Analysis and Comments on the 2015 AADM/AADSM Clinical Practice Guidelines for Treatment of Obstructive Sleep Apnea with Oral Appliances©

Although the purpose of a guideline is to help with clinical decision making, the 2015 AASM-AADSM falls short in making some fundamental decisions about the available appliances, which appliances are most effective, which appliances should be used for each level of sleep disordered breathing, and how do they compare with cpap. Unfortunately, the categories chosen of non-custom, custom, and custom titratable appliances are not helpful in distinguishing the primary outcome of interest to most practitioners of efficacy in reduction of AHI/RDI.

The following questions or comments were applied to the same literature and analysis found in the guidelines:

1. Are all of the appliances discussed commercially available in the United States?
2. Which appliance corresponds to each identified study?
3. Which appliances achieved the CPAP criteria of a reduction of AHI to <5 and >50% reduction?
4. Which appliances achieved the oral appliance criteria of a reduction of AHI to <10 and >50% reduction?
5. Can a protrusive mechanism be identified that accounts for greater success?
6. Is there any information concerning vertical?
7. Are there titration protocols mentioned?

These first four questions were applied using the information on page 49 which identified the custom, titratable OAs for OSA (AHI, RDI, REI). A chart listing the specific appliance with the study was created. The chart also listed the appliances which are not commercially available. Secondly, the studies that did not reduce the AHI/RDI below 10 or had less than 50% reduction were identified. A new chart was created listing the appliances, along with the study to allow a practitioner to choose a commercially available device to meet the level of severity of an OSA patient.

A number of pages from the guidelines have been reproduced with comments. These are fairly self-explanatory.

Finally, the protrusive mechanisms for most titratable devices fall under four categories:

1. bilateral compression (bc),
2. bilateral traction (bt)
3. midline compression (mc)
4. midline traction (mt).

Some devices that are available under these categories are:

1. Bilateral compression
    a. Herbst
    b. Somnomed
    c. PM positioner
    d. Dorsal
    e. Somnomed Herbst

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2. Bilateral traction
    a. EMA
    b. Norvall
    c. Silent Night
3. Midline compression
    a. Klearway
    b. Lamberg
    c. Silencer
4. Midline traction
    a. TAP

As mentioned in the discussion in the Guidelines, there are many more questions to be answered, particularly relating to dental morbidity and vertical. However, as the study says, morbidity is generally minor and is not of concern to most patients.

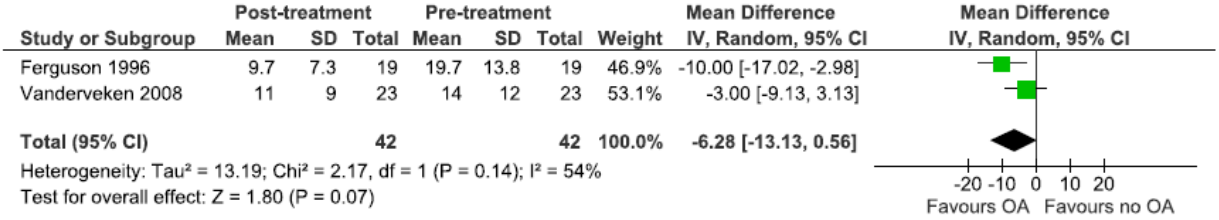
Based on this document, it may reasonably be concluded that a midline traction oral appliance should be the treatment of choice for moderate to severe OSA and if that fails, a cpap would be recommended secondarily.

Tap titration protocol

1. ***Hoekema***, Multiple PSG until maximum protrusion is reached or success of <10 AHI
2. ***Holly***, Titration in sleep lab after accommodation period

TAP average vertical, ***Hoekema*** 13.5mm, ***Holly*** 11 mm vertical.

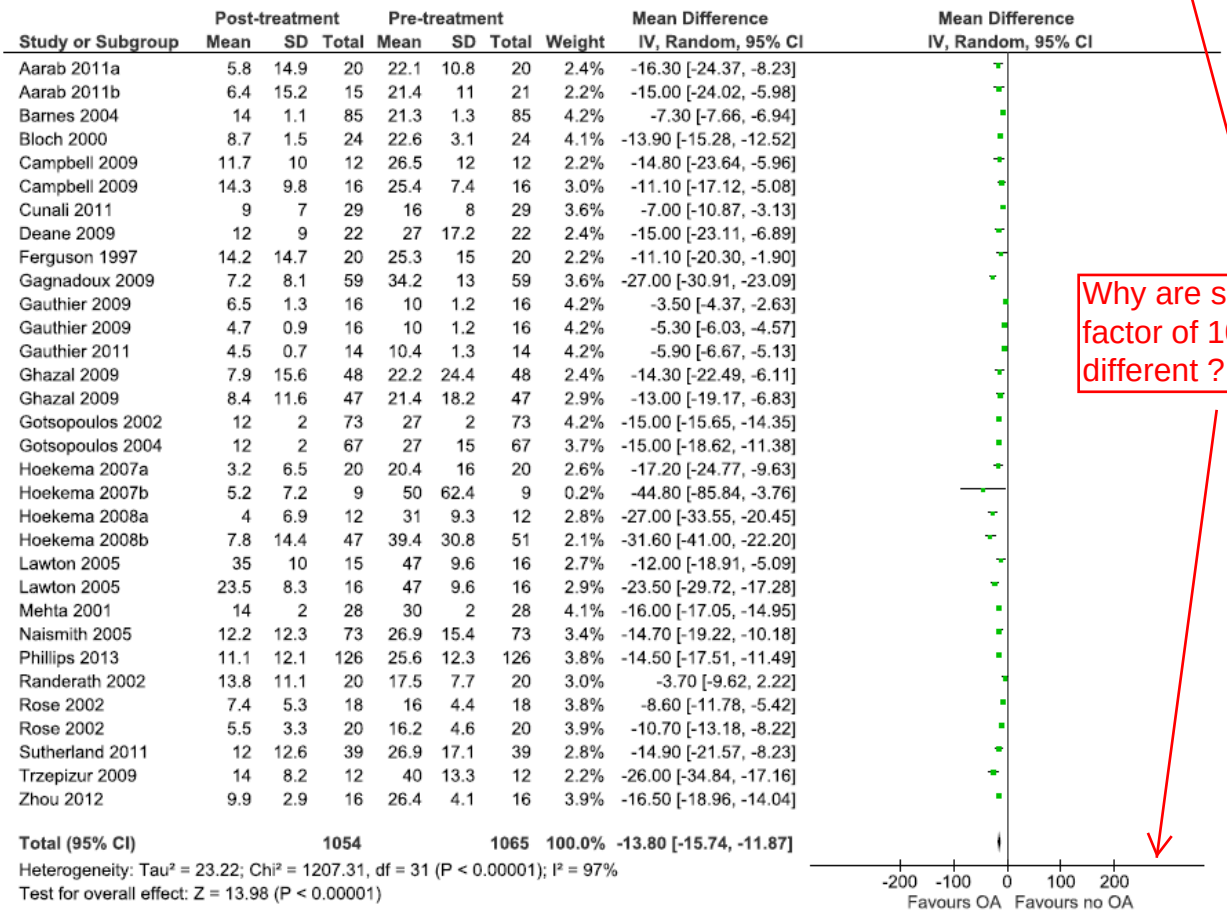
Figure 11. Non-Custom OAs for OSA (AHI/RDI/REI)



Study or Subgroup	Post-treatment Mean	SD	Total	Pre-treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ferguson 1996	9.7	7.3	19	19.7	13.8	19	46.9%	-10.00 [-17.02, -2.98]
Vanderveken 2008	11	9	23	14	12	23	53.1%	-3.00 [-9.13, 3.13]
Total (95% CI)			**42**			**42**	**100.0%**	**-6.28 [-13.13, 0.56]**

Heterogeneity: Tau² = 13.19; Chi² = 2.17, df = 1 (P = 0.14); I² = 54%
Test for overall effect: Z = 1.80 (P = 0.07)

Figure 12. Custom, Titratable OAs for OSA (AHI/RDI/REI)



Study or Subgroup	Post-treatment Mean	SD	Total	Pre-treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Aarab 2011a	5.8	14.9	20	22.1	10.8	20	2.4%	-16.30 [-24.37, -8.23]
Aarab 2011b	6.4	15.2	15	21.4	11	21	2.2%	-15.00 [-24.02, -5.98]
Barnes 2004	14	1.1	85	21.3	1.3	85	4.2%	-7.30 [-7.66, -6.94]
Bloch 2000	8.7	1.5	24	22.6	3.1	24	4.1%	-13.90 [-15.28, -12.52]
Campbell 2009	11.7	10	12	26.5	12	12	2.2%	-14.80 [-23.64, -5.96]
Campbell 2009	14.3	9.8	16	25.4	7.4	16	3.0%	-11.10 [-17.12, -5.08]
Cunali 2011	9	7	29	16	8	29	3.6%	-7.00 [-10.87, -3.13]
Deane 2009	12	9	22	27	17.2	22	2.4%	-15.00 [-23.11, -6.89]
Ferguson 1997	14.2	14.7	20	25.3	15	20	2.2%	-11.10 [-20.30, -1.90]
Gagnadoux 2009	7.2	8.1	59	34.2	13	59	3.6%	-27.00 [-30.91, -23.09]
Gauthier 2009	6.5	1.3	16	10	1.2	16	4.2%	-3.50 [-4.37, -2.63]
Gauthier 2009	4.7	0.9	16	10	1.2	16	4.2%	-5.30 [-6.03, -4.57]
Gauthier 2011	4.5	0.7	14	10.4	1.3	14	4.2%	-5.90 [-6.67, -5.13]
Ghazal 2009	7.9	15.6	48	22.2	24.4	48	2.4%	-14.30 [-22.49, -6.11]
Ghazal 2009	8.4	11.6	47	21.4	18.2	47	2.9%	-13.00 [-19.17, -6.83]
Gotsopoulos 2002	12	2	73	27	2	73	4.2%	-15.00 [-15.65, -14.35]
Gotsopoulos 2004	12	2	67	27	15	67	3.7%	-15.00 [-18.62, -11.38]
Hoekema 2007a	3.2	6.5	20	20.4	16	20	2.6%	-17.20 [-24.77, -9.63]
Hoekema 2007b	5.2	7.2	9	50	62.4	9	0.2%	-44.80 [-85.84, -3.76]
Hoekema 2008a	4	6.9	12	31	9.3	12	2.8%	-27.00 [-33.55, -20.45]
Hoekema 2008b	7.8	14.4	47	39.4	30.8	51	2.1%	-31.60 [-41.00, -22.20]
Lawton 2005	35	10	15	47	9.6	16	2.7%	-12.00 [-18.91, -5.09]
Lawton 2005	23.5	8.3	16	47	9.6	16	2.9%	-23.50 [-29.72, -17.28]
Mehta 2001	14	2	28	30	2	28	4.1%	-16.00 [-17.05, -14.95]
Naismith 2005	12.2	12.3	73	26.9	15.4	73	3.4%	-14.70 [-19.22, -10.18]
Phillips 2013	11.1	12.1	126	25.6	12.3	126	3.8%	-14.50 [-17.51, -11.49]
Randerath 2002	13.8	11.1	20	17.5	7.7	20	3.0%	-3.70 [-9.62, 2.22]
Rose 2002	7.4	5.3	18	16	4.4	18	3.8%	-8.60 [-11.78, -5.42]
Rose 2002	5.5	3.3	20	16.2	4.6	20	3.9%	-10.70 [-13.18, -8.22]
Sutherland 2011	12	12.6	39	26.9	17.1	39	2.8%	-14.90 [-21.57, -8.23]
Trzepizur 2009	14	8.2	12	40	13.3	12	2.2%	-26.00 [-34.84, -17.16]
Zhou 2012	9.9	2.9	16	26.4	4.1	16	3.9%	-16.50 [-18.96, -14.04]
Total (95% CI)			**1054**			**1065**	**100.0%**	**-13.80 [-15.74, -11.87]**

Heterogeneity: Tau² = 23.22; Chi² = 1207.31, df = 31 (P < 0.00001); I² = 97%
Test for overall effect: Z = 13.98 (P < 0.00001)

Appliances that achieved AHI<10 and 50% reduction,
FDA cleared, comercially available

Appliance Used	Study or Subgroup	Post Mean AHI	Pre Mean AHI	Total Pts	Severity	% improvement	Avalible US	Column4
MT device	Aarab 2011a	5.8	22.1	20	Moderate	74%	No	
MT device	Aarab 2011b	6.4	21.4	21	Moderate	70%	No	
MDSA	Barnes 2004	14	21.3	85	Moderate	34%	No	
Herbst	Bloch 2000	8.7	22.6	24	Moderate	62%	Yes	
MDSA	Campbell 2009	11.7	26.5	12	Moderate	56%	No	
MDSA	Campbell 2009	14.3	25.4	16	Moderate	44%	No	
Klearway	Cunali 2011	9	16	29	Moderate	44%	Yes	
Somnomed	Deane 2009	12	27	22	Moderate	56%	Yes	
Silencer	Ferguson 1997	14.2	25.3	20	Moderate	44%	Yes	
BT	Gagnadoux 2009	7.2	34.2	59	Severe	79%	No	
Klearway	Gauthier 2009	6.5	10	16	Mild	35%	Yes	
Silencer	Gauthier 2009	4.7	10	16	Mild	53%	Yes	
Klearway	Gauthier 2011	4.5	10.4	14	Mild	57%	Yes	
TAP	Ghazal 2009	7.9	22.2	48	Moderate	64%	Yes	
Herbst	Ghazal 2009	8.4	21.4	47	Moderate	61%	Yes	
Somnomed	Gotsopoulos 2002	12	27	73	Moderate	56%	Yes	
Somnomed	Gotsopoulos 2004	12	27	67	Moderate	56%	Yes	
TAP	Hoekema2007a	3.2	20.4	20	Moderate	84%	Yes	
TAP	Hoekema2007b	5.2	50	9	Severe	90%	Yes	
TAP	Hoekema2008a	4	31	12	Severe	87%	Yes	
TAP	Hoekema2008b	7.8	39.4	51	Severe	80%	Yes	
Twin Block	Lawton 2005	35	47	16	Severe	26%	Yes	
BT	Lawton 2005	23.5	47	16	Severe	50%	No	
Somnomed	Mehta 2001	14	30	28	Severe	53%	Yes	
Somnomed	Naismith 2005	12.2	26.9	73	Moderate	55%	Yes	
Somnomed	Phillips 2013	11.1	25.6	126	Moderate	57%	Yes	
Herbst	Randerath 2002	13.8	17.5	20	Moderate	21%	Yes	
Silencer	Rose 2002	7.4	16	18	Moderate	54%	Yes	
Activator	Rose 2002	5.5	16.2	20	Moderate	66%	No	
Somnomed	Sutherland 2011	12	26.9	39	Moderate	55%	Yes	
Herbst (modified)	Trzepizur 2009	14	40	12	Severe	65%	No	
Silent Night	Zhou 2012	9.9	26.4	16	Moderate	63%	No (FDA)	

Successful (CPAP Criteria)

AHI <5 and >50% decrease, Available in US

AHI> 30 (Severe)

Appliance Used	Study or Subgroup	Post_AHI	Pre_AHI	Total	Severity	% reduction
TAP	Hoekema2007b	5.2	50	9	Severe	90%
TAP	Hoekema2008a	4	31	12	Severe	87%
AHI>15 (Moderate)						
TAP	Hoekema2007a	3.2	20.4	20	Moderate	84%
				41		

Successful (Oral Appliance Criteria)

AHI <10 and >50% Decrease, Available in US

AHI >30 (Severe)

TAP	Hoekema2008b	7.8	39.4	51	Severe	80%
TAP	Holley 2011*	8.4	30	497	Severe	72%
* listed in bibliography, not RCT,				548		
AHI>15 (Moderate)						
TAP	Ghazal 2009	7.9	22.2	48	Moderate	64%

Total Papers On Tap : 6 Total participants 637

Herbst	Bloch 2000	8.7	22.6	24	Moderate	62%
Herbst	Ghazal 2009	8.4	21.4	47	Moderate	61%
Silencer	Rose 2002	7.4	16	18	Moderate	54%
Silencer	Gauthier 2009	4.7	10	16	Mild	53%
Silencer	Gauthier 2011	4.5	10.4	14	Mild	57%

Failure (Oral Appliance Criteria)

>10 AHI or <50% decrease or not available in the US

Appliance Used	Study or Subgroup	Post_AHI	Pre_AHI	Total	Severity	% reduction
Silencer	Ferguson 1997	14.2	25.3	20	Moderate	44%
Klearway	Gauthier 2009	6.5	10	16	Mild	35%
Klearway	Cunali 2011	9	16	29	Moderate	44%
Herbst	Lawton 2005	23.5	47	16	Severe	50%
Herbst	Randerath 2002	13.8	17.5	20	Moderate	21%
Somnomed	Deane 2009	12	27	22	Moderate	56%
Somnomed	Gotsopoulos 2002	12	27	73	Moderate	56%
Somnomed	Gotsopoulos 2004	12	27	67	Moderate	56%
Somnomed	Mehta 2001	14	30	28	Severe	53%
Somnomed	Naismith 2005	12.2	26.9	73	Moderate	55%
Somnomed	Phillips 2013	11.1	25.6	126	Moderate	57%
Somnomed	Sutherland 2011	12	26.9	39	Moderate	55%
MT device	Aarab 2011a	5.8	22.1	20	Moderate	74%
MT device	Aarab 2011b	6.4	21.4	21	Moderate	70%
Activator	Rose 2002	5.5	16.2	20	Moderate	66%
Silent Night	Zhou 2012	9.9	26.4	16	Moderate	63%

Various Pages from the draft of the Clinical Guidelines which has been accepted by the AADSM with notes and comments

Executive Summary

Clinical Practice Guidelines for the Treatment of Obstructive Sleep Apnea and Snoring with Oral Appliance Therapy: An Update for 2015

An American Academy of Sleep Medicine and American Academy of Dental Sleep Medicine Clinical Practice Guideline

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Introduction

Since the publication of the initial position statement by the American Academy of Sleep Medicine (AASM) in 1995, the clinical use of oral appliances (OAs) for the treatment of snoring and obstructive sleep apnea (OSA) has markedly increased. The most recent AASM practice parameters on the treatment of snoring and OSA with oral appliances was published in 2006 as "Practice Parameters for the Treatment of Snoring and Obstructive Sleep Apnea with Oral Appliances: An Update for 2005" with the accompanying systematic review paper "Oral Appliances for Snoring and Obstructive Sleep Apnea: A Review".[1,2] Since these publications, the scientific literature on OAs has grown considerably, particularly related to clinical outcomes after use of OAs. The purpose of this guideline is therefore to update the recommendations for the use of OAs in the treatment of OSA and snoring.

Methods

To develop this guideline, the AASM and American Academy of Dental Sleep Medicine (AADSM) commissioned a task force of four members, two sleep medicine physicians and two dentists, with expertise in the use of OAs. None of the task force members had any relevant conflicts. Eleven PICO (**P**atient, **P**opulation or **P**roblem, **I**ntervention, **C**omparison, and **O**utcomes) questions were developed based on both the questions raised in the 2006 AASM review paper[2]and practice parameter[1]and review of systematic reviews, meta-analyses, and guidelines published since then (Table 1). The AASM Board of Directors approved the final list of PICO questions before the targeted literature search was performed.

The literature search was performed by the AASM research staff using the PubMed and Embase databases. Though the search yielded all types of articles with various study designs, for most PICO questions the analysis was limited to only randomized controlled trials (RCTs). The RCTs that were cited in the 2006 AASM review paper [2] and 2006 practice parameter paper [1] were included for data analysis if they met the study inclusion criteria. For PICO questions 7 and 11, due to lack of RCTs, we relied on prospective observational studies. The PubMed database was searched from January 1, 2004 through July 31, 2012 and was updated again on February 28, 2013 to capture the latest literature. A

MT is only appliance that qualifies under this statement of a reduction of AHI of up to 25 per hour

4.2.1.1.2 Custom vs. Non-C

Custom OAs reduce AHI and RDI in adult patients with OSA. (Level of evidence: *Moderate*) Thirty-three RCTs including 1259 patients that assessed AHI with the use of custom OAs were identified. [9-11, 16-18, 20, 23, 26-32, 34-51] Overall, custom OAs were found to substantially reduce the AHI. Meta-analysis (Figure 10) showed the mean reduction in AHI/RDI/REI for custom OAs to be 13.89 events/hr (95% CI: 15.57, 12.20). Twenty-eight of the 33 RCTs included in the meta-analysis reported a greater than 50% reduction in AHI with the use of custom OAs in adult OSA patients. [10, 11, 16-18, 26, 27, 29, 30, 32, 34-51] Five RCTs reported a mean decrease in AHI of up to 25 events/hr with the use of custom OAs. [34, 38-40, 48]

Non-custom OAs reduce AHI/RDI/REI in adult patients with OSA. (Level of evidence: *Low*) Two RCTs including 42 adult patients with OSA that assessed AHI with the use of non-custom OAs were identified. [33, 49] Small improvements in AHI were reported. Meta-analysis (Figure 11) showed the mean reduction in AHI for non-custom OAs to be 6.28 events/hr (95% CI: -13.13, 0.56). It should be noted that the meta-analysis reports wide confidence intervals surrounding the mean reduction in AHI for each of the 2 RCTs that studied the efficacy of non-custom OAs.

34, and 48 are modified Herbst not available in the US
38,39,40 MT

A comparison of the results of the meta-analyses c ve a greater reduction in AHI in adult patients with OSA tha

4.2.1.1.3 Custom, Titratable vs. Custom, Non-Titratable OAs

Custom, titratable OAs reduce AHI/RDI/REI in adult patients with OSA. (Level of evidence: *Moderate*) A meta-analysis (Figure 12) of twenty-seven RCTs including 1054 patients showed the mean reduction in AHI/RDI/REI for custom, titratable OAs to be 13.80 events/hr (95% CI: 15.74, 11.87). [9, 11, 16-18, 20, 26-28, 30-32, 34-46, 48, 51] Twenty-two of the 27 RCTs included in the meta-analysis reported a greater than 50% reduction in AHI with the use of custom, titratable OAs in adult OSA patients. [11, 16-18, 26, 27, 30, 32, 34-40, 42-46, 48, 51] Five RCTs reported a mean decrease in AHI of up to 25 events/hr with the use of custom titratable OAs. [34, 38, 39] [40, 48] In an RCT conducted by Tan et al., the first 10 subjects were treated with a custom, non-titratable OA; but two subjects complained of inadequate nocturnal oral respiration and were unable to tolerate the device. [47] Therefore, the patients in the study were switched to a custom, titratable device for the remainder of the study. [47] For this reason, the study was excluded from the meta-analyses of custom, titratable and custom, non-titratable OAs.

Custom, non-titratable OAs reduce AHI/RDI/REI in adult patients with OSA. (Level of evidence: *Moderate*) A meta-analysis (Figure 13) of six RCTs including 164 adult patients with OSA showed the mean reduction in AHI for custom, non-titratable OAs to be 12.51 events/hr (95% CI: 15.23, 9.80). [10, 11, 23, 29, 49, 50] Four of the six RCTs included in the meta-analysis reported a greater than 50% reduction in AHI with the use of custom, non-titratable OAs. [10, 11, 29, 50]

A comparison of the results of the meta-analyses cited above suggests that custom, titratable and custom, non-titratable OAs achieve an equivalent reduction in AHI in adult patients with OSA.

MT has greatest improvement in minimum oxygen saturation for any OA

4.2.1.1.4 OAs vs. CPAP

CPAP reduces AHI/RDI/REI more than OAs in adult patients with OSA. (Level of evidence: *Moderate*) A meta-analysis performed on fifteen RCTs (9 of them published since the 2006 practice parameters paper) evaluated 491 patients assigned to an OA and 481 assigned to CPAP to assess the effect of these devices on AHI. [9, 10, 20, 26-28, 33, 34, 37-40, 44, 47, 48] The results are shown in Figure 14. In weighted analysis, OAs produced a significant mean reduction in AHI, however the mean reduction in AHI was 6.24 events/hr (95% CI: 8.14, 4.34) greater with CPAP than with OA.

A study by Gagnadoux et al. evaluating the effectiveness of OA vs. CPAP over a 2 month treatment period noted a complete response (>50% reduction in AHI to < 5 events /hr) in 73.2% of patients with CPAP and 42.8% with OA. [34] The odds of achieving an AHI ≤ 5 events/hr was 49 times greater, and the odds of achieving an AHI ≤ 10 events/hr was 89 times greater with the OA treated group compared to the control group, based on one RCT. The odds of achieving an AHI ≤ 5 events/hr after treatment were 3.6 times greater. [34] Ferguson et al. reported that achieving an AHI ≤ 10 events/hr was 1.9 times greater with CPAP than with OA. [9] The treatment duration with OA and CPAP in the above studies varied between 6 weeks and 4 months.

4.2.1.2 Oxygen Saturation

4.2.1.2.1 All Appliance Types

Oral appliances modestly improve minimum oxygen saturation in adult patients with OSA. (Level of evidence: *Moderate*) A meta-analysis was performed on all included trials that compared pre- and post-treatment oxygen saturation when treated with OAs vs. control group without OA. The results are shown in Figure 15. In a weighted analysis of 22 RCTs that assessed 946 adult OSA patients treated with OAs, the mean improvement in oxygen saturation was 3.09% (95% CI: 2.43, 3.76). [9, 16-18, 20, 28, 31-33, 35-45, 49, 51] The greatest improvements in minimum oxygen saturation with the use of OAs were reported by Hoekema et al. in 2007 and 2008; 13.0% (95% CI: 7.02, 18.98) and 12.1% (95% CI: 6.89, 17.31), respectively. [38, 39]. Custom, titratable appliances were used in these studies. [38, 39] Nine of the 22 RCTs included in the meta-analysis did not show a statistically significant improvement in oxygen saturation with the use of OAs. [9, 20, 31-33, 41, 45, 49, 51]

4.2.1.2.2 Custom vs. Non-Custom OAs

Custom OAs modestly improve minimum oxygen saturation in adult patients with OSA. (Level of Evidence: *Moderate*) A meta-analysis of 21 RCTs including 908 adult patients with OSA showed that the mean increase in minimum oxygen saturation for custom OAs to be 3.22% (95% CI: 2.54, 3.90). [9, 16-18, 20, 28, 31, 32, 35, 36, 38-45, 49, 51] The results are shown in Figure 16. Eight of the 21 RCTs included in the meta-analysis did not show a statistically significant improvement in oxygen saturation with the use of custom OAs. [9, 20, 31, 32, 41, 45, 49, 51]

Non-custom OAs do not significantly improve minimum oxygen saturation in adult patients with OSA. (Level of evidence: *Moderate*) Two RCTs including 42 adult patients with OSA investigated changes in minimum oxygen saturation with non-custom OAs. [33, 49] Meta-analysis (Figure 17) of these 2 studies

No difference in minimum oxygen desaturation with MT compared to CPAP

revealed a statistically insignificant mean decrease in minimum oxygen saturation of 0.29% (95% CI:-3.22, 2.64).

4.2.1.2.3 Custom, Titratable vs. Custom, Non-titratable OAs

Custom, titratable OAs modestly improve minimum oxygen saturation in adult patients with OSA. (Level of Evidence: *Moderate*) Meta-analyses were performed on 20 RCTs including 851 adult patients with OSA that assessed the impact of custom, titratable OAs on minimum oxygen saturation during their sleep. [9, 16-18, 20, 28, 31, 32, 35, 36, 38-45, 51] The results are shown in Figure 18. The weighted analysis showed a mean increase of 3.15% (95% CI: 2.46, 3.84) in minimum oxygen saturation using custom, titratable OAs.

Custom, non-titratable OAs modestly improve minimum oxygen saturation in adult patients with OSA. (Level of evidence: *Low*) A meta-analysis (Figure 19) of 3 RCTs including 57 patients showed a mean increase in minimum oxygen saturation of 4.70% (95% CI: -3.83, 13.22) when using custom, non-titratable OAs to treat adult patients with OSA. [45, 49, 51] Zhou et al. reported a statistically significant improvement in minimum oxygen saturation [51], while Vanderveken et al. and Rose et al. found no significant improvement. [45, 49]

A comparison of the results of the meta-analyses cited above suggests that custom, titratable and custom, non-titratable OAs achieve an equivalent improvement in minimum oxygen saturation in adult patients with OSA.

4.2.1.2.4 OAs vs. CPAP

CPAP improves minimum oxygen saturation slightly better than OAs in adult patients with OSA. (Level of evidence: *Moderate*) Nine RCTs (5 of them published since the 2006 practice parameters paper) evaluated a total of 346 adult patients with OSA randomized to OA and 354 to CPAP to evaluate the effect on oxygen desaturation. [9, 20, 28, 33, 37-40, 44] Meta-analysis (Figure 20) revealed the improvement in oxygen saturation was better with CPAP than with an OA (mean difference 3.11% (95% CI: 1.74, 4.48) higher with CPAP than with an OA). Of the 9 RCTs included in the meta-analysis, Ferguson et al. reported the greatest improvement in minimum oxygen saturation with the use of CPAP over OAs; 11.9% (95% CI: 6.71, 17.09). [9] Conversely, RCTs conducted by Hoekema et al. reported no significant differences in minimum oxygen saturation with OAs compared to CPAP. [38-40]

4.2.1.3 Arousal Index

4.2.1.3.1 All Appliance Types

Oral appliances reduce the arousal index in adult patients with OSA. (Level of evidence: *Moderate*) Fourteen RCTs (6 of them published since the 2006 practice parameters paper) assessed 704 adult patients with OSA randomized to OAs vs. a control group and found an overall reduction in arousal index with OAs. [11, 18, 20, 26-29, 32, 35, 36, 42-44, 47] A meta-analysis (Figure 21) comparing the pre- and

MT showed larger improvement of ESS scale than Somnomed or any other appliance.

4.2.2.2 Custom vs. Non-Custom OAs

Custom oral appliances reduce daytime sleepiness in adult patients with OSA. (Level of evidence: *Moderate*) Twenty-five RCTs including 948 patients were identified that evaluated the change in ESS with the use of custom OAs. [10, 11, 16-18, 23, 28-31, 34, 35, 37-44, 47-49, 51, 52] Reductions in ESS were modest. Meta-analysis (Figure 47) showed the mean reduction in ESS score for custom OAs to be 1.95 (95% CI: 2.03, 1.88). Phillips et al., in one of the largest studies with 108 subjects, found a significant ($p<0.01$) reduction in ESS from a baseline of 9.1±0.4 to 7.2±-0.4. [44] Others such as Hoekema et al. reported larger improvements in ESS score (12.9±5.6 to 4.8±5.4). [39]

Non-custom oral appliances do not significantly reduce daytime sleepiness in adult patients with OSA. (Level of evidence: *Moderate*) A single RCT including 23 patients assessed the effects of non-custom OA therapy on sleepiness in adult patients with OSA. The study reported an insignificant mean reduction in ESS of 1.0 (95% CI: -3.62, 1.62).

The evidence on the efficacy of custom and non-custom OAs for the improvement of subjective daytime sleepiness is presented in Figures 52 and 53, respectively.

4.2.2.3 Custom, Titratable vs. Custom, Non-Titratable OAs

Custom, titratable oral appliances reduce daytime sleepiness in adult patients with OSA. (Level of evidence: *Moderate*) Nineteen RCTs including 768 patients were identified that evaluated the change in ESS with the use of custom, titratable OAs. [11, 16-18, 28, 30, 31, 34, 35, 37-44, 48, 51] Reductions in ESS were modest. Meta-analysis (Figure 48) showed the mean reduction in ESS score for custom, titratable OAs to be 3.95 (95% CI: 4.61, 3.28).

Custom, non-titratable oral appliances reduce daytime sleepiness in adult patients with OSA. (Level of evidence: *High*) Eight RCTs including 156 patients were identified that evaluated the change in ESS with the use of custom, non-titratable OAs. [10, 11, 23, 29, 30, 49, 51, 52] Meta-analysis (Figure 49) showed the mean reduction in ESS score for custom, non-titratable OAs to be 3.65 (95% CI: 5.18, 2.13).

The evidence on the efficacy of custom, titratable and custom, non-titratable OAs for the improvement of subjective daytime sleepiness is summarized in Figures 54 and 55, respectively.

4.2.2.4 OAs vs. CPAP

OAs are equivalent to CPAP in reducing subjective daytime sleepiness in adult patients with OSA. (Level of evidence: *Low*) Meta-analyses were performed on 10 RCTs that compared measures of daytime sleepiness between OAs and CPAP (Figure 50). [10, 28, 34, 37-40, 44, 47, 48] The weighted analysis of 10 trials comparing changes in the ESS between OAs and CPAP found an insignificant increase of 0.08 (95% CI: -0.21, 0.38) in post-treatment measures of subjective sleepiness between these two therapies.

In an RCT of patients with mild to moderate OSA, Barnes et al. compared the impact of OAs and CPAP on daytime sleepiness. [28] Both treatments led to clinically and statistically significant improvements in

MT was equivalent to CPAP in improving daytime sleepiness

daytime sleepiness, with greater effects noted with CPAP therapy. [28] Compared with placebo, both treatments significantly improved subjective sleepiness as measured by the ESS ($p < 0.001$ for both OAs and CPAP). [28] There was no difference in the measured treatment effect between the two interventions. [28] The investigators did not observe improvements in objective sleepiness with either treatment. [28] However, the mean sleep latency on baseline maintenance of wakefulness testing (MWT) was normal among the cohort (30.7±0.9 minutes), and only 18.4% had objective somnolence prior to therapy. [28] Alertness, as measured by a visual analog scale, was improved with CPAP ($p < 0.001$) but unchanged with OAs. [28] In an RCT, Hoekema, et al. found that OAs performed similarly to CPAP in improving daytime sleepiness. [40] Specifically, ESS changed from 12.9±5.6 at baseline to 6.9±5.5 following treatment with an OA, compared with a change from 14.2±5.6 to 5.9±4.8 with CPAP. [40]

The evidence on the efficacy of OAs vs. CPAP for the improvement of subjective daytime sleepiness is presented in Figure 56.

4.2.3 Quality of Life

4.2.3.1 All Appliance Types

Oral appliances improve quality of life measures in adult patients with OSA. (Level of evidence: *Moderate*) This is an expansion of the statements and associated recommendations provided in the 2006 AASM Practice Parameters for the Treatment of Snoring and Obstructive Sleep Apnea with Oral Appliances. Since the publication of the 2006 practice parameters, several high quality clinical trials have established the benefits of OA therapy in improving QOL measures in patients with OSA.

Compared with no treatment or non-therapeutic (sham) therapy, treatment with OAs significantly improved QOL measures. A meta-analysis of eight RCTs exploring the impact of OAs on QOL was performed. [10, 28, 29, 31, 35, 39, 41, 44] The results are shown in Figure 57. Oral appliances were associated with significant improvements in QOL measures. In a weighted analysis, the mean improvement in the SF-36 scores was 6.41 (95% CI: 5.08, 7.75). In a study comparing a custom OA set at 75% of the maximum mandibular advancement to a similar OA that did not advance the mandible, Blanco et al. found that QOL was improved with therapy. [29] After 3 months of treatment, the overall FOSQ scores also improved by 27.1% from baseline in the mandibular advancement group ($p <0.001$, effect size 0.90). [29] In comparison, the non-advanced group experienced a -1.7% decline in FOSQ. [29] Similarly, Gauthier et al. conducted an RCT of patients using OAs for the treatment of OSA. [17] After a mean follow-up period of 40.9 months, mean overall FOSQ scores improved from 13.9±0.8 to 17.2±0.6 ($p \leq 0.01$). [17]

The evidence on the efficacy of OAs for the improvement in QOL is summarized in Figure 61.

4.2.3.2 Custom vs. Non-Custom OAs

Significantly greater improvement of FOSQ with MT than with Somnomed or other appliances

Custom appliances im *nea in adult patients with OSA.* (Level of Evidence: *Moderate*) The meta-analysis for all appliance types applies to custom OAs as all of the appliances were custom made. (Figure 57)

There was insufficient evidence to assess the efficacy of non-custom OAs for improvement in QOL.

4.2.3.3 Custom, Titratable OAs vs. Custom, Non-Titratable OAs

Custom, titratable appliances improve quality of life. (Level of Evidence: *Moderate*) Six RCTs including 2223 patients were identified that evaluated the change in SF-36 with the use of custom, titratable OAs. [28, 31, 35, 39, 41, 44] Meta-analysis (Figure 58) showed the mean reduction in SF-36 score for custom, titratable OAs to be 6.84 (95% CI: 5.42, 8.26).

Custom, non-titratable appliances do not improve quality of life in adult patients with OSA. (Level of Evidence: *Low*) Two RCTs including 102 patients were identified that evaluated the change in SF-36 with the use of custom, non-titratable OAs.[10, 29] Meta-analysis (Figure 59) showed no significant improvement in QOL for custom, non-titratable OAs; -0.95 (95% CI: -4.55, 2.64).

The evidence on the efficacy of custom, titratable and custom, non-titratable OAs for the improvement in QOL is summarized in Figures 62-63.

4.2.3.4 OAs vs. CPAP

OAs are nearly equivalent to CPAP for improving QOL in adult patients with OSA. (Level of evidence: *Low*) Meta-analyses were performed on 4 RCTs that compared measures of QOL between OAs and CPAP (Figure 60) and found that both therapies performed similarly; a clinically insignificant weighted mean improvement in SF-36 scores of 2.18 (95% CI: 1.10, 3.25) with CPAP compared to OAs. [10, 28, 40, 44] In an RCT of patients with mild to moderate OSA, Barnes et al. compared the impact of OAs and CPAP on several functional outcomes. [28] Both treatments led to clinically and statistically significant improvements in QOL, with greater effects noted with CPAP therapy. [28] Neither treatment was superior to placebo for changes in neuropsychologic function or improvements in mood. [28] In an RCT, Hoekema et al. found that OAs performed similarly to CPAP in improving QOL. [40] Specifically, FOSQ scores improved from 13.7±3.1 to 16.6±2.8 with OAs and from 13.9±3.7 to 16.7±3.1 with CPAP therapy. [40] Phillips et al. observed that baseline FOSQ scores improved from 16.3±0.2 to 17.3±0.2 with CPAP and 17.3±0.2 with an OA. [44] In addition, SF-36 scores related to Bodily Pain, Vitality, Social Function, Mental Health, and Mental Component had similar improvements with both therapies. [44]

The evidence on the efficacy of OA vs. CPAP for the improvement in QOL is presented in Figure 64.

4.2.4 Hypertension

4.2.4.1 All Appliance Types

Oral appliances have a modest impact on reducing blood pressure in adult patients with OSA. (Level of evidence: *Moderate*) This is a new clinical question that was not addressed in the 2006 AASM Practice

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