Cochrane Library

Cochrane Database of Systematic Reviews

Myofunctional therapy (oropharyngeal exercises) for obstructive sleep apnoea (Protocol)

Rueda JR, Mugueta-Aguinaga I, Vilaró J, Rueda-Etxebarria M

Rueda JR, Mugueta-Aguinaga I, Vilaró J, Rueda-Etxebarria M.
Myofunctional therapy (oropharyngeal exercises) for obstructive sleep apnoea.
Cochrane Database of Systematic Reviews 2019, Issue 10. Art. No.: CD013449.
DOI: 10.1002/14651858.CD013449.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Protocol]

Myofunctional therapy (oropharyngeal exercises) for obstructive sleep apnoea

José-Ramón Rueda[1], Iranzu Mugueta-Aguinaga[2], Jordi Vilaró[3], Mikel Rueda-Etxebarria[4]

[1]Department of Preventive Medicine and Public Health, University of the Basque Country, Leioa, Spain. [2]Respiratory Physiotherapy Unit, Rehabilitation Service, Pneumology, Biocruces Health Research Institute, Cruces University Hospital, Barakaldo, Spain. [3]Department of Health Sciences, Ramon Lull University, Barcelona, Spain. [4]Rehabilidom, Bilbao, Spain

Contact address: José-Ramón Rueda, Department of Preventive Medicine and Public Health, University of the Basque Country, Barrio Sarriena, S.N., Leioa, Bizkaia, E-48080, Spain. joseramon.rueda@ehu.eus.

Editorial group: Cochrane Airways Group
Publication status and date: New, published in Issue 10, 2019.

Citation: Rueda JR, Mugueta-Aguinaga I, Vilaró J, Rueda-Etxebarria M. Myofunctional therapy (oropharyngeal exercises) for obstructive sleep apnoea. *Cochrane Database of Systematic Reviews* 2019, Issue 10. Art. No.: CD013449. DOI: 10.1002/14651858.CD013449.

ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To evaluate the benefits and harms of myofunctional therapy (oropharyngeal exercises) for the treatment of obstructive sleep apnoea.

BACKGROUND

Description of the condition

Obstructive sleep apnoea (OSA) is a syndrome characterized by episodes of apnoea (complete cessation of ventilation) or hypopnoea (insufficient breathing) during sleep. Classical symptoms of the disease — such as snoring, unsatisfactory rest and daytime sleepiness — are experienced mainly by males; females report more unspecific symptoms such as low energy or fatigue, tiredness, initial insomnia and morning headaches (Evans 2014; Fietze 2018; Nigro 2018; Theorell-Haglöw 2018). OSA is associated with an increased risk of occupational injuries (Hirsch 2016), metabolic diseases (Patinkin 2017), cardiovascular diseases (Hou 2018; Sarkar 2018), mortality (Butler 2019; Marshall 2008), and being involved in traffic accidents (Gottlieb 2018; Tregear 2009).

Obesity is probably the single most important risk factor for OSA in adults (Carneiro 2018; Hnin 2018) and children (Andersen 2019). It is estimated that over 70% of people with OSA are obese, and the prevalence of OSA among obese people may be as high as 45% (Romero-Corral 2010). Obesity is a growing problem all over the world and the incidence and prevalence of OSA is predicted to increase in parallel with it (Blüher 2019; Garvey 2015). Socioeconomic status could be a risk factor for OSA and, coupled with obesity and disparities in health care, could influence the association between OSA and racial/ethnic minorities (Guglielmi 2019). Other factors that seem to play a relevant role in the genesis of OSA include an anatomically narrow or highly collapsible upper airway or problems related with muscle responsiveness, loop gain and pharyngeal dilator muscle activity (Eckert 2013; Carberry 2016).

Diagnosis of OSA includes polysomnography – a sleep study that includes overnight continuous monitoring of the patient, usually done in-hospital-, or home sleep apnoea testing in people presenting with a combination of symptoms, including excessive daytime sleepiness, loud snoring, witnessed apnoea episodes, or non-dipping nocturnal hypertension (Kapur 2017; Randerath 2018; Crinion 2019).

Published reviews have found wide variation in the reported prevalence of OSA, which is caused in part by substantial methodological heterogeneity in population prevalence studies, including differences in the diagnostic threshold used to define the cut-off level for the Apnea-Hypopnea Index (AHI) or the inclusion (or not) of excessive daytime sleepiness as necessary diagnostic criteria (Lozo 2016; Senaratna 2017). In adults, the prevalence of OSA with excessive daytime sleepiness could range from between 3% and 18% of men, and 1% and 17% of women (Franklin 2015; Jonas 2017; Mirrakhimov 2013; Sunwoo 2018; van der Spuy 2018). However, OSA in women is probably under-diagnosed, given the widespread belief that OSA is rare in women and that the symptomatology in women differs from classical symptoms of snoring and daytime somnolence (Garvey 2015). In children, prevalence could range from 1% to 6% (Bixler 2009; Li 2010; Katidis 2017; Tsukada 2018).

Description of the intervention

Myofunctional therapy for OSA is usually a multi-component intervention including several combinations of oropharyngeal exercises (Camacho 2017). Current proposals vary regarding the time frame of the treatment, the type and intensity of exercises to be included, and the delivery of the interventions (e.g. whether they are delivered by a professional, such as a speech pathologist, or self-administered by the patient using an app).

Therapy can include isotonic and isometric exercises involving several muscles and areas of the mouth, pharynx and upper respiratory tract, working on functions such as speech, breathing, blowing, suction, chewing or swallowing (Guimaraes 2009: de Felicio 2018).

How the intervention might work

Myofunctional therapy aims to improve to the functioning of upper airway dilator muscles that are essential to maintain pharyngeal patency (Guimaraes 2009; Folha 2015; Osman 2018). Muscular endurance exercises aim to improve the tone, tension and mobility of oropharyngeal muscles and soft tissues, in order to diminish airway closures during sleep (Diaferia 2017). The therapy also targets parapharyngeal fat pads, such as tongue fat, which are increased in OSA patients (Kim 2014).

A similar approach to that described above is purported to be useful for children with OSA (Guilleminault 2013).

Why it is important to do this review

Continuous positive airway pressure (CPAP) is considered the first treatment option for most people with OSA, however adherence to treatment is often suboptimal (Bakker 2019; Mehrtash 2019; Rotenberg 2016). Poor compliance with CPAP is probably due to the side effects of the treatment, which include discomfort, nasal congestion, abdominal bloating, mask leaks, claustrophobia and inconvenience of regular usage (Wozniak 2014). A Cochrane Review published in 2014 evaluated the efficacy of different interventions aimed at improving adherence in CPAP-naive people with severe sleep apnoea; it estimated that basal adherence to CPAP (four or more hours per night) could range from 28% to 59% in randomized controlled trials (RCTs), and found that some interventions could result in additional increases in adherence rates ranging from 14% to 26% (Wozniak 2014). However, significant numbers of patients would still remain non-adherent.

Although there are other possible treatment options for some patients with OSA, including oral appliances or surgery (Carvalho 2016; Jen 2018; Werz 2017), myofunctional therapy is noninvasive, inexpensive, and has no major risks. It could be a safe and acceptable option for many patients with OSA, and economically accessible for people and countries with lower incomes.

There are some published reviews on myofunctional therapy for OSA or snoring but they include in their analysis the results of observational studies which are not as reliable as randomized clinical trials for assessing the efficacy or safety of the compared interventions. Also, those reviews do not include evidence from new studies published recently (Camacho 2017; de Felicio 2018; Kayamori 2017).

It is necessary to have a reliable summary of available evidence from RCTs assessing the effects of myofunctional therapy on people with OSA to guide decision making for patients, professionals and funding agencies.

OBJECTIVES

To evaluate the benefits and harms of myofunctional therapy (oropharyngeal exercises) for the treatment of obstructive sleep apnoea.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomized controlled trials (RCTs). We will include studies reported in full text, those published as an abstract only and unpublished data.

Types of participants

We will include adults and children (below 18 years old) with a diagnosis of obstructive sleep apnoea, defined as five or more episodes of apnoea or hypopnoea per hour of sleep by polysomnography (PSG) or portable monitoring (Type I to Type III sleep monitors).

We will exclude studies where the included participants experience other types of sleep-disordered breathing, such as central sleep apnoea, or where obstructive sleep apnoea has developed after a stroke.

Types of interventions

We will include studies comparing myofunctional therapy (oropharyngeal exercises) with one of the following control groups.

1. Sham therapy or no intervention
2. Continuous positive airway pressure (CPAP)
3. Any other active intervention
4. Combination therapy: myofunctional therapy added to CPAP versus CPAP alone or CPAP plus sham myofunctional therapy
5. Waiting list

We will not include studies in which myofunctional therapy is part of a multi-component intervention and there is no possibility to assess the separate effect of myofunctional therapy.

We will include the following co-interventions, provided they are not part of the randomized treatment: exercise for weight loss and diet and sleep recommendations.

We anticipate the following comparisons.

1. Myofunctional therapy versus sham therapy
2. Myofunctional therapy versus no intervention or wait-list
3. Myofunctional therapy versus CPAP
4. Myofunctional therapy plus CPAP versus CPAP alone.

Types of outcome measures

Primary outcomes

1. Daytime sleepiness, measured by a validated scale or questionnaire (e.g. the Epworth Sleepiness Scale; Johns 1991)
2. Morbidity (including accidents and cardiovascular diseases) and mortality

Secondary outcomes

1. Quality of life, measured by a validated scale or questionnaire (e.g. the SF-36; Ware 1993)
2. Sleep quality, measured by a validated scale or questionnaire (e.g. the Pittsburgh Sleep Quality Index; Buysse 1989)
3. Adverse events/side effects
4. Apnoea-Hypopnoea Index (AHI), defined as the number of episodes of apnoea or hypopnoea per hour of sleep, measured objectively by polysomnography
5. Snoring

We will pool data for the short, medium and long term, defined as follows.

1. Short term: up to three months
2. Medium term: from three months to two years
3. Long term: more than two years

Search methods for identification of studies

Electronic searches

We will identify studies from searches of the following databases and trial registries.

1. Cochrane Airways Trials Register (Cochrane Airways 2019), via the Cochrane Register of Studies (all years to date)
2. Cochrane Central Register of Controlled Trials (CENTRAL), via the Cochrane Register of Studies (all years to date)
3. MEDLINE Ovid SP (1946 to date)
4. Embase Ovid SP (1974 to date)
5. US National Institutes of Health Ongoing Trials Register (clinicaltrials.gov)
6. World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch/)

The proposed MEDLINE search strategy is listed in Appendix 1. This will be adapted for use in the other databases. The search strategy was developed by the Cochrane Airways Information Specialist in collaboration with the review authors, and was peer-reviewed by another Cochrane Information Specialist using the Peer Review of Electronic Search Strategies (PRESS) checklist (McGowan 2016). All databases and trial registries will be searched from their inception to the present, and there will be no restriction on language or type of publication. Hand-searched conference abstracts and grey literature will be searched for through the Cochrane Airways Trials Register and the CENTRAL database.

Searching other resources

We will check the reference lists of all primary studies and review articles for additional references. We will search relevant manufacturers' websites for study information.

We will search on PubMed for errata or retractions from included studies published in full text and report the date this was done within the review.

Data collection and analysis

Selection of studies

Three review authors (IMA, JV and MRE) will screen the titles and abstracts of the search results independently and code them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. We will retrieve the full-text reports of all potentially eligible studies and three review authors (IMA, JV and MRE) will independently screen them for inclusion, recording the reasons for exclusion of ineligible studies. We will resolve any disagreement through discussion or, if required, we will consult another review author (JRR). We will identify and exclude duplicates and collate multiple reports of the same study so that each study, rather than each report, is the unit of interest in the review. We will record the selection process in sufficient detail to complete a PRISMA flow diagram and 'Characteristics of excluded studies' table (Moher 2009).

Data extraction and management

We will use a data collection form for study characteristics and outcome data, which has been piloted on at least one study in the review. Two review authors (IMA and MRE) will extract, in a duplicate manner, the following characteristics from the included studies.

1. Methods: study design, total duration of study, details of any 'run-in' period, number of study centres and location, study setting, withdrawals and date of study.
2. Participants: number (N), mean age, age range, gender, severity of condition, previous history of CPAP use, diagnostic criteria, baseline lung function, smoking history, inclusion criteria and exclusion criteria.
3. Interventions: intervention, comparison, concomitant interventions and excluded co-interventions.
4. Outcomes: primary and secondary outcomes specified and collected, and time points reported.
5. Notes: funding for studies and notable conflicts of interest of trial authors.

Two review authors (MRE and IMA) will independently extract outcome data from included studies. We will note in the 'Characteristics of included studies' table if outcome data were not reported in a usable way. We will resolve disagreements by consensus or by involving a third review author (JRR or JV). One review author (MRE) will transfer data into the Review Manager file (RevMan 2014). We will double-check that data are entered correctly by comparing the data presented in the systematic review with the study reports. A second review author (JRR) will spot-check study characteristics for accuracy against the study report.

Assessment of risk of bias in included studies

Two review authors (IMA and MRE) will assess risk of bias independently for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will resolve any disagreements by discussion or by involving another review author (JV or JRR). We will assess the risk of bias according to the following domains.

1. Random sequence generation
2. Allocation concealment
3. Blinding of participants and personnel
4. Blinding of outcome assessment
5. Incomplete outcome data
6. Selective outcome reporting
7. Other bias

We will judge each study as being at high, low or unclear risk of bias for each domain. We will provide a quote from the study report, together with a justification for our judgement, in the 'Risk of bias' table. We will summarize the 'Risk of bias' judgements across different studies for each of the domains listed. We will consider blinding separately for different key outcomes where necessary (e.g. for unblinded outcome assessment, risk of bias for all-cause mortality may be very different than for a patient-reported pain scale). Where information on risk of bias relates to unpublished data or correspondence with a trialist, we will note this in the 'Risk of bias' table.

When considering treatment effects, we will take into account the risk of bias for the studies that contribute to that outcome.

Assessment of bias in conducting the systematic review

We will conduct the review according to this published protocol and justify any deviations from it in the 'Differences between protocol and review' section of the systematic review.

Measures of treatment effect

We will analyse dichotomous data as odds ratios (ORs) and continuous data as the mean difference (MD) or standardized mean difference (SMD). If data from rating scales are combined in a meta-analysis, we will ensure they are entered with a consistent direction of effect (e.g. lower scores always indicate improvement).

We will undertake meta-analyses only where this is meaningful; that is, if the treatments, participants and the underlying clinical question are similar enough for pooling to make sense. We will describe skewed data narratively (for example, as medians and interquartile ranges for each group).

Where multiple trial arms are reported in a single study, we will include only the relevant arms. If two comparisons (e.g. drug A versus placebo and drug B versus placebo) are combined in the same meta-analysis, we will either combine the active arms or halve the control group to avoid double-counting.

If adjusted analyses are available (ANOVA or ANCOVA) we will use these as a preference in our meta-analyses. If both change-from-baseline and endpoint scores are available for continuous data, we will use change-from-baseline unless there is low correlation between measurements in individuals. If a study reports outcomes at multiple time points, we will use last one.

We will use intention-to-treat (ITT) or 'full analysis set' analyses where they are reported (i.e. those where data have been imputed for participants who were randomly assigned but did not complete the study), instead of completer or per-protocol analyses.

Unit of analysis issues

For dichotomous outcomes we will use participants, rather than events, as the unit of analysis (i.e. number of children admitted to hospital, rather than number of admissions per child). However, if rate ratios are reported in a study, we will analyse them on this basis. We will only meta-analyze data from cluster-RCTs if the available data have been adjusted, or can be adjusted, to account for the clustering.

Dealing with missing data

We will contact investigators or study sponsors in order to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when a study is identified as an abstract only). Where this is not possible, and the missing data are thought to introduce serious bias, we will take this into consideration in the GRADE rating for affected outcomes.

Assessment of heterogeneity

We will use the I^2 statistic to measure heterogeneity among the studies in each analysis. If we identify substantial heterogeneity we will report it and explore the possible causes using prespecified subgroup analyses.

Assessment of reporting biases

If we are able to pool more than 10 studies, we will create and examine a funnel plot to explore possible small-study and publication biases.

Data synthesis

We will use a random-effects model and perform a sensitivity analysis with a fixed-effect model.

'Summary of findings' table

We will create a 'Summary of findings' table using the following outcomes: daytime sleepiness, morbidity (including accidents and cardiovascular diseases) and mortality, quality of life, sleep quality, adverse events, AHI and snoring. Outcomes will be reported separately for short, medium and long term when data is available. We will use the five GRADE considerations (risk of bias, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of a body of evidence as it relates to the studies that contribute data for the prespecified outcomes. We will use the methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011), using GRADEpro GDT software (GRADEpro GDT). We will justify all decisions to downgrade the quality of studies using footnotes and we will make comments to aid the reader's understanding of the review where necessary.

Subgroup analysis and investigation of heterogeneity

We plan to carry out subgroup analyses for the following factors.

1. Gender (females versus males)
2. Age (18 years and younger versus older than 18 years)
3. Severity of OSA (mild versus moderate to severe)

We will use the following outcomes in subgroup analyses.

1. Daytime sleepiness
2. Morbidity (including accidents and cardiovascular diseases) and mortality
3. Serious adverse events

We will use the formal test for subgroup interactions in Review Manager 5 (RevMan 2014).

Sensitivity analysis

We plan to carry out sensitivity analyses for the primary outcomes, in which we remove the following.

1. Studies with a high risk of bias for key sources of potential bias (e.g. randomization, allocation concealment, blinding)
2. Studies with missing data

We will also compare the results from a fixed-effect model with those using a random-effects model.

We will undertake a further sensitivity analysis to investigate whether choice of summary statistic (OR or RR) is critical to the conclusions of the meta-analysis.

ACKNOWLEDGEMENTS

The Background and Methods sections of this protocol are based on a standard template used by Cochrane Airways.

Milo Puhan was the Editor for this protocol and commented critically on the protocol.

This project was supported by the National Institute for Health Research (NIHR), via Cochrane Infrastructure funding to the Cochrane Airways Group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS, or the Department of Health.

The authors and the Cochrane Airways editorial team are grateful to the following peer reviewers for their time and comments.

Samantha Cox, Cochrane Ear, Nose and Throat
Hayley Barnes, Alfred Hospital, Melbourne
Dr Anna Mohammadieh, St Vincent's Hospital and Royal North Shore Hospital, Sydney
Brian Stafford (consumer reviewer)
Mark Sidaway (consumer reviewer)

REFERENCES

Additional references

Andersen 2019

Andersen IG, Holm JC, Homøe P. Obstructive sleep apnea in children and adolescents with and without obesity. *European Archives of Oto-Rhino-Laryngology* 2019;**276**(3):871-8.

Bakker 2019

Bakker JP, Weaver TE, Parthasarathy S, Aloia MS. Adherence to CPAP: what should we be aiming for, and how can we get there?. *Chest* 2019;**155**(1):pii: S0012-3692(19)30032-7.

Bixler 2009

Bixler EO, Vgontzas AN, Lin HM, Liao D, Calhoun S, Vela-Bueno A, et al. Sleep disordered breathing in children in a general population sample: prevalence and risk factors. *Sleep* 2009;**32**(6):731-6.

Blüher 2019

Blüher M. Obesity: global epidemiology and pathogenesis. *Nature Reviews. Endocrinology* 2019;**15**(5):288-98.

Butler 2019

Butler MP, Emch JT, Rueschman M, Sands SA, Shea SA, Wellman A, et al. Apnea-Hypopnea event duration predicts mortality in men and women in the Sleep Heart Health Study. *American Journal of Respiratory and Critical Care Medicine* 2019;**199**(7):903-12.

Buysse 1989

Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research* 1989;**28**(2):193-213.

Camacho 2017

Camacho M, Guilleminault C, Wei JM, Song SA, Noller MW, Reckley LK, et al. Oropharyngeal and tongue exercises (myofunctional therapy) for snoring: a systematic review and meta-analysis. *European Archives of Oto-Rhino-Laryngology* 2018;**275**(4):849-55.

Carberry 2016

Carberry JC, Jordan AS, White DP, Wellman A, Eckert DJ. Upper airway collapsibility (Pcrit) and pharyngeal dilator muscle activity are sleep stage dependent. *Sleep* 2016;**39**(3):511-21.

Carneiro 2018

Carneiro G, Zanella MT. Obesity metabolic and hormonal disorders associated with obstructive sleep apnea and their impact on the risk of cardiovascular events. *Metabolism* 2018;**84**:76-84.

Carvalho 2016

Carvalho FR, Lentini-Oliveira DA, Prado LBF, Prado GF, Carvalho LBC. Oral appliances and functional orthopaedic appliances for obstructive sleep apnoea in children. *Cochrane Database of Systematic Reviews* 2016, Issue 10. [DOI: 10.1002/14651858.CD005520.pub3]

Cochrane Airways 2019

Cochrane Airways Trials Register. airways.cochrane.org/trials-register (accessed 16 April 2019).

Crinion 2019

Crinion SJ, Ryan S, Kleinerova J, Kent BD, Gallagher J, Ledwidge M, McDonald K, McNicholas WT. Nondipping Nocturnal Blood Pressure Predicts Sleep Apnea in Patients With Hypertension. *Journal of Clinical Sleep Medicine* 2019;**15**(7):957-63.

de Felicio 2018

de Felício CM, da Silva Dias FV, Trawitzki LVV. Obstructive sleep apnea: focus on myofunctional therapy. *Nature and Science of Sleep* 2018;**10**:271-86.

Diaferia 2017

Diaféria G, Santos-Silva R, Truksinas E, Haddad FLM, Santos R, Bommarito S, et al. Myofunctional therapy improves adherence to continuous positive airway pressure treatment. *Sleep Breath* 2017;**21**(2):387-95.

Eckert 2013

Eckert D, White DP, Jordan AS, Malhotra A, Wellman A. Defining phenotypic causes of obstructive sleep apnea. Identification of novel therapeutic targets. *American Journal of Respiratory and Critical Care Medicine* 2013;**188**(8):996-1004.

Evans 2014

Evans J, Skomro R, Driver H, Graham B, Mayers I, McRae L, et al. Sleep laboratory test referrals in Canada: sleep apnea rapid response survey. *Canadian Respiratory Journal [Revue Canadienne de Pneumologie]* 2014;**21**:e4-10.

Fietze 2018

Fietze I, Laharnar N, Obst A, Ewert R, Felix SB, Garcia C, et al. Prevalence and association analysis of obstructive sleep apnea with gender and age differences - Results of SHIP-Trend. *Journal of Sleep Research* 2018;**27**(5):e12770.

Folha 2015

Folha GA, Valera FC, de Felício CM. Validity and reliability of a protocol of orofacial myofunctional evaluation for patients with obstructive sleep apnea. *European Journal of Oral Sciences* 2015;**123**(3):165-72.

Franklin 2015

Franklin KA, Lindberg E. Obstructive sleep apnea is a common disorder in the population-a review on the epidemiology of sleep apnea. *Journal of Thoracic Disease* 2015;**7**(8):1311-22.

Garvey 2015

Garvey JF, Pengo MF, Drakatos P, Kent BD. Epidemiological aspects of obstructive sleep apnea. *Journal of Thoracic Disease* 2015;**7**(5):920-9.

Gottlieb 2018

Gottlieb DJ, Ellenbogen JM, Bianchi MT, Czeisler CA. Sleep deficiency and motor vehicle crash risk in the general

population: a prospective cohort study. *BMC Medicine* 2018;**16**(1):44.

GRADEpro GDT [Computer program]

McMaster University (developed by Evidence Prime). GRADEpro GDT. Version accessed prior to 5 June 2019. Hamilton (ON): McMaster University (developed by Evidence Prime), 2015.

Guglielmi 2019

Guglielmi O, Lanteri P, Garbarino S. Association between socioeconomic status, belonging to an ethnic minority and obstructive sleep apnea: a systematic review of the literature. *Sleep Medicine* 2019;**57**:100-6.

Guilleminault 2013

Guilleminault C, Huang YS, Monteyrol PJ, Sato R, Quo S, Lin CH. Critical role of myofascial reeducation in pediatric sleep-disordered breathing. *Sleep Medicine* 2013;**14**(6):518-25.

Guimaraes 2009

Guimarães KC, Drager LF, Genta PR, Marcondes BF, Lorenzi-Filho G. Effects of oropharyngeal exercises on patients with moderate obstructive sleep apnea syndrome. *American Journal of Respiratory and Critical Care Medicine* 2009;**179**(10):962-6.

Higgins 2011

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from training.cochrane.org/handbook.

Hirsch 2016

Hirsch Allen AJ, Park JE, Daniele PR, Fleetham J, Ryan CF, Ayas NT. Obstructive sleep apnoea and frequency of occupational injury. *Thorax* 2016;**71**(7):664-6.

Hnin 2018

Hnin K, Mukherjee S, Antic NA, Catcheside P, Chai-Coetzer CL, McEvoy D, et al. The impact of ethnicity on the prevalence and severity of obstructive sleep apnea. *Sleep Medicine Review* 2018;**41**(Oct):78-86.

Hou 2018

Hou H, Zhao Y, Yu W, Dong H, Xue X, Ding J, et al. Association of obstructive sleep apnea with hypertension: A systematic review and meta-analysis. *Journal of Global Health* 2018;**8**(1):010405.

Jen 2018

Jen R, Almeida FR, Brasher P, Doyle-Waters MM, Salzman J, Fleetham J. Oral appliances for obstructive sleep apnoea. *Cochrane Database of Systematic Reviews* 2018, Issue 9. [DOI: 10.1002/14651858.CD013131]

Johns 1991

Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;**14**(6):540-5.

Jonas 2017

Jonas DE, Amick HR, Feltner C, Palmieri Weber RP, Arvanitis M, Stine A, et al. Screening for obstructive sleep apnea in adults: an evidence review for the U.S. preventive services task force [internet]. *Evidence Synthesis* 2017;**146**:14-05216-EF-1.

Kapur 2017

Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. *Journal of Clinical Sleep Medicine* 2017;**13**(3):479-504.

Katidis 2017

Kaditis AG, Alonso Alvarez ML, Boudewyns A, Alexopoulos EI, Ersu R, Joosten K, et al. Obstructive sleep disordered breathing in 2–18 year-old children: diagnosis and management. *European Respiratory Journal* 2016;**47**(1):69-94.

Kayamori 2017

Kayamori F, Mandelbaum E. Effects of orofacial myofunctional therapy on the symptoms and physiological parameters of sleep breathing disorders in adults:a systematic review. *Revista CEFAC* 2017;**19**(6):868-78.

Kim 2014

Kim AM, Keenan BT, Jackson N, Chan EL, Staley B, Poptani H, et al. Tongue fat and its relationship to obstructive sleep apnea. *Sleep* 2014;**37**(10):1629-48.

Li 2010

Li AM, So HK, Au CT, Ho C, Lau J, Ng SK, et al. Epidemiology of obstructive sleep apnoea syndrome in Chinese children: a two-phase community study. *Thorax* 2010;**65**(11):991-7.

Lozo 2016

Lozo T, Komnenov D, Badr MS, Mateika JH. Sex differences in sleep disordered breathing in adults. *Respiratory Physiology and Neurobiology* 2017;**245**(Nov):65-75.

Marshall 2008

Marshall NS, Wong KK, Liu PY, Cullen SR, Knuiman MW, Grunstein RR. Sleep apnea as an independent risk factor for all-cause mortality: the Busselton Health Study. *Sleep* 2008;**31**(8):1079-85.

McGowan 2016

McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. *Journal of Clinical Epidemiology* 2016;**75**:40-6. [DOI: 10.1016/j.jclinepi.2016.01.021]

Mehrtash 2019

Mehrtash M, Bakker JP, Ayas N. Predictors of continuous positive airway pressure adherence in patients with obstructive sleep apnea. Lung 2019 Jan 7 [Epub ahead of print]; Vol. 197. [doi: 10.1007/s00408-018-00193-1]

Mirrakhimov 2013

Mirrakhimov AE, Sooronbaev T, Mirrakhimov EM. Prevalence of obstructive sleep apnea in Asian adults: a systematic review of the literature. *BMC Pulmonary Medicine* 2013;**13**(10):1-10.

Moher 2009

Moher D, Liberati A, Tetzlaff J, Altman D. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine* 2009;**6**(7):e1000097. [DOI: 10.1371/journal.pmed.1000097]

Nigro 2018

Nigro CA, Dibur E, Borsini E, Malnis S, Ernst G, Bledel I, et al. The influence of gender on symptoms associated with obstructive sleep apnea. *Sleep and Breathing* 2018;**22**(3):683-93.

Osman 2018

Osman AM, Carter SG, Carberry JC, Eckert DJ. Obstructive sleep apnea: current perspectives. *National Science of Sleep* 2018;**10**:21.

Patinkin 2017

Patinkin ZW, Feinn R, Santos M. Metabolic consequences of obstructive sleep apnea in adolescents with obesity: a systematic literature review and meta-analysis. *Child Obesity* 2017;**13**(2):102-10.

Randerath 2018

Randerath W, Bassetti CL, Bonsignore MR, Farre R, Ferini-Strambi L, Grote L, et al. Challenges and perspectives in obstructive sleep apnoea: report by an ad hoc working group of the Sleep Disordered Breathing Group of the European Respiratory Society and the European Sleep Research Society. *European Respiratory Journal* 2018;**52**(3):pii: 1702616.

RevMan 2014 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Romero-Corral 2010

Romero-Corral A, Caples SM, Lopez-Jimenez F, Somers VK. Interactions between obesity and obstructive sleep apnea—implications for treatment. *Chest* 2010;**137**(3):711-9.

Rotenberg 2016

Rotenberg BW, Murariu D, Pang KP. Trends in CPAP adherence over twenty years of data collection: a flattened curve. *Journal of Otolaryngology* 2016;**45**(1):43.

Sarkar 2018

Sarkar P, Mukherjee S, Chai-Coetzer CL, McEvoy RD. The epidemiology of obstructive sleep apnoea and cardiovascular disease. *Journal of Thoracic Disease* 2018;**10**(Suppl 34):S4189-4200.

Schünemann 2011

Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, Guyatt GH. Chapter 12: Interpreting results and drawing conclusions. Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration, 2011. Available from www.handbook.cochrane.org, 2011.

Senaratna 2017

Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al. Prevalence of obstructive sleep apnea in the general population: z systematic review. *Sleep Medicine Review* 2017;**34**(Aug):70-81.

Sunwoo 2018

Sunwoo JS, Hwangbo Y, Kim WJ, Chu MK, Yun CH, Yang KI. Prevalence, sleep characteristics, and comorbidities in a population at high risk for obstructive sleep apnea: a nationwide questionnaire study in South Korea. *PLOS One* 2018;**13**(2):e0193549.

Theorell-Haglöw 2018

Theorell-Haglöw J, Miller CB, Bartlett DJ, Yee BJ, Openshaw HD, Grunstein RR. Gender differences in obstructive sleep apnoea, insomnia and restless legs syndrome in adults - What do we know? A clinical update. *Sleep Medicine Review* 2018;**38**:28-38.

Tregear 2009

Tregear S, Reston J, Schoelles K, Phillips B. Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. *Journal of Clinical Sleep Medicine* 2009;**5**:573-81.

Tsukada 2018

Tsukada E, Kitamura S, Enomoto M, Moriwaki A, Kamio Y, Asada T, et al. Prevalence of childhood obstructive sleep apnea syndrome and its role in daytime sleepiness. *PLoS One* 2018;**13**(190):e0204409.

van der Spuy 2018

van der Spuy I, Zhao G, Karunanayake C, Pahwa P. Predictors of sleep apnea in the Canadian population. *Canadian Respiratory Journal* 2018;**2018**:6349790. [DOI: 10.1155/2018/6349790]

Ware 1993

Ware JE, Kosinski M, Dewey JE, Gandek B. SF-36 Health Survey: Manual and interpretation guide. Lincoln, RI: Quality Metric Inc 1993.

Werz 2017

Werz SM, Pfeifle M, Schrader F, Jurgens P, Briel M, Berg BI. Surgery for obstructive sleep apnoea in adults. *Cochrane Database of Systematic Reviews* 2017, Issue 9. [DOI: 10.1002/14651858.CD012770]

Wozniak 2014

Wozniak DR, Lasserson TJ, Smith I. Educational, supportive and behavioural interventions to improve usage of continuous positive airway pressure machines in adults with obstructive sleep apnoea. *Cochrane Database of Systematic Reviews* 2014, Issue 1. [DOI: 10.1002/14651858.CD007736.pub2]

APPENDICES

Appendix 1. MEDLINE (Ovid) search strategy

Ovid MEDLINE(R) ALL <1946 to April 15 2019>

#	Searches	Results
1	exp Sleep Apnea Syndromes/	32631
2	((sleep$ or nocturnal) adj2 (apnoea$ or apnoea$)).tw.	33371
3	(sleep$ adj2 disordered adj2 breathing).tw.	5870
4	((sleep$ or nocturnal) adj2 (hypopnea$ or hypopnoea$ or hypo-apnoea$ or hypo-apnea$ or apneic-hypopneic or apnoeic-hypopnoeic)).tw.	2344
5	(OSA or SAHS).ti,ab. and sleep$.tw.	11147
6	OSAHS.ti,ab.	1343
7	or/1-6	43202
8	Myofunctional Therapy/	309
9	myofunction$.tw.	432
10	exp Oropharynx/	13839
11	Tongue/	17654
12	Palate, Soft/	3900
13	(oropharyngeal$ or oropharynx or orofacial$ or tongue$ or soft palate).tw.	68836
14	or/10-13	87136
15	exp Exercise Therapy/	45793
16	(exercise$ or therapy$).tw.	1892170
17	15 or 16	1907618
18	14 and 17	8306
19	8 or 9 or 18	8766
20	7 and 19	427
21	(controlled clinical trial or randomized controlled trial).pt.	568244
22	(randomized or randomised).ab,ti.	566118
23	placebo.ab,ti.	202224
24	dt.fs.	2099633

(Continued)

25	randomly.ab,ti.	309763
26	trial.ab,ti.	538885
27	groups.ab,ti.	1926408
28	or/21-27	4488218
29	Animals/	6386163
30	Humans/	17669534
31	29 not (29 and 30)	4536680
32	28 not 31	3887284
33	20 and 32	101

CONTRIBUTIONS OF AUTHORS

JR Rueda wrote the final draft of the protocol and will write the draft of the full review. He is the contact person with the editorial base and co-ordinated the contributions from the co-authors and will be the guarantor of the final review.

I Mugueta-Aguinaga, J Vilaró and M Rueda-Etxebarria drafted the clinical sections of the Background. They will select the studies for the full review, extract data and conduct the 'Risk of bias' assessment.

Contributions of editorial team

Rebecca Fortescue (Co-ordinating Editor) edited the protocol, advised on methodology and approved the protocol prior to publication.

Chris Cates (Co-ordinating Editor) checked the planned methods.

Milo Puhan (Contact Editor) edited the protocol and advised on content.

Emma Dennett (Managing Editor) co-ordinated the editorial process, advised on content and edited the protocol.

Emma Jackson (Assistant Managing Editor) organized peer review and edited the references.

Elizabeth Stovold (Information Specialist) designed the search strategy and arranged for peer review of the search strategy.

DECLARATIONS OF INTEREST

JR Rueda: none known.

I Mugueta-Aguinaga: none known.

J Vilaró: none known.

M Rueda-Etxebarria: none known.

SOURCES OF SUPPORT

Internal sources

- JR Rueda receives salary from the University of the Basque Country, Spain.
- I Mugueta-Aguinaga receives salary from Osakidetza the Basque Country Health Service, Spain.
- M Rueda-Etxebarria receives salary from Rehabilidom, Spain.
- J Vilaró receives salary from the Ramon Lull University, Spain.

External sources

- The authors declare that no such funding was received for this systematic review, Other.