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The effectiveness of mandibular advancement device for the treatment of obstructive sleep apnea in adults: a systematic review

Master's Thesis

Supervisor

Prof. Kristina Lopatienė

Kaunas, 2020

FINAL MASTER‘S THESIS IS CONDUCTED AT THE DEPARTMENT OF ORTHODONTICS

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1. Is done by myself.

2. Has not been used at another university in Lithuania or abroad.

3. I did not used any additional sources that are not listed in the Thesis, and I provide a complete list of references.

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LITHUANIAN UNIVERSITY OF HEALTH SCIENCES
MEDICAL ACADEMY
FACULTY OF ODONTOLOGY
DEPARTMENT OF MAXILLOFACIAL SURGERY

The effectiveness of mandibular advancement device for the treatment of obstructive sleep apnea in adults: a systematic review

Master's Thesis

The thesis was done

by student ..... **Supervisor** .....
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..... **20….** ..... **20….**
(day/month) (day/month)

Kaunas, 2020

EVALUATION TABLE OF THE MASTER'S THESIS
OF THE TYPE OF SYSTEMIC REVIEW OF SCIENTIFIC LITERATURE

Evaluation: .....

Reviewer: .....
(scientific degree. name and surname)

Reviewing date: .....

No.	MT parts	MT evaluation aspects	Compliance with MT requirements and evaluation		
			Yes	Partially	No
1	**Summary (0.5 point)**	Is summary informative and in compliance with the thesis content and requirements?	0.3	0.1	0
2		Are keywords in compliance with the thesis essence?	0.2	0.1	0
3	**Introduc-tion, aim and tasks (1 point)**	Are the novelty, relevance and significance of the work justified in the introduction of the thesis?	0.4	0.2	0
4		Are the problem, hypothesis, aim and tasks formed clearly and properly?	0.4	0.2	0
5		Are the aim and tasks interrelated?	0.2	0.1	0
6	**Selection criteria of the studies, search methods and strategy (3.4 points)**	Is the protocol of systemic review present?	0.6	0.3	0
7		Were the eligibility criteria of articles for the selected protocol determined (e.g., year, language, publication condition, etc.)	0.4	0.2	0
8		Are all the information sources (databases with dates of coverage, contact with study authors to identify additional studies) described and is the last search day indicated?	0.2	0.1	0
9		Is the electronic search strategy described in such a way that it could be repeated (year of search, the last search day; keywords and their combinations; number of found and selected articles according to the combinations of keywords)?	0.4	0.1	0
10		Is the selection process of studies (screening, eligibility, included in systemic review or, if applicable, included in the meta-analysis) described?	0.4	0.2	0
11		Is the data extraction method from the articles (types of investigations, participants, interventions, analysed factors, indexes) described?	0.4	0.2	0
12		Are all the variables (for which data were sought and any assumptions and simplifications made) listed and defined?	0.4	0.2	0
13		Are the methods, which were used to evaluate the risk of bias of individual studies and how this	0.2	0.1	0

		information is to be used in data synthesis, described?			
14		Were the principal summary measures (risk ratio, difference in means) stated?	0.4	0.2	0
15	**Systemiza-tion and analysis of data (2.2 points)**	Is the number of studies screened: included upon assessment for eligibility and excluded upon giving the reasons in each stage of exclusion presented?	0.6	0.3	0
16		Are the characteristics of studies presented in the included articles, according to which the data were extracted (e.g., study size, follow-up period, type of respondents) presented?	0.6	0.3	0
17		Are the evaluations of beneficial or harmful outcomes for each study presented? (a) simple summary data for each intervention group; b) effect estimates and confidence intervals)	0.4	0.2	0
18		Are the extracted and systemized data from studies presented in the tables according to individual tasks?	0.6	0.3	0
19	**Discussion (1.4 points)**	Are the main findings summarized and is their relevance indicated?	0.4	0.2	0
20		Are the limitations of the performed systemic review discussed?	0.4	0.2	0
21		Does author present the interpretation of the results?	0.4	0.2	0
22	**Conclusions (0.5 points)**	Do the conclusions reflect the topic, aim and tasks of the Master's thesis?	0.2	0.1	0
23		Are the conclusions based on the analysed material?	0.2	0.1	0
24		Are the conclusions clear and laconic?	0.1	0.1	0
25	**References (1 point)**	Is the references list formed according to the requirements?	0.4	0.2	0
26		Are the links of the references to the text correct? Are the literature sources cited correctly and precisely?	0.2	0.1	0
27		Is the scientific level of references suitable for Master's thesis?	0.2	0.1	0
28		Do the cited sources not older than 10 years old form at least 70% of sources, and the not older than 5 years – at least 40%?	0.2	0.1	0
Additional sections, which may increase the collected number of points					
29	**Annexes**	Do the presented annexes help to understand the analysed topic?	+0.2	+0.1	0
30	**Practical recommen-dations**	Are the practical recommendations suggested and are they related to the received results?	+0.4	+0.2	0
31		Were additional methods of data analysis and their results used and described (sensitivity analyses, meta-regression)?	+1	+0.5	0

32		Was meta-analysis applied? Are the selected statistical methods indicated? Are the results of each meta-analysis presented?	+2	+1	0
General requirements, non-compliance with which reduce the number of points					
33	**General requirements**	Is the thesis volume sufficient (excluding annexes)?		15-20 pages (-2 points)	<15 pages (-5 points)
34		Is the thesis volume increased artificially?	-2 points	-1 point	
35		Does the thesis structure satisfy the requirements of Master's thesis?		-1 point	-2 points
36		Is the thesis written in correct language, scientifically, logically and laconically?		-0.5 point	-1 points
37		Are there any grammatical, style or computer literacy-related mistakes?	-2 points	-1 points	
38		Is text consistent, integral, and are the volumes of its structural parts balanced?		-0.2 point	-0.5 points
39		Amount of plagiarism in the thesis.	>20% (not evaluated)		
40		Is the content (names of sections and sub-sections and enumeration of pages) in compliance with the thesis structure and aims?		-0.2 point	-0.5 points
41		Are the names of the thesis parts in compliance with the text? Are the titles of sections and sub-sections distinguished logically and correctly?		-0.2 point	-0.5 points
42		Are there explanations of the key terms and abbreviations (if needed)?		-0.2 point	-0.5 points
43		Is the quality of the thesis typography (quality of printing, visual aids, binding) good?		-0.2 point	-0.5 points
***In total (maximum 10 points):**					

***Remark:** the amount of collected points may exceed 10 points.*

Reviewer's comments: _____

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Reviewer's name and surname Reviewer's signature

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1. Abstract

Summary

Obstructive sleep apnea (OSA) remains an ongoing concern due to its effects on sleep quality and its association with increased risk of health problems. Over the past decade mandibular advance devices (MAD) have been enthusiastically researched about in their effectiveness in the treatment of sleep apnea. This review evaluates the results of these studies for the purpose of acquiring a definitive answer to whether MADs should be used as a treatment for OSA. The aim of the present review is to assess effectiveness of MADs in treating patients with OSA, based on measurements obtained from polysomnography such as Apnea-Hypopnea Index (AHI) and sleep efficiency.

Material and methods

A detailed search was performed with the use of PubMed and ISI Web of Knowledge databases, covering the period from January 2015 to February 2020.

Result

Eleven studies were evaluated and 13 MADs were reviewed in order to determine the effectiveness of MADs in decreasing AHI. In total, the present review assessed the data of 519 patients. The articles presented a significant percentage of AHI reduction in patients treated with MADs, ranging from 22% to 75%. Of the 13 MADs assessed, 9 proclaimed $\geq$50% reduction in AHI. Out of the six studies that documented on sleep efficiency, three obtained a statistically significant improvement.

Conclusion

The current review demonstrated a significant improvement in AHI values after treatment with mandibular advancement device. MADs can therefore be considered a more inexpensive alternative for continuous positive airway pressure therapy (CPAP), however, no significant improvement was obtained in sleep efficiency.

Keywords: Obstructive sleep apnea, mandibular advancement device, mandibular advancement appliance, mandibular advancement splint, oral appliance.

2. Introduction

Patients with obstructive sleep apnea (OSA) experiences repetitive interruption of breathing during sleep as a result of complete or partial obstructions of one or multiple sites of the upper airway [1, 2]. This occurs due to narrowing or collapse of the pharynx which stops the flow of air [3]. It can also occur repeatedly at night and is often accompanied by reduced blood oxygen saturation and micro-arousals, resulting in snoring and sleep deprivation [4]. The severity of OSA is measured by using the apnea-hypopnea index (AHI) by assessing the average number of apnea or hypopnea events recorded per hour of sleep. The AHI values are classified as normal (AHI <5), mild (AHI 5-15), moderate (AHI 16–30), or severe (AHI >30) [5].

There are several risk factors linked with the development of OSA. Aging, for instance, is one of the contributing factors; other risk factors are obesity, male gender, increased neck circumference, tonsillar hypertrophy and anatomical abnormalities (e.g. micrognathia, retrognathia, macroglossia, an inferiorly placed hyoid bone). Additionally OSA can develop due to hormonal factors such as after menopause, and due to hypothyroidism and acromegaly [6-8].

Undiagnosed and untreated sleep apnea can lead to serious consequences such as decrease of life expectancy. Several studies have shown a link between OSA and increased risk of health problems, in particular there is an increased risk for cardiovascular diseases such as hypertension, coronary artery disease, cardiac arrhythmias, congestive heart failure and stroke. Furthermore increased risk of metabolic health, severe sleep deprivation and increased risk of motor vehicle accidents due to daytime sleepiness are some unfavorable outcomes of OSA [9]. In view of this research OSA patients can be expected to have a higher risk of mortality, there is a significant link between apnea severity and mortality; patients with AHI > 20 have an increased risk of mortality than those with AHI < 20 [10].

Despite the fact that this syndrome has significant negative outcomes, 90% of the patients with sleep apnea remain undiagnosed and are thus left untreated. Nonetheless the prevalence of OSA has increased in recent times as a result of the increasing obesity rates among adults. According to recent studies approximately 13% of the population aged to 30-49 years and 26% of the population aged 50-70 years suffers from moderate to severe OSA [11].

OSA patients are diagnosed by taking the history of the patient, assessing the clinical features, performing a physical examination and ultimately confirming with one of the three diagnostic tests; overnight polysomnography, split-night polysomnography or home monitoring. Overnight polysomnography is considered to be the gold-standard diagnostic test for OSA [12].

Polysomnographic diagnosis is carried out by a sleep technician in a laboratory by monitoring and

recording electroencephalogram (EEG), electrooculogram (EOG), electromyogram (EMG), respiratory effort, oxygen saturation, oronasal airflow and measuring the heart rate by electrocardiogram (ECG) during sleep [13]. The treatment of OSA varies based on the severity of the syndrome; no single treatment is applicable to all patients. Treatment options can include one or more of the following: (a) lifestyle changes; (b) continuous positive airways pressure (CPAP); (c) oral appliance; or (d) surgery. The goals of treating a patient with OSA are to reduce the AHI and to increase blood oxygen levels during sleep. Whereas, the success rate of a treatment is defined by achieving a reduction of more than 50% in AHI and/or an AHI of ≤5 [14].

Oral appliances can be categorized into two groups; tongue retaining devices and mandibular advancement devices (MADs). The most commonly used oral appliance devices are MADs, these appliance are also known as mandibular advancement splints (MAS) or mandibular advancement appliance (MAA) or mandibular repositioning appliances (MRA) (see Figure 1 in annexes). The devices can be customized or bought prefabricated over the counter. MADs aim to improve airway potency by protruding the mandible forward and thus preventing upper airway collapsibility at night. As the collapsibility of the pharynx is reduced, the amount of apneic events will decrease and daytime sleepiness and cardiovascular diseases can be improved [15-17].

Over the past decade MADs have been enthusiastically researched about in their effectiveness in the treatment of sleep apnea. This review evaluates the results of these studies for the purpose of acquiring a definitive answer to whether MADs should be used as a treatment for sleep apnea.

The aim of the study:

The current systematic review aims to assess the effectiveness of mandibular advancement devices in treating patients with obstructive sleep apnea, based on measurements obtained from polysomnography such as the apnea-hypopnea index and the sleep efficiency.

The objectives of the study:

1. To assess apnea-hypopnea index, pre-and post-treatment with mandibular advancement device in patients with OSA.
2. To assess the effect of MAD on sleep efficiency in patients with OSA.
3. To assess the outcomes of the included studies in order to obtain a definitive answer to whether MADs should be used as a treatment for sleep apnea.

3. Material and methods

3.1. Protocol

The present systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews (PRISMA) [17].

3.2. Focus question

The following clinical question was formulated according to the problem, intervention, comparison and outcome (PICO) process (table 1): How effective is mandibular advancement device as a treatment for obstructive sleep apnea?

Table 1. The framed focus question following the PICO framework.

Acronym	Definition	Description
P	Patient	Patients with obstructive sleep apnea
I	Intervention	Mandibular advancement advice
C	Comparison	Polysomnography data; pre-surgical and post-surgical
O	Outcome	AHI - events/h, mean and sleep efficiency %, mean
	Focus question	How effective is mandibular advancement device as a treatment for obstructive sleep apnea?

3.3. Information sources

An electronic search for English language articles was performed using PubMed and ISI Web of Knowledge from January 2015 to February 2020.

3.4. Search strategy

The literature search strategy was conducted in accordance to the PRISMA guidelines using PubMed and ISI Web of Knowledge electronic databases. A detailed search was conducted on the two electronic databases, the search covered the period from January 2015 to February 2020. Filter were applied for the search, only full text articles and articles written in english were included. Another filter applied was studies with human patients only and studies conducted on adults (>18). The search strategy on Pubmed included a combination of six search terms: “obstructive sleep apnea,” “sleep apnea,” “mandibular advancement splints,” “mandibular advancement appliance,” “oral appliances,” and “mandibular advancement device.” The same search terms was used for the other database. An electronic search was performed on other additional databases however, findings were not of relevance. The full electronic search strategy is described in table 2.

Table 2. Keywords used for the search strategy.

	Keywords
	1. Obstructive sleep apnea
OR	2. Sleep apnea
AND	3. Mandibular advancement device
OR	4. Mandibular advancement appliance
OR	5. Mandibular advancement splint,
OR	6. Oral appliance

3.5. Types of publications

This systematic review included only clinical studies in the English language done on humans. Publications conducted in pediatric patients, absence of full text or abstract, *in vitro* studies and articles published more than five years ago were excluded.

3.6. Types of studies

The present systematic review included randomized clinical trials, case-control studies, pilot studies, prospective and retrospective observational studies conducted on humans and published from January 2015 to February 2020. The last search was conducted in 5th of February 2020.

3.7. Types of participants

Subjects that were investigated with polysomnography for the confirmation of OSA and additionally underwent a follow-up polysomnography with the oral appliance *in situ* during sleep were included in this study.

3.8. Outcome variables

The primary outcome variable was the mean changes of AHI rates and the secondary outcome variable was the mean changes of sleep efficiency.

3.9. Inclusion criteria

The inclusion criteria for the studies were as follows: 1) studies conducted on adults (>18); 2) studies with human subjects; 3) only full-text articles; 4) studies written in the English language; 5) studies of patients with an apnea-hypopnea index of ≥ 5; and 6) The use of polysomnography pre- and post-treatment, with the use of any kind of mandibular advancement device.

3.10. Exclusion criteria

The exclusion criteria for the studies were as follows: 1) articles that were published more than five years ago; 2) studies conducted on animals; 3) systematic reviews and literature reviews; and 4) compromised periodontal health or dental status.

3.11. Data extraction and data items

The data items retrieved from the included articles were as follows: 1) first author and year of publication; 2) study design; 3) number of participants; 4) duration of the study; 5) inclusion criteria of the study; 6) mean age of the patients; 7) measurement method; 8) type of appliance used; 9) mandibular protrusion degree; 10) primary outcome (AHI); 11) secondary outcome (sleep efficiency); and 12) results of each study.

3.12. Statistical analysis

Meta-analysis of the data was not conducted due to significant heterogeneity between the studies included.

3.13. Risk of bias assessment

The bias assessment of each included study was performed by using The Quality Assessment Tool for Quantitative Studies [18]. The tool will evaluate six domains: selection bias, study design, confounders, blinding, data collection method and withdrawals or drop-outs.

3.14. Ethical approval

The ethical approval was received from the Bioethics Center at Lithuanian University of Health Sciences to conduct the current systematic review. Registration code: BEC-OF-145.

3. Results

3.1. Study selection

The search screened 275 articles, among these articles 39 were potentially relevant in accordance to the title and were thus assessed further by reviewing the abstract. Full versions were downloaded if the articles met the set criteria or if the abstract did not provide sufficient information. Subsequently, the full reports of the publications that were potentially significant to the review were retrieved for further assessment of eligibility. In total 18 full-text articles were evaluated in order to make the final judgment, in which seven records were excluded for absence of polysomnographic data pre- and post-treatment. Ultimately, eleven publications met the predefined criteria and were thus considered suitable for this review. Figure 1 demonstrates the PRISMA flow diagram which shows selection process of the studies. Table 3 summarizes the characteristics of the included studies.

Figure 2**.** Prisma flow diagram illustrating the selection process of the studies.

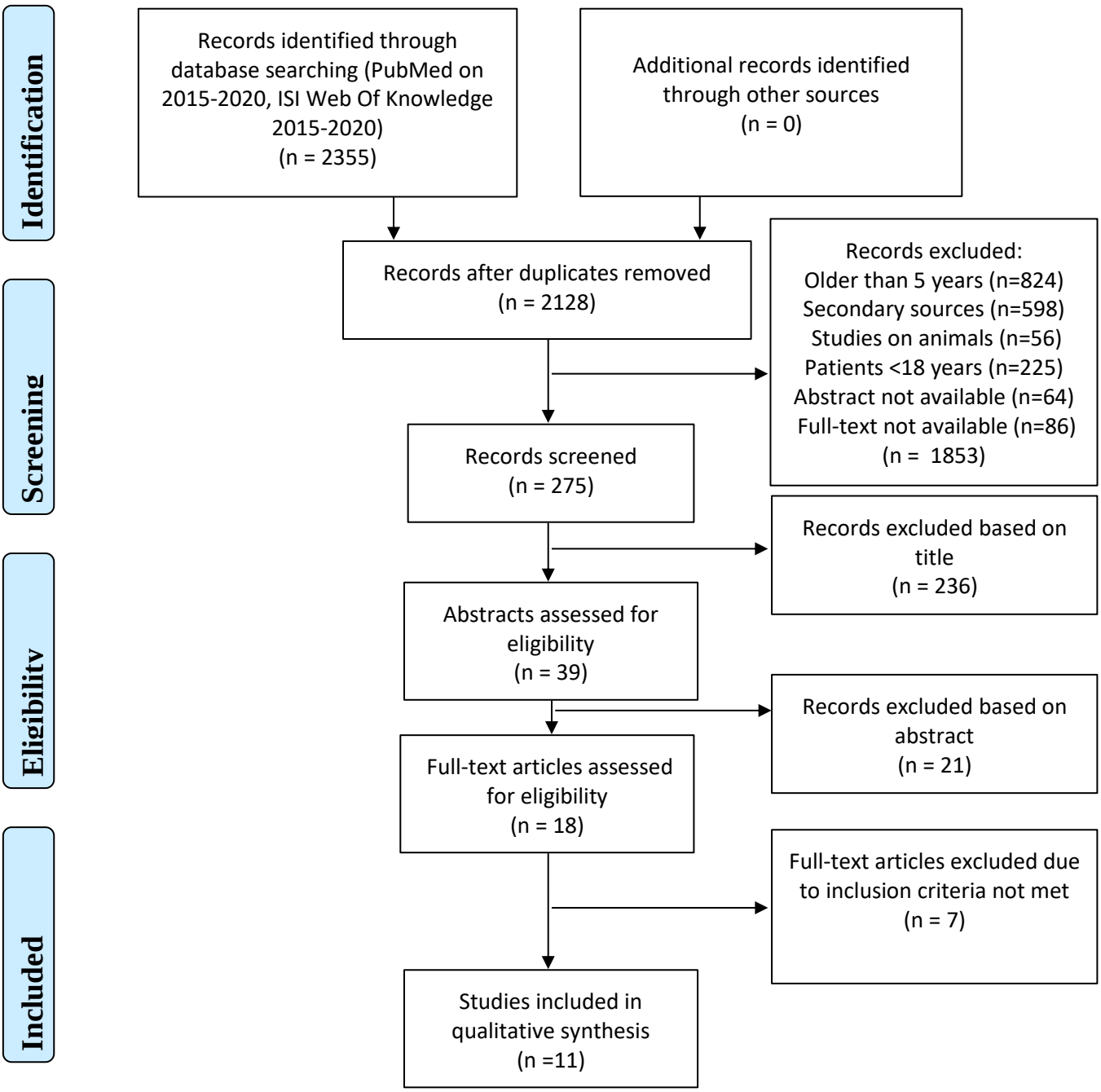


Table 3. Study characteristics of the included articles.

Author, Year, Reference	Study design and Duration	Number of Participants and Inclusion Criteria	Age in years, mean ± SD	Measurement Method
Marty et al. 2017 [26]	Pilot study; 2 months	N = 35, (AHI > 10), moderate-severe OSA	49.6 ± 14.1	PSG, Questionnaire
Pitarch et al. 2018 [27]	Prospective clinical trial; 6 months	N = 41, (AHI > 5/h)	54.5 ± 10.3	PSG, Questionnaire
Verburg et al. 2017 [28]	Retrospective study; 3 months	N = 137 MAD Somnodent = 67 MAD Herbst = 70 (AHI > 10)	Somnodent; 54.51 ± 10.23 Herbst; 55.59 ± 9.96	PSG
Marklund et al. 2015 [29]	Randomized clinical trial; 4 months	N = 91 Study group n = 46 Control group n = 45, (AHI < 30) Mild-moderate OSA	49.8 (10.6)	PSG, Questionnaire
Durán-Cantolla et al. 2015 [30]	Randomized controlled crossover clinical trial; 4 months	N = 38, (5 ≤ AHI < 30) mild to moderate OSA	46.2 + 9.1	PSG, questionnaire
Van Haesendonck et al. 2016 [31]	Prospective study; 4 months	N = 112, (AHI > 5) presence of OSA	47.9 ± 9.7	PSG, questionnaire
Nikolopoulou et al. 2017 [32]	Randomized controlled trial; 6 months	N = 57 MAD = 20 nCPAP = 18 Placebo = 19, (AHI ≥ 5) presence of OSA	50.4 ± 8.9	PSG, Questionnaire
Fernandez-Julian et al. 2018[33]	Case-control study ;6 months	N = 40 Study group = 30 Control group = 10, (AHI ≥ 15) moderate to severe	54.8 ± 10.1	PSG, Questionnaire
Wang et al. 2017 [34]	Prospective study;3 months	N = 60, (AHI > 5)	44.6 ± 11.0	PSG, Questionnaire
Umemoto et al. 2017 [35]	Prospective study;3 months	N = 52 , Twin-block group = 23 Fixed group = 29, (AHI ≥ 5)presence of OSA	Twin-block group; 52.9 ± 10.7 Fixed group; 53.8 ± 8.6	PSG, Questionnaire
Galic et al. 2016 [36]	Prospective study; 12 months	N = 15, (5 ≤ AHI ≤ 30) mild to moderate	51.2 ± 8.9	PSG, Questionnaire

3.2. Study exclusion

Seven studies were excluded after a full-text review due to absence of polysomnographic data pre-treatment and post-treatment [19-25].

3.3. Quality assessment

Only three of the included studies were randomized clinical trials. The quality and risk assessment was performed by using The Quality Assessment Tool for Quantitative Studies [18] and is represented in table 4. In summary, nine of the included studies were rated moderate, one study was rated weak and another one was rated strong.

Table 4. Bias assessment of the included studies.

Author	Selection bias	Study design	Confounders	Blinding	Data collection	Withdraw/drop-outs	Global rating
Marty et al. 2017 [26]	Strong	Moderate	Strong	Weak	Strong	Strong	Moderate
Pitarch et al. 2018 [27]	Strong	Moderate	Strong	Weak	Strong	Strong	Moderate
Verburg et al. 2017 [28]	Strong	Moderate	Strong	Weak	Strong	Strong	Moderate
Van Haesendonck et al. 2016 [31]	Strong	Moderate	Strong	Weak	Strong	Moderate	Moderate
Fernandez-Julian et al. 2018 [33]	Strong	Moderate	Strong	Weak	Strong	Strong	Moderate
Wang et al. 2017 [34]	Strong	Moderate	Strong	Weak	Strong	Strong	Moderate
Umemoto et al. 2017 [35]	Strong	Moderate	Strong	Weak	Strong	Weak	Weak
Galic et al. 2016 [36]	Strong	Moderate	Strong	Weak	Strong	Strong	Moderate
Nikolopoulou et al. 2017 [32]	Strong	Strong	Strong	Weak	Strong	Strong	Moderate
Duran-Cantolla et al. 2015 [30]	Strong	Strong	Strong	Strong	Strong	Strong	Strong
Marklund et al. 2015 [29]	Strong	Strong	Strong	Weak	Strong	Strong	Moderate

3.4. Study characteristics

Out of all the included articles, five were prospective cohort studies, three randomized control studies, one prospective cohort study, one pilot study and one case-control study, making up a total of 678 patients, in which 519 received MAD therapy. The follow-up period reported by the studies ranged from 2 to 12 months. The characteristics and outcome measures of the included trials are presented in table 3 and 5. Figure 3 demonstrates a summarized baseline and follow-up data of AHI score of the included studies.

Table 5. Outcome measures of the included studies.

Author, Year, Reference	Mandibular advancement device and protrusion degree	Outcome (AHI - events/h, mean)	Reduction of AHI (%)	Outcome (Sleep efficiency %, mean)	Results
Marty et al. 2017 [26]	Thermoplastic MAD (Oniris) Chairside Fabricated Mandibular Advancement Device Mean protrusion; 9.6 ± 1.8 mm	Baseline 34.1 ± 18.8 2 month follow- up; 12.78 ± 14.11 ($p < 0.001$)	62.52	N/A	A significant improvement can be observed in the apnea hypopnea index between the baseline and 2 month measure.
Pitarch et al. 2018 [27]	Custom-made adjustable acrylic appliance, DAM (Aditas, Asturias, Spain). Mean protrusion; 6.8 ± 1.7 mm,	Baseline; 22.5±16.8 3-6 month follow-up; 9.1±11.6 ($p \leq 0.05$)	59.55	Baseline; 83.6 ± 7.1% 3-6 month follow-up: 87.2 ± 6.8% (p = 0.0030)	AHI was improved significantly. The sleep efficiency increased significantly.
Verburg et al. 2017 [28]	MAD Somnodent and Herbst. Both are acrylic duo bloc titratable oral appliances. MAD is set at a constant vertical dimension	Somnodent Baseline; 18.47 3 month follow-up; 9.61 Herbst appliance Baseline; 22.66 3 month follow-up; 8.80	Somnodent = 47.96 Herbst appliance = 61.16	N/A	A significant decrease in AHI can be observed with both appliances.
Marklund et al. 2015 [29]	SR Ivocap Elastomer; Ivoclar Vivaden and Herbst teleskop mechanism screw. Mean protrusion; 6-7 mm	Study group Baseline: 15.6 ± 9.8 4 month follow- up: 6.7 ± 4.9 Control group: Baseline: 15.3 ± 10.5 4 month follow- up: 16.7 ± 10.0	57.05	Baseline: 90.7 ± 8.1% 4 month follow- up: 90.8 ± 9.3%	AHI was improved significantly. Sleep efficiency did not improve significantly.
Durán-Cantolla et al. 2015 [30]	Mandibular advancement device, KlearwayTM Mean protrusion; 8.6 ± 2.8 mm.	Baseline; 15.3 +10.2 4 month follow-up; 11.9 +15.5	22.22	Baseline: 87.1 ± 7.8% Follow-up: 88.8 ± 7.8%	MAD intervention not statistically significant. Sleep efficiency improvement not significant.
Van Haesendonck et al. 2016 [31]	Somnomed G2 (Somnomed Europe AG, Zurich, Switzerland) custom-made, titratable two-piece device Protrusion data N/A	Baseline; 24.5 ± 18.2 4 month follow-up; 12.0 ± 12.5 (p < 0.001)	51.02	N/A	AHI was decreased significantly in 112 patients.

Nikolopoulou et al. 2017 [32]	Individually adjustable MAD The MAD was set at 25% of the maximum protrusion in one patient, at 50% in 7 patients and at 75% in 12 patients	MAD group: Baseline; 22.1 ± 10.8 6 month follow-up; 5.8 Placebo Baseline; 20.1 ± 8.7 6 month follow-up; 14.9	73.75	N/A	Significant differences in the changes in AHI from baseline to follow-up can be noted.
Fernandez-Julian et al. 2018 [33]	Custom-made adjustable acrylic appliance, DAM (Aditas, Asturias, Spain). Initially at 50% of the maximal protrusion and later advanced by 0.5 to 1mm every 1-2 weeks until the patient was pleased.	Baseline; 28.7 6 month follow-up; 6.9 (P <.01.) Placebo; Baseline; 24 6 month follow-up; 23.8	75.95	N/A	A significant improvement can be observed in the apnea hypopnea index.
Wang et al. 2017 [34]	SomnoGuard SP. Titratable thermoplastic two-part device. Protrusion data N/A	Baseline; 21.9 3 month follow-up; 9.5 (< 0.001)	56.62	Baseline; 80.5 ± 13.6 % 3 month follow-up: 88.9 ± 7.9 % (< 0.001)	Statistically significant difference between the baseline and 3-month measure. AHI was decreased, whereas sleep efficiency significantly increased (all $p < 0.05$).
Umemoto et al. 2017 [35]	Twin-Block appliance and Fixed oral appliance 70% of the maximum protrusion	Twin-block Baseline; 20.6 ± 11.5 3 month follow-up; 14.7 ± 9.4 (p<0.001) Fixed appliance Baseline; 21.4 ± 15.2 3 month follow-up; 11.2 ± 9.7 (p<0.001)	Twin-block= 28.6 Fixed = 47.66	Twin-block Baseline; 75.0 ± 17.9 % 3 month follow-up; 77.2 ± 16.0 % (p=0.356) Fixed appliance Baseline; 79.5 ± 11.8 % 3 month follow-up; 82.7 ± 12.4 % (p= 0.177)	A significant difference can be observed in AHI before and after MAS treatment in both appliances.
Galic et al. 2016 [36]	Custom-made removable MAD (Silensor-sl, Erkodent) Mean protrusion; 7.0 ± 1.6 mm	Baseline: 22.9 ± 5.9 **3 months:** 11.2 ± 4.9 (p < 0.05) **1 year:** 9.7 ± 4.5 (p<0.001**)**	57.64	Baseline: 78.5 ± 17.3 % 1 year follow-up: 85.9 ± 10.5% (p= 0.437).	The mean AHI improved significantly. A notable difference between the baseline and 1-year measure can be seen. The sleep efficiency increased significantly.

N/A – Not available

3.5. Qualitative analysis

Galic et al. (2016)

This prospective study enrolled a total of 18 patients and 15 completed the entire study protocol. The inclusion criteria for the patients were as follows: (1) mild to moderate OSA ($5 \leq AHI \leq 30$); (2) at the minimum 6-8 healthy teeth; (3) protrusion of the jaw at minimum of 5 mm; (4) absence of cardiovascular disease or diabetes mellitus. Patients were excluded from the study for the following reasons: (1) abnormal dentition; (2) temporomandibular joint disorder; (3) periodontal disease; (4) respiratory or neurological disease or; (5) usage of drugs or alcohol abuse. Initially a physical examination was conducted on all the patients, a self-administrated questionnaire the Epworth Sleepiness Scale (ESS) was carried out and all measurements were obtained with polysomnography. The polysomnography test was performed at the baseline to determine OSA and at the time of 3-month and 1-year follow-up. All the participating patients received a custom-made MAD (Silensor- sl, Erkodent, Pfalzgrafenweiler, Germany) and were all treated by a qualified dentist. The appliance was adjusted at 50% of the maximum protrusion for each patient initially. In a four week period patients were allowed to adjust the appliance at the clinic until improvement was noted. The mean maximal mandibular protrusion was 68.8% ± 56%. Every day over a one year period the patients recorded bedtime, wake-up time and total amount of hours the device was used.

The mean AHI improved significantly between the baseline and 3-month follow-up (22.9± 5.9 to 11.2 ± 4.9, $P < 0.05$) but even more so between the baseline and 1-year follow up (22.9 ± 5.9 to 9.7±4.5, $P<0.001$). A total of 67% of patients had at least 50% decrease of AHI rates after 1-year of MAD therapy. In 53% of the patients the AHI values was decreased to <10 and a total of 4 (27 %) patients reached AHI <5. The sleep efficiency increased (78.5 ± 17.3% to 85.9 ± 10.5%) following the treatment.

Marklund et al (2015)

This randomized, single-blinded, parallel study enrolled a total of 96 patients and 91 completed the study. The inclusion criteria for the patients were as follows: (1) mild to moderate OSA ($5 \leq AHI \leq 30$); (2) daytime sleepiness (3) 20-70 years of age and; (4) body mass index lower than 35. Patients were excluded from the study for the following reasons: (1) Grade 3 or 4 tonsillar hypertrophy (accorindg to Friedman's staging system); (2) psychiatric diseases; (3) dementia; (4) untreated cavity or periodontal disease; (5) occupational drivers; (6) insufficient amount of teeth for retention and; (7) patients with a bias. The included patients completed the ESS questionnaire, Karolinska

Sleepiness Scale, a health survey, Oxford Sleep Resistance, and the Functional Outcomes of Sleep Questionnaire. Furthermore the participants underwent an overnight polysomnography for the assessment of the AHI and sleep quality. The participants were then divided into two groups assigned to receive MAD or placebo device treatment. Forty-five of the participants in the active oral appliance group used a two-part appliance (SR Ivo Elastomer Icoclar Vivadent) with a mean mandibular advancement of 6.8 mm. Forty-six of the participants in the placebo device group used a bilaminate splint with retention to the palate and a total of 89% of the patients used the device the whole night.

The mean AHI improved significantly between the baseline and 4-month follow-up (15.6 ± 9.8 to 6.7 ± 4.9) for the active oral appliance group however, the AHI values for the placebo device group was substantially different (15.3 ± 10.5 to 16.7 ± 10.0). Forty-nine percent of the patients in the active oral appliance group the AHI decreased below 5 whereas 11% of the patients in the placebo group had an AHI below 5. In the oral appliance group 89% of the patients wished to continue with the treatment. No significant difference was noted in sleep efficiency when comparing the oral appliance group with the placebo device group (90.7 ± 8.1% to 90.8 ± 9.3%).

Durán-Cantolla et al. (2015)

This randomized, placebo controlled, double blinded and crossover clinical trial study enrolled 42 patients and 38 completed the study. The inclusion criteria for the patients were as follows: (1) > 18 years old; (2) chronic snoring; (3) mild to moderate OSA (5 ≤ AHI < 30); and (4) have a roommate to submit information. Patients were excluded from the study for the following reasons: (1) high-risk professions; (2) moderate to severe somnolence; (3) coronary cardiopathy, acute vascular disease, pulmonary disease and chronic treatment with theohyllines; (4) periodontitis or temporomandibular joint problems; (5) <6 mm capacity of mandibular advancement and <10 teeth in each jaw; (6) cognitive disorders; (7) pregnancy. ESS questionnaire was used to measure somnolence and polysomnography was performed on all patients before and after the treatment.

The participants were then divided into two groups assigned to receive MAD or placebo device treatment. Initially a wash-out period was carried out for two weeks followed by 4 weeks of adaptation of the appliance and 12 weeks of treatment. The sequence was then repeated once more by switching the appliance but following the same protocol. In the present study the KlearwayTM device was used with a mean mandibular advancement of 8.6 ±2.8 mm. The same type of appliance was used for placebo device except in was set in centric occlusion.

No statistically significant difference was noted in the mean AHI values following the treatment with MAD (15.3 ± 10.2 to 11.9 ± 15.5). However, the placebo device increased the AHI from 15.3 ± 10.2 to 25.6 + 26.0 which was statistically significant. Fifty percent decrease in the AHI was achieved in 46.2% of the patients treated with MAD compared to 18.4% treated with placebo device. Patients treated with MAD achieved values of AHI < 5 in 31.6% of the patients compared to 15.8% for placebo device. However, in some cases the AHI values worsened when treated with MAD. In 10.3% of the cases the AHI increased by 50% compared to 31.6% for placebo device. Sleep efficiency improvement was not significant modified in neither MAD (87.1 ± 7.8% to 88.8 ± 7.8%) nor placebo device (88.9 ± 7.8%).

Marty et al. (2017)

This pilot study enrolled a total of 41 patients and 35 completed the entire study protocol. The inclusion criteria for the patients were as follows: (1) 18 to 80 years old; (2) moderate or severe OSA (AHI >10) Patients were excluded from the study for the following reasons: (1) < 8 teeth per dental arch; (2) dental infection or periodontal disease; (3) temporomandibular joint problems; (4) neurological or psychiatric disorders; (5) obesity; (6) clinical nasal obstruction; (7) bone disease; (8) patients with pacemaker. Initially a physical examination and polysomnography test was conducted on all the patients in addition ESS questionnaire, visual analogue scale and pittsburg sleep quality index were completed by the patients.

The appliance used in this study was a custom-fitted thermoplastic MAD (Oniris; Laboratoire Oniris, Chaville, France) with a mean maximal mandibular advancement of 9.6 ± 1.8 mm. After 30 to 45 days of using the appliance a polysomnography was performed and a final polysomnography was conducted after 50 to 60 days.

The mean AHI improved significantly between the baseline and 2-month follow-up, dropping from 34.1 ± 18.8 to 12.8 ± 14.1. Sixty-nine percent of the patients were considered to be responders meaning a decrease in the AHI of > 50% was obtained. Sixty percent were complete responders meaning the AHI decreased to < 10 at the end of the treatment and 9% were partial responders. In general a significant decrease was achieved between the baseline and the last check-up.

Pitarch et al. (2018)

This prospective clinical trial enrolled a total of 51 patients and 41 completed the entire study protocol. The inclusion criteria for the patients were as follows: (1) age > 18 years; (2) OSA (AHI > 5/h); (3) treatment failure with either CPAP or surgery. Patients were excluded from the study for the following reasons: (1) temporomandibular joint problems; (2) pregnant patients; (3) periodontal disease; (4) usage of medication that could interfere with the sleep stages; (5) < 10 teeth per dental

arch. Baseline data was collected by polysomnography test, ESS questionnaire and by a snoring visual analogue scale. The polysomnography was repeated after 3-6 months with the appliance in the mouth. The appliance used in this study was a custom-made appliance, DAM® (Aditas, Asturias, Spain) with a mean mandibular advancement of 6.8 ± 1.7 mm. The average AHI was reduced significantly between the baseline and 3-6-month follow-up (22.5 ± 16.8 to 9.2 ± 11.6). In 27 out of the 41 participants there was a AHI reduction of ≥ 50%, meaning there was a treatment success rate of 65.8%. With the appliance the sleep efficiency improved significantly (83.6 ± 7.1% to 87.2 ± 6.8% p = 0.0030)

Verburg et al. (2017)

This retrospective, cohort study enrolled a total 137 patients. The inclusion criteria for the patients were as follows: (1) OSA patients with AHI > 10. Patients were excluded from the study for the following reasons: (1) AHI < 10; (2) edentulous; (3) prosthesis; (4) only snoring. The AHI value was measured with a polysomnography test before the treatment and after at least 3 months of wearing the appliance. A standard questionnaire was not used due to the type of study. Two types of devices were used in this study; type "Somnodent-Flex" (MAD 1) and type "Herbst" (MAD 2). The MAD was set at a constant vertical dimension. Sixty-seven of the patients were treated with MAD 1 and 70 of the patients with MAD 2.

The average AHI was reduced significantly between the baseline and 3-month follow-up for both MAD 1 (18.47 to 9.61) and MAD 2 (22.66 to 8.80). A reduction of 48% was obtained in the AHI rates for patients treated with MAD 1 and 61% in patients treated with MAD 2. An AHI reduction of < 5 was obtained in 35.8% and 43.7% of the MAD 1 and MAD 2 patients, respectively. An AHI reduction of <10 was obtained in 61.2% and 67.6% of the MAD 1 and MAD 2 patients, respectively. The difference between the reductions of the AHI values between the two devices is 13% which is a relatively small difference in effectiveness between the two appliances.

Van Haesendonck et al. (2016)

In this prospective clinical trial 112 patient constituted the final sample. The inclusion criteria for the patients were as follows: (1) age > 18 years; (2) presence of OSA (AHI > 5). Patients were excluded from the study for the following reasons: (1) compromised dental status; (2) periodontal disease; (3) edentulous. All participants underwent a thorough clinical examination and data of the most recent polysomnography session was obtained before the study for the baseline recording. A final polysomnography test was performed during the follow-up with the device in situ. In total the patients in this study underwent two overnight polysomnography recordings. In addition the patients filled out ESS questionnaire and the visual analogue scale at the baseline as well as the time

of the follow-up. The MAD used in this study was a custom-made Somnomed G2® device (Somnomed Europe AG, Zurich, Switzerland).

The average AHI was reduced significantly between the baseline and 4-month follow-up (25±18 to 12±13 $p < 0.001$). Fifty-eight percent of the cases showed an AHI decrease of ≥ 50%. Approximately 31.3% had an AHI reduction of < 5 and 57.1% of the participants had obtained AHI < 10 events/h.

Nikolopoulou et al. (2017)

This randomized controlled trial enrolled a total of 64 OSA patients and 57 participants completed the entire study protocol. The inclusion criteria for the patients were as follows: (1) age > 18 years; (2) AHI of 5–45 events/h; (3) excessive daytime sleepiness. Patients were excluded from the study for the following reasons: (1) body mass index greater than 40; (2) usage of medication that could interfere with the sleep stages; (3) patients previously treated with nasal Continuous Positive Airway Pressure (nCPAP) or an oral appliance; (4) temporomandibular joint disorders; (5) periodontal disease or dental pain; (6) presence of other sleep disorders; (7) poor retention for a device. Epworth Sleepiness Scale questionnaire was used to measure somnolence and polysomnography was performed on all patients before and after 6 months of treatment. In total the patients in this study underwent two full polysomnography recordings. The participants were randomly divided into three groups assigned to an MAD, nCPAP or an intra-oral placebo device treatment (20 MAD patients, 18 nCPAP patients and 19 placebo patients). This study used individually adjustable for the MAD group device, REMstar Pro system for the nCPAP group and a thin hard acrylic resin palatal splint for the placebo group. The MAD was set at 25% of the maximum protrusion in one patient, at 50% in 7 patients and at 75% in 12 patients.

The mean AHI improved significantly between the baseline and 6-month follow-up (22.1 to 5.8), the AHI values for the placebo device group was substantially different (20.1 to 14.9). No statistically significant difference was noted in the mean AHI values between the MAD and nCPAP treatment ($P = 0.092$) however, the changes in AHI were significantly larger when compared to the placebo group ($P = 0.000$ and 0.002, respectively).

Fernandez-Julian et al. (2018)

A case-control study was conducted on the efficacy of a MAD versus no treatment. In total 40 patients completed the study, in which 30 were assigned to the study group and 10 to the control group. The inclusion criteria for the patients were as follows: (1) age > 18 years; (2) moderate-to-severe OSA (AHI ≥ 15); (3) refused CPAP treatment. Patients were excluded from the study for the following reasons: (1) somatic or psychiatric disease; (2) respiratory or cardiovascular disease; (3)

pregnant patients; (4) acute or chronic inflammatory disease; (5) body mass index greater than 32; (6) < 8 teeth per dental arch; (7) periodontal disease and temporomandibular disorder. A thorough assessment was executed at baseline and at 6 months by polysomnography test, ESS questionnaire, Functional Outcome of Sleep Questionnaire and by inflammatory markers. The oral appliance used in this study was a custom-made two-piece device (Aditas, Asturias, Spain). The mandibular position was set at 50% of the maximal protrusion and was later advanced by 0.5 to 1mm every 1-2 weeks until the patient was pleased.

The mean AHI improved significantly between the baseline and 6-month follow-up (28.7 to 6.9), the AHI values for the placebo device group was substantially different (24 to 23.8). An AHI reduction of <5/h was obtained in 23.3% of the patients whereas 40% of the patients achieved an AHI of <10/h. Treatment failure (AHI ≥ 10/h) in 36.6% of the patients was obtained.

Wang et al. (2017)

In this study 60 patients completed the entire study protocol. The inclusion criteria for the patients were as follows: (1) presence of OSA (AHI > 5); (2) patients diagnosed by polysomnography; (3) refused CPAP treatment. Patients were excluded from the study for the following reasons: (1) patients previously treated with surgery or CPAP; (2) anatomic abnormalities of the oral cavity; (3) dental defects; (4) weight change of >10% recently; (5) no partner to report information. A thorough evaluation was executed at baseline and after 3 months of wearing the device. The following evaluation was conducted; polysomnography test, ESS questionnaire, and acoustic pharyngometry. The device used in this study was a titratable thermoplastic MAD, the SomnoGuard SP So (Tomed GmbH, Köln, Germany). Patients were instructed trough a video on how to adjust the MAD at home and were later examined to ensure that the appliance was used correctly.

The mean AHI improved significantly between the baseline and 3-month follow-up (21.9 to 9.5) A total of 66.7% of patients had a reduction of ≥ 50% from baseline in the AHI and 60% were adherent to treatment. AHI was decreased, whereas sleep efficiency was significantly increased (80.5 ± 13.6 % to 88.9 ± 7.9 %).

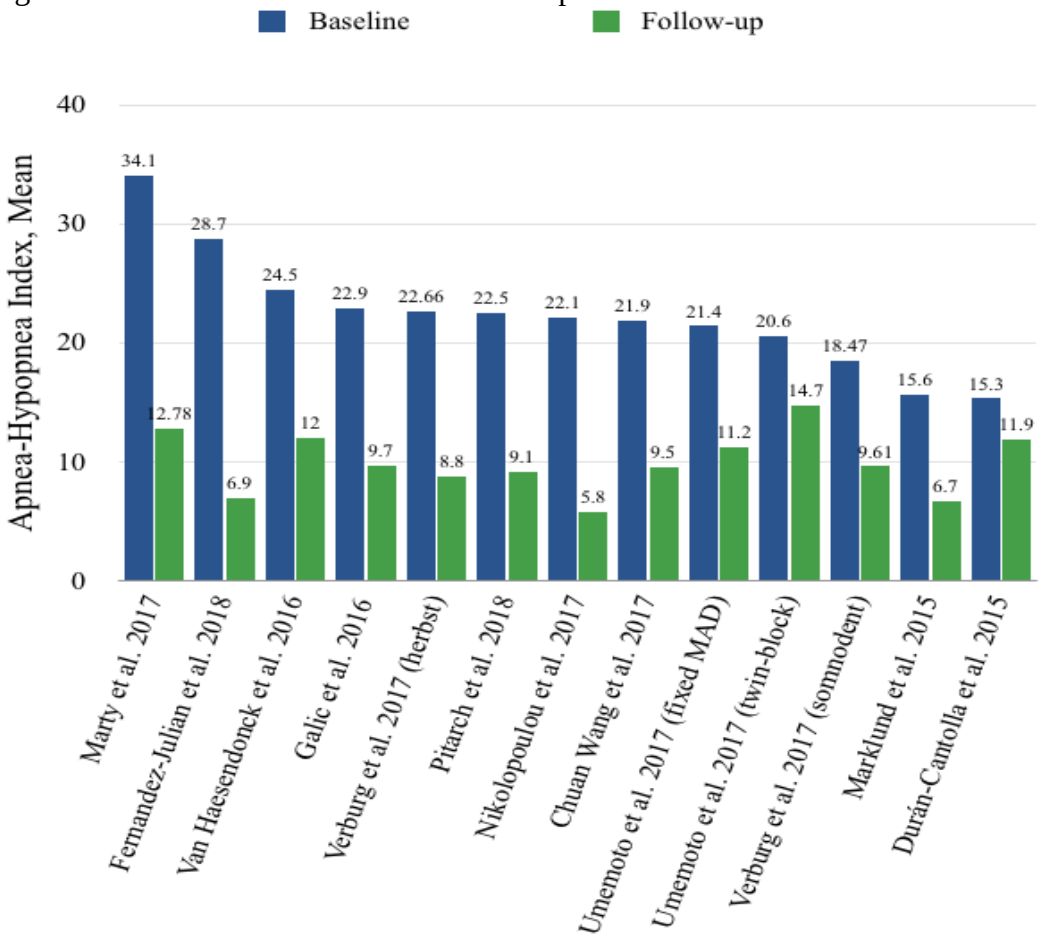
Umemoto et al. (2017)

In this study 52 patients completed the entire study protocol. The inclusion criteria for the patients were as follows: (1) presence of OSA (AHI > 5); (2) patients diagnosed by polysomnography; (3) non-responders to CPAP treatment. Patients were excluded from the study for the following reasons: (1) anodontia; (2) periodontitis; (3) severe malocclusion; (4) temporomandibular joint disorder. ESS questionnaire was used to measure somnolence and polysomnography was performed on all patients before and after 3 months of wearing the device. The participants were divided into

two groups assigned to receive a twin-block Silensor (Erkodent Gmbh, Tuttlingen, Germany) or a fixed MAS treatment. Twenty-three participants were in the twin-block group and 29 in the fixed group. The mandibular position was set at 70% of the maximal protrusion.

The mean AHI improved significantly between the baseline and 3-month follow-up for both the twin-block group (20.6 ± 11.5 to 14.7 ± 9.4) and the fixed group (21.4 ± 15.2 to 11.2 ± 9.7). An AHI improvement by >50% or to <5 was obtained in 21.7% of the patients in the twin-block group and 48.3% in the fixed group. AHI improvement by >25% with an AHI >5 was obtained in 39.1% of the patients in the twin-block group and 31.0% in the fixed group. An AHI improvement of <25% with an AHI >5 was considered to be non-responders. In the twin-block group 39.1% of the participants were non responders and 20.7% in the fixed group. Sleep efficiency improvement was not significantly modified in either the twin-block (75.0 ± 17.9 % to 77.2 ± 16.0 %) or the fixed appliance (79.5 ± 11.8 % to 82.7 ± 12.4 %).

Figure 3. Summarized baseline and follow-up data of AHI score of the included studies.



5. Discussion

5.1. Principal findings

Eleven studies were evaluated in order to determine the effectiveness of MADs in decreasing AHI. In the study conducted by Verburg et al. 2017 [28] two types of devices were used; Somnodent-flex and Herbst. Likewise two types of appliances, twin-block and fixed MAD, were applied in the study conducted by Umemoto et al. 2017 [35]. Ultimately 11 studies were evaluated however, 13 MADs were reviewed altogether. In total, the present systematic review assessed the data of 519 patients that received MAD therapy. The articles presented a significant percentage of AHI reduction in patients treated with MADs, ranging from 22% to 75%. The definition of treatment success in reports of MAD effectiveness varies greatly, therefore the criteria of success is described differently in each article. In this review treatment success is defined by a reduction of AHI by ≥50% from baseline or reduction of AHI to ≤5 events/h [13]. Of the 13 MADs assessed in the articles, 9 proclaimed a 50% reduction in AHI and thus met the criterion of success. The study conducted by Fernandez-Julian et al. 2018 [33] had the biggest change in terms of AHI, in which a change from 28.7 events/h to 6.9 events/h was documented. The minimum change was noted in the study conducted by Durán-Cantolla et al. 2015 [30] which recorded a change from 15.3 events/h to 11.9 events/h. Similar outcomes to this review were presented in other systematic reviews, for instance the study conducted by John et al [37] in 2018 or Noller et al. [38] in 2017 as well as in the study conducted by Serra-Torres et al. [39] in 2015. This increases the credibility of the results obtained in this review.

The strength of evidence concerning the secondary outcome variable is inferior compared to the primary outcome variable since only 6 out of 11 studies measured the sleep efficiency. All of the six studies reported a slight increase in sleep efficiency in patients treated with MAD, however, only three showed a statistically significant improvement.

The value of this review is the confirmation that MADs are an effective treatment option for OSA based on the positive outcomes of decreasing the AHI events/h and thus improving symptoms. Several studies adjusted the protrusion degree for every participant to ensure the maximum efficacy of the device; this can have affected the outcomes of the device. A dentist should therefore establish the optimal titration of the device which may not be the maximal possible protrusion, but instead the degree with the greatest response from the patient.

This review included participants diagnosed with mild, moderate or severe OSA. Despite the fact that research states that treatment success with MAD is lower in cases with severe degree of the

syndrome, [40] subjects with severe sleep apnea were not excluded. Even though MAD is not the first treatment option for patients with severe sleep apnea it can be a viable alternative for subjects that either refused or are struggling with other treatment methods (such as CPAP). The fact that severe cases should be included is also mentioned by White et al. [41] and Guimarães et al. [42]. A study performed on the mortality rates of severe OSA population established that patients that were intolerant to CPAP, but were treated with MAD, died less than patients that were left untreated [42]. Any improvement of the severity of the syndrome is better than none and therefore MAD can be considered as an alternative for CPAP treatment. Moreover, MADs are discreet when used and could have positive influence on the self-confidence of the subject.

The effectiveness of MAD therapy was evaluated by assessing the polysomnography recordings, which was performed in all of the studies included in this review. The method of choice for assessing AHI was polysomnography, to make sure that the same quality outcomes were obtained from all the participants. Utilizing other diagnostic methods, such as a polygraph might underscore AHI due to missing possible hypopneas [43].

5.2. Limitations and future scientific recommendations

Four limitations can be mentioned. First limitation to this study is that the number of patients in each study was rather small. Aside from the studies conducted by Verburg et al. 2017, [28] Van Haesendonck et al. 2016 [31] and Marklund et al. 2015 [29] which evaluated 137, 112, and 91 participants, receptively, all the remaining studies had less than 60 participants. Greater number of participants should be included in future studies, so that a more precise assessment of the efficacy of MAD treatment can be made. Nonetheless, 519 subjects were assessed, which can be considered large enough to make a conclusion from the outcomes.

Second, the search strategy was not limited to randomized controlled trials. Even though randomized controlled trials are considered to provide the most accurate information on the effectiveness of interventions, following selection process, only a limited number of articles were found, therefore various types of studies were included. As a result heterogeneity of the data occurred within the studies and therefore meta-analysis could not be conducted. Instead, a descriptive statistical analysis was conducted, which poses a threat to validity. This may have affected the quality and authenticity of the results of the included studies as well as on the results of this review.

Third, the follow-up period in the articles under review varied considerably, ranging from 2 to 12 months. Longer follow-up periods are necessary in order to evaluate the effectiveness of MAD in the longer term.

Fourth, various types of customized devices as well prefabricated devices were utilized in this study. Studies comparing custom-made and ready-made MADs states that the former offers clear advantages in performance, patient preference and compliance [44]. Despite the fact that the mechanism of action of these devices is similar, having different types of devices can be a possible confounder. Furthermore, as a result of the numerous different appliances available at the moment and lack of research being conducted on them, the question of which type of customized and prefabricated devices are the most efficient arises.

6. Conclusion

1. The 11 studies assessed in this review presented a significant percentage of AHI reduction in patients treated with MADs, ranging from 22% to 75%. Of the 13 MADs assessed, 9 proclaimed a treatment success by ≥50% reduction in AHI, meeting the set criteria of treatment success.
2. Six studies documented on the outcomes of sleep efficiency, all of the following reported a slight increase of sleep efficiency in patients treated with MADs, however, significant improvement was only obtained in three of the studies.
3. Considering the reduction in obtained in AHI, the effectiveness of MAD therapy in obstructive sleep apnea patients seems evident. Therefore one of the most effective appliances for treating patients with OSA is the mandibular advancement device. However, randomized controlled trials and long-term follow-up periods are required in order to draw a definite conclusion about the effectiveness of the treatment.

7. Practical recommendations

a. The practicing dental professional must play a more active role in identifying individuals at greatest risk for OSA.
b. Interdisciplinary team must work collectively during examination in order to obtain optimized treatment outcomes.
c. A qualified dentist needs to make a careful patient selection, MAD selection, and assess patient's compliance as well as the patient's expectations for successful treatment outcomes.

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9. Annexes

Figure 1. Example of a mandibular advancement device – Somnodent.