REVIEW

Oral Appliances for Snoring and Obstructive Sleep Apnea: A Review

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Abstract: We conducted an evidence-based review of literature regarding use of oral appliances (OAs) in the treatment of snoring and obstructive sleep apnea syndrome (OSA) from 1995 until the present. Our structured search revealed 141 articles for systematic scrutiny, of which 87 were suitable for inclusion in the evidence base, including 15 Level I to II randomized controlled trials and 5 of these trials with placebo-controlled treatment. The efficacy of OAs was established for controlling OSA in some but not all patients with success (defined as no more than 10 apneas or hypopneas per hour of sleep) achieved in an average of 52% of treated patients. Effects on sleepiness and quality of life were also demonstrated, but improvements in other neurocognitive outcomes were not consistent. The mechanism of OA therapy is related to opening of the upper airway as demonstrated by imaging and physiologic monitoring. Treatment adherence is variable with patients reporting using the appliance a median of 77% of nights at 1 year. Minor adverse effects were frequent whereas major adverse effects were uncommon. Minor tooth movement and small changes in the occlusion developed in some patients after prolonged use, but the long-term dental significance of this is uncertain. In comparison to continuous positive airway pressure (CPAP), OAs are less efficacious in reducing the apnea hypopnea index (AHI), but OAs appear to be used more (at least by self report), and in many studies were preferred over CPAP when the treatments were compared. OAs have also been compared favorably to surgical modification of the upper airway (uvulopalatopharyngoplasty, UPPP). Comparisons between OAs of different designs have produced variable findings. The literature of OA therapy for OSA now provides better evidence for the efficacy of this treatment modality and considerable guidance regarding the frequency of adverse effects and the indications for use in comparison to CPAP and UPPP.

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1.0 INTRODUCTION

THE STANDARDS OF PRACTICE COMMITTEE (SPC) IS CHARGED BY THE AMERICAN ACADEMY OF SLEEP MEDICINE (AASM) TO PRODUCE TOPICAL reviews and clinical guidelines and practice parameters for the use of clinicians. The Committee embraces the principles of evidence-based medicine including standardized methods for literature review and criterion-based ratings of research quality. The methods are consistent with guideline development methodology advocated by the American Medical Association (AMA). The AMA has certified previous guidelines for meeting their quality criteria.

In 1995, the then American Sleep Disorders Association (now the AASM) and its SPC produced a practice parameter regarding oral appliance (OA) use for snoring and obstructive sleep apnea (OSA).[1] In 2002 the AASM SPC created a task force to update the literature review in preparation for updating the related practice parameters regarding OA for OSA. The charge to the task force was to focus on new developments since 1995 and to seek specific answers to the following questions:

- What is the efficacy of OA in the treatment of snoring and obstructive sleep apnea in the short and long term?
- By what mechanisms do OA improve snoring and obstructive sleep apnea?
- Do patients use OA in the treatment of snoring and obstructive sleep apnea in the short and long term?
- What short- and long-term side effects, adverse effects or complications occur with the use of OA in the treatment of snoring and obstructive sleep apnea?
- How do OAs compare to nasal continuous positive airway pressure (CPAP), surgery and other therapies for the treatment of snoring and obstructive sleep apnea in terms of efficacy, treatment adherence, and preference?
- What device selection and procedures are best for implementing OA in the treatment of snoring and obstructive sleep apnea?

2.0 METHODS

Task force members were selected by SPC for their expertise in the topic, their willingness to abide by the procedures of the SPC for evidence-based parameter development, and the absence of conflict-of-interest regarding the devices and procedures under review.

The data for this review were assembled by searching PubMed for English language peer-reviewed publications containing the key words "oral appliance", "obstructive sleep apnea", "orthodontic appliances", and related terms. The search was restricted to adult patients. Of the 112 articles produced by this search, 45

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were rejected because they did not report original investigations, did not describe investigative methods adequately, were not studies of oral appliance therapy or reported data on fewer than 8 patients. Articles known to task force members that met the selection criteria but did not appear in the original search were added to the list. By this means 64 additional articles were added before January 2004, creating a list of 131 articles (Online Evidence Table). The same search process was repeated in July 2004 yielding 10 additional papers included for this review.

The task force first developed an abstract form in order to create a standardized database for the review, for the subsequent parameter development, and for the critical scrutiny of readers. The elements of this Evidence Table were selected to address the questions in the task force's charge. These data are contained in an Evidence Table, available in an online supplement. In addition, each paper was graded for research quality and evidentiary strength by reference to a scale advocated by Sackett[2] (Table 1). The studies and papers graded as Level I or II evidence are listed in Appendix 1 (Evidence Table, selected studies, Level I-II). This evidence table can be accessed on the web at http://www.aasmnet.org.

3.0 RESULTS

3.1 Overview Including Comments on Evidence Levels and Comparisons to Pre-1995.

The literature concerning OA therapy has grown exponentially since 1995, the year of publication of the original OA review and practice parameter.[1,3] Not only have more authors published their research, but also the types of investigations are much more varied. While most reports continue to be case series, as was the case at the time of the previous review, an important number of controlled treatment trials have now appeared, and these have strengthened the efficacy claims. Several extended follow-up studies have filled the substantial void present in 1995 regarding the long-term effects of OA. Further, comparisons to CPAP and other therapies allow a better positioning of OA therapy among the other treatment options for OSA.

Table 1—AASM Classification of Evidence

Recommendation Grades	Evidence Levels	Study Design
A	I	Randomized well-designed trials with low-alpha & low-beta errors*
B	II	Randomized trials with high-beta errors*
C	III	Nonrandomized controlled or concurrent cohort studies
C	IV	Nonrandomized historical cohort studies
C	V	Case series

ADAPTED FROM SACKETT(2)
*Alpha (type I error) refers to the probability that the null hypothesis is rejected when in fact it is true (generally acceptable at 5% or less, or $p<0.05$). Beta (Type II error) refers to the probability that the null hypothesis is mistakenly accepted when in fact it is false (generally trials accept a beta error of 0.20). The estimation of Type II error is generally the result of a power analysis. The power analysis takes into account the variability and the effect size to determine if sample size is adequate to find a difference in means when it is present (Power generally acceptable at 80-90%).

The quality of the research studies has improved substantially. Several randomized controlled trials have explored the efficacy of OA in comparison to other therapies or to placebo. Randomization is a feature of some of these studies, although not always directed at the outcome of interest. Five studies had randomized assignment of patients to OA therapy and placebo with assessment of baseline and treatment status, permitting a reliable assessment of treatment effect.[4-8] In other studies the use of random order of cross-over between OA and CPAP therapy controlled for the effect of treatment order, a potential confounder in this study design.[6,9-13] The standardization of diagnostic and outcome measures was reported in greater detail than in the earlier literature, probably reflecting an emerging consensus on outcome assessment and the availability of standardized instruments. As a result, of the 87 selected papers, 15 were rated Level I-II, whereas all of the studies reviewed in 1995 were at Level V quality. Of interest, the higher-grade studies did not differ significantly in their findings from those lower quality reports, producing a substantial concordance among most papers on the major issues.

The richness of the current literature produces challenges for the reviewer. Comparison of multiple studies must account for the effects of different OA designs and use, different patient populations, differences in OSA assessment and definitions of outcomes, and variations in follow-up time. The subsequent discussion acknowledges these differences in methodology, which in some cases limit meaningful comparisons.

3.2. What Is the Efficacy of Oral Appliances in the Treatment of Snoring and Obstructive Sleep Apnea in the Short and Long Term?

The first question to be addressed in this review of the recent research concerning OAs for the control of snoring and/or sleep apnea is: "Do they work?" Of the many studies reviewed, there were 41 that met adequate standards of evidence, and addressed the question of efficacy by providing objective sleep data before and after treatment. Ten of these studies were at Level I.[5,6,8-10,12,14-16] Data from a randomized controlled trial (RCT) of a mandibular repositioning appliance (MRA) and uvulopalatopharyngoplasty (UPPP) was reported in an initial manuscript[16] with additional data in 4 subsequent papers.[17-20] There were 5 Level II studies[4,7,13,21,22] and 1 Level III study.[23]There were 25 Level V studies.[24-48]

3.2.1 Devices Tested

Many different OAs with unique design features were tested in these studies. Most OAs were designed on the general principal that advancing the mandible, and holding it forward during sleep, would allow unobstructed breathing. Only a few studies reported using an appliance that only held the tongue forward. Some of these tongue-advancing appliances are "boil and bite" type devices, which can be fitted by the patients themselves, although the most widely used tongue device is custom made (tongue retaining device, TRD). Most of the MRAs studied require a dentist to make impressions from which to create a custom made device, or to adapt a pre-fabricated appliance to the patients' dimensions and adjust it to insure an optimal fit.

3.2.2 Subjects Tested

The number of subjects involved in the recent studies ranged from 8 to 257. Two studies reported on 10 or fewer subjects and 7

included more than 40 subjects. In 80% of the studies, the number of patients who completed the study was between 11 and 50. The studies differed in the length of time the patient wore the device before being re-tested (see Tables 3 and 4) and this may have affected follow-up and drop out rates. Reasons for dropping out of the study sometimes included OA side effects or lack of efficacy. Thus the rates of success may be somewhat inflated in some studies as they are reported results based upon those who could tolerate and use the appliance and who returned to be restudied. Drop out rates in the 15 Level I and II studies ranged from 0 to 38%, median 11.5%. Three of the newest and largest randomized trials used an intention-to-treat analysis that dealt with the drop out issue.[6,11,15] The remaining studies computed success rates based on the number of completed patients, and these success rates might be discounted by the drop out rate for a more conservative estimate of success.

Subject selection differed between the trials. Some investigators approached consecutive patients attending a sleep clinic with symptoms of OSA for recruitment, whereas other subjects were offered a place in a study because they had refused or failed another treatment. This "other treatment" was most often nasal CPAP but some studies involved those who failed to respond to UPPP surgery.[37] The typical selection criterion was a diagnosis of OSA with the severity of this disorder ranging from 5 to 30 respiratory events per hour. Some studies included subjects with more severe OSA (i.e., those in which there were more than 40 respiratory events per hour). Additional selection criteria in many of the studies included the presence of sufficient teeth to anchor the OAs and the ability of the subject to protrude the lower jaw at least 3 to 6 mm forward.

3.2.3 Criteria Utilized

The criterion for successful treatment differed from study to study. The most stringent definition of success was a reduction to less than five respiratory events per hour of sleep while the most liberal definition was a reduction of 50% or more from the baseline apnea-hypopnea index (AHI). Some studies used a respiratory disturbance index (RDI) obtained from respiratory sleep studies done in the laboratory or at home. Forty of the 41 studies report their findings as the percent of patients reaching 1 or more of the specific levels of improvement in AHI chosen (see Table 2). One of the randomized studies did not provide this information in the published paper but the data was provided by the authors.[22] All studies reported the mean AHI before and after wearing the appliance. However, when the initial range of severity is wide, a change in the mean AHI is less useful to the clinician than is the percent of patients reaching a specific treatment target particularly when this is provided according to AHI severity.

Eight studies of MRA therapy present treatment success results for an AHI of 5 or fewer respiratory events per hour of sleep. The average rate of success in these studies was 42%. Thirty studies of MRA therapy present the number of subjects achieving a post-treatment AHI of 10 or less and are listed in Table 2. An average of 52% of these patients' studies reached this level of control with the MRA. Ten studies present the most liberal criterion of successful treatment: a reduction of the baseline AHI by 50%. In these studies, 65% of the patients had a 50% reduction in AHI with the MRA. The success rate improves as the required level of control of OSA is lowered.

Other indicators of improved respiration, such as the minimum oxygen saturation level during sleep showed small increases generally in the range of 1 to 11%. For example, Yoshida[47] found a significant change in minimum saturation from 72 to 75% and Skinner and colleagues[46] found an increase from 76 to 82%. Many other studies found an improvement in minimum SaO_2.[4-6,22,28-32,36,37,39,40,43,48,49] or in other measures of oxygenation[7,14-16,42] but these improvements were not always statistically significant.[8-10,13,24,27,41,45] In some of the crossover studies comparing CPAP to an OA the minimum oxygen saturation improved with neither treatment[13] or with CPAP but not the MRA[9,10,12] or with both therapies.[6,23] Improvements in sleep structure were addressed in some studies. A significant reduction in the number of arousals was reported in some studies.[4,5,8,12-14] However, the mean arousal index was not always decreased[6] and CPAP was sometimes more effective at reducing arousals than MRA.[6]

The control of snoring has been less well studied than the control of apnea. This is largely due to the technical challenges of measuring the frequency and loudness of snoring in quantitative terms, such as the number of snores per hour and their intensity. Most studies relied on reports of improved snoring from the bed partner and in these studies, snoring was generally reported as substantially improved. Several studies measured snoring objectively.[5,14-16,38,40,44,50] Most studies reported significant reductions in snoring intensity[5,14,38,40] and the frequency of snores was significantly reduced in all but 1 study.[38] There was a placebo controlled RCT that assessed snoring severity in patients without OSA.[51] The MRA improved snoring intensity and frequency as reported by the bed partner more than did the placebo. Obviously, these subjective reports have limitations in their dependence upon bed partner reports. The overall effectiveness of OAs on snoring is a research question that needs further objective evaluation.

Changes in 1 of the commonest symptoms of OSA, excessive daytime sleepiness, were most often assessed by self-report. The Epworth Sleepiness Scale (ESS) was the most frequently used measure of subjective sleepiness. Significant reductions in the ESS were reported in many studies[4-6,8,9,12,14,15,21,41,44,46] but the improvement was not statistically significant in all studies[11,38] or did not differ between the appliance and placebo.[7] Visual analogue scales and spousal reports were also used. Four studies used objective measurements of sleepiness. Three studies[6,11,36] used the Maintenance of Wakefulness Test (MWT) and 1[5] used the Multiple Sleep Latency Test (MSLT). The MSLT improved with the MRA.[5] The MWT improved with the appliance in 1 study[36] but not in another.[6] However, there was no difference in MWT between CPAP and the MRA.[11] One study warned of the potential for bias because not all patients were willing to return for follow-up testing.[36] The final sample may have disproportionately included patients who had a good response to the MRA, as they may have been more willing to take part in the follow-up MWT testing. Objective measures of daytime sleepiness may provide additional information to the subjective measures of daytime sleepiness and the use of objective measures should be encouraged in future studies of the efficacy of OAs.

3.2.4 Variables Affecting Oral Appliance Efficacy

On the basis of this review there appear to be 4 variables that contribute to the effectiveness of oral appliances - the severity of the sleep apnea, the amount of mandibular protrusion of the

Table 2—Treatment Success Rates

Author	Device	Criteria						
		AHI<5	AHI<10	AHI<15	AHI<20	50% reduction	50% Reduction + AHI<10	50% Reduction + AHI<20
Barnes[6]	MRA		42/85 49%					
Barthlen[24]	SnoreGuard			5/8 62.5%		5/8 62.5%		
	TD			2/8 25%		2/8 25%		
Bloch[14]	Monobloc		18/24 75%					
	Herbst		16/24 67%					
Clark[23]	Herbst		4/21 19%					
Engleman[11]	MRA	9/48 19%	22/48 47%					
Esaki[26]	MRA			6/8 75%				
Eveloff[27]	Herbst		10/19 52.6%					
Ferguson[9]	Silencer		11/20 55%					
Ferguson[10]	SnoreGuard		12/25 48%					
Gao[28]	MRA		7/11 63.6%					
Gavish[29]	MRA		4/10 40%					
Gotsopoulos[5]	MRA	21/73 29%						
Hans[21]	SnoreGuard		4/13 31%	7/13 54%		7/13 54%		
Henke[30]	MRA		9/28 32%	12/28 43%		19/28 68%		
Ishida[31]	MRA					13/19 68%		
Johnston[7]	MRA		6/18 33%		9/18 50%			
Liu[32]	MRA		13/22 59%					
Lowe[33]	Klearway			27/38 71% Moderate (AHI 15-30) 16/20 80% Severe (AHI>30) 11/18 61%				
Marklund[35]	MRA		19/33 58%					
Marklund[34]	MRA		28/44 64% Mild (AHI<20) 17/21 81% Moderate (AHI 20-40) 9/15 60% Severe (AHI≥40) 2/8 25%			23/24 52% Mild (AHI<20) 10/21 48% Moderate (AHI 20-40) 10/15 67% Severe (AHI≥40) 3/8 38%		
Mehta[4]	MRA	9/28 32%	14/28 54%	21/28 75%				
Menn[36]	MRA		12/23 52.2%					16/23 70%
Millman[37]	Herbst		10/24 42%	14/24 58%		13/24 54%		
Neill[38]	MRA	4/19 21%						
Ng[39]	MRA	5/10 50%	6/10 60%					
O'Sullivan[40]	MRA				14/26 54%			
Pancer[41]	TAP		38/72 53%			61/75 81%		
Pellanda[42]	Serenox		9/15 62%					13/15 86.7%
Pitsis[8]	MRA	13/24 57%						
Randerath[13]	ISAD		6/20 30%					
Rose[22]	Silencor	6/21 29%	13/21 62%			11/21 52%	10/21 48%	
	Karwetzky	9/23 39%	14/23 61%			15/23 65%	10/23 43%	
Rose[43]	Karwetzky	58/81 72% All 27/31 87% Mild AHI 5-15 24/33 73% Moderate AHI 15-30 7/17 17% Severe AHI>30						
Sanner[25]	MRA						7/13 54%	
Schönhofer[44]	SnorBan		11/22 50%		14/22 64%		11/22 50%	
Schönhofer[45]	SnorEx –TD			6/23 26%				
Skinner[46]	TAP		7/14 50%	11/14 79%				
Tan[12]	Fixed MRA		9/14 64%					
	Silensor		7/10 70%					
Walker-Engström[15]	MRA @75%		22/42 52%					
	MRA @50%		13/42 31%					
Wilhelmsson[16]	MRA		29/37 78%					
Yoshida[47]	MRA		138/256 54%			169/256 66%		
Yoshida[48]	MRA		38/72 53%			44/72 61%		

MRA, the presence of positional sleep apnea (higher AHI in the supine than in the lateral sleep position), and the body mass index (BMI).

3.2.4.1 Severity of Respiratory Disturbance

There were 9 studies that analyzed the success of the treatment by the severity of the OSA.[13,33,36,38,40,41,43,52,53] Most of these studies found lower success rates in more severe OSA (as defined by AHI). The success rates in mild to moderate OSA averaged 57 to 81%. Success rates ranged between 14 and 61% among those subjects who were classified as severe (AHI defined as >30 in some studies and >40 in others). Comparisons between these studies are difficult as they differ in the definition of success (e.g., AHI less than 10 events per hour or a 50% reduction in the AHI). In addition, the devices involved varied in their design characteristics, for example, some could be titrated to an optimal position of advancement whereas others were single position. Several appliances were evaluated in more than 1 study (see Table 3). Different inclusion criteria and different treatment protocols may have affected the success rates in different studies using the same device. Overall, better success rates were seen in patients with lower AHI.

3.2.4.2 Degree of Protrusion

The degree of protrusion of the mandible varied from 6 to 10 mm. or from 50 to 75% of the maximum the patient could protrude the mandible on request. Mehta and coworkers[4] compared the patients' response to 2 devices, 1 that protruded the mandible and 1 that did not. The placebo device did not improve the AHI suggesting that it is protrusion that is necessary for the OA to be effective. Several studies have reported that increased amounts of mandibular protrusion produce greater reductions in respiratory events.[15,22,26,34,54] or in the number of 4% oxygen desaturations occurring during nocturnal oximetry.[55] The study by Walker-Engström and colleagues compared 2 different degrees of mandibular protrusion – 50% or 75% of maximum using the same device in both groups.[15] The MRA set at 75% reduced the AHI to < 10 in 52% of patients whereas the MRA set at 50% of maximum reduced the AHI to < 10 in 31% of patients. They did not find increased side effects with more protrusion. Some authors have found that increased protrusion may be more likely to cause occlusal change[56] but not all studies have found this relationship.[57]

Some studies assessed the amount of vertical opening of the OA and its impact on efficacy or side effects.[8,22,57,58] In 1 study[8] greater vertical opening caused more jaw discomfort but did not have an impact on efficacy. In another study[22] the authors compared appliances with different amounts of vertical opening - 1 was open 10 to 12 mm and the other MRA had 5mm of opening. The appliance with the greater opening was slightly more effective at lowering the AHI. The effect of the amount of vertical opening on efficacy and complications is unclear and further investigations are required.

3.2.4.3 Positionality of Sleep Disordered Breathing

Five studies[38,47,49,53,59] evaluated the severity of the breathing disorder by the rate of respiratory events in different sleep positions. Three studies[47,49,53] reported that there was a greater likelihood of success with OA therapy when the difference in the rate of respiratory events between supine and lateral sleep was larger. Two other studies[38,59] did not find that supine dependent OSA was associated with greater treatment success.

Table 3—Independent Studies With Same Device

Author	N	Device	Selection	Percent Success	ESS *		AHI		Follow-up Time	Protrusion
					Pre	Post	Pre	Post		
Barthlen[24]	8	Snore Guard	Severe OSA (AHI 25 to 137)	5/8 62% (AHI<15)			72.1±39.9	35.5±39.4	8 months	3-5mm
Ferguson[10]	25	Snore Guard	Mild to Moderate OSA (AHI 15-30)	12/25 48% (AHI<10)			19.7±13.8	9.7±7.3	4 months	7mm 7mm vertical
Hans[21]	13	Snore Guard	13 with OSA (AHI>10)	4/13 31% (AHI<10)	12.0±3.9	8.2±4.0	53.9±35.6	36.5±43.7	2 weeks	6-8mm 8 vertical
Bloch[14]	24	Herbst	AHI ≥ 5 or UARS unwilling and/or unable to use CPAP	16/24 66% (AHI<10)	13.1±0.9	8.8±0.7	22.6±3.1	8.7±1.5	1 week	10mm protrusion advanced as needed vertical 5-10 mm
Eveloff[27]	24	Herbst	OSA (AHI ≥ 10) CPAP failures or Patient choice	10/24 42% (AHI<10)			34.7±5.3	12.9±2.1	13 months	Individualized
Clark[23]	23	Herbst	OSA (AHI>15)	4/21 19% (AHI<10)			33.9.±14	19.9±12.8	2 weeks	65% of maximum protrusion
Millman[37]	24	Herbst	UPPP failures and AHI>10	10/24 42% (AHI<10)			37.2 ± 7.1	15.3±4.4	13 months	66-75% of maximum protrusion
Pancer[41]	75	TAP	Snoring or Mild to Severe OSA (72 had OSA)	38/72 53% (AHI<10)	11 ± 5	7 ± 3	44 ± 28	12 ± 15	12 weeks	Self-adjusted
Skinner[46]	14	TAP	Mild to Moderate OSA (AHI 10-40) or Severe OSA and CPAP failure	7/14 50% (AHI≤10)	12 ± 5	6 ± 4	34 ± 22	10 ± 5	6-8 weeks	Self-adjusted

* ESS=Epworth Sleepiness Scale

3.2.4.4 Effect of Body Mass Index

A higher body mass index (BMI) was associated with lower efficacy of the MRA in several studies[15,43,52] but not in all studies.[16,38] There is a relationship between BMI and positionality of sleep apnea with the higher the BMI the less likely there will be a marked difference in severity by sleep position. One long-term study found that weight gain was adversely associated with efficacy of the MRA.[49]

3.2.4.5 Summary and Conclusions Regarding Efficacy of Oral Appliances

Although the literature on efficacy shows a growing quality of the studies from those reported on in the previous review, there are many questions still to be answered fully. On the positive side there are more studies with large numbers of patients -- Barnes, 2004[6] N=85, Pancer, 1999[41] N=72, Yoshida, 2000[47] N=256 and Gotsopoulos, 2002[5] N=73. There are also better-designed studies, particularly randomized placebo controlled trials, as well as the use of crossover studies with the same subjects being given an oral appliance and CPAP in turn, or 2 different oral appliances. There are also longer-term follow-up studies assessing effectiveness over time. Two studies were as long as 4 and 5 years.[20,35] Nonetheless, there are still many issues remaining that need to be addressed. A central issue is the need to establish a uniform definition of treatment success that includes both objective criteria (AHI and oxygenation) along with symptoms (snoring and sleepiness). A second issue is that the patient characteristics associated with treatment success need to be fully determined. Most of the studies are significantly underpowered to find predictors of treatment outcome. A meta-analysis with pooling of data might be able to find what variables consistently predict treatment outcome. Additionally, the degree of severity is usually not reported separately for the lateral and supine sleep positions. This was recommended in the AASM guidelines.[1] Since the rate of breathing disturbance is often elevated in supine sleep and patients with more OSA when supine seem to achieve better results with an OA, the importance of obtaining this measurement should be emphasized.

Overall, those with mild to severe OSA have a 52% chance of being able to control their sleep apnea using an appliance. OAs are on the whole less effective than CPAP but may be better accepted by patients than nasal CPAP in studies where subjects used both treatments.[6,9,10,23] OA are not recommended as a first line treatment in patients with severe OSA (AHI greater than 40). However, these patients might consider an OA if they have failed CPAP[27] or upper airway surgery,[37] recognizing that the results of OA therapy in severe OSA are unpredictable.

3.3 Mechanisms of Action of Oral Appliances

Oral appliances may improve upper airway patency during sleep by enlarging the upper airway and/or by decreasing upper airway collapsibility (e.g., improving upper airway muscle tone).

3.3.1 Effects of Mandibular and Tongue Advancement on Upper Airway Size

Studies of the effect of OAs on upper airway size have found different effects. The differences are likely related to the differences in methodology. Simple active anterior movement of the tongue or mandible can increase cross sectional airway size in subjects with and without OSA.[60] Passive mandibular advancement during general anesthesia stabilizes the upper airway by increasing airway size in both the retropalatal and retroglossal area and by reducing closing pressure.[61]

Several studies have evaluated the effects of MRAs on upper airway size using upright lateral cephalometry with the films taken during wakefulness. These results are sometimes conflicting. In 2 studies an MRA increased the posterior airway space (PAS) in the majority of subjects.[62,63] In another study where the amount of protrusion was individualized in each patient there was no change in the size of the PAS with the appliance.[27] Other studies using upright lateral cephalometry have shown that MRA lower the tongue position, reduce the mandibular plane to hyoid distance (MPH), advance the mandible and widen the upper oropharynx (retropalatal and retroglossal) in some subjects.[32,62,64,65] One device opened the mandible (inter-incisal distance) by 12 to 18 mm and advanced the mandible by 3 to 5 mm increased airway size but caused the MPH distance to increase.[66]

Similar reductions in MPH,[67,68] and increases in airway size and cross-sectional area at multiple levels[65,67-71] have been seen using supine cephalograms.

Other imaging modalities (e.g., computed tomography, magnetic resonance imaging) have also demonstrated increases in pharyngeal airway size[28,62,72] and volume.[73] Direct imaging of the awake supine airway with videoendoscopy confirms that an MRA increases the cross-sectional area of the airway particularly in the velopharynx.[74]

Some studies have shown that greater amounts of mandibular protrusion are related to the ability of the appliance to reduce the AHI.[15,22,34,54] This suggests that increases in airway size are at least part of the mechanism for the effect of the MRA on apnea severity.

3.3.2 Effects of Mandibular and Tongue Advancement on Upper Airway Muscle Tone

Tongue retaining devices (TRDs) affect genioglossus muscle activity in patients with OSA (awake or asleep) but effects of the TRD on other upper airway muscles have not been evaluated.[75,76] A TRD worn during sleep with the tongue in the bulb reduced the AHI and decreased genioglossus EMG activity.[75,76] The mechanism for this effect is not certain.

One study found that upper airway muscle tone increased with an MRA except in the post-apnea period in the genioglossus where tone was lower.[77] Another study also found augmentation of genioglossus tone with mandibular advancement.[78] These studies suggest that activation of the upper airway muscles may contribute to upper airway patency. In a more recent placebo controlled trial the simple presence of an OA had no impact on the AHI or on oxygen saturation.[4] This study suggests that mandibular advancement is required for the appliance to improve OSA because the presence of an OA without advancement showed no clinical effect.

In summary OAs may increase upper airway size at multiple levels and this may be important in producing their clinical effect. Greater amounts of mandibular protrusion are associated with greater efficacy of the appliance in reducing the AHI. In addition to increasing the size of the upper airway, OAs may also improve upper airway tone. Whether this is a clinically important effect is uncertain.

Table 4—Reviewed Publications Reporting Side Effects and Patient Compliance

Author	N	Device	Side Effect or Complication	Frequency	Compliance	Length of Follow Up
Barthlen[24]						
(Level V)	8	Snore Guard	Minor/transient TMJ pain, salivation	Not stated	8/8	8 months
		TD	Tongue pain (severe)	3/8	5/8	8 months
		SPL	Gagging (severe)	6/8	2/8	8 months
Bloch[14]	24	Herbst	TMJ pain	7/24	100% using 4 to 7	22 weeks
(Level I)		Monobloc	Muscle discomfort	4/24	nights/week	
			Dental discomfort (all transient, minor)	3/24		
Bondemark[84]	32	MRA	Dental pain, salivation,	8/32	32/32	2 years
(Level V)			jaw stiffness	5/32		
			Muscle tenderness	3/32		
			Joint sounds	2/32		
			Deviation of mandible < 2 mm (all minor, transient)			
Cameron[79]	16	MRA	Unable to wear	2 of 16	14 of 16	4 weeks
(Level V)	(9 OSA RDI>10)		Transient uncomfortable teeth and jaw muscles, salivation	"Occasional"		
Clark[23]	23	Herbst	Severe TMJ pain	1 of 23	17 of 23 using nightly	3 to 10 months
(Level III)			Occasional TMJ pain	2 of 23	2 of 23 using occasionally	
Clark[80]	53	Herbst	Jaw or facial muscle pain	40%	32 of 53 using	1 year
(Level V)			Tooth pain	38%	regularly	2 years
			Jaw joint pain	30%	24 of 50 using	
			Dry mouth	30%	regularly	
			Temporary occlusal change self report	15%		
			Permanent occlusal change self report	26%		
Engleman[11]	48	MRA	Tooth, jaw or gum pain	69%	79% using > 3 hours	8 weeks
(Level I)			Excessive salivation	19%	per night	
			Poor retention	40%		
			Sleep disruption	25%		
			Dental crown damage	6%		
Eveloff[27]	19	Herbst	Muscle or TMJ discomfort or pain	None at follow-up	Not stated	13 months
(Level V)						
Ferguson[9]	20	Silencer	Sore teeth or muscles, salivation	13 of 20	70% using 7 nights	4 months
(Level I)			Mild side effects	45%	per week	
			Moderate Side effects	20%	25% using 5 nights	
			Severe effects	0%	per week	
			No side effects	35%	5% using 2 night per	
			TMJ dysfunction	0%	week	
Ferguson[10]	25	Snoreguard	Sore teeth, sore jaw, salivation	15 of 25	60% using 7 nights	4 months
(Level I)			Mild side effects	36%	per week	
			Moderate side effects	20%	36% using 5 nights	
			Severe Side effects	4%	per week	
			No side effects	40%	4% using 2 nights	
			TMJ dysfunction	0%	per week	
			Poor retention	24%		
Fritsch[81]	22	Monobloc or Herbst	Dry mouth	19 of 22	100%	Median 14 mos
(Level V)		(mostly minor and same	Tooth discomfort	13 of 22		
		for both appliances)	Salivation	12 of 22		
			Jaw pain	9 of 22		
			Stiffness/pain of muscles	8 of 22		
			Loosening of teeth	2 of 22		
Johnston[7]	18	MRA	Unable to tolerate	1	68% using every or	4 to 6 weeks
(Level II)			Excessive salivation	68%	almost every night	
			Temporary occlusal change in am	44%	79% using ≥ 4 hours	
			Temporary TMJ discomfort in am	42%	per night	
			Persistent occlusal change	10%		
			Persistent TMJ discomfort	1		
Kato[55]	37	MRA	Excessive salivation			
(Level V)			Transient discomfort or pain of the TMJ briefly after awakening	Common	Not stated	Not stated

Table 4—Continued

Liu[52] (Level V)	47	Klearway	Minor/transient salivation, mild jaw muscle and/or tooth discomfort	Not stated	Not stated	Not stated
			Occlusal changes	None		
Liu[32] (Level V)	22	MRA	Minor/transient TMJ or incisor discomfort	3 of 22	100%	6 months
			Salivation; resolved after 1 week	4 of 22		
Lowe[33] (Level V)	38	Klearway	Minor/transient salivation, jaw muscle and tooth discomfort	Not stated	8 -compliance Mean use = 6.8 hrs/night. Range = 5.6 - 7.5hrs	7.7 months
			Persistent mild TMJ and muscle pain	1 of 38		
			Occlusal change	0 of 38		
Marklund[35] (Level V)	33	MRA	Transient occlusal change	2 of 19	19 of 33 using 50 - 90% of nights/wk	5 years
			Decreased overjet; mean 0.9mm	1 of 33		
McGown[82] (Level V)	84 with OSA (AHI>10) and 42 snorers	Herbst and Modified Silensor	Discomfort	36%	69 of all 126 (55%) using regularly 51 of 84 with OSA (61%) using regularly 47 of 69 regular users wore nightly averaging 6.6h/night	Median 21 months
			TMJ pain	37%		
			Sleep disturbance	17%		
			Salivation	10%		
			Altered bite	13%		
			Occurred every night	41%		
			Discontinued due to discomfort	23%		
Mehta[4] (Level II)	24	MRA	Mild-mod/transient:		21 of 24 used nightly	Acclimatization period followed by one week of treatment
			Excessive salivation	50%		
			Gum irritation	20%		
			Mouth dryness	46%		
			Jaw discomfort	12.5%		
			Tooth grinding	12.5%		
Menn[36] (Level V)	29	MRA	Discomfort causing initial drop-out	3 of 29	16 of 23	Mean 3.4 years
			TMJ discomfort causing discontinuation over the long term	4 of 23		
			Significant/chronic TMJ problems	0 of 23		
Millman[37] (Level V)	24	Herbst	Discomfort, poor efficacy or poor retention causing early discontinuation	6 of 24	Not stated	13 months
Neill[38] (Level V)	19	MRA	Side effects causing discontinuation	5 of 19	53% used nightly 26% used > 3 nights/wk 21% used < 3 nights/wk 79% used all night	Median 6.5 weeks
			Mild side effects:	10 of 19		
			Jaw pain	5 of 19		
			Sore teeth and gums	8 of 19		
			Excessive salivation	2 of 19		
			Choking	2 of 19		
			Difficulty breathing	2 of 19		
			Poor retention	Not stated		
O'Sullivan[40] (Level V)	57	MRA	Mild and usually transient			Mean 3.5 months
			Mild jaw discomfort	38 of 57	45 of 57 used nightly 7 of 57 used occasionally 2 of 57 used rarely	
			Excessive salivation	11 of 57		
			Dry mouth	12 of 57		
			Bruxism	3 of 57		
			Gum irritation	4 of 57		
Pancer[41] (Level V)	121	TAP	Side effects sometimes/often:		86% used nightly	Average 1 year
			Tooth discomfort	60%		
			Gum discomfort	9%		
			Tongue discomfort	10%		
			Excessive salivation	48%		
			Jaw discomfort	40%		
Pantin[57] (Level V)	132	MRA	Mild / Temporary:		76% used nightly	Mean 31 ± 18 months
			Excessive salivation	30%		
			Dry mouth	23%		
			TMJ pain	26%		
			Dental discomfort	26%		
			Myofacial discomfort	25%		
			Occlusal changes	12%		
			Side effects causing discontinuation	8 of 132		
			Including TMJ pain	2 of 132		

Table 4—Continued

Rose[22] (Level II)	21	Silencor	Unable to tolerate	1 of 21	18 of 21 used nightly for at least 6 hours	6 to 8 weeks
			Temporary excessive salivation and tooth and gingival pain	Not stated		
	23	Karwetzky	Unable to tolerate – muscle pain or TMJ pain or excessive gag	3 of 23	20 of 23 used nightly for at least 6 hours	
			Temporary muscle or TMJ pain	5 of 23		
			Temporary excessive salivation	Not stated		
Rose[85] (Level V)	34	MRA	All described as minor:		Not stated	30 months
			Salivation	4 of 34		
			Dry mouth	2 of 34		
			TMJ pain	3 of 34		
			Muscle pain or stiffness	6 of 34		
			Tooth discomfort or pain	4 of 34		
			Occlusal change	2 of 34		
			Significant TMJ problems	0 of 34		
Schönhofer[44] (Level V)	22	SnorBan	Minor pain in TMJ	4 of 22	19 of 22	3 months
			Minor tension in muscles	4 of 22		
			Minor salivation	9 of 22		
			Minor gingival pressure marks	10 of 22		
			Minor oral narrowness	5 of 2		
			Severe TMJ pain, salivation, gingival pressure causing discontinuation	3 of 22		
Skinner[46] (Level V)	14	modified TAP	Excessive salivation	7%	13 of 14 using nightly at 6 to 8 weeks with mean use 5.5 ± 2 hrs/night 57% using nightly after 1 yr	6 to 8 weeks 1 year
			Minor/transient tooth discomfort	28%		
			Poor retention	21%		
			Side effects causing discontinuation	0%		
			TMJ pain	0%		
Tan[12] (Level I)	24	One piece MRA 10 Silensor 14	Mild jaw discomfort upon awakening	50%	Not stated	2 months
			Unable to tolerate	1 of 24		
Walker-Engstrom[15] (Level I)	32	MRA	Minor changes in occlusion	4 of 32	82%	1 year
			Major occlusal change and TMJ pain	1 of 32	62%	4 years
			New TMJ sounds	3 of 32		
Wilhelmsson[16] (side effect and compliance data in Tegelberg[17] (Level I)	49	MRA	Drop out due to side-effects (11 drop out due to other reasons)	1 of 49	73% using ≥ 5 nights per week	12 months
			Transient excessive salivation	4 of 37		
			Minor jaw stiffness	8 of 37		
			Minor/transient TMJ pain	1 of 37		
			Minor dry mouth	5 of 37		
			Severe TMJ dysfunction	2 of 37		
			Occlusal change	0 of 37		
Yoshida[47] (Level V)	232	MRA	Minor/transient TMJ or muscle pain	22 of 232	90% compliant (compliance not defined)	30.5 months
			Minor/transient salivation and dental pain	Not stated		
			Significant TMJ or muscle pain causing discontinuation	5 of 232		
Yoshida[48] (Level V)	72	MRA	Minor/transient TMJ pain, muscle pain	Not stated	Not stated	36 days
			Serious complications	None		

3.4 Treatment Adherence

The adherence data were based on patient self-reports except for 1 study that employed a compliance monitor (Table 4). The investigations focused on overall use during an extended period of time from 4 weeks to 5 years. The studies assessed appliance use on the number of days per week and the number of hours per night the appliance was worn. Overall adherence rates varied greatly between the different studies and this may be related to appliance design and to the follow-up protocol.

Only 1 study assessed the difference between categories of appliances (i.e., tongue devices (TD) versus MRAs[24] whereas all other reports evaluated MRAs. In this study, with an 8-month average follow-up, 100% adherence was seen in 8 patients with the MRA, 62% with the TD (5 of 8 patients) and 25% with the soft palatal lifter (2 of 8 patients). All 8 patients were tested with all 3 devices. Reasons for non-compliance were severe tongue pain (while using the TD) and gagging (with the soft palatal lifter).

Twelve studies evaluated self-reported adherence over a time period of less than 1 year. Adherence ranged from 100% with

an MRA[24,52] to 25%[24] in 2 of the reports, while the remaining investigations[10,20,23,38,40,41,44,46,79,80] reported adherence within the first year of a median use of 77% of nights at 1 year (studies included a median of 25 patients, range 8 to 121 patients). All but 1 of these investigations documented initial dropouts due to appliance intolerance, temporomandibular joint (TMJ) problems, refusal of CPAP (in a cross-over study), or failure to keep appointments. These dropouts ranged from 0 to 3 patients per study with none lost to follow up. In 1 study,[41] 13 of 134 (10%) patients were lost to follow up. In all of the investigations, the adherence was calculated based on those patients who completed the study and who were available for follow up.

Five reports assessed adherence rates between 1 and 2 years of treatment. Two reports used a "2-year follow up" whereas the others used a mean follow up of 24, 20 and 21.5 months. Adherence was 100%[58,81] in 2 of the studies, while the remaining trials[27,82,83] had a median adherence between the first two years of 76% (respective rates of 93, 55 and 83%). These studies also calculated adherence based on the reports of patients who completed the study and who were available for follow up. Two of the studies[58,81] had no dropouts and all patients were available for follow up (32 of 32 and 22 of 22 patients respectively). The remaining studies listed reasons for not completing the study as ineffectiveness, failed appointments, significant weight loss and appliance intolerance. Loss to follow up was described as due to change in residence, no telephone available and questionnaire not returned. The percentage of those original patients who completed the study and who were available for follow up ranged from 73% (14 of 19) to 100% (32 of 32). The largest study[82] had 76% (126 of 166) complete and available for follow up.

Five investigations evaluated adherence after a period of between 2 years and 5 years. Self-reported adherence rates ranged from a median of 48%[80] to 75%[35,36,57] to 90%[47] Adherence rates were based on those patients who completed the study and who were available for follow up which ranged from 100%[35] to 69%.[57]

Adherence rates tended to decrease with duration of use, with 1 study reporting 60% adherence at 1 year and 48% at 2 years.[80] Another report cited an adherence drop from 82% to 62% from year 1 to year 4.[20] These reports assessed 53 and 32 patients, respectively. The reasons for discontinuing appliance use included side effects, complications, and lack of efficacy.

Three reports indicated that all compliant patients used the device every night.[4,41,57] However, 7 studies showed that an average of 68% of patients used the device every night, 23% several nights per week and 8% less than several nights per week.[9,10,35,38,40,82,83] The patients evaluated for adherence were those who completed the protocol and were available for follow up.

Reported rates of adherence with the MRA were similar to the reported adherence rates with CPAP in 2 of the crossover studies.[9,10]

Two studies evaluated the numbers of hours per night that an appliance was used by the patient.[38,82] In 1 study the subjects reported an average use of 6.6 hours per night and the other reported "all night" use. In the only study using objective monitoring with a novel intra-oral compliance monitor, the authors found that patients averaged 6.8 hours of use per night with a range of 5.6 to 7.5 hours.[33] This objective data is in the same range as the patient self-reported hours of use.

3.5 Adverse Events

Thirty-eight articles evaluated more than 1,700 patients for side effects and complications from OAs in snoring and OSA patients (Tables 4 and 5). Surveys were used most often as the method to obtain information on side effects; however, tooth movement, skeletal changes and occlusal alterations were objectively quantified in some studies (Table 5).[56,57,81,83-86] Lack of a standard therapeutic protocol in the use of appliances and differences in appliance design confound the precise evaluation of side effects and complications from OA therapy. The vast majority of investigations focused on MRAs. Only 1 study looked at a TD and the soft palate lifter.

The available research suggests that side effects and complications may be grouped as follows:

1. Minor and temporary. These can occur at any stage during treatment, are minor in severity, tend to resolve in a short period of time or are easily tolerated if they do not resolve and they do not prevent regular use of the appliance
2. Moderate to severe and continuous. These can occur at any stage during treatment, are moderate to severe in intensity, tend not to resolve over time and may result in discontinuation of appliance use.

Commonly reported minor and temporary side effects included TMJ pain, myofascial pain, tooth pain, salivation, TM joint sounds, dry mouth, gum irritation and morning-after occlusal changes. These phenomena were observed in a wide range of frequency from 6% to 86% of patients.[4,32,33,38,40,41,44,52,57,81,84,85] Most authors described these effects as "transient", or "minor" and reported resolution within several days to several weeks with regular use and occasional adjustment of OA fit. There was no difference in the frequency of side effects between the Level V and the Level I and Level II studies.

More severe and continuous side effects included TMJ pain, myofascial pain, tongue pain (tongue devices only), gagging (soft palate lifter mostly), tooth pain, gum pain, dry mouth and salivation. Occasionally, these phenomena prevented continued use of the appliance.[24,36,38,57] Observation of these effects occurred within a range of 0% to 75% of patients.[9,10,20,23,24,36,38,44,47,57] Significant and persistent TMJ problems were rare. There was no difference in the frequency of more severe side effects or complications between the Level V and the Level I and II studies.

Four studies focused on the differences in appliance design (3 Level V, 1 Level III and 1 Level I). Two of the studies compared a non-adjustable, mono-block appliance with an adjustable 2-piece appliance and found no difference in side effects—Bloch[14] (Level I) and Fritsch[81](Level V). Another study compared hard versus soft appliances (both non-adjustable) and found more pronounced side effects with the hard appliance[56] (Marklund, Level III). One other study compared a non-adjustable, mono-block appliance with a tongue retaining device and a soft palate lifter[24] (Barthlen 2000 Level V). Severe gagging prevented use of the soft palate lifter in 6 of 8 patients and severe tongue pain prevented use of the TD in 3 of 8 patients.

Tooth movement, skeletal changes and occlusal alteration were studied in several Level V studies and 1 Level III study.[23] A mean decrease in overbite and overjet was reported in 7 studies[35,56,57,81,84-86] An anterior shift of the lower first molar was ob-

Table 5—Dental, Cephalometric and Occlusal Changes after Long-Term Oral Appliance Therapy

Author	N	Device	Dental, Cephalometric, Occlusal Changes	Frequency	Length of Follow Up
Bondemark[84] (Level V)	32	MRA	Dental tenderness, salivation, jaw stiffness,	8 of 32	2 years
			Dental cast analysis showed:		
			Mean decrease in overjet of 0.4mm		
			Mean decrease in overbite of 0.1mm		
			Molar relationship - more mesial sagittal		
Fransson[83] (Level V)	65	MRA	9% increase relative area of pharynx		2 years
			8% decrease area of velum		
			Proclined lower incisors by 1.5 deg		
Fritsch[81] (Level V)	22	Monobloc or Herbst	Cephalometric measurements:		Median 14 mos
			Mean retrusion of upper incisors (minor)		
			Mean decrease in SNB angle (minor)		
			Dental cast analysis:		
			Decrease in overjet mean -0.2mm		
			Decrease in overbite mean -0.4mm		
			Mesial displacement of mand. 1st molar mean -0.2mm		
Marklund[35] (Level V)	33	MRA	Transient occlusal change resolved during the day	2 of 19	19 patients at 5 years
			Decreased overjet: mean 0.9 mm		
Marklund[56] (Level V)	75	MRA – hard acrylic in 28 patients	Decreased overjet; median -0.6mm		Median 2.5 years
			Decreased overbite; median -0.5mm		
		Dental cast analysis	Mesial shift in mandibular 1st molar; median -0.5mm		
			Increased max. arch width 1st molar; median 0.1mm		
			Increased mand. arch width 1st molar; mean 0.2mm		
		MRA – soft acrylic in 47 patients	Decreased overjet; median -0.2mm		Median 2.2 years
		Dental cast analysis	Decreased overbite; median -0.3mm		
			Mesial shift in mandibular 1st molar; median -0.1mm		
			Increased max. arch width 1st molar; median 0.3mm		
			Increased mand. arch width 1st molar; median 0.2mm		
		Both appliances (no difference by device)	Subjective reports of occlusal change:		
			No observed effect on dentition	37 of 69	
			Changed in morning, resolved during day	28 of 69	
			Permanent change in occlusion	3 of 69	
			Unsure	1 of 69	
			Upper central incisor became elongated	1 of 69	
Pantin[57] (Level V)	132	MRA	Dental analysis:		Mean 31 months
			Joint noise; not originally present	8%	
			Increased mouth opening	28%	
			Decrease in overjet; 1 - 3mm	14%	
			Not aware of real change in occlusion	8 of 15	
			Erroneously perceived changed occlusion	9 of 16	
Robertson[86] (Level V)	100	MRA	Cephalometric changes:		6 - 30 months (6 month review intervals)
			Vertical condylar position		
			Increase in vertical face height		
			Dentoalveolar measurements:		
			Retroclination of upper incisors; 1.88 deg.		
			Proclination of lower incisors; 2.81 deg.		
			Decreased overbite; 1.02mm		
			Decreased overjet; 1.06mm		
Rose[85] (Level V)	34	MRA	Cephalometric analysis:		Mean 29.6 months
			Decrease overjet; mean 1.3mm		
			Decrease overbite; mean1.1mm		
			Lingual inclination of upper incisors		
			Labial inclination of lower incisors		
			Dental cast analysis:		
			Decrease overjet > 1mm	26%	
			Anterior positioning of the lower molar >1mm	23.50%	
			Posterior open bite	26%	

served in 4 studies.[56,81,84,85] Other changes included retrusion of upper incisors, protrusion of lower incisors and decrease in SNB angle.[81,83,85] Several other reports documented changes in arch width, joint noise, increased mouth opening, change in vertical condylar position, and increased face height.[56,57,86]

One report concluded that changes in the angulation of incisors tended to occur with increasing length of treatment, while conversely, skeletal changes tended to occur soon after the onset of treatment and were most likely attributed to a repositioning of the head of the condyle within the glenoid fossa.[86] In this study,

changes in the condylar vertical position were initially observed at the 6-month review period. Changes in the angulation of the incisor teeth were not evident then. Similar changes were evident at the 18-month review period with further retroclination of the maxillary incisors, along with significant reduction in overbite and overjet. Following 24 months of treatment, the first changes in mandibular incisor position were observed, with proclination of these teeth of a mean 2.2 degrees. The most significant dental changes were observed after 30 months of treatment with a mean 4.9 degrees proclination of the mandibular incisors and a reduction in overbite of a mean 1.82 mm. Another study concluded that overall, the changes observed were minor and clinically irrelevant, although in some cases they were more pronounced and therefore of clinical importance.[85] No relationship was found between manifestation of side effects and the degree of protrusion or the initial malocclusion.[57] Both of these studies were at evidence Level V.

Pantin and colleagues contacted 191 patients treated with an MRA over a 5-year period.[57] This study was evidence Level V. One hundred thirty-two patients agreed to a questionnaire survey with 106 agreeing to present for a clinical examination by a dentist.[57] Occlusal changes were assessed using shimstock passed through the occlusion with the patient biting in centric occlusion. In addition, a wax bite was taken to record the interarch relationship. This new bite registration was compared with the original bite registration. Fifteen of the 106 patients (14%) who were clinically examined after 5 years of treatment had evidence of occlusal change. Interestingly, 8 of these 15 patients were not aware of these changes. Conversely, 9 of 16 patients who reported bite changes had no clinical evidence of such changes.

The patients in the Pantin study[57] who were found to have occlusal changes were managed "conservatively", using temporary cessation or reduction in the use of the device together with remedial exercises each morning following appliance removal. The authors found that this approach was effective in many of the cases. The authors suggest that careful monitoring by a qualified dentist is central to the management of this complication and it may be reasonable to continue with treatment in the presence of occlusal change so long as it is not associated with unacceptable symptoms, is not overly progressive and that there is adequate posterior support. However, failure to respond to conservative management, especially if there is loss of posterior support, may necessitate permanent treatment cessation. This was the case with 2 of the patients in the Pantin study. However, this presents a clinical dilemma when the patient is unconcerned about the occlusal change and refuses to abandon the appliance citing that the perceived benefits of treatment outweigh the dentist's concern with the altered occlusion.

The Pantin group showed no relationship between the degree of mandibular advancement during treatment and the magnitude of occlusal alteration suggesting that any degree of mandibular advancement could cause occlusal changes in predisposed individuals. In addition, the absence of a relationship between class of pretreatment malocclusion and magnitude of occlusal change suggests that such a predisposition cannot be predicted from the characteristics of the occlusion before treatment in their population of 106 patients. The proportion of patients with occlusal changes increased with length of use up to 2 years and remained relatively constant thereafter. It appears that the patient's greatest period of vulnerability to occlusal changes is within the first 2 years of treatment.

3.5.1 Conclusion Regarding Complications of Oral Appliances and Implications for Follow-up for Oral Appliance Therapy

In conclusion, these investigations show that there are many potential side effects and complications associated with OA therapy but most are minor and temporary and do not significantly affect appliance use. Many of the minor side effects (discomfort or excessive salivation) improved even with continued appliance use. However, others are more significant and do not necessarily resolve over time and may lead to discontinuation of OA treatment. Some of the bite changes did not resolve with cessation of therapy and more information is needed about the significance of these occlusal changes and the risks of long-term appliance use. Conceivably, these changes may be due to frank tooth movement, remodeling of the TMJ complex or neuromuscular adaptation that may have an influence on the posture of the mandible. The response of some patients to exercises suggests that it may be related to a failure to reposition the mandible into the glenoid fossa. Additional cephalometric, radiographic and clinical studies are needed to elucidate the importance of these changes.

3.6 Comparison of Oral Appliance Therapy with Other Therapies

The major advance in the clinical science of OA therapy is its evaluation in controlled clinical trials. In comparison to the case series reviewed in 1995,[3] more recent studies with improved design have compared OA to CPAP, OA to palatal surgery, and several OA types to each other (Tables 6 and 7). The list includes 13 studies with Level I-V evidence grade. These studies have helped define the role of OA in the context of the other commonly used therapies.

MRA have been compared to CPAP in seven studies, six Level I-II studies (Tables 6 and 7) and 1 Level III study. In each study, the design was a crossover of the 2 treatments with random allocation of order. Efficacy was compared to baseline at the end of treatment periods from 2 weeks to 4 months with 1 to 2 week separation or 'wash-out' periods between the treatments. The 2 most recent studies[6,11] had substantial numbers of patients, 51 and 104 respectively. Thus based on consideration of methodology as well as the consistency of findings, this literature appears valid and credible.

In each of the crossover studies CPAP reduced the AHI to low levels in nearly all patients, whereas OA failed to do so in a third or more of patients (Table 6). There was little or no effect on other outcomes between the 2 therapies. For example, in a study of mild-moderate OSA,[6] CPAP and OA significantly improved sleepiness and other neurobehavioral outcomes over placebo, but the difference between the therapies was not significant over a broad range of outcomes. In a group of more severe patients,[11] CPAP produced a better effect than OA on subjective but not objective sleepiness as well as on several functional outcome scales. One potential explanation for this discrepancy in outcomes is imperfect treatment adherence with CPAP and better acceptance of the OA. In 1 study, average CPAP use was 4.2 nights per week for 3.2 hours per night (objective time counter), compared to OA use of 5.3 nights for 5.5 hours per night (by diary).[6]

The effect on treatment preference is complex (Table 6). Patients may find OA therapy easier to use than and this might translate to a preference for OA therapy in the earlier studies. Howev-

Table 6—Comparison of OA to Other OSA Therapies in Treatment Trials

Author	N	Comparison	Design	Main Findings
Barnes[6] (Level I)	114	CPAP and Placebo	Crossover	In mild-moderate OSA, OA and CPAP improve quality of life, sleepiness and neuro-behavior to similar degrees.
Barthlen[24] (Level V)	8	MRA, TD, SPL	Crossover	An MRA (Snore Guard) reduces AHI in most patients, but TD does not and SPL is not tolerated
Clark[23] (Level III)	23	MRA and CPAP	Crossover	CPAP was more efficacious but more patients preferred the OA.
Engleman[11] (Level 1)	51	MRA and CPAP	Crossover	CPAP improves objective measures of OSA and symptoms better than MRA.
Ferguson[9] (Level I)	24	MRA and CPAP	Crossover	CPAP was more effective in reducing AHI but patient satisfaction was greater with the MRA.
Ferguson[10] (Level I)	27	MRA and CPAP	Crossover	CPAP was more efficacious, but was used less, and the MRA was preferred.
Randerath[13] (Level I)	20	MRA and CPAP	Crossover	CPAP is more efficacious than MRA but subjective benefit is the same; CPAP is used less and MRA is rated "easier to use".
Tan[12] (Level 1)	24	MRA and CPAP	Crossover	OA and CPAP produce similar improvement in OSA and sleepiness but MRA is preferred.
Wilhelmsson[16] (Level I)	95	MRA vs UPPP	RCT	OA is more effective than UPPP at 1 year.
Walker-Engström[15] (Level I)	86	MRA at 50 or MRA at 75% maximum protrusion	RCT	The MRA with more anterior protrusion (75% of maximum) was more effective at reducing the AHI than the same MRA with less protrusion (50%).
Bloch[14] (Level I)	24	Herbst vs. Monobloc	Crossover with MRA	Herbst and Monobloc OA are equally effective in reducing AHI but Monobloc reduces symptoms more and is preferred
Rose[22] (Level I)	26	Silencor MRA vs. Activator MRA	Crossover with MRA	Both reduced daytime sleepiness, snoring and improved sleep quality, but the Activator was more effective at lowering the AHI.
Pitsis[8] (Level I)	23	MRA- 4 mm or MRA-14 mm interincisal opening	Crossover with MRA	MRAs with different amounts of opening (4 vs. 14 mm) have similar efficacy for OSA but the less open MRA was preferred.

er, studies with a focus on functional outcomes[6,11] showed either a preference for CPAP or no difference. For example, 1 study found no difference in treatment preference but demonstrated consistently better performance by CPAP in AHI, sleepiness assessed by the Epworth Sleepiness Scale, and several outcome scales, 1 general, the other OSA specific.[11] Furthermore, a subset of 18 patients with mild OSA (AHI < 15) that were sleepy did very well with CPAP and 14 of these 18 subjects preferred that treatment.

Limitations of these studies must be acknowledged. Most of the studies were done with fixed position appliances that did not allow adjustment of the OA to optimize treatment effect. Also CPAP treatment adherence was substantially limited in the earlier studies. Arguably, the studies did not represent best practice for CPAP or for OAs by contemporary standards, and current practice may produce different outcomes.

These studies have been used to recommend OA for consideration as primary therapy in mild to moderate OSA patients. Although it is recognized that CPAP is better at reducing the AHI when it is used, limited adherence results in less than perfect effectiveness (i.e., a patient actually using the efficacious therapy). Those who advocate more liberal use of OA therapy hypothesize that a patients' greater willingness to use OA, when efficacious, might translate into good long-term outcomes. A major difficulty in this area is the lack of consensus regarding the medical risk of persistent low levels of sleep related breathing disorders. The important lesson from these studies is that treatments must be evaluated for efficacy in various domains including treatment acceptance and adherence. Although CPAP is more effective at lowering the AHI, OA and CPAP appear to be similar in milder OSA with respect to improvements in symptoms, acceptance and adherence. Patient preference for a treatment should be given consideration in the selection of OA therapy as an alternative to CPAP in mild to moderate cases of OSA.

MRAs have been compared to upper airway surgery in 1 study[16] and a series of subsequent reports.[17-20] This randomized parallel group study was performed in 95 OSA patients. At 1 year of follow-up, OA therapy produced a greater proportion of successfully treated (AHI < 5) patients (78% vs. 51%), although quality of life assessment showed greater 'contentment' in the surgical group.[18] At 4 years, the loss to follow-up was significant; however, among those available for re-evaluation, efficacy was greater in the OA group and 62% were still using this therapy whereas 25% of UPPP patients had selected an additional therapy. This study emphasizes the incomplete success rates with both OA and UPPP and the further decline in effectiveness over time. Furthermore, in this randomized study, OA performed at least as well and arguably better than UPPP.

Different types of MRAs have been compared in a number of studies. In addition to the studies that met selection criteria for this paper, 2 others of lower evidence levels, were identified.[87,88] Taken together, these studies indicate that MRAs are generally effective in reducing snoring and OSA and appear to be more easily utilized and more often effective than a TRD, a soft palatal lifter, and a labial shield. Comparisons between different MRAs are limited with no general conclusions possible about a preferred design or technique.

3.7 Issues Regarding Patient Management, Device Selection, and

Table 7—Effect of MRA or CPAP Treatment on AHI and Epworth Sleepiness Scale (ESS) in 7 Crossover Studies

Author	Total N	AHI			ESS			Treatment Success	Treatment Success	
		Baseline	CPAP	MRA	Baseline	CPAP	MRA	CPAP	MRA	Criterion
Barnes[6]	104	21.3 ±12.8	4.8 ±4.7	14.0 ±10.1	10.2 ±4.7	9.2 ±3.8	9.2 ±3.7	Not stated	49%	AHI <10
Clark[23]	23	33.9 ±14.3	11.2 ±3.9	19.9 ±12.8				52%	19%	AHI <10
								81%	57%	AHI <20
Engleman[11]	51	31 ±26	8 ±6	15 ±16	14 ±4	8 ±5	12 ±5	34%	9%	AHI <5
								66%	47%	AHI <10
Ferguson[9]	24	26.8 ±11.9	4.2 ±2.2	13.6 ±14.5	10.7 ±3.4	5.1 ±3.3	4.7 ±2.6	70%	55%	AHI <10, improved symptoms
Ferguson[10]	25	24.5 ±8.8	3.6 ±1.7	9.7 ±7.3				62%	48%	AHI <10, symptoms improved
Randerath[13]	20	17.5 ±7.7	3.2 ±2.9	13.8 ±11.1				100%	30%	AHI <10
Tan[12]	24	22.2 ±9.6	3.1 ±2.8	8.0 ±10.9	13.4 ±4.6	8.1 ±4.1	9.2 ±5.1	Not stated	67%	AHI <10

Cost

3.7.1 Pretreatment Assessment

The American Academy of Sleep Medicine[1] and the Academy of Dental Sleep Medicine[89] recommend a protocol for the management of OA therapy in patients who are being treated for snoring or OSA and define the roles of the physician and dentist in the provision of appliance therapy.

Before treating either snoring or OSA with an OA, an assessment by a sleep clinician is required. This person is usually a physician. An objective assessment of sleep and breathing should be conducted.[90] If the clinician decides that the patient is a good candidate for OA therapy, based upon the advantages and limitations of this treatment, a referral is made to the dentist that includes the necessary clinical information. Such information may include a copy of the polysomnogram, the ESS score, and a letter of referral with any other pertinent medical information.

The dentist assesses the patient's dental suitability for OA therapy. The evaluation includes a dental history, and a complete intra-oral examination. This includes a soft tissue, periodontal, TMJ, and nocturnal bruxism assessment. The occlusion is assessed and the teeth and restorations are examined. Dental records are obtained and may include dental radiographs, and a panoramic survey. Some practitioners obtain a cephalometric radiograph in order to monitor long-term dental and craniofacial change. However, the precise utility of cephalometry has not been demonstrated. The dentist obtains informed consent about the risks and benefits of OA therapy.

3.7.2 Dental Contraindications

Patients need to have an adequate number of healthy teeth (not compromised by periodontal disease) in the upper and lower dental arch to use an MRA. The exact number of teeth necessary for adequate support of an MRA has not been identified but consensus holds that at least 6 to 10 teeth in each arch is desirable. Consensus opinion is that the patient should have the ability to protrude the mandible forward and open the jaw widely without significant limitation in order to be fitted with an MRA. Moderate to severe TMJ problems or an inadequate protrusive ability may be contraindications to OA therapy. Not all TMJ problems are a contraindication to OA therapy--mild TMJ problems may be lessened by the forward jaw position. Significant bruxism may be a contraindication to OA therapy. Some patients may damage the appliance if they have severe bruxism or may have increased pain if the appliance rigidly holds them in a single fixed position. Patients with full dentures are generally unable to use an MRA but some of these patients may be treated with a TD.

3.7.3 Appliance Selection

The dentist chooses whether an MRA or TD is appropriate based on the number of healthy teeth, status of the TMJ and patient preference. Information about OAs that have received 510k market clearance from the Food and Drug Administration (FDA) for the treatment of snoring or OSA is available at the Academy of Dental Sleep Medicine website (http://www.dentalsleepmed.org/FDAClearance.aspx). Some appliances are indicated for snoring only and some for both snoring and OSA therapy.

3.7.3.1 Mandibular Repositioning Devices

MRAs may be pre-fabricated (e.g., "boil and bite") or custom, and may be single position devices, or partly to fully adjustable. Some fixed position appliances can be remade with additional advancement but this is generally time consuming and needs to be done by the dentist or dental laboratory. Diagnostic plaster models are obtained as appropriate for the specific oral appliance. Non-custom appliances are fit to the patient in the dental office. Custom appliances are fabricated by the dentist in coordination with a dental laboratory and are delivered to the patient when manufacture is complete.

3.7.3.2 Tongue Repositioning Devices

TDs are used in patients with large tongues, or when there are contraindications to use of an MRA. Some TDs are custom made for the patient (e.g., tongue retaining device (TRD)) but some devices are prefabricated. To use the TRD the patient advances the tongue into the bulb while squeezing the bulb to create negative suction. The patient experiments with the amount of forward positioning of the tongue that is required to decrease snoring and symptoms. Once the patient is using the appliance routinely, overnight testing is required to assess the clinical response objectively.

3.7.4 Appliance Delivery

The dentist fits the appliance and teaches the patient how to use the appliance, how to care for it, how to adjust it (if that is a feature of the design) and what side effects and complications to look for. The initial position for an MRA is usually set between 50 and 75% of maximum mandibular protrusion or less if the patient cannot tolerate that much protrusion initially. Single jaw position MRA appliances are sometimes remade if the initial jaw position proves to be to far forward and causes side effects or if it is not set far forward enough to relieve snoring and OSA symptoms. Adjustable or titratable MRA appliances allow the mandible to be moved forward in increments over weeks to months. The rate of advancement and the amount of protrusion is individualized. If an optimal therapeutic position cannot be achieved (e.g., persisting snoring) the appliance is set at the maximum forward position that does not produce significant side effects. The patient may continue therapy if the patient is receiving benefit at this position. These appliances are titrated to symptom improvement or resolution and then the patient has a follow-up overnight evaluation of the impact of the OA on the AHI and other sleep variables. Some practitioners advocate using home monitoring of sleep during the clinical titration process. They suggest that this will provide objective data as to the efficacy of the OA and allow optimization of the MRA prior to the final overnight study. We did not find studies evaluating this approach to appliance titration.

A newer method of implementing MRA therapy involves overnight titration in a sleep laboratory. This was first reported in a study that used an appliance that had to be removed from the patient's mouth and adjusted manually.[91] More recently titration has been done with a temporary appliance and without awakening the patient. The appliance is advanced either by a hydraulic system[92] or by remote control.[93] The ability to reduce the AHI during the titration study was highly predictive of success when a permanent MRA was used for chronic therapy.[93] Overnight titration of an MRA remains an experimental approach but if the technology were more widely available, it might allow the identification of patients who will achieve adequate control of their OSA with an MRA before they purchase a custom appliance.

3.7.5 Dental Follow-up

The dentist should observe appliance usage, side effects, complications and the degree of advancement of the appliance at follow-up visits, initially at 1 to 2 week intervals. The dentist should also monitor the subjective changes in the patient's symptoms of OSA. The appliance may need repairs, adjustments, further advancement or even replacement with a different device if side effects develop or if there is an inadequate subjective or objective improvement. No studies have reported on the ideal frequency of follow-up visits, but regular assessment in the early weeks and months of therapy is important to manage side effects, promote compliance and reduce the potential for early discontinuation due to any difficulties the patient may have using the appliance. Following initial adaptation to the OA, regular dental assessment becomes even more critical to evaluate and manage possible complications such as tooth movement, skeletal change or occlusal alteration. In this regard, it may be prudent for the dentist to evaluate each patient every 6 months for the first several years and annually thereafter to ensure the integrity of the oral structures.

3.7.5.1 Oral Appliance Practitioners

The dentist who provides therapy with OAs for the management of sleep related breathing disorders should have adequate knowledge and skill to provide safe and effective treatment. Therefore, the dental clinician must be thoroughly familiar with the sleep-induced changes in the physiology of various organ systems including, but not limited to, the neurological, musculoskeletal, cardiac and respiratory systems, as well as possess a good knowledge of the symptoms associated with sleep related breathing disorders. In addition, the dental practitioner should be proficient in understanding various diagnostic and follow-up testing modalities including, but not limited to, the polysomnographic evaluation, MSLT, MWT, ESS and pulse oximetry and be adept at interacting with medical sleep specialists and other attending physicians for the purposes of proper diagnosis, treatment and follow-up.

Finally, the dentist who provides therapy with OAs should understand the functional characteristics and design variations of many different OAs and must be able to recognize and manage the side effects and complications associated with MRAs and TDs, especially concerning occlusal changes, tooth movement and temporomandibular joint symptoms. In this regard, the prudent practitioner understands the implications of life-long therapy and the importance of regular, periodic, follow-up examinations.

Qualified practitioners are those who are board-certified as Diplomates of the American Board of Dental Sleep Medicine or others who have undertaken comprehensive training in sleep medicine and/or sleep-related breathing disorders with an emphasis on the scientific literature and the use of an appropriate protocol for diagnosis, treatment and follow-up. Treatment provided by individuals who have little or no training and education in this unique multi-disciplinary area should be discouraged.

3.7.6 Medical Follow up

Once a satisfactory improvement in snoring and subjective OSA symptoms has taken place, the patient is referred back to the attending sleep clinician for a clinical assessment and/or repeat overnight assessment. Medical follow-up is also necessary to evaluate treatment response and to assess for recurrence of symptoms of OSA. It is recommended that a follow-up polysomnogram or an attended cardiorespiratory sleep study verify effectiveness of the OA.[1] This recommendation is supported by the evidence from Level I, II and V studies that found some patients to have an increase in AHI with OA treatment.[9,21,30,63,94]

3.7.7 Costs for Oral Appliance Therapy

Definitive data concerning the cost of OA therapy are lacking. The initial cost to the patient includes the cost of the consultation, of the dental records needed to manufacture the appliance, and for the appliance. Cost increases occur when cephalometric radiographs or other dental or airway imaging studies are performed as part of the assessment procedure. Other direct patient costs include the fees covering time spent fitting, adjusting and monitoring the therapy. Production costs may vary depending upon whether the device is custom-made in a dental laboratory or is an off-the-shelf (prefabricated) appliance. Consensus opinion indicates that dental laboratory costs for custom-made devices may range from $100 to over $600 depending upon the design and the

quality of the appliance. Costs for prefabricated devices can range from $45 to over $100. Service fees can vary greatly depending on the clinical protocol, actual time spent caring for the patient, and geographical economic factors. Lack of standardization for the use of OAs is problematic and patterns of practice among individual dentists are distributed among a broad spectrum. At present, many dentists report service fees that range from $200 to $2,500.

Only 1 investigation to date[95] explored clinical practice among dentists treating OSA. The participants surveyed by the authors included 124 dentists who were members of the Academy of Dental Sleep Medicine (formerly the Sleep Disorders Dental Society). This group may not be representative of all dentists treating snoring and sleep apnea patients with OAs. This survey revealed that 25 different devices were used by the participants in the following categories: custom-fit (45%), prefabricated (14%), TD (7%), and adjustable (34%). The dentists were found to adjust the appliances overall an average of 2.5 times (range 0 to 6). The average total cost to the patient for treatment according to the participants of this study published in 1997, excluding any reimbursement, was $933 (range $400 to $2,450). Computation of continuing costs is difficult in view of the paucity of data on the long-term durability of OAs. However, appliance repair, replacement and annual or biannual follow-up visits will factor in as continuing costs for the OA patient. The patterns of practice for non-Academy dentists are unknown. The Academy strongly emphasizes close cooperation between dentists and sleep clinicians in order to provide optimal care to patients. They also emphasize regular clinical follow-up of oral appliance patients.

4.0 CONCLUSION

The literature describing OA therapy for OSA has improved dramatically in the last few years in terms of both quantity and quality. This systematic review has found randomized controlled studies comparing MRAs to CPAP, placebo, other appliances and surgery (UPPP) as well as large case series with comprehensive long-term follow-up. The studies included in this systematic review included patients mostly with mild or moderate OSA but some studies did include patients with severe OSA. The efficacy of OAs was established for controlling OSA in some but not all patients with treatment success (AHI less than or equal to 10) achieved on average in 52% of patients.

The success rates from each study must be interpreted carefully as many studies reported results based primarily upon those subjects who could adapt to the appliance and who returned for clinical follow-up. CPAP is more effective than MRAs at improving the AHI and in improving oxygenation but many patients preferred the MRA to CPAP for long-term treatment in studies where both treatments were used. MRAs are more effective than UPPP in terms of reducing the AHI. Results of OA therapy vary depending upon appliance design and the amount of advancement. They are less effective in patients with more severe OSA or with a higher BMI.

Most patients report improvements in sleep quality and excessive daytime sleepiness. Treatment adherence is variable with a median appliance use of 77% of nights at 1 year (by self-report). They are well tolerated by most patients. Side effects are common but generally minor and include excessive salivation, muscle and tooth discomfort and occasionally joint discomfort. These symptoms usually improve over time. TMJ complications rarely occur. Tooth movement and malocclusion are noted in some patients especially after 1 or more years of treatment but the occlusal changes are frequently reversible. The long-term dental importance of these changes is uncertain but they may lead to treatment discontinuation.

Comparative studies of OA to CPAP and UPPP have helped define the role of OA therapy in patients with OSA. An important limitation of OA therapy includes the lower levels of effectiveness in terns of reducing the AHI and improving oxygenation when compared to CPAP. Therefore, OAs are not indicated as first-line therapy for patients with severe OSA, severe daytime sleepiness or in patients who have very low oxygen saturation levels during sleep. They may be indicated in patients who have failed other treatments even if they have severe OSA although results are less predictable in this group.

Published literature now provides evidence for the efficacy of OAs in the treatment of patients with mild to moderate OSA and provides considerable guidance regarding the development of adverse effects that occur with long-term treatment. They play a role in a selected group of patients in whom an alternative to CPAP is desired. OA therapy represents a unique opportunity for dentists and doctors to provide care for patients with OSA. With collaboration and good communication between the dentist and the sleep clinician, many patients with snoring or OSA can be treated effectively.

5.0 Future Directions

Future studies are needed to evaluate the effect of different appliance designs upon the success rate for reducing the AHI and improving sleep and symptoms. Standard AHI criteria for success should be established as well as standard protocols for follow-up and documenting adverse effects. Future comparisons of OA to CPAP therapy may provide different results from studies done several years ago because of improvements in both modalities of therapy. Objective measurements of snoring and treatment adherence should also be obtained. Ongoing refinements of appliance design may eventually lead to improved outcomes with fewer complications. Head to head comparisons of different appliances and different design features may provide more information as to the key design elements that are related to treatment efficacy, adherence and complications (e.g., open or closed vertical dimension). The newer titratable appliances may improve outcomes but optimal treatment protocols need to be defined. In particular, the role of home monitoring in the optimization of the amount of mandibular protrusion needs to be determined. The role of these appliances, particularly MRA, in adolescents and children has yet to be evaluated in a comprehensive or systematic way. Studies addressing these issues will advance the field of OA therapy and improve the care being delivered to patients with OSA.

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Abbreviations and Definitions

AHI	Apnea-Hypopnea Index: the frequency of apneas and/or hypopneas per hour of recorded sleep.
CPAP	Continuous Positive Airway Pressure: a respiratory therapy used to maintain upper airway patency in sleep.
ESS	Epworth Sleepiness Scale: a standardized self-rating scale of subjective sleepiness.
MRA	Mandible repositioning appliance: an oral appliance designed to advance the mandible relative to the maxilla.
MSLT	Multiple Sleep Latency Test: a standardized polygraphic procedure to objectively measure sleepiness in a series of nap attempts during the usual wake period.
MWT	Maintenance of Wakefulness Test: a standardized polygraphic procedure to objectively measure sleepiness similar to MSLT except that the subject attempts to remain awake in a sleep-inducing setting.
OA	Oral Appliance: a device inserted in the mouth to modify the upper airway for the treatment of snoring and obstructive sleep apnea.
OSA	Obstructive Sleep Apnea: breath cessation for no less than 10 seconds (in adults) caused by upper airway obstruction in sleep; also, a generic term for a clinical condition of complete or partial obstructed breathing events that cause impaired sleep and breathing.
PSG	Polysomnography: a standardized recording technique to assess sleep and breathing.
RCT	Randomized controlled (treatment) trial.
TD	Tongue Device: an oral appliance used to hold the tongue in the anterior mouth for the treatment of snoring and obstructive sleep apnea.
UPPP	Uvulopalatopharyngoplasty: a surgical procedure to remove the uvula and modify the soft palate for the treatment of snoring and obstructive sleep apnea.