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Review

Efficacy of Mandibular Advancement Devices in the Treatment of Mild to Moderate Obstructive Sleep Apnea: A Systematic Review

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Abstract

Background: Mandibular advancement devices (MADs) are widely used for mild-to-moderate obstructive sleep apnea (OSA). We aimed to synthesize recent evidence on their clinical effectiveness and tolerability. **Methods**: A systematic review was conducted. Ten studies were included, evaluating MAD therapy in adults with mild-to-moderate OSA. The review reported on standard outcomes, including the apnea-hypopnea index (AHI), oxygenation, daytime sleepiness (Epworth Sleepiness Scale, ESS), quality of life, adherence, and adverse events. Risk of bias was also assessed. **Results**: Across the included studies, MADs consistently reduced AHI from baseline and improved ESS and/or snoring. In head-to-head comparisons, MADs generally yielded smaller reductions in AHI than CPAP but achieved comparable improvements in symptoms and quality of life, with higher nightly adherence. Reported adverse effects were mostly mild and transient. **Conclusions**: MAD therapy is an effective and generally well-tolerated option for adults with mild-to-moderate OSA and for the patients intolerant to CPAP, although average AHI reduction is smaller than with CPAP. Given the low certainty and heterogeneity of current evidence, high-quality randomized trials with objective adherence tracking and standardized titration are needed.

Keywords: obstructive sleep apnea (OSA); mandibular advance device (MAD); apnea hypopnea index (AHI); continuous positive airway pressure (CPAP); polysomnography (PSG)

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1. Introduction

About 25% of men and 15% of women suffer from obstructive sleep apnea (OSA), a prevalent disease that is more common in obese subjects [1–6]. It is characterized by repetitive episodes of partial or complete obstruction of the upper airway during Rem and

non-Rem sleep, a reduction in oxygen saturation in the blood which activates inflammatory mechanisms and impairs glucose metabolism, and a sixfold increased risk of developing diabetes and cardiovascular illnesses [7–9]. It is associated with many symptoms and comorbidities: excessive daytime sleepiness, neurocognitive problems, obesity, type 2 diabetes mellitus, exacerbation of chronic obstructive pulmonary disease and reduced quality of life [10–17]. OSA is also thought to be a risk factor for ischemic stroke and cardiovascular disease on its own [18–21]. The patient's clinical history may include loud snoring, nocturnal awakening, gasping or choking episodes during sleep, unrefreshing sleep, morning headaches, excessive daytime sleepiness [22–29], etc. This review focuses on obstructive sleep apnea (OSA), characterized by recurrent upper airway collapse during sleep. If complete airway obstruction occurs due to negative inspiratory pressure, apnea occurs; if the obstruction is partial, hypopnea or snoring occurs [30–34]. This review addresses obstructive sleep apnea (OSA) only; central sleep apnea is outside the scope and was excluded from our analysis. The body's muscle tone normally relaxes during sleep, and at the throat, the airways made up of soft tissue walls may collapse [35–38].

1.1. Diagnosis

Obstructive sleep apnea (OSA) is diagnosed by quantifying the apnea–hypopnea index (AHI, events/hour). Estimates suggest that only ~20% of affected adults have received a formal diagnosis [39–43]. The AHI can be derived from in-laboratory polysomnography (PSG) or from validated home sleep apnea testing (HSAT; type-III devices), according to clinical context and guideline recommendations. Conventional cut-offs classify OSA as normal (<5 events/hour), mild (5–14.9), moderate (15–29.9), and severe ($\geq$30) [44–50]. Imaging modalities like cone-bean computed tomography (CBCT), magnetic resonance imaging (MRI) and Drug-Induced Sleep Endoscopy (DISE) are not diagnostic tests for OSA: they are adjuncts for phenotyping and treatment planning, including MAD candidacy [51–56]. The lateral cephalogram is the most commonly utilized in clinical practice, although only providing a two dimensional image [57–62]. To estimate the severity of sleep apnea, a correlation index is established based on the number of events per hour recorded with polysomnography, called the "apnea-hypopnea index" (AHI) [63–67]. AHI values below 5 are regarded as normal, those between 5 and 15 as very mild, between 15 and 30 as moderate and those over 30 as severe.

1.2. Treatment

In order to prevent excessive daytime sleepiness, neuropsychiatric, and cardiovascular abnormalities, the best treatment for OSA should be able to restore breathing during sleep [68–72]. Therapy begins with lifestyle measures (weight management when indicated, avoidance of alcohol and sedatives). Continuous positive airway pressure (CPAP) is the standard non-invasive treatment for OSA, particularly in severe disease, although adverse effects may limit adherence. Since its inception in the early 1980s, continuous positive airway pressure (CPAP) has been the main treatment of choice for OSA [73–78]. It is linked to a number of adverse effects including nasal congestion, discomfort brought on by pressure sensation and air leak, skin intolerance from skin inflammation, claustrophobia, and. All these adverse effects could lead the patient to long-term adherence problems. There is a general consensus that patients with AHI $\geq$30 events/hour (severe) and OSA-related symptoms should receive CPAP therapy. But it is unclear whether CPAP is indicated in patients with mild to moderate OSA ((AHI = 5–14.9) (AHI = 15–29) events/hour (mild–moderate)) [79–81]. Other alternatives include maxillomandibular and pharyngeal surgery. Reported surgical outcomes vary widely by procedure, airway anatomy, and success

definitions; surgery is generally reserved for carefully selected patients after comprehensive airway evaluation.

Therefore, in clinical setting, the MAD is regarded as an alternative for treating OSA in patients who have a low body mass index, cannot tolerate CPAP, or have upper airway resistance syndrome [82–87]. MADs advance the mandible to enlarge and stabilize the upper airway, reducing collapsibility during sleep (Figure 1). Contemporary practice uses titration rather than a fixed advancement: devices are typically adjusted to ~50–75% of the patient's maximal comfortable protrusion (commonly ≈5–8 mm in adults), with incremental adjustments guided by symptoms and objective sleep metrics. Short term adverse effects (e.g., dental discomfort, salivation, morning occlusal changes) are usually mild and transient; longer-term dental/skeletal adaptations may occur and warrant monitoring. This increases the upper airway's patency, which makes the airway less likely to collapse or narrow. Numerous studies have suggested that MAD be used to treat mild-to-moderate OSA [88–92]. A subset of patients, including some with severe OSA, are intolerant of CPAP; in such cases, MAD may be considered as an alternative or adjunct, recognizing that efficacy tends to decrease with increasing disease severity. MAD is an excellent choice for treating snoring and obstructive sleep apnea syndrome since it is easy to use and quite comfortable which can result in greater patient adherence [93,94]. In selected cases, combining MAD with nasal CPAP can lower the pressure required and improve comfort and adherence. These designs avoid the issues of air leaks and claustrophobia associated with CPAP treatment. Short term complications include jaw pain, tooth sensitivity and salivary hypersecretion, while long-term complications may involve changes in the geometry of the teeth and facial skeleton [95–98].



Figure 1. An example of a MAD.

1.3. Young Patients

Recent research has found a correlation between OSA and facial dysfunction deformity. Children who breathe via their mouths have been found to exhibit cephalometric patterns resembling those of adults with OSA [99]. OSA in childhood causes major neuropsychomotor and physical problems. Childhood OSA is associated with neurocognitive and behavioral deficits, impaired school performance, and adverse growth and cardiometabolic outcomes. Therefore, it must be identified and treated as soon as possible in an effort to pre-

vent or lessen its effects, which are extremely detrimental to a child's healthy growth [42]. Although adenotonsillectomy and continuous positive airway pressure (CPAP) have been the recommended treatments for OSA in children, there hasn't been complete success in curing this syndrome. Minimally invasive therapies have been suggested more lately [100], including speech therapy and intra-oral and extra-oral devices [101]. Since MAD improves AHI scores, it has been utilized as one of the intraoral devices to treat OSA in children; however, it is not possible to infer that MAD is an effective treatment for pediatric OSA [102].

2. Materials and Methods

2.1. Protocol and Registration

This systematic review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The review protocol was registered at The International Prospective Register of Systematic Reviews Registry guidelines (PROSPERO ID: 1006206).

2.2. Search Processing

A search on PubMed, Scopus, and Web of Science was performed to find papers that matched the topic of OSA, dating within 10 years, in English. The search strategy was created by combining terms relevant to the study's purpose. The following Boolean keywords were applied: ": "mandibular advancement device" OR "mandibular advancement splint" OR "oral appliance" OR "dental appliance" OR "MAD" OR "MAS" AND "obstructive sleep apnea" OR "OSA".

Article screening strategy	Keywords: A: "mandibular advancement device" OR "mandibular advancement splint" OR "oral appliance" OR "dental appliance" OR "MAD" OR "MAS" B: "obstructive sleep apnea" OR "OSA" Boolean Indicators: "A" OR "B" Timespan: within 10 years Electronic databases: Pubmed; Scopus; Web of Science

2.3. Inclusion Criteria

The following inclusion criteria were considered:

- Studies that investigated the use of MAD in patients suffering from OSA;
- Randomized clinical trials;
- Studies with *open access* written in English;
- Full-text articles;
- Studies that were published in the last 10 years.

Papers that did not match the above criteria were excluded.

2.4. Exclusion Criteria

The exclusion criteria were as follows:

- Animal studies;
- In vitro studies;
- Off-topic studies;
- Reviews, retrospective studies, case series and case reports, letters to the authors or comments;
- Non-English-language studies.

2.5. PICO Question

The review was conducted using the PICO criteria:

- Participants: Individuals with mild to moderate OSA, which was confirmed through overnight polysomnography (PSG). Participants: adults (≥18 y) with mild–moderate OSA (AHI 5–30 events/h) diagnosed by polysomnography or type-III HSAT Both male and female.
- Interventions: application of MAD
- Comparisons: different MAD in conservative management (no/standard care, lifestyle, positional) and alternative therapies (CPAP, surgery, weight loss).
- Outcomes: Treatment of OSA to improve quality of life and reduce the risk of cardiovascular complications, apnea-hypopnea index (AHI), oxygen saturation, and sleep quality.

2.6. Data Processing

Three reviewers (C.C., F.C., S.S.) independently consulted the databases to collect the studies and rated their quality based on selection criteria. During the screening phase, we excluded articles that did not fit the topic by reading the manuscript title and the abstract. The full texts of the remaining articles were read to conduct an eligibility analysis, according to the inclusion criteria. The selected articles were downloaded in Zotero (Version 6.0.15). Any divergence between the four authors was settled by a discussion with one senior reviewer (F.I.).

2.7. Article Identification Procedure

The appropriateness evaluation was performed independently by two reviewers, C.C and F.C. An additional manual search was conducted to increase the number of articles available for full text analysis. English language articles that met the inclusion criteria were taken into consideration, and duplicates and items that did not qualify were marked with the reason that they were not included.

2.8. Study Evaluation

The article data were independently evaluated by the reviewers using a special electronic form designed according to the following categories: authors, year of study, aim of the study, materials and methods, and results.

2.9. Quality Assessment

Two reviewers, D.D.V and S.S., evaluated the included papers' quality using the ROBINS-I tool (Cochrane Bias Methods Group and the Cochrane Non Randomised Studies of Interventions Methods Group Creative Commons Attribution Non Commercial No Derivatives 4.0 International License). In order to evaluate the possibility of bias in the outcomes of non-randomized trials comparing the health impacts of two or more therapies, ROBINS-I was created. Each of the seven evaluated points was given a bias degree. F.I., the third reviewer, was consulted in the case of disagreement until a consensus was reached. The reviewers were instructed on how to use the ROBINS-I tool and adhered to the guidelines in order to assess the potential for bias in seven different domains: confounding, participant selection, intervention classification, deviations from intended interventions, missing data, outcome measurement, and choice of reported results. Discussion and consensus were used to settle any differences or conflicts amongst reviewers in order to improve the assessments' objectivity and uniformity. In situations when agreement could not be reached, the final decision was made by a third reviewer. An extensive assessment of potential biases in the non-randomized studies included in this study was made possible by

the use of ROBINS-E for bias assessment. This contributed to the overall evaluation of the caliber and dependability of the results by pointing out the evidence base's advantages and disadvantages. The writers of this review were able to reach more informed interpretations and conclusions based on the facts at hand by taking the risk of bias into account.

3. Results

3.1. Study Selection and Characteristics

Figure 2 shows the flow diagram of a systematic review carried out using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting criteria. The diagram describes the search strategy, inclusion, and exclusion of publications at each stage of detection.

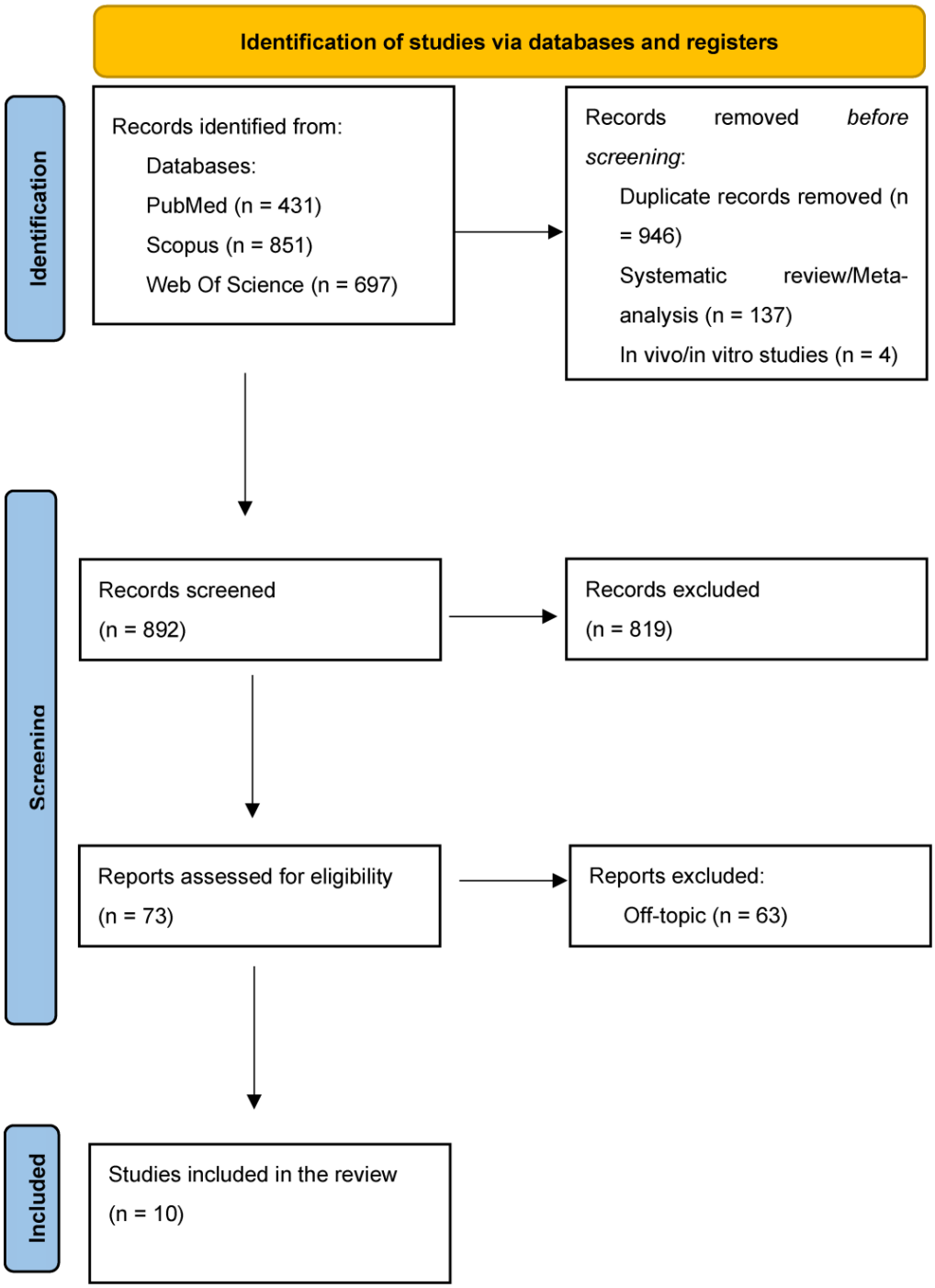


Figure 2. PRISMA flow chart.

A total of 1979 publications were identified in three databases, including PubMed (431), Web of Science (697), and Scopus (851). After screening, 946 duplicated articles, 4 in vivo/invitro studies, 137 systematic reviews were excluded. Then 819 articles were excluded by the analysis of title and abstract, leading to 73 records assessed for eligibility. After eligibility, 10 studies were included in the finale analysis. Across the included studies, MADs produced clinically meaningful reductions in apnea-hypopnea index (AHI) and improvements in daytime sleepiness (e.g., Epworth Sleepiness Scale) in mild–moderate OSA. Compared with CPAP, MADs generally achieved smaller AHI reductions but similar improvements in symptoms/quality of life, with higher nightly adherence in several studies. Adverse events were mostly mild and transient (dental discomfort, salivation, morning occlusal changes), while long-term dental/skeletal adaptations were variably reported and require monitoring. The process is summarized in Figure 2.

3.2. Quality Assessment and Risk of Bias

The risk of bias across the included studies has been systematically evaluated and summarized in Table 1.

Table 1. Bias assessment.

Authors (Year)	D1	D2	D3	D4	D5	D6	D7	Overall
Agarwal S.S et al., 2023 [103]	-	-	-	+	+	-	+	-
Bosschieter P.F.N. et al., 2022 [104]	+	+	-	-	-	+	+	-
Ciavarella D. et al., 2023 [105]	-	+	-	+	-	+	-	-
Fichera G. et al., 2020 [106]	-	+	-	-	-	+	-	-
On S.W. et al., 2024 [107]	-	+	-	-	-	-	-	-
Pahkala R. et al., 2020 [108]	-	+	-	-	+	+	+	+
Pitarch R.M. et al., 2018 [109]	-	+	-	-	-	-	+	-
Shete C.S. et al., 2017 [110]	+	+	+	+	+	-	-	+
Verburg F.E. et al., 2018 [111]	-	+	-	-	-	+	+	-
Zhu N. et al., 2024 [112]	-	+	+	+	-	-	+	+

Domains:
D1: Bias due to confounding.
D2: Bias arising from measurement of the exposure.
D3: Bias in selection of participants into the study (or into the analysis).
D4: Bias due to post-exposure interventions.
D5: Bias due to missing data.
D6: Bias arising from measurement of the outcome.
D7: Bias in Selection of the Reported Result

! Very High
X High
- Some Concerns
+ Low
? No information

The quality assessment was based on seven key domains: confounding bias, measurement of exposure, participant selection, post-exposure interventions, missing data,

measurement of outcomes, and selection of reported results. These domains were used to evaluate potential threats to the internal validity of each study. Overall, the majority of the included studies demonstrated a moderate risk of bias, with some methodological concerns. For instance, there were only minor problems with exposure and outcome measurement in Pitarch R.M. et al. (2018) [109]. However, the profiles of On S.W. et al. (2024) [107] and Agarwal S.S. et al. (2023) [103] were more mixed, exhibiting low bias in some categories but raising questions about participant selection and confounding that could limit the findings' generalizability.

While Verburg F.E. et al. (2018) [111] identified some risk of bias concerning post-exposure interventions, Fichera G. et al. (2020) [106] expressed some concerns with the selection of reported outcomes and missing data. More significant biases were present in Ciavarella D. et al. (2023) [105] and Pahkala R. et al. (2020) [108], particularly in the domains of confounding and missing data, which may have distorted their findings. Overall bias rates were modest in studies like Shete C.S et al. (2017) [110].

Lastly, issues with participant selection and outcome assessment were raised by Zhu N. et al. (2024) [112] and Bosschieter P.F.N. et al. (2022) [104], which may have affected the reliability of their findings. These recurring "some concerns" problems in numerous studies underscore the need for improved study designs in order to lessen bias and increase the validity of results.

The question in the domains evaluated in the ROBINS encompasses the following:

3.3. Clinical Outcomes

Mandibular advancement device (MAD) therapy was associated with clinically meaningful improvements across multiple outcome measures. In terms of respiratory parameters, reductions in the Apnea–Hypopnea Index (AHI) from baseline were observed in the majority of cohorts included across the ten studies. For instance, Pitarch et al. reported a decrease from 22.5 to 9.1 events per hour, Pahkala et al. from approximately 40 to 25, Ciavarella et al. from around 28 to 16, Shete et al. from approximately 30 to 20, On et al. from 32.8 to 12.9, Zhu et al. from over 30 to 14.8, and Agarwal et al. from approximately 35 to 25 events per hour. Improvements in daytime symptoms were also consistently documented. Studies reporting the Epworth Sleepiness Scale (ESS) showed notable reductions, such as Pitarch (12 to 7), Ciavarella (15 to 10), On (14 to 9), and Agarwal (12 to 8), suggesting decreased daytime sleepiness following MAD therapy. These improvements were often accompanied by reductions in snoring indices, and enhanced patient-reported sleep quality was assessed. Several studies also examined oxygenation and upper airway parameters. On et al. documented an increase in minimum SpO_2, while Shete et al. reported both improved oxygen saturation and an increase in upper pharyngeal airway volume. Ferraz et al. observed anteroposterior enlargement of the airway with the device in situ, supporting the anatomical efficacy of MADs in improving upper airway patency. When directly compared with continuous positive airway pressure (CPAP), MADs generally produced smaller reductions in AHI. However, they yielded comparable benefits in terms of symptom relief and quality of life. Notably, patient acceptance and adherence appeared to be higher with MAD therapy, particularly in individuals with low CPAP tolerance, as illustrated in the study by Fichera. Nonetheless, objective adherence monitoring was inconsistently reported across the studies, limiting comprehensive evaluation of long-term compliance. Adverse events associated with MAD therapy were primarily mild and transient, including dental discomfort, excessive salivation, and temporary morning occlusal changes. However, some studies noted the potential for longer-term dental and skeletal adaptations, which underscores the importance of ongoing monitoring during prolonged use.

Overall, MAD therapy yielded consistent within-group AHI reductions and improvements in symptoms across mild–moderate OSA cohorts, with mild/transient adverse effects and variable but generally favorable acceptance compared with CPAP. When directly compared, MADs typically produced smaller AHI decreases than CPAP yet similar gains in ESS/quality of life in several studies; objective adherence was inconsistently tracked. Given clinical/methodological heterogeneity and low overall study quality, our conclusions are conservative and emphasize the need for higher quality trials with standardized titration and objective adherence sensors (Table 2).

Table 2. Analysis of results.

Authors	Number of Patients	Study Design	AHI (Pre/Post)	ESS (Pre/Post)	Other Parameters
Agarwal S.S. et al., 2023 [103]	30 (18 M, 12 F)	CPAP vs. MAD	Pre: 35 → Post: 25	Pre: 12 → Post: 8	Satisfaction higher in MAD vs. CPAP
Bosschieter P.F.N. et al., 2022 [104]	58	Non-custom MAD vs. Custom MAD	Pre: 16.3 → Post: 10.7 (custom), Pre: 16.3 → Post: 7.8 (non-custom)	Pre-baseline: Not reported → Post: questionnaires indicated improvement post-treatment." (p = 0.005)	Adherence improvement
Ciavarella D. et al., 2023 [105]	29 (15 M, 14 F)	Customizable MAD	Pre: 28 → Post: 16	Pre: 15 → Post: 10	↑ SpO_2, ↑ quality of life
Fichera G. et al., 2020 [106]	18 (15 M, 3 F)	MAD	Pre: 40 → Post: 35	Pre: 16 → Post: 12	MAD comparable to CPAP
On S.W. et al., 2024 [107]	14 (<20 years)	Autotitrating MAD	Pre: 32.8 → Post: 12.9	Pre: 14 → Post: 9	↑ SpO_2 minima
Pahkala R. et al., 2020 [108]	58 (39 M, 19 F)	MAD	Pre: 40 → Post: 25	Pre: 16 → Post: 10	Quality of life, snoring improvement
Pitarch R.M. et al., 2018 [109]	41	MAD	Pre: 22.5 → Post: 9.1	Pre: 12 → Post: 7	Snoring index reduction
Shete C.S. et al., 2017 [110]	37	MAD	Pre: 30 → Post: 20	Pre: 15 → Post: 10	↑ Airway volume, ↑ SpO_2
Verburg F.E. et al., 2018 [111]	137	MAD 1 vs. MAD 2	No significant difference	Not reported	No significant difference in AHI
Zhu N. et al., 2024 [112]	20	MAD	Pre: >30 → Post: 14.8	Pre: 12 → Post: 10	Symptom improvement with titration

↑ = Increase.

4. Discussion

The included studies collectively indicate that MADs lower AHI and improve daytime symptoms in adults with mild–to–moderate OSA; however, heterogeneity in designs and outcome definitions together with limited objective adherence data—constrains the certainty of these findings [113–117]. While this systematic review highlights the efficacy of MADs, it's crucial to acknowledge the significant real-world challenges that limit their successful clinical implementation for mild to moderate OSA. These translational obstacles, including device tolerability, patient adherence, and the need for a multidisciplinary care model, represent key barriers to optimizing patient outcomes.

Device tolerability is one of the most commonly reported issues. Side effects such as dental discomfort, excessive salivation, dry mouth, temporomandibular joint (TMJ) pain, and occlusal changes have been described in the literature, potentially reducing patient willingness to continue treatment over time. While many of these effects are transient and improve with adaptation, a proportion of patients may ultimately discontinue therapy because of persistent intolerance.

The articles reviewed provide a comprehensive evaluation of the efficacy of MAD in treating OSA, with many studies confirming its positive impact on the AHI, oxygen saturation and sleep quality [118–122] (Figure 3). However, the success of MAD therapy is influenced by several factors such as the type of device, patient characteristics, and

anatomical variations [123–129]. This discussion explores the types of MAD, their clinical efficacy, and factors influencing treatment outcomes, while also addressing the limitations of the current body of research.

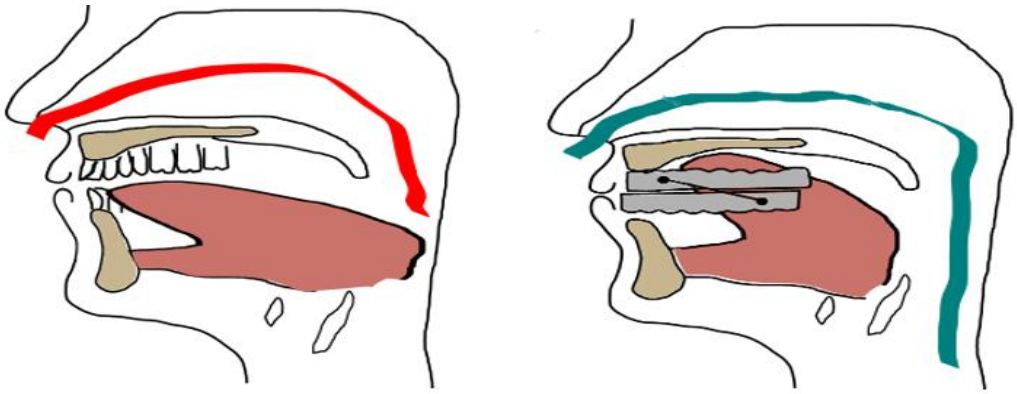


Figure 3. Mechanistic rationale of MAD therapy: tongue posture and upper airway patency.

4.1. Types and Mechanisms of Action of MAD

The type of MAD and the possibility of titration play a crucial role in treatment success [130–137]. These can be custom-made or prefabricated, with fixed or adjustable mandibular advancement to improve treatment efficacy and tolerability. Patient selection and device fitting are key factors for achieving the best therapeutic outcomes [138–142].

Agarwal S.S. et al., 2023 [103] and On S.W. et al., 2024 [107] have shown that non-customized devices, when properly adjusted, particularly self-adjustable ones, demonstrate significant improvement in patients. Agarwal observed that the AHI of patients decreased from 35 to approximately 25, while the ESS improved from 12 to 8, suggesting better sleep quality and a reduction in the severity of OSA. Similarly, On et al. reported a reduction in AHI from 32.8 to 12.9 and a decrease in ESS from 14 to 9, in addition to a significant improvement in minimal oxygen saturation (SpO_2). This data supports the theory that non-customized MADs can be more effective than fixed devices, as they better adapt to the individual needs of patients.

In contrast, Bosschieter P.F.N. et al., 2022 [104] examined the difference between non-customized and custom-made MADs, emphasizing that customization leads to better outcomes. Patients treated with custom-made MADs showed a reduction in AHI from 16.3 to 10.7, compared to a reduction from 16.3 to 7.8 in patients treated with non-customized devices. Although ESS data were not reported, this study suggests that device customization may lead to better results, especially in terms of reducing the AHI. In a study of 137 patients, Verburg F.E. et al., 2018 [111] compared the use of two different types of MADs. The results showed no significant differences between the two devices, neither in terms of reduction in AAI nor improvement in ESS. However, no detailed data on treatment adoption were reported, and the absence of significant differences suggests that other variables, such as patient selection, may play an important role in clinical outcomes.

4.2. Clinical Efficacy and Predictive Factors

Several studies have evaluated the efficacy of MADs using parameters such as AHI and ESS, documenting significant improvements in OSA treatment. Ciavarella D. et al., 2023 [105] treated 29 patients with a custom-made MAD, showing a reduction in AHI from 28 to approximately 16 and in ESS from 15 to 10. Additionally, improvements in oxygenation and quality of life were reported, indicating that custom-made MADs are particularly effective in patients with mild to moderate OSA. Pahkala R. et al., 2020 [108] reported similar results in a group of 58 patients treated with MADs, with a reduction in

AHI from 40 to 25 and a decrease in ESS from 16 to 10. This data highlights the efficacy of MADs but also the importance of accurate patient selection to optimize results. Fichera G. et al., 2020 [106] observed a reduction in AHI from 40 to approximately 35 and in ESS from 16 to 12 in 18 patients treated with MADs. Although these improvements are notable, the values do not reach the extreme reductions observed in other studies. This suggests that while MADs can be effective, they may not always be the first line treatment for severe OSA, where CPAP may be preferable. Pitarch R.M. et al., 2018 [109] highlighted that in 41 patients treated with MADs, AHI dropped from 22.5 to 9.1, while ESS decreased from 12 to 7, along with a significant reduction in the snoring index. This data suggests that MADs not only improve AHI and ESS but also reduce snoring, a common symptom in OSA patients. Shete C.S. et al., 2017 [110] documented a reduction in AHI from 30 to approximately 20 and in ESS from 15 to 10 in 37 patients treated with MADs. Furthermore, an improvement in upper airway volume and oxygenation was observed, suggesting that MADs not only reduce AHI but also lead to anatomical improvements in the upper airways. Zhu N. et al., 2024 [112] recorded a reduction in AHI from 35 to 25 and in ESS from 12 to 8 in 18 patients treated with MADs. Additionally, patients showed symptom improvement due to a titration process, which allowed for an optimal adaptation of the device to individual needs.

4.3. Translational Challenges: Tolerability, Adherence, and Multidisciplinary Care

The success of MAD therapy for OSA primarily depends on appropriate patient selection and a comprehensive clinical evaluation [143–149]. Ideal candidates for MAD treatment include patients with mild to moderate OSA, those who cannot tolerate CPAP, and individuals with favorable anatomical profiles. Pre-treatment evaluations, such as polysomnography and upper airway examinations, are essential to establish an accurate diagnosis and guide therapeutic decisions [150–153]. The titration process is crucial for ensuring the best device function and minimizing side effects such as temporo mandibular joint (TMJ) pain, occlusal changes, and increased salivation [154–158]. Regular follow-up visits are necessary to monitor adherence and device adjustments, ensuring the patient's continuous progress [159–167].

In clinical practice, the adoption of MADs poses challenges. Device tolerability remains one of the most problematic aspects, as many patients report side effects such as dental discomfort, dry mouth, TMJ pain, and hypersalivation. While these symptoms may decrease over time with adaptation, a certain number of patients may discontinue treatment due to persistent intolerance. Furthermore, adherence is a critical determinant of treatment success, yet it tends to decrease over time. This decline is often influenced by the subjective perception of benefit, socioeconomic conditions, and individual motivation, posing a significant hurdle to long-term efficacy. Unlike with CPAP, objective adherence monitoring with MADs is still limited, highlighting the need to develop more effective monitoring tools. Given these challenges, the optimal implementation of MAD therapy fundamentally requires a multidisciplinary approach. This collaborative model, involving specialists in sleep medicine, otolaryngologists, and pulmonologists, is not merely beneficial but essential for personalizing therapeutic strategies and managing comorbidities. This collaborative model supports a more personalized and holistic therapeutic strategy, optimizing both device use and clinical outcomes.

4.4. Limitations of the Study and Future Research

Although this review provides valuable insights into the efficacy of mandibular advancement devices (MADs) for the treatment of obstructive sleep apnea (OSA), several limitations must be acknowledged. The heterogeneity in study designs, sample sizes, and patient characteristics limits the generalizability of the findings. Moreover, most available

studies focus on short to medium-term outcomes, leaving the long-term impact of MAD therapy, particularly on OSA-related comorbidities such as hypertension and cardiovascular disease, insufficiently explored. Another critical issue is the frequent reliance on subjective measures, such as patient reported sleep quality, which may introduce bias and hinder the comparability of results. Future research should prioritize large scale randomized controlled trials (RCTs) to assess the long-term effectiveness of MADs, including their impact on OSA related comorbidities like hypertension and cardiovascular disease. Concurrently, efforts should be made to improve treatment tolerability, enhance adherence, and develop standardized multidisciplinary care pathways. Investigating genetic and anatomical predictors of therapeutic success may also help refine patient selection and improve clinical outcomes. A deeper understanding of the anatomical and functional changes induced by MADs over time could help bridge the gap between clinical trials and real worlds application. In this context, future studies should explore the integration of digital sensors into MADs to enable continuous monitoring of adherence and treatment effectiveness, as well as the use of artificial intelligence-based titration systems to optimize mandibular protrusion in a personalized manner, thereby improving both efficacy and tolerability. Additionally, combining MAD therapy with positional therapy or other multimodal strategies may represent a promising approach to further enhance clinical outcomes. Although CPAP remains the most cost-effective option for patients with severe OSA, real world studies suggest that MADs may offer favorable cost benefit profiles in mild to moderate cases due to higher levels of patient acceptance and adherence. Indeed, while nightly use of CPAP often declines over time, MADs are generally associated with greater comfort, portability, and social acceptability, leading to sustained adherence in many patients. This higher long-term compliance may partially offset their initial cost and reinforce the role of MADs as a valuable therapeutic alternative in clinical practice.

5. Conclusions

Mandibular advancement devices (MADs) represent a potentially effective and generally well tolerated treatment option, particularly for patients with mild to moderate obstructive sleep apnea (OSA). However, due to the overall low methodological quality of the available studies, definitive conclusions regarding their comparative efficacy especially in relation to different device types (e.g., titratable vs. fixed, customized vs. non-customized) remain premature. While some evidence suggests that MADs may produce favorable anatomical changes in the upper airway, contributing to symptom improvement, these findings should be interpreted with caution. Further high quality randomized controlled trials with standardized titration protocols, objective adherence monitoring, and consistent outcome measures are needed to confirm the long-term effectiveness of MADs and to identify predictors of treatment success. Careful patient selection and ongoing follow-up remain essential components of effective MAD therapy.

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Abbreviations

Abbreviation	Definition
OSA	Obstructive sleep apnea
MAD	Mandibular advancement devices
AHI	Apnea-hypopnea index
ESS	Epworth Sleepiness Scale
UA	Upper airway
PSG	Polysomnography
CPAP	Positive pressure airway devices

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