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REVIEW ARTICLES

Factors influencing adherence to oral appliance therapy in adults with obstructive sleep apnea: a systematic review and meta-analysis

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Study Objectives: The review aimed to identify the factors influencing adherence to oral appliance therapy in adults with obstructive sleep apnea.
Methods: The protocol was initially registered with the International Register of Systematic Reviews (Prospero: CRD42019122615) prior to undertaking a comprehensive electronic search of databases and references without language and date restrictions. Quality assessment was undertaken using the Cochrane Collaboration's risk of bias tool and Quality in Prognosis Studies (QUIPS) tool.
Results: Studies exhibited low or unclear risk of bias for the domains assessed by the respective quality assessment tools. The influence of independent variables such as disease characteristics, patient characteristics, appliance features, and psychological and social factors on adherence levels was also assessed. There was a total of 31 included studies, which consisted of 8 randomized controlled trials, 2 controlled clinical trial, 7 prospective cohorts, 11 retrospective cohorts, and the remaining 3 studies were a case-series, case-control, and a mixed-methods. All 31 included studies were subject to qualitative analysis, with only 4 studies included in the quantitative analysis. Results of the meta-analysis demonstrated increased adherence with custom-made appliances, with a pooled mean difference of −1.34 (−2.02 to −0.66) and low levels of heterogeneity ($I^2 = 0\%$).
Conclusions: A weak relationship was observed between objective adherence and patient and disease characteristics, such as age, sex, obesity, apnea-hypopnea index, and daytime sleepiness, to oral appliance therapy. Nonadherent patients reported more side effects with oral appliance therapy than users and tended to discontinue the treatment within the first 3 months. Custom-made oral appliances were preferred and increased adherence reported in comparison to ready-made appliances. Further research is imperative to examine the relationship between psychosocial factors and adherence to oral appliance therapy.
Keywords: obstructive sleep apnea, patient adherence, oral appliance therapy, dental sleep medicine
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INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by the repeated episodic collapse of the upper airway during sleep, with resultant sleep deprivation.[1] Severe long-term effects of this disease include excessive daytime sleepiness, cognitive dysfunction, hypertension, impaired quality of life, and increased cardiovascular morbidity and mortality.[2]

Based on the severity of OSA there are 2 main treatment modalities, continuous positive airway pressure (CPAP) and oral appliances (OA)[3]. Both treatments are lifelong, with sustained adherence to treatment of paramount importance. Successful treatment may lead to improvements in quality of life, considerable cost saving to the health provider, and a reduction in the risk of motor vehicle collisions and cardiovascular disease.[4]

CPAP is mainly used for those with moderate to severe OSA and highly effective and regarded as the gold standard of treatment.[5] However, side effects such as pressure sores, mask dislodgement, claustrophobia, air leakage, and nasal congestion have made it unpopular and intolerable among patients. According to a recent update of the American Academy of Sleep Medicine guidelines, OA therapy (OAT) can be prescribed to

those with mild to moderate OSA, particularly if they express it as a preference. OAT remains the second-line treatment of choice for patients who refuse or are unable to tolerate CPAP therapy.[6]

OAT reduces daytime sleepiness and improves the apnea-hypopnea index (AHI) by posturing the mandible and maintaining an open pharyngeal airway.[7] However, studies have consistently demonstrated that CPAP is more effective than OAT at reducing sleep-disordered breathing and achieving complete control of OSA.[8] Despite the greater effect of CPAP on objective polysomnographic parameters, it does not appear to be more effective at achieving better health outcomes. It seems that the higher efficacy of CPAP is offset by greater OAT adherence. Adherence with CPAP is reportedly over 1 h/night lower than with OA.[9] This discrepancy may explain why, despite the superior efficacy of CPAP, as determined by the AHI, no significant differences were observed in terms of quality of life and cognitive and functional outcomes.[10]

The short-term efficacy of OAT has been studied in many randomized controlled trials (RCTs), with encouraging results in all age groups.[11–15] However, long-term studies report an unchanged or only minor decrease in the efficacy of OAT.[16–20] Rose et al[19] observed an increase in the mean AHI, from 4.2 to 8.3 events/h after 2 years of OAT. Deterioration in OSA severity

Figure 1—A PRISMA flow diagram shows the number of articles identified at each stage of the search.
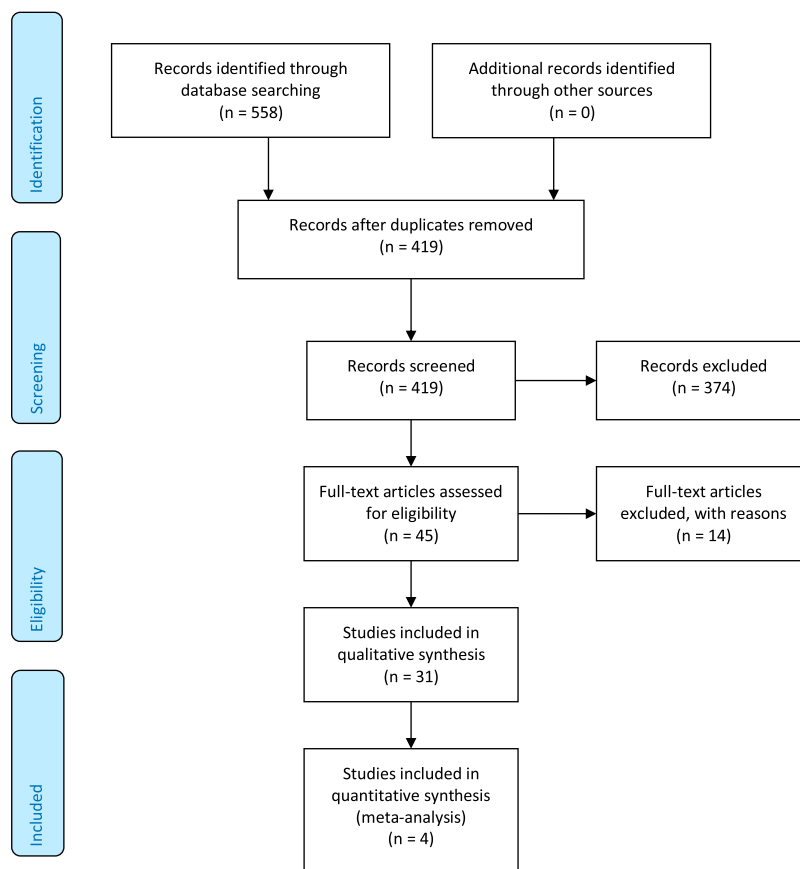
and a loss of OA efficacy were found in a small sample of patients (n = 9) treated continuously for more than 15 years.[21] However, OAT was reported to be effective in two-thirds of patients (n = 279) after 3 years of treatment.[22] Despite the limited number of long-term studies, no significant changes appear to have been detected in the efficacy of OAT.[17,18,20] Notwithstanding this, a decrease in blood pressure is reported from OAT compared with a placebo and equivalent to that of CPAP in the relatively small samples studied.[24–27]

Adherence with OAT has until recently been limited to self-reported data, with the inherent risks of overreporting. Based on this subjective reporting, adherence with OA therapy appears to decline over time, Hoffstein et al reported a wide range of adherence (4–76%) in the first year of appliance use[23]. In a further study, adherence after 1 year was 83%[24] declining to 62–64% after 4 to 6 years.[25,26] The ability to assess adherence objectively provides a more valid measure of a treatment modality's effectiveness. With CPAP therapy, the presence of an inbuilt adherence monitor has provided valuable insight into the limitations of self-reported use, with patients overestimating by up to 1 hour.[27] More recently, Vanderveken et al[28] and Johal et al[29] reported on the safety and feasibility, at 3 and 18 months, respectively, of objective measurement techniques with OAT in the same cohort of patients who demonstrated a range of sleep-disordered breathing from snoring to OSA.

Thus, the current review aims to assess the factors influencing adherence to OAT in adults with obstructive sleep apnea and the potential effectiveness of interventions to promote improved adherence.

METHODS

Following the registration of the protocol with the International Register of Systematic Review (Prospero: CRD42019122615), a systematic review of the literature was undertaken to identify studies exploring the factors influencing adherence to oral appliance therapy in patients. The search strategy was designed to access both published and unpublished materials and comprised three stages:

1. A search of MEDLINE Ovid and Embase to identify relevant keywords contained in the title, abstract, and subject descriptors.
2. Terms identified in this way and the synonyms used by respective databases were then used in an extensive search of the literature.
3. Reference lists and bibliographies of the articles collected from those identified in stage 2 were searched.

The initial search terms were "obstructive sleep apnea", "oral appliance", and "patient adherence" and "compliance." Articles indexed in the following database with no restrictions in relation to the date of publication and language of the article were searched: Ovid, Embase, Scopus, Cochrane Library, and Web of Science. Primary authors and experts in the field of sleep

Table 1—Characteristics and principal outcomes of the included studies.

Sr. No.	Study	Study Design	Participants & Settings	Exposure (Patient or Disease Characteristics, Type of Appliance, Psychological or Social Factor)	Outcome (Increased/Decreased or No effect on Adherence)	Appliance	Measurement of Adherence	Intervention for Adherence
1	Clark et al, 2000[57]	Retrospective observational study	Orofacial Pain & Oral medicine, University of California (n = 53, M/F: 46/7, Mean age: 55.7 y, Mean AHI < 30 events/h	Side effects	Decreased adherence	Herbst Appliance	Self-reported	Nil
2	McGown et al, 2001[52]	Retrospective observational study	Middlesex Hospital, RNTNE Hospital, RLH (n = 126, Mean AHI < 30 events/h)	Patient Characteristics	No association with adherence	Modified Adjustable Silensor and Herbst Device	Self-reported	Nil
				Side effects	Decreased adherence			
				Psychological (Self-perceived changes) and Social factors	Increased adherence			
3	Rose et al, 2002[53]	Retrospective observational study	Respiratory Care, University Hospital of Frieburg, Germany (n = 188, M/F: 168/23, Mean age: 54.4 y)	Patient & Disease Characteristics	No association with adherence	Custom-made OA (Esmarch IPG)	Self-reported	Nil
				Side effects	Decreased adherence			
				Psychological (Self-perceived Changes)	Decreased adherence			
4	De Almeida et al, 2005[26]	Retrospective observational study	University of British Columbia, Canada (n = 544, M/F: 202/49, Mean age: 49.9 y, Mean AHI: 30.25 events/h)	Patient & Disease characteristics	No association with adherence	Oral Appliance	Self-reported	Nil
				Side effects	Decreased adherence			
				Social factors (Bed partners satisfaction)*	Increased adherence			
5	Izci et al, 2005[51]	Retrospective observational study	Department of Sleep Medicine, Edinburgh University (n = 144, M/F: 114/30, Mean age: 51 y, Mean AHI: 24 events/h)	Patient characteristics	No association with adherence	Mandibular Repositioning Splint	Self-reported	Nil
				Psychological factors (Marital Satisfaction)**	Increased adherence			
				Side effects	Decreased adherence			
6	Bates et al, 2006[56]	Prospective observational study	Department of Orthodontics, Victoria Hospital (n = 121, M/F: 83/38, Mean age: 49.55 y, Mean AHI: 18.21 events/h)	Side effects	Decreased adherence	Mandibular Repositioning Splint	Self-reported	Nil
7	Vanderveken et al, 2008[41]	Randomized Control trial	University of Antwerp, Belgium (n = 35, M/F: 29/6, Mean age: 49 y, Mean AHI: 14 events/h)	Appliance fabrication and titration procedure (Ready-made OA vs Custom-made OA)	Increased adherence with Custom-made OA	Ready-made OA (SnoreGuard Plus) and Custom-made OA	Self-reported	Nil

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Table 1—Characteristics and principal outcomes of the included studies. (continued)

Sr. No.	Study	Study Design	Participants & Settings	Exposure (Patient or Disease Characteristics, Type of Appliance, Psychological or Social Factor)	Outcome (Increased/ Decreased or No effect on Adherence)	Appliance	Measurement of Adherence	Intervention for Adherence
8	Ghazal et al, 2009[20]	Randomized Control trial	Respiratory Care, University Hospital of Freinburg, Germany (n = 103, M/F: 48/55, Mean age: 50.5 y, Mean AHI: 34.5 events/h)	Patient & Disease characteristics	No association with adherence	IST and Thornton Anterior Positioner (TAP)	Self-reported	Nil
				Appliance Fabrication (IST vs TAP)	Increased adherence with IST			
9	Tsuda et al, 2010[49]	Prospective observational study	Kyushu Dental University, Japan (n = 47, M/F: 40/7, Mean age: 53.1 y, Mean AHI: 21.3 events/h)	Patient & Disease Characteristics (BMI and ESS)	Decreased adherence in association with higher ESS and BMI	Boil- Bite Appliance (TheraSnore)	Self-reported	Nil
				Side effects	Decreased adherence			
10	Cunali et al, 2011[32]	Randomized Control trial	Federal University of Sao Paulo, Brazil (n = 29, M/F: 10/19, Mean age: 48.5 y, Mean AHI: 17 events/h)	Intervention-Support Therapy	Increased adherence	OA (Brazilian Repositioning device BRD)	Self-reported	Support Therapy (Mandibular Exercises)
11	Brette et al, 2012[46]	Prospective observational study	Antoine-Beclere & Argenteuil Hospitals (n = 140, M/F: 108/32, Mean age: 62 y, Mean AHI: 27 events/h)	Patient & Disease Characteristics	Decreased adherence	Custom-made adjustable device (OPM4 J device)	Self-reported	Nil
				Social Support	Decreased adherence			
				Appliance characteristics	Decreased adherence			
12	Freidman et al, 2012[55]	Case series	Advanced Centre for Specialty Care, Chicago (n = 180, M/F: 130/50, Mean age: 61.5 y, Mean AHI: 33.9 events/h)	Side effects	Decreased adherence	Ready-made OA (SomnoGuard AP) and Custom-made OA (Thornton Adjustable Positioner TAP 3)	Self-reported	Nil
				Appliance Fabrication (Ready-made OA vs Custom-made OA)	Increased adherence with Custom-made OA			
13	Zhou et al, 2012[39]	Randomized Control trial	Department of Orthodontics, Tongji University (n = 16, M/F: 13/3, Mean age: 45.23 y, Mean AHI: 38 events/h)	Appliance fabrication and titration procedure (Monobloc OA vs two-piece OA)	Increased adherence with Monobloc OA	Monobloc OA (Activator) and Bibloc OA (Silent Nite)	Self-reported	Nil
14	Dieltjens et al, 2013[54]	Case-control study	University of Antwerp, Belgium (n = 82, M/F: 56/26, Mean age: 49.5 y, Mean AHI: 18 events/h)	Psychological factors (Type D personality)	Decreased adherence	Custom-made Mono Bloc OA and Custom-made Bibloc titratable OA (RespiDent Butterfly)	Self-reported	Nil

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Table 1—Characteristics and principal outcomes of the included studies. (continued)

Sr. No.	Study	Study Design	Participants & Settings	Exposure (Patient or Disease Characteristics, Type of Appliance, Psychological or Social Factor)	Outcome (Increased/ Decreased or No effect on Adherence)	Appliance	Measurement of Adherence	Intervention for Adherence
15	Ingman et al, 2013[48]	Retrospective observational study	Department of Oral & Maxillofacial Diseases, Helsinki University Hospital (n = 96, M/F: 68/28, Mean age: 50.5 y, Mean AHI: 18.4 events/h)	Patient characteristics (length of the maxilla, mandible and soft palate, oropharyngeal space, crepitation at TMJ)	Increased adherence with shorter mesio-distal length of the maxilla and mandible, and crepitation at right TMJ	Mandibular Advancement Splint	Self-reported	Nil
16	Lee at al, 2013[35]	Nonrandomized control trial	Department of Otorhinolaryngology, Seoul National University (n = 153, M/F: 138/15, Mean age: 51.2 y, Mean AHI: 32.8 events/h)	Appliance fabrication and titration procedure (Monobloc OA vs Bibloc OA)	Increased adherence with Bibloc OA	Monobloc and Bibloc OA	Self-reported	Nil
17	Quinnell et al, 2014[37]	Randomized Control trial	Papworth Hospital Sleep Centre, (n = 90, M/F: 72/81, Mean age: 50.9 y, Mean AHI: 13.8 events/h)	Appliance fabrication (Boil-Bite vs Semibespoke vs Be-spoke)	Increased adherence with the Be-spoke oral appliance	Boil-bite OA (Sleep pro 1), Semibespoke OA (Sleep pro 2), and Bespoke OA	Self-reported	Nil
18	Wang et al, 2014[38]	Randomized Control trial	Dept. of Otorhinology, Hospital of Anhui Medical University (n = 22, M/F: 22/0, Mean age: 51.9 y, Mean AHI: 48.16 events/h)	Appliance Type (Adjustable OA vs Nonadjustable OA)	Increased adherence with the adjustable OA	Rod Type OA (Erkodent Silensor) and Controllable appliance (Twin Bloc)	Self-reported	Nil
19	Dieltjens et al, 2015[33]	Prospective observational study	Antwerp University Hospital, Belgium (n = 51, M/F: 38/13, Mean age: 49.3 y, Mean AHI: 14.9/h, Mean AHI: 18.4 events/h)	Patient (Anthropometric) & Disease characteristics (Polysomnographic measure)	No association with adherence	Custom-made titratable OA (RespiDent Butterfly)	Objective (Theramon Sensors)	Nil
				Side effects	Decreased adherence			
20	Prescinotto et al, 2015[44]	Retrospective observational study	Federal University of Sao Paulo, Brazil (n = 28, M/F: 9/19, Mean age: 48.8 y, Mean AHI; 17.5 events/h)	Patient characteristics (upper airway abnormalities)	No association with adherence	Custom-made OA	Self-reported	Nil
21	Attali et al, 2016[22]	Prospective observational study	Pitié-Salpétrière, France (n = 279, M/F: 98/81, Mean age: 58 y, Mean AHI: 26 events/h)	Appliance factors	Decreased adherence	Ready-made OA (Naval Resmed) and Custom-made OA (Somnodent SomnoMed)	Self-reported	Nil
				Side effects	Decreased adherence			
				Psychological factors	Decreased adherence			
22	Carballo et al, 2016[42]	Retrospective observational study	Veterans Affairs Medical Centre, Brazil (n = 33, M/F: 32/1, Mean age: 71.4 y)	Psychological and social factors	No association with Adherence	Oral Appliance	Self-reported	Nil
23	Makihara et al, 2016[58]	Retrospective observational study	Kyushu Dental University, Japan (n = 48, M/F: 35/13, Mean age: 64.9 y)	Side effects	Decreased adherence	Boil-Bite Appliance (TheraSnore)	Self-reported	Nil
				Psychological factors	Decreased adherence			

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Table 1—Characteristics and principal outcomes of the included studies. (continued)

Sr. No.	Study	Study Design	Participants & Settings	Exposure (Patient or Disease Characteristics, Type of Appliance, Psychological or Social Factor)	Outcome (Increased/ Decreased or No effect on Adherence)	Appliance	Measurement of Adherence	Intervention for Adherence
24	Nerfeldt et al, 2016[43]	Prospective intervention study	Department of Clinical Science, Karolinska Institute Stockholm, Sweden (n = 66, M/F: 37/35, Mean Age: 48.5 y, Mean AHI: 16 events/h)	Disease Characteristics (Arousers vs Desaturaters)	Increased adherence in arousers	Monobloc titratable OA	Self-reported	Nil
25	Vecchierini et al, 2016[50]	Prospective intervention study	Multicenter (n = 369, M/F: 273/96, Mean age: 52.6 y, Mean AHI: 29.5 events/h)	Side effects	Decreased adherence in the early stages of the treatment	Custom-made OA (Narval)	Self-reported	Nil
26	Al-Dharrab et al, 2017[36]	Randomized Control trial	Faculty of Dentistry, King Abdul-Aziz University (n = 12, M/F: 2/10, Mean age: 46 y, Mean AHI: 26 events/h)	Appliance fabrication and titration procedure (Titratable vs Nontitratable)	Increased adherence with Titratable appliance	Custom-made titratable OA (Foresta Dent, Bite Jumping screw) and nontitratable OA	Self-reported	Nil
27	Gagnadoux et al, 2017[34]	Nonrandomized control trial	University of Angers and Saint-Antoine Hospital, France (n = 158, M/F: 104/54, Mean age: 54 y, Mean AHI: 27.7 events/h)	Appliance fabrication and titration procedure (Ready-made OA vs Custom-made OA)	Increased adherence with Custom-made OA	Ready-made OA (BluePro) and Custom-made OA (Somnodent and Amo Device)	Self-reported	Nil
28	Haviv et al, 2017[59]	Mixed-methods	Department of Oral Medicine, Hebrew University (n = 52, M/F: 48/4, Mean age: 56.75 y, Mean AHI ≤ 40 events/h)	Side effects	Decreased adherence	Herbst Device	Self-reported	Nil
				Psychological factors	Decreased adherence			
29	Johal et al, 2017[40]	Randomized Control trial	Royal London Dental Hospital, Queen Mary University of London, (n = 35, M/F: 21/14, Mean age: 44.9 y, Mean AHI: 13.3 events/h)	Appliance fabrication and titration procedure (Ready-made OA vs Custom-made OA)	Increased adherence with Custom-made OA	Ready-made OA (Snoreshield) and Custom-made OA	Self-reported	Nil
30	Nishigawa et al, 2017[47]	Retrospective observational study	Department of General Dentistry, Tokushima University Hospital Japan (n = 40, M/F: 28/12, Mean age: 57.8 y)	Side effects	Decreased adherence	Herbst Appliance	Self-reported	Nil
				Psychological factors	Decreased adherence			
31	Saglam-Aydinatay et al, 2018[45]	Retrospective observational study	Department of Orthodontics, Hacettepe University, Ankara, Turkey (n = 69, M/F: 52/17, Mean age: 54.4 y, Mean AHI < 30 events/h)	Patient & Disease Characteristics	No association with adherence	Monobloc OA and Twin-bloc OA	Self-reported	Nil
				Side effects	Decreased adherence			
				Psychological (Self-perceived changes) and social factors	Increased adherence			

*Improvement reported by the partner in the patient's snoring. ** Marital quality and bed sharing. AHI = apnea-hypopnea index, BMI = body mass index, F = female, M = male, OA = oral appliance, TAP = Thornton anterior positioner.

Table 2—Factors of influence on oral appliance adherence.

Factors	Decreased Adherence	Increased Adherence	No Significant Association with Adherence	Caveat
Patient and disease characteristics			Anthropometric characteristics (age, sex, obesity)	
			Disease severity	
			Baseline sleepiness	
			Polysomnographic parameters	
			Anatomical characteristics (length of the maxilla, mandible and soft palate, oropharyngeal space, crepitation at TMJ)	
			Upper airway or facial skeletal abnormalities	
	Desaturaters (patients with oxygen desaturations)	Arousers (patients with respiratory arousals)		Significant improvement in the ESS among the arousers
		OA therapy as the first line of treatment		Strong predictor for treatment continuation
		Complete symptom resolution		Contributes to the perception of OSA but not a strong predictor alone
Appliance fabrication and titration	Monobloc OA	Bi-Bloc OA		Relatively free mandibular movement
	Ready-made (Nontitratable) OA	Custom-made (Titratable) OA		More reported side-effects with ready-made as compared to custom-made
	Patients not using the OA for > 2 years			More likely to discontinue the treatment
		Regular dental follow-up		Helps in minimizing early side-effects which lead to early discontinuation of the treatment
Psychological and social factors	Lack of perceived benefits			Leads to early discontinuation of the treatment, consistent factor
		Support from their bed partners		Improved sleep quality of the bed partner with OA use is associated with increased adherence

ESS = Epworth Sleepiness Scale, OA = oral appliance, TMJ = temporomandibular joint.

and respiratory medicine were contacted. The additional literature search included Google Scholar to identify any other relevant published work. An example of the search strategy used is shown in **Table S1** in the supplemental material.

The title and abstracts of the studies identified were assessed independently by 2 reviewers (H.T., A.J.) and were included or excluded based on the following PEO criteria:

1. Population: Adults with OSA receiving oral appliance therapy
2. Exposure of interest: Disease characteristics, patient characteristics, appliance features, and psychological and social factors
3. Outcome: Adherence
4. Study design: Prognostic studies both retrospective or prospective observational in nature and randomized or nonrandomized controlled trials

5. Exclusions: Studies comparing CPAP or surgical intervention with oral appliance therapy were excluded

The first 2 reviewers (H.T., A.J.) obtained full-text reports of studies meeting the selection criteria for screening, and any disagreement was resolved by consulting a third reviewer to reach a consensus (T.N.).

Risk of bias and quality assessment in individual studies

Two authors independently assessed the risk of bias of the included studies (H.T., A.J.; **Figure 1**, and any disagreements were resolved by further discussion and consensus. Due to the diversity in the design of the included studies, 2 different tools were used to assess their quality. RCTs were assessed using the Cochrane Collaboration's risk of

bias tool.[30] The following 5 domains were considered: random sequence generation, allocation concealment, blinding of outcome assessors, incomplete outcome data, and selective reporting. The domain blinding of participants and personnel was not considered due to the nature of the questions addressed by this review. Observational studies were critically appraised using the Quality in Prognosis Studies (QUIPS) tool.[31] This tool assesses the risk of bias in studies of prognostic factors and comprises 6 domains: study participation, study attrition, prognostic factor management, outcome measurement, study confounding, and statistical analysis and reporting.

Data items and collection

The influence of independent variables such as disease characteristics, patient characteristics, appliance features, and psychological and social factors on the outcome, ie, adherence, reported in the included studies was recorded and categorized based on these factors. The findings of the studies were synthesized in a narrative manner. Information regarding study design, sample size, participants and settings, type of oral appliance used, strategies or interventions employed to increase adherence, and method of adherence measurement (objective or self-reported) were recorded (**Table 1** and **Table 2**).

Meta-analysis

A meta-analysis was performed using Review Manager (RevMan; Version 5.3. Copenhagen, The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) for studies with low and/or unclear risk of bias, similar study design, and comparing 2 types (ready-made vs custom-made) oral appliances prescribed for patients with OSA in regards to patient adherence. Results were analyzed using forest plots with weighted mean differences between ready-made vs custom-made appliances in relation to patient adherence, ie, mean nightly (hours) use of the appliance. The studies were weighted using the inverse variance method and tested for heterogeneity using the Chi square test to assess the significance of heterogeneity and I^2 statistics to measure the diversity between studies. Pooled studies with $I^2 < 25\%$ were regarded as homogenous, and those with $I^2 > 75\%$ were considered to demonstrate high heterogeneity. A fixed-effects model was used and a P value of less than .05 was considered statistically significant, reported along with the 95% confidence interval.

RESULTS

Following the removal of duplicates, 419 articles were considered eligible for screening of the title and abstract. The abstracts were assessed against the selection criteria, with 45 articles considered eligible for full-text screening. Subsequently, fourteen studies were excluded (**Table S2**), with a total of 31 studies included in the review, which consisted of 8 RCTs, 2 controlled clinical trials, 7 prospective cohorts, 11 retrospective cohorts, while the remaining 3 studies were a case-series, case-control, and a mixed-methods study (**Figure 2**). All

Figure 2—Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

31 included studies were subject to qualitative analysis, with 4 studies subject to a meta-analysis. All included studies were undertaken in academic medical centers or sleep centers (**Table S3**).

The majority of the included studies investigated the influence of side effects (45%), disease and patient characteristics (41%), and appliance characteristics (32%) on patient adherence. The efficacy of strategies or interventions to increase patient adherence to OAT in adult patients with OSA was assessed in only a single study.[32] While a self-reported measure of adherence was used in the majority of included studies, objective monitoring of adherence was reported in just 1 study.[33] Studies that considered psychological and social factors (38%) focused on the impact of constructs, such as bed-partner satisfaction levels (improvement reported in the patient's snoring by their partner), self-perceived changes, and type D

personality (a combination personality type of negative affectivity and social inhibition) on oral appliance adherence.

Risk of bias within studies

The risk of bias (**Figure 1**) assessment for random sequence generation, allocation concealment, blinding of outcome assessors, incomplete outcome data, and selective reporting was assessed for the included RCTs (n = 8) and controlled clinical trials (n = 2). The majority of these studies demonstrated a low or unclear risk of bias for the above domains. Only 2 studies[34,35] demonstrated a high risk of bias for random sequence generation, otherwise a low risk of bias was assessed in relation to selective reporting for all included studies. In terms of allocation concealment, 5 studies[20,36–38] demonstrated an unclear risk of bias, 3 studies[32,40,41] indicated a low risk of bias, and a high risk of bias was observed in 2 studies.[34,35] Due to no clear description concerning blinding of outcome assessors, 7 studies[20,32,35–39] exhibited an unclear risk of bias and a low risk of bias was observed in the rest of the 3 studies.[34,40,41] High risk of bias for incomplete outcome data was observed in only 1 study,[34] whereas the remaining 9 studies[20,32,35–41] exhibited a low risk of bias. The findings along with the comments for the judgement are summarized in **Table S4**.

Similarly, observational studies (n = 21) were found to demonstrate a low or moderate risk of bias concerning study participation, study attrition, prognostic factor management, outcome management, study confounding, and statistical analysis and reporting. Four studies[42–45] exhibited a moderate risk of bias for study participation, whereas the remaining studies (n = 17) indicated a low risk of bias. All studies demonstrated a low risk of bias for the domains-outcome measurement and statistical analysis and reporting. In terms of study attrition, 3 studies[43,46,47] exhibited a moderate risk of bias, while a low risk of bias was observed in the remaining studies. Furthermore, 8 studies[33,43–46,48–50] demonstrated a low risk of bias for prognostic factor measurement, and remaining studies exhibited a moderate risk of bias. The majority of the studies indicated a moderate risk of bias for study confounding, while a low risk of bias was observed in 2 studies[33,51] (**Table S5**).

Qualitative study analysis

Patient and disease characteristics

The current review identified 13 studies exploring the influence of patient and disease characteristics, which reported neither supine-dependent OSA, age, obesity, sex, or sleepiness to be related to OAT tolerability.[20,26,33,43–46,48,49,51–54] There were no significant sex differences detected in relation to the cessation of appliance use. Neither disease severity or baseline sleepiness was found to be a predictor of OAT adherence.[26] While the above-reported studies relied upon self-reported adherence, an additional single study found no correlation between objective adherence and anthropometric characteristics, polysomnographic parameters, or excessive daytime sleepiness.[33] Furthermore, among the 13 studies included, 1 study found no significant association between adherence and the following patient anatomical characteristics: upper airway or facial skeletal

abnormalities, such as pharyngeal alterations ($P = .62$), retrognathia ($P = .34$), Class II dental occlusion ($P = .64$), craniofacial alterations ($P = .44$), or nasal alterations ($P = .38$)[44]. Although the findings are not statistically significant, these should be viewed carefully as the authors relied upon self-reported adherence, rather than objective adherence.

Appliance fabrication and titration

In terms of appliance factors, 11 studies examined the influence of appliance fabrication and titration on OAT adherence.[20,34–41,54,55] One study compared the modified Herbst appliance (IST) with the Thornton anterior positioner (TAP), which differed in their ability to open the mouth during sleep in a protrusive position.[20] Although the TAP was more effective in treating OSA, its long-term acceptance was less than that of the IST.[20]

Three studies comparing Mono-Bloc OA with Bi-Bloc OA, with regards to their adherence, have reported rather conflicting results.[35,39,54] Zhou and Lou[37] suggested that monobloc appliance should be considered, as almost half of the patients preferred the appliance to the bibloc device. However, the findings were based on a very small sample size (n = 16). On the contrary, a large prospective single-center study, with a sample size of 153 patients, observed an adherence rate of 83.3% with the Bi-Bloc OA and 68.8% with the Mono-Bloc OA, at 1 year ($P = .04$). The authors concluded that the relatively free mandibular movement may explain the difference in adherence rates.[35] Similarly, Dieltjens et al,[54] while examining the association between Type D personality (a combination personality type of negative affectivity and social inhibition) and OAT adherence, observed a higher discontinuation rate with monobloc OAT in comparison to bi- or duo-bloc appliance (95% confidence interval, 1.77–47.09; $P = .008$) when adjusted for Type D personality, age, sex, and decrease in AHI. However, the findings of the above studies should again be interpreted with caution as they failed to assess adherence using an objective measure and the marked differences in study designs.

Seven studies evaluating the impact of ready-made (nonadjustable/nontitratable) and custom-made OAT observed an overwhelming patient-reported preference for custom-made OAT in comparison to ready-made devices.[34,36–38,40,41,55] The adherence was higher with the custom-made OAT despite more reported dental discomfort ($P = .03$).[34] In an additional RCT with a crossover design, Johal et al reported a response rate of only 24% with a ready-made OAT vs the 64% in the custom-made OAT[39]. It has to be acknowledged that adherence was assessed from self-reports and can be at risk of bias. More recently, the addition of objective adherence monitors has served to confirm the reported levels of self-reported adherence with OAT.[28,29]

Side effects

Side effects, such as dental pain, muscular pain, and excessive salivation associated with OAT may prevent early acceptance of the device and contribute to nonadherence.[56] Moreover, side effects arising from long-term OAT use, such as bite change, may also lead to poor patient adherence.[22,33,52,57] The current review identified 14 studies examining the influence of early and long-term side effects on OAT adherence.[22,26,33,47,49–53,55,56–59]

Figure 3—Forest plot of patient-reported adherence for custom-made oral appliance and ready-made oral appliance.
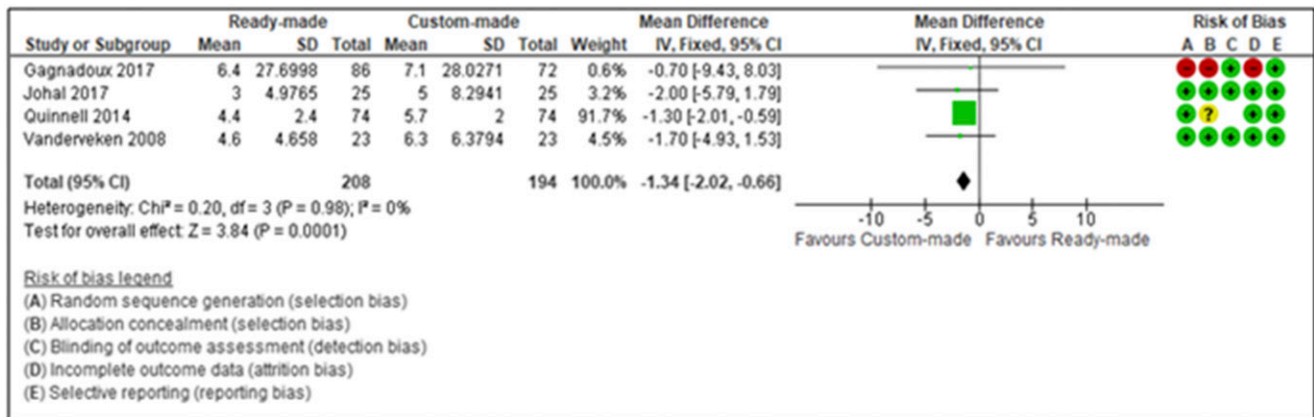
The forest plot demonstrates 4 studies that indicate increased patient adherence with custom-made appliances in comparison to ready-made appliances. The squares represent the point estimate of the corresponding studies. The area of each square is proportional to the study's weight in the meta-analysis, and the lateral points (horizontal line) indicate the confidence intervals of the respective study. The overall effect or the summary estimate is plotted as a diamond, and the lateral points demonstrate the confidence intervals of the estimate. A mean difference of zero (vertical line) indicates no effect; studies with confidence intervals crossing the vertical line are inconclusive. Powerful studies have narrower confidence intervals. In the graph, the Quinnell study and the overall effect estimate have narrow confidence intervals that do not cross zero, indicating that the meta-analysis could be considered as statistically significant.

The most common self-reported reason for discontinuing the treatment was a lack of treatment effect or discomfort or pain on OAT use, consistent with other reported studies.[22,45,51,56,57] Furthermore, early discontinuation (< 2 years) of treatment was observed due to side effects, discomfort, and inefficacy. In contrast, patients discontinued treatment due to no specific reasons after 2 or more years.[22] Additionally, the higher rates of treatment discontinuation with ready-made OAT was found to be associated with higher reported side effects in comparison to the custom-made OAT.[34,37,40,41]

Psychological and social factors

Among the 31 included studies, 12 studies[22,26,42] examined the influence of the psychological and social factors on OAT adherence. One study reported low rates of perceived effectiveness, self-efficacy, and social support for OAT as a cohort (n = 39) of older patients had low expectation for positive outcomes.[42] However, given that other included studies identified psychological factors, such as a lack of perceived benefits by the patients and their bed partner, and cognitive perceptions such as complete symptom resolution as influential on OAT adherence, the above findings are highly contentious.[22,26,47,51,53,59] Likewise, 2 studies identified that social factors, such as poor marital satisfaction (marital quality and bed sharing frequency) ($P < .04$), support from their partner, and shame caused by the disease symptoms to be associated with continued usage of OAT.[45,51] Nevertheless, the above findings should be viewed carefully due to marked differences in study designs and lack of objective assessment of adherence.

Quantitative analysis

A meta-analysis was undertaken in relation to the use of ready-made OAT vs custom-made OAT with regards to patient adherence (**Figure 3**). Based on these studies,[34,37,40,41] increased adherence was observed with custom-made appliances, with a pooled mean difference of −1.34 (−2.02 to −0.66), with low levels of heterogeneity ($I^2 = 0\%$).

<div style="background:red;color:white">DISCUSSION</div>

Given that oral appliances are removable and have to be used indefinitely, adherence to treatment is of utmost importance for achieving successful therapy.[6] However, adherence to OAT for OSA is highly variable.[14] The current review observed that the relationship between OAT adherence and patient and disease characteristics such as age, sex, obesity, AHI, and daytime sleepiness is relatively weak. Furthermore, no association was observed between objective adherence and anthropometric characteristics, polysomnographic parameters, and excessive daytime sleepiness. It also appears that disease severity and sleepiness may not be associated with OAT adherence. The majority of the included studies exploring the impact of patient and disease characteristics, were retrospective in nature and highly heterogeneous in terms of study participants.

Dieltjens et al conducted a prospective clinical trial to identify the determinants of objective adherence to OAT in patients with OSA.[32] Previous studies on OAT adherence have relied upon patient-reported adherence, which is subject to overestimation.[26,60] Moreover, objective compliance monitors with OAT have only been introduced recently.[28] The trial (n = 51) observed no correlation between objective adherence and anthropometric characteristics, polysomnographic parameters, and excessive daytime sleepiness. Nevertheless, the authors did emphasize the influence of socially disturbing snoring, reporting objective adherence correlated significantly with a decrease in socially disturbing snoring, as reported by

the partner compared with baseline visual analog scale scores for snoring without the appliance.[35] Nerfeldt and Friberg[43] investigated the difference between "arousers" (patients with respiratory arousals) and "desaturaters" (patients with oxygen desaturations) in terms of adherence rates. The authors observed that patients with greater numbers of arousal showed higher adherence (85%) than among the "desaturaters" (55%; P = .034). It was reasoned that the above difference in adherence rate was due to a significant improvement in the Epworth Sleepiness Score among the arousers (Epworth Sleepiness Score ≥ 10), which was not seen among the desaturaters. Furthermore, OAT as a first-line treatment was reported to be a strong predictor (odds ratio 1.77, 95% confidence interval 1.03–3.03; P = .0375) for treatment continuation.[22] Similarly, complete symptom resolution (odd ratio 1.78, 95% confidence interval 1.03–3.03, P = .0384) was also a strong predictor for OAT adherence.[22] These findings support an important role for disease chronicity in terms of patient adherence, which was similar to those reported for other chronic diseases.[61] They also reinforce the link between disease chronicity and long-term treatment persistence, while indicating that patients intolerant of or nonadherent with CPAP are more likely to discontinue OAT.[22] However, Izci et al[51] in a large sample (n = 144) of patients with OSA demonstrated that usage of OAT was not significantly affected by whether a patient was CPAP nonadherent or a refuser (P > .3). Nonetheless, the findings of the above studies should be interpreted with caution, as the studies failed to provide an objective measure of adherence and also due to the marked differences in study design and participant settings with regards to race and ethnicity. However, Johal et al demonstrated excellent long-term objective adherence with OAT in a sample of 42 patients with OSA, who were CPAP intolerant[28].

Nonetheless, it is interesting to evaluate these findings in the context of CPAP adherence. A weak association between patient and disease characteristics, such as disease severity, AHI, oxygen desaturation, and Epworth Sleepiness Score on CPAP adherence has been observed.[62–64] Although nasal resistance influences initial CPAP acceptance, nasal anatomy, not necessarily patient-reported nasal complaints, may be influential on CPAP adherence.[64–67] Furthermore, initial CPAP adherence appears to be closely associated with higher neighborhood socioeconomic factors, independent of individual demographic and clinical factors.[68] These findings suggest that socio-environmental factors are important in terms of patient adherence among patients with OSA. Studies have also examined race as influential on CPAP adherence, all of which have reported lower CPAP adherence in African Americans compared with Caucasian users.[69,70] Factors such as race and ethnicity-based differences in OAT adherence were not examined, as no studies have been published exploring such factors. Similarly, a low socioeconomic index is only considered a barrier to accessing OAT, as its influence on treatment adherence is yet to be explored.[71] Thus, additional studies are needed to understand and help characterize the individual considerations needed for initiating and managing OA treatment within diverse patient groups.

In terms of appliance characteristics, both patient-reported adherence and preference favored the use of custom-made appliances. The preference was not only reflected in the higher number of nights per week but also the number of hours per night that the appliance was used.[40,41] The findings are consistent with a recent systematic review and meta-analysis.[72] Moreover, as OAT for OSA is entirely dependent on patient behavior, patient preference or acceptance cannot be disregarded. However, the majority of the studies were limited to self-reported use and lacked an objective adherence measurement. This reflects the relatively recent introduction of objective adherence monitors.[28] Notwithstanding this, a lack of retention with the ready-made OAT was the most frequently cited reason for discomfort and nonadherence.[37,40,41,49,55]

In relation to side effects, nonusers experienced 1 or more adverse effects and tend to discontinue the treatment earlier, ie, within the first 3 months, whereas those who use the device for longer periods experienced milder problems.[52,58] In a questionnaire-based retrospective study, nonusers reported a higher average number of side effects than users.[52] Similarly, Makihara et al[58] reported that one-third of the nonusers discontinued the OAT within the first month and 40% within in the next 3 months. The most common reasons for discontinuation of treatment were discomfort or lack of treatment effects.[26,52,57] Specifically, pain originating from the masticatory muscles or the temporomandibular joints may be one of the main reasons for poor adherence or abandonment.[32] Consequently, Cunali et al[32] randomized 29 OSA adult patients with temporomandibular disorders into 2 groups, the exercise support therapy group and placebo therapy (PT) group, and they were evaluated prior to and 120 days after OAT. The authors observed higher treatment adherence in the support therapy group (P < .05) compared to the placebo therapy group, as there was a significant reduction of pain intensity in the former group (P < .05) but not in the latter. Long-term occlusal changes may occur with OAT,[26] as such, dental follow-up may be useful in encouraging adherence while limiting possible side effects and the risk of cessation of treatment in long-term OAT users. In terms of the influence of sex, in a retrospective study (n = 251), women experienced and reported more side effects and seemed to have a greater tendency to abandon treatment than men, as 46.8% of the women who answered a questionnaire based-survey had discontinued the use of OAT compared to the 32.8% of men.[26] However, given that the study was retrospective, with data collection from patients at different time intervals, the findings should be interpreted with caution.[26]

Psychological and social factors, such as mood and perception of treatment benefits, and bed partner satisfaction levels were significantly correlated with OAT use.[51] Dieltjens et al identified that self-reported adherence to OAT was significantly lower for adults with OSA and Type D personality, a combination personality type of negative affectivity and social inhibition, compared to patients with OSA without the said personality type[53]. These findings are in agreement with similar observations reported by Brostrom et al[73] in regards to lower CPAP adherence with type D personality. Objective adherence was found to be significantly correlated with a more pronounced decrease in socially disturbing snoring.[33] Research shows that adoption of new health behavior, like a

new physical activity routine or adhering to a prescribed medication regimen, is a challenging endeavor, involving a variety of social, emotional, and cognitive factors.[74] However, evidence in terms of psychological and social factors with regards to OAT adherence is highly underrepresented, which contrasts with the volume of literature concerning CPAP adherence. Efforts to enhance patient education ranging from telephone support to home visits, motivational enhancement, or augmented support,[75,76] have been shown to improve CPAP adherence when compared to standard care. It has also been suggested in a recent Cochrane review that educational, supportive, and behavioral interventions may increase CPAP usage to varying degrees.[77] However, no studies evaluating the efficacy of the above-mentioned interventions in relation to OAT adherence were identified in this review. Evidence concerning the impact of psychological factors, such as patient's perceptions, self-efficacy, and social support on OAT adherence is highly underrepresented in the field of sleep medicine in comparison to various sleep apnea treatments. Therefore, further research is imperative for the development of tailor-made interventions to enhance adherence in patients with low mood and/or psychological disorders.

Strengths and limitations

This is the first systematic review to assess the factors influencing adherence or nonadherence in adult patients with OSA on OAT. To limit publication bias, comprehensive search strategies were implemented along with the use of Covidence, a core component of Cochrane's review toolkit. The review followed the PRISMA reporting guidelines, and the Cochrane Handbook of systematic review was used for risk of bias assessment for the included RCTs.

In terms of limitations, the search yield was limited to 8 RCTs demonstrating low or unclear risk of bias. Furthermore, the application of a meta-analysis in nonrandomized controls trials leads to bias arising from methodological issues and marked differences in study designs. Another possible limitation is the limited evidence identified concerning the impact of psychological and social factors and the effect of strategies or interventions to improve OA adherence.

CONCLUSIONS

A weak relationship was observed between objective OAT adherence and patient and disease characteristics such as age, sex, obesity, AHI, and daytime sleepiness. Nonadherent patients reported more side effects than users and tended to discontinue treatment within the first 3 months. Increased patient adherence was identified with custom-made OAT in comparison to ready-made OA. The review identified limited evidence concerning the influence of psychological and social factors on OAT adherence. Given that majority of the studies relied upon patient-reported adherence, the review observed a considerable lack of objective adherence monitoring.

Further research would be beneficial to describe the determinants of adherence, such as risk perception, self-efficacy, and outcome expectancy and to facilitate patient education and development of tailor-made interventions to enhance

adherence to OAT. Similarly, the lack of objective adherence monitoring necessitates the need for future studies that assess adherence objectively.

ABBREVIATIONS

AHI, apnea-hypopnea index
CPAP, continuous positive airway pressure
IST, Herbst appliance
OA, oral appliance
OAT, oral appliance therapy
OSA, obstructive sleep apnea
RCT, randomized controlled trial
TAP, Thornton anterior positioner

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