81.6±9.0</td>
<td>0.09</td>
</tr>
<tr>
<td>Range</td>
<td>61.0-96.0</td>
<td>72.0-96.0</td>
<td>61.0-92.0</td>
<td></td>
</tr>
</tbody>
</table>

*Note: M = Males; F = Females*
Table 9 illustrates patient characteristics of the whole group, and of groups I and II (see Appendix 9 for individual patient measurements).

The patients (79% males) were, in general, middle aged, overweight and had a wide range of OSA severity from mild to severe. The mean age (± sd) was 48.0 yrs ± 9.2 with a mean body mass index (± sd) of 29.4 kg/m² ± 3.1 and a baseline AHI (± sd) of 26.8/hr± 16.5. All patients completed a baseline polysomnograph.

Randomisation of the sample to Group I (ABB) and Group II (BAA) resulted in two groups of 12 patients each. There was no significant difference in baseline characteristics (age, sex, BMI, neck circumference, AHI and MinSaO₂) between the two groups.

5.2.1 Severity Of OSA

The patients ranged in their pre-treatment or baseline AHI from 10.0/hr to 68.0/hr. Because of the considerable variation (± sd 16.5), the patients were classified into either mild (baseline AHI<20/hr), moderate (baseline AHI 20-40/hr) or severe OSA (baseline AHI>40/hr). Figure 12 represents the percentage breakdown of the three classes of OSA severity within the sample.

Figure 12. Classification Of OSA Severity

The only significant difference (p < 0.05) in baseline characteristics, between the 3 OSA severity classes, was in the mean BMI (Table 10). Adjusting for multiple comparisons, this difference was significant (p < 0.05) between the mild and severe OSA groups only (Table 11). No significant difference in the mean age, neck circumference and baseline MinSaO₂ was detected between the groups.
Table 10. OSA Severity And Mean BMI

<table>
<thead>
<tr>
<th>OSA Severity</th>
<th>N</th>
<th>Mean BMI ± sd (kg/m²)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>11</td>
<td>28.0 ± 2.1</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>7</td>
<td>29.2 ± 3.8</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>6</td>
<td>32.4 ± 2.0</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>24</td>
<td>29.4 ± 3.1</td>
<td></td>
</tr>
<tr>
<td>Between groups</td>
<td></td>
<td></td>
<td>0.015*</td>
</tr>
</tbody>
</table>

*p<0.05

Table 11. Multiple Comparisons Between OSA Severity For Mean BMI

<table>
<thead>
<tr>
<th>OSA Severity</th>
<th>OSA Severity</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Moderate</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>0.013*</td>
</tr>
<tr>
<td>Moderate</td>
<td>Mild</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>0.138</td>
</tr>
<tr>
<td>Severe</td>
<td>Mild</td>
<td>0.013*</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>0.138</td>
</tr>
</tbody>
</table>

*p<0.05

5.2.2 Clinical Data

A summary of the clinical characteristics for the whole sample group is illustrated in Table 12.

Table 12. Clinical Characteristics Of The Sample Group

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acclimatisation (weeks)</td>
<td>19.7 ± 8.8</td>
<td>5.0 - 40.0</td>
</tr>
<tr>
<td>Actual advancement with MAS (mm)</td>
<td>7.5 ± 1.8</td>
<td>5.0 - 11.5</td>
</tr>
<tr>
<td>Maximum jaw protrusion (mm)</td>
<td>9.6 ± 1.8</td>
<td>6.0 - 13.0</td>
</tr>
<tr>
<td>Actual advancement (% of maximum jaw protrusion)</td>
<td>78.2 ± 8.4</td>
<td>62.5 - 88.9</td>
</tr>
</tbody>
</table>

The mean acclimatisation period between issuing the appliance and the one week washout prior to the first sleep study was 19.7 weeks ± 8.8. During this period,
patients had on average 3 visits to the author for adjustments to their MAS. The
mean actual advancement of the lower jaw using the MAS was 7.5 mm ± 1.8, which
as a percentage of maximum jaw protrusion was 78.2% ± 8.4.

The advancement, carried out in increments during the acclimatisation period, varied
for each patient (range 5.0 mm - 11.5 mm) and depended on their ability to advance
their mandible as far as was comfortably possible. In two patients (8%), the
symptoms of snoring, sleep quality and daytime sleepiness worsened with additional
advancement, having previously improved with lesser advancement. In these
patients the appliance had to be rewound to a level that was consistent with optimum
subjective improvement in OSA symptoms.

5.3 Cephalometric Analysis

The individual cephalometric measurements of the sample are presented in Appendix
10. Group data for males (M), females (F) and the total sample (T) are presented in
Table 13, as are comparative data for normal subjects derived from the literature.
Table 13. A Comparison Of Sample Cephalometric Measurements And Normative Values

<table>
<thead>
<tr>
<th>Cephalometric Variable</th>
<th>Group (T=total, M=male, F=female)</th>
<th>OSA Sample n = 24, M = 19, F = 5</th>
<th>Mean ± SD</th>
<th>Mean ± SD</th>
<th>N</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BaSN (degrees)</td>
<td>T</td>
<td>126.7 ± 4.6</td>
<td>130.6 ± 4.6</td>
<td>58</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>127.1 ± 4.9</td>
<td>129.4 ± 5.4</td>
<td>27</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>125.1 ± 3.0</td>
<td>131.7 ± 4.2</td>
<td>31</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>SN (mm)</td>
<td>T</td>
<td>77.3 ± 4.4</td>
<td>69.1 ± 3.1</td>
<td>58</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>78.6 ± 3.0</td>
<td>71.5 ± 3.0</td>
<td>27</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>72.2 ± 5.3</td>
<td>67.0 ± 1.9</td>
<td>31</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>ANS-pm (mm)</td>
<td>T</td>
<td>56.3 ± 3.7</td>
<td>54.7 ± 3.8</td>
<td>58</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>57.2 ± 3.1</td>
<td>57.2 ± 3.3</td>
<td>27</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>52.8 ± 4.0</td>
<td>52.6 ± 2.2</td>
<td>31</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Co-A (mm)</td>
<td>T</td>
<td>92.5 ± 4.9</td>
<td>85.8 ± 4.6</td>
<td>58</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>94.0 ± 3.7</td>
<td>88.7 ± 4.3</td>
<td>27</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>87.1 ± 5.3</td>
<td>83.3 ± 2.9</td>
<td>31</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Go-Gn (mm)</td>
<td>T</td>
<td>82.6 ± 5.6</td>
<td>75.2 ± 5.8</td>
<td>58</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>84.5 ± 4.5</td>
<td>79.2 ± 4.0</td>
<td>27</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>75.5 ± 3.2</td>
<td>71.7 ± 3.9</td>
<td>31</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>SNA (degrees)</td>
<td>T</td>
<td>80.7 ± 3.9</td>
<td>81.2 ± 3.8</td>
<td>58</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>80.4 ± 4.2</td>
<td>82.0 ± 4.6</td>
<td>27</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>81.7 ± 2.6</td>
<td>80.5 ± 3.4</td>
<td>31</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>SNB (degrees)</td>
<td>T</td>
<td>77.0 ± 3.8</td>
<td>78.7 ± 3.8</td>
<td>58</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>77.3 ± 3.9</td>
<td>79.7 ± 4.5</td>
<td>27</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>75.9 ± 3.5</td>
<td>77.9 ± 3.4</td>
<td>31</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>ANB (degrees)</td>
<td>T</td>
<td>3.6 ± 2.3</td>
<td>2.3 ± 2.3</td>
<td>58</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>3.1 ± 1.9</td>
<td>2.0 ± 2.9</td>
<td>27</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>5.8 ± 2.8</td>
<td>1.6 ± 2.4</td>
<td>31</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>LAFH (mm)</td>
<td>T</td>
<td>74.9 ± 6.2</td>
<td>63.5 ± 6.1</td>
<td>58</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>75.8 ± 6.6</td>
<td>66.6 ± 6.1</td>
<td>27</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>71.4 ± 2.4</td>
<td>60.7 ± 4.5</td>
<td>31</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>TPFH (mm)</td>
<td>T</td>
<td>87.9 ± 7.3</td>
<td>76.0 ± 6.1</td>
<td>58</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>90.3 ± 6.2</td>
<td>80.5 ± 4.0</td>
<td>27</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>78.9 ± 2.3</td>
<td>72.0 ± 4.1</td>
<td>31</td>
<td>ns</td>
<td></td>
</tr>
</tbody>
</table>
### Table 13 (cont’d)

<table>
<thead>
<tr>
<th>Cephalometric Variable</th>
<th>Group (T=Total, M=Male, F=Female)</th>
<th>OSA Sample (n=24), M=19, F=5</th>
<th>Normative Data</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>SN-Mp (mm)</td>
<td>T 35.8 ± 4.9</td>
<td>33.1 ± 6.1</td>
<td>58</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>M 34.8 ± 4.7</td>
<td>31.8 ± 6.8</td>
<td>27</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>F 39.4 ± 4.0</td>
<td>34.3 ± 5.9</td>
<td>31</td>
<td>ns</td>
</tr>
<tr>
<td>H-Mp (mm)</td>
<td>T 23.9 ± 5.9</td>
<td>12.0 ± 3.8</td>
<td>30</td>
<td>0.0009</td>
</tr>
<tr>
<td></td>
<td>M 24.4 ± 5.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>F 22.0 ± 7.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>C2C4-SN (degrees)</td>
<td>T 113.7 ± 6.0</td>
<td>97.7 ± 5.7</td>
<td>51</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>M 113.3 ± 6.2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>F 115.4 ± 5.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Phw-spt (mm)</td>
<td>T 12.3 ± 3.5</td>
<td>10.1 ± 2.8</td>
<td>101</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>M 12.5 ± 3.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>F 11.6 ± 3.6</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>pm-P (mm)</td>
<td>T 41.4 ± 6.5</td>
<td>41.2 ± 4.4</td>
<td>36</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>M 41.5 ± 6.8</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>F 41.1 ± 6.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PAS (mm)</td>
<td>T 9.4 ± 3.1</td>
<td>14.0 ± 2.2</td>
<td>30</td>
<td>0.018</td>
</tr>
<tr>
<td></td>
<td>M 9.9 ± 3.1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>F 7.4 ± 2.4</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SPT (mm)</td>
<td>T 10.9 ± 1.7</td>
<td>10.0 ± 1.7</td>
<td>36</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>M 11.2 ± 1.7</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>F 9.6 ± 1.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>TI (mm)</td>
<td>T 87.4 ± 6.3</td>
<td>83.3 ± 5.3</td>
<td>36</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>M 89.1 ± 5.2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>F 80.8 ± 6.2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>THt (mm)</td>
<td>T 43.4 ± 3.1</td>
<td>41.1 ± 3.6</td>
<td>36</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>M 44.3 ± 2.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>F 40.0 ± 3.8</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Note:** Normative data for most of the measurements are from Bhatia and Leighton (1993). Normative data for TI, THt, pm-P and SPT are from Tangugsorm et al., (1995b) (part II); H-Mp and PAS from Guilleminault et al., (1984); Phw-spt adapted from Solow et al., (1996) and C2C4-SN from Solow and Tallgren, (1976).
The cephalometric variables found to be significantly different (p < 0.05) from the normative data were:

<table>
<thead>
<tr>
<th>Cephalometric Variable</th>
<th>Variation From The Norm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SN</td>
<td>Length increased</td>
</tr>
<tr>
<td>LAFH</td>
<td>Distance increased (female group only)</td>
</tr>
<tr>
<td>H-Mp</td>
<td>Distance increased</td>
</tr>
<tr>
<td>C2C4-SN</td>
<td>Angle increased</td>
</tr>
<tr>
<td>PAS</td>
<td>Distance decreased</td>
</tr>
</tbody>
</table>

5.3.1 Analysis Of Errors Of Cephalometric Measurements

Appendix 11 summarises mean difference, sd of the difference, the calculated errors and the reliability index of the repeated cephalometric measurements. The cephalometric variables with the most variation were Co-A, Tl and pm-P. This outcome was due to the difficulty of consistently identifying these points. However, the high correlation between the two sets of readings indicated a high estimate of reproducibility.

5.4 Subjective Outcomes Based On Questionnaires

Data were compiled from Questionnaire 1 (completed at the initial orthodontic examination) and Questionnaire 2 (completed at the end of the acclimatisation period). All patients (n=24) completed Questionnaires 1 and 2. Nineteen patients received help from their bed partners in answering questions related to snoring. The five patients who were single received assistance from family members or friends in answering these questions.

5.4.1 Patient Compliance With The MAS

(Q: In the last month, how often did you use the Oral Appliance?)

The compliance rate was 87.5% (measured by the number of patients wearing the appliance every day). Three patients (12.5%) stated they wore the appliance for on average 3-4 days a week.
5.4.2 Effect Of The MAS On Snoring

(Q: How would you rate the effect of the Oral Appliance on your snoring?)

Figure 13 illustrates the degree of improvement in snoring reported by the subjects at the end of the acclimatisation period after using the MAS. Overall 96% of patients and sleeping partners reported varying improvement in snoring. Patient # 14 found no improvement in snoring.

Figure 13. Effect Of The MAS On Snoring

5.4.3 Effect Of The MAS On Daytime Sleepiness

(Q: How would you grade your daytime sleepiness / fatigue in the last month for the 8 situations listed in the questionnaires?)

Comparing the pre-treatment and post-acclimatisation ESS scores, there was a significant reduction in the mean Epworth Sleepiness Score with the MAS from a pre-treatment value of 10.1 ± 1.1 to 3.9 ± 0.64 (p<0.01) for the whole group (Figure 14).

The MAS resulted in some improvement in the Epworth Sleepiness Score (ESS) in 23 patients (96%) at the end of the acclimatisation period. One patient (patient # 5) showed no change in the ESS score.
5.4.4 Effect Of The MAS On Sleep Quality

(Q: How would you rate the quality of your sleep?)

The MAS resulted in a subjective improvement in sleep quality in 21 of the 23 patients (91%) who reported "unrefreshing sleep" prior to MAS treatment. Two patients (patient # 5 and # 22) found no change in sleep quality. One patient (patient # 15) reported that the sleep quality diminished from "refreshed" to "slightly unrefreshed" with the MAS. Figure 15 illustrates the distribution of the sample in the different categories of sleep quality before and after use of the MAS.
5.4.5 Effect Of The MAS On Level Of Tiredness On Waking

(Q: How would you grade your level of tiredness on waking?)

Of the 23 patients who complained of tiredness on waking prior to treatment, the MAS resulted in a subjective improvement in 18 patients (78%). Five subjects (patient #5, #6, #7, #22 and #24) found no change in level of tiredness on waking with the MAS. Figure 16 illustrates the distribution of the sample into the different categories of tiredness on waking before and after use of the MAS.

![Figure 16. Effect Of The MAS On Level Of Tiredness](image)

5.4.6 Effect Of The MAS On Sleeping Arrangement

(Q: Since obtaining the appliance, has your sleeping arrangement changed?)

Table 14 shows that 4 out of 8 (50%) couples resumed sleeping together as a result of an improvement in snoring with the MAS.

Table 14. Effect Of The MAS On Sleeping Arrangement

<table>
<thead>
<tr>
<th>Patient’s Sleeping Arrangement</th>
<th>Before MAS</th>
<th>After MAS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (% of patients)</td>
<td>Number (% of patients)</td>
</tr>
<tr>
<td>Patients who were single</td>
<td>5 (21%)</td>
<td>5 (21%)</td>
</tr>
<tr>
<td>Patients with partners</td>
<td>19 (79%)</td>
<td>19 (79%)</td>
</tr>
<tr>
<td>Couples who slept in different rooms because of the snoring</td>
<td>8 (33%)</td>
<td>4 (17%)</td>
</tr>
</tbody>
</table>
5.4.7 Side Effects Experienced With The MAS

(Q: Have you encountered any difficulties with the appliance?)

The MAS was well tolerated by 21 patients (87.5%). In these patients, the side effects were described as mild to moderate, with symptoms lasting less than 3 weeks and did not preclude continuing use of the MAS. Two patients (8.3%) did not experience any side-effects whilst using the MAS.

The side effects experienced with the MAS were jaw discomfort, excess salivation, dryness of the mouth, grinding of the teeth and soft tissue irritation. Figure 17 illustrates the distribution of the sample who reported these side effects with some patients complaining of more than one side effect.

Figure 17. Side Effects Experienced By Patients Using The MAS

![Bar chart showing side effects]

Appendix 12 details the type of side effect experienced by patients, the severity (mild, moderate or severe), frequency (rarely, sometimes or often) and duration (< 2 weeks; 2-3 weeks; > 3 weeks).

Jaw discomfort of mild to moderate severity, lasting between 20 minutes to half an hour on waking, was experienced by three patients (12.5%). Two of these patients continued to experience this side effect for longer than 3 weeks. However, no patient developed any symptoms of temporomandibular joint dysfunction.

Excessive salivation, experienced by 12 patients (50%) was a transient phenomenon in 6 patients, resolving within 3 weeks. The remaining half of the group continued to experience this side effect for longer than 3 weeks.
Eleven patients (45.8%) experienced dryness of the mouth. This persisted for longer than 3 weeks in 10 patients (41.7%).

Three patients (12.5%) reported that the MAS resulted in a bruxing habit. This continued for more than 3 weeks in two of the patients.

Soft tissue irritation of mild to moderate severity, although experienced by five patients (20.8%) was only temporary and was resolved in all patients within 2-3 weeks.

5.4.8 Patient Satisfaction With The MAS

(Q: How would you rate your satisfaction with the appliance?)

(Q: Would you like to continue to use the Oral Appliance?)

Twelve (50%) patients were very satisfied with the MAS, 11 (46%) were satisfied and one patient was dissatisfied. Overall, 96% of the patients said they would like to continue to use the MAS because of an improvement in their symptoms.

5.5 Objective Outcomes Based On Sleep Study Data

The variables were tested for possible gender differences by two-tailed t-tests. No differences were found at the 5% significance level. In the following analysis, therefore, male and female data were pooled.

5.5.1 Carry-over, Period And Sequence Effects

The study design allowed assessment of treatment effects while simultaneously taking into account carry-over, period and sequence effects. There were no significant sequence effects found in this study. Carry-over and period effects identified during the analysis are noted in the relevant sections.

The sleep study measurements involved sleep architecture, snoring and respiratory variables.

5.5.2 Sleep Architecture Variables

The mean total sleep time (TST) (min), % of total sleep time spent supine, sleep stage in REM and NREM sleep, arousal index and sleep efficiency between treatment with the MAS and placebo is listed in Table 15.
Table 15. Effect Of The MAS On Sleep Architecture

<table>
<thead>
<tr>
<th>Sleep Architecture Variables</th>
<th>Placebo Mean ± SEM</th>
<th>MAS Mean ± SEM</th>
<th>p Value (*significant difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Sleep Time (min)</td>
<td>365.1 ± 5.2</td>
<td>367.7 ± 5.0</td>
<td>0.240</td>
</tr>
<tr>
<td>TST Spent Supine (%)</td>
<td>50.8 ± 3.9</td>
<td>52.0 ± 3.7</td>
<td>0.183</td>
</tr>
<tr>
<td>REM Sleep (min)</td>
<td>59.9 ± 3.7</td>
<td>75.9 ± 3.7</td>
<td>0.010*</td>
</tr>
<tr>
<td>NREM Sleep (min)</td>
<td>305.2 ± 4.0</td>
<td>291.8 ± 4.0</td>
<td>0.000*</td>
</tr>
<tr>
<td>TST in REM (%)</td>
<td>16.4 ± 1.0</td>
<td>20.6 ± 1.0</td>
<td>0.003*</td>
</tr>
<tr>
<td>TST in NREM (%)**</td>
<td>83.6 ± 0.9</td>
<td>79.4 ± 0.8</td>
<td>0.002*</td>
</tr>
<tr>
<td>Arousal Index (/hr)</td>
<td>40.9 ± 1.7</td>
<td>27.5 ± 1.7</td>
<td>0.000*</td>
</tr>
<tr>
<td>Sleep Efficiency (%)</td>
<td>85.8 ± 1.2</td>
<td>85.7 ± 1.2</td>
<td>0.3111</td>
</tr>
</tbody>
</table>

Note: * p < 0.05

** There was a significant period effect detected by the model (p=0.038)

There was a significant difference in the sleep staging between REM and NREM sleep when the MAS was used compared to the placebo. The mean proportion of time spent in NREM decreased from 83.6% ± 0.9 to 79.4% ± 0.8 (p<0.01) and that of REM sleep increased from 16.4% ± 1.0 to 20.6% ± 1.0 (p<0.01) with the use of the MAS. This represented a 25.6% increase in the mean proportion of time spent in REM sleep.

The mean arousal index improved significantly with the use of the MAS by 32.8% (p<0.01).

There was no significant difference in mean total sleep time, sleep efficiency and % time spent supine (p>0.05) for treatment with MAS and placebo.

5.5.3 Snoring Variables

The data on the snoring variables: snoring frequency, mean and maximum snoring intensity are reported on a subset of the total sample. Complete snoring data were available in 19 of the subgroup of 22 patients in whom snoring was quantified.

As there was no carry over or period effect with respect to the snoring variables listed above, sleep study data from sequences ABB and BAA for the 19 patients were pooled for the statistical analysis. These results are outlined in Table 16.
Table 16. Effect Of The MAS On Snoring Variables

<table>
<thead>
<tr>
<th>Snoring Variables</th>
<th>Placebo Mean ± SEM</th>
<th>MAS Mean ± SEM</th>
<th>p Value (*significant difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Snoring Frequency in TST (hr)</td>
<td>421.9 ± 27.0</td>
<td>223.0 ± 25.6</td>
<td>0.000*</td>
</tr>
<tr>
<td>Mean Snoring Intensity (dB)</td>
<td>52.5 ± 0.4</td>
<td>49.2 ± 0.4</td>
<td>0.000*</td>
</tr>
<tr>
<td>Maximum Snoring Intensity (dB)</td>
<td>71.9 ± 1.3</td>
<td>68.5 ± 1.2</td>
<td>0.224</td>
</tr>
</tbody>
</table>

*p < 0.001

Over the total sleep time, the MAS was associated with a significant improvement in both mean snoring frequency and intensity (p<0.01). The background noise in the sleep laboratory room ranged from 32 - 37 dB on the nights of measurement.

The mean snoring frequency decreased by 47% with the use of the MAS compared to the placebo, from 421.9/hr ± 27.0 to 223.0/hr ± 25.6 (p<0.01).

The MAS was also significantly effective in reducing the mean snoring intensity from 52.5dB ± 0.4 (placebo) to 49.2dB ± 0.4. This represented a 3.3dB decrease in the mean snoring intensity (p<0.01).

There was no significant difference in the mean maximum snoring intensity (p>0.05) with the use of the MAS.

5.5.4 Respiratory Variables

Comparison of the means for MinSaO₂, AHI, total time spent in apnoea, hypopnoea and apnoea + hypopnoea for the various sleep stages between MAS and placebo is provided in Table 17.
Table 17. Effect Of The MAS On Respiratory Variables

<table>
<thead>
<tr>
<th>Respiratory Variables</th>
<th>Placebo Mean ± SEM</th>
<th>MAS Mean ± SEM</th>
<th>p Value (%significant difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MinSaO₂ (%)</td>
<td>86.7 ± 0.6</td>
<td>90.7 ± 0.6</td>
<td>0.000*</td>
</tr>
<tr>
<td>AHI (hr)</td>
<td>29.9 ± 1.8</td>
<td>14.4 ± 1.8</td>
<td>0.000*</td>
</tr>
<tr>
<td>Total time spent in apnoea in REM sleep (min)</td>
<td>5.1 ± 1.0</td>
<td>3.2 ± 1.0</td>
<td>0.172</td>
</tr>
<tr>
<td>Total time spent in apnoea in NREM sleep (min)</td>
<td>23.3 ± 4.4</td>
<td>10.9 ± 4.3</td>
<td>0.049*</td>
</tr>
<tr>
<td>Total time spent in hypopnoea in REM sleep (min)</td>
<td>9.0 ± 1.2</td>
<td>8.7 ± 1.2</td>
<td>0.871</td>
</tr>
<tr>
<td>Total time spent in hypopnoea in NREM sleep (min)**</td>
<td>30.3 ± 4.6</td>
<td>24.9 ± 4.6</td>
<td>0.219</td>
</tr>
<tr>
<td>Total time spent in apnoea + hypopnoea in REM sleep (min)</td>
<td>14.4 ± 1.4</td>
<td>11.6 ± 1.4</td>
<td>0.334</td>
</tr>
<tr>
<td>Total time spent in apnoea + hypopnoea in NREM sleep (min)***</td>
<td>65.8 ± 4.5</td>
<td>23.9 ± 4.4</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

* p < 0.05  
** There was a significant carry-over effect detected by the model (p=0.002)  
*** There was a significant period effect detected by the model (p=0.012)

There was a significant increase (p<0.01) in the mean MinSaO₂ by 4.6% with the use of the MAS compared to the placebo.

There was a significant reduction (p<0.01) of 51.8% in the mean AHI of the overall group with the use of the MAS when compared to the placebo. Improvement in AHI was not related to the order of use of the MAS in the study [no significant sequence effect (p>0.05)].

The effect of sleep stage on total time spent in apnoea, hypopnoea and apnoea and hypopnoea combined was considered between the MAS and placebo. The MAS resulted in a reduction in the mean total time spent in these respiratory variable...
Measurements compared to the placebo for both REM and NREM sleep stages. This reduction was significant in the following measurements:

i) Mean total time spent in apnoea in NREM decreased by 53.2% from 23.3 min ± 4.4 to 10.9 min ± 4.3 (p<0.05).

ii) Mean total time spent in apnoea and hypopnoea in NREM decreased by 63.7% from 65.8 min ± 4.5 to 23.9 min ± 4.4 (p<0.01).

5.5.5 Effect Of Placebo On AHI

There was no significant change in AHI between baseline AHI and placebo (p>0.05) for both sequences (ABB and BAA).

Table 18. Baseline And Placebo AHI Means For Groups I And II

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline AHI (/hr)</th>
<th>Placebo AHI (/hr)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SEM</td>
<td>Mean±SEM</td>
<td></td>
</tr>
<tr>
<td>Group 1 (ABB)</td>
<td>26.0 ± 4.4</td>
<td>29.1 ± 7.1</td>
<td>0.534</td>
</tr>
<tr>
<td>Group II (BAA)</td>
<td>29.5 ± 5.9</td>
<td>30.8 ± 5.5</td>
<td>0.868</td>
</tr>
</tbody>
</table>

5.6 Treatment Outcome

A reduction in AHI with the use of the MAS occurred in 91.7% (22 patients) of the sample (refer to Appendix 13). One patient (patient #13) showed no change in AHI between MAS and placebo and in patient #9 the AHI increased with the use of the MAS.

There was a mean percentage change in AHI of 55.7%\textsuperscript{13} ± 6.5. The percentage change in AHI ranged from a maximum of 92.8% (15.2 to 1.1 events/hr in patient #18) to a minimum reduction of -18.8% (8.0 to 9.5 events/hr in patient #9).

The subjects were classified into 3 categories (Treatment Success, Partial Success and Treatment Failure) as defined in the methodology. This is illustrated in Figure 18.

\textsuperscript{13} The percentage change in AHI was calculated using the formula: \( \frac{\text{AHI(Placebo)} - \text{AHI(MAS)}}{\text{AHI(Placebo)}} \times 100 \).

For the sequence ABB, the average of the AHI with MAS from sleep studies 2 and 3 was used. For the sequence BAA, the average of the AHI with placebo from sleep studies 2 and 3 was used.
There were nine (37.5%) patients who were classified as Treatment Success because the MAS resulted in a return of the AHI to less than 5/hr and a resolution of clinical symptoms.

Six (25%) patients were classified as Partial Success. In this group of patients, the AHI remained above 5/hr with the use of the MAS but it was effective in resulting in a greater than 50% reduction in the AHI with an improvement in clinical symptoms. There were nine patients (37.5%) in whom the AHI remained greater than 5/hr and there was less than 50% reduction in the AHI with the use of the MAS. These patients were classified as Treatment Failures.

*Figure 18. Treatment Outcome In The OSA Sample*

The MAS resulted in a successful outcome ranging from complete to partial success in 62.5% of patients.
5.6.1 Treatment Outcome And OSA Severity

Figure 19 illustrates the distribution of the treatment outcomes within the different classes of OSA severity.

\[ \text{Figure 19. Treatment Outcome And OSA Severity} \]

\[
\begin{array}{c|c|c|c|c|c|c|c|c}
\hline
\text{OSA Severity} & \text{N=24} & \text{Treatment Success} & \text{Partial Success} & \text{Treatment Failure} \\
\hline
\text{Mild OSA} & 10.7\% & 8.3\% & 8.3\% & 8.3\% \\
\text{Moderate OSA} & 20.8\% & 12.5\% & 8.3\% & 8.3\% \\
\text{Severe OSA} & 15.0\% & 8.3\% & 8.3\% & 8.3\% \\
\hline
\end{array}
\]

5.6.2 Treatment Outcome And Sample Characteristics

A one-way ANOVA showed that there was no significant difference (p>0.05) in the variables of mean age, BMI, neck circumference, baseline AHI and MinSaO\textsubscript{2}, acclimatisation period, percentage of actual mandibular advancement and absolute mandibular advancement with the MAS, between the treatment outcome groups.

5.6.3 Treatment Outcome And Cephalometric Variables

A one-way ANOVA found a significant difference in the mean SNB and mean SN-Mp between the treatment outcome groups (Table 19).

Adjusting for multiple comparisons (Table 20), the mean SNB was significantly different (p=0.022) between the Treatment Success group (SNB=75.3° ± 3.7) and the Treatment Failure group (SNB=79.8° ± 2.3). However, the multiple comparison test did not reveal any significant difference (p>0.05) in the mean SN-Mp between any two pairs of the treatment outcome group.

There was no significant difference in any of the other cephalometric variables between the outcome groups.
Table 19. Treatment Outcome And Cephalometric Variables

<table>
<thead>
<tr>
<th>Cephalometric Variable</th>
<th>N</th>
<th>Mean ± sd</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNB (degrees)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment Success</td>
<td>9</td>
<td>75.3 ± 3.7</td>
<td></td>
</tr>
<tr>
<td>Partial Success</td>
<td>6</td>
<td>75.5 ± 3.7</td>
<td></td>
</tr>
<tr>
<td>Treatment Failure</td>
<td>9</td>
<td>79.8 ± 2.3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>77.0 ± 3.8</td>
<td></td>
</tr>
</tbody>
</table>

Between groups: 0.013*

Mandibular plane to SN line (degrees)

<table>
<thead>
<tr>
<th>Treatment Outcome</th>
<th>N</th>
<th>Mean ± sd</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Success</td>
<td>9</td>
<td>37.6 ± 2.1</td>
<td></td>
</tr>
<tr>
<td>Partial Success</td>
<td>6</td>
<td>37.8 ± 4.9</td>
<td></td>
</tr>
<tr>
<td>Treatment Failure</td>
<td>9</td>
<td>32.6 ± 5.6</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>35.8 ± 4.9</td>
<td>0.038*</td>
</tr>
</tbody>
</table>

Between groups: 0.038*

*p<0.05

Table 20. Multiple Comparisons Between Treatment Outcome For Mean SNB

<table>
<thead>
<tr>
<th>Treatment Outcome</th>
<th>Treatment Outcome</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Success</td>
<td>Treatment Failure</td>
<td>0.022*</td>
</tr>
<tr>
<td></td>
<td>Partial Success</td>
<td>1.000</td>
</tr>
<tr>
<td>Partial Success</td>
<td>Treatment Failure</td>
<td>0.058</td>
</tr>
<tr>
<td></td>
<td>Treatment Success</td>
<td>1.000</td>
</tr>
<tr>
<td>Treatment Failure</td>
<td>Partial Success</td>
<td>0.058</td>
</tr>
<tr>
<td></td>
<td>Treatment Success</td>
<td>0.022*</td>
</tr>
</tbody>
</table>

*p<0.05

Figure 20 illustrates that in the antero-posterior dimension, patients in the Treatment Success group had a mandible that was retropositioned relative to the anterior cranial base compared to patients in the Treatment Failure group.

Figure 20. Relationship Between SNB And Treatment Outcome
Figure 21 illustrates that in the vertical dimension, patients in the Treatment Success group had an increased SN-Mp angle compared to patients in the Treatment Failure group.

*Figure 21. Relationship Between SN-Mp And Treatment Outcome*
5.7 Predictors Of Response

A multiple regression model for predicting AHI with the MAS, using stepwise selection, by subjecting cephalometric, baseline anthropometric and polysomnographic data identified the following specific parameters as significant variables: neck circumference, Phw-spt, baseline AHI and SN-Mp.

The mathematical relationship, of these four variables, to predict AHI with the use of MAS was then derived:

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

\[
 r^2 = 82\% \quad s = 8.06
\]

*Note:* 
\( r^2 \) refers to the percentage of variability that is explained by the regression equation 
\( s \) refers to the average standard deviation of the residuals from the regression model

A normal probability plot of the residuals fitted a straight line, supporting a normal distribution.

The regression coefficients are listed in Table 21.

*Table 21. Regression Coefficients*

<table>
<thead>
<tr>
<th>Model</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>t-ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>19.42</td>
<td>32.66</td>
<td>0.60</td>
<td>0.60</td>
</tr>
<tr>
<td>NC</td>
<td>1.32</td>
<td>0.56</td>
<td>2.35</td>
<td>0.03*</td>
</tr>
<tr>
<td>Phw-spt</td>
<td>-2.71</td>
<td>0.59</td>
<td>-4.62</td>
<td>0.00*</td>
</tr>
<tr>
<td>Base AHI</td>
<td>0.38</td>
<td>0.12</td>
<td>3.15</td>
<td>0.01*</td>
</tr>
<tr>
<td>SN-Mp</td>
<td>-0.99</td>
<td>0.38</td>
<td>-2.60</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

*P<0.05

Age, BMI, baseline MinSaO₂, and all remaining cephalometric variables were tested and not found to be significant.
6. DISCUSSION

6.1 Introduction

The use of oral appliances in the treatment of snoring and OSA has been the subject of detailed review (Schmidt-Nowara et al., 1995). Mandibular advancement using an oral appliance was first considered as a treatment for upper airway obstruction and mandibular hypoplasia in infants, as early as 1902 (Robin, 1934). More recently, a variety of OAs have been proposed for the treatment of OSA (Lowe, 1994).

There is considerable controversy in the literature regarding the use of OAs in the treatment of snoring and OSA. During the past decade, there have been several OAs introduced into the market with claims of reducing snoring and OSA, but very few appliances have been tested for efficacy in a clinical trial. Many studies have been case series or individual case reports, raising questions about the validity of conclusions.

Therefore, one aim of the present study was to test the clinical efficacy of a MAS in the treatment of snoring and OSA using a prospective, randomised, placebo-controlled, cross-over study design. A further aim was to evaluate the treatment outcome both objectively and subjectively in order to highlight the importance of follow-up polysomnography in all patients treated with OAs. A unique MAS was used, with features that incorporated ideal design features suggested by Battagel (1996). To predict AHI using this MAS, a mathematical model using step-wise multiple regression analysis was derived.

6.2 Experimental Design

6.2.1 Patient Selection

The sample selected for the study may not be a true representation of the population of patients with sleep apnoea. Patients were selected from a particular clinic (Centre of Sleep Disorders and Respiratory Failure, St. George Hospital), which had an interest in dental therapies for OSA. This may have resulted in referral bias. In addition, patients chose to use the OA as a treatment option rather than the conventionally advocated CPAP leading to a further potential for sample bias. The
sample size was also small. Hence, the applicability of the results to the general OSA population must be reviewed with some caution.

Despite these sampling errors, the validity and significance of the results in this study, both statistically and clinically, are important because of the strength of the study design employed.

6.2.2 Study Design

The experimental design used in this study was a prospective, randomised, placebo-controlled, cross-over study with an extra-period (ABB-BAA).

Cross-over trials are widely used in clinical practice and medical research. In a cross-over trial each experimental subject receives two or more different treatments in an order that depends on the particular design for the trial. The main advantage is that the treatments are compared ‘within subjects’. That is, every subject provides a direct comparison of the treatments they have received.

This is to be contrasted with the ‘parallel group trial’. In this latter trial each subject receives only one of the possible treatments. The subjects are randomly divided into groups and each group is assigned one of the treatments being compared.

A cross-over design was selected for this study because it is superior to the parallel group design with the same numbers of subjects in terms of precision, power and costs (Chassan, 1970; Brown, 1980). In addition, from an ethical viewpoint, the cross-over design allows all patients to receive the ‘active’ treatment. In a parallel design, half the group would not receive the ‘active’ intervention.

The ABB/BAA is a higher order design because it includes more than two treatment periods, and is superior to the simplest cross-over design known as the 2x2 design (AB/BA) (Jones and Kenward, 1989). These authors have suggested avoiding the 2x2 design from a statistical viewpoint because it suffers from two disadvantages. Firstly, the test for carry-over or period effect lacks power in the AB/BA design, because it is based on between-subject comparisons. Secondly, assumptions need to be made to draw any conclusions about carry-over, period and sequence effects because these effects cannot be analysed separately.

The ABB/BAA design not only has a greater power than the 2x2 design to detect carry-over, period and sequence effects simultaneously but does so without the
necessity of having to make assumptions. In the present study a significant (p<0.05) carry-over effect was detected for “total time spent in hypopnoea in NREM sleep” and period effects were found for “proportion of total sleep time in NREM sleep and “total time spent in apnoea and hypopnoea in NREM sleep”. Despite the carry-over and period effects, the author was still able to estimate treatment effects, demonstrating the benefits of this design.

The ABB/BAA design has also proved to be an optimal design when compared to other 3 period dual sequences, such as ABA/BAB and AAB/BBA, because it provides minimum variances of the estimators, and these estimators are uncorrelated (Jones and Kenward, 1989).

For the reasons provided above, the 3 period cross-over design ABB/BAA was selected as the preferred study design model for this research and provided the power to enable statistical analysis of the results.

6.2.2.1 Placebo

In previous 2 period cross-over studies (Clark et al., 1996; Ferguson et al., 1996; Ferguson et al., 1997), treatment with OAs has been compared with CPAP as opposed to a placebo.

This is the first placebo-controlled cross-over trial using OAs to be reported in the literature. For the purposes of this study, it was felt necessary to show that what actually brings about an improvement in OSA using the MAS, is the antero-posterior advancement of the mandible. In order to demonstrate this, the lower appliance on its own acted as the placebo.

To avoid introducing any bias, patients were advised that the lower appliance may confer a benefit to their condition. However, results from the sleep studies, comparing the placebo to the MAS, have conclusively shown that the MAS is more efficacious in treating the OSA compared to the placebo. In addition, there was no significant difference between placebo and baseline AHI, indicating the placebo did not have a significant impact on the treatment outcome.
6.3 Characteristics Of The MAS

6.3.1 MAS Design

The MAS used in this study is of a unique design originating from one of the research advisers. It was modified by the author to include a screw for serial advancement. The important aspect of this appliance is the unique flange and slot design of the upper and lower appliances respectively. This important feature allows retention of the mandible in a forward position, so that the lower jaw is prevented from dropping back with the patient in the supine position, while keeping the vertical dimension of the appliance to a minimum.

Appliances such as the Esmarch Device (Mayer and Meier-Ewert, 1995), mandibular advancement splint (O'Sullivan et al., 1995) and Snore-Guard (Schmidt-Nowara et al., 1991; Ferguson et al., 1996) have an increased vertical dimension compared with the MAS used in the current study. For example, the vertical opening of the OA used by O'Sullivan and colleagues (1995) is 10 mm and that used by Ferguson and colleagues (1996) is 7 mm. The rationale for this aspect of the appliance design is not provided by these authors, but one possibility is that the resulting soft tissue stretch, obtained by opening the mandible beyond the free-way space, helps to prevent the mandible from dropping back from the advanced position.

It has been suggested that an appliance with an increased vertical dimension would tend to hinge the mandible down and back thereby reducing the overall effect of increasing the airway dimension in the antero-posterior plane from the mandibular advancement (Battagel, 1996). However to date, there is no research to show that an appliance with a reduced vertical opening is any more effective, with respect to obtaining an increased airway or giving improved patient comfort, than an appliance with an increased opening.

Another unique feature of the MAS design used in the present study is that it incorporated an advancement screw in the lower appliance. This allowed for incremental adjustment of the MAS at the chairside to reposition the mandible anteriorly.
6.3.2 Optimal Advancement With The MAS

An acclimatisation period with the MAS was important because it allowed patients to adjust to the initial advancement, so that on subsequent visits they were able to protrude their mandible further forward. The present study found considerable inter-individual variation in the advancement required for maximum subjective improvement in OSA symptoms. This study is therefore unable to conclude what the optimal acclimatisation period is and what the optimal advancement should be.

Some studies (Clark et al., 1993; O'Sullivan et al., 1995) have suggested 75% of maximum jaw protrusion as an optimum level of advancement, but there is no scientific basis for this.

A method of ascertaining the optimum advancement for each patient would have been to titrate the advancement of the appliance to an objective response such as AHI or arterial oxygen saturation during a single night of polysomnography. This is an area for further research.

6.3.2.1 Potential Limitations

The clinical measurements to assess actual advancement and maximum jaw protrusion were strictly speaking not measured along a standardised reference plane and they do not reflect the changes in the airway dimension. Therefore their validity as clinically useful measurements must be questioned.

In addition, firm conclusions cannot be drawn regarding the advancement feature of the MAS as being the only aspect that resulted in an improvement in OSA treatment outcome. There was a difference in the vertical dimension between the MAS (upper and lower appliances) and the placebo (lower appliance only), which may also have influenced the outcome.

6.4 Sample Characteristics

6.4.1 Anthropometric Data

The study sample anthropometric characteristics were representative of the general OSA population with respect to age, BMI, neck circumference and gender as reported in the literature.
The prevalence of OSA in the general population has been shown to be more common in males, aged greater than 40 years, who have a BMI greater than 25 kg/m² (Guilleminault and Dement, 1978). The age and BMI of patients in this study were equivalent to the OSA population as stated in the literature. The gender ratio of 4 males:1 female observed in this study is also in keeping with the results from previous studies (Guilleminault and Dement, 1978).

Neck circumference was measured because it reflects obesity in the region of the upper airway. The mean neck circumference of 40.4 cm ± 3.9 found in this study is similar to the neck circumference value of 42.7 cm ± 3.2 reported by Ferguson et al. (1995) in a group of 161 OSA patients.

6.4.2 Severity Of OSA

Patients in this study ranged in baseline AHI from 10.0/hr to 68.0/hr. Baseline AHI was used to classify patients into 3 groups of severity: Mild OSA (46% of patients in study), Moderate OSA (29%) and Severe OSA (25%). These three categories were based on supervisor selected AHI values (as detailed in Section 3.15.2) because no accepted international classification system for OSA severity exists. The use of AHI as an index of severity may be inappropriate, as it does not always correlate with the degree of daytime hypersomnolence (Guilleminault et al., 1991), but it is the most objective tool available at present. The distribution of patients into the OSA severity categories was undertaken to assess whether OSA severity had an effect on treatment outcome with the use of the MAS.

When evaluating for differences in baseline characteristics between the 3 severity categories, a significant difference was found in mean BMI. The mean BMI of the severe OSA group was significantly higher than the mean BMI of the mild OSA group.

Both BMI and neck circumference are measures of obesity and have been shown to correlate with apnoea severity (Davies et al., 1992). The present study, however, did not find a significant difference in the mean neck circumference between the severity groups. This finding was most likely the result of a small sample size.

Although obesity has been implicated as a major risk factor in the development of OSA (Battagel, 1996), some studies (Tsuchiya et al., 1992; Ferguson et al., 1995)
conclude there is a spectrum of upper airway soft-tissue and craniofacial abnormalities among OSA patients. These studies have identified that not all patients with OSA are obese and some of these non-obese patients have an abnormal craniofacial structure.

6.4.3 Cephalometric Abnormalities In OSA Patients

The following cephalometric variables of the OSA patients in this study were found to be significantly different from normative data: Length of the anterior cranial base, hyoid bone position and head posture, pharyngeal diameters (posterior airway space and width of pharynx at maximum soft palate width) and lower anterior face height. These findings are discussed below, followed by a critique in the use of cephalometric measurements in sleep apnoea research.

6.4.3.1 Length Of The Anterior Cranial Base (SN)

The length of the anterior cranial base was significantly increased in OSA patients compared to normative data. This finding was in contrast to other studies which have reported a reduction in anterior cranial base length (Bacon et al., 1990; Tangnugsum et al., 1995a; Battagel and L’Estrange, 1996). The significance of this finding is uncertain and may represent a spurious result.

6.4.3.2 Hyoid Bone Position (H-Mp) And Head Posture (C2C4-SN)

An increased hyoid bone to mandibular plane distance and an extended head position have been commonly reported in OSA patients.

Studies by Riley et al. (1983); Jamieson et al. (1986); Lowe et al. (1986) and Lyberg et al. (1989) have all reported a significant increase in the distance of the hyoid bone to the mandibular plane in OSA patients. The patients in the present study were found to have an increased mandibular plane to hyoid distance compared to the norm.

Patients were also found to have an increased craniocervical angulation (C2C4-SN), which has been reported previously (Solow and Tallgren, 1976; Solow et al., 1993, 1996; Petri et al., 1994).

Studies have been unable to identify an increased H-Mp distance and an increased C2C4-SN angulation as causative factors in the development of OSA. The
contemporary view regarding an inferiorly positioned hyoid bone and an extended head position is a smaller than optimal airway induces flexion or extension of the head for better airway patency, which in turn elicits an inferior-positioned hyoid bone (Winnberg et al., 1988; Pae, 1989). These physiological adaptations probably serve to lift away the base of the tongue and the soft palate from the posterior pharyngeal wall in order to alleviate the obstruction. These findings therefore support an increased H-Mp distance and an increased C2C4-SN angulation as effects, rather than as causative factors, of OSA.

The position of the hyoid bone relative to the mandible seems to have a direct effect on ventilation. In a study by Mayer and Meier-Ewert (1995), hyoid bone position was the only cephalometric parameter which had a correlation with minimal oxygen saturation and percentage change in apnoea index. The closer the mandible and hyoid bone were moved with the mandibular advancement device (Esmarch device), the more oxygen saturation and apnoea index improved.

6.4.3.3 Pharyngeal Diameters : Posterior Airway Space (PAS) And Width Of Pharynx At Maximum Soft Palate Width (Phw-Spt)

The PAS was first described by Riley et al. (1983). It is defined as the distance between the posterior pharyngeal wall and the dorsal surface of the base of the tongue, measured on the line that intersects point Go and B point. Most studies (Jamieson et al., 1986; Lyberg et al., 1989; Andersson and Brattsrom, 1991; Tangugssorn et al., 1995b) measuring airway diameters in OSA patients report a reduction in the measurement of this variable compared to the controls. This study also found a significantly reduced PAS.

However, other studies (Yildirim et al., 1991; Solow et al., 1996) found no significant difference in the PAS between the OSA patients and controls.

PAS is used in most studies of airway dimensions in OSA, but its validity must be questioned. This measurement is based on a reference line determined by facial skeletal morphology. From a physiological point of view it would seem more relevant to have this defined by the anatomy of the airway itself. Even though endoscopic (Borowiecki et al., 1978; Rojoweski et al., 1984) and computer tomography (Shepard, 1990a) studies have reported the narrowest segment to be
located most often in the retropalatal region, no studies have been carried out measuring the precise anatomical location of the narrowest sagittal pharyngeal airway diameter.

A recent study, by Solow et al., (1996) using lateral cephalometry also found the most narrow airway diameter to be behind the soft palate. The present study looked at the width of the airway behind the maximum soft palate thickness (Phw-spt), but the finding was not significant.

6.4.3.4 Lower Anterior Face Height (LAFH)

The increased LAFH in the female group was the only gender difference detected in the OSA sample. However, the sample size of five females is too small to draw any conclusions.

6.4.3.5 Limitations In The Use Of Cephalometry In Sleep Apnoea Research

Making interpretations of the airway from cephalometric measurements can be inaccurate. A cephalometric measurement is made from a two dimensional image of a complex three dimensional structure and this therefore creates limitations as no information is provided on the transverse dimension.

Some authors discuss the possibility that flexion or extension of the head could influence the dimensions of the oropharyngeal airway (Rubinstein et al., 1987; Davies and Stradling, 1990). To take this factor into account cephalometric radiographs of the subjects in this study were taken in the standing natural head position.

Also, it has been shown that subject posture may affect cephalometric measurements (Yildirim et al., 1991). Caution must therefore be exercised when relating results of upright cephalometry to events occurring during sleep in the supine position.

Changes in airway tone and compliance from wakefulness to sleep, as well as potential unreliability of interpretation based on isolated parameters of airway caliber tone, are other confounding factors in the use of standard cephalometry.

Assessment of dynamic structures of the airway, such as the tongue and soft palate present many difficulties, which influences the reliability of these measurements (Miles et al., 1995).
A major consideration in all cephalometric studies is the control population used for comparison. The normative data used in this study are from a recently published manual by Bhatia and Leighton (1993), and from other published papers (Solow and Tallgren, 1976; Guilleminault et al., 1984; Tangugsorn et al., 1995b; Solow et al., 1996).

Racial origin, age and gender are three important factors to consider when comparing cephalometric data. The patients comprising the normative data were of Caucasian origin. There was one patient of Asian origin in the current study (patient # 5), whose comparison with normative data may not have been accurate.

The means and standard deviations for the normal group, presented in Table 13, are those of 20 year old subjects. The mean age of the patients in this study was 48.0 yrs ± 9.2. There is minimal change in the dentofacial complex after 20 years of age and therefore it is reasonable to use this data for the adults in the present study.

Another consideration is relatively few females with OSA that have been evaluated. They are usually grouped with males, and hence any possible gender differences remain unclear.

Despite these drawbacks, the upright cephalogram remains the most popular clinical tool to assess upper airway size for preliminary diagnostic purposes because it is simple and cost effective to use.

6.4.4 Potential Limitations In The Statistical Analysis Of Sample Characteristics

In the statistical analysis for multiple comparisons, the Bonferroni Adjustment was used to identify significant differences between pairs of means. A recent paper (Perneger, 1998) has advocated against using the Bonferroni Adjustment because it can be misleading and often unnecessary with an increased likelihood of Type II errors. However, in the present thesis as there was no pre-established hypothesis for the situations in which the Bonferroni Adjustment was carried out, the author believes that use of this statistical analysis was valid.
6.5 Interactions Between Airway Obstruction And Facial Development

Abnormal growth of the dentofacial complex is thought to result from a combination of genetic and environmental factors. An important environmental factor appears to be airway obstruction resulting in oral breathing. One hypothesis is that oral breathing consequent to upper airway obstruction produces postural changes that may alter dentofacial growth (McNamara, 1973). It has been proposed that nasal obstruction leads to modification of head posture, which may influence facial development (Solow and Kreiborg, 1977). Of interest is the finding by Solow et al. (1991) that this postural sequel to airway obstruction is also present in patients with OSA.

There is evidence that upper airway obstruction from hypertrophied adenoids results in increased craniocervical angulation, decreased mandibular size, retrognathia and steep inclination of the mandibular plane (Linder-Aronson, 1970; Solow et al., 1984). These features, which were similar to those identified in adult OSA patients, led to the concept that OSA may have evolved during childhood before becoming clinically apparent in adult life. This theory is supported by Guilleminault and colleagues (1989). They demonstrated that cephalometric abnormalities were associated with persistent snoring and upper airway obstruction in adolescents, who had undergone tonsillectomy and adenoidectomy for upper airway obstruction before puberty.

However, the present study did not provide any direct evidence for the observed deviations in craniofacial variables when compared to the norm.

Animal studies support the link between airway obstruction and craniofacial development. Pilot studies involving the suturing of a plastic block in the posterior palate of the rhesus monkey that obstructed the oral airway, resulted in a forward posturing of the tongue and the development of an anterior open bite (Harvold, 1968). A subsequent study, with matched controls, revealed that suturing an acrylic block into the palatal vault of the monkeys led to an increase in facial height, decreased maxillary arch length, decreased maxillary and mandibular intercanine distance, and alteration of tongue and mandibular morphology (Harvold et al., 1973).
In addition to the observed skeletal changes in these rhesus monkeys, it was demonstrated that neuromuscular activity in numerous facial muscles was altered, with consequent effects on facial development (Miller et al., 1984; Harvold et al., 1981). When the obstruction was removed at a sufficiently early age, there was a partial regression of the anatomical changes, but the altered neuromuscular activity persisted (Vargervick et al., 1984; Miller et al., 1984).

Whilst it would appear reasonable to speculate that OSA in adults results from genetic and developmental factors that determine craniofacial growth, differences between man and animals exist. There is a difference between the anatomy of the airway, temporomandibular joints and location of jaw muscles between humans and monkeys. Therefore, postural responses and muscle recruitment are not the same between the two species. Also, in contrast to the rhesus monkey, man is not an obligate nose breather. Although, most individuals who snore, and patients with OSA, are mouth breathers during sleep (Sher, 1990), oral breathing can usually occur without major changes in oral posture in man (Warren et al., 1984). This raises an interesting question “At what percentage does oral breathing become clinically significant in causing craniofacial changes”? The current literature has been unable to resolve this airway controversy.

6.6 Efficacy Of The MAS

Efficacy, as defined by the Oxford Dictionary, is the power to produce the result intended or desired.

The ASDA report (1995) on OSA suggested treatment objectives for patients with primary snoring without features of OSA or upper-airway resistance is to reduce the snoring to a subjectively acceptable level. For patients with OSA, the desired outcome of treatment includes the resolution of symptoms and clinical signs of OSA and the normalisation of the AHI and oxyhaemoglobin saturation. The problem with this report is that the conclusions are based on studies (Clark et al., 1993; Eveloff et al., 1994) whose strength of evidence must be questioned because of poor study designs. In addition, the ASDA report fails to define the normalised levels of AHI and oxyhaemoglobin saturation.
The present study has confirmed the efficacy of the newly designed MAS in treating OSA and snoring evidenced by objective and subjective criteria. The study demonstrated a significant objective improvement in AHI, arterial oxygen saturation, sleep architecture, snoring frequency and intensity. The subjective improvement was supported by a symptomatic improvement in snoring from partner reports together with improved social situation.

6.6.1 Efficacy Of MAS In Snoring

6.6.1.1 Objective Evaluation

O'Sullivan and colleagues (1995) were the first to quantify snoring in the laboratory. They found an 18% reduction in snoring frequency and a 15.8% reduction in snoring intensity in the proportion of snores ≥50dB. However, their study utilised a case series design, which did not take into account any carry-over effect of the appliance. Each patient in the study had only one sleep study where they slept half the night with the MAS and the other half without the appliance.

In the present study snoring was quantified in 22 of the 24 patients who completed the full protocol. Two patients could not be objectively evaluated because equipment was unavailable. The snoring data of 3 patients within this subgroup of 22 had to be excluded from the analysis because of technical problems. Therefore, the final analysis on the laboratory snoring data were based on 19 patients.

Both snoring frequency and intensity reduced significantly in the present study. The 47% reduction in mean snoring frequency (from 421.9/hr ± 27.0 to 223.0/hr ± 25.6) is substantially improved when compared with results from O'Sullivan’s study (1995) in which there was an 18% reduction (from 660.0/hr to 540.0/hr) with the use of the MAS.

The 3.3dB reduction in mean sound level of snoring in the current study was considerable because in dB terms it represents over a two fold reduction in sound intensity\(^1\). O'Sullivan and colleagues (1995) based their evaluation on the proportion of snores ≥ 50dB and found that the mean percentage of snores ≥ 50dB decreased from 42.0% to 26.2% with the use of the MAS.

6.6.1.2 Subjective Evaluation

Analysing questionnaires 1 and 2 in the present study, 23 of the 24 subjects found an improvement in their snoring. This finding is consistent with studies (Table 3 in Section 1.5.3.3) which also evaluated snoring from patient reports. The improvement in snoring using the MAS resulted in a positive outcome for four couples. These patients and their bed partners previously slept separately because of the snoring and were able to resume sleeping in the same room as a result of the MAS.

Three of the patients in the present study also reported their snoring was "cured" and this was supported by their partners.

Comparing subjective to objective outcomes, it was found the MAS did not cure snoring. The snoring intensity was not reduced to the minimum level at which snoring was set for this study (5dB greater than background noise of 32-37dB).

6.6.2 Efficacy Of MAS In OSA

6.6.2.1 Objective Evaluation

1. Effect On AHI

This study found a significant reduction in mean AHI of 51.8%, for patients using the MAS. This result is similar to that reported by Schmidt-Nowara et al. (1991) (AHI reduced by >50%); Clark et al. (1993, 1996) (AHI reduced by 75% and 39% respectively); Eveloff et al. (1994) (AHI reduced by 63%); O'Sullivan et al. (1995) (AHI reduced by 46%); and Ferguson et al. (1996, 1997) (AHI reduced by 51% and 44% respectively).

By evaluating the association between sleep stage and total time spent in apnoea and hypopnoea, a reduction in the duration spent in apnoea in NREM sleep was found to be the main reason for the reduction in the overall apnoea-hypopnoea index. To our knowledge this finding has not been previously reported in the literature.
2. **Effect On Arterial Blood Oxygenation**

A significant improvement in arterial blood oxygenation was found assessed by minimum arterial blood oxygen saturation, when the MAS was used. This supports the results from Schmidt-Nowara *et al.* (1991); Clark *et al.* (1993, 1996); and O’Sullivan *et al.* (1995). However, other studies (Eveloff *et al.*, 1994; Ferguson *et al.*, 1996, 1997) have not shown a significant change in this variable.

Although MinSaO$_2$ values may only represent a single worst-case obstructive event, what they do indicate is that the airway becomes less obstructed with the MAS compared to the placebo.

3. **Effect On Sleep And Sleepiness**

Polysomnographic assessments of sleep with the MAS and placebo in this study demonstrated a significant reduction in NREM sleep, a significant increase in REM sleep and a significant reduction in the arousal index when the MAS was used. This is indicative of a return to normal sleep physiology.

The case review studies (Table 4 in Section 1.5.3.3), which used other mandibular repositioning appliances, also found similar changes in these variables. A randomised prospective cross-over study by Ferguson *et al.*, (1996) using the Snore-Guard appliance and, a prospective cross-over study by the same group (Ferguson *et al.*, 1997) where the AMP was used, found no significant change in sleep architecture variables with these appliances.

6.6.2.2 **Subjective Evaluation**

In the present study, the significant improvement in sleep variables in patients using the MAS, was reflected in the majority of patients by a reduction in daytime sleepiness, level of tiredness and improved sleep quality, assessed using a validated questionnaire.

According to Johns (1991), the mean Epworth Sleepiness Score (ESS) for subjects with a history of normal sleep habits without apnoea is 6. In this study, the mean score for the whole group following treatment with the MAS improved. Individually, 20 patients (83%) had a post treatment score ≤ 6.
An additional finding was two patients who achieved Treatment Success (measured by AHI<5/hr) still reported "moderately unrefreshing" sleep (patient # 23) and "moderate tiredness" on waking (patients # 20 and # 23) with the MAS. This finding is consistent with Hoffstein et al. (1988) who has suggested that snoring associated increases in upper airway resistance, while not sufficient to cause a significant decrease in airflow (ie an apnoea or hypopnoea), could cause an arousal thereby diminishing sleep quality. Prior to treatment with the MAS, these patients had reported "very unrefreshed sleep" (patient # 23) and complained of feeling "very tired" in their responses on waking (patients # 20 and # 23). Hence, the MAS resulted in some subjective improvement in sleep quality in these patients.

However, strong conclusions cannot be drawn on the clinical efficacy of the MAS on sleep quality by relying on subjective data alone. A more appropriate method to assess the level of tiredness and daytime sleepiness would be to use an objective test such as the Multiple Sleep Latency Test (Carskadon and Dement, 1982; Carskadon et al., 1986).

6.6.3 Treatment Success

6.6.3.1 Definition Of Treatment Success

A major controversy in OSA treatment relates to what constitutes treatment success. One definition is that successful treatment should eliminate or prevent all apnoeas and hypopnoeas from occurring as does tracheostomy and nasal CPAP. An alternate definition is that the AHI should return to normal or below a predetermined level at which the study defined OSA. Treatment Success for this study was defined as: “a resolution of symptoms and a reduction in AHI to < 5/hr”. This is the most stringent treatment success criterion using OAs in the literature. Other MAS studies have used the following criteria to define treatment success:

- Post treatment AHI < 10/hr (Eveloff et al., 1994; Ferguson et al., 1996; Ferguson et al., 1997).
- Post treatment AHI < 15/hr (Clark et al., 1993). Another study by Clark et al. (1996), failed to define what treatment success was, even though success was claimed with the AMP.
- Post treatment AHI < 20/hr (O'Sullivan et al., 1995).
• Reduction in pretreatment AHI by 50% plus a reduction in post treatment AHI < 10/hr (Bonham et al., 1988).

6.6.3.2 Comparison Of Treatment Success With Other Studies

Objective Evaluation

Based on the objective criteria set for this study, the treatment success rate of 37.5% is lower than rates reported by Eveloff et al., 1994 (53%); Ferguson et al., 1996 (48%) and 1997 (55%) and O'Sullivan et al., 1995 (54%). This could be explained by the strict criteria used in the current study to measure clinical success. Also, the high success rate (55%) reported by Ferguson et al. (1997) was due to 11 patients being classified as treatment successes (AHI <10/hr), but 4 of these patients already had a baseline AHI <10/hr prior to treatment with the AMP. The author believes these patients should have been excluded when measuring the success rates.

Subjective Evaluation

In the current study, 12 subjects (50%) were “very satisfied” and another 11 subjects (46%) were “satisfied” with the MAS. The same 23 subjects (96%) stated they wanted to continue to use the MAS because they perceived a conferred health benefit. This signifies a high success rate based on a subjective evaluation.

6.6.3.3 Comparison Of Objective And Subjective Evaluation

The importance of using objective methods to assess outcome is clearly borne out by these results, which contrast to the subjective results of treatment outcome. This is critical because, even though most of the patients felt subjectively better, there were 15 patients (62.5%) who had an AHI value greater than 5/hr with use of the MAS. Six of these 15 patients were Partial Success and nine were Treatment Failures. This indicates OSA was not totally controlled with the appliance. It is postulated that in these patients, MAS treatment, although abolishing some apnoeas, shifts OSA towards an upper airway resistance syndrome.

Of the nine Treatment Failures, all but one (patient # 14) reported subjective improvements.
These findings have implications in treatment as described below.

1. **Objective Polysomnographic Monitoring**

   Post appliance testing to insure adequate control of apnoeic activity is critical to the safe use of these devices. Currently, the only way to accurately assess treatment efficacy is by overnight sleep monitoring.

2. **Treatment Failures or Technical Failures**

   Those patients who are not clinical successes require follow-up and a change in treatment strategy to control the OSA. If appropriate treatment is not instituted there is a potential risk of medical complications, especially related to cardiovascular morbidity.

   Some patients may have been technical failures and therefore require further advancement or modification of the MAS to achieve clinical success. In the present study this could have been true for the patients in the Partial Success and Treatment Failure group who should be re-assessed to ensure that their outcome was not influenced by technical problems with the MAS.

   Assessment for technical failure is currently being carried out at the Centre of Sleep Disorders and Respiratory Failure, St. George Hospital. The MAS is modified or adjusted to further advance the mandible and patients re-evaluated in the sleep laboratory. In this way, failures resulting from technical problems with the MAS should be overcome.

   Other patients may require CPAP therapy. Where conservative, medical or dental measures have failed then surgery, either alone or in combination with the above treatment modalities could be offered as a final option.

3. **Predicting Treatment Response**

   A reduction in AHI does not constitute adequate treatment for all patients with OSA. A clinical tool to predict treatment response with the OA therapy would identify which patients are most likely to benefit.
6.6.4 Potential Limitations

A limitation in the current study was that it relied on a patient's stated compliance with the oral appliance. Covert monitoring, although technically difficult, could allow objective measurement of compliance. A microchip that senses body heat has been developed for the OA (Fleetham et al., 1996).

There may have been an element of responding to the questionnaire in a socially desirable way (social desirability response bias). The patients were aware that the study was investigating the effectiveness of the oral appliance. Therefore, this may have affected their answers. The discrepancy between subjective and objective measures supports this.

Sleep quality and daytime sleepiness could have been measured objectively using a vigilance test such as the Multiple Sleep Latency Test (Carskadon and Dement, 1982). However, this test is labour intensive and not as easy to administer compared to the validated questionnaire using the Epworth Sleepiness scale.

There are limitations to the use of polysomnography. Firstly, the measurements are carried out in a sleep laboratory, which is a very different environment to the patient's home. Portable monitoring devices are available but these systems have not been fully validated (Flemons, 1996). Secondly there is night-to-night variability in the apnoea index. However, studies have demonstrated that one polysomnograph is sufficient to identify OSA in 94% of the subjects (Mendelson, 1994). Further, the effect of placebo and MAS were assessed in the same environment in this study.

6.7 Mechanism Of Action Of The MAS Appliance

This study does not provide direct evidence of how the MAS brought about an improvement in AHI, blood arterial oxygenation, snoring frequency and intensity.

The proposed mechanism of action of the MAS in the treatment of OSA is that it increases upper airway size and influences tongue muscle activity (Ahlgren, 1979; Lowe, 1990) thereby improving airflow to the lungs. Whether this is achieved by increasing the vertical dimension or via antero-posterior changes in the mandibular posture or a combination of both, remains to be confirmed. Our study design (with placebo) would suggest that advancement is critical to success.
To bring about an improvement in snoring, the MAS has to reduce the vibration of the soft tissues. Possible mechanisms that have been suggested (Lugaresi et al., 1984) include:

- an increase in oropharyngeal and hypopharyngeal dimensions with an associated reduction in turbulent airflow in the region and/or
- an increase in passive tension within the pharyngeal wall

More information about the mechanism of action of mandibular advancement could be obtained by computerised tomography and magnetic resonance imaging. These newer technologies may provide further insights into how OAs affect airway dimensions.

An important finding in this study was that one subject (patient # 9) developed more severe OSA with MAS treatment than placebo. It is speculated that the MAS increased the vertical space between the upper and lower incisors causing a downward rotation of the mandible and a decrease in upper airway size. This may explain why the severity of OSA increased with the appliance compared to the placebo.

6.8 Compliance With The MAS

The compliance rate with the MAS was 87.5%. This compares favourably with the rates reported by other studies using mandibular repositioning devices.

The data on long-term compliance of OAs are limited and are all based on patient reports. Compliance rates vary in different studies and may be related to the length of follow up. Compliance with OA use ranged from 100% in 14 patients followed for 3 to 21 months (Ichioka et al., 1991), to 75% in 68 patients questioned after 7 months (Schmidt-Nowara et al., 1991), to 52% in 24 patients queried after 3 years (Clark et al., 1993).

Although nasal CPAP is considered to be the gold standard treatment for OSA, with respect to its efficacy, long-term compliance rate ranges from 50%-80%, with less symptomatic patients more likely to discontinue treatment (Ferguson, 1996). An alternative mode of OSA treatment which is not only efficacious but also well accepted and tolerated by the patients is required for long-term management of OSA patients.
Since the MAS is well accepted by most patients and is clinically successful in a group of OSA patients, it could provide a viable alternative to CPAP, for some patients.

6.9 Side Effects With The MAS

The MAS was well tolerated by 21 patients (87.5%). The side effects that were reported by these patients were of mild to moderate intensity and most symptoms resolved within three weeks. Jaw discomfort (in 2 patients), salivation (in 6 patients), dryness of the mouth (in 10 patients) and grinding of the teeth (in 2 patients) were the side effects that persisted for more than three weeks.

Jaw discomfort, reported as persistent by two patients, was a muscular tenderness on waking. This was most likely to be muscle fatigue resulting from the forward position of the jaw. The jaw discomfort lasted for about half an hour after removing the MAS and neither of these patients reported any further discomfort during the remainder of the day.

Dryness of mouth was the most common side effect, persisting for more than three weeks, suggesting that an oral mode of respiration may have been used by those patients.

Patients who reported grinding with the MAS had a previous history of bruxism. Since disarticulating the teeth did not resolve this parafunctional habit, factors other than occlusion must be responsible for this side-effect. The contemporary view regarding the aetiology of bruxism supports this view as stress has been implicated as a cause for this condition.

The long-term side effects of the MAS need further evaluation. Because of time constraints, this study could not research any long-term effects and therefore could not provide any insight into whether the MAS has any permanent and significant long-term effects on the dentition, the facial skeleton or the temporomandibular joint. To date these important questions remain unanswered in the literature.

6.10 Predictors Of Treatment Response For The Current Study

It is clinically important to be able to identify which OSA patients would benefit from mandibular advancement splint therapy. Alternative treatment modalities could
then be offered to patients unlikely to benefit from this form of treatment. The
manufacture and fitting of a MAS followed by polysomnographic sleep study
requires considerable time and financial commitment. Wastage of resources would
be prevented if treatment outcome could be predicted.

Stepwise multiple regression analysis using the study baseline anthropometric,
cephalometric and polysomnographic data, on the 24 subjects, allowed formulation
of a mathematical relationship to predict post treatment AHI with a mandibular
advancement splint.

This model indicates that AHI with the MAS is positively correlated with neck
circumference and baseline AHI and, negatively correlated with the width of the
pharynx (Phw-spt) and angulation of the mandibular plane to the anterior cranial base
(SN-Mp). These variables in combination, not individually, best predict the AHI with
the MAS.

Prospective evaluation of a randomised population of patients with OSA would be
required to validate this model.

Although this model for predictors of treatment response is based on the combination
of the 4 variables acting simultaneously, it is important to understand what each of
the variables signifies:

**Neck circumference** reflects obesity in the region of the upper airway and suggests
that obesity mediates its effects in OSA through fat deposition in the neck. It has
been shown that NC correlates with several soft-tissue variables measured from
lateral cephalometry (Davies and Stradling, 1990) and correlates better than BMI
with apnoea severity (Davies et al., 1992). Therefore, it is suggested that this
measurement is routinely carried out for OSA patients.

**Baseline AHI** has previously been shown to predict success with OA. In three
studies (Schmidt-Nowara et al., 1991; Eveloff et al., 1994; O'Sullivan et al., 1995)
success was related to the initial AHI. In the latter study where untreated AHI was
between 20 and 60 (n=17), 12 subjects (70%) had a reduction in AHI to below 20
with the MAS. Where untreated AHI exceeded 60 (n=9) two subjects (22%) had an
AHI below 20 with the MAS. However, other studies (George, 1987; Lowe et al.,
1990; Clark et al., 1993; Eveloff et al., 1994) have reported a substantial
improvement in patients with an AHI > 60, but these were case reports with small sample size.

This present study found four Treatment Successes in the mild OSA group (36%), three in the moderate OSA group (43%) and two in the severe OSA group (33%). These findings differ from those of O'Sullivan et al. (1995), which suggest patients with milder OSA are more likely to benefit from mandibular repositioning appliances. However, firm conclusions cannot be drawn in the current study as the patient numbers within the three OSA severity classes were small.

The cephalometric predictor, **Phw-spt**, indicates that by increasing the width of the pharyngeal airspace at the level of the maximum soft palate thickness, the MAS brings about an increased airflow. This in turn will reduce the apnoeas and hypopnoeas and thereby lower the AHI. In fact, one mechanism of action proposed for the MAS, is that it advances the soft palate (Bonham et al. 1988; Lowe, 1994) thereby increasing the pharyngeal airspace. Whether this actually happens at the level of Phw-spt is uncertain.

The relationship of **SN-Mp** to post treatment AHI suggests that patients with a higher SN-Mp angle are likely to have an improved AHI with MAS compared to those with a lower SN-Mp angle. In the present study, there was a significant difference in mean SN-Mp angle between the three treatment outcome groups. However, statistical tests for multiple comparisons did not reveal a significant difference in the mean SN-Mp between any two specific outcome groups.

### 6.11 Evaluation Of Other Predictors Of Treatment Response Models From The Literature

Eveloff and colleagues (1994) performed lateral cephalometry in 19 OSA patients with and without a mandibular repositioning appliance, and compared the responders with non-responders. They found that a shorter soft palate and a decreased distance between the hyoid bone and the mandibular plane were associated with a successful treatment outcome. Subjecting cephalometric and polysomnographic data to stepwise regression analysis, they derived the following model with five independent variables to predict post treatment AHI:

\[
\text{AHI with MAS} = 8.957 + 0.228(\text{baseline AHI}) - 1.162(\text{SNA}) + 1.015(\text{PAS}) + 0.851(\text{MP-H}) + 0.607(\text{PFH}) \quad [r^2 = 0.74]
\]
Another study (Mayer and Meier-Ewert, 1995), only investigated cephalometric predictors for mandibular advancement in OSA. They submitted the cephalometric and treatment efficacy data of 44 patients (measured as Apnoea Index) with and without the Esmarch device to a regression analysis, and concluded that a combination of a narrower SNB angle, wider SNA angle, shorter soft palate and narrow oropharynx (PAS) gave the maximal efficacy with the Esmarch device.

To date, none of these models have been validated using a prospective study.

6.12 Recommendations For Future Research

Future research recommendations are as follows:

1. The mathematical model derived to predict treatment response should be clinically validated with a larger sample size using a prospective study design, before firm conclusions can be drawn regarding predictors of response.

2. Patients need to be followed up long term to:
   - Confirm improvement in health outcomes are maintained
   - Investigate the changes to the dentition, skeleton and temporomandibular joint

3. There are currently at least twenty-five different OAs in the market. Prospective, randomised controlled trials with a larger sample size, should be undertaken to compare specific appliances to each other and to evaluate effectiveness in patients with varying degrees of OSA severity.
   These trials should include:
   - An objective assessment of daytime sleepiness and performance
   - Covert compliance monitoring

4. The exact mechanism of action of MAS in snoring and OSA during sleep is unknown. Computerised tomography and magnetic resonance imaging, although expensive techniques, could be used to elucidate this unresolved question.

5. Further research needs to be conducted into a combined treatment with the surgical procedure, UPPP and OAs, in patients where UPPP does not completely relieve OSA.
6. The aetiology and management of OSA in children has not been fully investigated and requires further research. This may indicate a role for orthodontists in the diagnosis and management of snoring and OSA where it is possible that the identification and treatment of children at “high risk” for developing OSA may prevent the disorder.
7. CONCLUSIONS

The conclusions that can be drawn from this study are as follows:

1. The MAS is well tolerated and accepted by a majority of the OSA patients.

2. Results indicate that there is an objective (sleep study analysis) and subjective (questionnaire analysis) improvement in OSA using the MAS.

3. From the group of subjects who had a subjective improvement in OSA, not all were Treatment Successes. This highlights the importance of a post-treatment follow-up sleep study to assess treatment outcome. OSA has long-term medical consequences if untreated and therefore subjects with uncontrolled OSA should be provided with alternative modes of therapy.

4. An objective means of predicting treatment response to mandibular advancement was formulated using the following baseline variables:
   - **Baseline AHI** available from the initial diagnostic polysomnogram
   - **Neck circumference** available from anthropometric measurements
   - **Phw-spt and SN-Mp**, both available from lateral cephalometric analysis

   The following model to predict post treatment AHI was derived using the above independent variables

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

   \[
   r^2 = 82\% \quad s = 8.06
   \]

5. Orthodontists can play an important role in the multidisciplinary management of OSA patients through the use of:
   - cephalometric analysis to aid in the diagnosis and treatment planning
   - OA therapy
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APPENDICES

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APPENDIX 1. DEFINITION OF SLEEP STAGES

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

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

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

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

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APPENDIX 2. CONSENT FORM

ST GEORGE HOSPITAL AND UNITED DENTAL HOSPITAL

RESEARCH STUDY INTO “TREATMENT OF SNORING AND OBSTRUCTIVE SLEEP APNOEA WITH A MANDIBULAR ADVANCEMENT SPLINT”

PARTICIPANT CONSENT FORM

I, ...........................................................................................................(name) of
...........................................................................................................(address)

have read this consent form, and have discussed the study with Dr Peter Cistulli and understand the purpose of this study. I am aware of the procedures involved in the study, including any inconvenience, discomfort or side effects, and of their implications.

I freely choose to participate in this study and understand that I can withdraw at any time.

I also understand that the research study is strictly confidential.

I hereby agree to participate in this study.

Name of Participant: ................................................................. Name of Investigator: .................................................................

........................................................................................................

Signature of Participant: ................................................................. Signature of Investigator: .................................................................

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Date: ................. Date: .................
APPENDIX 3. PATIENT INFORMATION SHEET

ST GEORGE HOSPITAL AND UNITED DENTAL HOSPITAL

RESEARCH STUDY INTO

“TREATMENT OF SNORING AND OBSTRUCTIVE SLEEP APNOEA WITH A MANDIBULAR ADVANCEMENT SPLINT”

SUBJECT INFORMATION STATEMENT

You are invited to take part in a research study titled the “Treatment of Snoring and Obstructive Sleep Apnoea with a Mandibular Advancement Splint”.

The objective of this study is to find out how effective the use of a mandibular advancement splint (MAS) is in the treatment of snoring and/or sleep apnoea. A mandibular advancement splint is a dental appliance that holds the lower jaw forward during sleep.

You have been selected as a participant because you are a snorer and/or have sleep apnoea.

The study is being conducted by:

- Dr Peter Cistulli, Specialist Physician & Director at the Centre for Sleep Disorders & Respiratory Failure, St. George Hospital
- A/Professor M. Ali Darendeliler, Head- Discipline of Orthodontics, United Dental Hospital
- Dr Atul Mehta, Orthodontic Registrar and MDSc student, United Dental Hospital
- Dr Richard Palmisano, Honorary Orthodontic Consultant, St George Hospital

In order to participate in this study, the following time commitment is required by you. All appointments will be conducted at St George Hospital, 36 Belgrave St, Kogarah 2217.

Baseline investigations

*The first appointment is to be attended by you and your partner. Approximately 2-3 appointments will be required to complete baseline investigations.*

Baseline investigations will include the following:

- Dental examination - this consists of a routine dental checkup to ascertain the health of your teeth and gums.
- Routine dental X rays - the x-rays are part of the routine clinical assessment of patients who snore and have sleep apnoea.
APPENDIX 3 (CONT’D)

- Impressions - upper and lower impressions of your teeth will be taken for construction of the dental appliance. You will then be given a follow-up appointment approximately two weeks after the impression is taken to issue you with your custom made appliance. The appliance consists of a plastic plate which fits over the upper and lower teeth with grooves in the plates to hold the lower jaw forward. They are similar to small upper and lower mouth guards. The appliance is worn only during sleep.

- Initial sleep questionnaire - to be completed by you and your partner during the first appointment.

Sleep Studies

Three sleep studies will be performed, each approximately one week apart following completion of the baseline investigations. The sleep studies will be conducted overnight at the Sleep Laboratory at St George Hospital (address as above). Patients will be required to spend the night at the Sleep Laboratory during each of the three sleep studies.

Due to the nature of the study design, you must understand that the Mandibular Advancement Splint will only be given to you at specific times during the study. This is an important aspect of the study and requires your full co-operation.

Follow-up Questionnaire

A follow-up questionnaire will need to be completed by you and your partner to understand in more detail the effects of the Mandibular Advancement Splint on your snoring and/or sleep apnoea.

Side-effects of Treatment

The dental appliance may cause minor discomfort when first fitted but this can be easily alleviated by adjusting the appliance.

Dental Appliance

The dental appliance remains the property of the Sleep Disorders Centre, at St. George Hospital.

Confidentiality

All aspects of the study, including results, will be strictly confidential and only the investigators named above will have access to information on participants. A report of the study may be submitted for publication, but individual participants will not be identifiable in such a report.

Voluntary Participation

Participation in this study is entirely voluntary; you are in no way obliged to participate. Whatever your decision, please be assured that it will not affect your medical treatment or relationship with medical staff.
APPENDIX 3 (CONT’D)

Contact Details

When you have read this information, Dr Peter Cistulli / Dr Atul Mehta will discuss it with you further and answer any questions you may have. If you have any questions at any stage of the study, please feel free to contact Dr Atul Mehta at the United Dental Hospital (PH: 9282-0388) or Dr Peter Cistulli at the Sleep Disorders Centre, St. George Hospital (PH: 3502696).

Ethics Approval

This study has been approved by the United Dental Hospital Ethics Committee. Any person with concerns or complaints about the conduct of this research study can contact the Chairman of the Ethics Review Committee on 02 9282 0240.

This information sheet is for you to keep.
APPENDIX 4. ORTHODONTIC HISTORY AND EXAMINATION

**General**

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**Dental History**

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**Extra-Oral Examination**

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APPENDIX 4 (CONT’D)

Intra-Oral Examination

Oral Hygiene : Teeth present : 87654321 / 12345678
               :                    87654321 / 12345678
CPITTN : Caries : 87654321 / 12345678
          :                     87654321 / 12345678

Intra-Oral Examination (cont’d)

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

Functional Evaluation

Jaw function/TMJ complaint now : No □ Yes □
If yes, specify :

History of pain : No □ Yes □
If yes, duration :

History of joint sounds : No □ Yes □
TM Joint tenderness to palpation : No □ Yes □
If yes, which joint : Right □ Left □
Muscle tenderness to palpation : No □ Yes □
If yes, where :
APPENDIX 4 (CONT’D)

Range of motion: Maximum opening : __________ mm
          Right excursion       : __________ mm
          Left excursion        : __________ mm
          Protrusion            : __________ mm

CR/CO discrepancy : __________ mm

Exaggerated GAG reflex : No □ Yes □

Initial Advancement : __________ mm

Subsequent Advancement : __________ mm

Final Advancement     : __________ mm
APPENDIX 5. SLEEP QUESTIONNAIRE - 1

NAME : ___________________________ DATE: __________________

PATIENT NUMBER : ___________________________

Please consult with your spouse/sleeping partner when answering these questions.

1. Do you snore
   Yes□ No□
   If you answered No then proceed to Question 4

2. Snoring Frequency:
   On average, how many days/night during the last month have you snored or been told that you snore? Tick one of the following:
   □ Rarely: once/week
   □ Sometimes: 1-2/week
   □ Frequently: 3-4/week
   □ Almost always: 5-7/week
   □ Do not know

3. Snoring Intensity:
   During the past month has your snoring been:
   Tick one of the following:
   □ Only slightly louder than heavy breathing
   □ About as loud as mumbling or talking
   □ Louder than talking
   □ So loud that it can be heard through a closed door
   □ Do not know

Information for the questions 1; 2 & 3 above provided by: (a) You □ (b) Your Partner □ or (c) Both □

4. How would you grade your daytime sleepiness / fatigue in the last month for the following situations: Use the following scale to choose the most appropriate number for each situation:

   (0) Never doze
   (1) Slight chance of dozing
   (2) Moderate chance of dozing
   (3) High chance of dozing
( ) Sitting and reading
( ) Watching TV
( ) Sitting, inactive in a public place (e.g., a theatre, meeting)
( ) As a passenger in a car for an hour without a break
( ) Lying down to rest in the afternoon when circumstances permit
( ) Sitting and talking to someone
( ) Sitting quietly after a lunch without alcohol
( ) In a car, while stopped for a few minutes in the traffic

5. How would you rate the quality of your sleep?

Tick one of the following:

☐ Refreshing
☐ Slightly unrefreshing
☐ Moderately unrefreshing
☐ Very unrefreshing

6. How would you grade your level of tiredness on waking?

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

7. Do you live with a partner ☐ or as a Single person ☐

8. If you live with a partner do you:

☐ share the same bedroom
☐ sleep in different rooms because of the snoring
☐ sleep in different rooms for a reason other than snoring

9. Age:....... yrs....... months

Any comments:

____________________________________________________________________________

____________________________________________________________________________

Thank you for your cooperation
APPENDIX 6. SLEEP QUESTIONNAIRE - 2

This questionnaire pertains to the period of Appliance use

NAME: ________________________  DATE: ________________

PATIENT NUMBER: ________________________

Please consult with your spouse/sleeping partner when answering these questions.

1. In the last month, did you use the Oral Appliance - Tick one of the following:
   - [ ] Regularly: Everyday of the week
   - [ ] Occasionally: 3-4/week
   - [ ] Rarely: 1-2/week
   - [ ] Not at all

2. Do you snore while using the appliance
   - [ ] Yes
   - [ ] No

   If you answered No then proceed to Question 3

3. Snoring Frequency: On average, how many days/ nights during the last month have you snored or been told that you snore? Tick one of the following:
   - [ ] Never
   - [ ] Rarely: once/week
   - [ ] Sometimes: 1-2/week
   - [ ] Frequently: 3-4/week
   - [ ] Almost always: 5-7/week
   - [ ] Do not know

4. Snoring Intensity: During the past month has your snoring been:
   - [ ] Only slightly louder than heavy breathing
   - [ ] About as loud as mumbling or talking
   - [ ] Louder than talking
   - [ ] So loud that it can be heard through a closed door
   - [ ] Do not know
5. How would you rate the effect of the Oral Appliance on your snoring:

Tick one of the following:

☐ Snoring cured
☐ Snoring much improved
☐ Snoring improved
☐ Snoring slightly improved
☐ No improvement

6. Did you involuntarily remove the Oral Appliance on any night? ☐ Yes  ☐ No

If yes, why? ...........................................................................................................

7. Did the Oral Appliance loosen with time? ☐ Yes  ☐ No

8. If you stopped using the Oral Appliance:

Why did you stop? ...................................................................................................

9. When did you stop? ☐ less than a week after obtaining the appliance

☐ After 1 week
☐ After 2 weeks
☐ After 3 weeks

10. How would you grade your daytime sleepiness / fatigue in the last month (whilst using the Oral Appliance at night) for the following situations: Use the following scale to choose the most appropriate number for each situation:

(0) Never doze

(1) Slight chance of dozing

(2) Moderate chance of dozing

(3) High chance of dozing

☐ Sitting and reading
☐ Watching TV
☐ Sitting, inactive in a public place (eg a theatre, meeting)
☐ As a passenger in a car for an hour without a break
☐ Lying down to rest in the afternoon when circumstances permit
☐ Sitting and talking to someone
☐ Sitting quietly after a lunch without alcohol
☐ In a car, while stopped for a few minutes in the traffic
11. How would you rate the effect of the Oral Appliance on your degree of daytime sleepiness/fatigue:
   - Cured
   - Improvement
   - Same
   - Unsure

12. How would you rate the quality of your sleep with the appliance?
   Tick one of the following:
   - Refreshing
   - Slightly unrefreshing
   - Moderately unrefreshing
   - Very unrefreshing

13. How would you rate the effect of the Oral Appliance on the quality of your sleep:
   - Large improvement
   - Improvement
   - Same
   - Unsure

14. How would you grade your level of tiredness on waking whilst using the Oral Appliance?
   - Not tired
   - Slightly tired
   - Moderately tired
   - Very tired

15. How would you rate the effect of the Oral Appliance on the level of tiredness on waking:
   - Large improvement
   - Improvement
   - Same
   - Unsure
16. Since obtaining the Oral Appliance has your sleeping habit changed:

- Yes. Sleep in the same room.
- No change. Still sleep in different rooms because of snoring.
- No change. Sleep in different rooms for a reason other than snoring.

17. Have you encountered any difficulties with the appliance?  Yes  No

18. If yes to Q 17 then which of the following side effects did you experience with the Oral Appliance:

<table>
<thead>
<tr>
<th>SIDE EFFECT</th>
<th>SEVERITY</th>
<th>FREQUENCY</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Jaw discomfort</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>If yes then:</td>
<td>If yes then:</td>
<td>□ less than a week</td>
</tr>
<tr>
<td>No</td>
<td>□ Mild</td>
<td>□ Rarely</td>
<td>□ 1 week</td>
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<tr>
<td>If No, then go to (b)</td>
<td>□ Moderate</td>
<td>□ Sometimes</td>
<td>□ 2 weeks</td>
</tr>
<tr>
<td></td>
<td>□ Severe</td>
<td>□ Often</td>
<td>□ 3 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>□ &gt; 3 weeks</td>
</tr>
<tr>
<td>(b) Excess Salivation</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>If yes then:</td>
<td>If yes then:</td>
<td>□ less than a week</td>
</tr>
<tr>
<td>No</td>
<td>□ Mild</td>
<td>□ Rarely</td>
<td>□ 1 week</td>
</tr>
<tr>
<td>If No, then go to (c)</td>
<td>□ Moderate</td>
<td>□ Sometimes</td>
<td>□ 2 weeks</td>
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<tr>
<td></td>
<td>□ Severe</td>
<td>□ Often</td>
<td>□ 3 weeks</td>
</tr>
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<tr>
<td>(c) Dryness of mouth</td>
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<td></td>
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<td>If yes then:</td>
<td>□ less than a week</td>
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<tr>
<td>No</td>
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<td>□ Rarely</td>
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<td>□ Severe</td>
<td>□ Often</td>
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<td>(d) Grinding of teeth at night</td>
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<tr>
<td>No</td>
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<tr>
<td>(e) Soft tissue irritation</td>
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<td>If yes then:</td>
<td>□ less than a week</td>
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<td>No</td>
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<td>□ 1 week</td>
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<td>□ Sometimes</td>
<td>□ 2 weeks</td>
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<td></td>
<td>□ Severe</td>
<td>□ Often</td>
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<tr>
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<td></td>
<td></td>
<td>□ &gt; 3 weeks</td>
</tr>
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</table>
19. Any other side effects not mentioned:

20. Did the side effects prevent you from using the Oral Appliance? □ Yes  □ No

21. How would you rate your satisfaction with the appliance?
   □ Very satisfied
   □ Satisfied
   □ Dissatisfied
   □ Very dissatisfied

22. Would you like to continue to use the Oral Appliance? □ Yes  □ No

*Any comments:*


Thank you for your cooperation
APPENDIX 7. LETTER FOR GROUP I PATIENTS

<Patient Address>

<Date>

Dear <Patient Name>

I am writing to inform you that you have been selected for a research study and have been placed in Group I. The purpose of this letter is to describe to you what each of the three sleep studies will involve.

<table>
<thead>
<tr>
<th>Sleep Study</th>
<th>Category</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep Study 1</td>
<td>AI</td>
<td>Only lower splint to be worn. (Upper splint is NOT to be worn). The following morning you should take both the splints home with you to wear every night until the second sleep study.</td>
</tr>
<tr>
<td>Sleep Study 2</td>
<td>BI</td>
<td>You will be given upper and lower splint to wear during sleep study. The following morning you should take both the splints home with you to wear every night until the final sleep study.</td>
</tr>
<tr>
<td>Sleep Study 3</td>
<td>BI</td>
<td>You should wear upper and lower splint during sleep study.</td>
</tr>
</tbody>
</table>

You will shortly be contacted by Jenny to book three appointments for the above sleep studies, if you have not already been contacted by her.

Jenny will also ask you to hand in your appliance two weeks before the first sleep study. This is to ensure that all patients start the sleep studies at the same point. This is an important part of the study and I would be grateful if you can comply with this request. A week before the first sleep study (ie a week after having handed in both the appliances) you will then collect your lower splint ONLY from Jenny and wear this every night until your first sleep study. It is essential that you bring in your lower appliance with you for your first sleep study.

If you have a cold/flu, please inform Jenny by contacting St George Hospital on 9350 2696.

If you are unclear about any of these instructions or have any questions, you can contact me at the United Dental Hospital on 9282 0388 or at home in the evenings on 9399 5669.

Kindly bring this letter with you when attending each sleep study and show it to the chief sleep study technician.

Many thanks for all your co-operation in this study.

Yours sincerely

Dr A S Mehta
APPENDIX 8. LETTER FOR GROUP II PATIENTS

Dr Atul S Mehta
Orthodontic Registrar
United Dental Hospital
2 Chalmers Street
Surrey Hills NSW 2010

<Patient Address>

<Date>

Dear <Patient Name>

I am writing to inform you that you have been selected for a research study and have been placed in Group II. The purpose of this letter is to describe to you what each of the three sleep studies will involve.

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<tr>
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<td>BII</td>
<td>You will be given upper and lower splint to wear during sleep study. The following morning the upper splint is kept by the technician. The lower splint should be taken home by you and worn every night until the second sleep study.</td>
</tr>
<tr>
<td>Sleep Study 2</td>
<td>All</td>
<td>Only lower splint to be worn (Upper splint is NOT to be worn). The following morning the lower splint should be taken home by you and worn every night until the second sleep study.</td>
</tr>
<tr>
<td>Sleep Study 3</td>
<td>All</td>
<td>Only lower splint to be worn (Upper splint is NOT to be worn).</td>
</tr>
</tbody>
</table>

You will shortly be contacted by Jenny to book three appointments for the above sleep studies, if you have not already been contacted by her.

Jenny will also ask you to hand in your appliance two weeks before the first sleep study. This is to ensure that all patients start the sleep studies at the same point. This is an important part of the study and I would be grateful if you can comply with this request. A week before the first sleep study (ie a week after having handed in both the appliances) you will then collect both your upper and lower splints and wear them every night until your first sleep study. It is also essential that you bring in both your appliances when you come for your first sleep study.

If you have a cold/flu, please inform Jenny by contacting St George Hospital on 9350 2696.

If you are unclear about any of these instructions or have any questions, you can contact me at the United Dental Hospital on 9282 0388 or at home in the evenings on 9399 5669.

Kindly bring this letter with you when attending each sleep study and show it to the chief sleep study technician.

Many thanks for all your co-operation in this study.

Yours sincerely

Dr A S Mehta
APPENDIX 9. INDIVIDUAL PATIENT CHARACTERISTIC DATA

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Patient Group</th>
<th>Age (years)</th>
<th>Sex: male 1, female 0</th>
<th>Weight (kg)</th>
<th>Ht (m)</th>
<th>BMI (kg/m²)</th>
<th>Neck Circumference (cm)</th>
<th>Baseline AHI (hour)</th>
<th>Baseline MinSaO (%)</th>
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## Appendix 10. Individual Patient Cephalometric Measurements

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<thead>
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<th>Patient Number</th>
<th>Ba-SN (degrees)</th>
<th>SN (mm)</th>
<th>ANS-pin (mm)</th>
<th>Co-A (mm)</th>
<th>Go-Gn (mm)</th>
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APPENDIX 11. ANALYSIS OF ERRORS OF CEPHALOMETRIC MEASUREMENTS

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MD: Orthodontics
APPENDIX 13 (CONT’D)

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<th>Average of AHI.2 and AHI.3</th>
<th>% Change AHI</th>
<th>Treatment Outcome</th>
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Notes:

1) The percentage change in AHI was calculated using the formula: \[
\text{AHI (placebo)} - \text{AHI (MAS)} \times 100 / \text{AHI (placebo)}
\]

For the sequence ABB, the average of the AHI with MAS from sleep studies 2 and 3 was used. For the sequence BAA, the average of the AHI with placebo from sleep studies 2 and 3 was used.

2) Success is defined as a return of AHI < 5/hr; Partial Success is defined as ≥ 50% reduction in AHI but AHI ≥ 5/hr; Failure is defined as < 50% reduction in AHI.