



## Long-Term Effectiveness and Safety of Maxillomandibular Advancement for Treatment of Obstructive Sleep Apnea

Scott B. Boyd, DDS, PhD<sup>1,2</sup>; Arthur S. Walters, MD<sup>1</sup>; Peter Waite, DDS, MD, MPH<sup>3</sup>; Susan M. Harding, MD<sup>4</sup>; Yanna Song, MS<sup>5</sup>

<sup>1</sup>Department of Neurology, Sleep Disorders Division, Vanderbilt University School of Medicine, Nashville, TN; <sup>2</sup>Department of Oral and Maxillofacial Surgery, Vanderbilt University School of Medicine, Nashville, TN; <sup>3</sup>Department of Oral and Maxillofacial Surgery, University of Alabama at Birmingham, Birmingham, AL; <sup>4</sup>Division of Pulmonary, Allergy and Critical Care Medicine, University of Alabama at Birmingham, Birmingham, AL; <sup>5</sup>Department of Biostatistics, Vanderbilt University School of Medicine, Nashville, TN

**Study Objective:** To determine the long-term clinical effectiveness and safety of maxillomandibular advancement (MMA) for the treatment of moderate to severe obstructive sleep apnea (OSA).

**Methods:** A prospective two-center cohort study design was used to evaluate OSA patients who underwent MMA > 2 years ago. The primary outcome measure was the apnea-hypopnea index (AHI). Secondary outcome measures included blood pressure (BP), sleepiness (Epworth Sleepiness Scale [ESS]), and quality of life (Functional Outcomes of Sleep Questionnaire [FOSQ]).

**Results:** 30 adult patients (80% men, age 50.5 ± 9.6 years [mean ± SD]) participated in the study. The AHI decreased from a mean of 49 to 10.9 events/h ( $p < 0.0001$ ) at the time of long-term evaluation (6.6 ± 2.8 years after MMA), with 46.7% of patients obtaining an AHI < 5 and 83.4% of patients attaining an AHI ≤ 15 events/h. The mean diastolic BP decreased from 83.7 to 79.0 mm Hg ( $p < 0.05$ ). ESS decreased from a mean of

12.1 to 6.0 ( $p < 0.01$ ). FOSQ increased from a mean of 12.6 to 17.3 ( $p < 0.05$ ). Few long-term treatment-related adverse events occurred, which had minimal impact on quality of life (QOL).

**Conclusions:** MMA is a clinically effective and safe long-term treatment for most patients with moderate-to-severe OSA as demonstrated by significant decreases in AHI, diastolic BP, and subjective sleepiness, with concomitant significant improvements in QOL. The results of this small cohort study suggest that MMA should be considered as the alternative treatment of choice for patients with severe OSA who cannot fully adhere to CPAP therapy.

**Keywords:** obstructive sleep apnea, maxillomandibular advancement, apnea-hypopnea index, cohort study, treatment outcome, quality of life, daytime sleepiness, safety

**Citation:** Boyd SB, Walters AS, Waite P, Harding SM, Song Y. Long-term effectiveness and safety of maxillomandibular advancement for treatment of obstructive sleep apnea. *J Clin Sleep Med* 2015;11(7):699–708.

Moderate-to-severe obstructive sleep apnea (OSA) is a common disorder, which is estimated to be present in approximately 13% of men and 6% of women aged 30 to 70 years.<sup>1</sup> OSA occurs when there is complete or partial collapse of the upper airway during sleep resulting in chronic intermittent hypoxia (CIH), sympathetic activation, and sleep fragmentation. Important clinical consequences of OSA include: excessive daytime sleepiness, impaired cognitive function, diminished quality of life (QOL), and an increased risk of motor vehicle crashes.<sup>2–6</sup> OSA is associated with hypertension, diabetes, and an increased risk of cardiovascular events, including stroke and death; thus making OSA a significant public health concern.<sup>7–13</sup> Furthermore, OSA is a chronic disease that commonly requires lifelong management.<sup>14</sup>

Currently, continuous positive airway pressure (CPAP) therapy is the accepted first-line therapy for OSA.<sup>15</sup> Significant improvements in objective and subjective sleepiness, blood pressure (BP), QOL, and neurocognitive function are noted with CPAP use.<sup>15–17</sup> Furthermore, treatment of severe OSA with CPAP reduces the risk of cardiovascular events.<sup>11</sup> CPAP non-adherence or the inability to tolerate CPAP is the major barrier to adequate therapy of OSA. When CPAP adherence is defined as > 4 hours of nightly use, 46% to 83% of OSA

### BRIEF SUMMARY

**Current Knowledge/Study Rationale:** Since a relatively large number of patients with severe OSA will not fully adhere to CPAP therapy—presumably leaving them at continued high risk for cardiovascular events and a diminished quality of life—it is extremely important to have alternative therapies available that can effectively treat severe OSA over a patient's lifetime. To the best of our knowledge, no studies have comprehensively and concomitantly examined the long-term effectiveness and safety of maxillomandibular advancement (MMA) as an alternative therapy to CPAP. We conducted this study to determine if MMA is a clinically effective and safe long-term treatment for OSA patients, as measured by changes in the apnea-hypopnea index (AHI), blood pressure (BP), sleepiness, and quality of life (QOL).

**Study Impact:** Our results show that MMA produces substantial and sustained reductions in the AHI, diastolic BP, and subjective sleepiness with concomitant improvements in QOL. Importantly, MMA has a good risk-benefit ratio, as these successful outcomes were achieved in the context of minimal long-term treatment-related adverse outcomes. The results of this study provide compelling evidence to suggest that MMA should be the alternative treatment of choice for patients with severe OSA who cannot fully adhere to CPAP.

patients are considered to be non-adherent.<sup>18</sup> This leaves many patients untreated and at increased risk for cardiovascular events and decrements in QOL.

Several short term observational studies show that maxillo-mandibular advancement surgery (MMA) may be a clinically effective alternative therapy for patients with moderate-to-severe OSA who are not effectively treated with CPAP.<sup>19–26</sup> MMA involves surgical facial advancement by concomitant maxillary and mandibular osteotomies, thus enlarging the caliber of the posterior upper airway space. Although the level of evidence is low, substantial and consistent short-term reductions in the apnea-hypopnea index (AHI) are observed following MMA.<sup>25,26</sup> Preliminary short-term reports also indicate that MMA may result in improvement in subjective sleepiness,<sup>27,28</sup> health-related QOL,<sup>29</sup> and BP.<sup>22</sup>

Limited data evaluate the long-term efficacy of MMA other than reporting the AHI.<sup>30–32</sup> However, there are other important outcome measures beyond the AHI. We hypothesize that MMA is a clinically effective long-term treatment for patients with moderate-to-severe OSA, as measured by changes in AHI, BP, sleepiness and QOL. The specific aims of this study were to determine the long-term efficacy of MMA on sleep disordered breathing, BP, subjective sleepiness, % REM sleep and QOL in patients with moderate-to-severe OSA. Furthermore, the safety of MMA was comprehensively examined using a novel approach which included concomitant subjective assessment of treatment related symptoms and objective physical examination to facilitate determination of the risk-benefit ratio of MMA.

## METHODS

### Study Design and Patient Recruitment

This study was a prospective 2-center observational cohort study to determine the long-term effectiveness and safety of MMA. The study cohort was composed of patients who had previously undergone MMA for treatment of moderate-to-severe OSA after failing to adequately adhere to CPAP therapy at Vanderbilt University Medical Center (VUMC) between 1997 and 2007 and at the University of Alabama at Birmingham (UAB) between 2006 and 2010. At a minimum of 2 years following MMA, patients were recruited to complete a history and physical examination, overnight attended polysomnography (PSG), and questionnaires evaluating sleepiness, QOL and treatment-related symptoms. This research protocol was approved by the Vanderbilt University IRB (Human Research Protection Program) and the IRB at UAB, and ethical standards were used to conduct the study.

Screening criteria used to identify potential candidates for inclusion in the study included: (1) adults aged  $\geq 18$  years, (2) diagnosis of moderate-to-severe OSA (AHI  $> 15$  events/h) as determined by preoperative overnight in-laboratory diagnostic attended PSG, (3) inability to tolerate or adequately adhere to CPAP therapy, (4) postoperative overnight in-laboratory PSG documenting short-term changes (3 to 6 months) in AHI after MMA, and (5) a follow-up period post MMA  $\geq 2$  years. Exclusion criteria included: (1) previous facial surgery not related to the treatment of OSA, (2) inadequate existing data preoperatively, (3) inability or unwillingness to return for long-term evaluation, and (4) inability or unwillingness to provide written informed consent. BMI and/or anatomic criteria were not

used to determine inclusion or exclusion of patients from the cohort.

A focused electronic medical record query at VUMC identified 72 patients meeting screening criteria. An attempt was then made to contact each patient for participation in this study. Contact was made with 44.4% (32/72) of the cohort, and 30.6% (22/72) of the total patients agreed to participate. Seven of the 10 patients who did not agree to participate stated that they did not have any subjective symptoms of OSA—including excessive daytime sleepiness and QOL issues—and perceived no benefit in returning for participation. The remaining 3 patients indicated that subjectively they had OSA symptoms, but their symptoms were not as severe as prior to surgery.

The same focused medical record query was conducted at UAB, which identified 25 patients who met screening criteria. Contact was made with 32% (8/25) of the cohort, and each of the 8 patients agreed to participate.

After informed consent, patients underwent the long-term evaluation including a history and physical examination, overnight attended PSG, Epworth Sleepiness Scale, QOL instruments and questions related to treatment-related symptoms. Additionally, each patient's medical record was retrospectively reviewed to obtain preoperative history, physical examination, PSG (pre-MMA and short-term post-MMA) and survey data. Also, perioperative inpatient records and post-surgical outpatient clinical records were systematically reviewed to identify the type and severity of all adverse events potentially related to MMA.

### Outcomes

The primary outcome measure was long-term changes in AHI after surgical treatment, as measured preoperatively and again more than 2 years after MMA surgery. The magnitude of this change as well as the proportion of patients reaching an AHI  $< 5$  events/h and an AHI of  $\leq 15$  events/h with resolution of OSA symptoms was also calculated. Additionally, short-term changes in the AHI after surgical treatment (as measured at preoperation and again 3–6 months after MMA surgery) were also calculated. The short-term changes in the AHI were additionally calculated for MMA patients who did not participate in long-term evaluation for the purpose of comparing study participants and non-participants to determine if any selection bias existed in recruitment of MMA patients for the study. Secondary outcome measures included changes in office BP, subjective sleepiness as measured by the Epworth Sleepiness Scale (ESS),<sup>33,34</sup> %REM sleep, and sleep-specific quality of life as measured by either the Functional Outcomes of Sleep Questionnaire (FOSQ [at UAB])<sup>35</sup> or the Sleep Apnea Quality of Life Index (SAQLI [at VUMC]).<sup>36,37</sup> The oxygen desaturation index (ODI3) (the number of times per hour of sleep that the blood oxygen saturation drops by 3 percentage points from baseline) and the percentage of sleep time with oxygen saturation  $< 90\%$  were measured to determine the magnitude of chronic intermittent hypoxia at long-term follow-up. The proportion of patients with an ODI3  $< 5$  events/h and an ODI3  $\leq 15$  events/h was also calculated. Demographic characteristics and other secondary outcomes measures included age (years), gender, BMI ( $\text{mg}/\text{kg}^2$ ), length of long-term follow-up after surgery (years), and comorbid medical conditions. Comparisons were

conducted between VUMC and UAB patients to determine if significant differences existed between the sites for baseline characteristics as well as changes in the outcome measures.

Additionally, adverse events and treatment-related symptoms that developed after MMA were assessed. A comprehensive systematic review of the preoperative, perioperative, and postoperative medical records were completed for each patient to identify all adverse events associated with MMA surgery. Furthermore, the long-term clinical evaluation also identified potential long-term adverse events. The SAQLI (VUMC) was used to determine the presence and severity of treatment related symptoms.

### Surgical Procedures

All MMA procedures were completed using standardized surgical techniques, as previously published including: (1) total Le Fort I maxillary osteotomy and (2) bilateral sagittal split ramus osteotomies of the mandible.<sup>20,24,38</sup> Both maxillary and mandibular osteotomies were stabilized with bone plate and screw fixation.

### Long-Term Evaluation

Eligible consented patients returned for the comprehensive long-term evaluation. A detailed history and physical examination was completed, including a functional examination of the facial structures: nose, temporomandibular joints, muscles of mastication, trigeminal and facial nerve function, dental occlusion, and oropharynx. Static light touch sensation of the upper lip, lower lip, and chin were objectively examined using Semmes-Weinstein Monofilaments (North Coast Medical Inc., Morgan Hill, CA) assessing the maxillary and mandibular branches of the trigeminal nerve. A lateral cephalometric radiograph was compared to the preoperation radiograph to determine the magnitude and direction of movement from the MMA surgery.

Participants completed the ESS (0–24) with scores > 10 representing excessive or pathologic sleepiness.<sup>33,34</sup> These ESS results were compared to preoperative ESS scores to determine the long-term changes in subjective sleepiness after MMA.

The SAQLI<sup>36,37,39</sup>—a reliable and valid instrument to address sleep-specific QOL—was administered to VUMC study participants. The SAQLI contains 5 domains: Daily Functioning (A), Social Interactions (B), Emotional Functioning (C), Symptoms (D), and Treatment-Related Symptoms (E). In domain D, there is a positive impact section that uses a visual analogue scale (VAS)—ranging from no impact (0) to extremely large impact (10)—where the patient rates the improvement in QOL since treatment. In domain E, the patient is specifically questioned about the presence of a wide variety of treatment-related symptoms including, but not limited to, symptoms related to MMA surgery. Symptom questions specific to MMA included: (1) numbness or pain of the lips and chin, (2) limitation in jawing opening, (3) worsening of facial appearance, (4) popping or clicking of the jaw joints, (5) movement of the teeth so that the upper and lower teeth no longer meet properly, and (6) difficulty chewing. Additionally, the patient had the opportunity to add any adverse symptoms that were not on the list to comprehensively assess all treatment-related symptoms. The patient then rated the magnitude of identified symptoms using

a 7-point Likert-type scale with responses ranging from no problem to a very large problem. The patient then completed a VAS—ranging from no impact (0) to extremely large impact (10)—to rate the overall negative impact that the treatment-related symptoms have had on their QOL.

The Functional Outcomes of Sleep Questionnaire (FOSQ)<sup>35</sup>—a reliable and valid self-administered instrument to address sleep specific QOL—was completed by each MMA patient treated at UAB since patients routinely completed the FOSQ preoperatively. The preoperative and long-term FOSQ scores were then compared to determine the long-term changes in the FOSQ.

A standard multichannel overnight attended PSG was completed for all study participants at the time of the long-term evaluation. Each study was conducted and scored using the rules, terminology, and technical specifications developed by the American Academy of Sleep Medicine.<sup>40</sup>

Scoring of all of the long-term studies—conducted at both VUMC and UAB—was performed by a single experienced registered polysomnographic technologist at VUMC and then reviewed and interpreted by one board-certified sleep medicine specialist (A.W.)—both of whom were blinded to the clinical status and previous PSG results of the patient. To facilitate accurate comparison to the preoperative PSG, each long-term study was scored using the same hypopnea scoring rules that were used to score the preoperative PSG for that particular patient. None of the preoperative studies scored respiratory event related arousals (RERAs). The results of the prospective long-term PSG were then compared to the preoperative PSG findings to determine long-term changes. Additionally, comparisons were made to the short-term post-MMA PSG results to assess the relationship between short and long-term changes in the AHI after MMA.

### Data Collection and Statistical Analysis

Sample size calculations were performed to determine if MMA produced a clinically significant improvement in OSA, as defined by a long-term AHI  $\leq 15$  events/h, with the AHI as the primary outcome measure. Preliminary data at baseline derived from the cohort of 72 patients undergoing MMA at VUMC between 1997 and 2007 demonstrated a mean preoperative AHI of 53 events/h. The sample size calculation was structured to detect a difference in means of 38 events/h (e.g., a first condition mean of 53 events/h and a second condition mean of 15 events/h, assuming a standard deviation of differences of 28 events/h, using a paired t-test with a 0.05 two-sided significance level). A sample size of 16 was calculated to have a 90% power to detect a difference in the stated mean AHI values. The study sample intentionally exceeded the 16 patients for the purpose of determining the long-term changes in other important outcome measures (BP, ESS, QOL, adverse events) where insufficient data exist to assess these changes in these outcomes.

Data were directly entered into a customized clinical research database (REDCap) that was designed to store all demographic, polysomnographic, clinical, and questionnaire data collected at the preoperative and post-surgical time intervals. Data were then analyzed using the statistical software SAS for Windows (Version 9.1.3, SAS Institute, Cary, NC) and



R (The R Foundation, Vienna, Austria). Descriptive statistical analysis was performed for all demographic and outcome variables preoperatively and at the long-term postoperative evaluation. Data are reported as mean  $\pm$  standard deviation, median and interquartile range (IQR) for continuous variables, and frequency and percent for categorical variables. The Wilcoxon signed rank test was used to compare the unadjusted treatment effect for each of the outcome measures, and 95% confidence intervals (CI) were calculated for the mean change in each of the outcome measures. The Cohen's *d* test was used to calculate the effect size for changes in the diastolic blood pressure (DBP). Spearman rank correlation coefficients were calculated to assess the association between long-term changes in AHI and BMI. The Mann-Whitney U and Pearson  $\chi^2$  tests were used for subgroup analysis to test for differences between those patients who did and did not have uvulopalatopharyngoplasty (UPPP), as well as for those patients who did and did not have genioglossal advancement. The Mann-Whitney U test was also used to test for differences in the short-term changes in AHI (primary outcome measure) between those MMA patients who did and did not participate in the study to assess for selection bias. Mann-Whitney U and Pearson  $\chi^2$  tests were also used to test for differences between VUMC and UAB patients for demographic baseline characteristics as well as changes in outcome measures. Only one surgeon performed the MMA procedures at VUMC (S. Boyd) and only one at UAB (P. Waite), so differences in outcomes are expressed as institutional differences. For all analyses, a *p* value of  $< 0.05$  was considered statistically significant. Differences in AHI were expressed as the mean change ( $\pm$  SD) with treatment at each time interval. Additionally, the mean percent reduction in the AHI (preoperative AHI minus postoperative AHI divided by preoperative AHI), and the proportion of patients reaching specific levels of treatment effectiveness (AHI  $< 5$  events/h; AHI  $\leq 15$  events/h with no significant symptoms of sleepiness) were determined. Patients were classified for severity of OSA as: normal (AHI  $< 5$  events/h), mild (AHI 5–15 events/h), moderate (AHI  $> 15$ –30 events/h), or severe (AHI  $> 30$  events/h).

## RESULTS

### Patient Characteristics

The cohort included 30 adult patients (mean age of  $50.5 \pm 9.6$  years, range: 32–74 years) who were primarily overweight (preoperative BMI  $29.1 \pm 4.1$  kg/m<sup>2</sup>), men (80%), with severe OSA (baseline AHI  $49.0 \pm 20.0$  events/h). Comorbid conditions present preoperatively included hypertension (26.7%), depression (27.6%), diabetes (6.5%), coronary artery disease (3.6%), cardiac dysrhythmias (3.6%), and hypothyroidism (3.6%). Per inclusion criteria, prior to performing MMA, all patients had attempted CPAP and were unable to tolerate or adequately adhere to therapy.

At the time of long-term evaluation, patients were, on average,  $> 6$  years status/post MMA surgery (mean =  $6.6 \pm 2.8$  years, range 2.1–11.2 years; median = 6.3, IQR 4.2 to 9.1). The magnitude of maxillary advancement was 7 mm (mean =  $7.0 \pm 2.3$  mm, range 2.5 to 11.1 mm; median = 7.3, IQR 5.6 to 9.0) and the magnitude of mandibular advancement was about 9 mm

(mean =  $9.2 \pm 3.3$  mm, range 2.8 to 18.9 mm; median = 9.6, IQR 7.4 to 10.3) as measured at the long-term evaluation. No significant clockwise (CW) or counter-clockwise (CCW) rotational movements of the maxillomandibular complex occurred as measured by changes in the angle of the occlusal plane (OP) (pre-MMA OP,  $14.9 \pm 5.4$  degrees vs long-term post-MMA OP,  $15.4 \pm 6.5$  degrees,  $\Delta$ OP,  $0.5 \pm 3.6$  degrees; *p*  $> 0.05$ ). Preoperatively,  $> 40\%$  of the study group had mandibular deficiency with a skeletal class II malocclusion (pre-MMA, I = 55.6%; II = 40.7% [II-1 = 36.4%; II-2 = 63.6%]; III = 3.7%); 72.7% of class II patients underwent concomitant correction of their malocclusion with MMA surgery, so that at the long-term evaluation the vast majority of patients had normal class I occlusion (long-term post-MMA, I = 93%; II = 7% [II-2 = 100%]; III = 0%).

### Outcomes

Surgical treatment by MMA resulted in a substantial and sustained reduction in the AHI. The mean AHI decreased 76.9% from a preoperative value of 49.0 events/h to a long-term value of 10.9 events/h (*p*  $< 0.0001$ ), with a mean change of  $-37.8$  events/h (95% CI:  $-47.4$  to  $-28.2$ ). The median AHI decreased 88.4% from 45.0 to 5.2 (**Table 1**). At long-term, 46.7% of patients reached an AHI of  $< 5$  events/h and 83.4% of patients obtained an AHI of  $\leq 15$  events/h with concomitant resolution of sleepiness (ESS  $\leq 10$ ; **Table 2**). The long-term results were a continuation of the initial significant decrease in the AHI score that was observed shortly after surgery (pre-MMA AHI  $49.0 \pm 20.0$  vs AHI short-term post-MMA  $9.1 \pm 7.9$ ; *p*  $< 0.0001$ ; **Figure 1**). There was no significant change in the AHI score between the short-term and long-term time intervals (*p*  $> 0.05$ ). Furthermore, no significant differences were found when comparing the short-term changes in the AHI between the MMA patients who did and those who did not participate in the study (participants short-term  $\Delta$ AHI  $-39.4 \pm 20.0$  vs non-participants short-term  $\Delta$ AHI  $-44.5 \pm 28.4$ ; *p*  $> 0.05$ ).

The long-term mean ODI3 was 9.7 events/h (**Table 1**), and the mean percentage of sleep time with oxygen saturation  $< 90\%$  was  $7.2 \pm 13.3$  (median = 1.2; IQR = 0.1 to 9.9); 56.7% of patients reached an ODI3  $< 5$  events/h and 80% of patients obtained an ODI3  $\leq 15$  events/h. However, changes in ODI3 and percentage of sleep time with oxygen saturation  $< 90\%$  following MMA could not be calculated because no preoperative values were available.

Long-term decreases in systolic and diastolic blood pressure (DBP) were observed, with diastolic changes reaching the level of statistical significance (preoperative DBP  $83.7 \pm 9.7$  to long-term DBP  $79.0 \pm 8.5$ , *p*  $< 0.05$ ;  $\Delta$ DBP =  $-4.8 \pm 10.9$ ; 95% CI:  $-9.0$  to  $-0.7$ ; **Table 1**). The magnitude of the change in DBP represents a medium effect size (Cohen's *d* = 0.515).

A significant improvement in subjective sleepiness was observed following MMA, with the mean ESS score decreasing from 12.1 to 6.0 (*p*  $< 0.01$ ;  $\Delta$ ESS =  $-5.6 \pm 5.9$ ; 95% CI:  $-10.5$  to  $-0.7$ ; **Table 1**). At long-term evaluation, 90% of the study cohort had a normal level of subjective sleepiness (ESS  $\leq 10$ ) compared to pre-operation, where only 41.7% of patients had normal values. A significant improvement in the percentage of REM sleep was also observed (*p*  $< 0.05$ ;  $\Delta\%$  REM sleep =  $6.5 \pm 12.4$ ; 95% CI: 0.5 to 12.5; **Table 1**). There was significant improvement in

**Table 1**—Primary and secondary outcome measures.

Outcome	Pre-MMA	Long Term	Change	p value
Primary outcome				
AHI score, mean ± SD	49.0 ± 20.0	10.9 ± 15.0	-37.8 ± 25.7	< 0.0001
Median	45.0	5.2	-37.7	
Interquartile range	38.0 to 61.0	1.9 to 12.2	-49.1 to -19.9	
Secondary outcomes				
ESS score, mean ± SD	12.1 ± 4.9	6.0 ± 3.9	-5.6 ± 5.9	< 0.01
Median	12.0	5.0	-8.0	
Interquartile range	8.0 to 13.2	4.0 to 7.5	-11.0 to -4.0	
% REM Sleep score, mean ± SD	10.3 ± 9.4	16.6 ± 7.5	6.5 ± 12.4	< 0.05
Median	9.4	14.8	8.1	
Interquartile range	0.75 to 18.0	11.3 to 20.3	-0.70 to -14.1	
FOSQ score, mean ± SD	12.6 ± 3.6	17.3 ± 2.4	4.7 ± 3.9	< 0.05
Median	11.6	17.6	4.7	
Interquartile range	10.0 to 15.0	14.8 to 19.5	2.2 to 7.3	
Blood Pressure (mm Hg)				
Systolic, mean ± SD	136.0 ± 13.0	133.0 ± 13.0	-3.5 ± 18.0	> 0.05
Median	136.0	132	-2.0	
Interquartile range	127 to 146	125 to 142	-19.0 to 11.0	
Diastolic, mean ± SD	83.7 ± 9.7	79.0 ± 8.5	-4.8 ± 10.9	< 0.05
Median	83.0	77.5	-3.0	
Interquartile range	78 to 90.5	73.0 to 85.0	-10.0 to 3.0	
ODI3 score, mean ± SD				
Median		9.7 ± 14.0		
Interquartile range		4.7		
		1.5 to 10.8		

P values shown are based on Wilcoxon signed rank test for differences between baseline and long term. AHI, apnea-hypopnea index; ESS, Epworth Sleepiness Scale; REM, rapid eye movement; FOSQ, Functional Outcomes of Sleep Questionnaire; ODI3, oxygen desaturation index-the number of times per hour of sleep that the blood oxygen saturation drops by 3 percentage points from baseline.

QOL measurement long-term in both the FOSQ scores (UAB patients) ( $p < 0.05$ ;  $\Delta$ FOSQ =  $4.7 \pm 3.9$ ; 95% CI: 1.1 to 8.3; **Table 1**) and the SAQLI (VUMC patients) following MMA surgery (**Figure 2**). Furthermore, MMA surgery had minimal negative long-term impact on their QOL stemming from potential adverse events following MMA surgery (**Figure 2**). All of the observed changes in the outcome measures occurred despite a significant long-term increase in BMI (preoperative BMI  $29.1 \pm 4.1$  kg/m<sup>2</sup> to long-term BMI  $30.5 \pm 4.0$  kg/m<sup>2</sup>,  $p < 0.01$ ). However, no significant association was found between long-term changes in BMI and long-term changes in the AHI for the entire study cohort ( $r = 0.2143$ ,  $p > 0.05$ ).

**Site Analysis**

No significant preoperative differences in BMI (VUMC,  $28.2 \pm 2.7$  kg/m<sup>2</sup> vs UAB,  $33.1 \pm 6.8$  kg/m<sup>2</sup>,  $p > 0.05$ ), gender (VUMC 77% men vs UAB 88% men,  $p > 0.05$ ), or AHI (VUMC baseline AHI  $49 \pm 17$  events/h vs. UAB baseline AHI  $48 \pm 28$  events/h,  $p > 0.05$ ) were observed between VUMC and UAB patients, although UAB patients were significantly older (VUMC,  $48.3 \pm 7.8$  years vs UAB,  $56.6 \pm 12.0$  years,  $p < 0.05$ ). Furthermore, no significant preoperative differences in ESS (VUMC,  $11.4 \pm 4.2$  vs UAB,  $14.0 \pm 7.2$ ,  $p > 0.05$ ), %REM sleep (VUMC,  $9.5 \pm 9.7$  vs UAB,  $12.6 \pm 8.9$ ,  $p > 0.05$ ), SBP (VUMC,  $137 \pm 11$  vs UAB,  $134 \pm 18$ ,  $p > 0.05$ ), or DBP

**Table 2**—Comparisons of AHI severity at pre-MMA and long term post-MMA.

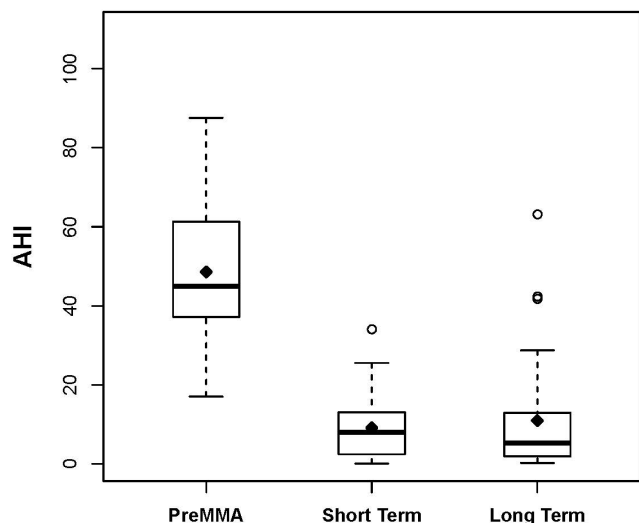
AHI Severity	Pre-MMA	Long Term
< 5	0 (0)	46.7 (14)
5–15	0 (0)	36.7 (11)*
> 15–30	16.7 (5)	6.7 (2)
> 30	83.3 (25)	10.0 (3)

Shown are total percentage of study cohort (total number of patients) at designated AHI severity level for the specified treatment interval. \*All patients had no significant subjective sleepiness (ESS  $\leq 10$ ) and no concomitant cardiopulmonary disease. MMA, maxillomandibular advancement; AHI, apnea-hypopnea index.

(VUMC,  $84.4 \pm 9.6$  vs UAB,  $82.0 \pm 10.2$ ,  $p > 0.05$ ) were observed between VUMC and UAB patients.

There were no significant differences between VUMC and UAB patients for long-term changes in AHI (VUMC,  $-40.4 \pm 20.0$  vs. UAB,  $-30.1 \pm 29.8$ ,  $p > 0.05$ ), ESS (VUMC,  $-5.3 \pm 5.1$  vs UAB,  $-6.3 \pm 9.3$ ,  $p > 0.05$ ), %REM sleep (VUMC,  $4.7 \pm 10.3$  vs UAB,  $11.7 \pm 17.7$ ,  $p > 0.05$ ), SBP (VUMC,  $-3.8 \pm 18.5$  vs UAB,  $-2.8 \pm 17.9$ ,  $p > 0.05$ ), or DBP (VUMC,  $-4.7 \pm 11.0$  vs UAB,  $-5.0 \pm 11.4$ ,  $p > 0.05$ ). Furthermore, no significant differences were found when comparing the magnitude of short-term changes in AHI between patients

**Figure 1**—Comparisons of short-term and long-term changes in AHI scores following surgical treatment by maxillomandibular advancement (MMA).



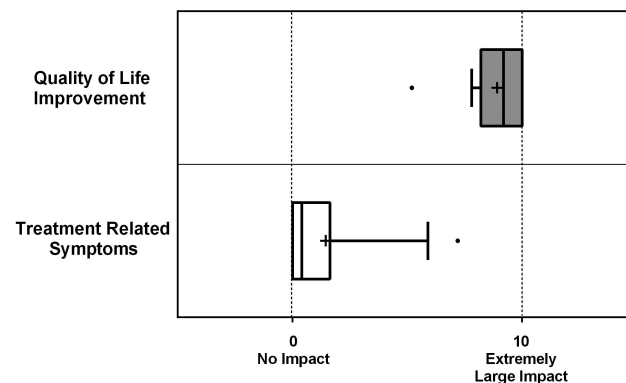
The bottom and top of the box represent the 25<sup>th</sup> percentile (lower quartile) and 75<sup>th</sup> percentile (upper quartile), which is bisected by the median value; black diamond represents the mean value; whiskers are used to represent the upper and lower values within 1.5 interquartile range (IQR) of the upper and lower quartiles, respectively; circles represent outlier values—which are defined as values more than 1.5 IQRs below the lower quartile or above the upper quartile. Surgical treatment resulted in a significant short-term decrease in the AHI score (pre-MMA AHI, 49.0 ± 20.0 vs AHI short-term post-MMA, 9.1 ± 7.9;  $p < 0.0001$ ). Surgical treatment also resulted in a significant long-term decrease in the AHI score (pre-MMA AHI, 49.0 ± 20.0 vs long-term AHI after MMA, 10.9 ± 15.0;  $p < 0.0001$ ). There were no significant differences in changes in the AHI scores between the short-term and long-term time intervals ( $p > 0.05$ ).

who did and did not participate in the study (VUMC Participants  $\Delta$ AHI  $-38.7 \pm 17.1$  vs VUMC Non-Participants  $\Delta$ AHI  $-43.4 \pm 29.2$ ,  $p > 0.05$ ; UAB Participants  $\Delta$ AHI  $-41.4 \pm 27.8$  vs UAB Non-Participants  $\Delta$ AHI  $-46.9 \pm 26.4$ ,  $p > 0.05$ ).

### Subgroup Analysis

To determine the potential additive impact of UPPP on changes in AHI, the study cohort was stratified by those patients who had MMA performed alone ( $n = 14$ ) and those patients who had surgical treatment consisting of UPPP in combination with MMA (UPPP/MMA) ( $n = 16$ ). UPPP was most commonly performed prior to MMA (68.8%, 11/16), while others had UPPP performed concomitantly with MMA (18.8%, 3/16); or less frequently following MMA (12.5%, 2/16). The UPPP procedures were completed by multiple surgeons using similar techniques as first described by Fujita et al.<sup>41</sup> There were no statistically significant differences found between the 2 subgroups preoperatively for age ( $p > 0.05$ ), BMI ( $p > 0.05$ ), AHI ( $p > 0.05$ ), and length of follow-up after MMA ( $p > 0.05$ ), but there were significantly more men in the UPPP/MMA group (MMA, 64% vs. UPPP/MMA, 94%;  $p < 0.05$ ). Surgical treatment resulted in a significant long-term decrease in the AHI score in each group: MMA (preoperative AHI 50.0 ± 20.0 vs

**Figure 2**—Impact of MMA treatment on quality of life as measured by the Sleep Apnea Quality of Life Index (SAQLI).



The left side of the boxes represent the 25<sup>th</sup> percentile (lower quartile) and 75<sup>th</sup> percentile (upper quartile), which is bisected by the median value; + sign represents the mean value; whiskers are used to represent the upper and lower values within 1.5 interquartile range (IQR) of the upper and lower quartiles respectively; black circle represent outlier values—which are defined as values more than 1.5 IQRs below the lower quartile or above the upper quartile. The results show that the study group perceived a very large improvement in their quality of life following MMA surgery (mean ± SD, 8.9 ± 1.2; median, 9.2; IQR, 8.3 to 10.0) with very minimal negative impact on their quality of life from symptoms that developed following MMA surgery (mean ± SD, 1.4 ± 2.3; median, 0.4; IQR, 0.0 to 1.5).

long-term AHI after MMA 8.0 ± 10.7,  $p < 0.001$ ) and UPPP/MMA (preoperative AHI 47.0 ± 21.0 vs long term AHI after UPPP/MMA 13.4 ± 17.9,  $p < 0.001$ ). The mean change in the AHI scores were larger for those patients undergoing MMA alone, but the magnitude of change did not reach the level of statistical significance (MMA  $\Delta$ AHI =  $-42 \pm 22$  vs. UPPP/MMA  $\Delta$ AHI  $-34 \pm 24$ ,  $p > 0.05$ ).

To determine the potential impact of genioglossal advancement (GA) on changes in the AHI scores the study cohort was stratified by patients who did ( $n = 9$ ) and did not ( $n = 21$ ) have GA. Genioglossal advancement was performed using standard surgical techniques as previously published.<sup>20,24,38</sup> No significant differences in the preoperative AHI were found between the 2 groups (GA+ preoperative AHI, 52 ± 24 vs GA- preoperative AHI, 47 ± 18,  $p > 0.05$ ). The mean change in the AHI scores were larger for those patients undergoing concomitant GA, but the magnitude of change did not reach the level of statistical significance (GA+,  $\Delta$ AHI =  $-46 \pm 22$  vs. GA-  $\Delta$ AHI  $-34 \pm 23$ ,  $p > 0.05$ ).

### Adverse Events

No patient had perioperative cardiac, respiratory, or neurologic adverse events associated with MMA surgery. The airway was managed during surgery with intubation in all patients, and no tracheotomies were performed. No patient required re-intubation for perioperative control of the airway. The estimated average blood loss was 343.0 ± 166.7 mL, and only 1 patient received a blood transfusion. No patient experienced complications requiring return to the operating room.



The average length of hospitalization was  $2.3 \pm 0.6$  days and no patient required readmission following discharge. Wound infections occurred in 6.7% (2/30) of patients and were effectively treated by local measures and oral antibiotics, without the use of intravenous antibiotics or re-hospitalization. Five patients (5/30, 16.7%) underwent outpatient removal of bone fixation plates after osseous healing of the maxillary and mandibular osteotomies.

Few adverse functional outcomes were observed following MMA surgery. Preoperatively, 31% (9/30) of patients had teeth malocclusion, and each of these patients had the malocclusion corrected as a component of MMA surgery. Few patients (6.7%, 2/30) developed malocclusion as a result of MMA, correlating well with the results of the SAQLI, where 4.8% of VUMC patients perceived an abnormality in the relation of their teeth after surgery. No objective reduction in mandibular mobility occurred after MMA (preoperatively mean  $47.7 \pm 6.7$  mm vs. long-term mean  $47.9 \pm 7.8$  mm). Physical examination showed temporomandibular joint (TMJ) function was unchanged or improved after surgery as measured by the percentage of patients with masticatory muscle pain (preoperative 3.3% vs. long-term 0%) or clinically evident TMJ disk displacement with reduction (preoperative 30% vs. long-term 17.9%). This correlated well with the SAQLI results, where 14.3% of the VUMC patients perceived popping and clicking of the jaws after surgery. No patient developed a motor deficit of the facial nerve following surgery. No patients exhibited anesthesia of the lips or chin, as measured objectively by light touch sensation, but 40% of MMA patients subjectively perceived a decrease in sensation. However, those patients with decreased sensation rated the change as no problem to only a small to moderate problem in relationship to their QOL. Few patients (13.8%) perceived a worsening of their facial appearance after MMA.

## DISCUSSION

This study evaluated the long-term clinical effectiveness and safety of maxillomandibular advancement (MMA) for the treatment of moderate-to-severe OSA. Clinical outcomes included AHI, BP, subjective sleepiness, %REM sleep, and QOL. To the best of our knowledge, this is the first time that long-term MMA outcomes have been presented in such a comprehensive fashion. Our primary outcomes measure, AHI, shows that MMA is a clinically effective long-term treatment for patients with moderate-to-severe OSA, with AHI reaching the normal range (AHI < 5 events/h) in 46.7% of patients and 83.4% of patients attaining an AHI of  $\leq 15$  events/h without significant subjective sleepiness (ESS  $\leq 10$ ) or cardiopulmonary comorbidities. Furthermore, significant improvements in secondary outcomes were observed including decreases in diastolic BP and subjective sleepiness, and significant improvements in QOL. The addition of UPPP or genioglossal advancement, as adjunctive surgical procedures, did not add significant benefit beyond MMA performed alone. Few adverse events were observed objectively and subjectively following MMA surgery, including long-term sequelae. Surprisingly these long-term results were achieved despite significant weight gain compared to the preoperative state. The average length of follow-up for

this study—greater than six years—indicates that the clinical effectiveness of MMA is likely to endure for many years.

The mean long-term AHI reduction of 76.9% observed in this study is comparable to the results of three studies that have reported mean long-term reductions in the AHI ranging from 69% to 84% following MMA performed as the primary procedure<sup>30,31</sup> or as staged surgical therapy, consisting of UPPP in combination with MMA.<sup>32</sup> The results of this study are also comparable to the results of a recent systematic review and meta-analysis that reported an overall mean reduction in the AHI of 87% when MMA was performed as a primary procedure.<sup>25</sup> The consistency of the findings of substantial and sustained reductions in the AHI following MMA across many sites provides further support for the generalizability of our results. Also, the magnitude of the mean reduction in the AHI following MMA is significantly larger than that observed for other surgical procedures used to treat OSA including UPPP (33%), laser assisted uvulopalatopharyngoplasty (18%), upper airway radiofrequency treatment (34%), and soft tissue implants (26%).<sup>25</sup> More recently, upper airway stimulation by an implantable device has been advocated as a treatment for moderate-to-severe OSA, but the reported results of a mean reduction in the AHI by about 52%, from 32.0 events/h at baseline to 15.3 events/h one year after surgery is significantly less than the results achieved with MMA.<sup>42</sup>

Currently, there is one report that examined the comparative effectiveness of MMA and CPAP therapy for the treatment of severe OSA. Vicini et al.<sup>43</sup> performed a randomized clinical trial comparing MMA and auto-titrating positive airway pressure (APAP) where all patients were evaluated in the home setting by a level 3 unattended sleep study. They found that after one year of treatment—by either surgery or APAP—that both groups showed a significant improvement in mean AHI (pre-MMA AHI, 56.8; post-MMA AHI, 8.1 vs. pre-APAP AHI, 50.3; post-APAP AHI, 6.3) and ESS (pre-MMA ESS, 11.6; post-MMA ESS, 7.7 vs. pre-APAP ESS, 11.2; post-APAP ESS, 5.9) levels with no significant differences noted between the two groups.

Oral appliances, including mandibular advancement devices (MAD), are also an alternative therapy that can successfully treat patients with mild OSA, but they have not been shown to be consistently successful in treating moderate and severe OSA.<sup>44,45</sup> A recent retrospective study compared the effectiveness of MMA and MAD device in patients with moderate-to-severe OSA. MMA was significantly more efficient in achieving therapeutic success (AHI < 15 events/h and at least 50% reduction from baseline) than MADs, with an odds ratio of 3.22.<sup>45</sup> Like CPAP, oral appliances are a compliance-based therapy and, therefore, require lifelong use to provide consistent clinically effective care. Furthermore, devices and supplies need to be replaced at different time intervals.

The modest reductions in blood pressure observed in this study are equivalent to the decreases found after CPAP treatment. We observed mean decreases in office systolic (SBP) and diastolic (DBP) blood pressure of  $-3.5$  mm Hg and  $-4.8$  mm Hg, respectively, after MMA; compared to SBP and DBP reductions of  $-3.2$  mm Hg and  $-2.9$  mm Hg, respectively, following CPAP treatment as reported in a recent systematic review and meta-analysis.<sup>46</sup>

The significant long-term reductions in subjective sleepiness after MMA observed in this study are equivalent or slightly better than the reductions in sleepiness reported for OSA patients who are adherent to CPAP therapy. Ninety percent of the patients in this study had normal ESS scores ( $ESS \leq 10$ ) after MMA, with a mean long-term reduction in ESS scores of 5.6. These results are comparable to a recent meta-analysis,<sup>47</sup> which showed that high use of CPAP ( $> 4$  h average nightly use) was associated with a 4.2 ESS score reduction, as well as a study by Antic et al., who reported that  $> 7$  hours of CPAP use resulted in normalization of ESS scores in 80.6% of patients with moderate to severe OSA.<sup>16</sup> Additionally, a meta-analysis by Patel et al. showed that patients with severe OSA ( $AHI > 30$  events/h) and excessive sleepiness ( $ESS \geq 11$ ) had a mean reduction in ESS scores of 4.75.<sup>48</sup> Our long-term MMA results are also analogous to the short-term MMA follow-up reports of Datillo and Drooger<sup>27</sup> and Goodday and Bourque<sup>28</sup> who reported normalization of ESS scores in 100% and 90% of patients, respectively. Therefore it appears that the significant short-term reductions in subjective sleepiness after MMA are maintained on a long-term basis.

The significant improvement in total FOSQ scores observed in this study are comparable to the significant improvements after 3 months of CPAP therapy for moderate-to-severe OSA.<sup>16</sup> The mean long-term improvements in FOSQ scores of 4.7 found in this study are better than the mean change score of 3.2 reported after two years of CPAP use<sup>49</sup> and a mean change of 2.9 following hypoglossal nerve stimulation.<sup>42</sup> Our long-term MMA results are similar to the short-term changes in FOSQ scores following MMA reported by Lye et al. who observed a mean change in FOSQ scores of 4.5.<sup>29</sup> Therefore it appears that the short-term improvements in QOL after MMA may be maintained on a long-term basis.

The surgical approach for most patients in our study group was to perform standard maxillomandibular advancement without significant rotation of the complex. We observed a mean mandibular advancement of 9.2 mm with no significant CCW or CW rotation of maxillomandibular complex as measured by changes in the OP. Riley and Powell have recommended a mandibular advancement of at least 10 mm<sup>32</sup>—which is slightly more than what was achieved in this study—although few data exist to demonstrate a strong correlation between the magnitude of surgical advancement and the subsequent changes in the AHI. CCW rotation of the maxillomandibular complex for treatment of OSA has been shown to increase the size of the posterior upper airway space, significantly reduce the AHI, and may even improve facial appearance in patients with severe mandibular deficiency, a high mandibular plane, and a convex facial profile.<sup>50,51</sup> Most patients in this study did not display these facial characteristics, so CCW rotation of the maxillomandibular complex was not routinely performed. Few patients (13.8%) in this study reported any worsening of facial esthetics after MMA, and most patients with preexisting skeletal Class II malocclusion had their mandibular deficiency concomitantly corrected by standard MMA surgery. Currently it is unknown if CCW rotational movements provide larger reductions in AHI beyond the significant reductions in AHI that have been observed with standard MMA.<sup>52</sup>

The long-term results of this study show that MMA patients do not experience a significant number of treatment-related adverse outcomes. The few minor perioperative adverse events observed did not result in any significant long-term sequelae. Furthermore, MMA did not adversely affect masticatory function as measured by mandibular mobility, temporomandibular joint function, neuro-sensation, and dental occlusion. Additionally, the few adverse events that occurred had minimal long-term impact on QOL as measured by the SAQLI. These findings occurred despite the fact that MMA patients generally have several characteristics that may be associated with adverse surgical outcomes including older age, larger mandibular and maxillary movements, and comorbid medical conditions. The combination of the safety profile and the observed clinical effectiveness demonstrates that MMA has a very good risk-benefit ratio.

No published studies have used the systematic comprehensive long-term approach to examining the safety of MMA employed in this study, but some investigators have observed similar short-term results. Holty et al. conducted a systematic review and meta-analysis of 22 published studies on MMA, finding a major complication rate of 1% and relatively few minor complications in patients who were followed an average of 5 months (range 3–7.7 months) after surgery. Minor adverse events included malocclusion, minor hemorrhage, local infections successfully treated with antibiotics, frequent neurosensory changes of the inferior alveolar nerve which commonly resolved by 12 months, and worsening of facial appearance noted in a low percentage of patients.<sup>26</sup> Similarly, Blumen et al. reported in their group of fifty patients that no serious complications occurred following MMA, with the most frequent local complication being mental nerve sensory loss, which patients considered as secondary to the positive surgical outcome.<sup>53</sup>

There are several potential limitations to our study. Importantly, this is an observational study in contrast to the preferred randomized clinical trial, which allows for better control of potential confounding variables. Additionally, the sample size of this study is relatively small and is limited to two centers. There is also a potential concern for selection bias as long-term outcomes were assessed in less than 50% of the total MMA cohort at both institutions. However, no difference in the short-term efficacy of MMA—as measured by changes in the AHI after MMA—was observed between those patients who participated in the study and those who did not. This finding significantly diminishes the likelihood of any selection bias, especially since we did not observe any significant deterioration in the efficacy of MMA between the short-term and long-term post-MMA time intervals. This study examined several important outcome measures—AHI, subjective sleepiness, QOL, BP—but there are other important health-related and functional outcomes that need to be examined including neurocognitive function and more measures of cardiovascular health. Ideally, larger prospective multicenter studies will be conducted in the future to comprehensively assess the effectiveness and safety of MMA to better define the generalizability of the results of this study and the overall impact of MMA on the health of patients with moderate-to-severe OSA, especially in patients who are unable to tolerate CPAP.



## CONCLUSIONS

Our results note that MMA is a clinically effective long-term treatment for patients with moderate-to-severe OSA as it predictably produces substantial and sustained reductions in AHI, BP, and subjective sleepiness, with concomitant significant improvements in QOL. Importantly, MMA has a good risk-benefit ratio, as these successful outcomes were achieved in the context of minimal short-term and long-term treatment-related adverse outcomes. In comparison to published results of other treatment options for patients with severe OSA, the magnitude of improvement in clinical outcomes after MMA is superior to other surgical procedures, oral appliance therapy and more recently, upper airway stimulation. Furthermore, MMA appears to produce results that are similar to the outcomes for patients who are fully adherent to CPAP therapy. Since a relatively large number of patients with severe OSA will not fully adhere to CPAP therapy—presumably leaving them at continued high risk for cardiovascular events and a diminished quality of life—it is extremely important to have alternative therapies available that can effectively treat severe OSA over a patient's lifetime. The results of this study provide compelling evidence to suggest that MMA meets these needs and should be the alternative treatment of choice for patients with severe OSA who cannot fully adhere to CPAP therapy.

## ABBREVIATIONS

AHI, apnea-hypopnea index  
 BMI, body mass index  
 BP, blood pressure  
 CCW, counter-clockwise  
 CI, confidence interval  
 CIH, chronic intermittent hypoxia  
 CPAP, continuous positive airway pressure  
 CW, clockwise  
 DBP, diastolic blood pressure  
 ESS, Epworth Sleepiness Scale  
 FOSQ, Functional Outcomes of Sleep Questionnaire  
 GA, genioglossal advancement  
 MAD, mandibular advancement device  
 MMA, maxillomandibular advancement  
 OSA, obstructive sleep apnea  
 QOL, quality of life  
 RERAs, respiratory even related arousals  
 SAQLI, Sleep Apnea Quality of Life Index  
 UPPP, uvulopalatopharyngoplasty  
 VAS, visual analogue scale

## REFERENCES

1. Peppard PE, Young T, Barnett JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol* 2013;177:1006–14.
2. Moore P, Bardwell WA, Ancoli-Israel S, Dimsdale JE. Association between polysomnographic sleep measures and health-related quality of life in obstructive sleep apnea. *J Sleep Res* 2001;10:303–8.
3. Moyer CA, Sonnad SS, Garetz SL, Helman JI, Chervin RD. Quality of life in obstructive sleep apnea: a systematic review of the literature. *Sleep Med* 2001;2:477–91.

4. Reimer MA, Flemons WW. Quality of life in sleep disorders. *Sleep Med Rev* 2003;7:335–49.
5. George CF, Smiley A. Sleep apnea & automobile crashes. *Sleep* 1999;22:790–5.
6. Ellen RL, Marshall SC, Palayew M, Molnar FJ, Wilson KG, Man-Son-Hing M. Systematic review of motor vehicle crash risk in persons with sleep apnea. *J Clin Sleep Med* 2006;2:193–200.
7. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *Sleep Heart Health Study. JAMA* 2000;283:1829–36.
8. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med* 2000;342:1378–84.
9. Young T, Peppard P, Palta M et al. Population-based study of sleep-disordered breathing as a risk factor for hypertension. *Arch Intern Med* 1997;157:1746–52.
10. Punjabi NM, Shahar E, Redline S, Gottlieb DJ, Givelber R, Resnick HE. Sleep-disordered breathing, glucose intolerance, and insulin resistance: the Sleep Heart Health Study. *Am J Epidemiol* 2004;160:521–30.
11. Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *Lancet* 2005;365:1046–53.
12. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005;353:2034–41.
13. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 2002;165:1217–39.
14. Epstein LJ, Kristo D, Strollo PJ Jr, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med* 2009;5:263–76.
15. Giles TL, Lasserson TJ, Smith BH, White J, Wright J, Cates CJ. Continuous positive airways pressure for obstructive sleep apnoea in adults. *Cochrane Database Syst Rev* 2006;3:CD001106.
16. Antic NA, Catcheside P, Buchan C, et al. The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in patients with moderate to severe OSA. *Sleep* 2011;34:111–9.
17. Weaver TE, Maislin G, Dinges DF, et al. Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 2007;30:711–9.
18. Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. *Proc Am Thorac Soc* 2008;5:173–8.
19. Bettge G, Pepin JL, Veale D, Deschaux C, Raphael B, Levy P. Obstructive sleep apnea syndrome. fifty-one consecutive patients treated by maxillofacial surgery. *Am J Respir Crit Care Med* 2000;162:641–9.
20. Boyd SB, Walters AS, Song Y, Wang L. Comparative effectiveness of maxillomandibular advancement and uvulopalatopharyngoplasty for the treatment of moderate to severe obstructive sleep apnea. *J Oral Maxillofac Surg* 2013;71:743–51.
21. Hochban W, Conradt R, Brandenburg U, Heitmann J, Peter JH. Surgical maxillofacial treatment of obstructive sleep apnea. *Plast Reconstr Surg* 1997;99:619–26; discussion 27–8.
22. Prinsell JR. Maxillomandibular advancement surgery in a site-specific treatment approach for obstructive sleep apnea in 50 consecutive patients. *Chest* 1999;116:1519–29.
23. Riley RW, Powell NB, Guilleminault C. Obstructive sleep apnea syndrome: a review of 306 consecutively treated surgical patients. *Otolaryngol Head Neck Surg* 1993;108:117–25.
24. Waite PD, Wooten V, Lachner J, Guyette RF. Maxillomandibular advancement surgery in 23 patients with obstructive sleep apnea syndrome. *J Oral Maxillofac Surg* 1989;47:1256–61; discussion 62.
25. Caples SM, Rowley JA, Prinsell JR, et al. Surgical modifications of the upper airway for obstructive sleep apnea in adults: a systematic review and meta-analysis. *Sleep* 2010;33:1396–407.
26. Holty JE, Guilleminault C. Maxillomandibular advancement for the treatment of obstructive sleep apnea: a systematic review and meta-analysis. *Sleep Med Rev* 2010;14:287–97.
27. Dattilo DJ, Drooger SA. Outcome assessment of patients undergoing maxillofacial procedures for the treatment of sleep apnea: comparison of subjective and objective results. *J Oral Maxillofac Surg* 2004;62:164–8.
28. Goodday R, Bourque S. Subjective outcomes of maxillomandibular advancement surgery for treatment of obstructive sleep apnea syndrome. *J Oral Maxillofac Surg* 2012;70:417–20.

29. Lye KW, Waite PD, Meara D, Wang D. Quality of life evaluation of maxillomandibular advancement surgery for treatment of obstructive sleep apnea. *J Oral Maxillofac Surg* 2008;66:968–72.
30. Conrath R, Hochban W, Brandenburg U, Heitmann J, Peter JH. Long-term follow-up after surgical treatment of obstructive sleep apnoea by maxillomandibular advancement. *Eur Respir J* 1997;10:123–8.
31. Jaspers GW, Booij A, de Graaf J, de Lange J. Long-term results of maxillomandibular advancement surgery in patients with obstructive sleep apnoea syndrome. *Br J Oral Maxillofac Surg* 2013;51:e37–9.
32. Riley RW, Powell NB, Li KK, Troell RJ, Guilleminault C. Surgery and obstructive sleep apnea: long-term clinical outcomes. *Otolaryngol Head Neck Surg* 2000;122:415–21.
33. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;14:540–5.
34. Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep* 1992;15:376–81.
35. Weaver TE, Laizner AM, Evans LK, et al. An instrument to measure functional status outcomes for disorders of excessive sleepiness. *Sleep* 1997;20:835–43.
36. Flemons WW, Reimer MA. Development of a disease-specific health-related quality of life questionnaire for sleep apnea. *Am J Respir Crit Care Med* 1998;158:494–503.
37. Flemons WW, Reimer MA. Measurement properties of the calgary sleep apnea quality of life index. *Am J Respir Crit Care Med* 2002;165:159–64.
38. Boyd SB. Management of obstructive sleep apnea by maxillomandibular advancement. *Oral Maxillofac Surg Clin North Am* 2009;21:447–57.
39. Lacasse Y, Godbout C, Series F. Independent validation of the Sleep Apnoea Quality of Life Index. *Thorax* 2002;57:483–8.
40. Iber C, Ancoli-Israel S, Chesson A, Quan SF. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. Westchester, IL: American Academy of Sleep Medicine, 2007.
41. Fujita S, Conway W, Zorick F, Roth T. Surgical correction of anatomic abnormalities in obstructive sleep apnea syndrome: uvulopalatopharyngoplasty. *Otolaryngol Head Neck Surg* 1981;89:923–34.
42. Strollo PJ Jr, Soose RJ, Maurer JT, et al. Upper-airway stimulation for obstructive sleep apnea. *N Engl J Med* 2014;370:139–49.
43. Vicini C, Dallan I, Campanini A, et al. Surgery vs ventilation in adult severe obstructive sleep apnea syndrome. *Am J Otolaryngol* 2010;31:14–20.
44. Jalbert F, Lacassagne L, Bessard J, Dekeister C, Paoli JR, Tiberge M. [Oral appliances or maxillomandibular advancement osteotomy for severe obstructive sleep apnoea in patients refusing CPAP]. *Rev Stomatol Chir Maxillofac* 2012;113:19–26.
45. Garreau E, Wojcik T, Bouscaillou J, Ferri J, Raoul G. [Comparative effectiveness of maxillomandibular advancement surgery versus mandibular advancement device for patients with moderate or severe obstructive sleep area]. *L'Orthodontie française* 2014;85:163–73.
46. Schein AS, Kerkhoff AC, Coronel CC, Plentz RD, Sbruzzi G. Continuous positive airway pressure reduces blood pressure in patients with obstructive sleep apnea: a systematic review and meta-analysis with 1000 patients. *J Hypertens* 2014;32:1762–73.
47. Crawford MR, Bartlett DJ, Coughlin SR, et al. The effect of continuous positive airway pressure usage on sleepiness in obstructive sleep apnoea: real effects or expectation of benefit? *Thorax* 2012;67:920–4.
48. Patel SR, White DP, Malhotra A, Stanchina ML, Ayas NT. Continuous positive airway pressure therapy for treating sleepiness in a diverse population with obstructive sleep apnea: results of a meta-analysis. *Arch Intern Med* 2003;163:565–71.
49. Doff MH, Hoekema A, Wijkstra PJ, et al. Oral appliance versus continuous positive airway pressure in obstructive sleep apnea syndrome: a 2-year follow-up. *Sleep* 2013;36:1289–96.
50. Doff MH, Jansma J, Schepers RH, Hoekema A. Maxillomandibular advancement surgery as alternative to continuous positive airway pressure in morbidly severe obstructive sleep apnea: a case report. *Cranio* 2013;31:246–51.
51. Lin CH, Liao YF, Chen NH, Lo LJ, Chen YR. Three-dimensional computed tomography in obstructive sleep apnoeics treated by maxillomandibular advancement. *Laryngoscope* 2011;121:1336–47.
52. Knudsen TB, Laulund AS, Ingerslev J, Homoe P, Pinholt EM. Improved apnea-hypopnea index and lowest oxygen saturation after maxillomandibular advancement with or without counterclockwise rotation in patients with obstructive sleep apnea: a meta-analysis. *J Oral Maxillofac Surg* 2015;73:719–26.
53. Blumen MB, Buchet I, Meulien P, Hausser Hauw C, Neveu H, Chabolle F. Complications/adverse effects of maxillomandibular advancement for the treatment of OSA in regard to outcome. *Otolaryngol Head Neck Surg* 2009;141:591–97.

## ACKNOWLEDGMENTS

The authors thank David Adkins and Alison Green for their contributions to data collection and analysis.

## SUBMISSION & CORRESPONDENCE INFORMATION

**Submitted for publication November, 2014**

**Submitted in final revised form January, 2015**

**Accepted for publication January, 2015**

Address correspondence to: Scott B. Boyd, DDS, PhD, Research Professor, Vanderbilt University School of Medicine, CCC 3322 MCN 2103, 1161 21st Ave. S., Nashville, TN 37232-2103; Tel: (615) 343-6832; Fax: (615) 322-2793; Email address: scott.boyd@vanderbilt.edu

## DISCLOSURE STATEMENT

This was not an industry supported study. This investigation was supported in part by a Research Support Grant Award from the Oral and Maxillofacial Surgery Foundation and in part by Vanderbilt CTSA award No. UL1TR000445 from the National Center for Advancing Translational Sciences. Its contents are solely the responsibility of the authors and do not necessarily represent official views of the National Center for Advancing Translational Sciences or the National Institutes of Health. Dr. Walters has received research support from and has consulted for UCB Pharma and MundiPharma. Dr. Harding has received royalties from UpToDate. The other authors have indicated no financial conflicts of interest. All work associated with this study was performed at Vanderbilt University, Nashville, TN and University of Alabama at Birmingham, Birmingham, AL.