Oral appliances for obstructive sleep apnoea (Review)

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[Intervention Review]

Oral appliances for obstructive sleep apnoea

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ABSTRACT

Background

Obstructive sleep apnoea-hypopnoea (OSAH) is a syndrome characterised by recurrent episodes of partial or complete upper airway obstruction during sleep that are usually terminated by an arousal. Nasal continuous positive airway pressure (CPAP) is the primary treatment for OSAH , but many patients are unable or unwilling to comply with this treatment. Oral appliances (OA) are an alternative treatment for OSAH.

Objectives

The objective was to review the effects of OA in the treatment of OSAH in adults.

Search strategy

We searched the Cochrane Airways Group Specialised Register. Searches were current as of June 2008. Reference lists of articles were also searched.

Selection criteria

Randomised trials comparing OA with control or other treatments in adults with OSAH .

Data collection and analysis

Two authors independently extracted data and assessed trial quality. Study authors were contacted for missing information.

Main results

Seventeen studies (831 participants) met the inclusion criteria. All the studies had some shortcomings, such as small sample size, under-reporting of methods and data, and lack of blinding. OA versus control appliances (six studies): OA reduced daytime sleepiness in two crossover trials (ESS score -1.81; 95%CI -2.72 to -0.90), and improved apnoea-hypopnoea index (AHI) (-10.78 events/hr; 95% CI -15.53 to -6.03 parallel group data - five studies). OA versus CPAP (ten studies): There was no statistically significant difference in symptoms for either parallel or crossover studies, although OAs were less effective than CPAP in reducing apnoea-hypopnoea index in parallel and crossover studies. CPAP was more effective at improving minimum arterial oxygen saturation during sleep compared with OA. In two small crossover studies, participants preferred OA therapy to CPAP. OA versus corrective upper airway surgery (one study): Symptoms of daytime sleepiness were initially lower with surgery, but this difference disappeared at 12 months. AHI did not differ significantly initially, but did so after 12 months in favour of OA.

Authors' conclusions

There is increasing evidence suggesting that OA improves subjective sleepiness and sleep disordered breathing compared with a control. CPAP appears to be more effective in improving sleep disordered breathing than OA. The difference in symptomatic response between these two treatments is not significant, although it is not possible to exclude an effect in favour of either therapy. Until there is more definitive evidence on the effectiveness of OA in relation to CPAP, with regard to symptoms and long-term complications, it would appear to be appropriate to recommend OA therapy to patients with mild symptomatic OSAH, and those patients who are unwilling or unable to tolerate CPAP therapy. Future research should recruit patients with more severe symptoms of sleepiness, to establish whether the response to therapy differs between subgroups in terms of quality of life, symptoms and persistence with usage. Long-term data on cardiovascular health are required.

PLAIN LANGUAGE SUMMARY

Oral appliances for treating sleepiness, quality of life and markers of sleep disruption in people with obstructive sleep apnoea/hypopnoea (OSAH)

OSAH is characterized by recurrent episodes of partial or complete upper airway obstruction during sleep, leading to a variety of symptoms including excessive daytime sleepiness. The current first choice therapy is CPAP that keeps the upper airway patent during sleep. However, this treatment can be difficult for some patients to tolerate and comply with on a long-term basis. OA are now widely used as an alternative to CPAP therapy. They are designed to keep the upper airway open by either advancing the lower jaw forward or by keeping the mouth open during sleep. This review found that OA should not be considered as first choice therapy for OSAH, where symptoms and sleep disruption are severe. There has not been a sufficient amount of research that examines the effects of OA compared with CPAP in terms of symptoms and quality of life. Although CPAP was clearly more effective at reducing the disruption to sleep, some people with OSAH may prefer using them if they are found to be tolerable and more convenient than CPAP. When an active OA was compared with an inactive OA , there were improvements in daytime sleepiness and apnoea/hypopnoea severity. OA may be more effective than corrective upper airway surgery. Further research should consider whether people with more distinctly severe symptoms respond in a similar way to those patients represented in the studies we have included in the review.

BACKGROUND

Obstruction of the upper airway during sleep may result in snoring, and reduction (hypopnoea) or cessation (apnoea) of airflow. In adults apnoea is defined as cessation of airflow for greater than 10 seconds. Hypopnoea is defined as a 50% or greater decrease in airflow, often accompanied by hypoxaemia or arousal. The obstructive sleep apnoea-hypopnoea (OSAH) syndrome is defined as a patient suffering five or more apnoeas/hypopnoeas per hour of sleep with daytime symptoms, and is a relatively common condition occurring in 2 to 4% of males and 1 to 2 % of females in middle age (Young 1993).

The pathophysiology of OSAH involves factors that relate to the anatomical dimensions of the upper airway, upper airway resistance and upper airway muscle activity during sleep (Hudgel 1992).

The patient with OSAH often presents because of symptoms noticed by their bed partner, who will often report that the patient snores loudly followed by an apnoea associated with respiratory effort and terminated by an awakening and resumption of loud snoring. The patient then resumes sleep and the cycle may repeat itself many times during the night. Excessive daytime sleepiness and an impairment of cognitive function are often present due to sleep fragmentation and patients may experience other symptoms including mood disturbance, decreased libido and social withdrawal (ASDA 1995). Several epidemiological studies have reported associations between OSAH and health related outcomes such as cardiac arrhythmias, systemic and pulmonary hypertension, ischaemic heart disease and cerebrovascular disease (Shahar 2001). There is some evidence that OSAH may be linked to sleepiness and road traffic accidents which has medico legal implications,

with some countries requiring drivers suffering with OSAH to report this to the appropriate licensing authority (RCP 1993; Wright 1997).

The diagnosis of OSAH is usually made by polysomnography, which also provides an indication of severity (ASDA 1995). Polysomnography involves recording during sleep of chest and abdominal movements, oxyhaemoglobin saturation, airflow, ECG tracing, sleep state (EEG, EOG and EMG), activity whilst asleep, and arousals. The number of episodes of apnoea and hypopnoea per hour of sleep is calculated from the polysomnogram and is referred to as the apnoea-hypopnoea index (AHI). Severity of OSAH has two components: severity of daytime sleepiness and AHI (AASM 1999). Epworth Sleepiness Score is currently the most widely used assessment of subjective sleepiness and apnoea hypopnoea index is the most widely used assessment of sleep disordered breathing from overnight monitoring. Both measurements have their limitations but should be considered independent outcomes in evaluating the effectiveness of OSAH treatment.

Treatment options for OSAH include behavioural modification such as weight loss, alcohol avoidance and alteration of sleeping position (Shneerson 2001; Smith 2006); CPAP (Giles 2006); and a range of upper airway surgical procedures (Sundaram 2005). OA that modify the upper airway size are increasingly prescribed to patients with OSAH. Upper airway muscle activity decreases during sleep, leading to increased collapsibility of the pharyngeal tissues, mandibular opening and posterior displacement of the tongue. These changes result in narrowing of the oropharyngeal and hypopharyngeal airway (Hudgel 1992). A variety of OA are available whose primary actions are to advance the mandible or tongue and thus increase the upper airway size. Another, less accepted theory of their mode of action, is that OA cause stretch-induced activation of the pharyngeal motor system, reducing soft tissue laxity and airway collapse (Ono 1996).

Side-effects have been reported with the use of OA including discomfort in the temporo-mandibular joint, teeth or facial musculature, bite change, excessive salivation or dryness of the mouth (Clark 2000). The effectiveness of OA in the treatment of patients with OSAH, and their relative efficacy in comparison to the other available modalities of treatment is unclear. Previous reviews of OAs in the treatment of OSAH have only reported evidence from case series reports (Schmidt-Nowara 1995), or in comparison to CPAP (Giles 2006), and their place in guidelines suggests that they are not considered first-line therapy (SIGN 2003).

OBJECTIVES

To determine the clinical effectiveness of OA in the treatment of OSAH in adults.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials.

Types of participants

Participants with a diagnosis of OSAH, as defined as five or more apnoeas or hypopnoeas per hour of sleep are eligible for inclusion. There are no gender restrictions. Participants will be restricted to those over the age of 16 years.

Types of interventions

Treatment group: any intraoral prostheses for OSAH
Control group: other surgical or non-surgical intervention, or no intervention.

Types of outcome measures

Primary outcomes

Primary outcome measures were daytime sleepiness as measured by a validated sleep apnoea symptom score and the number of apnoeas and hypopnoeas per hour of sleep (AASM 1999).

Secondary outcomes

1. Quality of life (using a validated scale);
2. Cognitive function (using a validated scale);
3. Side effects associated with use of OA;
4. Oxygen desaturation indices;
5. One year mortality;
6. Patient preference.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Airways Group Specialised Register, together with an additional search on MEDLINE for citations containing “sleep” and (“apnoea” or “apnea” or hypopnoea“ or ”hypopnea“) or ”sleep disordered breathing“ or ” sleep related respiratory disorder(s)“ in any of the fields. We then identified any possible randomised controlled trials using the strategy developed by the Cochrane Collaboration.

The text words used in the initial searches were:
oral OR intraoral OR dental OR tongue OR mandib* OR mandib* advancement AND splint OR appliance OR prosth* OR device OR continuous positive airway* pressure OR CPAP OR (adenotonsil*) OR (tonsil*) OR (adenoid*) OR (surg* and palate) OR (surg* and uvula) OR (surg* and pharynx) OR (uvulopharyngoplasty) OR (UPPP) OR (UVPP) OR (UPP) OR (palatoplasty) OR (pharyngoplasty) OR (palatopharyngoplasty) OR (PPP) OR (uvulopalatoplasty) OR (LAUP) OR (tracheostomy) OR (mini-tracheostomy) OR (surg* and maxillo-facial) OR (surg* and maxillofacial) OR (genioglossal advancement) OR (maxillo-mandibular advancement) OR (maxillo-mandibular osteotomy) OR (maxillary advancement) OR (maxillary osteotomy) OR (mandibular osteotomy) OR (intrapalatine resection) OR (tongue volume reduction) OR (inferior sagittal osteotomy) OR (hyoid bone suspension) OR (hyoid suspension) OR (hyoid myotomy) OR (surg* and upper-airways) OR (surg* and nasal) OR (septoplasty) OR (polypectomy).
To update the review, we carried out further searches of the Specialised Register in June 2008 and the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 2, 2008). The search was amended and the text words used were:
(oral* OR intraoral* OR intra-oral* OR dental* OR tongue* or mouth* or jaw* OR mandib* OR "mandib* advancement*" or splint* or prosth* or appliance or device)

Searching other resources

To locate additional RCTs we:

- checked the reference lists of relevant review articles, and references of all identified RCTs;
- contacted the NHS Centre for Reviews and Dissemination, the National Health Technology Assessment Programme the NHS National Research register and the Aggressive Research Intelligence Facility;.
- contacted local and national sleep laboratories and experts in the fields of sleep and respiratory medicine, and ENT surgery;.
- contacted other Cochrane Review Groups to identify citations found by handsearching of journals (such as surgical journals).

Data collection and analysis

Selection of studies

The authors (JL, TL) independently reviewed the titles, abstracts, and citations to assess potential relevance for full review. From the full text, the reviewers independently assessed studies for inclusion based on the criteria for population, intervention, study design and outcomes. There was no disagreement between the reviewers on the inclusion and exclusion of studies. Any disagreement over study inclusion would have been resolved by a third reviewer (JF).

Data extraction and management

The reviewers independently extracted data from included trials and entered results into the Cochrane Collaboration software program (Review Manager). No information regarding outcomes needed to be estimated from graphs. Should future studies be published with such presentation of data, two reviewers will estimate it independently. Data extraction included the following items:

1. Population: age, gender, number of patients studied, patient demographics, withdrawals.
2. Intervention: type (type of OA).
3. Control: medical (type, dose, route of delivery, duration), mechanical (type, delivery), other surgical (type).
4. Outcomes: as above
5. Design: method of randomisation and allocation concealment

Assessment of risk of bias in included studies

We assessed the bias protection of each study by assessing randomisation procedures and blinding. Given the nature of the questions we have addressed in this review, blinding is not likely to be possible for oral appliance and CPAP or surgical comparisons. This assessment is in line with guidance described in chapter 8 of the Cochrane Handbook (Handbook 2008).
Each study was assessed for validity on a 0-5 scale, method of Jadad 1996:
Was the study described as randomised?(1 = yes, 0 = no)
Was the study described as double-blind?(1 = yes, 0 = no)
Was there a description of withdrawals and drop outs? (1 = yes, 0 = no)
Was the method of randomisation well described and appropriate? (1 = yes, 0 = no)
Was the method of double-blinding well described and appropriate?(1 = yes, 0 = no)
Deduct 1 point if methods of randomisation or blinding were inappropriate.

Data synthesis

We combined all included trials using Review Manager. For continuous variables, we calculated the results of individual studies as a fixed-effect weighted mean difference (WMD) or standardised mean difference (SMD), with 95% confidence intervals (95% CI). For dichotomous variables, a fixed-effect odds ratio (OR) with 95% CI, were calculated for individual studies. For pooled effects, heterogeneity was tested using the Breslow-Day test; $P < 0.1$ was considered to be statistically significant. If heterogeneity was observed, we used a random-effects model to calculate the results.

Subgroup analysis and investigation of heterogeneity

In the presence of heterogeneity, we performed the following sensitivity analysis using:

1. Females versus males;
2. Random-effect versus fixed-effect modelling.

No data stratified by severity were presented.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search

For details of search history, see Table 1. An annual search update in June 2008 identified 26 new references. Four references were linked with previously included studies (Gotsopoulos 2002; Hoekema 2006). Three references were considered as new studies for this updated review but were excluded (Friedman 2008; Saletu 2007; van der Sweep 2006: see Characteristics of excluded studies).

Table 1. Search history

Date	Detail
All years to June 2005	References identified: 705 Unique studies retrieved: 55 (three unpublished) Studies failing to meet the entry criteria of the review: 37 Studies included: 16 Awaiting translation: 2
June 2005 to June 2007	References identified: 38 Unique studies retrieved: 4 Studies not complete: 1 Studies failing to meet the entry criteria of the review: 2 Studies meeting review entry criteria: 1

Included studies

Seventeen individual trials (32 references) met the review inclusion criteria of the review. There was no disagreement about study inclusion between reviewers. One study is ongoing (Fairbairn 2004), and one study is available as an interim analysis and does not contribute data to this review (Cibele 2006). For a full description of each eligible trial see Characteristics of included studies.

Design

All included studies were randomised and controlled. Eleven trials were of crossover design and seven were parallel group trials (Blanco 2005; Fleetham 1998; Hans 1997; Hoekema 2006; Hoekema 2007a; Lam 2007; Tegelberg 1999). Observer blinding was reported in Engleman 2002.

Participants

The participants in the studies suffered from mixed severity of OSAH, from mild to severe, as defined by AHI. The majority of participants were men of middle-age. In all studies there was polysomnographic confirmation of sleep apnoea, except for Johnston 2002 where home oximetry was used as the basis of determining oxygen desaturation indices.

Interventions

Ten trials compared an OA with CPAP (Barnes 2004; Engleman 2002; Ferguson 1997; Fleetham 1998; Hoekema 2006; Lam 2007; Olson 2002; Randerath 2002; Tan 2002), six trials compared an OA with a control OA (Blanco 2005; Durán 2002; Gotsopoulos 2002; Hans 1997; Johnston 2002; Mehta 2001) and one trial compared an OA with surgery (Tegelberg 1999). Active OA therapy consisted of mandibular advancement devices. Control OA therapy consisted of devices which were placed in the mouth that did not protrude the mandible. Only data from the OA versus CPAP comparison from (Barnes 2004) were entered in the review, as we felt that the data from the OA versus placebo pill comparison was not an adequate mean of establishing efficacy. Lam 2007 allocated participants to receive conservative management on top of either CPAP or OA, and also as a separate treatment arm.

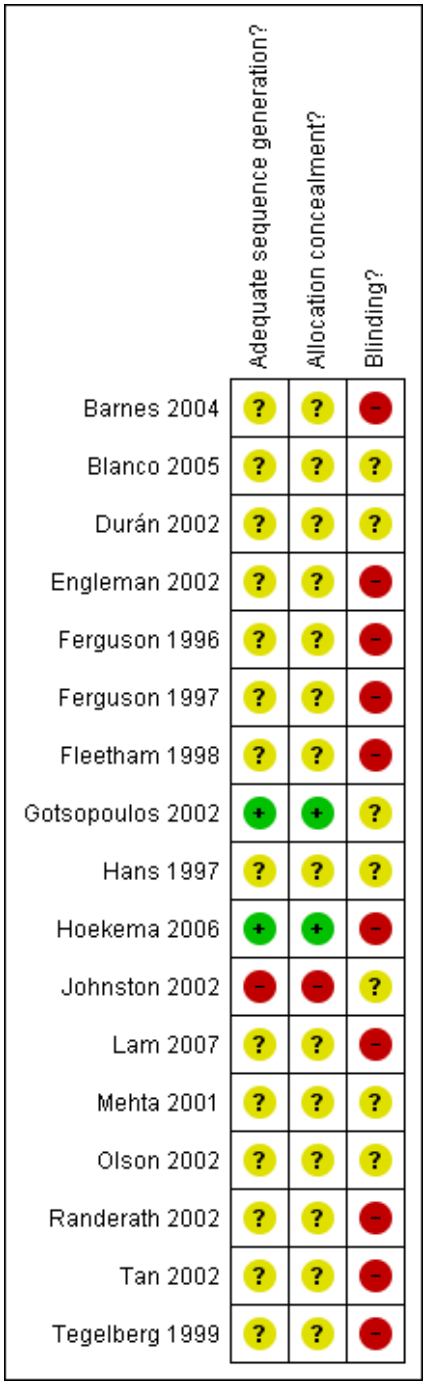
Duration

The studies lasted for between two weeks to one year. One study conducted a four year follow-up (Tegelberg 1999).

Risk of bias in included studies

Availability of information regarding the allocation of participants to treatment groups was generally poor. A summary of judgements for allocation generation, concealment and blinding is given in Figure 1. The information we have used as the basis for these judgements is provided in Characteristics of included studies. Overall there was a limited amount of information available which meant that many of our judgements were left as 'unclear'. Where information was available regarding randomisation procedures, they were adequate in protecting studies from selection bias.

Figure 1. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Blinding procedures were not possible for CPAP or surgical comparisons. Barnes 2004 was a three arm crossover trial reporting the effects of OA, CPAP and a dummy pill. We have retained data only for the OA and CPAP comparisons since data from the OA and dummy pill comparison may be particularly prone to detection bias. Other studies describe a control appliance (Blanco 2005; Durán 2002; Hans 1997), or an attempt by study personnel to present an inactive appliance as an alternative therapy in a single-blind manner (Gotsopoulos 2002; Johnston 2002; Mehta 2001). Jadad scores are provided for each study in Characteristics of included studies.

Effects of interventions

We have used the different comparisons to display the results. Some unpublished data have been made available to the reviewers. Subgroup analysis by severity of OSAH was not possible due to the heterogeneous populations recruited in the studies. Random-effects modelling has been compared with fixed-effect modelling if heterogeneity was observed, in order to determine the impact of variability between studies on the pooled results. Data from four crossover studies (Gotsopoulos 2002; Johnston 2002; Mehta 2001; Randerath 2002) have been analysed as parallel and crossover group data as the trialists made first arm data available upon request. Crossover scores were extracted from the published article.

Active oral appliance versus control oral appliance

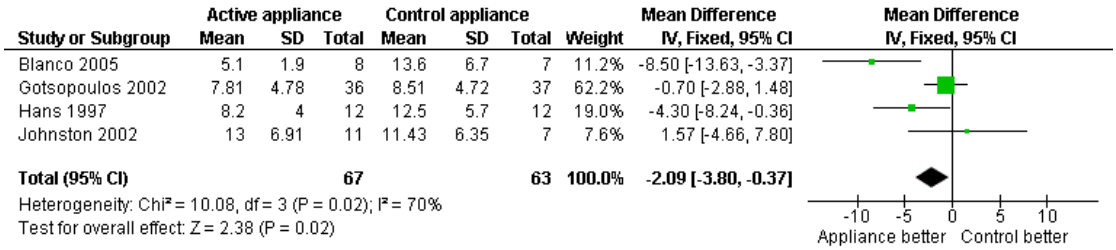
Six trials reported data for this comparison (Blanco 2005; Durán 2002; Hans 1997; Gotsopoulos 2002; Johnston 2002; Mehta 2001). Mandibular advancement devices were compared with devices that did not protrude the mandible.

Epworth Sleepiness Score

Parallel/First arm crossover studies (Blanco 2005; Gotsopoulos 2002; Hans 1997; Johnston 2002):

Pooled analysis generated a heterogeneous but significant result (-2.09; 95% CI -3.8 to -0.37, I2 = 70.2%, Figure 2). Random-effects modelling gave a non-significant result (-2.95; 95% CI -6.69 to 0.79). The addition of data from Blanco 2005 may have introduced a degree of variation. This may be explained by the somewhat more censored nature of the data from this study. No intention-to-treat analysis was undertaken in this trial, and there was an attrition rate of 20%. The overall attrition rate could explain the more significant difference on symptoms in the active treatment group, whereby those who remained in the study perceived the most benefit.

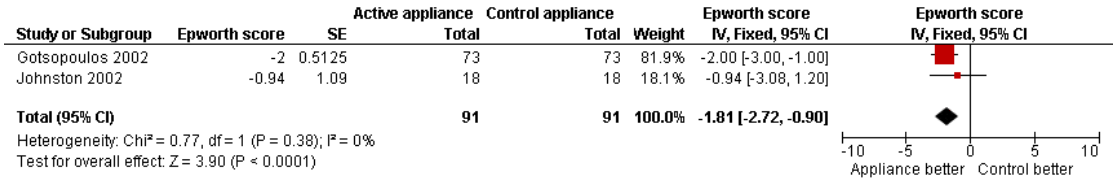
Figure 2. Forest plot of comparison: 1 Active oral appliance versus control appliance, outcome: 1.1 Epworth sleepiness score - first arm data/parallel studies.



Crossover studies (Gotsopoulos 2002; Johnston 2002):

Pooled analysis gave a significant difference in favour of active OAs of -1.81; 95%CI -2.72 to -0.90, Figure 3.

Figure 3. Forest plot of comparison: 1 Active oral appliance versus control appliance, outcome: 1.2 Epworth sleepiness score - crossover studies.



Apnoea Hypopnea Index

Parallel/First arm crossover studies (Blanco 2005; Gotsopoulos 2002; Hans 1997; Johnston 2002; Mehta 2001):
There was a significant effect in favour of active treatment (-10.78 events/hrI; 95%CI -15.53 to -6.03, Analysis 1.3).
Crossover studies (combined scores) (Durán 2002; Gotsopoulos 2002; Johnston 2002;Mehta 2001):
Data from Durán 2002; Gotsopoulos 2002; Johnston 2002 and Mehta 2001 and gave a significant treatment effect in favour of active OA (-15.15 events/hr; 95% CI -19.40 to -10.89, Analysis 1.4).

Minimum arterial oxygen saturation

Parallel/First arm crossover studies (Gotsopoulos 2002; Johnston 2002; Mehta 2001):
There was no significant effect in favour of active appliances (1.79%; 95% CI -0.29 to 3.87, Analysis 1.7).
Crossover studies (combined scores) (Gotsopoulos 2002; Mehta 2001):
There was a significant difference of 3.39%; 95% CI 2.25 to 4.54, Analysis 1.8).

Arousal Index

Parallel/First arm crossover studies (Blanco 2005; Gotsopoulos 2002; Mehta 2001):
Overall there was a statistically significant effect in favour of active OA compared with control: WMD-10.66 arousals/hr; 95% CI -16.03 to -5.29, Analysis 1.5.
Crossover studies (combined scores) (Gotsopoulos 2002; Mehta 2001):
There was a significant difference of -10.72 arousals/hr; 95% CI -15.05 to -6.39, Analysis 1.6.

Blood pressure outcomes

Crossover studies (Gotsopoulos 2002)
Active oral appliance therapy led to lower blood pressure compared with control for certain measurements of diurnal/nocturnal blood pressure. Confirmatory work is required.

Withdrawals

Parallel/First arm crossover studies (Blanco 2005; Hans 1997; Johnston 2002)
There was no significant difference between active and control OA (OR 0.83; 95% CI 0.24 to 2.86, Analysis 1.9).

Crossover studies (combined data) (Gotsopoulos 2002)
Gotsopoulos 2002 reported 12 withdrawals over the course of the study. Reasons cited were refusal to participate after receiving CPAP (one), work interference (three), permanent relocation interstate (two), extended overseas trip (one), self-perceived improvement in OSAH symptoms with OA during phase 1 (one), self-perceived improvement during acclimatisation phase (one).

Side effects/tolerability

Parallel/First arm crossover studies
No data available.
Crossover studies (combined data) (Gotsopoulos 2002; Johnston 2002; Mehta 2001)
Gotsopoulos 2002 reported that participants given the active OA suffered side effects more frequently than those given the control device. Side effects reported were jaw discomfort ($p < 0.0001$; control versus active OA); tooth tenderness ($P < 0.0001$; control versus active OA) and excessive salivation ($P < 0.05$; control versus active OA). Mehta 2001 reported that side effects were mild-moderate, and included: excessive salivation (50%), gum irritation (20%), mouth dryness (46%), jaw discomfort (12.5%) and bruxism (12.5%). Control and active OA data were not separated. The active OA was well tolerated by 21/24 participants who completed the protocol. Control OA data were not reported. Johnston 2002 reported that 68% participants wore the OA every, or almost every, night. Eighty-four per cent of participants complained that the device fell out of their mouth on more than two nights per week. Forty-two per cent of participants complained of jaw discomfort on waking. Johnston 2002 did not report control OA data on tolerability.

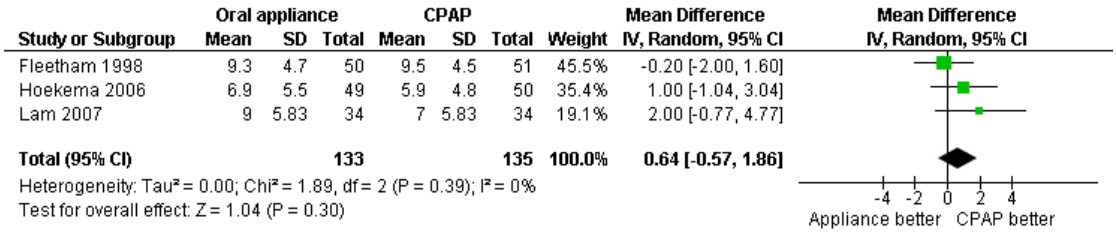
Oral appliance versus CPAP

Ten trials were identified which compared an OA to CPAP (Barnes 2004; Engleman 2002; Ferguson 1996; Ferguson 1997; Fleetham 1998; Hoekema 2006; Lam 2007; Olson 2002; Randerath 2002; Tan 2002). Three had a parallel group design (Fleetham 1998; Hoekema 2006; Lam 2007) and the remaining studies were crossover trials.

Epworth Sleepiness Score

Parallel/First arm crossover studies (Fleetham 1998; Hoekema 2006; Lam 2007):
No statistically significant difference: 0.64; 95% CI -0.57 to 1.86, Figure 4).

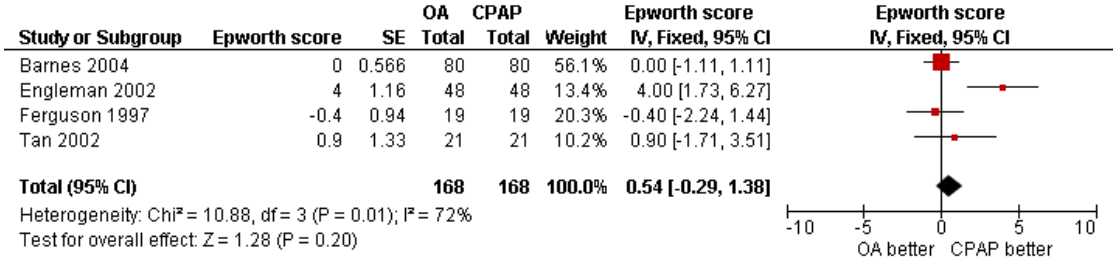
Figure 4. Forest plot of comparison: 2 Oral appliance versus continuous positive airways pressure, outcome: 2.1 Epworth sleepiness scale - first arm data/parallel studies.



Crossover studies (combined scores) (Barnes 2004; Engleman 2002; Ferguson 1997; Tan 2002):

There were conflicting scores for Epworth scores between the studies. There was a statistically significant effect in favour of CPAP over OAs in Engleman 2002 (of four units, P < 0.001). None of the three other trials reported a significant difference between the two groups on Epworth scores (Barnes 2004; Ferguson 1997;Tan 2002). There was a high degree of heterogeneity when pooled (I^2 72.4%). With fixed-effect modelling, the pooled estimate was 0.54; 95% CI -0.29 to 1.38, Figure 5. With random-effects modelling the result was 0.98 (95% CI -0.8 to 2.76). Although neither result was significant, the variation between the studies may be attributed to different OA design or treatment adherence.

Figure 5. Forest plot of comparison: 2 Oral appliance versus continuous positive airways pressure, outcome: 2.2 Epworth sleepiness score - crossover studies.



Randerath 2002 reported no difference on an in-house symptom score.

Apnoea Hypopnea Index

Parallel/First arm crossover studies (Fleetham 1998; Hoekema 2006; Lam 2007; Randerath 2002):

CPAP was more effective in suppressing apnoea and hypopnea than OA (8.13 events/hr; 95% CI 5.57 to 10.69, Analysis 2.3). Although the level of statistical heterogeneity for this outcome was high (I^2 60%), random effects modelling did not alter the statistical significance or the direction of the effect.

Crossover studies (combined scores) (Barnes 2004; Engleman 2002; Ferguson 1996; Ferguson 1997; Olson 2002; Randerath 2002; Tan 2002).

There were significant differences in AHI between OA and CPAP treated participants in favour of CPAP. When pooled these data generated a difference of 7.97 events/hr; 95% CI 6.38 to 9.56, Analysis 2.4.

Quality of life scores

Parallel/First arm crossover studies (Fleetham 1998; Lam 2007; Olson 2002):
Overall, there was no statistically significant difference between treatment groups on the SAQLI score (-0.03; 95% CI -0.35 to 0.28, Analysis 2.5).
Crossover studies (combined scores) (Barnes 2004; Engleman 2002; Tan 2002):
Tan 2002 used a scale where low scores were indicative of good health. Scores in the OA group were 10.20 +/-9.90 in the OA group and 6.50 +/-5.90 in the CPAP group (P < 0.001 after both treatments). Engleman 2002 reported component scores from the SF-36, which showed a significant effect in favour of CPAP versus OA on health transition and mental component scores (health transition: OA: 2.9 +/- 0.8; CPAP: 2.4 +/-0.8, P = 0.001; mental: OA: 48 +/-11; CPAP: 52 +/-10, P = 0.008). No significant difference was detected on the physical component score. The HADS anxiety and depression scores did not differ significantly. Barnes 2004 and Engleman 2002 also reported data on the Functional Outcomes of Sleep Questionnaire. There was no statistically significant difference between CPAP and OAs (-0.18; 95% CI -0.42 to 0.07), but there was a high degree of heterogeneity (I2 88.8%). Random-effects modelling gave a non-significant result with wider confidence intervals (-1.44 to 0.51). In the absence of additional data sets for this measurement, the numerous possible explanations of the conflicting results such as subtle differences in the design of the OA, study design and severity could influence the response to therapy. It is noteworthy that Engleman 2002 which reported superiority of CPAP over OA on other outcomes such as AHI, ESS also reported superiority over OA on FOSQ outcome data.
Tan 2002 also measured bed-partner health and daytime sleepiness, but did not detect a significant difference between treatment with CPAP and OA. Both treatments improved these scores compared with baseline. Data were not entered as it was not clear whether all participants in the study had bed partners or not.

Cognitive performance

Crossover studies (combined scores) (Barnes 2004; Engleman 2002)
Engleman 2002 did not detect a significant difference on cognitive performance scores. No other trial reported data on cognitive performance. Barnes 2004 reported no significant difference between CPAP and OA on word association, psychomotor vigilance, or maintenance of wakefulness tasks.

Minimum arterial oxygen saturation

Parallel/First arm crossover studies (Fleetham 1998; Lam 2007; Randerath 2002):
There was a significant effect in favour of CPAP compared with OA (4.59%; 95% CI 2.55 to 6.64, Analysis 2.13).
Crossover studies (combined scores) (Barnes 2004; Ferguson 1996; Ferguson 1997; Randerath 2002):
Although there was significant heterogeneity observed (I^2 61.9%), both fixed and random-effects modelling detected significant differences between the two treatment groups in favour of CPAP (Fixed: 5.16%; 95% CI 3.25 to 7.06); Random: 5.64%; 95% CI 2.48 to 8.8).

Arousal Index

Parallel/First arm crossover studies (Fleetham 1998; Lam 2007; Randerath 2002):
When pooled these data were statistically significant in favour of CPAP with both fixed-effects modelling (WMD 5.21 arousals/hr; 95% CI 2.48 to 7.94, Analysis 2.15).

Crossover studies (combined scores) (Barnes 2004; Ferguson 1996; Ferguson 1997; Olson 2002; Randerath 2002; Tan 2002):
There was a significant difference in favour of CPAP (2.24 arousals/hr; 95% CI 0.04 to 4.05, Analysis 2.16).

Blood pressure outcomes

Parallel/First arm crossover studies (Lam 2007)
No statistically significant differences were observed on systolic and diastolic blood pressure in Lam 2007.
Crossover studies (Barnes 2004)
One study reported data for this outcome. There were no significant differences between CPAP and OA in mean 24 hour systolic and diastolic pressure. OA treatment led to lower mean nocturnal diastolic pressure.

Withdrawals

Parallel/First arm crossover studies (Barnes 2004; Engleman 2002; Hoekema 2006; Lam 2007; Fleetham 1998; Randerath 2002):
There was a greater likelihood of withdrawal in those treated with OA compared with CPAP (OR 2.05; 95% CI 1.15 to 3.67, Analysis 2.21).
Crossover studies (Ferguson 1996; Ferguson 1997; Tan 2002):
Ferguson 1996 reported one drop out occurred during wash-in period and one dropped out in the first treatment period due to relocation (OA) and in Ferguson 1997 one drop-out occurred in the OA period declining follow-up. Three refused to crossover from appliance to CPAP, two of whom were treatment successes. Tan 2002 reported three dropouts from the study (two from the CPAP group and one from the OA group).

Side effects/tolerability

Parallel/First arm crossover studies (Fleetham 1998):
Fleetham 1998 did not report data on tolerability of either treatment.
Crossover studies (combined scores) (Engleman 2002; Ferguson 1996; Ferguson 1997; Randerath 2002):

Both treatment options lead to different, but noticeable and potentially important adverse effects. Jaw and oral pain occurred more frequently with OA than with CPAP (OR 18; 95% CI 8.62 to 37.57, two studies, N = 67). There were no differences in participants who were free from side effects (OR 0.57; 95% CI 0.24 to 1.36, two studies, N = 45). Individual studies reported higher rates of excessive salivation and appliance removal during sleep with OA, but higher rates of leak, dry upper airway, stuffy nose, and inconvenience with CPAP.

Patient preference

Barnes 2004; Engleman 2002; Ferguson 1996; Ferguson 1997; Olson 2002; Tan 2002): Due to the fact that preference outcomes from crossover studies are not paired, we have not pooled preference data. Out of 15 participants who were deemed treatment successes (reduction in AHI to < 10 and relief of symptoms) on both an OA and CPAP, 13 preferred treatment with an OA and two preferred treatment with CPAP (Olson 2002). The trial by Olson 2002 only considered the preferences from participants whose quality of life (SAQLI) score improved by one or more during either appliance or CPAP treatment. Engleman 2002 reported preference from all participants regardless of treatment success or failure. There was no difference between OA and CPAP preference (19 participants preferred OA and 25 preferred CPAP (four were unaccounted for), P = 0.194). Barnes 2004 reported that more participants preferred CPAP to OA (44% versus 30%), and that their bed partners also preferred this treatment option to OA (40% versus 36%). This was a large study and the expression of preference was made irrespective of treatment success of either option. A placebo pill was also introduced in this study, and such an option may have appealed to those who liked the convenience of this option, especially in milder patients who may not perceive as great a benefit as those with more severe OSAH.

Oral appliance versus surgery

One study (Tegelberg 1999) reported data for this comparison.

Subjective sleepiness score

An unvalidated questionnaire was developed in order to determine daytime sleepiness. No numerical values were reported, but a statistically significant difference was detected at six months, the group treated with surgery experienced less daytime sleepiness compared with the dental appliance group (P < 0.05). At twelve months this difference was not apparent.

Apnoea Hypopnea Index

Mean AHI was not statistically different between OA and surgery at six months (6.6 versus 8.6 respectively). At 12 months, there was a statistically significant difference between the groups, with a mean AHI in the OA group of 6.0 (95% CI 3.0 to 8.9) and an increase in the surgery group to 10.4 (7.6 to 13.2), P < 0.05. At four year follow-up there was a significant difference reported in the success rate in AHI for the OA (72% versus 35% - success defined as greater than 50% reduction in AHI). The difference between the two groups on mean scores was significant (7.2 versus 14.2 in the OA and uvulopalatopharyngoplasty groups respectively, P < 0.001).

Oxygen desaturation

Oxygen desaturation indices were reported. At six months, there was no significant difference (6.4 versus 8.0 in the appliance and surgery groups respectively). At 12 months the difference was non-significant (6.1 versus 9.3 in the appliance and surgery groups). At four year follow-up, oxygen desaturation index (ODI) was 6.7 and 13.1 in the OA and uvulopalatopharyngoplasty groups respectively, P < 0.01.

Quality of life

Quality of life was reported via three component sections of an overall questionnaire - the Minor Symptoms Evaluation-Profile (MSE-P), which has been validated in the assessment of central nervous system related symptoms during cardiovascular pharmacotherapy among hypertensive patients, but not in the assessment of patients with OSA. The three sections reported were: vitality, contentment and sleep. There were improvements in both groups compared with baseline. Vitality improved by 5.4 (95% CI 0.1 to 10.7), P < 0.05 in the OA group compared with 9.7 (95% CI 5.0 to 14.4), P < 0.001 in the surgery group. Sleep improved by 19.5 (95% CI 13.5 to 25.5), P<0.001 in the OA group compared with 22.6 (95% CI 16.9 to 28.3), P < 0.001 in the surgery group. At 12 months, there was a significant difference detected in favour of surgery on the contentment component (33.7 versus 27.4 in appliance and surgery groups respectively, P < 0.05). No differences were detected between the groups on the other two components.

Withdrawals

Withdrawals were reported for the OA group as follows: 12 participants withdrew from the OA group - four prior to treatment, two due to discomfort, one due to an allergic reaction with the OA , three due to perceived lack of efficacy one due to epilepsy and one due to maxillary cancer. Three participants withdrew from the group treated with surgery, two reversed their decision about participation and one was diagnosed with gastric cancer.

DISCUSSION

OAs are widely prescribed for the treatment of OSAH both as primary therapy and as an alternative to patients who are unable to tolerate CPAP. There are currently a large number of different OAs available for the treatment of OSAH. Until the mid to late 1990s the majority of studies of the effectiveness of OAs in OSAH were short term, uncontrolled, small and retrospective. More recently the quality of OA clinical research has become more rigorous and this review has identified 17 randomised controlled trials involving 831 participants with varied severity of OSAH. Review of these trials suggests that OAs are effective in improving subjective sleepiness and indices of sleep disordered breathing in selected patients with OSAH, are less effective than CPAP in improving indices of sleep disordered breathing but that certain patients prefer them. We remain uncertain as to the equivalence of OA and CPAP in terms of symptoms; the confidence intervals include a potentially meaningful difference in symptoms, but they also include unity. One study measured bed-partner health and sleepiness, another measured loudness of snoring rated by bed partners, and a third study incorporated preference data from bed partners. However, the data are not definitive because of the small patient numbers and inadequate assessment of efficacy with patient-oriented outcomes in the assembled studies.

The issues concerning the effectiveness of OA treatment in OSAH are very similar to those outlined for CPAP therapy (Giles 2006). Ethical concerns have been expressed about the use of placebo controls in OSAH randomised controlled trials (Hans 1997). However, sham nasal CPAP has been successfully used in OSAH randomised controlled trials and has shown a measurable placebo effect (Jenkinson 1999). The best achievable placebo in an OA treatment study would be an OA that had no effect on the vertical mouth opening or mandibular position. However, the inconvenience of this without any likely benefit would tend to bias in favour of an OA which had an effect on the vertical mouth opening and/or mandibular position, unless the benefits could be measured after subtracting the side effects of the treatment.

Compared with control, OAs have been shown to reduce symptoms of sleepiness associated with OSAH, and also to reduce AHI, arousals and minimum saturation. There is some evidence that OAs lead to lower blood pressure from one study. This effect requires replication in future trials. Further assessment of OAs with control should consider quality of life measures.

There is increasing evidence that CPAP is effective in improving daytime sleepiness, quality of life and blood pressure (Giles 2006; Patel 2003). This review suggests that OAs are less effective than CPAP in improving indices of sleep disordered breathing, but the evidence on subjective outcomes is less certain. Symptoms and indices of quality of life (arguably more powerful indications of how patients perceive therapeutic benefit than indices of sleep disordered breathing) have shown equivocal or conflicting results. The number of studies, and the somewhat mixed severity of baseline symptoms reported in their respective populations restrict meaningful exploration via subgroup analysis. Further work in more distinct study populations will help to establish whether particular characteristics (such as disease severity and burden) predispose patients to accept one treatment modality over another, to accept them equally well, or to accept neither. If the superiority of CPAP in reducing AHI, arousals and minimum saturation reflects a more intensive, invasive intervention and is independent of improvement in symptoms, then people who start treatment with fewer symptoms do not stand to perceive the same degree of benefit as do those with more pronounced sleepiness. However, if sleep disordered breathing is left inadequately controlled, the long-term risk of cardiovascular morbidity may be significant (Mooe 2001). Studies contributing data on AHI (11) outnumber those contributing data on ESS (seven) or quality of life (five). The use of subjective outcomes is a priority for additional research in this area.

The relative effects outlined above and the different side-effect profiles of these treatments also shed some light on to some of the findings on study withdrawal and preference. It should be noted that there was a higher withdrawal rate in OA treatment groups compared with CPAP. Where this occurs in crossover studies, this alters the characteristic of the study population at the end of treatment, such that trialists collect data from participants who have adhered to both treatment regimens. This is compounded when preference data are sought, because this can only be recorded in participants who have been exposed to all treatments assessed, leaving preference in crossover trials theoretically prone to order effects.

Across the studies there was no consistent preference for one intervention over another, with individual study results indicating discordant directions and degrees of preference for the two treatments. Exploration of these differing effects between trials is difficult, but there have been within-study subgroup analyses. Engleman 2002 suggested that preference for OA was stronger in those with milder daytime sleepiness, and less impairment in quality of life when compared with those expressing preference for CPAP. Those who preferred CPAP also used it for longer than those who preferred OA. Although baseline AHI did not correlate with preference in Engleman 2002, Barnes 2004 reported that in a mild subgroup of participants with AHI <15, more people expressed a preference for OAs than for CPAP. When studies considered preference in relation to a treatment response rather than baseline characteristic, there appeared to be a strong preference for OAs over CPAP (Ferguson 1996; Ferguson 1997; Olson 2002). The largest study to date has attempted to record overall preference irrespective of whether treatments were deemed successful or not (Barnes 2004). The number of participants preferring CPAP differed depending on whether the trialists asked which option was more convenient or which one was more effective, with many indicating that the placebo was easiest to use. There are clearly complex reasons why some people prefer OAs and others CPAP,

and this may be related to baseline psychological factors and disease severity, as well as subsequent response to treatment and tolerance of side-effects. Preference has been measured in numerous OSAH trials where different types of CPAP machines have been compared (Haniffa 2004). However, despite a numerically superior preference for auto-CPAP over fixed pressure machines in these studies, this does not seem to lead to superior amounts of usage (Haniffa 2004). Whilst preference is a powerful, subjective way of determining which option was regarded as superior in participants in these studies, this reflects only short-term exposure. Barnes 2004 also measured self-reported compliance with OA, and this indicated that where the OA were thought to have been effective, they were reportedly used more. Continued acceptance with treatment may be predicted by psychological determinants, and evidence from qualitative sources would be helpful in elucidating the interaction between perceived treatment success, willingness to persist with treatment, and psychological and emotional factors (Wild 2004).

Self-reported treatment compliance with OAs was high as reported in six studies (Barnes 2004; Ferguson 1997; Gotsopoulos 2002; Mehta 2001; Randerath 2002; Tegelberg 1999), though objective usage data are harder to capture for OAs than for CPAP.

Evidence from one trial comparing OA with a surgical procedure suggests that an OA was more effective than uvulopalatopharyngoplasty in improving indices of sleep disordered breathing. However, the significance of this finding is questionable as there is no definitive evidence of the effectiveness of this type of corrective upper airway surgery (Sundaram 2005). Further work is required to determine the most effective type of OA but until there is definitive evidence of the effectiveness of OA treatment the value of comparing different types of appliance is also debatable. Several studies have compared devices of different design (Bloch 2000; Luks 1996; Pitsis 2002; Rose 2002). Bloch 2000 reported no significant difference in efficacy between appliances, whilst Rose 2002 and Pitsis 2002 suggested that appliance design is important to treatment success and patient preference.

There are some data from a crossover study on blood pressure which indicates a reduction in certain measures when participants are treated with OA. In one measure, OA blood pressure was lower than CPAP. Repeated recording in future studies would help to quantify the effect compared with control. There is a need to monitor other conditions thought to be associated with OSAH. Successful long-term management of this condition is likely to be defined not merely by subjective response and associated adherence, but also by cardiovascular morbidity. Although predictors of treatment success have been proposed they have never been systematically validated (Mehta 2001). There are limited data on long-term complications. The results of this review justify well designed, large scale, randomised controlled trials to assess the effectiveness and cost effectiveness of OA treatment.

AUTHORS' CONCLUSIONS

Implications for practice

Although the data are limited by the relatively small number of patients studied and methodological weaknesses, such as lack of blinding, there is increasing evidence that OA improves subjective sleepiness and indices of sleep disordered breathing over an inactive control. CPAP and OA both led to improvements in AHI compared with baseline, but the magnitude of improvement favoured CPAP. Symptomatic response varied between the studies, and reinforces the need for additional trials using symptom and quality of life outcomes in the future. Participants were more likely to withdraw from OA therapy than from CPAP, although patients who respond to both treatments appear to prefer the use of an OA over CPAP. There may be various factors which determine which patients are more likely to persist with CPAP and OA, and studies in more distinct patient subgroups, or exploration of patient subgroups within studies, would help to this end. On the basis of evidence in this review it would appear appropriate to offer OA therapy to patients with mild symptomatic OSAH, and those who are unwilling or unable to persist with CPAP therapy. This recommendation is drawn from evidence of limited duration. Long-term effects of these two treatments and their impact on cardiovascular health are not currently evaluable.

Implications for research

Although the evidence base to support the use of CPAP in OSAH is strong, its relative effects compared with OA require further elucidation.

1. Additional well designed, large scale randomised controlled trials comparing active and control OA are required in patients with OSAH to determine which groups of patients are most likely to benefit from OA treatment, how these patients can be identified, how much benefit can be achieved and with what cost, side effects and complications.

2. These trials should have patient and investigator blinding and perform an intention to treat analysis. Adequate procedures to protect studies against selection bias should be detailed in study reports.

3. Crossover studies should also include tests of carryover and period effects. These trials should also use standardised, validated instruments to measure subjective outcomes.

4. There is a need to clarify the relative effects of OAs and CPAP in terms of symptoms and quality of life. The effect estimate for ESS did not exclude a difference in favour of either intervention, and this outcome in particular would benefit from additional usage of ESS in future trials. These findings would provide valuable insights in to how patients offered either of these therapies respond subjectively, and whether they seek alternative treatments to manage their OSAH.

5. There are very few studies of sufficient duration or size to estimate whether CPAP or OA are effective in improving cardiovascular health such as reducing stroke and heart attacks. Further studies should consider measuring these outcomes.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Barnes 2004

Methods	Three-way crossover trial. Patients randomised to three arms CPAP, MAS and Placebo.
Participants	80 middle aged patients with mild to moderate OSA. Male 64 females 16, mean age 47; baseline ESS mean 10.7; AHI: 21.3. Inclusion criteria: AHI 5-30;
Interventions	Nasal CPAP versus OA versus Placebo tablet. Study duration: 12 weeks
Outcomes	ESS, FOSQ, ODI 4%, AHI, MWT, SF-36
Notes	Two week wash out period between each treatment. Intention-to-treat analysis Jadad Score=2

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	No	OA & CPAP compared with dummy pill (single-blind)

Blanco 2005

Methods	Randomised, parallel group trial. Method of allocation: not clear.
Participants	24 participants randomised. Data presented on 15 participants who completed the study. Mean age: 55 years; BMI: 26.8; AHI: 24-33; ESS: 14.7-16.3. Inclusion criteria: AHI >/= 10; two OSA symptoms. Exclusion criteria: Poor dentition; >75years; BMI: >40
Interventions	OA versus control OA. Control OA same as active without advancement
Outcomes	AHI; symptoms; quality of life; tolerability
Notes	

Risk of bias

Blanco 2005 (*Continued*)

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	Unclear	Presentation of control intervention different; information on whether it was described as being an alternative treatment to intervention not available

Durán 2002

Methods	Randomised, crossover trial. Method of allocation: not clear.
Participants	44 participants recruited. 38 participants completed the study (4 women). Mean age: 46.5 (SEM 9.2); BMI: 27.7 (SEM 3.2); AHI: 15.3 (SEM 10) Inclusion criteria: Mild OSA and snoring (AHI >5).
Interventions	OA versus OA in centric occlusion. Study duration: unclear. Study preceded by a 12-18 week acclimatisation period.
Outcomes	AHI; symptoms; tolerability
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	Unclear	Presentation of control intervention different; information on whether it was described as being an alternative treatment to intervention not available

Engleman 2002

Methods	Randomised crossover study comparing oral appliance and CPAP. Randomisation was stratified by severity of OSA defined by AHI of less than or equal to 15. Randomisation was conducted by blocks of 4.
Participants	12 women and 36 men completed the trial (51 were recruited). Baseline age 46 +/-9, baseline AHI 31+/-26, baseline Epworth 14 +/-4. Inclusion criteria: Age 18-70, AHI 5 or more, 2 or more symptoms of OSA including sleepiness (Epworth score of 8 or more) and driving impairment. Exclusion criteria: Patients with fewer than 4 teeth remaining in either arch, coexisting narcolepsy, periodic limb movement (more than 10 per hour), major medical illness, shift work, or residency more than 50 miles from Edinburgh.
Interventions	Participants randomised to either CPAP or one of two OA devices (occlusal and non-occlusal coverage). Duration: 4 months (2 months on each treatment).
Outcomes	AHI, subjective efficacy, symptom score, Epworth score, FOSQ, SF-36 health transition, physical and mental component scores.
Notes	Jadad score 3

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	No	OA and CPAP compared

Ferguson 1996

Methods	Randomised, prospective, crossover study. Unblinded comparison of oral appliance and nasal CPAP. Study duration 8 months
Participants	24 male and 3 female participants were recruited. Age range 25-72. Inclusion criteria AHI 15-50, patients residing in the metropolitan Vancouver area. Exclusion criteria <10 teeth in both maxillary and mandibular arches.
Interventions	After a two week wash-in period participants were randomised to either oral appliance or CPAP for 4 months. A 2 week wash-out period was followed by a second 4 month crossover treatment period.
Outcomes	AHI, Apnoea index, Total sleep time, desaturations <90%, minimum SaO2, sleep efficiency, arousals, symptom score (in-house), patient satisfaction,

Ferguson 1996 (*Continued*)

Notes	Jadad score 2	
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	No	OA and CPAP compared

Ferguson 1997

Methods	Randomised, prospective, crossover study. Unblinded comparison of oral appliance and nasal CPAP. Study duration 8 months	
Participants	19 male and 5 female participants were recruited. Age mean (SD) = 44(10.6). BMI: 32 +/-8.2; AHI 26.8 +/-11.9. Inclusion criteria AHI 15-50. Exclusion criteria <10 teeth in either maxillary or mandibular arches.	
Interventions	After a two week run-in period participants were randomised to either oral appliance or CPAP for 4 months. A 2 week wash-out period was followed by a further 4 month crossover treatment period.	
Outcomes	AHI, Apnea index, total sleep time, desaturations <90%, minimum SaO2, sleep latency, NREM, REM, arousals, Epworth sleepiness score.	
Notes	Jadad score 2	
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	No	OA and CPAP compared

Fleetham 1998

Methods	Randomised, prospective, unblinded parallel group study comparing oral appliance with nasal CPAP. Study duration 3 months
Participants	101 patients were recruited. Inclusion criteria AHI>10. 51 participants were randomised to receive CPAP and 50 were randomised to receive OA therapy. 96 men were recruited. Baseline demographics: AHI: CPAP: 37.6 +/-22.8; OA: 38.7 +/-22.2. Min SaO2: CPAP: 75.8 +/-12.7; OA: 73.6 +/-11.8. Age: CPAP: 49.0 +/-9.4; OA: 46.2 +/-11.3. ESS: CPAP: 12.8+/-4.1; OA: 11.1 +/-4.9. BMI: CPAP: 32.0 +/-5.5; OA: 31.4 +/-5.7. SAQLI: CPAP: 4.2 +/-1.1; OA: 4.2 +/-1.0.
Interventions	Participants were randomised to either oral appliance or nCPAP for a period of three months.
Outcomes	AHI, Epworth sleepiness score, minimum SaO2, Quality of life index.
Notes	Jadad score 1

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	No	OA and CPAP compared

Gotsopoulos 2002

Methods	Randomised, crossover study. Double-blind comparison of oral appliance with inactive control device. 4 week duration. Randomisation was conducted by random number generator in blocks of 4.
Participants	73 participants analysed out 85 recruited. 59 were males. Mean age: 48 +/-11. Baseline AHI: 27 +/-2; Min Sao2: 86 +/-1%. ESS: 11 Inclusion criteria: RDI >10, with symptoms of OSAS. Age >20, mandibular protrusion >3 mm. Exclusion criteria: Central SA, psychiatric disease, narcotics + sedatives, dental disease, exaggerated gag reflex.
Interventions	Active or inactive oral appliance (active device was mandibular advancement splint). 1 week wash-in period followed by 4 weeks of treatment. 1 week wash-out followed by second treatment regimen.
Outcomes	AHI, Epworth sleepiness score, Min Sa O2, Sleep architecture, snoring, multiple sleep latency test, self-reported compliance, tolerability, treatment satisfaction.
Notes	Jadad score 3

Gotsopoulos 2002 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer generated randomisation schedule
Allocation concealment?	Yes	Investigators unaware as to order of treatment group assignment
Blinding? All outcomes	Unclear	Two treatments not identical in presentation, but control treatment described as alternative treatment to participants (single-blind)

Hans 1997

Methods	Randomised parallel group study of oral appliance and minimally active oral appliance. Study duration two weeks.
Participants	24 adult volunteers were recruited. Age 51.9(12.3)Inclusion criteria RDI<30. Exclusion criteria systemic diseases other than OSAS, pregnant women, prisoners, minors, mentally disabled, edentulous, previous surgical treatments for snoring or apnoea, significant non-OSAS sleep disorders, RDI >30.
Interventions	Participants were randomised to either active oral appliance or minimally active oral appliance.
Outcomes	RDI, Epworth sleepiness score,
Notes	Jadad score 1

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	Unclear	Presentation of control intervention different; information on whether it was described as being an alternative treatment to intervention not available

Hoekema 2006

Methods	Randomised parallel group trial of CPAP and OA. Study duration: 8 weeks. Method of randomisation: not clear. Blinding: not performed.
Participants	103 participants. Local outpatient unit Inclusion criteria: >20 years; polysomnographically confirmed sleep apnoea; Exclusion criteria: Prior treatment for OSA; clearly reversible morphological airway abnormalities; endocrine dysfunction; severe cardia disease; periodic limb movement; extensive periodontal disease/tooth decay; active temporomandibular joint disease (including severe bruxism); restrictions in mouth opening or advancement of mandible; partial/complete edentulism (< 8 teeth in upper or lower jaw).
Interventions	Oral appliance versus CPAP
Outcomes	Treatment success; ESS; AHI; FOSQ; SF-36; HADS
Notes	Jadad score 3

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	'The clinical epidemiologist (BS) for the study made computer-generated randomization sequences, balancing for disease severity. The randomization sequences were used for selecting random permuted blocks with lengths of 2, 4, and 6
Allocation concealment?	Yes	'The randomization sequences were concealed and administered by Department of Oral and Maxillofacial Surgery staff. After each person's serial number and diagnosis of disease severity were provided, the treatment was disclosed. Each serial number could be provided only once.'
Blinding? All outcomes	No	OA and CPAP compared

Johnston 2002

Methods	Randomised crossover trial of oral appliance versus 'placebo' appliance. Study duration: 4-6 weeks followed by change to other appliance. Method of randomisation: toss of coin. Participants informed that two different types of oral appliance would be tested - one with proven efficacy and one without. Statistical test: paired t test
Participants	21 participants recruited from a dedicated sleep clinic. Mean age: 55.10 +/-6.87. 16 M. OSA diagnosis confirmed by home oximetry study (10 + desatu-

Johnston 2002 (*Continued*)

	rations per hour). AHI: 31.93 +/-21.18; ESS: 13.90 +/-6.90; ODI: 30.69 +/-18.82; BMI: 31.63 +/-5.94. Inclusion criteria: >/= 10 desaturations per hour Exclusion criteria: Concurrent pulmonary disease; inadequate number of sound teeth.
Interventions	Mandibular Advancement Appliance (MAA) versus placebo device
Outcomes	AHI, ODI, ESS, tolerability, compliance
Notes	Jadad score 3

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	No	Coin toss
Allocation concealment?	No	No concealment of allocation
Blinding? All outcomes	Unclear	Two treatments not identical in presentation, but control treatment described as alternative treatment to participants (single-blind)

Lam 2007

Methods	Randomised parallel group trial of CPAP versus oral appliance therapy. Study duration: 10 weeks. Method of randomisation: not specified.
Participants	68 participants with OSA (mean baseline AHI 22). Inclusion criteria: AHI >5-40 and ES >9 for those with AHI 5-20. Exclusion criteria: Excessive sleepiness, unstable medical diseases, coexistence of sleep disorders, upper airway surgery, pregnancy
Interventions	OA versus CPAP (conservative management given as a control group and not considered by this review)
Outcomes	AHI, Quality of life, sleepiness
Notes	Jadad score 2.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available

Blinding? All outcomes	No	OA versus CPAP compared

Mehta 2001

Methods	Randomised crossover trial of oral appliance and control oral plate. Study duration 3 weeks. Patients were blinded as to likely superior efficacy of the double plate appliance over the single plate.
Participants	28 adult participants were recruited. Age 48 (9), BMI 29.4(3.1), baseline AHI 27(17), min SaO2 85(8). Inclusion criteria at least 2 symptoms of OSA and AHI>10. Exclusion criteria periodontal disease, esentulism, exaggerated gag reflex, regular use of sedatives.
Interventions	Participants were randomised to three periods (ABB/BAA) of oral appliance or control plate after an acclimatization period.
Outcomes	AHI, minimum SaO2, snoring frequency,mean snoring intensity, maximum snoring intensity, total sleep time, REM, NREM, total sleep time spent supine, arousal index, sleep efficiency.
Notes	Jadad score 3

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Described as randomised; other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	Unclear	Two treatments not identical in presentation, but control treatment described as alternative treatment to participants (single-blind)

Olson 2002

Methods	Randomised crossover study. Comparison of oral appliance and nasal CPAP. Study duration 14 weeks
Participants	24 patients were included. Baseline AHI 8.1-36.9. Inclusion criteria AHI>15, or apnoea index >5, or AHI>5 and arousal index >15. Exclusion criteria poor dentition, temporomandibular joint pain, or previous treatment with oral appliances or nCPAP
Interventions	Participants were randomised to six week treatment periods of oral appliance or CPAP separated by a two week wash-out period.
Outcomes	Total sleep time, sleep efficiency, %REM sleep, AHI, Arousal index, Sleep apnoea quality of life index

Olson 2002 (*Continued*)

Notes	Jadad score 3

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	Unclear	OA versus CPAP compared

Randerath 2002

Methods	Randomised, crossover single centre trial. Comparison of CPAP with oral appliance. Study duration 12 weeks.
Participants	20 Participants with mild-moderate sleep apnoea were included in the study. 16 men; mean age: 56.5 +/-10.2; BMI: 31.2 +/-6.4; AHI: 17.5 +/-7.7. Inclusion criteria: AHI: 5-30, clinical symptoms of OSAS. Exclusion criteria: AHI >30, temporomandibular joint disorders, bruxism, participants with gaps in their teeth preventing fitting of device.
Interventions	Participants underwent 1 night polysomnography with both treatment modes, followed by 6 weeks treatment with either OA or CPAP in random order. Participants then crossed over to the other treatment.
Outcomes	AHI; Snoring (epochs/h); SaO2 (%); TST (min); Wake after sleep onset; Sleep stage 1, 2, 3, 4; REM sleep; Arousals per/h; Respiration-induced arousals, per/h of TST.
Notes	Jadad score 1

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	No	OA versus CPAP compared

Tan 2002

Methods	Randomised crossover study. Comparison of oral appliance and CPAP. Study duration 4 months
Participants	24 patients were recruited. Mean age: 50.9 +/- 10.1.Epworth sleepiness score: 13.4 +/- 4.6; AHI: 22.6 +/- 9.6; O2 desaturation: 7.1 +/- 2.7. Arousals/hr: 19.3 +/- 9.6. Three participants withdrew.
Interventions	Two months of CPAP and oral appliance in random order. Two week wash-out.
Outcomes	AHI, O2 desaturation, Epworth sleepiness score, general symptoms, daytime somnolence score, partner's assessment, duration of apnoeas, arousals/hr, sleep efficiency, REM sleep.
Notes	Jadad score 3

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Described as randomised, other information not available
Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	No	OA versus CPAP compared

Tegelberg 1999

Methods	Randomised, parallel group study. Single-blind comparison of surgery versus oral appliance. Study duration: 1 year.
Participants	95 male participants were recruited. Age: 20-65, baseline AHI: 15.7-23.3. Inclusion criteria: AHI between 5 and 25, age between 20 and 65. Exclusion criteria: Mental illness, drug misuse, significant nasal obstruction, insufficient teeth, pronounced dental malocclusion, severe cardiovascular disease, neurological disease, respiratory disease. At 4 year follow-up, OA group: N = 32, UPPP group: N = 40.
Interventions	Participants were randomised to either oral appliance or surgical intervention (uvulopalatopharyngoplasty). Participants randomised to receive UPP were followed up at regular intervals.
Outcomes	AHI, AI, oxygen desaturation index, snoring index, clinical dysfunction score, QOL scores
Notes	Jadad score: 3

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Described as randomised, other information not available

Tegelberg 1999 (*Continued*)

Allocation concealment?	Unclear	Information not available
Blinding? All outcomes	No	OA versus surgery

OSAS = Obstructive Sleep Apnoea Syndrome; AI = Apnoea Index; AHI = Apnoea Hypopnea Index; CPAP = Continuous Positive Airways Pressure; nCPAP = nasal CPAP; OA = Oral Appliance; BMI = Body Mass Index; SAQLI = Sleep Apnoea Quality of Life Index; ESS = Epworth Sleepiness Score; RDI = Respiratory Disturbance Index; ODI = Oxygen Desaturation Index; UPPP = Uvulopalatopharyngoplasty; TST = Total Sleep Time; SF-36 = Short-form 36; HADS: Hospital anxiety and depression score

Characteristics of excluded studies *[ordered by study ID]*

Athen 1999	Case series
Bloch 2000	Comparison of two types of mandibular devices
Bushell 1991	Randomised cross over which excluded OSA.
Cistulli 1998	Before and after study
Clark 1996	Non-randomised allocation to treatment groups
David 2000	Before and after study.
Dort 2003	Tongue-retaining device.
Eckhart 1998	Review article of splint characteristics
Eroshina 2001	Non-randomised before and after study.
Eveloff 1994	Before and after study

(*Continued*)

Friedman 2008	Study of surgically inserted palatal implants
Fritsch 2000	Review article
Ichioka 1995	Case series
Kato 2000	Before and after study
Lamont 1998	Non-randomised case series
Lawton 2005	Comparison of two types of mandibular devices
Liu 2000	Case series.
Lowe 2000	Before and after study
Luks 1996	Comparison of two types of mandibular devices
Marklund 1998	Non-randomised before and after study - identified from additional electronic search
Menn 1996	Non-randomised before and after study - identified from bibliography of Gotsopoulos 2002
Moore 2000	New product report, no data regarding efficacy
Neill 2002	Split night protocol
O'Sullivan 1993	Uncontrolled randomised study
O'Sullivan 1995	Uncontrolled randomised study
Ono 1996	Case control trial reporting genioglossus EMGs
Pillar 2004	Different OAs compared
Pirila-Parkkinen '99	Case controlled trial in children
Pitsis 2002	Comparison of two types of mandibular devices
Rose 2002	Comparison of two types of mandibular devices
Rose 2002b	Long-term assessment of oral appliance in non-randomised cohort study
Saletu 2007	Laboratory based short term crossover study
Schonhofer 1997	Review article
Schonhofer 1997b	Before and after study

(*Continued*)

Sjoholm 1994	Unable to determine suitability based on full text article. No reply from study investigators.
Skinner 2004	Study assessing the effects of a collar. Whilst this was a form of mandibular advancement, it was not within the scope of the review which was specifically concerned with oral appliances.
Turk 2005	Not randomised.
van der Sweep 2006	Assessment of chin straps in CPAP users.
van der Veken 2005	Comparison of two different oral devices.
Villa 2002	Randomised trial in children
Walker-Engstrom 2003	Randomised study - this was excluded as there was no placebo/inactive control. This study compared different degrees of mandibular advancement (50% versus 75%)
Winkels 1997	Non-randomised case series
Yoshida 1998	Case series

Characteristics of ongoing studies *[ordered by study ID]*

Cibele 2006

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	

Fairbairn 2004

Trial name or title	
Methods	

Fairbairn 2004 (*Continued*)

Participants	Patients with Obstructive sleep apnoea syndrome (OSAS)
Interventions	CPAP versus MAS
Outcomes	Steering simulation
Starting date	
Contact information	
Notes	

DATA AND ANALYSES

Comparison 1. Active oral appliance versus control appliance

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Epworth sleepiness score - first arm data/parallel studies	4	130	Mean Difference (IV, Fixed, 95% CI)	-2.09 [-3.80, -0.37]
2 Epworth sleepiness score - crossover studies	2	182	Epworth score (Fixed, 95% CI)	-1.81 [-2.72, -0.90]
3 Apnoea Hypopnea Index - first arm/parallel studies	5	156	Mean Difference (IV, Fixed, 95% CI)	-10.78 [-15.53, -6.03]
4 Apnoea Hypopnea Index - crossover studies	4	310	AHI/hr (Fixed, 95% CI)	-15.15 [-19.40, -10.89]
5 Arousals - first arm data/parallel studies	3	112	Mean Difference (IV, Fixed, 95% CI)	-10.66 [-16.03, -5.29]
6 Arousals - crossover studies	2	194	Arousals/hr (Fixed, 95% CI)	-10.72 [-15.05, -6.39]
7 Minimum saturation - first arm data/parallel studies	3	117	Mean Difference (IV, Fixed, 95% CI)	1.79 [-0.29, 3.87]
8 Minimum saturation - crossover studies	2	194	% (Fixed, 95% CI)	3.39 [2.25, 4.54]
9 Withdrawals - first arm/parallel studies	3	65	Odds Ratio (M-H, Fixed, 95% CI)	0.83 [0.24, 2.86]
10 Quality of life (FOSQ)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
11 Blood pressure outcomes	1		mmHg (Fixed, 95% CI)	Totals not selected
11.1 Systolic BP (24hr)	1		mmHg (Fixed, 95% CI)	Not estimable
11.2 Systolic BP (diurnal)	1		mmHg (Fixed, 95% CI)	Not estimable
11.3 Systolic BP (nocturnal)	1		mmHg (Fixed, 95% CI)	Not estimable
11.4 Diastolic BP (24hr)	1		mmHg (Fixed, 95% CI)	Not estimable
11.5 Diastolic DP (diurnal)	1		mmHg (Fixed, 95% CI)	Not estimable
11.6 Diastolic BP (nocturnal)	1		mmHg (Fixed, 95% CI)	Not estimable
11.7 Mean BP (24hr)	1		mmHg (Fixed, 95% CI)	Not estimable
11.8 Mean BP (diurnal)	1		mmHg (Fixed, 95% CI)	Not estimable
11.9 Mean BP (nocturnal)	1		mmHg (Fixed, 95% CI)	Not estimable

Comparison 2. Oral appliance versus continuous positive airways pressure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Epworth sleepiness scale - first arm data/parallel studies	3	268	Mean Difference (IV, Random, 95% CI)	0.64 [-0.57, 1.86]
2 Epworth sleepiness score - crossover studies	4	336	Epworth score (Fixed, 95% CI)	0.54 [-0.29, 1.38]

3 Apnoea Hypopnea Index - first arm data/parallel studies	4	283	Mean Difference (IV, Random, 95% CI)	9.08 [4.78, 13.38]
4 Apnoea Hypopnea Index - crossover studies	7	464	AHI/hr (Fixed, 95% CI)	7.97 [6.38, 9.56]
5 Quality of life score (SAQLI) - first arm data/parallel studies	3	192	Mean Difference (IV, Fixed, 95% CI)	-0.03 [-0.35, 0.28]
6 Quality of life - crossover studies	1		General Health score (Fixed, 95% CI)	Totals not selected
7 Functional outcomes of sleep questionnaire - crossover studies	2	256	FOSQ Units (Fixed, 95% CI)	-0.18 [-0.42, 0.07]
7.1 Total Score	2	256	FOSQ Units (Fixed, 95% CI)	-0.18 [-0.42, 0.07]
8 Short-form 36 (quality of life) - crossover studies	2		SF36 units (Fixed, 95% CI)	Totals not selected
8.1 Physical component score	1		SF36 units (Fixed, 95% CI)	Not estimable
8.2 Mental component score	1		SF36 units (Fixed, 95% CI)	Not estimable
8.3 Total score	1		SF36 units (Fixed, 95% CI)	Not estimable
9 Hospital Anxiety Depression Scale - parallel group trials	0		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 Anxiety	0		Mean Difference (IV, Fixed, 95% CI)	Not estimable
9.2 Depression	0		Mean Difference (IV, Fixed, 95% CI)	Not estimable
10 Hospital Anxiety Depression Scale - crossover studies	1		HADS Units (Fixed, 95% CI)	Totals not selected
10.1 Anxiety	1		HADS Units (Fixed, 95% CI)	Not estimable
10.2 Depression	1		HADS Units (Fixed, 95% CI)	Not estimable
11 Cognitive performance - SteerClear	1		Cows hit (Fixed, 95% CI)	Totals not selected
12 Maintenance of Wakefulness test (MWT) - crossover studies	2	256	Mins (Fixed, 95% CI)	0.69 [-1.56, 2.94]
13 Minimum saturation (%) - first arm data/parallel studies	3	189	Mean Difference (IV, Fixed, 95% CI)	4.59 [2.55, 6.64]
14 Minimum saturation - crossover studies	4	279	% (Fixed, 95% CI)	5.16 [3.25, 7.06]
15 Arousals - first arm data/parallel studies	3	189	Mean Difference (IV, Fixed, 95% CI)	5.21 [2.48, 7.94]
16 Arousals - crossover studies	6	367	Arousals/hr (Fixed, 95% CI)	2.24 [0.43, 4.05]
17 Blood pressure outcomes - crossover studies	1		mmHg (Fixed, 95% CI)	Totals not selected
17.1 Mean 24hr arterial pressure	0		mmHg (Fixed, 95% CI)	Not estimable
17.2 Mean 24hr systolic BP	1		mmHg (Fixed, 95% CI)	Not estimable
17.3 Mean 24hr diastolic BP	1		mmHg (Fixed, 95% CI)	Not estimable
17.4 Mean diurnal arterial pressure	0		mmHg (Fixed, 95% CI)	Not estimable
17.5 Mean nocturnal arterial pressure	0		mmHg (Fixed, 95% CI)	Not estimable
17.6 Mean nocturnal diastolic	1		mmHg (Fixed, 95% CI)	Not estimable
18 Blood pressure outcomes (parallel studies)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
18.1 Mean 24hr arterial pressure	0		Mean Difference (IV, Fixed, 95% CI)	Not estimable
18.2 Mean 24hr systolic BP	0		Mean Difference (IV, Fixed, 95% CI)	Not estimable

18.3 Mean 24hr diastolic BP	0		Mean Difference (IV, Fixed, 95% CI)	Not estimable
18.4 Mean morning systolic BP	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
18.5 Mean evening systolic BP	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
18.6 Mean morning diastolic BP	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
18.7 Mean evening diastolic BP	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
19 Patient Preference	4		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
20 Patient preference - treatment success in both arms	2		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
21 Withdrawals - first arm data/ parallel studies	6	411	Odds Ratio (M-H, Fixed, 95% CI)	2.05 [1.15, 3.67]
22 Side-effects by type - crossover studies	2		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
22.1 Pressure on face	1	38	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.20 [0.05, 0.85]
22.2 Pressure in mouth	1	38	Peto Odds Ratio (Peto, Fixed, 95% CI)	7.81 [0.47, 129.75]
22.3 TMJ pain	2	134	Peto Odds Ratio (Peto, Fixed, 95% CI)	18.00 [8.62, 37.57]
22.4 Removal during sleep	1	96	Peto Odds Ratio (Peto, Fixed, 95% CI)	3.50 [1.43, 8.57]
22.5 Sleep disruption	1	96	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.67 [0.28, 1.61]
22.6 Excessive salivation	1	96	Peto Odds Ratio (Peto, Fixed, 95% CI)	8.88 [2.27, 34.79]
22.7 Tooth damage	1	96	Peto Odds Ratio (Peto, Fixed, 95% CI)	7.71 [0.78, 75.97]
22.8 Leak	1	96	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.11 [0.03, 0.37]
22.9 Dry upper airway	1	96	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.12 [0.02, 0.74]
22.10 Stuffy nose	1	96	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.12 [0.03, 0.49]
22.11 Inconvenience	1	96	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.12 [0.02, 0.63]
23 Side-effects by severity - crossover studies	2		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
23.1 None	2	86	Odds Ratio (M-H, Fixed, 95% CI)	0.57 [0.24, 1.36]
23.2 Mild	2	86	Odds Ratio (M-H, Fixed, 95% CI)	5.19 [1.65, 16.30]
23.3 Moderate	2	86	Odds Ratio (M-H, Fixed, 95% CI)	1.02 [0.35, 2.95]
23.4 Severe	2	86	Odds Ratio (M-H, Fixed, 95% CI)	0.23 [0.04, 1.16]
24 Preference - treatment success in either treatment arm	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 3. Oral appliance versus surgery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Apnoea Hypopnea Index	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 6 months	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.2 1 year	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.3 4 years	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
2 Oxygen desaturation index	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 6 months	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.2 1 year	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.3 4 years	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable

3 Withdrawals/loss to follow up	1	Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 Active oral appliance versus control appliance, Outcome 1 Epworth sleepiness score - first arm data/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 1 Active oral appliance versus control appliance

Outcome: 1 Epworth sleepiness score - first arm data/parallel studies

Study or subgroup	Active appliance N	Mean(SD)	Control appliance N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Blanco 2005	8	5.1 (1.9)	7	13.6 (6.7)		11.2 %	-8.50 [-13.63, -3.37]
Gotsopoulos 2002	36	7.81 (4.78)	37	8.51 (4.72)		62.2 %	-0.70 [-2.88, 1.48]
Hans 1997	12	8.2 (4)	12	12.5 (5.7)		19.0 %	-4.30 [-8.24, -0.36]
Johnston 2002	11	13 (6.91)	7	11.43 (6.35)		7.6 %	1.57 [-4.66, 7.80]
Total (95% CI)	**67**		**63**			**100.0 %**	**-2.09 [-3.80, -0.37]**

Heterogeneity: Chi² = 10.08, df = 3 (P = 0.02); I² =70%

Test for overall effect: Z = 2.38 (P = 0.017)

Analysis 1.2. Comparison 1 Active oral appliance versus control appliance, Outcome 2 Epworth sleepiness score - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

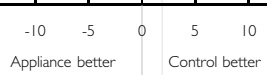
Comparison: 1 Active oral appliance versus control appliance

Outcome: 2 Epworth sleepiness score - crossover studies

Study or subgroup	Active appliance N	Control appliance N	Epworth score (SE)	Epworth score IV,Fixed,95% CI	Weight	Epworth score IV,Fixed,95% CI
Gotsopoulos 2002	73	73	-2 (0.5125)		81.9 %	-2.00 [-3.00, -1.00]
Johnston 2002	18	18	-0.94 (1.09)		18.1 %	-0.94 [-3.08, 1.20]
Total (95% CI)					**100.0 %**	**-1.81 [-2.72, -0.90]**

Heterogeneity: Chi² = 0.77, df = 1 (P = 0.38); I² =0.0%

Test for overall effect: Z = 3.90 (P = 0.000097)



Analysis 1.3. Comparison 1 Active oral appliance versus control appliance, Outcome 3 Apnoea Hypopnea Index - first arm/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 1 Active oral appliance versus control appliance

Outcome: 3 Apnoea Hypopnea Index - first arm/parallel studies

Study or subgroup	Active appliance N	Mean(SD)	Control appliance N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Blanco 2005	8	9.6 (12.1)	7	11.7 (7.9)		21.6 %	-2.10 [-12.33, 8.13]
Gotsopoulos 2002	36	13.54 (12.95)	37	24.22 (14.12)		58.5 %	-10.68 [-16.89, -4.47]
Hans 1997	12	21.1 (21.4)	12	46.8 (46.9)		2.7 %	-25.70 [-54.87, 3.47]
Johnston 2002	12	18.04 (18.08)	8	40.9 (21.21)		7.0 %	-22.86 [-40.77, -4.95]
Mehta 2001	12	11.65 (9.38)	12	29.11 (24.46)		10.3 %	-17.46 [-32.28, -2.64]
Total (95% CI)	**80**		**76**			**100.0 %**	**-10.78 [-15.53, -6.03]**

Heterogeneity: $Chi^2 = 6.30$, df = 4 (P = 0.18); $I^2 = 37\%$

Test for overall effect: Z = 4.45 (P < 0.00001)

Analysis 1.4. Comparison 1 Active oral appliance versus control appliance, Outcome 4 Apnoea Hypopnea Index - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 1 Active oral appliance versus control appliance

Outcome: 4 Apnoea Hypopnea Index - crossover studies

Study or subgroup	Active appliance N	Control appliance N	AHI/hr (SE)	AHI/hr IV,Fixed,95% CI	Weight	AHI/hr IV,Fixed,95% CI
Dum 2002	38	38	-14 (5.4439)		15.9 %	-14.00 [-24.67, -3.33]
Gotsopoulos 2002	73	73	-15 (3.71)		34.3 %	-15.00 [-22.27, -7.73]
Johnston 2002	20	20	-14.82 (5.367)		16.4 %	-14.82 [-25.34, -4.30]
Mehta 2001	24	24	-16 (3.755)		33.4 %	-16.00 [-23.36, -8.64]
Total (95% CI)					**100.0 %**	**-15.15 [-19.40, -10.89]**

Heterogeneity: Chi² = 0.10, df = 3 (P = 0.99); I² =0.0%

Test for overall effect: Z = 6.97 (P < 0.00001)

Analysis 1.5. Comparison 1 Active oral appliance versus control appliance, Outcome 5 Arousals - first arm data/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

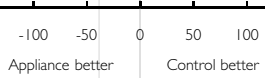
Comparison: 1 Active oral appliance versus control appliance

Outcome: 5 Arousals - first arm data/parallel studies

Study or subgroup	Active appliance N	Mean(SD)	Control appliance N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Blanco 2005	8	16 (11.5)	7	34.4 (23.8)		7.7 %	-18.40 [-37.75, 0.95]
Gotsopoulos 2002	36	26.01 (13.1)	37	34.26 (14.1)		74.1 %	-8.25 [-14.49, -2.01]
Mehta 2001	12	23.63 (8.5)	12	40.85 (20.62)		18.1 %	-17.22 [-29.84, -4.60]
Total (95% CI)	**56**		**56**			**100.0 %**	**-10.66 [-16.03, -5.29]**

Heterogeneity: Chi² = 2.23, df = 2 (P = 0.33); I² =10%

Test for overall effect: Z = 3.89 (P = 0.00010)



Analysis 1.6. Comparison 1 Active oral appliance versus control appliance, Outcome 6 Arousals - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

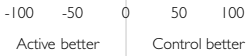
Comparison: 1 Active oral appliance versus control appliance

Outcome: 6 Arousals - crossover studies

Study or subgroup	Active appliance N	Control appliance N	Arousals/hr (SE)	Arousals/hr IV,Fixed,95% CI	Weight	Arousals/hr IV,Fixed,95% CI
Gotsopoulos 2002	73	73	-8 (2.99)		54.6 %	-8.00 [-13.86, -2.14]
Mehta 2001	24	24	-14 (3.28)		45.4 %	-14.00 [-20.43, -7.57]
Total (95% CI)					**100.0 %**	**-10.72 [-15.05, -6.39]**

Heterogeneity: Chi² = 1.83, df = 1 (P = 0.18); I² =45%

Test for overall effect: Z = 4.85 (P < 0.00001)



Analysis 1.7. Comparison 1 Active oral appliance versus control appliance, Outcome 7 Minimum saturation - first arm data/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 1 Active oral appliance versus control appliance

Outcome: 7 Minimum saturation - first arm data/parallel studies

Study or subgroup	Active appliance N	Mean(SD)	Control appliance N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Gotsopoulos 2002	36	88.11 (6.65)	37	86.7 (4.9)		60.0 %	1.41 [-1.28, 4.10]
Johnston 2002	12	77.75 (11.23)	8	76.25 (8.17)		6.0 %	1.50 [-7.01, 10.01]
Mehta 2001	12	90.67 (2.81)	12	88.17 (5.64)		34.0 %	2.50 [-1.07, 6.07]
Total (95% CI)	**60**		**57**			**100.0 %**	**1.79 [-0.29, 3.87]**

Heterogeneity: Chi² = 0.23, df = 2 (P = 0.89); I² =0.0%

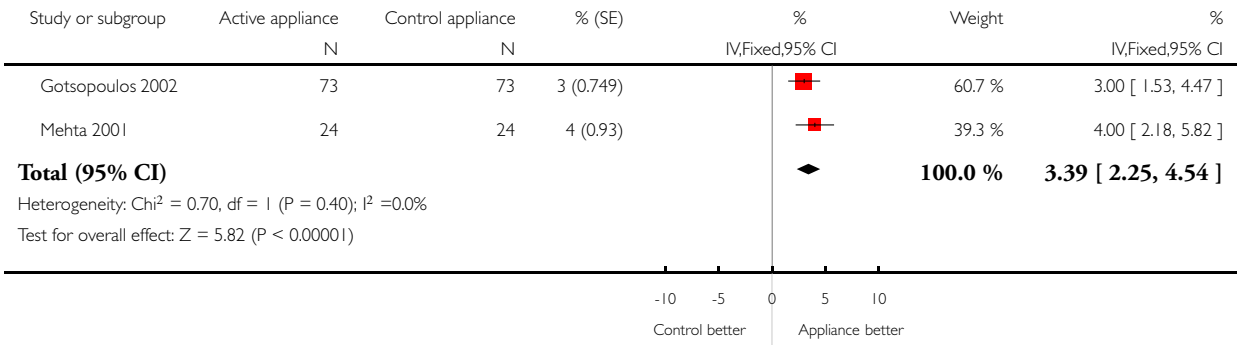
Test for overall effect: Z = 1.68 (P = 0.092)

Analysis 1.8. Comparison 1 Active oral appliance versus control appliance, Outcome 8 Minimum saturation - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 1 Active oral appliance versus control appliance

Outcome: 8 Minimum saturation - crossover studies

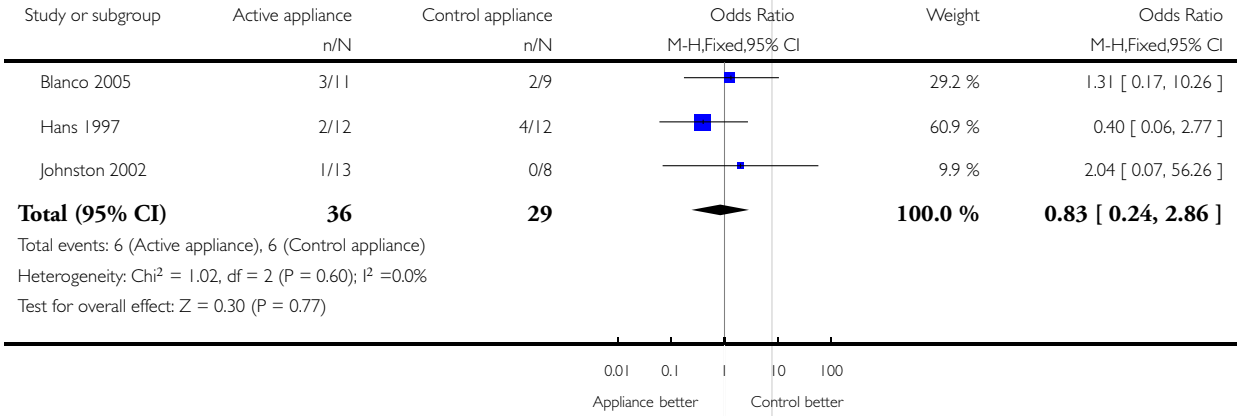


Analysis 1.9. Comparison 1 Active oral appliance versus control appliance, Outcome 9 Withdrawals - first arm/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 1 Active oral appliance versus control appliance

Outcome: 9 Withdrawals - first arm/parallel studies



Analysis 1.10. Comparison 1 Active oral appliance versus control appliance, Outcome 10 Quality of life (FOSQ).

Review: Oral appliances for obstructive sleep apnoea

Comparison: 1 Active oral appliance versus control appliance

Outcome: 10 Quality of life (FOSQ)

Study or subgroup	Active appliance N	Mean(SD)	Control appliance N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Blanco 2005	8	99.3 (14.4)	7	82.3 (13.9)		17.00 [2.66, 31.34]

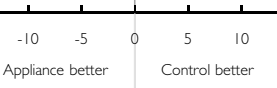
Analysis 1.11. Comparison 1 Active oral appliance versus control appliance, Outcome 11 Blood pressure outcomes.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 1 Active oral appliance versus control appliance

Outcome: 11 Blood pressure outcomes

Study or subgroup	Active appliance N	Control appliance N	mmHg (SE)	mmHg IV,Fixed,95% CI	mmHg IV,Fixed,95% CI
1 Systolic BP (24hr)					
Gotsopoulos 2002	67	67	-1.5 (0.7)		-1.50 [-2.87, -0.13]
2 Systolic BP (diurnal)					
Gotsopoulos 2002	67	67	-3 (1)		-3.00 [-4.96, -1.04]
3 Systolic BP (nocturnal)					
Gotsopoulos 2002	67	67	0.1 (1.3)		0.10 [-2.45, 2.65]
4 Diastolic BP (24hr)					
Gotsopoulos 2002	67	67	-1.6 (0.5)		-1.60 [-2.58, -0.62]
5 Diastolic DP (diurnal)					
Gotsopoulos 2002	67	67	-3.1 (0.8)		-3.10 [-4.67, -1.53]
6 Diastolic BP (nocturnal)					
Gotsopoulos 2002	67	67	-0.4 (0.9)		-0.40 [-2.16, 1.36]
7 Mean BP (24hr)					
Gotsopoulos 2002	67	67	-1.5 (0.5)		-1.50 [-2.48, -0.52]



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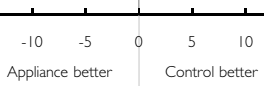
Study or subgroup	Active appliance N	Control appliance N	mmHg (SE)	mmHg IV,Fixed,95% CI	mmHg IV,Fixed,95% CI
8 Mean BP (diurnal)					
Gotsopoulos 2002	67	67	-3.2 (0.8)		-3.20 [-4.77, -1.63]
9 Mean BP (nocturnal)					
Gotsopoulos 2002	67	67	-0.3 (1)		-0.30 [-2.26, 1.66]



Analysis 2.1. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 1 Epworth sleepiness scale - first arm data/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

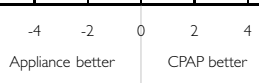
Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 1 Epworth sleepiness scale - first arm data/parallel studies

Study or subgroup	Oral appliance N	Mean(SD)	CPAP N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Fleetham 1998	50	9.3 (4.7)	51	9.5 (4.5)		45.5 %	-0.20 [-2.00, 1.60]
Hoekema 2006	49	6.9 (5.5)	50	5.9 (4.8)		35.4 %	1.00 [-1.04, 3.04]
Lam 2007	34	9 (5.83)	34	7 (5.83)		19.1 %	2.00 [-0.77, 4.77]
Total (95% CI)	**133**		**135**			**100.0 %**	**0.64 [-0.57, 1.86]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.89$, df = 2 (P = 0.39); $I^2 = 0.0\%$

Test for overall effect: Z = 1.04 (P = 0.30)

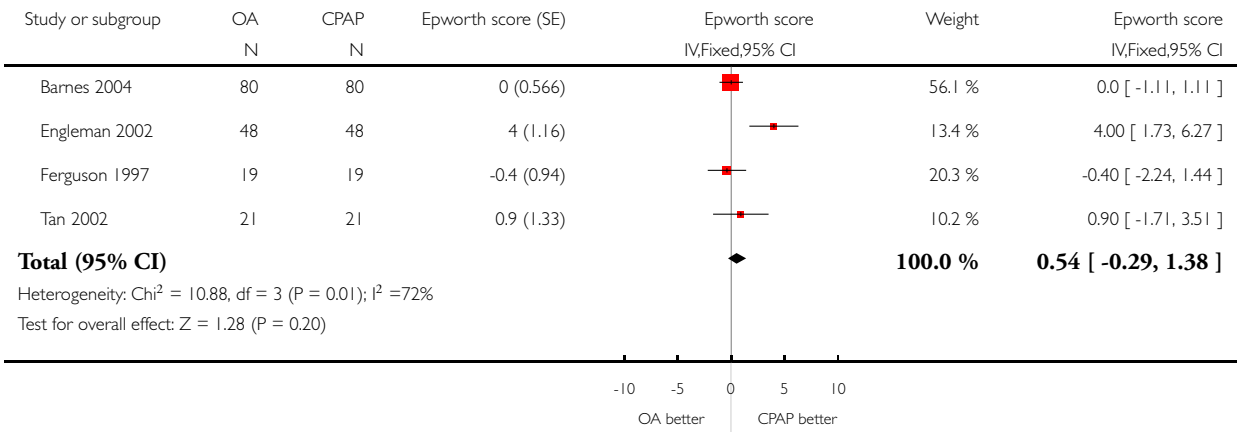


Analysis 2.2. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 2 Epworth sleepiness score - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 2 Epworth sleepiness score - crossover studies

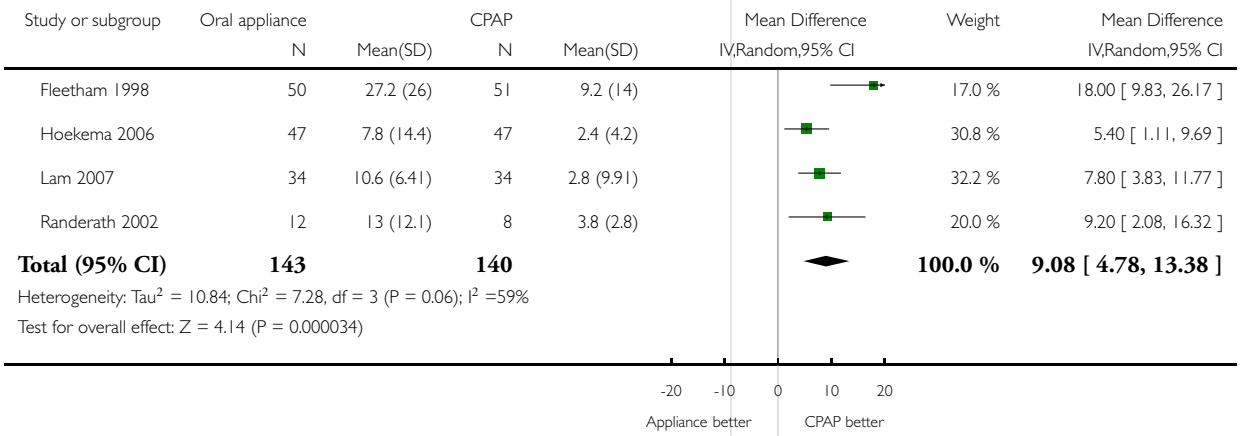


Analysis 2.3. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 3 Apnoea Hypopnea Index - first arm data/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 3 Apnoea Hypopnea Index - first arm data/parallel studies



Analysis 2.4. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 4 Apnoea Hypopnea Index - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 4 Apnoea Hypopnea Index - crossover studies

Study or subgroup	OA N	CPAP N	AHI/hr (SE)	AHI/hr IV,Fixed,95% CI	Weight	AHI/hr IV,Fixed,95% CI
Barnes 2004	80	80	9.2 (1.209)		45.0 %	9.20 [6.83, 11.57]
Engleman 2002	48	48	7 (2.06)		15.5 %	7.00 [2.96, 11.04]
Ferguson 1996	19	19	14 (4.54)		3.2 %	14.00 [5.10, 22.90]
Ferguson 1997	20	20	10 (3.72)		4.7 %	10.00 [2.71, 17.29]
Olson 2002	24	24	5.1 (2.11)		14.8 %	5.10 [0.96, 9.24]
Randerath 2002	20	20	10.6 (3.9)		4.3 %	10.60 [2.96, 18.24]
Tan 2002	21	21	4.9 (2.29)		12.5 %	4.90 [0.41, 9.39]
Total (95% CI)					**100.0 %**	**7.97 [6.38, 9.56]**

Heterogeneity: Chi² = 7.42, df = 6 (P = 0.28); I² =19%

Test for overall effect: Z = 9.83 (P < 0.00001)

Analysis 2.5. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 5 Quality of life score (SAQLI) - first arm data/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 5 Quality of life score (SAQLI) - first arm data/parallel studies

Study or subgroup	Oral appliance N	Mean(SD)	CPAP N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Fleetham 1998	50	4.7 (1.3)	51	4.8 (1.2)		41.3 %	-0.10 [-0.59, 0.39]
Lam 2007	34	5.5 (0.58)	34	5.5 (1.17)		51.1 %	0.0 [-0.44, 0.44]
Olson 2002	11	4.49 (1.32)	12	4.38 (1.45)		7.7 %	0.11 [-1.02, 1.24]
Total (95% CI)	**95**		**97**			**100.0 %**	**-0.03 [-0.35, 0.28]**

Heterogeneity: Chi² = 0.16, df = 2 (P = 0.93); I² =0.0%

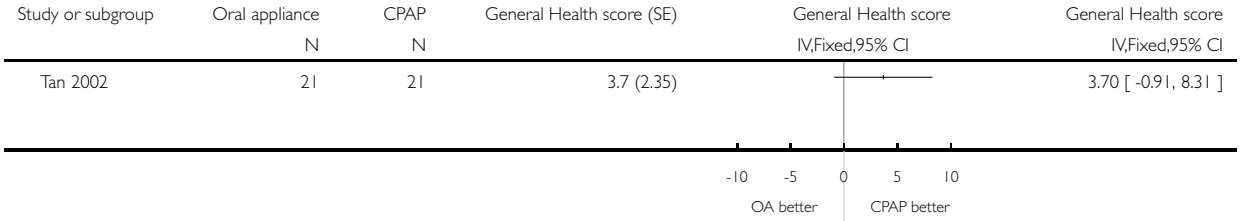
Test for overall effect: Z = 0.21 (P = 0.84)

Analysis 2.6. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 6 Quality of life - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 6 Quality of life - crossover studies

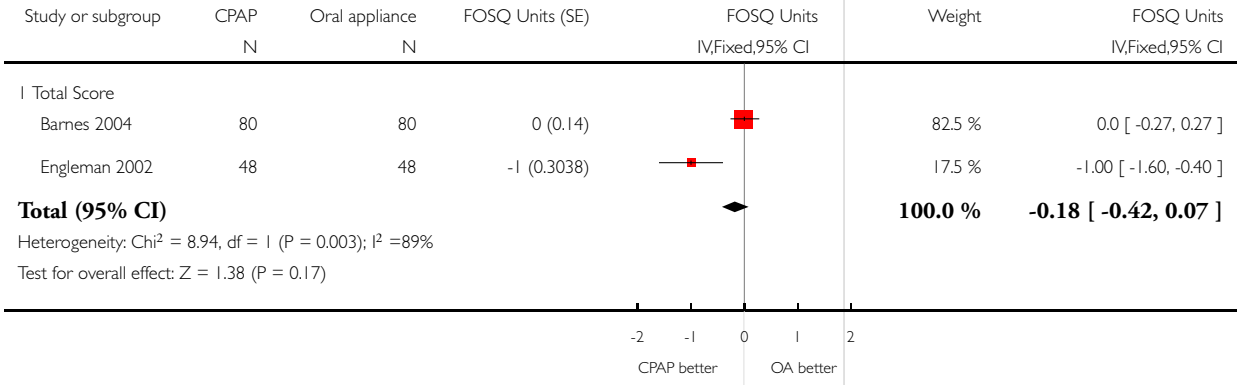


Analysis 2.7. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 7 Functional outcomes of sleep questionnaire - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 7 Functional outcomes of sleep questionnaire - crossover studies



Analysis 2.8. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 8 Short-form 36 (quality of life) - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 8 Short-form 36 (quality of life) - crossover studies

Study or subgroup	Oral appliance N	CPAP N	SF36 units (SE)	SF36 units IV,Fixed,95% CI	SF36 units IV,Fixed,95% CI
1 Physical component score					
Engleman 2002	48	48	0 (0)		0.0 [0.0, 0.0]
2 Mental component score					
Engleman 2002	48	48	0 (0)		0.0 [0.0, 0.0]
3 Total score					
Barnes 2004	80	80	-0.4 (1.6989)		-0.40 [-3.73, 2.93]

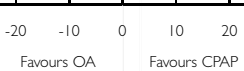
Analysis 2.10. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 10 Hospital Anxiety Depression Scale - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 10 Hospital Anxiety Depression Scale - crossover studies

Study or subgroup	CPAP N	OA N	HADS Units (SE)	HADS Units IV,Fixed,95% CI	HADS Units IV,Fixed,95% CI
1 Anxiety					
Engleman 2002	48	48	0 (8.67)		0.0 [-16.99, 16.99]
2 Depression					
Engleman 2002	48	48	1 (0.5399)		1.00 [-0.06, 2.06]



Analysis 2.11. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 11 Cognitive performance - SteerClear.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 11 Cognitive performance - SteerClear

Study or subgroup	OA N	CPAP N	Cows hit (SE)	Cows hit IV,Fixed,95% CI	Cows hit IV,Fixed,95% CI
Engleman 2002	48	48	1 (0.89)		1.00 [-0.74, 2.74]

Analysis 2.12. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 12 Maintenance of Wakefulness test (MWT) - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 12 Maintenance of Wakefulness test (MWT) - crossover studies

Study or subgroup	CPAP N	OA N	Mins (SE)	Mins IV,Fixed,95% CI	Weight	Mins IV,Fixed,95% CI
Barnes 2004	80	80	0.4 (1.27)		82.0 %	0.40 [-2.09, 2.89]
Engleman 2002	48	48	2 (2.7063)		18.0 %	2.00 [-3.30, 7.30]
Total (95% CI)					**100.0 %**	**0.69 [-1.56, 2.94]**

Heterogeneity: $Chi^2 = 0.29$, df = 1 (P = 0.59); $I^2 = 0.0\%$

Test for overall effect: Z = 0.60 (P = 0.55)

Analysis 2.13. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 13 Minimum saturation (%) - first arm data/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 13 Minimum saturation (%) - first arm data/parallel studies

Study or subgroup	CPAP N	CPAP Mean(SD)	Oral appliance N	Oral appliance Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Fleetham 1998	51	84.8 (7.7)	50	76.9 (13.2)		23.3 %	7.90 [3.67, 12.13]
Lam 2007	34	87.2 (16.91)	34	81 (9.33)		9.9 %	6.20 [-0.29, 12.69]
Randerath 2002	8	88.1 (2.3)	12	84.9 (3.4)		66.8 %	3.20 [0.70, 5.70]
Total (95% CI)	**93**		**96**			**100.0 %**	**4.59 [2.55, 6.64]**

Heterogeneity: Chi² = 3.78, df = 2 (P = 0.15); I² =47%

Test for overall effect: Z = 4.41 (P = 0.000010)

Analysis 2.14. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 14 Minimum saturation - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

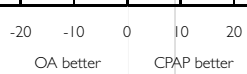
Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 14 Minimum saturation - crossover studies

Study or subgroup	Oral appliance N	CPAP N	% (SE)	% IV,Fixed,95% CI	Weight	% IV,Fixed,95% CI
Barnes 2004	80	80	4.1 (2.059)		22.3 %	4.10 [0.06, 8.14]
Ferguson 1996	19	20	4.9 (1.76)		30.5 %	4.90 [1.45, 8.35]
Ferguson 1997	20	20	11.9 (2.65)		13.4 %	11.90 [6.71, 17.09]
Randerath 2002	20	20	3.4 (1.67)		33.8 %	3.40 [0.13, 6.67]
Total (95% CI)					**100.0 %**	**5.16 [3.25, 7.06]**

Heterogeneity: Chi² = 7.87, df = 3 (P = 0.05); I² =62%

Test for overall effect: Z = 5.31 (P < 0.00001)



Analysis 2.15. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 15 Arousals - first arm data/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 15 Arousals - first arm data/parallel studies

Study or subgroup	Oral appliance N	Mean(SD)	CPAP N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Fleetham 1998	50	16.9 (13.3)	51	9 (8.6)		38.9 %	7.90 [3.52, 12.28]
Lam 2007	34	21.6 (14.58)	34	16.3 (10.5)		20.4 %	5.30 [-0.74, 11.34]
Randerath 2002	12	17.2 (4.9)	8	14.6 (4.7)		40.7 %	2.60 [-1.68, 6.88]
Total (95% CI)	**96**		**93**			**100.0 %**	**5.21 [2.48, 7.94]**

Heterogeneity: Chi² = 2.88, df = 2 (P = 0.24); I² =31%

Test for overall effect: Z = 3.74 (P = 0.00018)

Analysis 2.16. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 16 Arousals - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 16 Arousals - crossover studies

Study or subgroup	Oral appliance N	CPAP N	Arousals/hr (SE)	Arousals/hr IV,Fixed,95% CI	Weight	Arousals/hr IV,Fixed,95% CI
Barnes 2004	80	80	5.5 (2.76)		11.2 %	5.50 [0.09, 10.91]
Ferguson 1996	19	20	0.1 (4.26)		4.7 %	0.10 [-8.25, 8.45]
Ferguson 1997	19	19	2.7 (3.51)		6.9 %	2.70 [-4.18, 9.58]
Olson 2002	24	24	-0.1 (2.26)		16.7 %	-0.10 [-4.53, 4.33]
Randerath 2002	20	20	2.9 (1.61)		32.9 %	2.90 [-0.26, 6.06]
Tan 2002	21	21	1.8 (1.76)		27.5 %	1.80 [-1.65, 5.25]
Total (95% CI)					**100.0 %**	**2.24 [0.43, 4.05]**

Heterogeneity: Chi² = 2.97, df = 5 (P = 0.71); I² =0.0%

Test for overall effect: Z = 2.43 (P = 0.015)

Analysis 2.17. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 17 Blood pressure outcomes - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 17 Blood pressure outcomes - crossover studies

Study or subgroup	Oral appliance N	CPAP N	mmHg (SE)	mmHg IV,Fixed,95% CI	mmHg IV,Fixed,95% CI
1 Mean 24hr arterial pressure					
2 Mean 24hr systolic BP					
Barnes 2004	80	80	-0.6 (1.5612)		-0.60 [-3.66, 2.46]
3 Mean 24hr diastolic BP					
Barnes 2004	80	80	-0.4 (1.0612)		-0.40 [-2.48, 1.68]
4 Mean diurnal arterial pressure					
5 Mean nocturnal arterial pressure					
6 Mean nocturnal diastolic					
Barnes 2004	80	80	-2.7 (1.204)		-2.70 [-5.06, -0.34]

Analysis 2.18. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 18 Blood pressure outcomes (parallel studies).

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 18 Blood pressure outcomes (parallel studies)

Study or subgroup	OA N	Mean(SD)	CPAP N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 Mean 24hr arterial pressure						
2 Mean 24hr systolic BP						
3 Mean 24hr diastolic BP						
4 Mean morning systolic BP						
Lam 2007	34	125.9 (19.24)	34	123 (14.58)		2.90 [-5.21, 11.01]
5 Mean evening systolic BP						
Lam 2007	34	129.8 (21.57)	34	124.9 (19.83)		4.90 [-4.95, 14.75]
6 Mean morning diastolic BP						
Lam 2007	34	73.4 (11.66)	34	71.8 (12.83)		1.60 [-4.23, 7.43]
7 Mean evening diastolic BP						
Lam 2007	34	75.9 (11.66)	34	74 (12.24)		1.90 [-3.78, 7.58]

Analysis 2.19. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 19 Patient Preference.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 19 Patient Preference

Study or subgroup	Oral appliance n/N	CPAP n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Barnes 2004	24/80	35/80		0.55 [0.29, 1.06]
Engleman 2002	19/44	25/44		0.58 [0.25, 1.34]
Ferguson 1997	10/19	6/19		2.41 [0.64, 9.03]
Tan 2002	17/21	4/21		18.06 [3.87, 84.28]

Analysis 2.20. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 20 Patient preference - treatment success in both arms.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 20 Patient preference - treatment success in both arms

Study or subgroup	Oral appliance n/N	CPAP n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Ferguson 1996	6/7	1/7		36.00 [1.80, 718.68]
Ferguson 1997	7/8	1/8		49.00 [2.53, 948.62]

Analysis 2.21. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 21 Withdrawals - first arm data/parallel studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

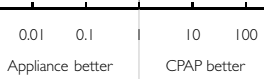
Outcome: 21 Withdrawals - first arm data/parallel studies

Study or subgroup	Oral appliance n/N	CPAP n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Engleman 2002	1/25	2/26		11.6 %	0.50 [0.04, 5.89]
Fleetham 1998	23/50	11/51		36.3 %	3.10 [1.30, 7.38]
Barnes 2004	9/34	7/34		31.7 %	1.39 [0.45, 4.29]
Randerath 2002	1/12	0/8		3.2 %	2.22 [0.08, 61.40]
Lam 2007	4/34	1/34		5.4 %	4.40 [0.47, 41.60]
Hoekema 2006	2/51	2/52		11.7 %	1.02 [0.14, 7.53]
Total (95% CI)	**206**	**205**		**100.0 %**	**2.05 [1.15, 3.67]**

Total events: 40 (Oral appliance), 23 (CPAP)

Heterogeneity: Chi^2 = 3.50, df = 5 (P = 0.62); I^2 =0.0%

Test for overall effect: Z = 2.43 (P = 0.015)

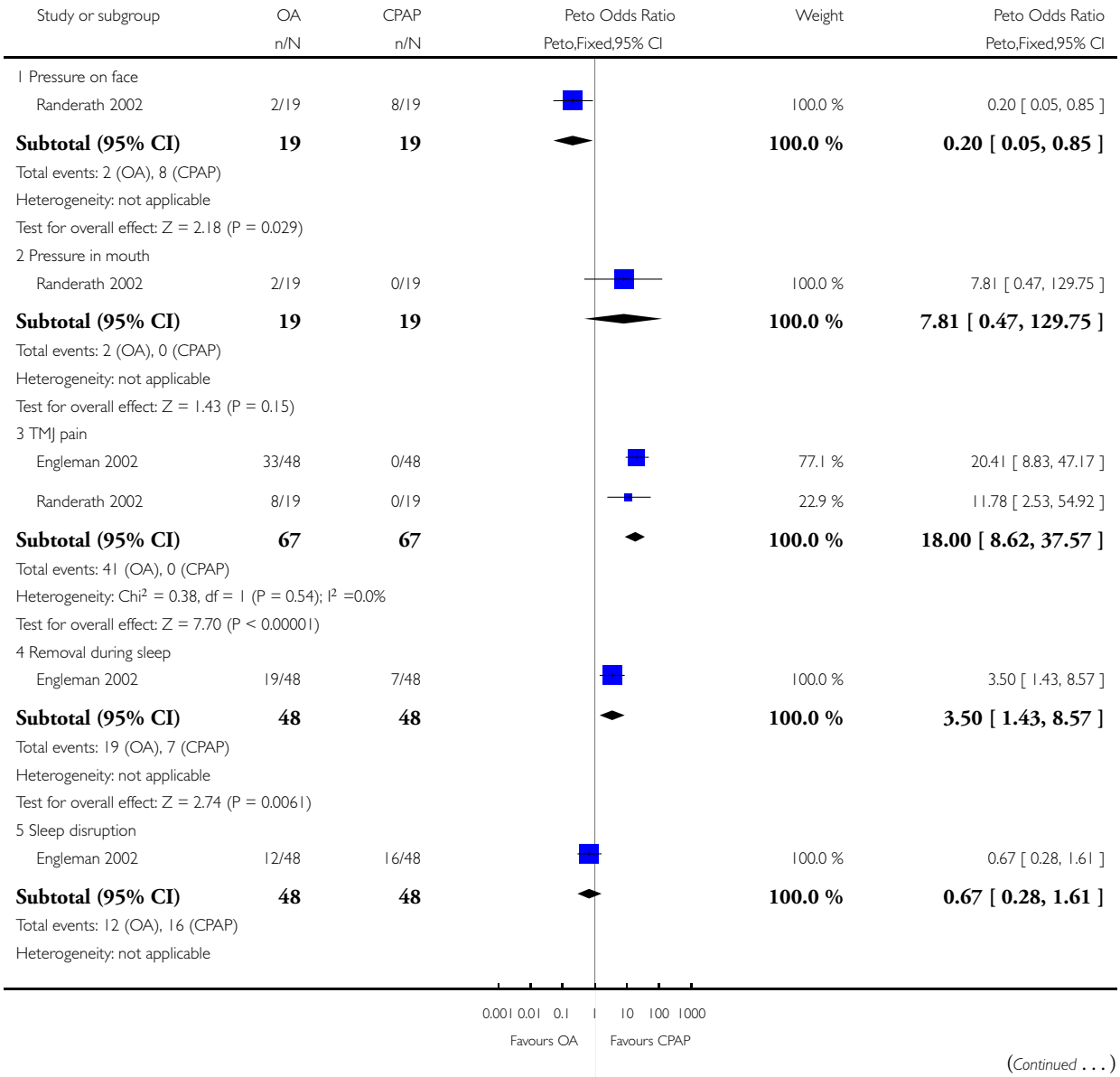


Analysis 2.22. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 22 Side-effects by type - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 22 Side-effects by type - crossover studies



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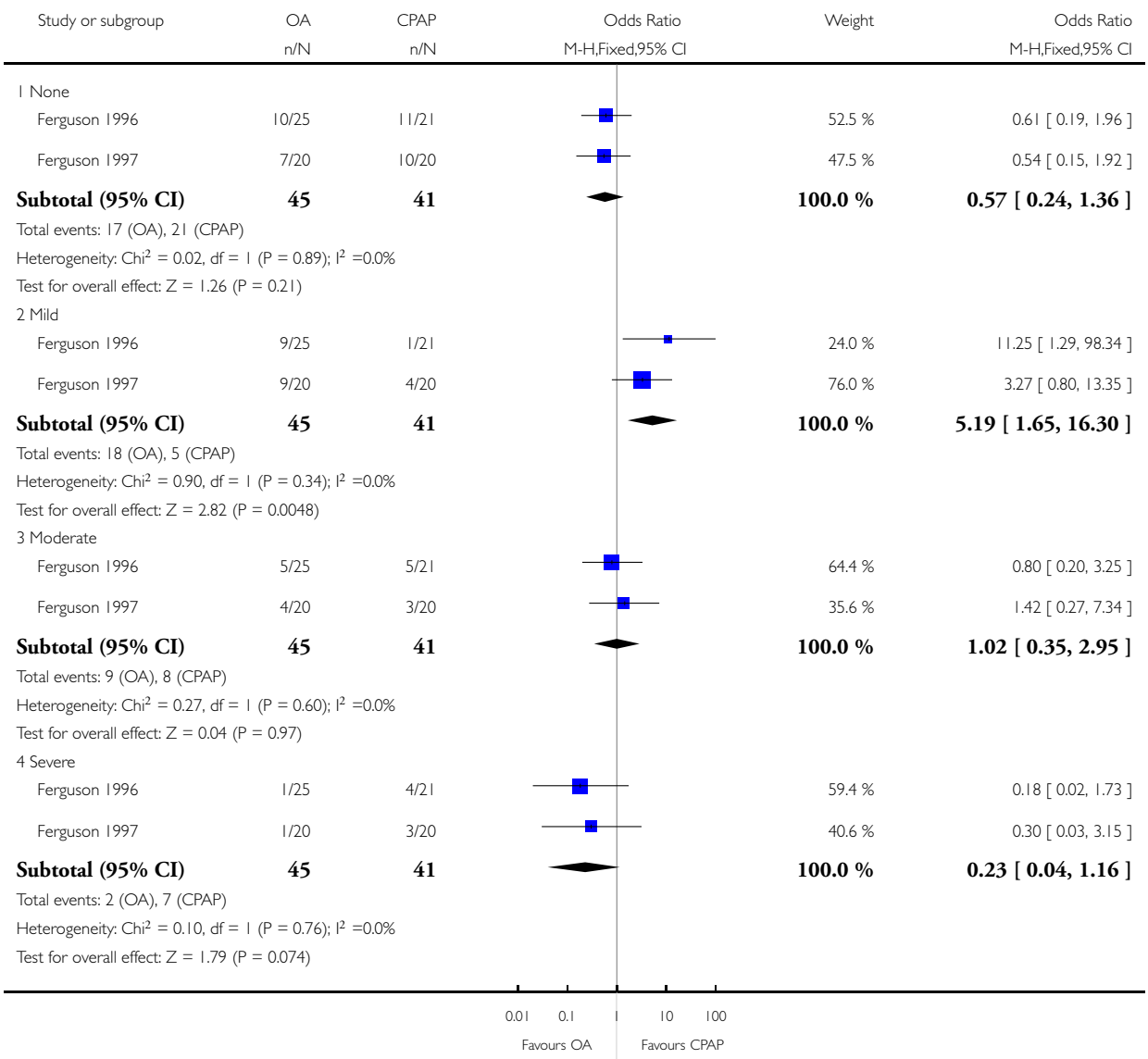
Study or subgroup	OA n/N	CPAP n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Test for overall effect: Z = 0.89 (P = 0.37)					
6 Excessive salivation					
Engleman 2002	9/48	0/48		100.0 %	8.88 [2.27, 34.79]
Subtotal (95% CI)	**48**	**48**		**100.0 %**	**8.88 [2.27, 34.79]**
Total events: 9 (OA), 0 (CPAP)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.13 (P = 0.0017)					
7 Tooth damage					
Engleman 2002	3/48	0/48		100.0 %	7.71 [0.78, 75.97]
Subtotal (95% CI)	**48**	**48**		**100.0 %**	**7.71 [0.78, 75.97]**
Total events: 3 (OA), 0 (CPAP)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.75 (P = 0.080)					
8 Leak					
Engleman 2002	0/48	11/48		100.0 %	0.11 [0.03, 0.37]
Subtotal (95% CI)	**48**	**48**		**100.0 %**	**0.11 [0.03, 0.37]**
Total events: 0 (OA), 11 (CPAP)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.51 (P = 0.00045)					
9 Dry upper airway					
Engleman 2002	0/48	5/48		100.0 %	0.12 [0.02, 0.74]
Subtotal (95% CI)	**48**	**48**		**100.0 %**	**0.12 [0.02, 0.74]**
Total events: 0 (OA), 5 (CPAP)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.28 (P = 0.022)					
10 Stuffy nose					
Engleman 2002	0/48	8/48		100.0 %	0.12 [0.03, 0.49]
Subtotal (95% CI)	**48**	**48**		**100.0 %**	**0.12 [0.03, 0.49]**
Total events: 0 (OA), 8 (CPAP)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.94 (P = 0.0033)					
11 Inconvenience					
Engleman 2002	0/48	6/48		100.0 %	0.12 [0.02, 0.63]
Subtotal (95% CI)	**48**	**48**		**100.0 %**	**0.12 [0.02, 0.63]**
Total events: 0 (OA), 6 (CPAP)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.52 (P = 0.012)					
Test for subgroup differences: Chi^2 = 113.47, df = 10 (P = 0.00), I^2 =91%					

Analysis 2.23. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 23 Side-effects by severity - crossover studies.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 23 Side-effects by severity - crossover studies



Analysis 2.24. Comparison 2 Oral appliance versus continuous positive airways pressure, Outcome 24 Preference - treatment success in either treatment arm.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 2 Oral appliance versus continuous positive airways pressure

Outcome: 24 Preference - treatment success in either treatment arm

Study or subgroup	Oral appliance n/N	CPAP n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Olson 2002	12/15	3/15		16.00 [2.67, 95.75]

Analysis 3.1. Comparison 3 Oral appliance versus surgery, Outcome 1 Apnoea Hypopnea Index.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 3 Oral appliance versus surgery

Outcome: 1 Apnoea Hypopnea Index

Study or subgroup	Oral appliance N	Mean(SD)	Surgery N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 6 months						
Tegelberg 1999	37	6.6 (8.8)	43	8.6 (7.2)		-2.00 [-5.56, 1.56]
2 1 year						
Tegelberg 1999	37	5.9 (9)	43	10.4 (9.3)		-4.50 [-8.52, -0.48]
3 4 years						
Tegelberg 1999	32	7.2 (7.2)	40	14.2 (10.3)		-7.00 [-11.05, -2.95]

Analysis 3.2. Comparison 3 Oral appliance versus surgery, Outcome 2 Oxygen desaturation index.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 3 Oral appliance versus surgery

Outcome: 2 Oxygen desaturation index

Study or subgroup	Oral appliance N	Mean(SD)	Surgery N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 6 months						
Tegelberg 1999	37	6.4 (8.5)	46	8 (8)		-1.60 [-5.18, 1.98]
2 1 year						
Tegelberg 1999	37	6.1 (9.8)	43	9.3 (9.9)		-3.20 [-7.53, 1.13]
3 4 years						
Tegelberg 1999	32	6.7 (6.8)	40	13.1 (10.7)		-6.40 [-10.47, -2.33]

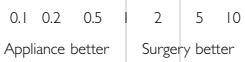
Analysis 3.3. Comparison 3 Oral appliance versus surgery, Outcome 3 Withdrawals/loss to follow up.

Review: Oral appliances for obstructive sleep apnoea

Comparison: 3 Oral appliance versus surgery

Outcome: 3 Withdrawals/loss to follow up

Study or subgroup	Oral appliance n/N	Surgery n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Tegelberg 1999	12/49	3/46		4.65 [1.22, 17.74]



WHAT'S NEW

Last assessed as up-to-date: 12 August 2008.

13 August 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 2, 2002

Review first published: Issue 4, 2003

13 August 2008	New search has been performed	Literature search run in June 2008. Additional data for an included study obtained from study investigators.
1 June 2007	New search has been performed	Literature search re-run. One new trial was identified but did not contribute data to the review (Hoekema 2006). One study published in full and previously available as a conference abstract contributed data to the comparison OA versus CPAP. This did not alter the conclusions of the review.
12 September 2005	New citation required and conclusions have changed	Three new trials met the inclusion criteria of the review (Barnes 2004; Blanco 2005; Lam 2003). The inclusion of these data had a small impact on the findings of the review. More evidence has come to light that CPAP is more effective at suppressing apnoea, although the impact on symptoms between the two treatments remains not significantly different. Some data now call in to question whether our previous observation that OAs were preferred to CPAP. It appears that this is not always so, and that there are several important psychological factors which could influence preference over a short-term trial, including perceived benefit.

CONTRIBUTIONS OF AUTHORS

JL developed the protocol with editorial input from JW. TL and JL went through search results, extracted and entered data. TL and JL developed the analysis with additional input from JF. TL , JL and JF contacted study authors and obtained unpublished data. The analysis was developed by JL and TL. JF and JL wrote and developed the discussion and conclusions. JW offered editorial support for the analysis and interpretation of the studies.

DECLARATIONS OF INTEREST

Prof John Fleetham was a trial investigator on several of the trials and has been the lead investigator in one study.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- NHS Research and Development, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

*Orthodontic Appliances; Continuous Positive Airway Pressure; Randomized Controlled Trials as Topic; Sleep Apnea, Obstructive [*therapy]

MeSH check words

Adult; Female; Humans; Male