

# A systematic review of the efficacy of oral appliance design in the management of obstructive sleep apnoea

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**SUMMARY** Oral appliances (OAs) are increasingly advocated as a treatment option for obstructive sleep apnoea (OSA). However, it is unclear how their different design features influence treatment efficacy. The aim of this research was to systematically review the evidence on the efficacy of different OAs on polysomnographic indices of OSA. A MeSH and text word search were developed for Medline, Embase, Cinahl, and the Cochrane library. The initial search identified 1475 references, of which 116 related to studies comparing OAs with control appliances. Among those, 14 were randomized controlled trials (RCTs), which formed the basis of this review. The type of OA investigated in these trials was mandibular advancement devices (MADs), which were compared with either inactive appliances (six studies) or other types of MADs with different design features.

Compared with inactive appliances, all MADs improved polysomnographic indices, suggesting that mandibular advancement is a crucial design feature of OA therapy for OSA. The evidence shows that there is no one MAD design that most effectively improves polysomnographic indices, but that efficacy depends on a number of factors including severity of OSA, materials and method of fabrication, type of MAD (monobloc/twin block), and the degree of protrusion (sagittal and vertical).

These findings highlight the absence of a universal definition of treatment success. Future trials of MAD designs need to be assessed according to agreed success criteria in order to guide clinical practice as to which design of OAs may be the most effective in the treatment of OSA.

## Introduction

Obstructive sleep apnoea (OSA) is the most common sleep-related breathing disorder that is increasingly recognized as a serious public health issue (Cistulli and Grunstein, 2005). Population-based studies from the USA, Europe, and Australasia estimate a prevalence of approximately 3–7 per cent in adult middle-aged males and 2–5 per cent in middle-aged females (Young *et al.*, 1993; Bearpark *et al.*, 1995; Bixler *et al.*, 1998; European Respiratory Society and European Lung Foundation, 2003; Ip *et al.*, 2004). It has been suggested that OSA is as common in developing as in industrialized countries (Punjabi, 2008). However, the lack of awareness among the general public and health profession means that an estimated 80–90 per cent of people with OSA are as yet undiagnosed (Young *et al.*, 1997; Davey, 2003).

There is growing evidence that untreated OSA is associated with a range of adverse cardiovascular health outcomes, such as hypertension (Peppard *et al.*, 2000), stroke, congestive heart failure, arterial fibrillation (Shahar *et al.*, 2001; Ng *et al.*, 2005), increased risk of motor vehicle accidents (Haraldsson *et al.*, 1990), excessive daytime sleepiness, and impaired quality of life and social life (Johnston *et al.*, 2002; Ng *et al.*, 2005).

Treatment options for OSA include behavioural modification, such as weight loss programmes, alcohol

avoidance, and alteration of sleeping position (Shneerson and Wright, 2001; Smith *et al.*, 2006), a range of upper airway surgical procedures (Bridgman and Dunn, 2000; Sundaram *et al.*, 2005), pharmacological regimen (Smith *et al.*, 2006; Jayaraman *et al.*, 2008), and continuous positive airway pressure (CPAP; Weaver and Chasens, 2007). CPAP is the current treatment of choice as it has been successfully used to treat the symptoms of the majority of OSA patients (Elshaug *et al.*, 2007); however, its efficacy is highly reliant on patient compliance. Due to CPAP's cumbersome nature, many patients fail to comply, especially those with mild to moderate OSA. This, combined with poor tolerability, outweighs perceived treatment benefit (Meurice *et al.*, 1994; Engleman *et al.*, 1996; Johnston *et al.*, 2002; Ng *et al.*, 2005; Giles *et al.*, 2006).

Oral appliances (OAs) offer a non-invasive treatment option for patients with OSA, which is considered less cumbersome than CPAP (Hoffstein, 2007). The American Academy of Sleep Medicine recommends OA therapy for patients with mild to moderate OSA and for those with more severe OSA who cannot tolerate CPAP and refuse surgery (Kushida, 2006). A recent Cochrane review suggested that OAs have similar treatment efficacy for mild to moderate OSA as CPAP and provided evidence that supports the use of OAs in clinical practice (Lim *et al.*, 2006).

A variety of OAs are available that can broadly be classified as: tongue-retaining devices, soft palate-lifting devices, and mandibular advancement devices (MADs). The primary action of OAs is to increase and stabilize the oropharyngeal and/or hypopharyngeal airway space (Lim *et al.*, 2006). MADs are the most commonly prescribed devices in the treatment of OSA. While MADs are more effective than other types of OAs in treating OSA (Hoekema *et al.*, 2004), it has been emphasized that the design features of the various appliances may have an impact on treatment efficacy (Chan *et al.*, 2007). However, there are few studies that have investigated this. Understanding which type or design of MAD is most effective in the treatment of OSA is imperative in informing evidence-based practice. This review aims to summarize evidence available on the efficacy of different MADs on the objective polysomnographic indices of OSA.

## Materials and methods

In order to identify studies relevant to the field of OA treatment for OSA, a computerized database search was carried out using Medline, Embase, Cinahl, and the Cochrane Library, including the Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, Cochrane Database of Methodology Reviews, Cochrane Methodology Register, Health Technology Assessment Database, and NHS Economic Evaluation Database. The search strategy including the MeSH and text words applied in the initial search was (((“Sleep Apnea, Obstructive”[Mesh]) OR (obstructive sleep AND (apnoea OR apnea)) OR (sleep AND (breathing disorder\* OR respiratory disorder\*))) AND (“Orthodontic Appliances”[Mesh]) OR (oral AND (device\* OR appliance\* OR splint)) OR (dental AND (device\* OR appliance\* OR splint)) OR (orthodontic AND (device\* OR appliance\* OR splint)) OR (mandib\* AND advancement\*))).

No language limitations were set and the search was limited to human studies. If articles contained the search thesaurus anywhere, they were selected to constitute a list of potentially eligible studies to be included in this review.

Titles and abstracts of study references on this list were reviewed by two independent researchers (AA and CM), who then agreed whether they were relevant to the theme of this review—studies exclusively focusing on OA therapy as OSA treatment modality (Figure 1). In cases where the researchers disagreed about which articles were relevant, consensus was reached by discussion. In order to select papers that lend themselves to assess the impact of appliance design on objective treatment effect, the list of abstracts was reviewed again and only studies whose title and abstract clarified that they investigated (1) MAD versus other MAD, (2) MAD versus inactive OA, or (3) the same MAD but with varying degrees of mandibular advancement or vertical

bite opening were selected to remain on the list of potential studies suitable for this review.

Full text articles of those potential studies were then obtained and evaluated to identify ‘effective’ papers and eligibility for methodological appraisal according to the American Association of Sleep Medicine (Sackett, 1993; Table 1). The reference lists of papers deemed eligible were searched manually for additional relevant publications, which were added to the list of potential studies to be included in this review (reference linkage). Papers were reviewed and grouped according to the following MAD design outcome measures: (1) studies comparing MADs with inactive control OAs, (2) studies comparing one-piece MADs with one-piece MADs, (3) studies comparing two-piece MADs with two-piece MADs, and (4) studies comparing one-piece MADs with two-piece MADs. All papers not specifically falling into one of these outcome groups were excluded from the list of potential eligible studies.

## Results

### *Literature search*

Initially, 1478 references (Figure 1) were retrieved from the primary database searches, among them 470 duplicate references. An additional 467 references were excluded by two independent reviewers based on abstract and title as the studies were not limited to OA therapy as the treatment modality of OSA. Of the remaining 538 study references, a further 425 were excluded as they did not meet the criteria for inclusion (Figure 1). Full texts of the remaining 113 papers were obtained. An additional three articles were identified by reference linkage as potentially relevant papers and subsequently added to the list. Among the 116 studies, 6 could be categorized (Table 1) as evidence level I (randomized well-designed trials with low alpha and beta error) and 8 as level II evidence (randomized trials with high alpha and beta error). Forty-three studies were found to reach evidence level III (non-randomized concurrently controlled studies). No studies could be found for level IV (non-randomized historically controlled studies) while 59 studies were categorized as evidence level V (case series). Based on this classification of evidence, all 14 level I and II randomized controlled trials (RCTs) were finally selected to form the basis of this review.

### *Overview of RCT study design, subjects’ OSA severity, and outcome measures*

Nine of the 14 RCTs used a cross-over design with the remaining five employing a parallel design (supplementary Table S1 is available at *European Journal of Orthodontics* online). The study duration ranged from 2 weeks to 12 months with an active treatment phase of 1–12 weeks per arm for cross-over studies and 2 weeks to 12 months for parallel design studies. Half of the reviewed studies

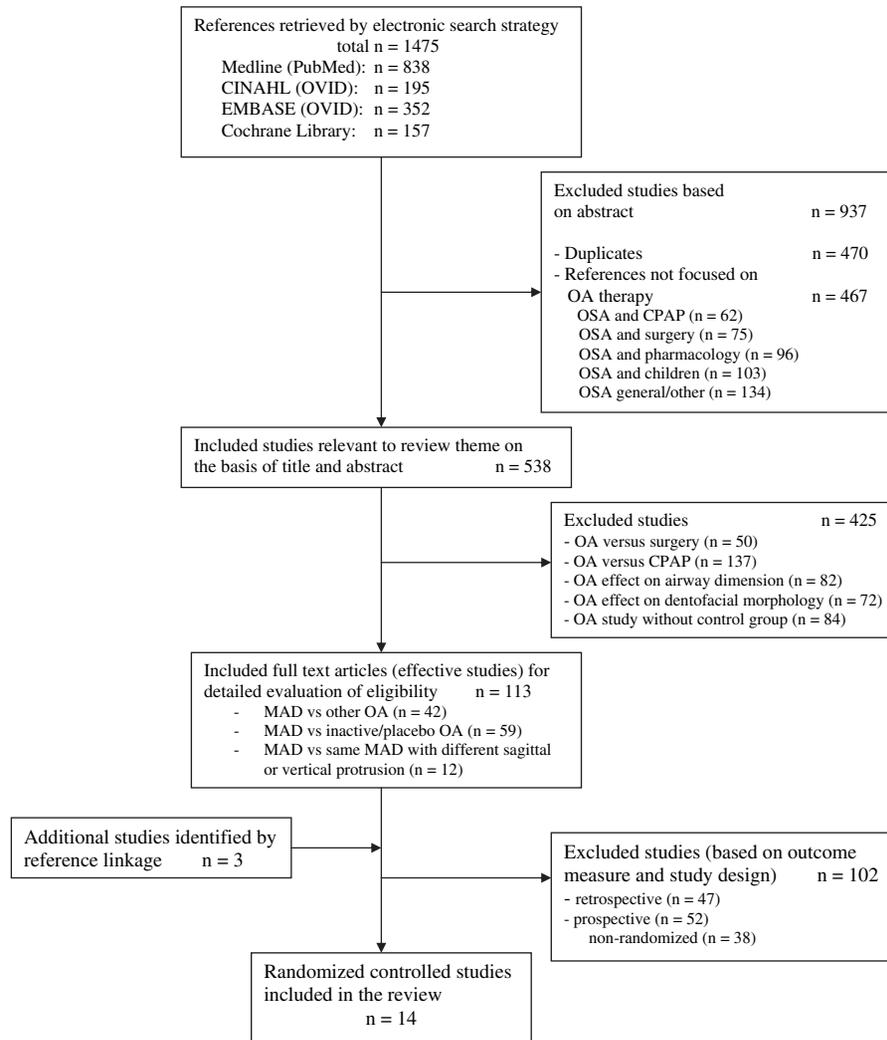


Figure 1 Flow diagram of study selection procedure.

Table 1 American Academy Sleep Medicine Classification of Evidence (Adapted from Sackett, 1993).

Evidence levels	Study design
I	Randomized well-designed trials with low alpha and beta error*
II	Randomized trials with high alpha and beta error*
III	Non-randomized concurrently controlled studies
IV	Non-randomized historically controlled studies
V	Case series

\*Alpha (Type I error) refers to the probability that the null hypothesis is rejected when in fact it is true (generally acceptable at 5 per cent or less or  $P < 0.05$ ). Beta (Type II error) refers to the probability that the null hypothesis is mistakenly accepted when in fact it is false (generally trials accept a beta error of 0.20). The estimation of Type II error is generally the result of a power analysis. The power analysis takes into account the variability and the effect size to determine if sample size is adequate to find a difference in means when it is present (power generally acceptable at 80–90 per cent).

specified an acclimatization period during which the patient adapted to the device, which varied from 2 to 40 weeks. All but two cross-over studies (Johnston *et al.*, 2002; Gauthier *et al.*, 2009) included a wash-out period between treatment arms, which ranged from 1 to 4 weeks. One study did not specify if a wash-out period was included in the protocol (Bloch *et al.*, 2000). The sample size of the target populations varied considerably from 16 to 93 subjects, with the majority of studies specifying a sample size between 20 and 30 subjects. An indication of the severity of OSA was provided in five studies (Mehta *et al.*, 2001; Gotsopoulos *et al.*, 2002; Rose *et al.*, 2002a; Vanderveken *et al.*, 2008; Gauthier *et al.*, 2009) with patients mostly in the mild to moderate range. However, three studies (Mehta *et al.*, 2001; Gotsopoulos *et al.*, 2002; Lawton *et al.*, 2005) included mild to severe OSA patients and one investigated the effect of two degrees of mandibular protrusion on severe OSA patients (Walker-Engström *et al.*, 2003).

The primary outcome assessed in 11 papers was the index of respiration expressed as the apnoea/hypopnoea index (AHI) and three papers used the respiratory disturbance index (RDI). Most studies presented mean AHI/RDI values and one (Lawton *et al.*, 2005) presented median values. The polysomnographic definition of OSA in all studies was based on an AHI or RDI of more than 10.

#### *Overview of MAD designs*

All of the reviewed studies provided some detail on the design of the MAD used; however, some were more specific than others. Three studies used commercially available appliances (Hans *et al.*, 1997; Rose *et al.*, 2002a; Gauthier *et al.*, 2009), whereas others only detailed the design features of the MAD tested (one- or two-piece; Bloch *et al.*, 2000; Mehta *et al.*, 2001; Gotsopoulos *et al.*, 2002; Johnston *et al.*, 2002; Pitsis *et al.*, 2002; Tegelberg *et al.*, 2003; Walker-Engström *et al.*, 2003; Blanco *et al.*, 2005; Lawton *et al.*, 2005; Petri *et al.*, 2008; Vanderveken *et al.*, 2008). Several studies (Hans *et al.*, 1997; Rose *et al.*, 2002a; Blanco *et al.*, 2005; Vanderveken *et al.*, 2008) described the materials used to construct the appliances. All but one study (Lawton *et al.*, 2005) provided details regarding the degree of mandibular protrusion. For most studies, this was reported as a percentage of maximum mandibular protrusion (50–95 per cent) and in millimetres (range from 3 to 13 mm; Bloch *et al.*, 2000; Mehta *et al.*, 2001; Gotsopoulos *et al.*, 2002; Johnston *et al.*, 2002; Pitsis *et al.*, 2002; Tegelberg *et al.*, 2003; Walker-Engström *et al.*, 2003; Gauthier *et al.*, 2009). The remaining studies either indicated only the percentage of maximum mandibular protrusion (Rose *et al.*, 2002a; Blanco *et al.*, 2005; Petri *et al.*, 2008; Vanderveken *et al.*, 2008) or specified the advancement in millimetres only (Hans *et al.*, 1997). The amount of vertical opening in millimetres (range 1–14 mm) was provided in 10 studies (Hans *et al.*, 1997; Bloch *et al.*, 2002; Gotsopoulos *et al.*, 2002; Johnston *et al.*, 2002; Pitsis *et al.*, 2002; Rose *et al.*, 2002a; Walker-Engström *et al.*, 2003; Blanco *et al.*, 2005; Petri *et al.*, 2008; Gauthier *et al.*, 2009).

#### *Efficacy of MAD design in the management of OSA*

*Studies comparing MADs with inactive control OAs.* Six studies compared a MAD with inactive control devices (Hans *et al.*, 1997; Mehta *et al.*, 2001; Gotsopoulos *et al.*, 2002; Johnston *et al.*, 2002; Blanco *et al.*, 2005; Petri *et al.*, 2008). The control appliances were designed not to advance the mandible. Four studies observed a significant reduction between baseline and follow-up AHI/RDI for patients wearing a custom-made two-piece MAD (Mehta *et al.*, 2001; Gotsopoulos *et al.*, 2002; Johnston *et al.*, 2002) and a commercial thermoplastic one-piece design resulted in a significant reduction between baseline and follow-up AHI/RDI for patients wearing the MAD (SnoreGuard; Hans *et al.*, 1997). These studies also showed a significant

difference between the MADs and the inactive control devices. No success criteria were specified in the latter study, but the authors reported that 90 per cent ( $n = 16$ ) of patients using the MAD showed improvements in RDI scores. According to the predetermined success criteria, Gotsopoulos *et al.* (2002), Johnston *et al.* (2002), and Mehta *et al.* (2001) found that two-thirds of patients were successfully treated with the custom-made two-piece MAD. In the study of Petri *et al.* (2008), the MAD was shown to significantly improve AHI results, and for 30 per cent of patients, the treatment was completely successful and partially successful in 15 per cent. Interestingly, Blanco *et al.* (2005) found that both the inactive device and the active MAD significantly improved the patients' mean AHI score and all patients met the set criteria for successful treatment irrespective of which appliance was used. Neither of the two latter studies reported whether there was a difference between the MADs and inactive control devices.

*Studies comparing one-piece MADs with one-piece MADs.* Three studies (Tegelberg *et al.*, 2003; Walker-Engström *et al.*, 2003; Vanderveken *et al.*, 2008) fell into this group. Vanderveken *et al.* (2008) found that a custom-made monobloc MAD significantly improved subjects' AHI ( $P < 0.01$ ) when compared with a thermoplastic monobloc MAD. The custom-made MAD resulted in significantly higher treatment success (60 versus 31 per cent;  $P < 0.05$ ). Two studies (Tegelberg *et al.*, 2003; Walker-Engström *et al.*, 2003) compared 50–75 per cent of maximum mandibular protrusion in the same one-piece MAD. All MADs significantly improved subjects' AHI ( $P < 0.001$ ), but when comparing the results, neither study found a significant difference between the two appliance groups. Walker-Engström *et al.* (2003) found that half (21) of subjects wearing a MAD with 75 per cent maximum mandibular protrusion and one-third (11) of subjects wearing the 50 per cent maximum mandibular protrusion MAD met the criteria for normalization (AHI less than 10). Tegelberg *et al.* (2003) found that 50 per cent maximum mandibular protrusion MAD achieved normalization in 79 per cent of subjects, whereas the 75 per cent maximum mandibular protrusion MAD achieved normalization in 73 per cent. In both studies, the difference was not significant.

*Studies comparing two-piece MADs with two-piece MADs.* Three studies (Pitsis *et al.*, 2002; Lawton *et al.*, 2005; Gauthier *et al.*, 2009) belonged to this category. Gauthier *et al.* (2009) compared two different commercially produced two-piece MADs (Silencer and Klearway). Both appliances significantly improved patients' mean RDI in favour of the Silencer ( $P \leq 0.05$ ). In the study of Lawton *et al.* (2005), the Herbst MAD and the twin block MAD both improved AHI values; however, there was no significant difference between the appliances. No treatment success criteria were detailed, but the authors reported that the AHI in two subjects with severe OSA worsened with the twin

block but improved with the Herbst MAD. Pitsis *et al.* (2002) investigated the effect of different vertical openings (4 and 14 mm) with the same degree of mandibular protrusion in two otherwise identical two-piece MADs. Both devices significantly improved AHI scores ( $P < 0.001$ ), but no comparison between appliances was reported. According to the predetermined success criteria, the MAD with 4 mm interincisal opening resulted in treatment success in 74 per cent of patients, whereas the MAD with 14 mm interincisal opening achieved success in 61 per cent of patients. Chi-square statistics of the two groups showed no statistical significance ( $P = 0.82$ ).

*Studies comparing one-piece MADs with two-piece MADs.* Two studies (Bloch *et al.*, 2000; Rose *et al.*, 2002a) were included in this category. No difference in reducing AHI was found between the monobloc and the Herbst MAD investigated by Bloch *et al.* (2000). Seventy-five per cent of subjects using the monobloc and 67 per cent of Herbst MAD users were treated successfully and achieved a reduction of AHI below 10 events per hour. Chi-square statistics of the two groups showed no statistical significance ( $P = 0.82$ ). Rose *et al.* (2002a) compared a two-piece soft polyethylene Silencor MAD with an acrylic one-piece Karwetzky MAD and while both devices significantly improved the RDI ( $P < 0.01$ ), there was a significant difference ( $P < 0.01$ ) between the two appliances in favour of the Karwetzky MAD. No specific success criteria were detailed, but improvements in symptoms were reported by 53 per cent of subjects with the Silencor and 66 per cent of subjects with the Karwetzky MAD.

## Discussion

Within the past decade, an increasing number of studies have investigated the efficacy of MADs as a treatment option for OSA (Figure 1). The included studies (effective articles) in this review were all RCTs and the majority employed a cross-over study design, which allows for 'within subject' comparison. However, a key feature of the cross-over design is the inclusion of a wash-out period in order to decrease the chance of bias due to a carry-over effect (Bland and Peacock, 2004). The results of such cross-over studies without wash-out periods should be interpreted with caution as they may falsely ascribe the joint effect of the two appliances to the effect of the appliance worn by patients in the second treatment arm. Only one study included severe OSA patients; most reviewed studies analysed the success of the treatment in mild to moderate OSA patients. The American Academy of Sleep Medicine recommends OA therapy for patients with mild to moderate OSA and for patients with more severe OSA who cannot tolerate CPAP and refuse surgery (Kushida, 2006), although others maintain that severe OSA patients should not be excluded from OA treatment (Henke *et al.*, 2000; Eveloff, 2002). Three of the reviewed studies (Mehta *et al.*, 2001; Gotsopoulos *et al.*, 2002; Walker-Engström *et al.*, 2003)

that included mild to severe OSA patients found MAD treatment effective in up to 63 per cent. In subjects with mild to moderate OSA, MAD treatment efficacy was found in up to 79 per cent. The findings correspond with other studies that investigated OAs efficacy in terms of severity of OSA and generally found lower treatment success rates with more severe OSA (Liu and Lowe, 2000; Rose *et al.*, 2002b). It is important to bear in mind that comparison of the studies is difficult as the definition of treatment success varied greatly. Studies in this review defined success as a reduction of AHI/RDI either by 50 per cent, below five events per hour, or below 10 events per hour, and some defined success as patient satisfaction. The reported range for treatment failure in those studies was 0–37 per cent (Mehta *et al.*, 2001; Gotsopoulos *et al.*, 2002; Blanco *et al.*, 2005; Vanderveken *et al.*, 2008). The reported rate of treatment failure in the study by Petri *et al.* (2008) (56 per cent for the MAD) is the highest for all reviewed articles that detailed failure criteria. Therefore, depending on the definition of success/failure criteria, the rates of reported success may be biased and different from study to study. In order to compare studies using MADs as a treatment modality for OSA and carry out a meta-analysis, a uniform definition of treatment success should be established.

The fact that the majority of studies showed that inactive control devices have no effect on polysomnographic indices (AHI or RDI) highlight that mandibular advancement is crucial to the efficacy of MADs. Walker-Engström *et al.* (2003) suggested that there is a relationship between the degree of advancement and the efficacy of MADs as those with greater mandibular advancement proved to be more efficient in improving OSA polysomnographic indices. These findings correspond with those of other studies (Marklund *et al.*, 1998; de Almeida *et al.*, 2002) showing increasing efficacy of MADs with greater degrees of mandibular advancement. However, it has been shown that some OSA patients experience an increase in airway obstruction when wearing devices with a high degree of maximum advancement (Lamont *et al.*, 1998). Tegelberg *et al.* (2003) did not find greater improvement in AHI in patients wearing a MAD with the greater advancement and recommended that OA treatment for mild to moderate OSA patients should start with no more than 50 per cent mandibular advancement. Therefore, it is important for the clinician to acknowledge that the optimum degree of advancement may not necessarily be the maximum achievable degree of protrusion for all OSA patients.

Few studies have assessed the potential role of the amount of vertical opening of MADs as a treatment modality for OSA. Pitsis *et al.* (2002) compared MADs with the same degree of mandibular protrusion but with different bite openings (4 and 14 mm). No difference was found between the two MADs, which suggest that the amount of vertical opening does not impact on efficacy.

Blanco *et al.* (2005), Hans *et al.* (1997), and Lawton *et al.* (2005) found an improvement in patients' RDI/AHI while wearing an inactive appliance. Although inactive appliances

aim to alter normal bite opening as little as possible, there is generally some degree of opening due to the thickness of the appliance, thus making the appliance not fully inactive. This can introduce a placebo effect and may therefore potentially bias the results. Evidence from studies using inactive control devices is conflicting and should therefore be interpreted with this in mind, or researchers should aim to find a way to eliminate this potential bias.

Vanderveken *et al.* (2008) found that the custom-made soft elastomeric MAD was significantly more effective in improving patients' AHI than the thermoplastic control MAD. Treatment success was significantly greater with the custom-made MAD. This suggests that tailor-made appliances may show greater efficacy in improving patients' polysomnographic indices of OSA. Clear deductions regarding whether materials used in the fabrication of the appliances influence treatment outcome cannot be made as there are no studies specifically investigating this issue. Most studies that use appliances of different materials also include other features, such as type of retention and vertical opening (Rose *et al.*, 2002a) or various degrees of mandibular protrusion (Tegelberg *et al.*, 2003; Walker-Engström *et al.*, 2003).

In this review, all types of MADs investigated proved to be effective in terms of improving AHI or RDI scores from baseline, therefore, supporting the findings of Hoekema *et al.* (2004) that MADs are generally effective irrespective of their various design features. However, Lawton *et al.* (2005) suggested that different design features may affect the polysomnographic indices of OSA in particular patients. That study compared a twin block MAD with a Herbst device and the authors found that for two OSA patients, the AHI worsened with the twin block, but improved with the Herbst device. Only two studies found a significant difference between the two MADs tested (Rose *et al.*, 2002a; Gauthier *et al.*, 2009) and observed efficacy in terms of RDI reduction for the two-piece Silencer MAD and one-piece Karwetzky MAD, respectively. While the vertical opening was similar in the two MADs, the degree of protrusion, the materials of the appliances, as well as the basic design feature (one- versus two-piece) were different.

It is as yet unclear which type of MAD will bring about the desired treatment effect for patients with OSA, especially severe OSA, and further research directly comparing different appliances and different designs is needed to shed light on this issue. The most effective MAD seems to be the one that is most acceptable to the patient and meets criteria for success at the same time. This highlights the role of a trained dental practitioner in the treatment of OSA as MADs need to be chosen on an individual basis and regularly supervised in order to achieve the desired efficacy.

## Conclusions

This review identified 14 high-quality trials comparing MADs of various designs to inactive devices or other MADs with

different design features in mostly mild to moderate OSA patients. All MADs proved successful in improving AHI/RDI and comparison with inactive appliances suggests that mandibular advancement is crucial in terms of establishing efficacy. The evidence as to whether MAD designs have an impact on polysomnographic indices is conflicting and more research is needed to investigate how different design features may affect the AHI or RDI in certain patients. There is no 'one fits all' MAD—the choice of which MAD is 'best' in improving polysomnographic indices depends on a variety of factors ranging from severity of OSA, materials used and method of fabrication, and design features to individually determined sagittal/vertical protrusion. A consensus should be reached on how to define treatment success and failure in order to perform a meta-analysis of study findings to guide clinical practice.

## Funding

General Research Fund, Hong Kong (project no. HKU 772809M).

## Supplementary material

Supplementary Table S1 is available at *European Journal of Orthodontics* online.

## Acknowledgements

The authors wish to thank Mrs Julia Chan from the Yu Chun Keung Medical Library for her assistance in the development of the search syntax and strategy and Dr Susan Bridges of the Faculty of Dentistry, The University of Hong Kong for appraisal of the manuscript.

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