BMJ Open

Apnoea–hypopnoea indices determined via continuous positive airway pressure (AHI-CPAP$_{flow}$) versus those determined by polysomnography (AHI-PSG$_{gold}$): a protocol for a systematic review and meta-analysis

Fanny Bertelli,[1,2] Carey Meredith Suehs ,[3,4] Jean Pierre Mallet,[3,5] Marie Caroline Rotty,[2] Jean Louis Pepin,[6] Frédéric Gagnadoux ,[7] Eric Matzner-Lober,[8] A Bourdin,[2,3,5] Nicolas Molinari,[1,4] Dany Jaffuel[3,5,9]

For numbered affiliations see end of article.

Correspondence to
Dr Carey Meredith Suehs; careysuehs@protonmail.com

ABSTRACT

Introduction To date, continuous positive airway pressure (CPAP) remains the cornerstone of obstructive sleep apnoea treatment. CPAP data describing residual sleep-disordered breathing events (ie, the CPAP-measured apnoea–hypopnoea indices (AHI-CPAP$_{flow}$)) is difficult to interpret because it is an entirely different metric than the polysomnography (PSG) measured AHI gold standard (AHI-PSG$_{gold}$). Moreover, manufacturer definitions for apnoea and hypopnoea are not only different from those recommended for PSG scoring, but also different between manufacturers. In the context of CPAP initiation and widespread telemedicine at home to facilitate sleep apnoea care, there is a need for concrete evidence that AHI-CPAP$_{flow}$ can be used as a surrogate for AHI-PSG$_{gold}$.

Methods and analysis No published systematic review and meta-analysis (SRMA) has compared the accuracy of AHI-CPAP$_{flow}$ against AHI-PSG$_{gold}$ and the primary objective of this study is therefore to do so using published data. The secondary objectives are to similarly evaluate other sleep disordered breathing indices and to perform subgroup analyses focusing on the inclusion/exclusion of central apnoea patients, body mass index levels, CPAP device brands, pressure titration modes, use of a predetermined and fixed pressure level or not, and the impact of a 4% PSG desaturation criteria versus 3% PSG on accuracy. The Preferred Reporting Items for SRMA protocols statement guided study design. Randomised controlled trials and observational studies of adult patients (≥18 years old) treated by a CPAP device will be included. The CPAP intervention and PSG comparator must be performed synchronously. PSGs must be scored manually and follow the American Academy of Sleep Medicine guidelines (2007 AASM criteria or more recent). To assess the risk of bias in each study, the Quality Assessment of Diagnostic Accuracy Studies 2 tool will be used.

Ethics and dissemination This protocol received ethics committee approval on 16 July 2020 (IRB_MTP_2020_07_2020000404) and results will be disseminated via peer-reviewed publications.

Strengths and limitations of this study

► This will be the first systematic review and meta-analysis to compare published data for apnoea–hypopnoea indices determined via continuous positive airway pressure devices (AHI-CPAP$_{flow}$) versus the gold standard determined by polysomnography (AHI-PSG$_{gold}$) in terms of accuracy.

► Given that AHI-CPAP$_{flow}$ and AHI-PSG$_{gold}$ are often used interchangeably, the results of this study will fill a pertinent knowledge gap particularly suited to the context of in-home CPAP initiation and the associated increase in telemedicine.

► This study will also evaluate how different parameters (central apnoea inclusion/exclusion, body mass index, oxygen saturation thresholds and device-specific summary measures) affect accuracy, and may therefore impact practice, study design or analyses.

► The main limitations of this study, as for most systematic reviews and meta-analyses, are likely to result from a paucity of eligible publications and their methodological quality.

► In the context of patients requiring long-term CPAP-management, why a single night point estimate (like AHI-PSG$_{gold}$) is considered as a gold standard rather than longitudinally repeated measurements (like AHI-CPAP$_{flow}$) requires consideration.

PROSPERO/Trial registration numbers CRD42020159914/NCT04526366; Pre-results

INTRODUCTION
Description of the condition
Nearly 1 billion adults aged 30–69 years are affected by obstructive sleep apnoea (OSA), including 425 million with moderate to severe OSA requiring treatment according to

current recommendations.[1] In 2020, continuous positive airway pressure (CPAP) remains the cornerstone of OSA treatment.[2 3]

Several studies have shown that CPAP therapy can effectively reduce upper airway obstruction with subsequent improvements in daytime sleepiness, sleep quality and quality of life.[3–5] OSA treatment with CPAP has been demonstrated to be cost-effective in various countries with different healthcare systems.[6–10] The treatment and monitoring of OSA is therefore gaining recognition as an increasingly important public health issue. Considering the number of patients to be diagnosed and monitored on a long-term basis, there is a need for simplified diagnostic and monitoring methods. Because initiation of CPAP at home demonstrated equivalent effects on patient outcomes when compared with an in-laboratory titration approach,[3] the 2019 American Academy of Sleep Medicine (AASM) guidelines recommended that CPAP therapy be initiated using either auto-CPAP at home or in-laboratory CPAP titration in adults with OSA and no significant comorbidities.[2] In addition, it was suggested that clinicians use telemonitoring-guided interventions during the initial period of CPAP therapy in adults with OSA.[2]

Description of the interventions

In clinical practice, to summarise data and conclude with an OSA diagnosis, the high-dimensional data contained within a polysomnography (PSG) is reduced down to the number of apnoea or hypopnoea events occurring per hour, that is the 'apnoea–hypopnoea index (AHI)'. As underlined by the 2013 American Thoracic Society Statement, CPAP data describing residual sleep-disordered breathing events are difficult to interpret.[11] CPAP devices rely only on a reduction in airflow for determining AHI and a recording time (corresponding to the length of time the device is turned on associated with a measurable breathing signal irrespective of the sleep/awake patient status), whereas PSG includes more data such as respiratory flow patterns, electroencephalogram (EEG) arousal, total sleep time, respiratory effort and oxyhaemoglobin desaturation measures. AHI determined by CPAP data (hereafter termed 'AHI-CPAP$_{flow}$' corresponding to the ratio between an airflow reduction and a recording time) is a different metric than the gold standard AHI determined by PSG (hereafter termed 'AHI-PSG$_{gold}$' corresponding to an airflow reduction associated with EEG arousal and/or oxyhaemoglobin desaturation and total sleep time). The extent to which the AHI-CPAP$_{flow}$ can be used interchangeably with or as a surrogate for AHI-PSG$_{gold}$ is unclear. Moreover, the manufacturer definitions for apnoea, hypopnoea and flow limitations are not only different from those recommended for PSG scoring, but also different among manufacturers (online supplementary appendix 1).[11–13] Depending on how a given manufacturer defines an event, the PSG percentage of desaturation and event considered, the differences in

total sleep time versus recording time, AHI-CPAP$_{flow}$ can theoretically overestimate or underestimate AHI-PSG$_{gold}$.[11]

Why it is important to do this review?

Considering the increasing use of in-home auto-CPAP titration and associated telemedicine initiatives (both for titration and long-term monitoring), the issue of whether or not AHI-CPA$_{flow}$ is a valid surrogate for AHI-PSG$_{gold}$ should be resolved.

Objectives

To date, no published systematic review and meta-analysis (SRMA) has compared AHI-CPAP$_{flow}$ and AHI-PSG$_{gold}$. Therefore, the primary objective of this study is to compare published data for AHI-PSG$_{gold}$ and AHI-CPAP$_{flow}$ in patients treated by CPAP. The secondary objectives are to evaluate, in a manner similar to the primary objective, data for apnoea index (AI), hypopnoea index (HI), respiratory disturbance index (RDI) and respiratory effort-related arousals (RERAs) and to perform subgroup analyses focusing on the inclusion/exclusion of central apnoea patients, body mass index (BMI) levels, CPAP device brands, pressure titration modes, use of a predetermined and fixed pressure level or not, and the impact of a 4% PSG desaturation criteria versus 3% PSG on index accuracy.

METHODS AND ANALYSIS

The Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols statement guided the design of this protocol (see online supplementary appendix 2 for the checklist).[14 15] The study is sponsored by the University Hospitals of Montpellier, Montpellier, France. Registration was submitted to PROSPERO (https://www.crd.york.ac.uk/PROSPERO/) on 6 February 2020, and first published on 28 April 2020, with updates on 21 August 2020 and 23 March 2021. Any changes or amendments made to the protocol will be tracked and dated on PROSPERO.

Study eligibility criteria

Detailed eligibility criteria were designed to take into account the relevant patient population, interventions, comparators, outcomes and statistical analysis/study types.[16]

Patient population

Studies reporting results for adult patients (≥18 years old) treated by a CPAP device will be included.

Intervention/comparator

The intervention of interest is the measure of residual sleep-disordered breathing events by a CPAP device during a given night. The comparator of interest is the simultaneous measure of the residual sleep-disordered breathing events by a PSG during the same night of CPAP treatment. The CPAP intervention and PSG comparator

must be performed synchronously, and the CPAP device name and series must be mentioned in the study.

Outcome measures

The main outcome is the mean difference between $AHI\text{-}CPAP_{flow}$ and $AHI\text{-}PSG_{gold}$ measures (and the associated SD for the mean difference). Secondary outcomes include analogous results for other frequently co-occurring indices: AI, HI, RDI or RERA.

PSG scoring must be manually performed by a qualified physician or technician using 2007 AASM recommended/alternative criteria or more recent AASM criteria. The scoring criteria used in the study must be detailed. In particular, oxyhaemoglobin desaturation level (3% or 4%), and apnoea and hypopnoea scoring criteria must be mentioned.

Statistical analyses/study types

The primary analysis will synthesise estimates for the average of individual differences between measures made via PSG minus those made via CPAP. Such individual differences are most conveniently provided by Bland-Altman test results. However, any of the following analysis types, comparing the aforementioned PSG versus CPAP data, are also of interest: scatter plots, correlation coefficients, differences in central tendency or any type of conformity test. We will include randomised controlled trials and observational studies published in English. Case series will be included but not case reports. Meta-analyses will be excluded. In general, because we are focused on a within-patient comparison, we expect more observational studies than randomised controlled trials. In addition, each arm of a randomised trial can be considered an independent estimate of PSG–CPAP differences.

Information sources

We will perform a search in MEDLINE (PubMed), Embase, Web of Science and the Google Scholar database. Additional studies will be sought by manually checking the references of included studies and relevant reviews. Searches will be restricted to publications appearing from 2007 onwards (to the day of search results, with an update just before publication). A supplementary search for ongoing/unpublished trials will be made using the https://www.clinicaltrials.gov/ website.

Search strategy

Our search strategy was developed using the following key concepts: AHI, CPAP, PSG and adults. For each key concept, we will also use acronyms such as PSG or current terms used by specialists as search terms. These search terms will be combined using Boolean operators "AND" and "OR". The full electronic strategy is presented in the online supplementary appendix 3.

Study selection

Figure 1 summarises the study selection process. At least two authors will screen the titles and abstracts yielded from the literature searches, independently and in duplicate. The exclusion criteria listed in box 1 will be used and sequentially deployed so as to help populate the future study flowchart (based on figure 1). Articles, which appear to meet our inclusion criteria, will be downloaded in full. Disagreements will be resolved by consensus or a third review author. We will identify and exclude duplicates, and collate multiple reports of the same study.

Data collection

Two reviewers will use pretested data collection forms to collect data independently and in duplicate. Disagreements will be resolved by consensus or by a third reviewer/author.

The data of interest include those for describing the articles analysed, and those pertaining to outcomes, and will be managed in spreadsheets (Microsoft Excel). In the first group, the following will be tabulated: author(s), journal, year of publication, study type (eg, retrospective cohort, randomised controlled trial), population size(s), mean BMI for the population(s), a short description of the OSA population, the AASM criteria applied during the study (eg, 2007 or 2012), the oxyhaemoglobin desaturation level used (3% or 4%), major exclusion criteria, device information (brand, model and mode if pertinent), the pressure mode used (eg, fixed, automatic, manual) and information concerning predetermined pressure levels used (eg, physician-determined vs CPAP-determined). Outcomes are a minima those issuing from Bland-Altman analyses (mean difference (PSG_{gold} minus $CPAP_{flow}$) and the associated SD, SE, lower limit of agreement and upper limit of agreement for each of the following: AHI, AI, HI, RDI and RERA).

Missing data

Where necessary, we will contact the authors of studies to obtain missing data/information. In cases where authors are unreachable or for some reason missing data cannot be provided, but a way to glean such data is available (for eg, from the pixels of a scatter plot), such will be tolerated and indicated. In the discussion section of the review, the potential impact of any missing data will be discussed.

The Quality Assessment of Diagnostic Accuracy Studies 2 tool[17] will be used to assess full article quality and risk of bias. The latter is a specialised tool for diagnostic accuracy studies that addresses four domains (patient selection, index test, reference standard, and flow and timing), assessing the risk of bias for each. Two independent reviewers will assess the methodological quality of selected articles and disagreements about scoring will be resolved by a third reviewer.

If a sufficient number of studies are available (at least ten is suggested), a funnel plot will be used to graphically summarise the extent of publication bias. Additionally, the Egger test[18] will be used to measure funnel plot asymmetry with statistical significance set at $p < 0.05$.

The overall quality of findings will be assessed using the Grading of Recommendations Assessment, Development and Evaluation system.
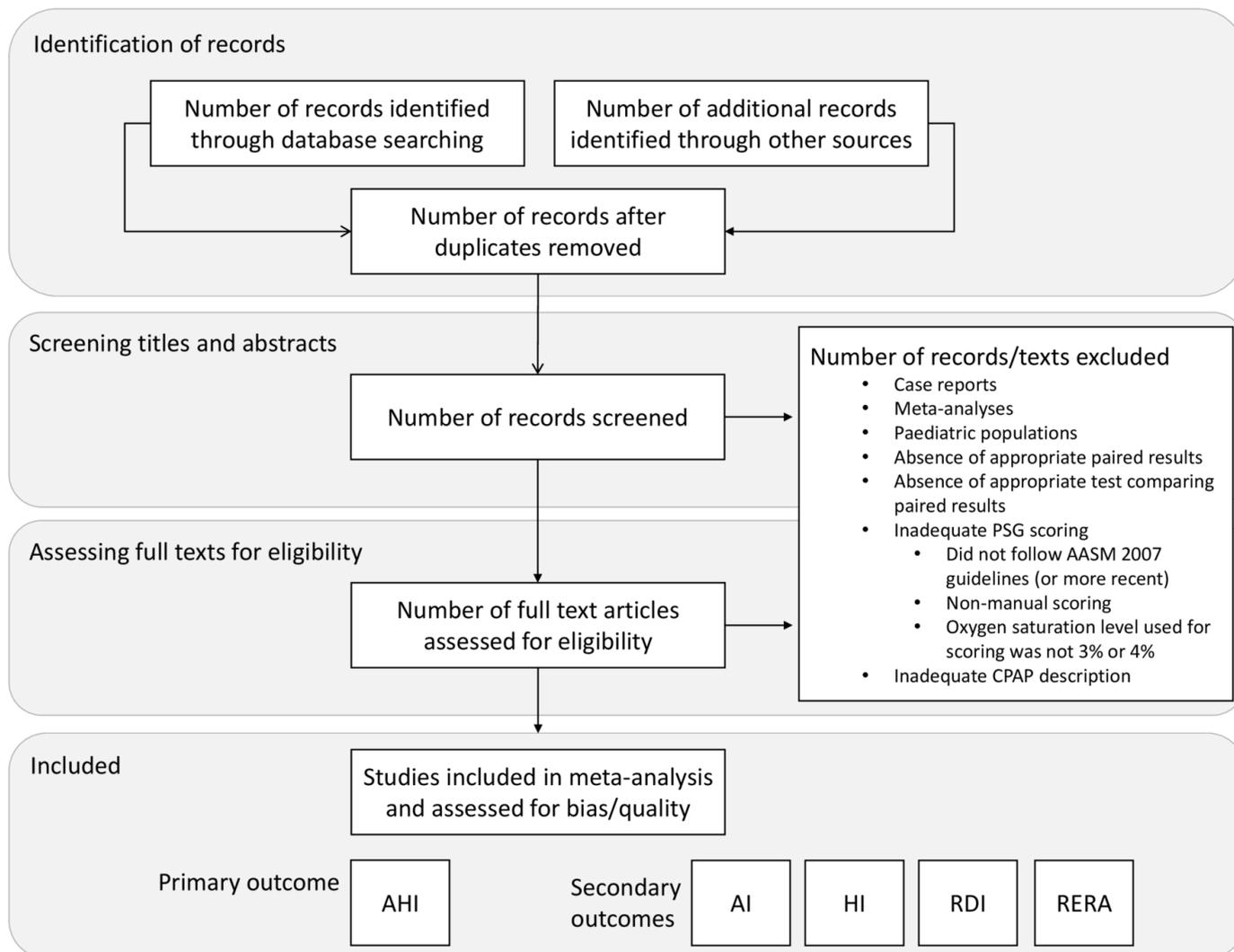
Figure 1 The proposed study flowchart. AASM, American Academy of Sleep Medicine; AHI, apnoea–hypopnoea index; AI, apnoea index; CPAP, continuous positive airway pressure; HI, hypopnoea index; PSG, polysomnography; RDI, respiratory disturbance index; RERA, respiratory effort related arousal.

Data synthesis

If we identify a sufficient number of studies with homogeneous populations and characteristics, we will carry out meta-analyses of primary (AHI-CPAP$_{flow}$ vs AHI-PSG$_{gold}$) and secondary outcomes using parametric analyses. In case of a low number of studies or studies with small sample sizes, we will adjust the methods and estimators used (regardless of the number and quality of studies found, a systematic narrative review will be written). Differences in means (PSG$_{gold}$ minus CPAP$_{flow}$) will be evaluated both as directional differences and as absolute values. Meta-analysis will be performed using a random-effects model to avoid homogeneity problems between studies results. The heterogeneity among studies included in each meta-analysis will be assessed with the Q-test statistic.

Analyses will be performed in the R statistical programming environment.[19] Meta-analysis will be conducted using the meta package.[20]

Subgroup analysis and investigation of heterogeneity

Subgroup analyses will be performed as described in the secondary objectives. If a sufficient number of studies are included in this review, we will perform sensitivity analyses to assess the consistency and robustness of our results.

Patient and public involvement

The present work is based on a review of relevant studies and does not include original patient data. Therefore, patients or public are not involved in this review protocol.

Protocol amendments

Any amendments to this protocol will be reported in PROSPERO with the justification and date of modification.

ETHICS AND DISSEMINATION

This protocol was approved by the Internal Review Board at the Montpellier University Hospitals on 16 July 2020

Box 1   Sequential exclusion process

All (full scientific) study designs and publication types written in English and reporting Bland-Altman test results (or other tests suggesting the presence of the required data) between simultaneous, paired, polysomnography (PSG)-derived and continuous positive airway pressure (CPAP)-derived data describing sleep disordered breathing. To achieve this, the following exclusion criteria will be sequentially applied to search results:

► Duplicates.
► Does not refer to a full scientific article (eg, case reports are excluded).
► Meta-analysis.
► Paediatric populations (populations <18 years are excluded).
► Absence of appropriate paired results: synchronised PSG-derived and CPAP-derived data must be reported for ≥1 of the following measures: apnoea–hypopnoea indices, apnoea index, hypopnoea index, respiratory disturbance index and respiratory effort related arousals.
► Absence of appropriate test comparing paired results: the study must use ≥1 of the following tests to compare the previously mentioned PSG-derived versus CPAP-derived data: a Bland-Altman or correlation test, other conformity tests or tests of differences in central tendency.
► Inappropriate PSG scoring 1: PSG-derived variables must be coded following the American Academy of Sleep Medicine 2007 (or more recent) guidelines.
► Inappropriate PSG scoring 2: PSG-derived variables must be scored manually.
► Inappropriate PSG scoring 3: oxygen desaturation level used for scoring must be mentioned and at 3% or 4%.
► Inappropriate CPAP description: brand/device names must be mentioned.

(IRB_MTP_2020_07_202000404). The results of this study will be disseminated via peer-reviewed publications.

DISCUSSION

Because AHI-CPAP$_{flow}$ is a different metric than the AHI-PSG$_{gold}$, the extent to which the AHI-CPAP$_{flow}$ can be used interchangeably with or as a surrogate for AHI-PSG$_{gold}$ is unclear. Furthermore, differences in apnoea/hypopnoea definitions between manufacturers are a potential additional limitation to the accuracy of the AHI-CPAP$_{flow}$ measures. To date, no review and meta-analysis has addressed this subject. Considering the number of patients requiring CPAP-monitoring, an auto-CPAP home titration is recommended as an alternative option to in-laboratory PAP titration for patients without comorbidities and an initial telemedicine monitoring is proposed.[2][3] In addition, for most of the recent randomised clinical trials, CPAP efficiency was based on the AHI-CPAP$_{flow}$ rather than on the AHI-PSG$_{gold}$.[21][22]

If we demonstrate the existence of significant differences between AHI-CPAP$_{flow}$ and AHI-PSG$_{gold}$, our conclusions may have major consequences not only in daily practice but also for the design of future studies, with a crucial need for increased PSG evaluation of CPAP effectiveness. In this regard, although subgroup analyses on central apnoea patients and BMI are of interest to the clinician, the potentially small number of studies may not allow us to perform these statistical analyses.

In the context of CPAP-treated patients requiring long-term management, whether a one night point estimate (like AHI-PSG$_{gold}$) could be considered as a gold standard to evaluate CPAP efficiency rather than a night-by-night serial measurement (like AHI-CPAP$_{flow}$) is also questionable.[23] Night-by-night AHI variation has been demonstrated not only for the PSG measures in stable patients[23] but also for the unstable patients with underlying cardiovascular diseases for example.[24] For certain patients, there is no doubt that significant night-to-night AHI variability exists, which can limit the diagnostic value of a single night measurement regardless of the nature of said measurement.

Aside from AHI-CPAP$_{flow}$ accuracy, the question that also arises is the existence of an AHI-CPAP$_{flow}$ threshold above which a more interventionist attitude should be adopted to avoid clinical consequences such as loss of CPAP-adherence and/or symptom recurrence. To date, this question remains debated. Whereas the AASM 2019 statement suggests that clinicians use telemonitoring-guided interventions during the initial period of CPAP therapy, no guiding AHI-CPAP$_{flow}$ threshold was proposed.[2] The 2013 American Thoracic Society statement has speculated that an AHI-CPAP$_{flow}$ over 10/h might be associated with a risk of CPAP-non-adherence (≤4 hours/day, 70% of the days),[11] but this was not the case when this threshold was tested for 650 long-term CPAP-treated patients.[25] On the other hand, in a 12 285 patient cohort, an AHI-CPAP$_{flow}$ >5/h (22% of the studied population) was associated with a statistically lower CPAP usage (mean of 5.75 vs 6.00 hours/night).[26]

To interpret individual AHI-CPAP$_{flow}$ scores, care must also be taken to properly account for patient symptoms (ie, symptoms not only in terms of CPAP efficiency but also in terms of patient-reported side effects like patient-reported-leaks). In this regard, for telemedicine care, patient questionnaires are likely to play a complementary role in addition to CPAP-reported data.[27]

Regardless of our review and meta-analysis results, there is an urgent need to standardise the respiratory event definitions used by device manufacturers. The current variability limits the usefulness of AHI-CPAP$_{flow}$ in clinical practice. Eight years after the American Thoracic Society statement and despite a clear recommendation on this issue,[11] no progress in this direction has been made. The results of AHI-CPAP$_{flow}$ versus AHI-CPAP$_{gold}$ SRMA will be interpreted and discussed in this context.

Author affiliations
[1]IMAG, CNRS, Univ Montpellier, CHU Montpellier, Montpellier, France
[2]Association pour l'assistance et la réhabilitation à domicile (Apard) groupe Adène, Montpellier, France
[3]Department of Respiratory Diseases, Univ Montpellier, CHU Montpellier, Montpellier, France

[4]Department of Medical Information, Univ Montpellier, CHU Montpellier, Montpellier, France

[5]PhyMedExp (INSERM U 1046, CNRS UMR9214), Montpellier University, Montpellier, France

[6]Department of Physiology, Sleep and Exercise, Univ Grenoble Alpes, CHU Grenoble, Grenoble, France

[7]Department of Pulmonology, CHU Angers, Angers, France

[8]CREST UMR 9194, ENSAE formation continue, Malakoff, France

[9]Pulmonary Disorders and Respiratory Sleep Disorders Unit, Polyclinic Saint-Privat, Boujan sur Libron, France

Twitter Carey Meredith Suehs @SuehsCarey

Contributors All authors contributed to conceptualising and designing the study. FB, CMS and DJ drafted the manuscript. JPM, MCR, JLP, FG, EML, AB and NM commented on important intellectual content and made revisions. All authors read and approved the final version of the manuscript. CMS and DJ accept full responsibility for the finished manuscript and controlled the decision to publish.

Competing interests AB reports grants, personal fees, non-financial support and other from AstraZeneca, grants, personal fees and other from GSK, grants, personal fees, non-financial support and other from Boeringher Ingelheim, personal fees, non-financial support and other from Novartis, personal fees and other from Teva, personal fees and other from Regeneron, personal fees, non-financial support and other from Chiesi Pharmaceuticals, personal fees, non-financial support and other from Actelion, other from Gilead, and personal fees and non-financial support from Roche, outside the submitted work. FG reports grants and personal fees from ResMed, personal fees and non-financial support from Sefam, personal fees from Cidelec, personal fees and non-financial support from Novartis, personal fees and non-financial support from Nyxoah, non-financial support from Boehringer Ingelheim, grants and personal fees from Philips Respironics, and non-financial support from Asten, outside the submitted work. DJ reports personal fees from Philips Healthcare, from ResMed, personal fees and non-financial support from Sefam, personal fees from Lowenstein, personal fees from GSK, from Boehringher Ingelheim, grants and personal fees from Novartis, personal fees and non-financial support from AstraZeneca, personal fees from Chiesi Pharmaceuticals and personal fees from Sanofi, outside the submitted work. JLP reports grants and other from Air Liquide Foundation, grants, personal fees and other from AGIR a dom, grants, personal fees and other from AstraZeneca, grants and other from Fisher & Paykel, grants and other from Mutualia, grants, personal fees and other from Philips, grants, personal fees and other from ResMed, grants and other from VitalAire, personal fees from AstraZeneca, personal fees from Boehringer Ingelheim, personal fees from Jazz Pharmaceuticals, personal fees from NightBalance and personal fees from Sefam, outside the submitted work. NM and CMS report grants from AstraZeneca, outside the submitted work.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer-reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

ORCID iDs
Carey Meredith Suehs http://orcid.org/0000-0002-2175-3496
Frédéric Gagnadoux http://orcid.org/0000-0002-4231-5102

REFERENCES

1 Benjafield AV, Ayas NT, Eastwood PR, *et al*. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *Lancet Respir Med* 2019;7:687–98.

2 Patil SP, Ayappa IA, Caples SM, *et al*. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of sleep medicine clinical practice guideline. *Journal of Clinical Sleep Medicine* 2019;15:335–43.

3 Patil SP, Ayappa IA, Caples SM, *et al*. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of sleep medicine systematic review, meta-analysis, and grade assessment. *Journal of Clinical Sleep Medicine* 2019;15:301–34.

4 Weaver TE, Maislin G, Dinges DF, *et al*. Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 2007;30:711–9.

5 Yu J, Zhou Z, McEvoy RD. Association of positive airway pressure with cardiovascular events and death in adults with sleep apnea: a systematic review and meta-analysis. *JAMA* 2017;318:156–66.

6 Kirsch DB, Yang H, Maslow AL, *et al*. Association of positive airway pressure use with acute care utilization and costs. *Journal of Clinical Sleep Medicine* 2019;15:1243–50.

7 Poullié A-I, Cognet M, Gauthier A, *et al*. Cost-Effectiveness of treatments for mild-to-moderate obstructive sleep apnea in France. *Int J Technol Assess Health Care* 2016;32:37–45.

8 Streatfeild J, Hillman D, Adams R, *et al*. Cost-Effectiveness of continuous positive airway pressure therapy for obstructive sleep apnea: health care system and societal perspectives. *Sleep* 2019;42.

9 Trakada G, Economou N-T, Nena E, *et al*. A health-economic analysis of diagnosis and treatment of obstructive sleep apnea with continuous positive airway pressure in relation to cardiovascular disease. The Greek experience. *Sleep and Breathing* 2015;19:467–72.

10 Wickwire EM, Albrecht JS, Towe MM, *et al*. The impact of treatments for OSA on Monetized health economic outcomes. *Chest* 2019;155:947–61.

11 Schwab RJ, Badr SM, Epstein LJ, *et al*. An official American thoracic Society statement: continuous positive airway pressure adherence tracking systems. The optimal monitoring strategies and outcome measures in adults. *Am J Respir Crit Care Med* 2013;188:613–20.

12 Berry RB, Budhiraja R, Gottlieb DJ. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. deliberations of the sleep apnea definitions Task force of the American Academy of sleep medicine. *J Clin Sleep Med JCSM Off Publ Am Acad Sleep Med* 2012;8:597–619.

13 Johnson KG, Johnson DC. Treatment of sleep-disordered breathing with positive airway pressure devices: technology update. *Med Devices* 2015;8:425–37.

14 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.

15 Shamseer L, Moher D, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;349:g7647.

16 Saaiq M, Ashraf B. Modifying "Pico" Question into "Picos" Model for More Robust and Reproducible Presentation of the Methodology Employed in A Scientific Study. *World J Plast Surg* 2017;6:390–2.

17 Whiting PF *et al*. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011;155:529–36.

18 Sterne JAC, Sutton AJ, Ioannidis JPA, *et al*. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;343:d4002.

19 R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R foundation for statistical computing, 2016. Available: https://www.R-project.org/

20 Schwarzer G, Carpenter JR, Rücker G. *Meta-Analysis with R*. Springer, 2015.

21 McEvoy RD, Antic NA, Heeley E, *et al*. Cpap for prevention of cardiovascular events in obstructive sleep apnea. *N Engl J Med Overseas Ed* 2016;375:919–31.

22 Peker Y, Glantz H, Eulenburg C, *et al*. Effect of positive airway pressure on cardiovascular outcomes in coronary artery disease patients with Nonsleepy obstructive sleep apnea. The RICCADSA randomized controlled trial. *Am J Respir Crit Care Med* 2016;194:613–20.

23 Roeder M, Bradicich M, Schwarz EI, *et al*. Night-to-night variability of respiratory events in obstructive sleep apnoea: a systematic review and meta-analysis. *Thorax* 2020;75:1095–102.

24 Linz D, Baumert M, Desteghe L, *et al*. Nightly sleep apnea severity in patients with atrial fibrillation: potential applications of long-term sleep apnea monitoring. *IJC Heart & Vasculature* 2019;24:100424.

25 Rotty M-C, Mallet J-P, Suehs CM, *et al*. Is the 2013 American thoracic Society CPAP-tracking system algorithm useful for managing non-adherence in long-term CPAP-treated patients? *Respir Res* 2019;20:209.

26 Bailly S, Daabek N, Jullian-Desayes I, *et al*. Partial failure of CPAP treatment for sleep apnoea: analysis of the French national sleep database. *Respirology* 2020;25:104–11.

27 Rotty M-C, Suehs CM, Mallet J-P, *et al*. Mask side-effects in long-term CPAP-patients impact adherence and sleepiness: the InterfaceVent real-life study. *Respir Res* 2021;22:17.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open

Supplementary appendix 1.

Apnoea and hypopnoea definitions by manufacturers.

Manufacturer	Apnoea definition	Hypopnoea definition
Resmed (S8, S9, S10 models)	A decrease in the 2-s moving average root mean square ventilation of 75% for at least 10 seconds	All of the following conditions are needed: - A decrease in the 2-s moving average root mean square ventilation below 50% for at least 12 seconds (S8) or 10 seconds (S9 and S10 models) - The hypopnea contains one or more partially obstructed breaths. - The hypopnoea is not immediately followed by an apnoea
Philips Respironics (System One Model)	A decrease in flow signal of >80% for at least 10 seconds	A decrease in flow signal of >40% for at least 10 seconds
Löwenstein (Prisma Models)	A flow signal ≤ 4l/minute for at least 10 seconds	A decrease in flow signal of >35% for at least 10 seconds
Fisher & Paykel InfoSmart software	A decrease in flow signal of >80% for at least 10 seconds	A decrease in flow signal of >40% for at least 10 seconds
SEFAM (Sbox models)	A decrease in flow signal of 100% for at least 10 seconds	A decrease in flow signal of >50% for at least 10 seconds
DeVilbiss Healtcare IntelliPAP AutoAdjust 2	A decrease in flow signal of >90% for at least 10 seconds	A decrease in flow signal of >50% for at least 10 seconds

Supplementary appendix 2. PRISMA-1 P Checklist.

Section / topic	Item No	Checklist item	Reported on lines
Administrative information			
Title:			
Identification	1a	Identify the report as a systematic review, meta-analysis, or both	1-4
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	Not applicable
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	76-77
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	5-39
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	325-330
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	267-269
Support:			
Sources	5a	Indicate sources of financial or other support for the review	331-334
Sponsor	5b	Provide name for the review funder and/or sponsor	156-157
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	331-334
Introduction			
Rationale	6	Describe the rationale for the review in the context of what is already known	99-142
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	139-152
Methods			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	164-194
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	196-201
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	203-207
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	217-220
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	209-215
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	217-218
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	219-230

Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	174-178
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	238-247
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	249-257
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I2, Kendall's τ)	249-251
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	261-263
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	251-258
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	243-247
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	246-247

SEARCH STRATEGY

This search strategy is inspired by / based on the supplementary file from the following article: *Yu J, Zhou Z, McEvoy RD, et al. Association of Positive Airway Pressure With Cardiovascular Events and Death in Adults With Sleep Apnea: A Systematic Review and Meta-analysis. JAMA. 2017;318(2):156–166. doi:10.1001/jama.2017.7967*

KEYWORDS

Sleep apnea*: SAS OR ("Apnoea") OR ("Hypopnea") OR ("Hypopnoea") OR ("Respiratory Disturbance Index"))*
Polysomnography
CPAP: *Continuous positive airway pressure*
Apnea hypopnea index:
Apnea hypopnea index flow: *Device residual events, treatment effectiveness*

PUBMED

1. (SLEEP APNEA)
2. (SLEEP APNOEA)
3. (SAS)
4. (APNEA)
5. (APNOEA)
6. (HYPOPNEA
7. (HYPOPNOEA)
8. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7
9. (CONTINUOUS POSITIVE AIRWAY PRESSURE)
10. CPAP
11. 9 OR 10
12. (POLYSOMNOGRAPHY)
13. PSG
14. (RESPIRATORY POLYGRAPHY)
15. RP
16. 12 OR 13 OR 14 OR 15
17. APNEA HYPOPNEA INDEX
18. APNOEA HYPOPNOEA INDEX
19. AHI
20. RESPIRATORY DISTURBANCE INDEX
21. RDI
22. 17 OR 18 OR 19 OR 20 OR 21
23. APNEA HYPOPNEA INDEX FLOW
24. APNOEA HYPOAPNOEA INDEX FLOW
25. AHI FLOW
26. RESPIRATORY DISTURBANCE INDEX FLOW
27. RDI FLOW
28. DEVICE RESIDUAL EVENTS
29. 23 OR 24 OR 25 OR 26 OR 27 OR 28
30. 8 AND 11 AND 16 AND 29

FILTERS:
- ❖ LANGUAGE: ENGLISH
- ❖ PUBLICATIONS FROM 01/01/2007 onwards

GOOGLE SCHOLAR

((device residual events) OR (rdi flow) OR (respiratory disturbance index flow) OR (ahi flow) OR(apnoea hypopnoea index flow) OR (apnea hypopnea index flow)) AND ((RDI) OR (respiratory disturbance index) OR (AHI) OR (apnoea hypopnoea index) OR (apnea hypopnea index)) AND ((polysomnography) OR (PSG)OR (respiratory polygraphy) OR (RP)) AND ((CPAP) OR (continuous positive airway pressure)) AND ((sleep apnoea)OR(SAS) OR (apnea) OR (apnoea) OR (hypopnoea) OR (sleep apnea) OR (hypopnea))

FILTERS:
- ❖ PUBLICATIONS FROM 2007 TO 2021
- ❖ LANGUAGE: ENGLISH

EMBASE

(sleep AND apnea OR (sleep AND apnoea) OR sas OR apnea OR apnoea OR hypopnea OR hypopnoea) AND (continuous AND positive AND airway AND pressure OR cpap) AND (polysomnography OR psg OR (respiratory AND polygraphy) OR rp) AND (apnea AND hypopnea AND index OR (apnoea AND hypopnoea AND index) OR ahi OR (respiratory AND disturbance AND index) OR rdi) AND (apnea AND hypopnea AND index AND flow OR (apnoea AND hypoapnoea AND index AND flow) OR (ahi AND flow) OR (respiratory AND disturbance AND index AND flow) OR (rdi AND flow) OR (device AND residual AND events))

FILTERS:
- ❖ PUBLICATIONS FROM 2007 TO 2021
- ❖ LANGUAGE: ENGLISH

WEB OF SCIENCE

((ALL=(SLEEP APNEA) OR ALL=(SLEEP APNOEA) OR ALL=(SAS) OR ALL=(APNEA) OR ALL=(APNOEA) OR ALL=(HYPOPNEA) OR ALL=(HYPOPNOEA))AND (ALL=(CONTINUOUS POSITIVE AIRWAY PRESSURE) OR ALL=(CPAP)) AND (ALL=(POLYSOMNOGRAPHY) OR ALL=(PSG) OR ALL=(RESPIRATORY POLYGRAPHY) OR ALL=(RP)) AND (ALL=(APNEA HYPOPNEA INDEX) OR ALL=(APNOEA HYPOPNOEA INDEX) OR ALL=(AHI) OR ALL=(RESPIRATORY DISTURBANCE INDEX) OR ALL=(RDI)) AND (ALL=(APNEA HYPOPNEA INDEX FLOW) OR ALL=(APNOEA HYPOAPNOEA INDEX FLOW) OR ALL=(AHI FLOW) OR ALL=(RESPIRATORY DISTURBANCE INDEX FLOW) OR ALL=(RDI FLOW) OR ALL=(DEVICE RESIDUAL EVENTS))) AND LANGUAGE: (English)

FILTERS:
- ❖ PUBLICATIONS FROM 2007 TO 2021