National Institute for Health and Care Excellence

Final

Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s

Evidence review M: Demonstration of efficacy

NICE guideline NG202

Intervention evidence review

August 2021

Final

Developed by the National Guideline Centre, hosted by the Royal College of Physicians

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1.1 Review question: How should efficacy of treatment be demonstrated?

1.2 Introduction

Having embarked on treatment for obstructive sleep apnoea/hypopnoea syndrome (OSAHS), obesity hypoventilation syndrome (OHS) and COPD-OSAHS overlap syndrome, it is important to assess whether this is working or if further therapy modifications are required. There has not been a standardised approach to this, nor have there been national guidelines, so practice varies between centres. Some have had a symptom focussed approach to assessing treatment efficacy, others have performed repeat sleep studies, others have used data available from downloads of positive airway pressure therapy. Newer widely available CPAP machines and telemonitoring allow more data on overnight sleep disordered breathing to be collected and potentially easily reviewed.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People being treated for OSAHS/OHS/ COPD-OSAHS overlap syndrome, stratified by: • disease severity (mild vs moderate vs severe) • condition (OSAHS/OHS/ COPD-OSAHS overlap syndrome) • type of treatment (CPAP vs surgery vs positional modifiers vs oral devices)
Interventions	• using ESS (Epworth Sleepiness Scale) • using AHI (Apnoea Hypopnea Index) • using ODI (Oxygen desaturation index) • using SAQLI (Calgary Sleep Apnea Quality of Life Index) • using partner reported symptoms • using hours of use • using ABG based CO_2 monitoring (for OHS only) • using transcutaneous CO_2 monitoring (for OHS only) Treatment to be adjusted during the period of measurements
Comparisons	Any of the above vs any other in isolation or combination
Outcomes	**Critical** • generic or disease specific quality of life measures (continuous) • mortality (dichotomous) **Important** • sleepiness scores (continuous, e.g. Epworth) • apnoea-hypopnoea index (continuous) • oxygen desaturation index (continuous) • CO_2 control (continuous) • hours of use (adherence measure, continuous) • minor adverse effects of treatment (rates or dichotomous)

	• driving outcomes (continuous) • neurocognitive outcomes (continuous) • impact on co-existing conditions: ○ HbA1c for diabetes (continuous) ○ cardiovascular events for cardiovascular disease (dichotomous) ○ systolic blood pressure for hypertension (continuous) All follow-up times will be included. Follow-up times will be grouped as: follow-up </=1 year and >1 year
Study design	• RCTs Minimum follow-up 1 month

1.4 Clinical evidence

1.4.1 Included studies

A search was conducted for studies on markers/indices/ measures to monitor treatment in patients with OSAHS/OHS/ COPD-OSAHS overlap syndrome. No relevant studies were identified.

See the excluded studies list in appendix I.

1.4.2 Summary of clinical studies included in the evidence review

No studies included in the review.

1.4.3 Quality assessment of clinical studies included in the evidence review

No studies included in the review.

1.5 Economic evidence

1.5.1 Included studies

No health economic studies were included.

1.5.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix G.

1.5.3 Health economic modelling

Original modelling was not conducted for this question.

1.5.4 Health economic evidence statements

No relevant economic evaluations were identified.

1.6 The committee's discussion of the evidence

1.6.1 Interpreting the evidence

1.6.1.1 The outcomes that matter most

The committee considered the outcomes of health-related quality of life and mortality as critical outcomes for decision making. Other important outcomes included sleepiness scores (continuous, e.g. Epworth), apnoea-hypopnoea index, oxygen desaturation index, CO_2 control, hours of use (adherence measure), minor adverse effects of treatment, driving outcomes, neurocognitive outcomes, impact on co-existing conditions, HbA1c for diabetes, cardiovascular events for cardiovascular disease, systolic blood pressure for hypertension.

There was no evidence available for any of the outcomes.

1.6.1.2 The quality of the evidence

No evidence was available for this review question.

1.6.2 Benefits and harms

OSAHS (CPAP, oral devices, positional modifiers)

There was no evidence on demonstrating efficacy for treatments for people with OSAHS, so the guideline committee made recommendations based on their experience and knowledge of current best practice.

The committee discussed that an ideal measure of treatment efficacy would demonstrate control of symptoms, control of AHI and uptake and adherence to therapy. The committee noted that there was a huge variation in practice in the use of monitoring methods/measures.

The committee agreed that the effectiveness of treatment with CPAP, mandibular advancement splints and positional modifiers in people with OSAHS should be assessed by reviewing the following: OSAHS symptoms, including the Epworth sleepiness scale and vigilance, for example when driving; severity of OSAHS, using AHI or ODI, adherence to therapy and telemonitoring data or download information from the device (if available).

The committee agreed that clinicians would want optimal control of symptoms after treatment. The symptoms could be snoring, witnessed apnoea, unrefreshing sleep, excessive sleepiness, nocturia, tiredness, insomnia, headaches, sleep fragmentation, ankle swelling, and cognitive dysfunction/memory impairment. However, they agreed that treatment efficacy cannot be decided on improvements of symptoms alone as it is an imprecise indicator of treatment success and some may be symptom-free at the outset.

The committee discussed that objective measures such as AHI or ODI should be used to assess the efficacy of CPAP/mandibular advancement splint /positional modifier treatment. The committee did not want to prescribe a threshold for AHI but agreed that the aim of the treatment is to achieve AHI <5. Committee members agreed that AHI<5 is the normal range, but they did not come to a consensus as AHI <5 is not always achieved after treatment.

The committee discussed the use of patient reported and objective adherence measures to assess efficacy of treatment. The committee noted that subjective reports of compliance often result in over reporting of adherence and cannot be reliably used. They agreed that it is responsibility of clinicians to use machine data and telemonitoring where available.

The committee stated that newer CPAP machines can track adherence, date ranges of use, number of nights used and not used, percentage of nights with use, percentage of nights with

use ≥ 4 hours or < 4 hours, average use on all nights, apnoea-hypopnoea index (AHI) and mask leak.

The committee identified several factors that commonly cause problems with CPAP that should be routinely reviewed if treatment is not working.

The committee agreed that in people using CPAP their understanding and experience of treatment should be explored, and mask type and fit and including checking for leaks , cleaning and maintaining equipment, nasal and mouth dryness, as well as other factors affecting sleep disturbance such as insomnia, restless legs, sleep hygiene, shift work, sleep routines should be reviewed. Careful history taking is required and further detailed investigation may be needed in some cases (for example polysomnography, monitoring of limb movements, or actigraphy), particularly when additional non-respiratory sleep disorders are suspected.

OSAHS may sometimes resolve, for example, because of weight loss or other lifestyle changes. The committee agreed that stopping treatment should be considered if this is suspected and the person monitored for the return of symptoms. A sleep study after at least 2 weeks without treatment may be needed to check whether OSAHS has resolved.The committee noted that CPAP is just one aspect of the treatment for OSAHS, and that monitoring should be tailored to the person's overall treatment plan, which may include lifestyle changes and weight management, modifying sedative drugs and alcohol, stopping smoking, and treating underlying lung disease and other comorbidities.

The committee discussed that reviewing symptoms as well as ESS, AHI and adherence to therapy is current practice and implementation of these recommendations will not change practice.

The committee agreed that if other therapies for OSAHS are used, such as customised mandibular advancement splint, or positional modifiers then assessment of their effectiveness should be measured once treatment has been optimised (e.g. after 3 months): on symptoms including ESS, and AHI or ODI measured by repeat sleep study.

Even though there was a lack of evidence on demonstrating efficacy for treatments for people with OSAHS, based on their experience the committee made strong recommendations hence they did not make any research recommendation for this topic.

OHS (non-invasive ventilation, CPAP)

There was no evidence for demonstrating efficacy for treatments for OHS, so the guideline committee made recommendations based on their experience and knowledge of current best practice. In OHS control of hypoventilation is demonstrated by improvement of symptoms, hypercapnia when awake and asleep, and oxygenation. It is important to optimise these in order to improve well-being and prognosis, and to reduce the risk of hospital admission.

The committee agreed that clinical effectiveness of treatment (CPAP/non-invasive ventilation) in people with OHS should be assessed by reviewing: symptoms of OSAHS and hypoventilation including ESS, and vigilance, for example when driving, severity of OSAHS, using AHI or ODI, adherence to therapy, an assessment of improvement in oxygenation and hypercapnia while awake and asleep and telemonitoring or download information from CPAP or non-invasive ventilation device.

The committee agreed that in people using CPAP their understanding and experience of treatment should be explored, and mask type and fit including checking for leaks , cleaning and maintenance of equipment, nasal and mouth dryness, other factors affecting sleep disturbance such as insomnia, restless legs, sleep hygiene, shift work, sleep routines should be reviewed.

The committee highlighted that in people with OHS, the need for oxygen therapy and adherence to this should be reviewed after treatment with non-invasive ventilation or CPAP has been optimised.

The committee noted that CPAP and non-invasive ventilation are just part the treatment for OHS, and that monitoring should be tailored to the person's overall treatment plan, which should also include lifestyle changes and weight management, modifying sedative drugs and alcohol, stopping smoking, and treating underlying lung disease and other comorbidities. The committee discussed that reviewing symptoms including ESS, AHI or ODI and adherence to therapy is current practice and implementation of these recommendations will not change practice.

The committee highlighted that in people with OHS, non-invasive ventilation or CPAP should be optimised first before reviewing requirement for long term oxygen therapy.

Even though there was a lack of evidence on demonstrating efficacy for treatments for people with OHS, based on their experience the committee made strong recommendations hence they did not make any research recommendation for this topic.

COPD-OSAHS overlap syndrome (non-invasive ventilation, CPAP, oxygen therapy*)*

COPD-OSAHS overlap syndrome is defined by the presence of COPD and OSAHS. Treatment for overlap syndrome is to address underlying COPD, OSA, or both.

There was no evidence for demonstrating efficacy for treatments for COPD-OSAHS overlap syndrome, so the guideline committee made recommendations based on their experience and knowledge of current best practice.

In COPD-OSAHS overlap syndrome, control of hypoventilation is demonstrated by improvement of daytime and night time oxygenation and hypercapnia; this is important to improve prognosis.

The committee agreed that clinical effectiveness of treatment (CPAP/non-invasive ventilation) in people with COPD-OSAHS overlap syndrome should be assessed by reviewing: symptoms of OSAHS and hypoventilation including ESS, and vigilance, for example when driving, severity of OSAHS using AHI or ODI, adherence to therapy, improvement in oxygenation and hypercapnia (if present) while awake and asleep , if present and telemonitoring or download information from CPAP or non-invasive ventilation device.

The committee agreed that in people using CPAP their understanding and experience of treatment should be explored, and mask type andfit including checking for leaks, nasal and mouth dryness, other factors affecting sleep disturbance such as insomnia, restless legs, sleep hygiene, shift work, sleep routines should be reviewed. They noted that sleep quality may be poor in COPD patients, with disruption from cough, wheeze, restless legs and medication.

In some patients with severe COPD and COPD-OSAHS overlap syndrome optimised treatment of the OSAHS may produce an objective improvement in indices such as the AHI or oxygen desaturation during sleep but fail to improve symptoms or quality of life for the patient. This would usually be because the severity of the person's COPD has the over-riding influence on quality of life. Since use of non-invasive ventilation or CPAP equipment adds to the burden of therapy, consideration should be given to the stopping these and using a symptom management approach. This requires careful discussion with the patient and their care givers, may also include discussions care planning (for example COPD exacerbation action plan and advance care planning) for those with severe COPD. The committee discussed that reviewing symptoms/sleepiness and adherence to therapy is current practice and implementation of these recommendations will not change practice.

The committee highlighted that in people with COPD-OSAHS overlap syndrome who are already having supplemental oxygen therapy, the need for oxygen therapy should be reviewed after treatment with non-invasive ventilation or CPAP has been optimised. Effective treatment with CPAP or non-invasive ventilation may improve the person's condition to the extent that they no longer fulfil the criteria for supplemental oxygen.

Even though there was a lack of evidence on demonstrating efficacy for treatments for people with COPD-OSAHS overlap syndrome, based on their experience the committee made strong recommendations hence they did not make any research recommendation for this topic.

1.6.3 Cost effectiveness and resource use

There were no economic or clinical evaluations identified for this review question. The committee therefore made consensus recommendations based on current practice.

Since treatments in these conditions are potentially for life it is important for cost effectiveness as well as for patient welfare to assess whether a treatment is working and then, if necessary, to modify or discontinue treatment.

The committee recommended assessing symptom control and, especially for CPAP and non-invasive ventilation factors that affect adherence. These assessments are already current practice. The frequency of monitoring is discussed in evidence report L.

Although control of symptoms is important, the committee agreed that treatment efficacy cannot be decided on improvements of symptoms alone as they are an imprecise indicator of treatment success and some people may be symptom-free at the outset. Therefore, they recommended the re-assessment of severity of OSAHS using AHI. For patients being treated with CPAP or non-invasive ventilation this is downloaded from the device itself and can be done remotely where there is telemonitoring – see Chapter L. However, for patients receiving other treatments this might require a home or hospital sleep study. For patients with OHS or overlap syndrome an assessment of improvement in oxygenation and hypercapnia would also be required.

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Appendices

Appendix A: Review protocols

Table 2: Review protocol: demonstration of efficacy

Field	Content
PROSPERO registration number	Not registered
Review title	Demonstration of efficacy
Review question	How should efficacy of treatment be demonstrated (for example, variable positive pressure titration device, oximetry, capnography or polysomnography titration)?
Objective	Determine the most clinically and cost-effective marker/index/ measure to monitor treatment in patients with OSAHS/OHS/COPD-OSAHS overlap syndrome.
Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikos The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
Condition or domain being studied	Obstructive sleep apnoea/hypopnoea syndrome is the most common form of sleep disordered breathing. The guideline will also cover obesity hypoventilation syndrome and COPD-OSAHS overlap syndrome (the coexistence of obstructive sleep apnoea/hypopnoea syndrome and chronic obstructive pulmonary disease).
Population	Inclusion: People being treated for OSAHS/OHS/ COPD-OSAHS overlap syndrome, stratified by: • Disease severity (mild vs moderate vs severe) • Condition (OSAHS/OHS/ COPD-OSAHS overlap syndrome) • Type of treatment (CPAP vs surgery vs positional modifiers vs oral devices) Severity: • Mild OSAHS: AHI >5 but <15 • Moderate OSAHS: AHI >/= 15 but <30 • Severe OSAHS: AHI >/= 30 When a mixed severity population is included the severity of the majority of the population will be used by taking the mean AHI of the patients included and the study will be downgraded for indirectness.

Intervention/Exposure/Test	• Using ESS (Epworth Sleepiness Scale) • Using AHI (Apnoea Hypopnea Index) • Using ODI (Oxygen desaturation index) • Using SAQLI (Calgary Sleep Apnea Quality of Life Index) • Using partner reported symptoms • Using hours of use • Using ABG based CO_2 monitoring (for OHS only) • Using transcutaneous CO_2 monitoring (for OHS only) Treatment to be adjusted during the period of measurements
Comparator/Reference standard/Confounding factors	Any of the above vs any other in isolation or combination
Types of study to be included	• RCTs Minimum follow-up 1 month
Other exclusion criteria	Non-English language studies. Conference abstracts
Context	-
Primary outcomes (critical outcomes)	• Generic or disease specific quality of life measures (continuous) • Mortality (dichotomous) All follow-up times will be included. Follow-up times will be grouped as: follow-up </=1 year and >1 year
Secondary outcomes (important outcomes)	• Sleepiness scores (continuous, e.g. Epworth) • Apnoea-Hypopnoea index (continuous) • Oxygen desaturation index (continuous) • CO_2 control (continuous) • Hours of use (adherence measure, continuous) • Minor adverse effects of treatment (rates or dichotomous) • Driving outcomes (continuous) • Neurocognitive outcomes (continuous) • Impact on co-existing conditions: ○ HbA1c for diabetes (continuous) ○ Cardiovascular events for cardiovascular disease (dichotomous) ○ Systolic blood pressure for hypertension (continuous) All follow-up times will be included. Follow-up times will be grouped as: follow-up </=1 year and >1 year
Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. EviBASE will be used for data extraction.

Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
Strategy for data synthesis	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). • GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. • WinBUGS will be used for network meta-analysis, if possible given the data identified. Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects.
Analysis of sub-groups	Subgroups that will be investigated if heterogeneity is present: • High risk occupational groups (for example heavy goods vehicle drivers) vs general population • Sleepiness – Epworth >9 vs Epworth 9 or less • Coexisting conditions – type 2 diabetes vs atrial fibrillation vs hypertension vs none • BMI – obese vs non-obese

Type and method of review	☒	Intervention
	☐	Diagnostic
	☐	Prognostic
	☐	Qualitative
	☐	Epidemiologic
	☐	Service Delivery
	☐	Other (please specify)
Language	English	
Country	England	
Anticipated or actual start date	NA – not registered on PROSPERO	
Anticipated completion date	NA – not registered on PROSPERO	
Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail SleepApnoHypo@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre	
Review team members	From the National Guideline Centre: Carlos Sharpin, Guideline lead Sharangini Rajesh, Senior systematic reviewer Audrius Stonkus, Systematic reviewer Emtiyaz Chowdhury (until January 2020), Health economist David Wonderling, Head of health economics Agnes Cuyas, Information specialist (till December 2019) Jill Cobb, Information specialist	
Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.	
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.	

Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10098
Other registration details	NA – not registered
Reference/URL for published protocol	NA – not registered
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
Keywords	-
Details of existing review of same topic by same authors	NA
Additional information	-
Details of final publication	www.nice.org.uk

Table 3: Health economic review protocol

Review question	**All questions – health economic evidence**
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded.

Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[34]

Inclusion and exclusion criteria

- If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile.
- If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded, then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile.
- If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.

Where there is discretion

The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'.
- Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the health economic analysis:

- The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

Sleep Apnoea search strategy 2 demonstration of efficacy

This literature search strategy was used for the following review;

- How should efficacy of treatment be demonstrated (for example, variable positive pressure titration device, oximetry, capnography or polysomnography titration)?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[34]

For more information, please see the Methods Report published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 4: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 6 July 2020	Exclusions Randomised controlled trials Systematic review studies Observational studies
Embase (OVID)	1974 – 6 July 2020	Exclusions Randomised controlled trials Systematic review studies Observational studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2020 Issue 7 of 12 CENTRAL to 2020 Issue 7 of 12	None
Epistemonikos (Epistemonikos Foundation)	Inception – 29 November 2018	None

Medline (Ovid) search terms

1.	exp Sleep Apnea Syndromes/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter/

10.	editorial/
11.	news/
12.	exp historical article/
13.	Anecdotes as Topic/
14.	comment/
15.	case report/
16.	(letter or comment*).ti.
17.	or/9-16
18.	randomized controlled trial/ or random*.ti,ab.
19.	17 not 18
20.	animals/ not humans/
21.	exp Animals, Laboratory/
22.	exp Animal Experimentation/
23.	exp Models, Animal/
24.	exp Rodentia/
25.	(rat or rats or mouse or mice).ti.
26.	or/19-25
27.	8 not 26
28.	(sleep* adj3 (tool* or index* or indic* or score* or scoring or scale*)).ti,ab.
29.	((spouse* or wife or wives or husband* or significant other* or partner* or family or families or care giver* or caregiver* or carer* or symptom*) adj (report* or observ* or watch* or note* or noting or hear* or listen*)).ti,ab.
30.	(out of hours or off hours).ti,ab.
31.	exp oximetry/ or capnography/ or polysomnography/
32.	(oximetry or capnogra* or capnometer or polysomnograph* or colorimetr* or conductometr* or potentiometr*).ti,ab.
33.	((carbon dioxide or CO2 or oxygen or O2) adj2 (monitor* or continuous*)).ti,ab.
34.	(blood gas adj2 (monitor* or continuous or test*)).ti,ab.
35.	Epworth Sleepiness Scale.ti,ab.
36.	Apnoea Hypopnea Index.ti,ab.
37.	Oxygen desaturation index.ti,ab.
38.	Calgary Sleep Apnea Quality of Life Index.ti,ab.
39.	(ESS or AHI or ODI or SQALI or ABG).ti,ab.
40.	or/28-39
41.	27 and 40
42.	Meta-Analysis/
43.	exp Meta-Analysis as Topic/
44.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
45.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
46.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
47.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
48.	(search* adj4 literature).ab.
49.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
50.	cochrane.jw.

51.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
52.	or/42-51
53.	randomized controlled trial.pt.
54.	controlled clinical trial.pt.
55.	randomi#ed.ti,ab.
56.	placebo.ab.
57.	randomly.ti,ab.
58.	Clinical Trials as topic.sh.
59.	trial.ti.
60.	or/53-59
61.	Epidemiologic studies/
62.	Observational study/
63.	exp Cohort studies/
64.	(cohort adj (study or studies or analys* or data)).ti,ab.
65.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
66.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
67.	Controlled Before-After Studies/
68.	Historically Controlled Study/
69.	Interrupted Time Series Analysis/
70.	(before adj2 after adj2 (study or studies or data)).ti,ab.
71.	exp case control study/
72.	case control*.ti,ab.
73.	Cross-sectional studies/
74.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
75.	or/61-74
76.	41 and (52 or 60 or 75)

Embase (Ovid) search terms

1.	exp Sleep Disordered Breathing/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter.pt. or letter/
10.	note.pt.
11.	editorial.pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.
14.	or/9-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15

17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/
20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	(rat or rats or mouse or mice).ti.
24.	or/16-23
25.	8 not 24
26.	(sleep* adj3 (tool* or index* or indic* or score* or scoring or scale*)).ti,ab.
27.	((spouse* or wife or wives or husband* or significant other* or partner* or family or families or care giver* or caregiver* or carer* or symptom*) adj (report* or observ* or watch* or note* or noting or hear* or listen*)).ti,ab.
28.	(out of hours or off hours).ti,ab.
29.	exp oximetry/ or exp capnometry/ or caponometer/ or polysomnography/
30.	(oximetry or capnogra* or capnometer or polysomnograph* or colorimetr* or conductometr* or potentiometr*).ti,ab.
31.	((carbon dioxide or CO2 or oxygen or O2) adj2 (monitor* or continuous*)).ti,ab.
32.	(blood gas adj2 (monitor* or continuous or test*)).ti,ab.
33.	Epworth Sleepiness Scale.ti,ab.
34.	Apnoea Hypopnea Index.ti,ab.
35.	Oxygen desaturation index.ti,ab.
36.	Calgary Sleep Apnea Quality of Life Index.ti,ab.
37.	(ESS or AHI or ODI or SQALI or ABG).ti,ab.
38.	or/26-37
39.	25 and 38
40.	systematic review/
41.	meta-analysis/
42.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
43.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
44.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
45.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
46.	(search* adj4 literature).ab.
47.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
48.	cochrane.jw.
49.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
50.	or/40-49
51.	random*.ti,ab.
52.	factorial*.ti,ab.
53.	(crossover* or cross over*).ti,ab.
54.	((doubl* or singl*) adj blind*).ti,ab.
55.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
56.	crossover procedure/
57.	single blind procedure/

58.	randomized controlled trial/
59.	double blind procedure/
60.	or/51-59
61.	Clinical study/
62.	Observational study/
63.	family study/
64.	longitudinal study/
65.	retrospective study/
66.	prospective study/
67.	cohort analysis/
68.	follow-up/
69.	cohort*.ti,ab.
70.	68 and 69
71.	(cohort adj (study or studies or analys* or data)).ti,ab.
72.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
73.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
74.	(before adj2 after adj2 (study or studies or data)).ti,ab.
75.	or/61-67,70-74
76.	exp case control study/
77.	case control*.ti,ab.
78.	cross-sectional study/
79.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
80.	or/75-79
81.	39 and (50 or 60 or 80)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Sleep Apnea Syndromes] explode all trees
#2.	(sleep* near/4 (apnea* or apnoea* or hypopnea* or hypopnoea*)):ti,ab
#3.	(sleep* near/4 disorder* near/4 breath*):ti,ab
#4.	(OSAHS or OSA or OSAS):ti,ab
#5.	(obes* near/3 hypoventil*):ti,ab
#6.	pickwick*:ti,ab
#7.	(OR #1-#6)
#8.	(sleep* near/3 (tool* or index* or indic* or score* or scoring or scale*)):ti,ab
#9.	((spouse* or wife or wives or husband* or significant other* or partner* or family or families or care giver* or caregiver* or carer* or symptom*) near/1 (report* or observ* or watch* or note* or noting or hear* or listen*)):ti,ab
#10.	(out of hours or off hours):ti,ab
#11.	MeSH descriptor: [Oximetry] explode all trees
#12.	MeSH descriptor: [Capnography] this term only
#13.	MeSH descriptor: [Polysomnography] this term only
#14.	(oximetry or capnogra* or capnometer or polysomnograph* or colorimetr* or conductometr* or potentiometr*):ti,ab
#15.	((carbon dioxide or CO2 or oxygen or O2) near/2 (monitor* or continuous*)):ti,ab
#16.	(blood gas near/2 (monitor* or continuous or test*)):ti,ab

#17.	Epworth Sleepiness Scale:ti,ab
#18.	Apnoea Hypopnea Index:ti,ab
#19.	Oxygen desaturation index:ti,ab
#20.	Calgary Sleep Apnea Quality of Life Index:ti,ab
#21.	(ESS or AHI or ODI or SQALI or ABG):ti,ab
#22.	(OR #8-#21)
#23.	#7 and #22

Epistemonikos search terms

1.	((title:((sleep apnea syndromes) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (disorder* OR breath*)) OR (OSAHS OR OSA OR OSAS) OR (obes* AND hypoventil*) OR pickwick*) OR abstract:((sleep apnea syndromes) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (disorder* OR breath*)) OR (OSAHS OR OSA OR OSAS) OR (obes* AND hypoventil*) OR pickwick*)))

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to sleep apnoea population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA – this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics and quality of life studies.

B.2.1 Health economic studies strategy

Table 5: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 6 July 2020	Exclusions Health economics studies
Embase	2014 – 6 July 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

	exp Sleep Apnea Syndromes/
1.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
2.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
3.	(OSAHS or OSA or OSAS).ti,ab.
4.	(obes* adj3 hypoventil*).ti,ab.
5.	pickwick*.ti,ab.
6.	or/1-6
7.	limit 7 to English language

8.	letter/
9.	editorial/
10.	news/
11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/9-16
17.	randomized controlled trial/ or random*.ti,ab.
18.	17 not 18
19.	animals/ not humans/
20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice).ti.
25.	or/19-25
26.	8 not 26
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/28-43
44.	27 and 44

Embase (Ovid) search terms

1.	exp Sleep Disordered Breathing/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.

6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter.pt. or letter/
10.	note.pt.
11.	editorial.pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.
14.	or/9-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/
20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	(rat or rats or mouse or mice).ti.
24.	or/16-23
25.	8 not 24
26.	health economics/
27.	exp economic evaluation/
28.	exp health care cost/
29.	exp fee/
30.	budget/
31.	funding/
32.	budget*.ti,ab.
33.	cost*.ti.
34.	(economic* or pharmaco?economic*).ti.
35.	(price* or pricing*).ti,ab.
36.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
37.	(financ* or fee or fees).ti,ab.
38.	(value adj2 (money or monetary)).ti,ab.
39.	or/26-38
40.	25 and 39

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Sleep Apnea Syndromes EXPLODE ALL TREES
#2.	(sleep* adj4 (apn?ea* or hypopn?ea*))
#3.	(sleep* adj4 disorder* adj4 breath*)
#4.	(OSAHS or OSA or OSAS)
#5.	(obes* adj3 hypoventil*)
#6.	(pickwick*)

#7.	#1 OR #2 OR #3 OR #4 OR #5 OR #6

B.2.2 Quality of life studies strategy

Table 6: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	1946 – 26 November 2019	Exclusions Quality of life studies
Embase	1974 – 26 November 2019	Exclusions Quality of life studies

Medline (Ovid) search terms

1.	exp Sleep Apnea Syndromes/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter/
10.	editorial/
11.	news/
12.	exp historical article/
13.	Anecdotes as Topic/
14.	comment/
15.	case report/
16.	(letter or comment*).ti.
17.	or/9-16
18.	randomized controlled trial/ or random*.ti,ab.
19.	17 not 18
20.	animals/ not humans/
21.	exp Animals, Laboratory/
22.	exp Animal Experimentation/
23.	exp Models, Animal/
24.	exp Rodentia/
25.	(rat or rats or mouse or mice).ti.
26.	or/19-25
27.	8 not 26
28.	quality-adjusted life years/
29.	sickness impact profile/
30.	(quality adj2 (wellbeing or well being)).ti,ab.
31.	sickness impact profile.ti,ab.

32.	disability adjusted life.ti,ab.
33.	(qal* or qtime* or qwb* or daly*).ti,ab.
34.	(euroqol* or eq5d* or eq 5*).ti,ab.
35.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
36.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
37.	(hui or hui1 or hui2 or hui3).ti,ab.
38.	(health* year* equivalent* or hye or hyes).ti,ab.
39.	discrete choice*.ti,ab.
40.	rosser.ti,ab.
41.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
42.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
43.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
44.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
45.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
46.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
47.	or/28-46
48.	27 and 47

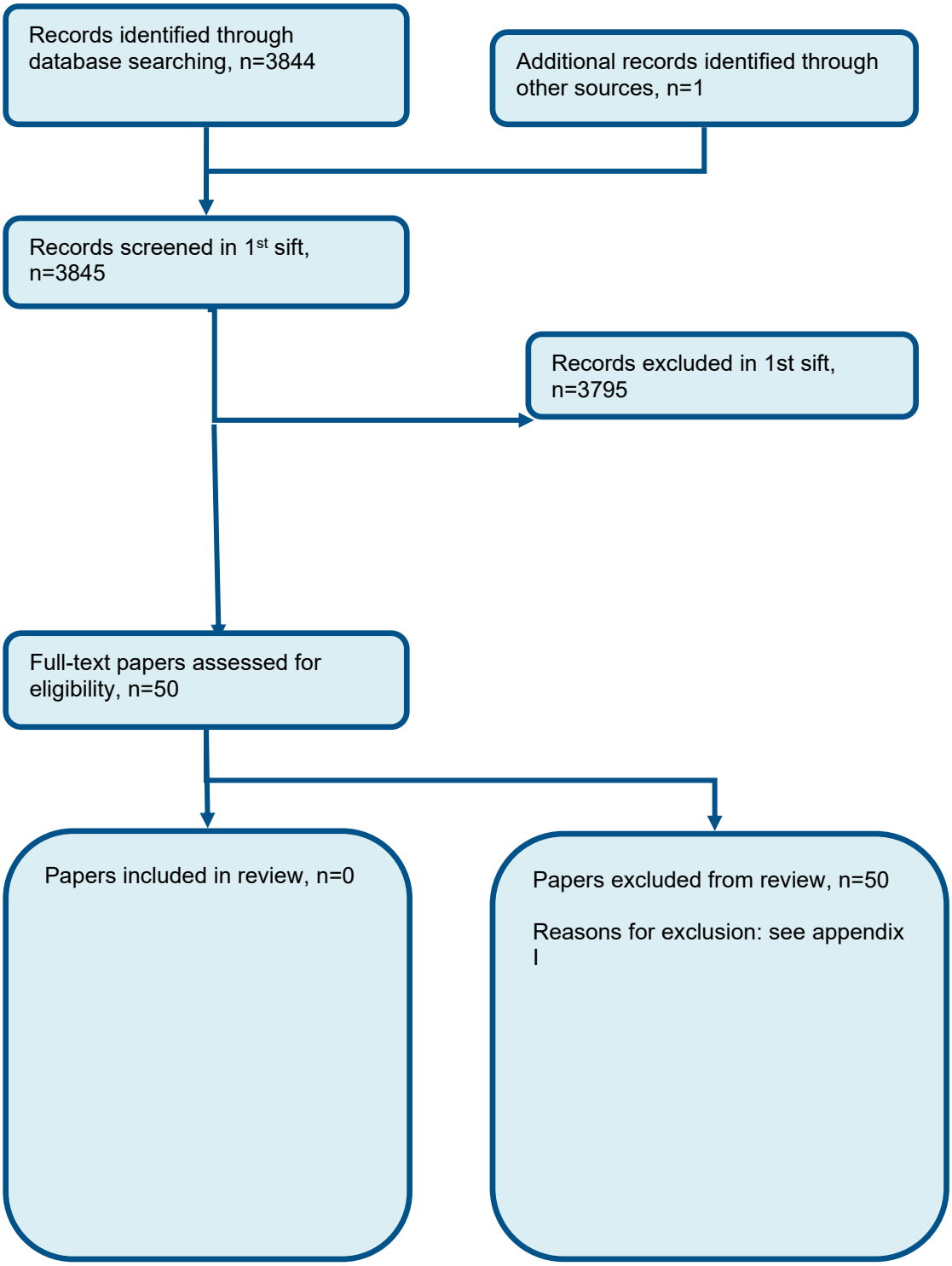
Embase (Ovid) search terms

1.	exp Sleep Disordered Breathing/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter.pt. or letter/
10.	note.pt.
11.	editorial.pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.
14.	or/9-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/
20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	(rat or rats or mouse or mice).ti.
24.	or/16-23

25.	8 not 24
26.	quality adjusted life year/
27.	"quality of life index"/
28.	short form 12/ or short form 20/ or short form 36/ or short form 8/
29.	sickness impact profile/
30.	(quality adj2 (wellbeing or well being)).ti,ab.
31.	sickness impact profile.ti,ab.
32.	disability adjusted life.ti,ab.
33.	(qal* or qtime* or qwb* or daly*).ti,ab.
34.	(euroqol* or eq5d* or eq 5*).ti,ab.
35.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
36.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
37.	(hui or hui1 or hui2 or hui3).ti,ab.
38.	(health* year* equivalent* or hye or hyes).ti,ab.
39.	discrete choice*.ti,ab.
40.	rosser.ti,ab.
41.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
42.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
43.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
44.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
45.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
46.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
47.	or/26-46
48.	25 and 47

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of demonstration of efficacy



Appendix D: Clinical evidence tables

No studies included in the review.

Appendix E: Forest Plots

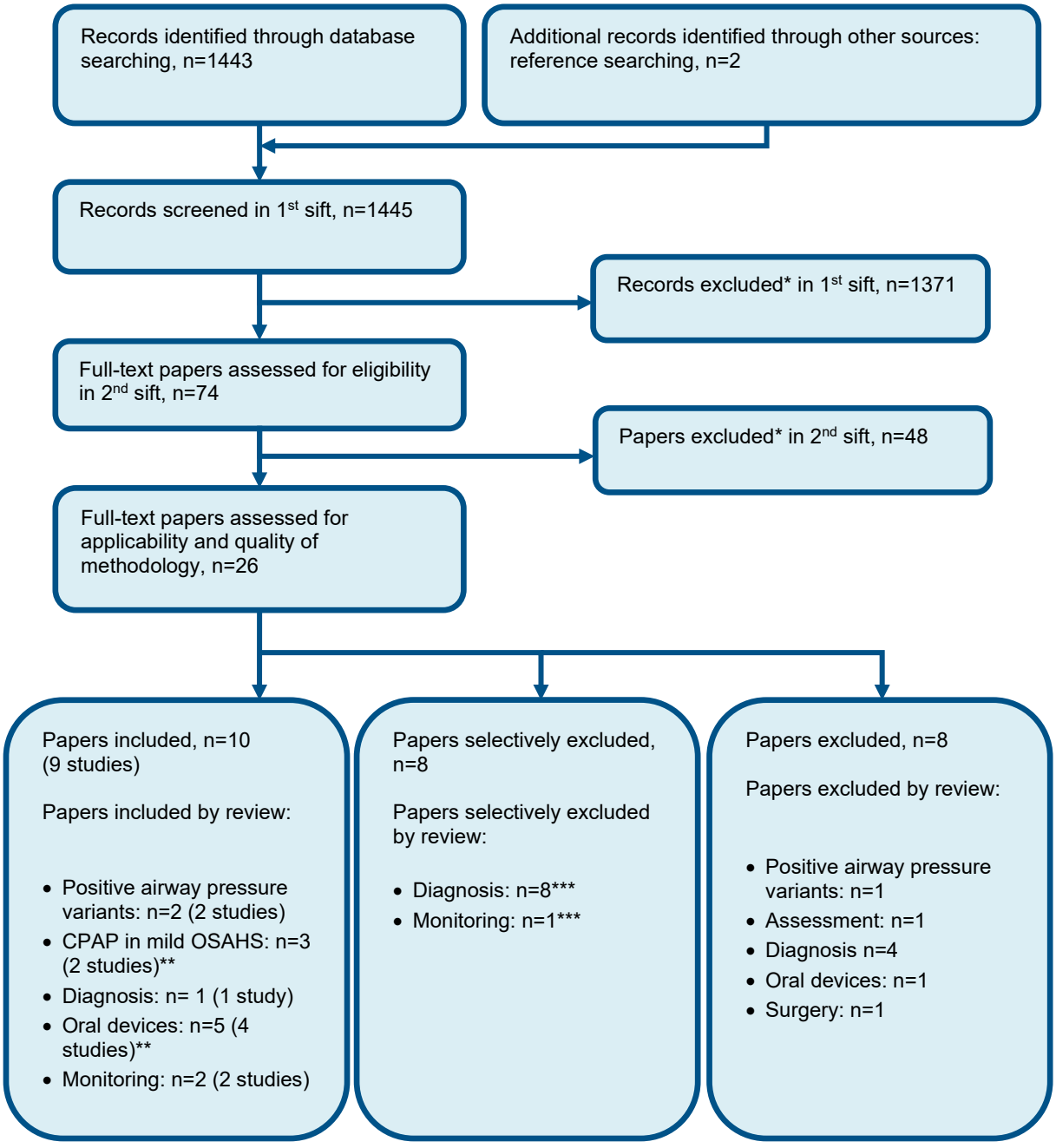
No studies included in the review.

Appendix F: GRADE tables

No studies included in the review.

Appendix G: Health economic evidence selection

Figure 2: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language
** Two studies (in three papers) were included for two different questions
*** One study was considered for two different questions

Appendix H: Excluded studies

H.1 Excluded clinical studies

Table 7: Studies excluded from the clinical review

Study	Exclusion reason
Ahmed 2010[1]	Literature review
Alvarez 2017[2]	Inappropriate intervention- study assessed reliability and accuracy of automated scoring of respiratory events provided by a home non-invasive ventilation device and of manual scoring using available flow and pressure traces obtained from these devices as compared with the results obtained by manual polygraphy scoring.
Arya 2014[3]	Inappropriate intervention- study evaluated patient's post-treatment subjective perception of the effectiveness of CPAP and mandibular advancement devices.
Baessler 2013[4]	Inappropriate intervention- study aimed to assess if treatment for sleep apnoea by CPAP will affect levels of inflammatory markers.
Baltaxe 2020[5]	Inappropriate population- people with chronic respiratory failure.
Berg 2020[6]	Inappropriate intervention- Friedman score. The study investigated the association between Friedman tongue position score (Friedman score) and CPAP or MAS compliance and AHI improvement in patients with non-severe OSA.
Bergeron 2018[7]	Inappropriate population – children
Budhiraja 2017[9]	Inappropriate intervention and comparison- CPAP vs no CPAP.
Brostrom 2018[8]	Validation of two questionnaires to measure shared decision-making during CPAP initiation.
Caminero 1997[10]	Not in English
Carrera 1998[11]	Study aimed to evaluate the impact upon the therapeutic decision of the definition of hypopnoea most commonly used in different labs, which is a reduction in airflow of 50% or more, accompanied by decrease of blood oxygen saturation of 4%
Choi 2016[12]	Inappropriate intervention- the purpose of the meta-analysis was to identify predictors of success after Uvulopalatopharyngoplasty.
Choi 2000[13]	Inappropriate intervention-study looked at 10 different derivatives of all night oximeter tracings in patients with OSA and compared their ability to predict the improvement in subjective sleepiness after 6 months of nCPAP therapy.
Choi 2001[14]	Inappropriate intervention- study aimed to assess changes in nasal continuous positive airway pressure (nCPAP) pressure requirements across time in OSA, and whether routine re titrations are indicated.

Study	Exclusion reason
Damiani 2013[15]	Inappropriate intervention-study compared titration effectiveness of two auto CPAP devices using different flow-based algorithms in patients with OSA.
Deng 2017[16]	Not in English
Ebben 2017[17]	Inappropriate intervention- the goal of the study was to develop new predictive models of CPAP that take into account the style of mask interface.
Georges 2013[18]	Conference abstract
Georges 2015[19]	Inappropriate intervention – study assessed validity and accuracy of AHI provided by home ventilators vs data scored manually during polysomnography in subjects on non-invasive ventilation for OHS.
Inoue 2016[20]	Study aimed to examine the relationship between subjective and objective sleepiness and to determine whether baseline objective sleepiness severity predicts the response to modafinil treatment for residual sleepiness in obstructive sleep apnoea syndrome patients.
Javaheri, 2020[21]	CPAP vs sham CPAP. To be considered for inclusion in CPAP in mild review.
Jonas 2017[22]	Inappropriate intervention- screening for obstructive sleep apnoea in adults
Kunisaki 2016[23]	Systematic review screened for relevant references.
Lee 2013[24]	Inappropriate intervention- the study aimed to develop an equation for optimal CPAP pressure based on data from Asian patients.
Leger 2016[25]	Inappropriate intervention- study evaluated the effectiveness of a novel device NOWAPI designed to assess compliance remotely in conjunction with any CPAP machine.
Masa 2011[26]	Inappropriate population- patients with suspected intermediate or high sleep apnoea and hypopnea syndrome.
Masa 2016[27]	Inappropriate intervention- the objective of the study was to assess the medium-term treatment efficacy of adding supplemental oxygen therapy to commonly prescribed treatment modalities in OHS.
Masa 2013[28]	Inappropriate population- patients with suspected OSA. Inappropriate intervention- home respiratory polygraphy vs polygraphy for diagnosis and treatment
Masa 2019[29]	Inappropriate intervention. Study included in CPAP in OHS review.
Masdeu 2010[30]	Study examined agreement among multiple sleep clinicians when presented with clinical data plus the full tracings and data obtained from unattended limited monitoring or full polysomnography.
McArdle 2015[31]	Inappropriate intervention-study assessed the efficacy of female specific auto-titrating continuous positive airway pressure (CPAP)

Study	Exclusion reason
	algorithm in pre-menopausal women relative to a standard auto titrating algorithm.
Mulgrew 2007[32]	Inappropriate intervention- conventional polysomnography vs ambulatory algorithm for titration of CPAP in patients with a high probability of moderate to severe OSA.
Nannapaneni 2014[33]	Retrospective chart review of OSA patients on PAP. The review evaluated the clinical utility of annual face to face follow-up visits in this group.
Ng 2019[35]	Inappropriate intervention- study aimed to evaluate the accuracy of the Berlin questionnaire in patients with suspected OSAS
Papadakis 2018[36]	Inappropriate population- children with snoring and tonsillar hypertrophy (4-10 years old)
Patout 2019[37]	Inappropriate intervention and comparison- study compared the physiological effectiveness of non-invasive ventilation set-up guided by polysomnography to limited respiratory monitoring and nurse-led titration in patients with COPD-obstructive sleep apnoea overlap.
Pilz 2000[38]	Inappropriate intervention- CPAP vs auto CPAP
Quintas-Neves 2016[39]	Systematic review aimed to assess and characterise the impact that different types of bariatric surgery have on obese OSA patients.
Rodrigues Thuler 2002[40]	Not in English
Rosen 2012[41]	Inappropriate intervention- home based portable monitoring and auto CPAP vs gold standard lab based polysomnography and CPAP titration for diagnosis and treatment of OSA.
Rosen 2015[42]	Inappropriate population - 5 to 9 year old habitually snoring children. Inappropriate intervention- adenotonsillectomy.
Sanchez-Quiroga 2018[43]	Inappropriate population-patients with suspected OSA. Inappropriate intervention- primary care physician's vs in lab specialised management.
Saur 2017[44]	Systematic review – screened for relevant references.
Schobel 2018[45]	Study aimed to investigate whether Peripheral arterial tonometry might be a useful tool to improve diagnostic work-up in OSA patients by better identifying residual sleep-disordered breathing due to insufficient CPAP-adjustment.
Suen 2019[46]	Narrative review
Sutherland 2014[47]	Inappropriate intervention- study aimed to assess the relationship between therapeutic CPAP pressure and mandibular advancement splints treatment response in treatment naïve OSA patients.

Study	Exclusion reason
Suzuki 2008[48]	Inappropriate intervention- the study evaluated the need for post-operative monitoring of oesophageal pressure in adult OSAHS patients who undergo tonsillectomy with UPPP.
Tam 2014[49]	Systematic review investigating the utility of outcome measures other than AHI for patients with OSA undergoing surgery.
Tedeschi 2013[50]	Inappropriate population- patients with high suspicion of OSA. Inappropriate intervention- home unattended portable monitoring and auto CPAP vs attended in lab program
Trikalinos 2007[51]	Not relevant intervention – technology assessment programme (USA) document on home diagnosis of obstructive sleep apnoea-hypopnoea syndrome.

H.2 Excluded health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2003 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below:

None.