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Mandibular advancement device effects on the upper airway anatomy and function: An umbrella review

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ABSTRACT

Study Objectives. To summarize systematic reviews regarding function and anatomy of the upper airway and subjective evaluations on breathing capability depending on the advancement and/or opening of the mandible. *Methods*. Four databases were searched based on inclusion criteria. Two independent reviewers evaluated abstracts of all articles for phase 1 and full text in phase2 of selection. PRISMA statement was used as a guideline; weaknesses were assessed using the AMSTAR2 tool. *Results*. 12 systematic reviews were included. Mandibular protrusion greater than 50% of maximum protrusion results in a decrease of AHI by an average of 62.3% and an increase in SaO_2. These findings correlate with dimensional changes in the upper airway; tongue, soft palate, and hyoid positions. Changes in the nasopharynx are minimal, however significant volumetric increase of the oropharynx after MAD use in growing patients was observed. Improved ESS scores were reported for all included studies in one review. All MAD designs reviewed in the study show potential to reduce AHI and RDI, with slightly lower AHI levels with those devices favouring more anterior than vertical mandibular movement. *Conclusions.* Devices that favour progressive mandibular advancement with less vertical opening have the potential to decrease AHI and increase SaO_2. Findings of this review can help clinicians determine titration amounts of mandibular advancement for specific patients and can help gauge the level of MAD efficacy on patients with sleep apnea.

Key words: Mandibular advancement, upper airway, mandibular opening, MAD, sleep apnea, AHI, oxygen saturation

Statement of significance:

Approximately 80 million Americans have sleep-disordered breathing (SDB); 1 out of 5 have Mild to Moderate obstructive sleep apnea (OSA), and 1 out of 15 have Moderate to Severe OSA. Part of the population diagnosed with SDB/OSA for any reason can't use CPAP. The alternate treatment is the mandibular advancement device (MAD). The MAD's function is to protrude and help stabilize the mandible to maintain a patent upper airway during sleep. MAD accounts for around 5% of the total OSA therapy in the USA, and some patients have indications to use MAD rather than CPAP. Therefore, it is of utmost importance to summarize the literature about MAD use and its effects on the respiratory capability of patients diagnosed with SDB.

Mandibular advancement device effects on the upper airway anatomy and function: An umbrella review

INTRODUCTION

Obstructive sleep apnea (OSA) is a breathing disorder that results in repetitive breathing cessation during sleep.[1,2] OSA has a high prevalence, affecting 9-38% of the adult population.[3] The cause of OSA is a combination of multiple anatomic and non-anatomic factors.[4,5] One of the common causes of OSA is related to upper airway collapse.[6] Although the gold standard of treatment is the continuous positive airway pressure (CPAP), low compliance rates between 30-60% [7] increase the need for alternative treatment methods.

Mandibular advancement devices (MAD) prevent upper airway collapse by moving the jaw forward and downward .[8,9] This anterior titration has been reported to increase the anteroposterior diameter and the cross-sectional area of the upper airway.[10,11] Several studies have shown that compared to non-advancement appliances, oral appliances that include mandibular advancement, and subsequent mandibular opening due to the condylar hinge angle, have significant benefits in preventing upper airway collapse.[9–13]

Several published systematic reviews have assessed the effect of mandibular advancement on the upper airway, and it is important to map and summarize their conclusions. The objective of an umbrella review is to highlight the strengths and weaknesses of previously published systematic reviews. In this view, this umbrella review aimed to summarize the findings of the effect of the MADs on the airway function, upper airway dimensions, and subjective self-reported evaluations

on breathing capability. Findings of this study can provide guidance when evaluating candidate profiles for patients in need of MAD treatment.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) was used as a guideline for the methodological approach of this study.[14]

Eligibility criteria

Systematic reviews about the effects of MADs on the upper airway anatomy and function were included in this umbrella review. The inclusion criteria consisted of any age range group in which the upper airway anatomy and/or ventilation was evaluated after mandibular advancement devices therapy. Randomized and non-randomized clinical trials were included in this review. Selected keywords included: upper airway, pharynx, oropharynx, nasopharynx, respiratory tract, mandibular advancement, mandibular advancement devices, orthodontics. Observational studies and animal studies were excluded. No limitations to publication year or language were imposed.

Information sources

The following databases were searched to identify systematic reviews related to our inclusion criteria: EMBASE, PubMed, Web of Science, and Scopus. Additionally, a hand search was carried out. The search was carried out in May 2020, and an update was performed in January 2021. The search results were exported to Rayyan Software (Qatar Computing Research Institute, Doha, Qatar),[15] in which the duplicates were excluded. (Figure 1)

Search

The excluded articles in phase 2 of selection are displayed in Appendix 1.

Selection of sources of evidence, Data charting process, and Data Items

Two reviewers (SGC and DK) evaluated titles and abstracts independently, using a web-based citation management program (Rayyan, Qatar Computing Research Institute, Doha, Qatar). The articles were screened in full text in the second phase by the same two reviewers, and, in cases of disagreement, a third reviewer was consulted (ML). The data were extracted by the second examiner (DK) and checked by the first author (SGC), and each article was recorded. The key features were listed such as authors, country, year, respiratory disturbance index (RDI), Apnea/Hypopnea Index (AHI), oxygen saturation (SaO_2), snoring index, Epwort's sleepiness scale (ESS), upper airway dimension, mandibular advancement, main results and AMSTAR results (Table 1).

Critical appraisal of individual sources of evidence

Critical and non-critical weaknesses were assessed using the AMSTAR 2 tool.[16] This tool focuses on the methodological quality of each systematic review.[16] The systematic reviews are ranked as high-quality, moderate quality, low quality, or critically low.[16]

Summary measures and synthesis of results

The studies were evaluated regarding changes in the upper airway, either dimensional or functional such as respiratory function (AHI and RDI) and SaO_2, described in Table 1. Information on AMSTAR's quality of evidence and journal of publication are displayed in table 2.

RESULTS

Selection and characteristics of sources of evidence

A total of 7693 articles were found through a comprehensive database search. After managing duplicates, 4359 studies were assessed based on the titles and abstracts. Thereafter, 4340 were excluded. The remaining 19 reviews were screened by assessing their full text. The references

of the included studies were also screened for possible new inclusions. In the end, 12 systematic reviews were included in this umbrella review.

Critical appraisal within sources of evidence

The AMSTAR 2 tool results shown in Table 1 are divided into 16 questions, and the results are displayed into four possible categories: High, Moderate, Low, and Critically Low quality of evidence. Six systematic reviews were ranked with *high* quality of evidence,[17–21,27] one received *moderate* rating,[22] and five received *low* rating.[23–28]

Results of individual sources of evidence

Airway functional changes

Bartolucci et al. (2016) discussed the amount of mandibular advancement and its effect on the respiratory function measured basically with AHI.[17] After evaluating 13 studies, they concluded that the mandibular advancement amount is not proportionate to the change in AHI.[17] The mean success rate among the assessed studies was 62.3% and was related to mandibular advancements from 25% to 89% of the maximum mandibular protrusion.[17] Sakamoto et al. also evaluated the amount of mandibular protrusion for effectiveness in respiratory pattern; they included only three studies in which 50% protrusion was compared to 75% mandibular protrusion.[25] They concluded that 50% advancement could be more effective in subjects diagnosed with mild OSA, whereas 75% advancement is more prone to effectively ameliorate OSA symptoms in patients diagnosed with severe OSA.[25]

Bartolucci et al., Marina et al., and Hoekema et al. evaluated the success rate of improving AHI and SaO_2 when mono-block and duo-block MADs were used.[18,21,24] Bartolucci showed a better improvement in both indices when the mono-block MAD was used.[18] Marina et al. corroborate with their results showing a decrease in AHI values and an increase in SaO_2.[24]

Although Hoekema et al. results showed that not all studies verified a statistical difference in the efficacy of mono-block compared to duo-block designs.[21]

One systematic review focused on the design of the oral appliances and their effects on reducing OSA symptoms.[28] They concluded that all different designs effectively reduce AHI and RDI; the significant correlation seems to be with the mandible advancement.[28]

Hoekema et al. evaluated the MAD efficacy and effects on co-morbidity linked to OSA symptoms.[21] All included studies but two evaluated MAD with 50% to 87% of the maximum mandibular protrusion; the other two studies mentioned a mandibular protrusion of 2.4mm to 6mm.[21] They verified that MAD is effective in decreasing AHI and increasing SaO_2.

Upper airway dimensional changes

Four systematic reviews evaluated the effect of functional appliance therapy on the airway dimensions in growing patients.[19,20,22,23] Their conclusion showed that functional appliance therapy allows the forward repositioning of the mandible, leading to an increase in the airway dimensions.[19,20,23] There is a change in the tongue, soft palate, and hyoid positions.[19,20] These effects also seem to be related to the reduction in AHI and increasing SaO_2.[19] Anusuya et al. reported the findings of some of the included studies showing that the change in the nasopharynx was minimal. However, the difference in the oropharynx was significant after the use of mandibular advancement treatment in growing subjects.[20]

Alsufyani et al. evaluated the CBCT usability in evaluating dimensional changes of the upper airway after mandibular advancement.[22] They reported results based on surgical advancement of the mandible and mandibular advancement using appliance therapy. Due to the aim of our study, we only included the data available related to the use of appliance therapy and that were not based on just a one-case description. Therefore only the data from two studies were

included in our umbrella review. Their protrusion amounts were 75% of the maximum mandibular protrusion and 4mm (±3.6mm). The authors reported a low quality of evidence showing a volumetric increase after using the Twin-block and Herbst appliances.[22]

Subjectively perceived symptoms

Only one systematic review reported just subjective evaluations.[26] Fourteen studies were included in which the perceived treatment efficacy was analyzed.[26] ESS was used in most of the included studies in Ahrens et al.'s systematic review; 12 studies showed improved ESS scores using MAD.[26] Other subjective tools were also used, such as fatigue severity scale, sleep disorder questionnaire, visual analog scale, and health-related quality of life questionnaires.[26] The majority of the patients reported MAD to be more efficient for treating OSA symptoms.[26]

Synthesis of results

Twelve systematic reviews were included in this study; all of them were written in English and published between 2004 and 2020. One study was from the United Kingdom, Canada,[22] Spain,[19] Neatherland[21] and Japan[25]; two from Italy[17,18]; two from India[20,24]; and three from China.[23,26,27] Six systematic reviews only included (Randomized Controlled Trial) RCTs.[17,18,20,21,25, 28]

DISCUSSION

The objective of this umbrella review was to summarize the findings of the effect of the MADs on the airway function, upper airway dimensions, and subjective self-reported evaluations on breathing capability. The findings of this umbrella review can provide guidance and awareness on how much effect MAD treatment can provide to patients with sleep apnea.

Airway functional changes

Bartolucci et al., reporting results of 13 studies and Sakamoto et al., based on three RCTs, agree that advances of around 50% would benefit patients diagnosed with mild to moderate OSA, both in terms of AHI improvement.[17,25] Few studies have evaluated if less than 50% of mandibular advancements based on the maximum protrusion is correlated with improved rates of AHI or not.[17] Mandibular advancements of 75% of the maximum mandibular protrusion could benefit patients diagnosed with severe OSA. However, it is possible to conclude that the improvement of AHI is not proportionate to the amount of mandibular advancement. Therefore, the amount of mandibular advancement could not be the only factor to affect AHI and improve OSA. The progressive mandible protrusion seems to be more suitable to titrate treatment according to each patient.

After reviewing 50 RCTs, Bartolucci et al. discussed improving the AHI and SaO_2 indices by comparing mono-block to duo-block MADs.[18] They reported that most of the studies included in their systematic review described better results in improving the AHI and SaO_2 when the mono-block device was used.[18] Their explanation for the better results with the mono-block is related to the lower vertical increase by the mono-block generating a smaller rotation of the mandible and consequently a greater mandibular advancement. This idea is in agreement with Mayoral et al.[13] On the other hand, the lack of control in vertical opening with the duo-block could be mitigated with the use of elastics. Conversely, Hoekema et al.[21] reported one study that showed no difference in AHI and SaO_2 between mono-block and duo-block devices.

Hoekema et al.[21] evaluated MAD efficacy, and their results also showed an improvement in SaO_2 compared to the placebo. Yet, no difference was found in AHI and ESS when different

vertical heights were tested; although the tendency was the patients prefer the ones with lower vertical dimension.[21] Their findings are contrary to the idea that the greater the vertical opening, the greater the decrease in the dimension of the oropharynx, due to the posterior rotation of the mandible, which could compromise the AHI.

Marina et al.[24] compared the custom-made to the pre-fabricated MADs. Throughout six included studies, four of them concluded that both types improve AHI and oxygen saturation, also agreeing with Ahrens et al.[27] One other did not show a difference in AHI with both types of appliances, while one showed that both types improved AHI. However, the custom-made appliance had a better result than the pre-fabricated one. In agreement with Marina et al.,[24] Serra-Torres et al.[19] and Ahrens et al.[27] also reported better outcomes with the custom-made appliances. The individualized selection of an oral appliance accounting for the MAD characteristics such as fabrication material, tooth anatomy and angulation, number of teeth present, device extension, and propulsion system is crucial. Possible allergies to some materials, retention, and strength and thickness are important factors for the patient's comfort and health. Materials, retention, extension and propulsion systems are interconnected and should be taken into account when choosing a MAD. For instance, the propulsion system affects the force vectors, and therefore also the retention. Moreover, the propulsion system will affect the comfort of the patient according to their sleep position.

Upper airway dimensional changes

Anusuya et al.[20] reported no increase in the nasopharynx region after the use of functional appliance for the mandibular advancement in growing patients. However, they found an increase

in the oropharynx region. Likewise, Xiang et al.[23] reported an increase in the oropharynx after using functional mandibular advancement appliance in growing patients in which dimensional changes were measured without the appliance in place before and after therapy. Conversely, Serra-Torres et al.[19] reported an increase in the velopharynx area in adult patients. Mandibular advancement increases antero and lateral dimensions of the velopharynx and oropharynx by displacing the suprahyoid and genioglossus muscles anteriorly; increasing tension on the palatoglossal and palatopharyngeal muscles of the soft palate, and lateral movement of the pharyngeal arches which would influence airway space. Xiang's review assessed growing patients without sleep disordered breathing.

Subjectively perceived symptoms

Hoekema et al. reported some studies showing an improvement in the ESS score compared to a placebo device,[21] but others showed no difference. Although, one systematic review mentioned a subjective improvement in breathing even with the inactive appliance (no mandibular protrusion) in place.[26] This could be due to the placebo effect or a slight vertical opening increase due to splint thickness. However, Hoekema et al. mentioned that the control devices are created to minimally increase the vertical mandibular opening.[21] Regarding one-block or duo-block, Hoekema et al.[21] reported no differences in the ESS according to one study.

Conclusion of studies graded as high quality through AMSTAR

Six studies were graded high quality according to AMSTAR, five of them were based on adult patients and one in children.[17,18,19,20,21,28] Three of them were based only in RCT studies.[17,18,28]

Their main conclusions are: 1) According to 50 articles, the monoblock device showed higher effectiveness than the duo block, however the authors reported this conclusion as with very low quality of evidence.[18] 2) According with 8 articles, functional appliances enlarge oropharynx in children.[20] 3) AHI improvement is not proportionate to the amount of mandibular advancement, based on 13 articles.[17] 4) AHI, oxygen saturation, snoring and daytime sleepiness improve with the MAD therapy, also there is an increase in the upper airway area, these results were based on 22 articles.[19] 5) Accordingly, based on 17 studies, another systematic review described improvement in AHI and daytime sleep with MAD therapy.[28]

Additional information

Hoekema et al. suggest that MAD treatment did not significantly change the maximum mouth opening, lateral movement, or protrusion.[21] However, one study in their systematic review showed an increased mouth opening in 28% of patients.[21] Among the systematic reviews included in this study, a significant variability in the results of individual studies was seen.[27] Still differences in study design, sample size, type of MAD, amount of advancement or opening, patients' compliance, and long-term effect studies lead to one conclusion that no one appliance fits all patients and symptoms.

The material of the devices (thermoplastic, acrylic, acrylic-metal, printed nylon), the retention mode, and the design of the devices (attached bilateral compression, attached bilateral traction, attached midline traction, attached bilateral interlocking, unattached bilateral interlocking) were not described. However, all of them could contribute to the efficiency (efficacy + adherence) of the MAD.

Future directions

Since compliance is a crucial characteristic of this therapy, more studies in this area are necessary. The effectiveness of MADs in edentulous patients is still unclear. Moreover, studies evaluating MADs long-term effects and side effects are needed.

In addition, imaging studies with evaluation of ventilation rather than AHI, might be of great interest. Lately, authors have reported the importance of not only evaluate OSA through one index – AHI – instead the variability of severity of OSA is also linked with Oxygen saturation for example.[30] Therefore, future studies need to take into consideration a list of parameters such as oximetry, sleep stage shifts, arousal, sleep efficiency, snoring, etc.

CONCLUSION

- In summary, a titratable custom-made MAD seems to be the best appliance for decreasing the AHI and increasing SaO_2, moreover, the lowest vertical increase possible and control of mouth opening seems to improve the subjective evaluation by the patient. Multiple factors influence the efficacy of the MAD, including the severity of OSA, degree of protrusion, appliance design, and fabrication materials. Therefore, the best MAD is the one that matches all these requirements for each particular patient.

The compilation of the information from 12 systematic reviews suggests that:

- A decrease in the AHI and an increase in the SaO_2 is related to mandibular protrusion of at least 50% of the maximum mandible protrusion rate. The progressive mandible protrusion seems to be more suitable to titrate treatment according to each patient.

- All device designs have the potential to reduce AHI and RDI.
- An improvement in the subjective respiratory efficiency using ESS was seen.
- There is strong evidence suggesting that the oropharynx space is increased, and there is a change in the position of the tongue, hyoid bone, and soft palate.
- Functional appliance therapy results showed significant improvement in oropharyngeal dimensions in Class II malocclusion subjects with retrognathic mandibles.

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List of figure caption

Figure 1: Flow chart

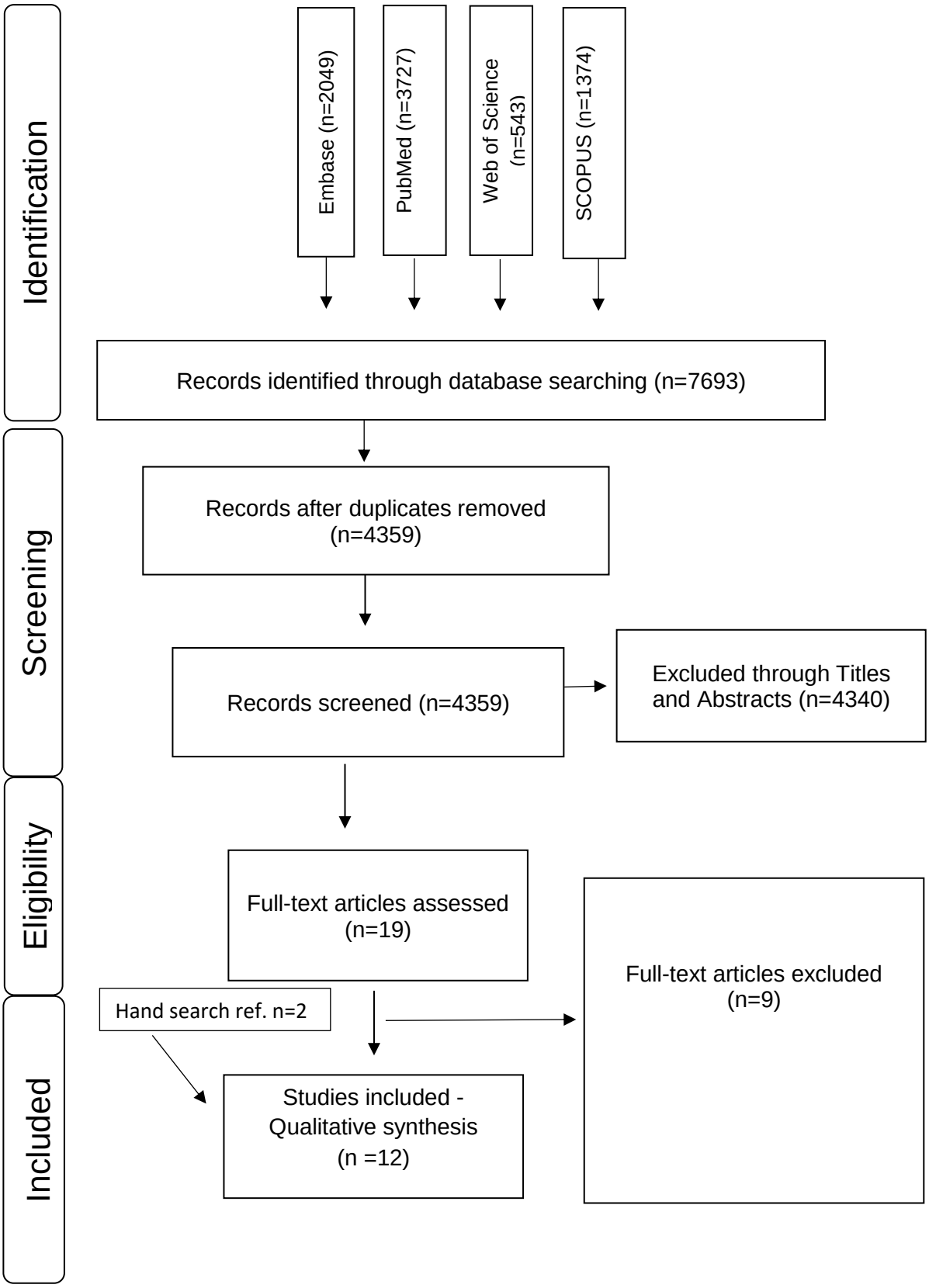

Figure 1 – Flowchart of literature search and study selection.

Table 1 - Summary of characteristics of included articles

(Critical appraisal tool- AMSTAR) https://amstar.ca/Amstar_Checklist.php

Author, year, and country	Number of articles included	Type of treatment and description	^RDI	#AHI	% SaO2	Snoring Index	Epwort's sleepiness scale (ESS)	Upper airway dimensions	Hyoid and other measurements	Main Results	AMSTAR
Bartolucci et al. 2021 Italy	50	Mono-bloc and Duo-block mandibular advancement devices and its effects on AHI and SaO_2		82% of the Mono-block therapy and 54% of the duo-block demonstrated success rate improving AHI	10% of the Mono-block therapy and 3% of the duo-block demonstrated success rate improving O_2S					Mono-block devices showed a higher effectiveness when compared to due-block devices, however with a very low quality of evidence, according to the authors.	High quality
Anusuya et al. 2019 India	8	Changes in pharyngeal airway dimensions following functional appliance therapy in skeletal Class II malocclusion in growing patients.						Average change in **nasopharynx**, between control and treatment groups (mm): CG: 91.85±159.25 TG: 133.12±133.35 (insignificant change) **Oropharynx:** CG: 168.54±325.71 TG: 414.21±394.51 (prominent effect) **Hypopharynx**: CG: 0.54±1.56. TG: 1.01±1.89	Changes in hyoid bone (mm): 1.81±2.50 Both removable and fixed functional appliances produced a significant increase in the hyoid bone distance. Changes were more prominent in the horizontal than vertical direction.	Functional appliance treatment has a significant effect on the improvement of the oropharyngeal airway, but minimum effect on the nasopharynx. Removable functional appliances (ie. Twin blocks) produced the better improvement in the upper airway dimension such as the oropharynx and hypopharynx than fixed appliances.	High quality

Sakamoto et al. 2019 Japan	3	Crossover and parallel trials, which compare results for OSA patients using MAD with 50% and 75% protrusion.	Mean difference between 50% and 75% protrusion Respiratory rate 1.89 95% CI [0.36, 9.92]	Mean difference between 50% and 75% protrusion: 0.38 95%CI [-0.89, 1.65]		Mean difference between 50% and 75% protrusion: 0.09 95% CI [0.05, 0.13]	Mean difference between 50% and 75% protrusion: 1.07 95% CI [-0.09, 2.24]			In mild to moderate OSA cases, 50% protrusion might be effective, whereas for severe cases, >70% may be more effective.	Low quality
Marina et al. 2019 India	6	Research question was if two types of MADs (custom made vs. pre-fabricated) affect the AHI, ESS, and SaO_2		Average without appliance: 27.34±5.08 Average with type A appliance: 7.08±2.27 Average with type B appliance: 8.93±2.72	Average without appliance: 10.88±4.97 Average with type A appliance: 6.24±2.94 Average with type B appliance: 5.28±3.09		Average without appliance: 9.54±6.33 Average with type A appliance: 6.59±4.50 Average with type B appliance: 7.03±5.0			Both the custom-made and prefabricated MADs reduced the severity of symptoms of OSA. MADs can reduce AHI when evaluated objectively, and can reduce ESS when evaluated subjectively.	Low quality
Xiang et al. 2017 China	7	Change in pharyngeal airway after treatment with a functional appliance. Types used were: Forsus, Twin block, Activator with/without headgear.						Superior Pharyngeal Space: 1.73mm/yr [1.13, 2.32] Middle Pharyngeal Space: 1.68mm/ yr [1.13, 2.23] Inferior Pharyngeal Space: 1.21mm/ yr [0.48, 1.95]	Appliances can force mandibular advancement with an annual increase in SNB angle by 1.79°/yr S-PNS: 0.83° [-0.19, 1.86] SN-GoGN: 1.19mm/yr [0.50, 1.89] (significant difference found in the mandibular plane angle)	"The oropharynx dimensions were most affected by the functional appliances compared to the nasopharynx and hypopharynx. Early treatment with functional appliances has positive effects on the upper airway, especially on oropharyngeal dimensions. The forward repositioning of the mandible and adaptive changes to the soft palate, increasing airway dimensions, help decrease the airway resistance."	Low quality

Bartolucci et al. 2016 Italy	13	AHI changes relative to mandibular advancement amounts		Improvement in AHI was seen in mandibular advancements of 25% to 89% of the maximum protrusion						Advancement amounts higher than 50% do not significantly influence the success rate of AHI (AHI improvement is not proportionate with mandibular advancement increase).	High quality
Serra-Torres et al. 2016 Spain	22	MADs used included: Klearway, Twin-block, Herbst, custom-made duo-block, custom-made mono-block.		AHI % reduction: 21% to 80%. 16 out of 22 studies reported at least 50% reduction in the AHI	Average oxygen saturation, from initial to post-treatment (%): 86.08±6.04 to 90.8±3.91		Average ESS, from initial to post-treatment: 9.99±4.72 to 6.84±3.5	5 out of 22 studies measured velopharynx dimensions and found an increase in it		"MAD increase the area of the airway and bring the soft palate, tongue, and hyoid bone forward activating the masseter and submental muscles, preventing closure."	High quality
Alsufyani et al. 2013 Canada	2 *	"Dimensional changes in the upper airway after appliance therapy in subjects with mild to moderate OSA. Twin-block and Herbst were used in the included studies						One study showed the total airway volume increased by 1.1±0.2 cm3 with twin-block. The other study showed an increase in the oropharynx to be 2.8±4.4 cm3 after the use of Herbst.		Although there was an increase in the airway volume, the studies had a low quality of evidence according to the authors of this systematic review	Moderate quality
Ahrens et al. 2011 China	14	Oral appliance design and its effect on OSA symptoms treatment outcomes		MAD therapy improves polysomnographic indices						"All MADs proved successful in improving AHI/RDI and comparison with inactive appliances suggests that mandibular advancement is crucial in terms of establishing efficacy."	Low quality

Ahrens et al. 2010 China	14	Subjective evaluation of MAD compared with either inactive appliances or MAD with different designs.					"Subjects and sleep partners both recorded that MADs significantly reduced snoring frequency, choking, cessation of breathing, the number of arousals, daytime sleepiness frequency of morning headache daytime aggressive reaction, and decreased libido."			"There is no MAD design that most effectively influences subjectively perceived treatment efficacy. Efficacy depends on materials and methods used for fabrication, type of MAD (monoblock or Twinblock), and the degree of sagittal and vertical protrusion."	Low quality
Lim et al. 2006 UK	17	Out of the 17 articles, 6 trials compared OA with a control OA, which consisted of devices that did not protrude the mandible.		There was a significant effect in favor of active treatment (-10.78 events/hr; 95%CI -15.53 to -6.03	Minimum arterial oxygen saturation For cross over studies, there was no significant effect in favor of active appliances (1.79% with 95% confidence interval [-0.29, 3.87])		Active appliance: 8.53±10.91 Control appliance: 37.47±5.87 Mean difference with 95% confidence interval: -2.09 [-3.80, -0.37]			OA improves subjective sleepiness and indices of sleep-disordered breathing over an inactive control. Additionally, OA leads to improvement in the AHI compared to the baseline. Blood pressure: active oral appliance therapy led to lower blood pressure compared to the control appliances	High Quality

Hoekema et al. 2004 Netherlands	16	Evaluation of the efficacy and safety of OA while treating OSA		Improvement of AHI and SaO_2 was seen among the included studies.	Improvement of AHI and SaO_2 was seen among the included studies.					"Oral appliances are effective in the treatment of OSA, although a placebo effect should be considered. (…)Although definite conclusions are not possible, efficacy of OA treatment appears to be related to the degree of mandibular advancement. Moreover, appliance design, like the amount of bite opening or the means of mandibular fixation, may affect subjective parameters of success."	High Quality

[*]Alsufyani et al 2013 evaluated in their Systematic Review changes in the upper airway after MAD or surgery, since surgery was not the focus of this Umbrella Review, we reported only the results based on MAD;[^]RDI= Respiratory disturbance index; [#]AHI= Apnea/Hypopnea Index; [%] SaO2= Oxygen saturation

Table 2 – Additional information of included articles

Author, year, and country	Journal of publication	Type of study	AMSTAR
Bartolucci et al. 2020 Italy	Journal of Oral Rehabilitation	SR + Meta analysis	High quality
Anusuya et al. 2019 India	Trends in Orthodontics	SR	High quality
Sakamoto et al. 2019 Japan	International Journal of Environmental Research in Public Health	SR	Low quality
Marina et al. 2019 India	Drug invention Today	SR	Low quality
Xiang et al. 2017 China	International Journal of Pediatric Otorhinolaryngology	SR + Meta analysis	Low quality
Bartolucci et al. 2016 Italy	Sleep Breath	SR + Meta analysis	High quality
Serra-Torres et al. 2016 Spain	The Laryngoscope	SR	High quality
Alsufyani et al. 2013 Canada	Sleep Breath	SR	Moderate quality
Ahrens et al. 2011 China	European Journal of Orthodontics	SR	Low quality
Ahrens et al. 2010 China	American Journal of Orthod Dentofacial Orthop	SR	Low quality
Lim et al. 2006 UK	Cochrane Database Systematic Review	SR	High Quality
Hoekema et al. 2004 Netherlands	Crit Rev Oral Biol Med	SR	High Quality