



## CLINICAL REVIEW

# Mandibular advancement device design: A systematic review on outcomes in obstructive sleep apnea treatment



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## SUMMARY

Obstructive Sleep Apnea (OSA) is often treated with Mandibular Advancement Devices (MADs). It is unclear whether particular design features are superior to others in terms of OSA alleviation. In order to facilitate clinical decision-making, this systematic review summarizes the objective and subjective outcomes of different available MAD designs. Studies comparing different MAD designs in OSA treatment were searched. After screening 1887 titles and abstracts, 20 original RCTs and six cohort studies were included. 14 articles were systematically reviewed in a meta-analysis. The decrease in AHI was significantly different between some of the MAD designs. The clinical relevance of the observed differences was however limited. Monoblock appliances performed more favorable, compared to bilateral thrust (effect size: -0.37; CI: -1.81 to 0.07). Midline traction appliances performed more favorable, compared to other designs. Custom appliances performed more favorable, compared to thermoplastic appliances (effect size: 0.86; CI: -0.62 to 2.35). Furthermore, there were no clinically relevant differences between MAD designs in reduction of ESS, compliance, preference, side effects, and cost effectiveness. With respect to the included trials, presently there is not one superior custom MAD design in OSA treatment regarding the effect on AHI reduction, ESS improvement, compliance, preference, side effects, cost effectiveness, and other disease-related outcomes. We confirm custom MAD designs perform superior to thermoplastic MAD designs.

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## Introduction

## Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is one of the most common sleep-related breathing-disorders [1]. Upper airway anatomy, muscle responsiveness, arousal threshold, high loop gain, and other non-

anatomical characteristics like obesity, gender, aging, and alcohol consumption are important factors affecting its severity [1–4]. OSA is associated with daytime sleepiness, lack of concentration, loud snoring, and increased risk of cardiovascular diseases [5,6]. The gold standard for the diagnosis of OSA is polysomnography (PSG), a comprehensive sleep study which yields, amongst other outcomes, the apnea-hypopnea index (AHI) [2,4,7]. In addition to reducing AHI-values, OSA treatment should have good compliance, improve subjective outcomes and have minimal side effects.

## Mandibular advancement devices

A mandibular advancement device (MAD) is a primary treatment option for mild to moderate OSA patients, and for severe OSA

*Abbreviations:* AHI, apnea hypopnea index; MAD, mandibular advancement device; OSA, obstructive sleep apnea; PG, polygraphy; PSG, polysomnography; RCT, randomized controlled trial; RDI, respiratory disturbance index.

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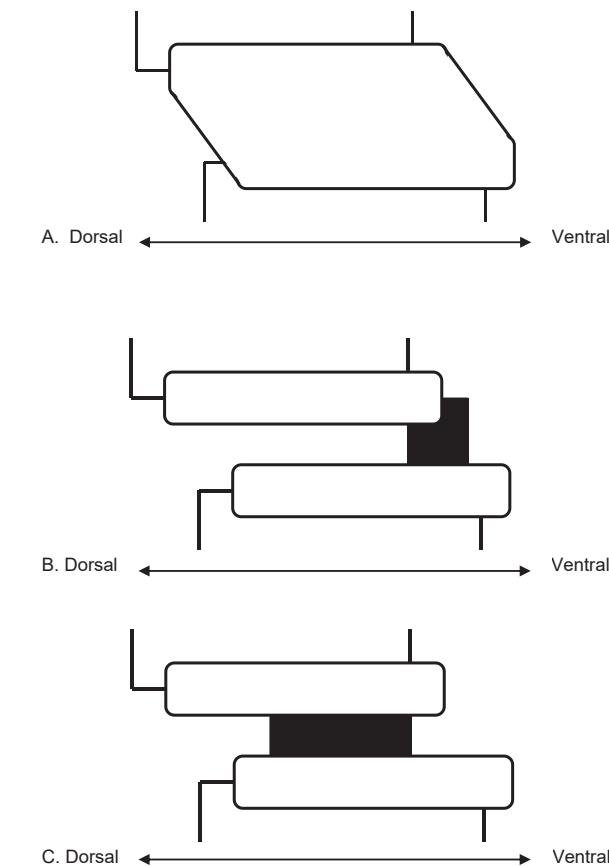
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patients who cannot tolerate continuous positive airway pressure (CPAP) [2,4]. MADs advance the mandible and tongue towards an anterior position, which consequently enlarges the upper airway and decreases its collapsibility during sleep. MADs come in different designs [8].

MAD's can be custom-made or prefabricated. Custom-made appliances are usually more expensive, made in a dental laboratory, and require dental impressions or scans of the upper and lower dentition. Prefabricated appliances, as “boil and bite” or thermoplastic appliances, are usually cheaper, sold over-the-counter, made from thermoplastic material, and do not require a dental laboratory for production. Prefabricated appliances can be fitted by a dentist, otolaryngologist, or even by patients themselves.

Another aspect in design is the fact that MADs can be titratable or non-titratable. Non-titratable appliances are usually one-piece or “monoblock” appliances, implying that the upper and lower jaw are rigidly connected. Titratable appliances consist of a separate upper and lower part, for example “biblock” or “duoblock” appliances. They may be distinguished into “midline traction” appliances, where the upper and lower part are connected in the frontal area of the appliance, and “bilateral thrust” appliances, where the upper and lower part are connected in the lateral or (pre-)molar area of the appliance (Fig. 1) [8,9]. Current guidelines suggest to use a custom titratable device [2].



**Fig. 1.** Lateral view of different design features in oral appliances. A: monoblock appliance, B: midline traction appliance, C: bilateral thrust appliance. The monoblock is a one-piece non-titratable appliance, at which the upper and lower jaw are rigidly connected. The midline traction and the bilateral thrust appliance are titratable appliances. In case of a midline traction design, the upper and lower part are connected in the frontal area of the device. In case of a bilateral thrust design, the upper and lower part are connected in the lateral or (pre-)molar area of the device.

**Objective**

This systematic review aims to answer the following question: what is the effect of MAD design on AHI reduction, improvement of sleepiness according to the Epworth sleepiness scale (ESS), compliance, patient preference, side effects, and cost effectiveness in OSA management? We hypothesize that 1) a titratable MAD is associated with better objective and subjective treatment outcome and a favorable compliance compared with a non-titratable MAD, 2) a custom-made MAD is more comfortable and yields better objective and subjective treatment outcome and is associated with a more favorable compliance when compared with thermoplastic MAD.

The results of this review might facilitate clinical decision making, yielding recommendations for the preferable MAD design in OSA management.

**Materials and methods**

*Search strategy*

A literature search was performed based on the PRISMA-statement ([www.prisma-statement.org](http://www.prisma-statement.org)). Systematic searches were conducted (by JUV and two medical information specialists) in the databases PubMed, Embase.com, and the Cochrane Library (Wiley) from inception up to June 2021 (full search strategies in supplement).

*Selection process*

All articles comparing two or more different MAD designs with respect to efficacy were selected for further evaluation. Studies were eligible for further methodological assessment when they met the following criteria: 1) studied patients were diagnosed with OSA (AHI>5) based on an overnight sleep study, 2) studied patients were aged >18 years, 3) the study evaluated two or more different MAD designs, and 4) objective effects (AHI or RDI) of the different MAD's were analyzed at baseline and follow-up. Studies comparing the same MAD with different mandibular advancements or vertical dimensions, or with different patient characteristics, as AHI or BMI, were excluded. In case of non-consensus between the reviewers, studies were discussed in a joint meeting.

*Methodological appraisal*

After selecting eligible full text articles, the methodological quality of studies was assessed by both reviewers (JUV and BR). All articles were blinded regarding title, authors, and journal. The Cochrane risk of bias was used for quality assessment of RCTs [10](S7). The Network-Ottawa Scale was used for quality assessment of Cohort studies [11](S8).

*Presentation of data*

Information relating to study design, MAD design, number of included patients, success percentage, compliance, patient's preference, daily use, side effects, cost effectiveness, PSG or PG scores (AHI, RDI) and ESS scores were collected and summarized in tables. Differences were mentioned in p values; statistically significant differences were defined by a p < 0.05.

Data of all eligible RCTs including AHI values based on a full night PSG and/or data on ESS scores were included for a meta-analysis. PG data was not included in meta-analysis due to the possible underestimation of the disease severity [12]. ODI was included when desaturation percentage was mentioned. RevMan

Statistics was used to calculate differences regarding AHI and ESS outcomes (Review Manager 5.3 Copenhagen, The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Linear regression analyses were performed to determine differences for PSG and ESS outcomes between different MAD designs.

**Results**

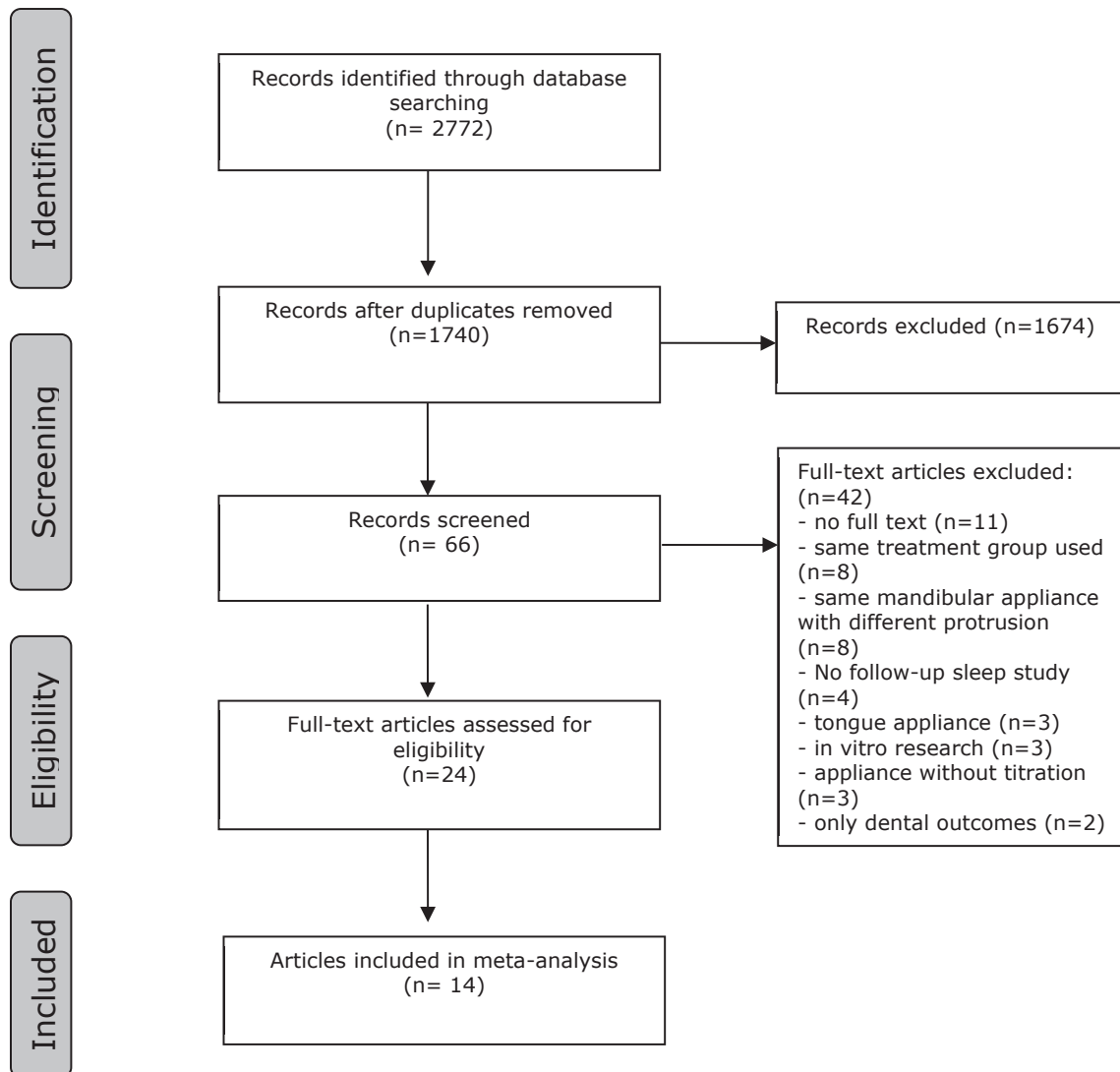
The literature search generated a total of 2949 references (1492-PubMed, 1098-Embase.com, 320-Cochrane Library). After removing duplicates, 1887 references remained. The reviewers screened all articles based on title and abstract. A total of 68 eligible full text articles were retrieved and evaluated according to the inclusion criteria (paragraph 2.2). 20 RCTs and six cohort studies, were selected (Fig. 2) and categorized into five different subgroups: 1) monoblock versus bilateral thrust appliances, 2) monoblock versus midline traction appliances, 3) bilateral thrust versus midline traction appliances, 4) bilateral thrust versus bilateral thrust appliances, and 5) thermoplastic appliances versus custom appliances. An overview of the used appliances is shown in supplement S2.

*Monoblock versus bilateral thrust*

*Background*

Baseline characteristics were comparable between all 11 RCTs [13–23] and two cohort studies [24,25] (Table 1). Mean mandibular protrusion was mentioned in all articles, except for one [16]. Mostly described as 70–80% of maximal protrusion [13–15,17–23], whereas Lee et al. and Isaacson et al. described 60% and 60–80%, respectively [24,25].

When evaluating the quality of the RCTs, selection bias was present in two RCTs [20,21]. Performance bias was present in all included RCTs [13,14,23,15–22]. In addition, in none of the studies a possible detection bias could be assessed because of a lack of detailed methodology. An attrition and reporting bias was present in one RCT [21]. Finally, other biases were observed in seven RCTs, such as a “homemade” monoblock device [13–16,18,21,22], short term use [14], and no dropouts reported during the study-period [22]. Evaluation of the quality of cohort studies yielded eight points for both studies, thereby demonstrating good quality [24,25](S7,S8).



**Fig. 2.** Flowchart of study selection.

**Table 1**  
Overview of the different studies comparing monoblock and bilateral thrust mandibular appliance design.

Author, year, reference	Study characteristics	Appliances	AHI/AHI			ESS		
			Baseline	Follow-up	Δ	Baseline	Follow-up	Δ
Al-Dharrab et al., 2017 [13]	RCT; Crossover study, 4-month follow-up, 2-week washout, 15 < AHI > 30, n = 12	Foresta dent bite jumping screw [1]	25.1 ± 4.9	1.60 ± 2.6 (p < 0.000)	1.19.1 ± 3.7 2.19.1 ± 3.7	11.3 ± 1.6	1.96 ± 0.9 2.94 ± 0.8	1.17 ± 1.3 2.18 ± 1.3
		Monoblock [2]		2.60 ± 2.5 (p < 0.000) NS	NS		NS	NS
Bloch et al., 2000 [14]	RCT; Crossover study, 156 days adaptation, 1-week per appliance follow-up, AHI > 5, n = 24	Herbst [1]	26.7 ± 3.3	1.87 ± 1.5 (p < 0.000)	1.18.0 ± 2.4 2.18.8 ± 2.5	13.5 (9.5 -16.0)	1.90 (6.5 -11.0)	1.45 (8.0 -13.5)
		Monoblock [2]		2.79 ± 1.6 (p < 0.000) NS	NS		2.90 (6.5 -10.0) NS	2.45 (8.0 -13.0) NS
Geoghean et al., 2015 [16]	RCT; Crossover study, 12-week follow-up, 2-week washout, AHI > 5, n = 45	Twinblock [1]	21.1 (14.2 -50.1)	1.15.2 (4.0-38.1) (p = 0.005)	1.5.9 (10.2 -44.1)			
		Monoblock [2]		2.5.9 (1.6-20.4) (p < 0.000) p = 0.02	NS	2.15.2 (12.6 -29.7)		
Isacsson et al., 2019 [17]	RCT; Parallel study, 6-week follow-up, AHI > 15, n = 313	Narval [1] (n = 123)	1.26.1 ± 14.3	1.12.3 ± 12.5 (p < 0.000)	1.13.8 ± 13.4	1.10 ± 4.8	1.6.7 ± 2.4 (p < 0.000)	1.3.3 ± 3.6
		Monoblock [2] (n = 139)	2.25.0 ± 14.5 NS	2.12.5 ± 12.9 (p < 0.000) NS	p = 0.011	2.9 ± 5.1 NS	2.6.1 ± 2.1 (p < 0.000) NS	2.2.9 ± 3.6 p = 0.048 NS
La Mantia et al., 2018 [18]	RCT; Crossover study, 10-week follow-up, 2-week washout, AHI > 10, n = 38	Twinblock [1]	28.5 ± 5.7	1.14.2 ± 4.5 (p = 0.003)	1.14.3 ± 5.1	13.5 ± 2.6	1.9.8 ± 2.1 (p = 0.031)	1.3.7 ± 2.4
		Monoblock [2]		2.8.5 ± 3.2 (p < 0.001) p = 0.032	2.20.0 ± 4.45 p < 0.000		2.9.4 ± 1.7 (p = 0.029) NS	2.4.1 ± 2.2 NS
Rose et al., 2002 [19]	RCT; Crossover study, 6-8-week follow-up, 2-3-week washout, 5 < AHI < 15, n = 26	Silencor [1]	1.16.0 ± 4.4	1.7.4 ± 5.3 (p < 0.01)	1.8.6 ± 4.9			
		Karwetzky [2]	2.16.2 ± 4.6 NS	2.5.5 ± 3.3 (p < 0.01) p < 0.05	2.10.7 ± 4.0 NS			
Sari et al., 2011 [20]	RCT; Parallel study, 1-month follow-up, 5 < AHI < 30, n = 24	Klearway [1] (n = 24)	1.18.8 ± 7.3	1.7.3 ± 3.3 p < 0.000	1.11.8 ± 5.3	1.11.3 ± 0.7	1.4.7 ± 1.0 (p < 0.001)	1.6.6 ± 0.9
		Mandibular Advancement Splint [2] (n = 24)	2.17.9 ± 6.8 NS	2.9.1 ± 4.9 (p = 0.009) NS	NS	NS	2.4.5 ± 0.9 (p = 0.003) NS	2.6.6 ± 1.3 NS
Tegelberg et al., 2020 [23]	RCT; Parallel study, 1-year follow-up, AHI > 5, n = 302	Narval [1] (n = 88)	1.25.0 ± 12.9	1.8.6	1.16.7 (-19.4 to -14.1)			
		Boxholm [2] (n = 104)	2.23.0 ± 13.6 NS	2.11.3	2.11.8 (-14.9 to -8.7) NS			
Umemoto et al., 2019 [21]	RCT; Parallel study, 3-month follow-up, AHI > 5, n = 52	Silencor [1] (n = 23)	1.20.6 ± 11.5	1.14.7 ± 9.4 p < 0.001	1.5.9 ± 7.0	1.8.4 ± 5.2	1.4.3 ± 3.6 (p < 0.001)	1.4.0 ± 3.7
		Monoblock [2] (n = 29)	2.21.4 ± 15.2 NS	2.11.2 ± 9.7 (p < 0.001) NS	NS	NS	2.4.8 ± 3.1 (p < 0.001) NS	2.4.6 ± 3.6 NS
Yanamoto et al., 2020 [15]	RCT; Crossover study, 4-week follow-up, 2-week washout, 5 < AHI < 30, n = 15	NK-connector [1]	12.5 (8.9 -17.0)	1.5.0 (2.6-12.0) p < 0.05	1.7.5 (5.8 -14.5)			
		DURAN [2]		2.5.8 (2.1-8.8) p < 0.05 NS	2.6.7 (5.5 -12.9) p < 0.05 NS			
Zhou et al., 2012 [22]	RCT; Crossover study, 3-month follow-up, 2-week washout, 5 < AHI < 30, n = 16	Silent Nite [1]	26.4 ± 4.1	1.9.9 ± 2.9 p < 0.01	1.16.5 ± 3.5	11.9 ± 2.7	1.8.0 ± 2.50 (p < 0.01)	1.3.9 ± 2.6
		Monoblock [2]		2.6.6 ± 2.3 p < 0.05	2.19.8 ± 3.2 p = 0.0096		2.7.9 ± 2.31 (p < 0.01) NS	2.4.0 ± 2.5 NS
Hyun Lee et al., 2012 [24]	COHORT; Parallel study, 3-month follow-up, AHI > 5, n = 153	Silencor [1] (n = 60)	1.30.9 ± 15.3	1.15.3 ± 12.6 (p < 0.001)	1.15.6 ± 14.0			
		Karwetzky [2] (n = 93)	2.34.7 ± 14.7 NS	2.12.5 ± 11.1 (p < 0.001) NS	2.22.2 ± 12.9 p = 0.0033			
Isacsson et al., 2017 [25]	COHORT; Parallel study, 1-year follow-up, AHI > 10 patients, n = 165	Resmed Narval [1] (n = 55)	1.22.0 ± 14.8	1.8.2 ± 14.8	1.13.8 ± 14.8	1.10.0 ± 4.2	1.7.4 ± 4.4	1.2.6 ± 4.3
		Boxholm [2] (n = 110)	2.23.0 ± 11.2 NS	2.10.3 ± 12.0 NS	2.12.7 ± 11.6 NS	NS	NS	2.3.1 ± 4.0 p = 0.000 NS

Bilateral-thrust [1], Monoblock [2].

AHI = Apnea Hypoapnea Index, RDI = Respiratory Disturbance Index, PSG = polysomnography, NS = not significant, RCT = Randomized controlled trial. (Mean ± Standard Deviation) or in case of not normally distributed data (Median (Q1-Q2)).

Depicted p values concern baseline and follow-up comparisons.

p-values indicated in bold concern comparisons between two treatments at follow-up or comparisons of the delta of an outcome.

Underlined when statistically different.

\*Rose et al. measured RDI instead of AHI. For calculations RDI values were used.

\*\*Al-Dharab, Isacsson 2017 and Tegelberg used a PG sleep study.

**Sleep study outcomes**

In four studies, bilateral thrust appliance had a significantly higher follow-up AHI compared with monoblock appliance [16,18,19,22]. Seven articles did not demonstrate a significant difference in follow-up AHI between the groups [13,14,17,20,21,24,25]. In four articles, delta AHI was significantly different between the groups [17,18,22,24]. In one of these, the delta AHI was significantly higher in bilateral thrust group [17]. The other three, had a significantly higher delta AHI in monoblock group [18,22,24].

When pooling the data, seven articles were included in the effect size calculation of delta AHI [14,17–22]. No significant difference in effect size was shown comparing both types (effect size: -0.37; CI: -1.81 to 0.07) (Fig. 3a).

In three studies ODI was mentioned. Two studies included an ODI 3% with baseline values of 6.7 (5.6–13.1) to 24.0 ± 12.8 and follow-up values of 2.3 (0.8–4.8) to 8.1 (p < 0.05) in the bilateral thrust group and to 1.9 (0.9–4.6) to 11.1 (p < 0.05) in the monoblock group (NS between groups) [15,23]. One study included an ODI 4% with baseline ODI 22.6 ± 6.4 and follow-up ODI 10.5 ± 4.1 in the bilateral thrust (p = 0.002) and 7.1 ± 2.8 (p < 0.001) in the monoblock group (p = 0.046 between groups).

**Subjective sleepiness**

ESS outcomes did not differ significantly between the groups.

When pooling the data, six articles were included in the effect size calculation of delta ESS [13,17,18,20–22]. No significant difference between both types were shown (effect size: 0.00; CI: -0.17 to 0.18) (Fig. 3b).

**Compliance, preference, side effects, and cost effectiveness**

In one article, compliance of bilateral thrust was significantly higher compared with monoblock [24]. However, in another study, compliance was higher in monoblock group [19].

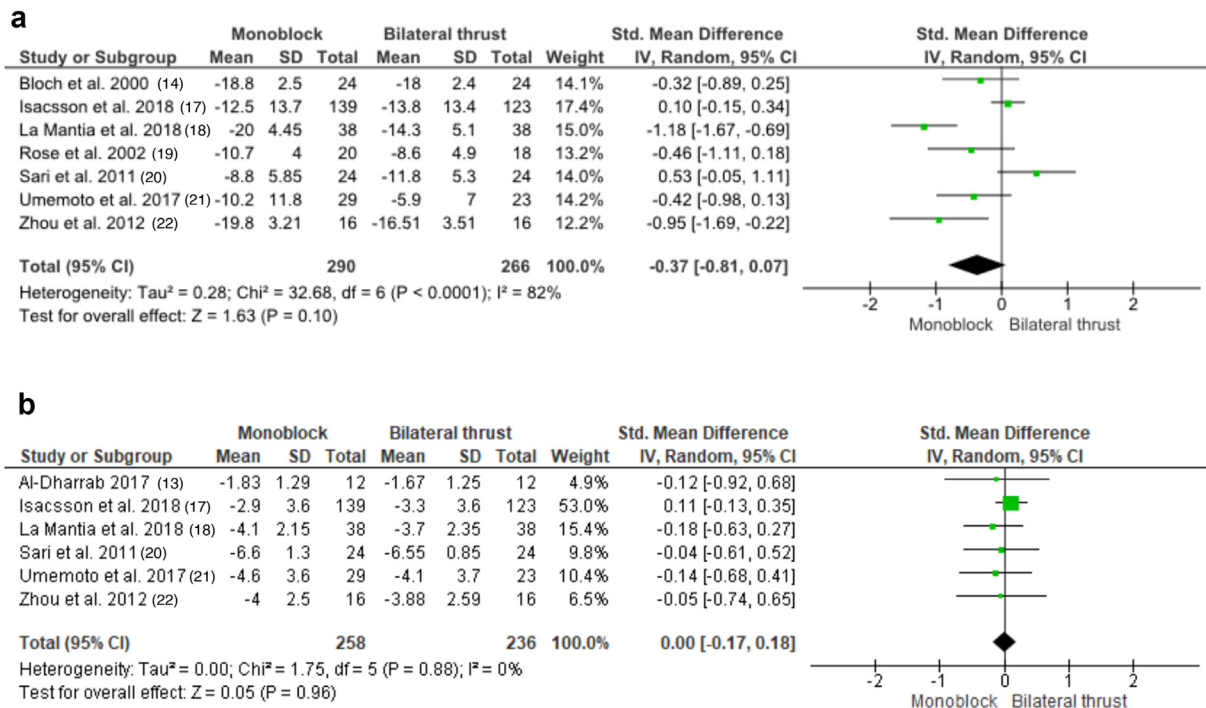
In three out of five articles, monoblock appliance scored higher on preference when compared with bilateral thrust appliance [13–15,19,22].

In five out of six studies, there was no difference between monoblock and bilateral thrust appliance in terms of side effects [13,14,20,23,25]. In one of these studies, after one year of follow up a posterior open bite had developed in bilateral thrust group in four out of 55 patients [25]. In two studies, more frequent side effects such as temporomandibular joint (TMJ) problems and tenderness in the masseter muscle were observed with monoblock appliance [15,19].

Cost effectiveness was described as that fixed MAD's should be selected whenever possible because of the cost effectiveness [13]. Another study described that bilateral thrust device was 17% more expensive in the first year of therapy compared to monobloc device [25](S3).

**Success**

Treatment success was mainly defined as AHI<10 and/or AHI>50% reduction, sometimes also including parameters as patient's satisfaction and relief of symptoms. Treatment success ranged in monoblock groups from 40 to 83% and in bilateral thrust groups from 42 to 92% [13,14,17,20–25]. In six articles, success rates, defined by a follow-up AHI<5, were higher in monoblock compared



**Fig. 3.** a: Effect sizes of mean difference in delta AHI values between monoblock and bilateral thrust appliances. b: Effect sizes of mean difference in delta ESS values between monoblock and bilateral thrust appliances.

to bilateral thrust [13,14,21,22,24,25]. In three studies, success rates, defined by a follow-up  $AHI < 5$ , were higher in bilateral thrust compared to monoblock [17,20,23].

#### Monoblock versus midline traction

##### Background

Baseline characteristics were comparable between monoblock and midline traction appliances in one cohort study [26]. A mean mandibular protrusion in both groups was not mentioned in the article. Follow-up examination was also done by an overnight PSG.

Evaluation of the quality with the Newcastle–Ottawa Quality Assessment Form yielded seven points, thereby demonstrating good study quality (S8).

##### Sleep study outcomes

Baseline AHI was  $30.1 \pm 24.4$  in monoblock group and  $29.7 \pm 24.1$  in midline traction group (NS). Follow-up AHI scores were  $10.0 \pm 12.4$  in monoblock group and  $7.5 \pm 9.7$  in midline traction group ( $p < 0.01$ ). Delta AHI scores was  $18.8 \pm 18.4$  in monoblock group to and  $22.6 \pm 16.9$  in midline traction group (NS).

ODI was not mentioned in the included study.

##### Subjective sleepiness

Baseline ESS scores were  $14.3 \pm 4.5$  in monoblock group and  $13.2 \pm 5.1$  in midline traction group (NS). Follow-up ESS scores were  $10.6 \pm 4.3$  in monoblock group and  $9.7 \pm 4.1$  in midline traction group (NS). Delta ESS scores were  $3.7 \pm 4.4$  in monoblock group and  $3.5 \pm 4.6$  in midline traction group (NS).

##### Compliance, preference, side effects, and cost effectiveness

Compliance, patient's preference, side effects, and cost effectiveness were not evaluated in this study.

##### Success

Patients experienced a mean AHI reduction of 65% in monoblock group and 74% in midline traction group (NS). Success defined by an  $AHI < 5$  was demonstrated in 47% of patients in monoblock group and 57% in midline traction group ( $p = 0.02$ ). Success defined by an  $AHI < 10$  with a resolution of sleepiness was demonstrated in 45% of patients in monoblock group and 66% in midline traction group ( $< 0.001$ ). Treatment success was significantly better in midline traction group when compared to monoblock group and generally successful ( $AHI < 5$ ) in women using midline traction appliance. In contrast, older men with a high BMI and relatively high baseline AHI were generally not successfully treated with monoblock appliance.

#### Bilateral thrust versus midline traction

##### Background

Baseline characteristics were comparable between all four RCTs [27–30] (Table 2). In all articles, delta protrusion from was not significantly different between the appliances [27–30].

When evaluating the quality of the RCTs, no selection bias or reporting bias was found in the included studies. A performance bias was observed in all four articles [27–30]. It was not possible to assess a detection bias because of a lack of detailed methodology. An attrition bias was diagnosed in one out of the three studies [27](S7).

##### Sleep study outcomes

Significant differences ( $p < 0.05$ ) on follow-up AHI and RDI between groups were observed at short-term follow-up, in favor of midline traction design [28,29]. Significant differences in delta RDI

were observed in two studies, both in favor of midline traction design [27,28]. A meta-analysis was not possible due to the quality of the sleep studies of three studies.

ODI was only mentioned in one of the included studies, however without desaturation percentage.

##### Subjective sleepiness

Delta ESS score at short-term follow-up was significantly different between groups in favor of the midline traction design [29]. The remaining three comparisons did not yield significant differences.

When pooling the data, there was no significant difference in delta ESS when comparing both types (effect size:  $-0.24$ ; CI:  $-0.87$  to  $0.38$ ) (Fig. 4).

##### Compliance, preference, side effects, and cost effectiveness

Daily use of the appliance was described in one study only (NS) [28].

Most patients preferred midline traction appliance (72%), whereas in another study most patients preferred bilateral thrust appliance (56%) [27,28].

In bilateral thrust group, there was a dropout of three out of 42 patients because of side effects, including dental side effects ( $n = 1$ ) and TMJ pain ( $n = 2$ ). In midline traction group, there was a dropout of four out of 46 patients because of side effects, including dental side effects ( $n = 2$ ) and TMJ pain ( $n = 2$ ) [29]. The number of short-term dropouts did not differ between the groups. However, it was significantly higher on the long-term, in midline traction group [28]. In addition, dropout rate was significantly higher in older patients [27].

Cost effectiveness was not evaluated in these studies (S4).

##### Success

When success was defined by  $RDI < 5$ ,  $RDI < 10$ , or  $RDI > 50\%$  reduction [28]. Respectively 63% ( $n = 10$ ), 75% ( $n = 12$ ), and 50% ( $n = 8$ ) of patients in bilateral thrust and 75% ( $n = 12$ ), 94% ( $n = 15$ ), and 63% ( $n = 10$ ) of patients in midline traction group were successfully treated. When success was defined by an  $AHI < 5$ . Short-term success was observed in 51% of patients in bilateral thrust compared to 79% of the patients in midline traction group [29]. When success was defined by  $REI < 10$  or  $REI > 50\%$  reduction, 55.6% ( $n = 20$ ) of midline traction and 69.4% ( $n = 25$ ) of bilateral thrust group were successfully treated [30].

#### Bilateral thrust versus bilateral thrust

##### Background

Different bilateral thrust appliances were compared in one RCT [31] and two cohort studies [32,33] (Table 3). Group 1 was defined as traction-based appliances, group 2 was defined as compression-based appliances. Meta-analysis in this section was not possible due to the cohort design of two studies.

Baseline characteristics were comparable between all articles. In only one study, mean protrusion was defined,  $11.2 \pm 2.4$  mm in group 1 and  $11.2 \pm 2.3$  mm in group 2 (NS) [33].

When evaluating the quality of the RCT, a selection bias, attrition bias, and reporting bias were not observed. However, a performance bias was observed. Besides, a detection bias was not possible to analyze because of a lack of detailed methodology. Evaluation of the quality of both cohort studies yielded eight points, indicating a good methodological quality [32,33] (S7,S8).

##### Sleep study outcomes

No significant differences could be demonstrated between the groups [31–33]. The difference in follow-up AHI values was

**Table 2**  
Overview of the different studies comparing bilateral thrust and midline traction appliance design.

Author, year, reference	Study characteristics	Appliances	AHI/RDI			ESS		
			Baseline	Follow-up	Δ	Baseline	Follow-up	Δ
Bishop et al., 2014 [27]	RCT; Crossover study, 5-8-week follow-up, 2-week washout, AHI>5, n = 24, n = 18 completed follow-up	Klearway [1] TAP 3 [2]	16.5 ± 3.2 <sup>a</sup>	1.10.3 ± 3.2 <sup>a</sup>	1.5.2 ± 3.2	12.2 ± 1.1	1.7.8 ± 1.1	1.4.4 ± 1.1
			NS	NS	2.8.8 ± 3.3	<u>p = 0.0017</u>	2.4.6 ± 1.1	
			NS	NS	2.7.7 ± 3.3 <sup>a</sup>	<b>p &lt; 0.05</b>	NS	
Gauthier et al., 2009 [28]	RCT; Crossover study 12-week follow-up, Unknown washout, AHI>5, n = 19, n = 16 completed follow-up	Klearway [1] Silencer [2]	10.0 ± 1.2 <sup>a</sup>	1.6.5 ± 1.3 <sup>a</sup>	1.3.5 ± 1.3	13.9 ± 1.3	1.9.3 ± 1.2	1.4.6 ± 1.3
			NS	<u>p &lt; 0.01</u>	2.5.3 ± 1.2	<u>p &lt; 0.001</u>	2.4.0 ± 1.3	
			NS	<u>p &lt; 0.001</u>	<b>p &lt; 0.000</b>	2.9.9 ± 1.3	<u>p &lt; 0.01</u>	NS
Ghazal et al., 2009 [29]	RCT; Parallel study 6 and 24-month follow-up, 5 < AHI<40, n = 103, Participated 6 months n = 95 Participated 24 months n = 45	IST [1] (short-term n = 47 and long-term n = 24)	1.21.5 ± 13.5	<b>Short-term</b>	<b>Short-term</b>	1.7.8 ± 4.26	<b>Short-term</b>	<b>Short-term</b>
			2.21.5 ± 16.9	1.11.1 ± 11.8	1.10.4 ± 12.7	2.9.5 ± 5.6	1.6.9 ± 5.3	<u>p &lt; 0.05</u>
		TAP [2] (short-term n = 48 and long-term n = 21)	2.6.7 ± 9.1	NS	2.14.8 ± 13.0	NS	2.4.5 ± 5.18	1.0.9 ± 4.8
			<u>p &lt; 0.05</u>	<b>Long-term</b>	<b>Long-term</b>	NS	<u>p &lt; 0.05</u>	2.5.0 ± 3.4
		1.4.6 ± 5.8	NS	2.16.1 ± 7.1	NS	1.7.3 ± 3.99	NS <sup>c</sup>	1.0.5 ± 4.7
		2.5.4 ± 5.1	<u>p &lt; 0.05<sup>c</sup></u>	NS	NS	2.8.4 ± 4.9	NS <sup>c</sup>	2.1.1 ± 5.0
NS	NS	NS	NS	NS	NS	NS		
Schneiderman et al., 2021 [30]	RCT; Crossover study 4-week follow-up, 1-week washout, AHI>15, n = 62, n = 36 completed follow-up	TAP1 [1] SomnoDent Flex [2]	1.32.6 (17.9)	1.9.3 (7.7)	1.25.3 ± 25.1 <sup>b</sup>	10.4 ± 5.4	6.0 ± 4.4	p = 0.001
			-41.8 <sup>b</sup>	-15.5 <sup>b</sup>	2.19.4 ± 20.6 <sup>b</sup>	NS	(not defined between groups)	
			2.36.1 (22.3)	2.13.1 (10.4)	NS	NS	NS	
			-57.9 <sup>b</sup>	-16.6 <sup>b</sup>	NS	NS	NS	NS

Bilateral Thrust [1], Midline traction [2].

AHI = Apnea Hypoapnea Index, RDI = Respiratory Disturbance Index, NS = not significant, PG = polygraphy, RCT = Randomized controlled trial. (Mean ± Standard Deviation).

Depicted p values concern baseline and follow-up comparisons.

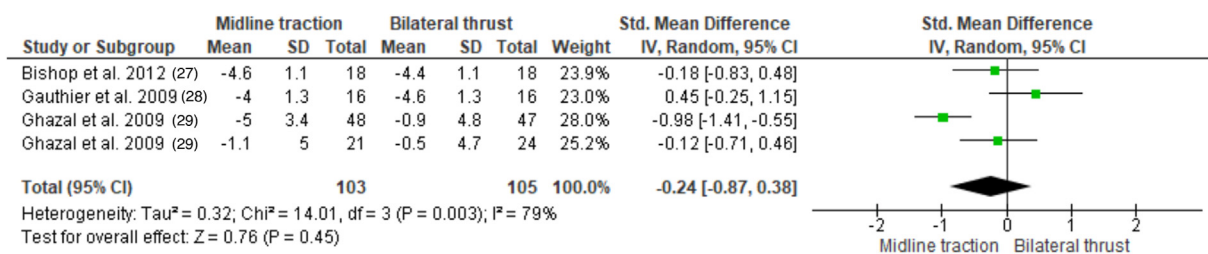
p-values indicated in bold concern comparisons between two treatments at follow-up or comparisons of the delta of an outcome.

Underlined when statistically different.

<sup>a</sup> Bisshop et al. and Gauthier et al. measured RDI calculated by PG.

<sup>b</sup> Schneiderman et al. measured REI.

<sup>c</sup> compared to short term follow-up.



**Fig. 4.** Effects sizes of mean difference in delta ESS values between midline traction and bilateral thrust appliances.

significantly different in one of the included studies favoring group 2 [32]. Due to inclusion of only one RCT, effect size for this group could not be calculated [31].

ODI was not mentioned in the included studies.

**Subjective sleepiness**

No significant differences were observed between the groups. Due to inadequate methodological quality of the RCT, effect size for this comparison was not calculated [31].

**Compliance, preference, side effects, and cost effectiveness**

21% of group 1 did not complete follow-up, whereas 19% of group 2 did not complete follow-up (NS) [33].

31% of patients (5/16) preferred group 1, while 56% of patients (9/16) preferred group 2 [31].

No significant differences between the appliances in either short- or long-term side-effects [31]. In another study, there was a significant more early pain to the masticatory muscles (p = 0.02) and long-term residual tongue pain (p = 0.04) in the compression-based design [33].

It was concluded that the groups are comparable. Because it's simple robust design, group 1 appliance is more cost effective compared to the complex design of the group 2 appliance [31] (S5).

**Success**

Treatment success defined by AHI<5 was observed in 28 and 36% of patients in group 1 and in 24 and 44% of patients in group 2 (NS) [32,33]. Treatment success defined by AHI<10 was observed in 61% of patients in group 1 and in 68% of patients in group 2 (NS). Treatment success defined by AHI<20 with an AHI>50% reduction

**Table 3**  
Overview of the different studies comparing bilateral thrust and bilateral thrust mandibular appliance design.

Author, year, reference	Study characteristics	Appliances	AHI			ESS		
			Baseline	Follow-up	Δ	Baseline	Follow-up	Δ
Lawton et al., 2005 [31]	<b>RCT</b> ; Crossover study, 4–6-week follow-up, 2-week washout, AHI>5, n = 16	Twin Block [1] Herbst [2]	45.5 (29.0 –68.0)	1.34.0 (9.0 –63.0) 2.24.5 (0.0 –45.0)	1.11.5 (19.0 –65.5) 2.21.0 (14.5 –56.5)	10.0 (2.0 –18.0)	1.8.5 (3.0 –17.0) 2.8.0 (4.0 –18.0)	1.1.5 (2.5 –17.5) 2.2.0 (3.0 –18.0)
Verburg et al., 2018 [32]	<b>COHORT</b> ; Parallel study, > 3-month follow-up, AHI>10, n = 137	Somnodent-Flex [1] (n = 67) Herbst [2] (n = 70)	1.18.5 ± 8.8 2.22.7 ± 13.7	1.9.6 ± 8.2 2.8.8 ± 10.1	1.8.9 ± 10.0 2.13.9 ± 15.0			
Vezina et al., 2011 [33]	<b>COHORT</b> ; Parallel study, > 2-year follow-up, AHI>0, n = 48	Narval [1] (n = 16) Herbst [2] (n = 32)	1.32.0 ± 16.7 2.27.4 ± 16.7	1.12.8 ± 12.3 2.14.8 ± 11.3	1.19.2 ± 14.5 2.12.6 ± 15.0	1.9.3 ± 7.1 2.10.4 ± 5.1	1.6.2 ± 3.4 2.9.0 ± 5.6	1.3.1 ± 5.3 2.1.4 ± 5.4

Bilateral Thrust [1], Bilateral Thrust Herbst appliance [2].

AHI = Apnea Hypoapne Index, NS = not significant, RCT = Randomized controlled trial.

(Mean ± Standard Deviation) or in case of not normally distributed data (Median (Q1–Q2)).

Depicted p values concern baseline and follow-up comparisons.

p-values indicated in bold concern comparisons between two treatments at follow-up or comparisons of the delta of an outcome.

Underlined when statistically different.

was observed in 61% of patients in group 1 and 52% of patients in group 2 (NS).

### Thermoplastic appliance versus custom appliance

#### Background

Baseline characteristics were comparable between all articles [34–38](Table 4). Thermoplastic appliance was set at 50 ± 20% or 8.0 mm ± 2.1, and custom appliance was set at 65 ± 10% or 8.0 mm ± 2.9 of maximum protrusion [36,38].

When evaluating the quality of the RCTs a selection bias was found in one article [34]. A reporting bias was observed in two studies [34,36]. A performance bias and a detection bias were present in two studies [35,36]. Evaluation of the quality of the cohort study yielded eight points, indicating good methodological quality [37] (S7,S8).

#### Sleep study outcomes

Follow-up AHI was significantly different between a monoblock thermoplastic appliance and a custom midline traction appliance (p < 0.001) favoring the custom appliance (35). In another study, delta AHI score was significantly different favoring the custom bilateral thrust appliance, compared to the thermoplastic bilateral thrust appliance (34).

When pooling the data, three studies were included in effect size calculation of delta AHI [34,36,38]. The AHI significantly improved with both types. However, no significant difference in effect size when comparing both thermoplastic and custom appliances was observed (effect size:0.86; CI:-0.62 to 2.35) (Fig. 5a).

ODI was mentioned in two studies. Baseline ODI 3% was 19.9 ± 2.1 in the thermoplastic group and 25.0 ± 2.4 in the custom MAD group. Follow-up ODI 3% was 8.5 ± 0.8 (p < 0.001) in the thermoplastic group and 12.9 ± 1.3 (p < 0.001) in the custom MAD group (p < 0.000 between groups) [34]. Baseline ODI 4% was 8.7 ± 6.2. Follow-up ODI 4% was 5.6 ± 6.3 (p < 0.001) in the thermoplastic group and 2.9 ± 3.2 (p < 0.05) in the custom MAD group (p < 0.001 between groups) [35].

#### Subjective sleepiness

A significant difference was observed between the thermoplastic and custom bilateral thrust groups in delta ESS in one article [34].

When pooling the data, three studies were included in the effect size calculation of delta ESS [34,36,38]. There were no significant differences in effect size when comparing thermoplastic and custom appliances (effect size:0.03; CI:-0.32 to 0.38) (Fig. 5b).

#### Compliance, preference, side effects, and cost effectiveness

Therapeutic use in nights per week and hours per night was significantly different between the appliances (p < 0.001) favoring custom appliances [35,36]. Dropouts were mainly seen in thermoplastic group (31–68%) when compared to custom group (24–49%) [34,37].

Preference for thermoplastic device varied from 9 to 24% and preference for custom device varied from 82 to 84% [35,38].

Side effects were described as none in one study [38]. Another study showed clearly more frequent side effects in the first couple of weeks with thermoplastic device in comparison with custom-made, with no differences at long-term [36].

Three studies mentioned the advantage of lower costs of thermoplastic in comparison to custom-made appliances [35,37,38](S6).

#### Success

In four studies, treatment success was defined as AHI<5 with >50% reduction or with ≥2 points drop in ESS score. Success in thermoplastic group varied from 17 to 52%, and in custom group from 26 to 72% [34,35,37,38]. Two articles observed significant differences between both appliances favoring custom group [34,38]. In one study success was defined as AHI<10 or an AHI>50% reduction, in 52% in thermoplastic group and 54% in custom group [36].

#### Discussion

This systematic review of the available literature regarding the effect of different MAD designs on AHI reduction, ESS improvement, compliance, preference, side effects, cost effectiveness, and other disease-related outcomes in OSA management indicates that different MAD designs do not differ significantly with respect to treatment outcome.

#### Methodology

Bias is reported due to limited information about the amount of protrusion and vertical dimension, or the fact that trade names



**Table 4**  
Overview of the different studies comparing thermoplastic and custom mandibular appliance design.

Author, year, reference	Study characteristics	Appliances	AHI/RDI			ESS		
			Baseline	Follow-up	Δ	Baseline	Follow-up	Δ
Gagnadoux et al., 2017 [34]	RCT; Parallel study, 6-month follow-up, AHI>5, n = 158	BluePro BlueSom (1a <sup>a</sup> ) (n = 86)	1a. 23.2 ± 1.6	1a. 7.9 ± 1.1	1a. 15.3 ± 1.4	1a. 9.9 ± 0.6	1a. 7.2 ± 0.6	1a. 2.7 ± 0.6
		AMO or Somnodent device (1b) (n = 72)	1 b. 32.2 ± 2.4	1 b. 13.2 ± 1.5	1 b. 19.0 ± 2.0	1 b. 9.4 ± 0.6	1 b. 6.5 ± 0.5	1 b. 2.9 ± 0.6
Johal et al., 2017 [35]	RCT; Crossover study, 3-month follow-up, 2-week washout, 5 < AHI < 15, n = 35	Snoreshield (2 <sup>a</sup> )	13.4 (11.6)	2.96 (4.8)	2.38 (8.2)	9.0 (5.0)	2.70 (4.5)	2.20 (4.8)
		Medical Dental Sleep Appliance [3]	-24.2)	-17.8)	-21.0)	-11.5)	-11.5)	-11.5)
Pepin et al., 2019 [36]	RCT; Parallel study, 2-month follow-up, AHI>15, n = 198	ONORIS (1a <sup>a</sup> ) (n = 69)	1a. 26.1 ± 11.1	1a. 14.2 ± 10.3	1a. 11.9 ± 9.4	NA	NA	1a. 3.8 ± 4.2
		TALI (1b) (n = 87)	1 b. 27.1 ± 9.8	1 b. 15.9 ± 10.3	1 b. 11.2 ± 10.8	2a. 7.0 ± 5.0	2a. 5.0 ± 4.0	2a. 2.0 ± 4.5
Vanderveken et al., 2008 [38]	RCT; Crossover study, 4-month follow-up, 1-month washout, AHI<40, n = 38	Somnoguard Plus (2a <sup>a</sup> )	14.0 ± 12.0	2a. 11.0 ± 9.0	2a. 3.0 ± 10.5	2 b. 6.0 ± 4.0	NS	2a. 2.0 ± 4.5
		Soft SR-Ivocap Elastomer (2b)	2 b. 27.1 ± 9.8	2 b. 6.0 ± 8.0	2 b. 8.0 ± 10.0	2 b. 6.0 ± 4.0	NS	2 b. 1.0 ± 4.5
Friedman et al., 2012 [37]	COHORT; Parallel study, 6-month follow-up, AHI>5, n = 180	Somnoguard AP (3a <sup>a</sup> ) (n = 123)	3a. 34.7 ± 24.2	3a. 10.0 ± 11.3	3a. 24.7 ± 12.9	3a. 26.9 ± 8.0	NS	NS
		TAP3 (3b) (n = 57)	3 b. 33.1 ± 23.1	3 b. 6.2 ± 15.1	3 b. 26.9 ± 8.0	NS	NS	NS

Bilateral Thrust (1), Monoblock (2), Midline Traction (3).

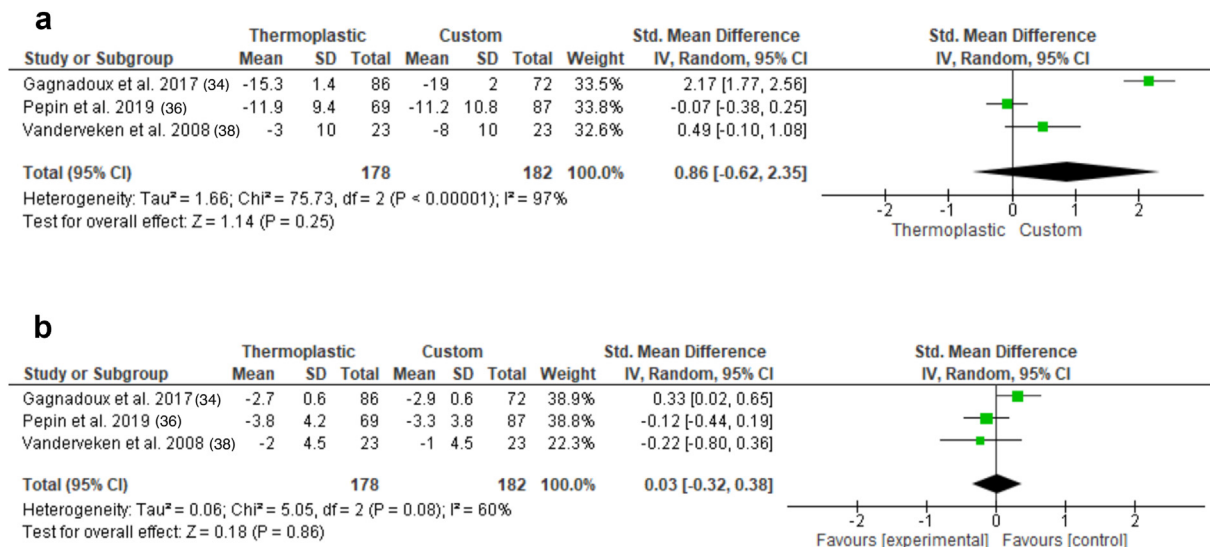
AHI = Apnea Hypoapnea Index, NS = not significant, RCT = Randomized controlled trial. (Mean ± Standard Deviation) or in case of not normally distributed data (Median (Q1-Q2)).

Depicted p values concern baseline and follow-up comparisons.

p-values indicated in bold concern comparisons between two treatments at follow-up or comparisons of the delta of an outcome.

Underlined when statistically different.

<sup>a</sup> Thermoplastic appliance.



**Fig. 5.** a: Effect sizes of mean difference in delta AHI values between thermoplastic and custom appliances. b: Effect sizes of mean difference in delta ESS values between thermoplastic and custom appliances.

were not mentioned or devices were “homemade”. These factors are important in treatment success. Not only in terms of AHI reduction, but also in terms of side effects [39,40]. Secondly, some studies use PSG for evaluating treatment outcomes, whereas others use a less comprehensive PG. Besides, bias could occur as a

carryover effect when applying a crossover design without, or with a limited, washout period. In CPAP treatment, there is some evidence that a carryover effect exists for some days, however in MAD therapy this has not been evaluated to date [41]. Finally, the difficulty of blinding for treatment could influence patient preferences

related to specific design features of the appliances. However, this is difficult to demonstrate. Also blinding clinicians for patient's treatment, is often unclear in the included studies and was only mentioned in three articles [17,34,38].

#### AHI reduction

When significant differences were observed in follow-up AHI between monoblock and bilateral thrust, this was in favor of monoblock design in articles comparing 16–45 patients after an eight to 12-week follow-up. These are relatively small populations and short follow-up periods. Besides, differences were small, effect size was low, and therefore probably of limited clinical relevance. They could be explained by the inability of mouth opening and thereby the inability of autorotation of the mandible while wearing the monoblock [14,22]. However, the inability of altering the advancement of the mandible without gross adjustments to the appliance is a disadvantage. Besides, monoblock design is associated with more pronounced muscular (i.e., mainly masseter) pain, possibly because of its more pronounced protrusive fixation of the mandible whereby no jaw movement is possible [15,20].

Significant differences observed in follow-up AHI between monoblock and midline traction, were in favor of midline traction appliance [26]. However, comparison on mandibular protrusion was not clearly described and only drawn on one article.

When significant differences on AHI outcomes were observed in bilateral thrust and midline traction appliances a more favorable effect of midline traction design was observed [27,28]. Dropout rate of patients was higher in older patients, probably because it is more difficult for them to accustom to the appliance [29]. This phenomenon could possibly be explained by restrictions in adaptation, which increases with age [42].

Advantages of the midline traction and the bilateral thrust appliances include the freedom of movement of the upper and lower jaw, the ease and subsequent potential for more pronounced mandibular advancement, and its relatively small design compared to the monoblock. It is possible that patients with sleep bruxism prefer more freedom of mandibular movement while wearing their MAD. This aspect may affect therapeutic compliance when comparing monobloc and other MAD designs. Positive aspects of midline traction appliance include relative inability of mouth opening, thereby preventing retrusion of the mandible when the device is *in situ*.

Significant differences in AHI outcomes were observed between thermoplastic and custom appliances, in favor of both [34,35]. In four studies, custom appliances resulted in more pronounced AHI improvements, which was only significant in one study [35–38]. Besides, due the low effect size, the differences were probably of limited clinical relevance. An important aspect which should be noted is the fact that the included studies comparing thermoplastic and custom appliances are not homogeneous due to differences in study design. In addition to different design features of the thermoplastic appliances, the custom appliances had either a monoblock, bilateral thrust or midline traction design. This heterogeneity hampers the direct comparison between the different included studies on this specific topic and limits generalizability. Thermoplastic appliances could possibly be less effective on long-term due to alterations in the thermoplastic material as a result of wear and temperature changes, which could reduce MAD retention. Overall disadvantages of thermoplastic designs include more side effects,

less pronounced treatment response and compliance due to a lack of retention, and difficulties in tolerating the device. However, its lower costs and the possibility of chair-side or homebased fitting by the patient are advantages.

#### ESS reduction

When comparing follow-up ESS, no significant or clinically relevant differences were observed between none of the designs. Based on ESS>10, patients are diagnosed with excessive daytime sleepiness [43]. In the included studies, baseline sleepiness was mostly less than 10, which indicates that most included patients did not experience severe sleepiness. Possibly, ESS questionnaire is not the best instrument to indicate sleepiness. However, it is still the most frequently used questionnaire in MAD related publications, and therefore included in this review.

#### General discussion/recommendations

When patients preference of appliance design is taken into account, aspects such as gender and BMI may be considered [33]. Besides, MAD design features such as the vertical dimension or the material from what the device is made needs to be considered in device selection. In addition, a high vertical dimension and therefore more pronounced stretching of the pharyngeal wall, may also be an important factor in increasing the airway lumen [19,22,25,44]. However, it could also result in more TMD pain [20]. Besides, a higher vertical dimension also creates a possible reduction of the maximum protrusive position and an increased posterior position or backward rotation of the mandible [39]. In addition, the amount of mandibular protrusion is very important in treatment success [45]. Most studies set the mandibular advancement at 70%. However, nowadays it is debated if there is a one size fits all position for optimal mandibular advancement. In a study by Pitsis et al. no significant differences were described in treatment effect between different vertical dimensions, however patient's preference in this study was clearly in favor of the lower vertical dimension [46]. Generally, a bulkier design, creates less space for the tongue and therefore potentially less airway space [31]. The above-mentioned characteristics are applicable for all appliance designs and may be affected by appliance material, patients' coaching, protrusive position, and vertical dimension of the specific device (S1). Preference was only clearly in favor of the custom when compared with thermoplastic appliances.

Preferably, the definite appliance selection should be made by dental specialists in accordance and adjusted to the patient, thereby introducing personalized medicine in MAD management. Cost aspects as appliance price and number of return visits are secondary factors which differ with every appliance design and per patient. Recommendations for the optimal MAD design and phenotyping of OSA patients are difficult to drawn and insufficiently supported by the current literature [47].

#### Conclusion

We conclude that different titratable and non-titratable MAD designs have an objectively and subjectively positive treatment outcome in most patients diagnosed with mild to moderate OSA. A clear clinically relevant distinction in favor of one of the appliances cannot be drawn. However, a custom-made MAD is more

comfortable, yields better objective and subjective treatment outcomes, and is associated with a more favorable compliance when compared with a thermoplastic MAD.

### Practice points

- Titratable and non-titratable MAD's have a comparable impact on AHI reduction, ESS improvement, compliance, cost effectiveness, and other disease-related outcomes in mild to moderate OSA
- Custom-made MAD's perform favorably in terms of treatment outcome, mainly due to a better compliance and patient preference with less side effects when compared with thermoplastic MAD's
- Given that there is no data to support one MAD design over another, appliance choice should be made by dental specialist following treatment guidelines, in accordance and adjusted to the patient choice, thereby introducing personalized medicine in MAD management

### Research agenda

- To help with clinical discussions-making, more prospective randomized studies are needed
- To develop personalized medicine in MAD management and to give specific recommendations for the optimal MAD design in specific phenotypes of OSA patients
- To optimize thermoplastic MAD design with a better retention and therefore compliance and treatment response

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### Conflicts of interest

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### Appendix A. Supplementary data

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