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The Comparative Effectiveness, Harms, and Cost of Care Models for the Evaluation and Treatment of Obstructive Sleep Apnea (OSA): A Systematic Review

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Investigators:
    Principal Investigators:
        Ken M. Kunisaki, MD, MS
        Wajahat Khalil, MD

    Co-Investigators:
        Erin Koffel, PhD
        Loretta Pfannes, MD

    Research Associates:
        Eva Koeller, BA
        Roderick MacDonald, MS

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PREFACE

The VA Evidence-based Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of particular importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. QUERI provides funding for four ESP Centers, and each Center has an active University affiliation. Center Directors are recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Centers. The ESP is governed by a Steering Committee comprised of participants from VHA Policy, Program, and Operations Offices, VISN leadership, field-based investigators, and others as designated appropriate by QUERI/HSR&D.

The ESP Centers generate evidence syntheses on important clinical practice topics. These reports help:

- · Develop clinical policies informed by evidence;
- · Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- · Set the direction for future research to address gaps in clinical knowledge.

The ESP disseminates these reports throughout VA and in the published literature; some evidence syntheses have informed the clinical guidelines of large professional organizations.

The ESP Coordinating Center (ESP CC), located in Portland, Oregon, was created in 2009 to expand the capacity of QUERI/HSR&D and is charged with oversight of national ESP program operations, program development and evaluation, and dissemination efforts. The ESP CC establishes standard operating procedures for the production of evidence synthesis reports; facilitates a national topic nomination, prioritization, and selection process; manages the research portfolio of each Center; facilitates editorial review processes; ensures methodological consistency and quality of products; produces "rapid response evidence briefs" at the request of VHA senior leadership; collaborates with HSR&D Center for Information Dissemination and Education Resources (CIDER) to develop a national dissemination strategy for all ESP products; and interfaces with stakeholders to effectively engage the program.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP CC Program Manager, at Nicole.Floyd@va.gov.

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INTRODUCTION

Obstructive sleep apnea (OSA) is a chronic condition that results from repeated closure of the upper airway during sleep resulting in reduced airflow (hypopnea) or complete airflow cessation (apnea) leading to cyclic sleep disruption. Subsequently, patients with OSA frequently experience excessive daytime sleepiness and decreased quality of life. However, not all individuals have excessive daytime sleepiness and symptoms are not required to make a diagnosis or obtain treatment. OSA has also been associated with a higher risk of myocardial infarction,[1,2] heart failure,[3] stroke,[4,5] and cognitive decline.[6,7] The severity of OSA can be categorized as mild, moderate, or severe based on the number of apnea and hypopnea events per hour (known as the apnea-hypopnea index [AHI]). An AHI of 5/hour to fewer than 15/hour is considered mild, 15/hour to fewer than 30/hour is considered moderate, and 30/hour or greater is considered severe. Continuous positive airway pressure (CPAP) effectively reduces AHI in most patients with OSA, improves blood pressure, and particularly in those with symptoms of excessive daytime sleepiness, improves quality of life and sleep symptoms.[8] CPAP use is also associated with a reduced risk of motor vehicle accidents.[9]

The estimated prevalence of mild to severe OSA based on AHI thresholds (AHI ≥ 5/hour) in the United States (2007-2010 data) among 30- to 70-year-olds regardless of symptom status is 34% for men and 17% for women.[10] The corresponding values for moderate to severe OSA (AHI ≥ 15/hour) are 13% for men and 6% for women. The prevalence of 30-70 year olds with AHI ≥ 5/hour and daytime sleepiness (Epworth Sleepiness Scale score > 10) is 14% for men and 5% for women. Current prevalence of abnormal AHI may be higher due to rising rates of obesity and increased testing for OSA due to heightened awareness of the condition. The proportion of persons with OSA who are asymptomatic or have unrecognized symptoms is unknown but a recent review estimated that 80% of individuals with AHI ≥ 5/hour may be undiagnosed.[11] The cost burden of diagnosing and treating OSA in the US in 2015 was estimated to be $12.4 billion while the cost burden of undiagnosed OSA in the US in 2015 was estimated to be $149.6 billion when costs of comorbidities and mental health, motor vehicle accidents, workplace accidents, and lost productivity were considered.[11] The authors acknowledged the difficulty of determining exact costs.

A prior evidence report and accompanying clinical practice guideline by the American College of Physicians (ACP) recommends that clinicians should target their assessment of OSA to individuals with unexplained daytime sleepiness.[12-14] This is largely because evidence is lacking on the effect of CPAP on improving many other outcomes, including diabetes, coronary heart disease events, and mortality, especially among individuals without daytime sleepiness. Furthermore, the ACP concluded that assessment of OSA in the absence of daytime sleepiness and treatment of persons with low AHI are both low-value care because evidence to date indicates that neither improves clinical outcomes.

A draft evidence report and recommendation statement from the US Preventive Services Task Force (USPSTF) indicated that evidence was insufficient to assess the net benefit of screening for and treatment of asymptomatic OSA.[15]

Specifically, the most evidence was available on CPAP and found that compared to sham intervention, CPAP reduced AHI, ESS score, and blood pressure. Although studies generally showed that treatment with CPAP reduced AHI to near-normal levels, the clinical significance of the small reductions in ESS score and blood pressure is uncertain. Further, given that most of the trials were conducted in referred patients or patients of sleep clinics, the applicability of this evidence to a screen-detected population (*ie*, detection of abnormal AHI in asymptomatic individuals or those without excessive daytime somnolence, including based on findings from "screening" questionnaires) is limited. Despite the consistent observational findings of an association between severe OSA and increased mortality, the USPSTF identified no studies that reported on change in AHI and associated change in mortality. Thus, it is unclear whether treatments that improve AHI would also improve mortality. The USPSTF found inadequate evidence on the link between change in the intermediate outcome (AHI) and reduction in the health outcome (mortality). While the USPSTF found evidence that treatment with CPAP can improve general and sleep-related quality of life in populations referred for treatment, the applicability of this evidence to screen-detected populations is unknown. The USPSTF also found inadequate evidence on whether treatment with CPAP improves other health outcomes (mortality, cognitive impairment, motor vehicle accidents, and cardiovascular or cerebrovascular events). Following release of the USPSTF report, results from a multi-site randomized trial were published and showed that CPAP was not effective for secondary prevention of cardiovascular events in those with established cardiovascular disease and moderate to severe OSA.[16]

Despite the data associating OSA with consequences to health and quality of life and the conclusions from other guideline groups, many persons with OSA remain undiagnosed. In 2005, the National Sleep Foundation administered the Berlin sleep apnea risk questionnaire (a questionnaire commonly used for OSA screening and/or case finding) by phone to a random sample of 1,506 US adults who agreed to complete the questionnaire and found that 31% of men and 21% of women met criteria for high OSA risk.[17] Obesity is a major risk factor for OSA and among those with a body mass index (BMI) of $\geq$ 30 kg/m^2 (25% of the sample), 57% had high risk for OSA.

In 2010, among 1.8 million US Veterans receiving outpatient care at 136 Veterans Affairs (VA) facilities, 37.4% had a BMI $\geq$ 30 kg/m^2, suggesting that a substantial portion of US Veterans are at high risk for OSA.[18] A recent analysis of Veterans Administration Informatics and Computing Infrastructure (VINCI) data between 2000 and 2010 showed that among 9.8 million Veterans, the age-adjusted prevalence of diagnosed sleep apnea was 0.4% in 2000 and had increased to 3.0% in 2010 (a relative increase of 650%).[19] As awareness of OSA by patients and providers continues to increase, and as BMI continues to increase in the US and globally,[20] healthcare systems such as the VA need to develop strategies to manage the increasing demand for sleep services. One strategy is to target screening and testing to those most likely to derive benefit from OSA treatment (*eg,* those with significant unexplained daytime sleepiness), as suggested by the ACP. Another strategy is to improve efficiency within healthcare systems by implementing innovative, less resource-intense models of care for OSA.

The traditional model of OSA evaluation and care relies upon primary care providers to refer patients with suspected OSA to a sleep specialist physician (SSP) for consultation. After an initial consultative visit, the SSP can order formal, in-lab polysomnogram (PSG) for diagnostic purposes and for those with confirmed OSA, a PSG for titration of CPAP pressures. The SSP would then typically initiate CPAP at the pressure suggested by the titration PSG, and then the

patient would follow up with the SSP at regular intervals for assessment of treatment compliance and efficacy. Given the rapidly rising requests for OSA diagnostic and treatment services, this traditional model is increasingly viewed as unnecessarily expensive and inefficient for the evaluation and treatment of patients at high risk of OSA. Recent data also indicate a decreasing supply of SSPs to care for patients with known or suspected OSA.[21]

Therefore, new models of OSA care have been proposed and implemented. These new models include home sleep testing (HST) for diagnostic purposes,[22] followed by treatment with an autotitrating CPAP (APAP) device,[23] which has internal algorithms to adjust CPAP pressure to keep the airway open during sleep. These models reduce PSG-associated costs and logistical barriers, yet typically still include consultation and follow up with a SSP. Other proposed models would reduce reliance on SSPs by including non-SSP providers such as nurses or primary care clinics to provide the bulk of OSA diagnosis and treatment.

Although several studies have been conducted to test some of these new models, systematic reviews are lacking. The Minneapolis VA's Evidence-based Synthesis Program (ESP) Center, in partnership with topic nominators and a Technical Expert Panel (TEP), was commissioned to systematically review the evidence regarding the comparative effectiveness, harms, and cost of these new models of OSA evaluation and treatment.

We addressed the following key questions:

Key Question 1. For adults with suspected OSA, what are the effectiveness/harms/resource utilization of case finding and care provided by practitioners who are not sleep physicians (including PCPs, PAs, NPs, technologists, nurses, and respiratory therapists), compared to case finding and care provided by sleep specialist physicians?

> **KQ1A.** Do effectiveness/harms/resource utilization vary by patient characteristics:
>   a. Unexplained daytime sleepiness/fatigue
>   b. AHI severity
>   c. Other risk factors or coexisting conditions associated with OSA (*eg,* obesity, neck circumference, treatment-resistant hypertension, diabetes, age, sex, race)
>   d. Symptoms (*eg,* nocturia, loss of libido, snoring, witnessed sleep "apnea")?

Key Question 2. For adults with suspected OSA, what are the effectiveness/harms/resource utilization of electronic consultation versus interactive (*eg*, in-person, telephone) consultation?

> **KQ2A.** Do effectiveness/harms/resource utilization vary by patient characteristics:
>   a. Unexplained daytime sleepiness/fatigue
>   b. AHI severity
>   c. Other risk factors or coexisting conditions associated with OSA (*eg,* obesity, neck circumference, treatment-resistant hypertension, diabetes, age, sex, race)
>   d. Symptoms (*eg,* nocturia, loss of libido, snoring, witnessed sleep "apnea")?

Key Question 3. For adults diagnosed with OSA, what are the effectiveness/harms/resource utilization (including cost avoidance) of using in-home autotitrating continuous positive airway

pressure (APAP) technology compared to standard continuous positive airway pressure (CPAP) titrated by in-lab PSG?

> **KQ3A.** Do effectiveness/harms/resource utilization vary by patient characteristics:
> a. Unexplained daytime sleepiness/fatigue
> b. AHI severity
> c. Other risk factors or coexisting conditions associated with OSA (*eg*, obesity, neck circumference, treatment-resistant hypertension, diabetes, age, sex, race)
> d. Symptoms (*eg,* nocturia, loss of libido, snoring, witnessed sleep "apnea")?

PICOTS AND ANALYTIC FRAMEWORKS (FIGURES 1A, 1B)

Population:

KQ1, KQ2: Adults with suspected obstructive sleep apnea (OSA) to include:
KQ3: Adults with diagnosed OSA

Intervention

KQ1: supervised practitioner or non-specialist licensed independent practitioner-led care (*ie,* PCP, PA, NP, nurse, technologist, or respiratory therapist) (for case finding *or* treatment)
KQ2: Electronic initial consultation (chart review or algorithm) (for case finding)
KQ3: Home auto-titrating continuous positive airway pressure (APAP)

Comparator

KQ1: Sleep specialist-led care (for case finding *or* treatment)
KQ2: Interactive (*eg,* in-person, telephone) initial consultation (case finding)
KQ3: In-center manual CPAP *titration*

Outcomes

Intermediate Outcomes: time to initiation of therapy; compliance; apnea-hypopnea index (AHI); oxygen saturation; continuous or scale score measures of sleep symptoms, urinary symptoms, cognitive ability, weight, BMI, libido, blood pressure, or HBA1c; harms (false positives/negative, overdiagnosis, patient safety/adverse events); costs

Clinical Outcomes: mortality; resource utilization; access to care; *minimally important differences* in sleep symptom scores, urinary symptom scores, libido, weight change, BMI, blood pressure, or HbA1c; quality of life; diagnosis of cognitive impairment; sleep symptom score below threshold; patient satisfaction

Timing: Any

Setting: Study done in North America, Europe, or Australia/New Zealand

Figure 1a. Analytic Framework – Key Questions 1 and 2

Case Finding
KQ1: Supervised practitioner or non-specialist LIP-led evaluation vs SSP
KQ2: Electronic consultation vs interactive

Intervention
KQ1: Supervised practitioner or non-specialist LIP-led care vs SSP

Adults with unexplained daytime sleepiness or at risk for OSA (*ie,* risk factors, coexisting conditions, or other symptoms)

PSG

OSA diagnosis

No OSA

Intermediate Outcomes
· Case finding/ diagnostic accuracy
· Time to initiation of therapy
· Compliance
· AHI
· Oxygen saturation
· Continuous measures of sleep and urinary symptom scores, cognitive ability, weight, BMI, libido, blood pressure, HbA1c

Clinical Outcomes
· Mortality
· Resource utilization (*eg,* hospitalizations)
· Access to care
· Minimally important differences in sleep symptom scores
· Normalization of AHI
· Quality of life
· Diagnosis of cognitive impairment
· Sleep symptom score below threshold
· Patient satisfaction

Harms (Case Finding)
· False positives/ negatives
· Overdiagnosis

Harms (Intervention)
· Patient safety/ adverse events
· Costs

Solid Arrow = Linkage; Dotted Arrow = Association; Curved Arrow leads to Harms (Ovals); AHI = Apnea Hypoxia Index; LIP = licensed independent practitioner; OSA = obstructive sleep apnea; PSG = polysomnography; SSP = sleep specialist physician

Figure 1b. Analytic Framework – Key Question 3
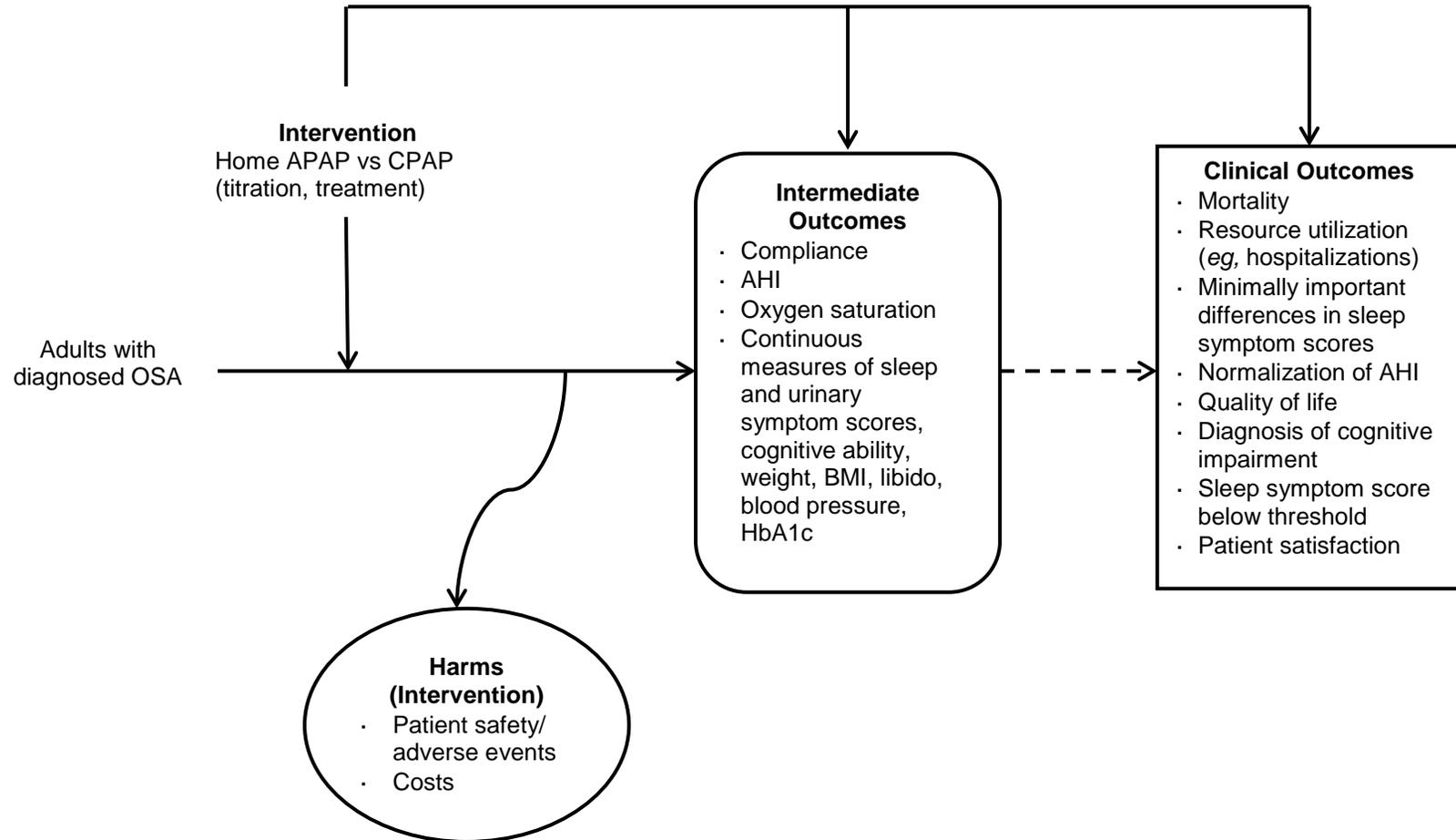
Solid Arrow = Linkage; Dotted Arrow = Association; Curved Arrow leads to Harms (Ovals); AHI = Apnea Hypoxia Index; APAP = Auto-adjusting Positive Airway Pressure; CPAP = C Positive Airway Pressure OSA = obstructive sleep apnea

METHODS

TOPIC DEVELOPMENT

This topic was nominated by Kathleen Sarmiento, MD, MPH, Director of Pulmonary Sleep Medicine, VA San Diego and W. Claibe Yarbrough, MD, National Program Director, Pulmonary/Critical Care/Sleep, on behalf of the Specialty Care Services (10P4E) – Pulmonary/Critical Care/Sleep National Program office. The evidence review examines the effectiveness and harms associated with different care models aimed at increasing access to care for Veterans who have obstructive sleep apnea.

SEARCH STRATEGY

We searched MEDLINE (Ovid) and CINAHL for articles published from 2000 through May 2016. Our search was limited to studies enrolling adults and published in the English language. The search for KQs 1 and 2 included the MeSH terms sleep apnea syndromes; sleep apnea, obstructive; health personnel; and remote consultation. The search for KQ3 included the MeSH terms home care services, continuous positive airway pressure, and calibration. The full search strategies are presented in Appendix A. We obtained additional articles by hand searching the reference lists of related systematic reviews and relevant studies.

STUDY SELECTION

All abstracts were independently reviewed by 2 trained investigators and research associates. We included studies of any design that reported results in adults with suspected or diagnosed OSA and were conducted in North America, Europe, Australia, or New Zealand. For KQ1 we excluded studies that did not include a comparison of a supervised practitioner or non-specialist licensed independent practitioner (*eg* primary care physician, physician's assistant, nurse, technologist, or respiratory therapist) to a SSP. We excluded studies evaluating the role of dentists or anesthesiologists. We also excluded studies in which the goal of the intervention was not case finding or care for OSA. For KQ2 we excluded studies that did not compare an electronic initial consultation, without patient contact, to an interactive initial consultation. For KQ3 we excluded studies that did not compare the use of APAP to CPAP for *titration* or *treatment* of OSA. We also excluded studies that used different diagnostic methods in those treated with APAP versus CPAP. In studies of *titration* we only included articles in which the APAP was used for titration at home and CPAP was manually titrated in a lab. We also excluded studies if they did not report any of our outcomes of interest (see PICOTS, above). There was no minimum follow-up duration.

Full-text reports of studies identified as potentially eligible were obtained for further review using the inclusion and exclusion criteria described above. Each article was independently reviewed by 2 investigators or research associates. Reasons for excluding a study at full-text review were noted and disagreements were decided by a third reviewer.

DATA ABSTRACTION

Study characteristics (location, setting, intervention groups, follow-up, aim of study, treatments, inclusion/exclusion criteria, and patient characteristics) as well as intermediate and clinical outcomes (time to initiation of therapy, compliance, AHI, oxygen saturation, sleep symptoms, urinary symptoms, cognitive ability, weight, BMI, libido, blood pressure, HbA1c, harms, overdiagnosis, adverse events, costs, mortality, resource utilization, access to care, quality of life, and patient satisfaction) were extracted onto evidence tables by one investigator or research associate and verified by another.

RISK OF BIAS ASSESSMENT

Trained research methodologists rated the risk of bias of individual studies as low, moderate, or high risk. One methodologist rated risk of bias and the rating was verified by a second investigator trained in risk of bias assessment. Discrepancies were resolved by discussion. For randomized controlled trials (RCTs), risk of bias ratings were based the following criteria: allocation sequence generation, allocation concealment, blinding, incomplete outcome data, and selective outcome reporting – a modification of the Cochrane approach to determining risk of bias.[24]

For observational studies, risk of bias was rated using criteria suggested in the Agency for Healthcare Research and Quality (AHRQ) Methods Guide: selection bias (use of appropriately comparable control group, design/analysis accounted for important confounding and modifying variables); masking of the outcome assessment (outcome assessor); use of intention-to-treat principles (*ie*, inclusion of all comparison group participants in outcomes analyses); attrition bias (if overall or differential dropout/loss to follow-up or exclusions a concern, missing data appropriately handled); and selective reporting of pre-specified outcomes.[25] Observational studies were considered high risk of bias unless all 5 criteria were addressed by the study authors. Studies that addressed all 5 criteria were considered medium or low risk of bias depending on how completely the criteria were addressed.

DATA SYNTHESIS

We created separate evidence tables for each KQ. We described and qualitatively compared the characteristics and findings of included studies. For KQ1 and KQ3, data were analyzed in Comprehensive MetaAnalysis Version 3 (Biostat, Englewood, New Jersey) using DerSimonian and Laird random effects models to calculate weighted mean differences (WMD) for compliance and standardized mean differences (SMD) for changes from baseline for Epworth Sleepiness Scale (ESS) and quality of life (SF-36) scores with corresponding 95% confidence intervals (CI). SMDs can be interpreted by using Cohen's definition of small (0.2), medium (0.5), and large (0.8) effect sizes.[26] Statistical heterogeneity among trials was assessed by using the I^2 test.[27] A score of 75% or greater may indicate considerable heterogeneity.

RATING THE BODY OF EVIDENCE

We assessed strength of evidence using the method described by Owens et al for the following outcomes: access to care, ESS, quality of life, compliance (hours of use per night), and adverse events. Strength of evidence for an outcome was rated as high, moderate, low, or insufficient. This rating was based on precision (degree of certainty in the estimate of effect), consistency

(direction of effect across included studies), directness (whether evidence links intervention directly to health outcomes), and risk of bias of the individual studies (as described above).[28] One methodologist rated strength of evidence and the rating was verified by a second. Discrepancies were resolved by discussion.

PEER REVIEW

A draft version of this report was reviewed by content experts as well as clinical leadership. Reviewer comments and our responses are presented in Appendix B and the report was modified as needed.

RESULTS

We reviewed 2,847 abstracts, 2,252 from MEDLINE and 595 from CINAHL. We excluded 2,493 abstracts and reviewed the full text of 354 references. During full-text review we excluded 323 articles leaving 31 eligible for inclusion. Hand searching pertinent trials and systematic review identified an additional 3 references. Figure 2 details the process.

LITERATURE FLOW

Figure 2. Literature Flow Chart
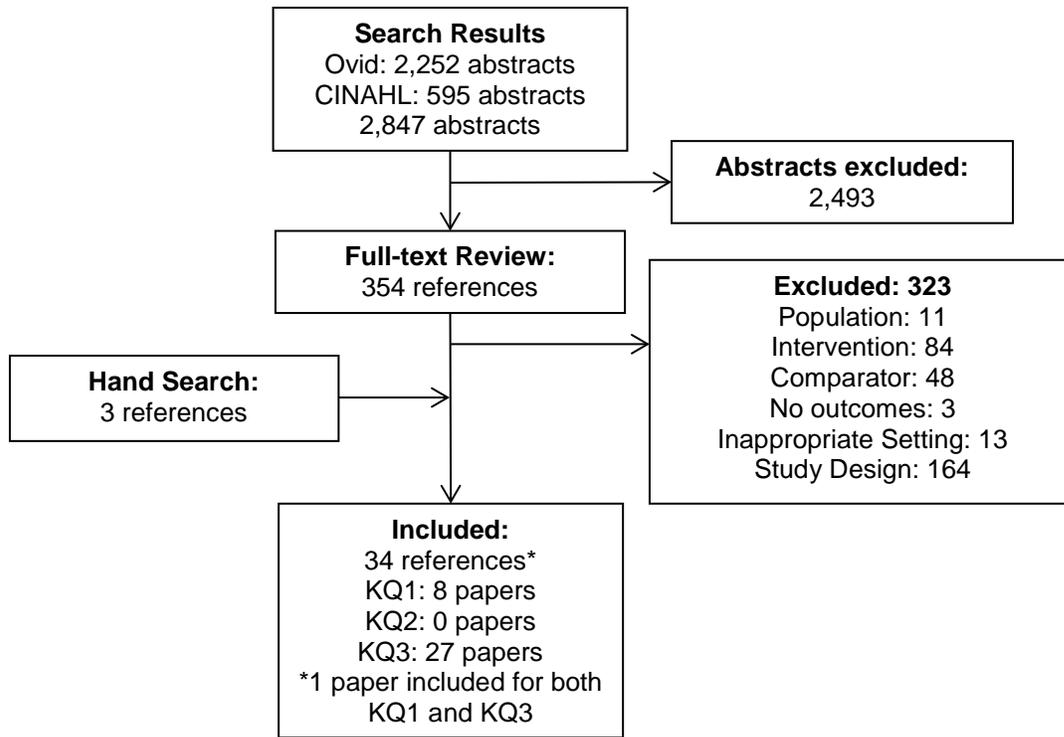
KEY QUESTION #1: For adults with suspected OSA, what are the effectiveness/harms/resource utilization of case finding and care provided by practitioners who are not sleep physicians (including PCPs, PAs, NPs, technologists, nurses, and respiratory therapists), compared to case finding and care provided by sleep specialist physicians?

Summary of Findings for Key Question #1

Case Finding

- No studies assessed the diagnostic accuracy of non-sleep-specialist nurse for case finding and referral.

- One retrospective study reported good agreement between a primary care pulmonologist and a SSP on what sleep test to order for patients referred by their family physician.

Care

- Clinical (*ie*, patient-centered) outcomes were infrequently and inconsistently reported. When reported there was no significant difference in clinical outcomes between OSA treated by primary care/nurses and SSPs. The strength of evidence for quality of life was moderate.

- Intermediate outcomes were more commonly reported. Sleep symptom scores were similar between groups (moderate strength of evidence).

- There was little evidence that treatment compliance differed between patients treated by SSPs and those not, including the proportion of patients with 4 hours or more of CPAP use on 70% or more of nights (moderate strength of evidence).

- Very few studies reported other intermediate outcomes. One reported a significantly lower residual AHI on CPAP in patients referred for PSG by non-sleep specialists and another found that the proportion of patients receiving CPAP within one month of their PSG was significantly higher in patients cared for by a SSP. Strength of evidence for access to care and adverse events was insufficient.

Overview of Studies – Table 1

Eight studies (n = 1,401; 4 RCTs) reported results for KQ1.[29-36] Study characteristics are summarized in Table 1 with more details in Appendix C, Table 1. Sleep physician care was compared to management by primary care in 4 studies (n = 564),[31-33,36] sleep-specialist nurses in 3 studies (n = 434),[29,30,34] and other non-sleep physicians in one study (n = 403).[35] The weighted mean age was 52 years and roughly half of the participants (54%) had hypertension. The mean BMI was 34 kg/m^2, ESS was 11.5, and AHI was 32/hour. Three studies (n = 678) reported that their patients had moderate or severe OSA (mean AHI ≥ 15/hour)[29,33,35] and 5 studies (n = 721) reported that their patients had mild OSA (mean ESS 11-14)[30-32] or moderate (mean ESS > 14) sleepiness.[29,33] Three studies (n = 415) required all participants to have symptoms of sleepiness (*ie,* ESS ≥ 8[30,31] or ESS ≥ 12[29]), and participants in these studies had a mean baseline ESS of

13.6 (mild sleepiness). Participants in the remaining 4 studies that reported ESS but did not require sleepiness had a mean baseline ESS of 10.5 (normal sleepiness). Three studies took place in Europe, 3 in North America, and 2 in Australia/New Zealand. Of the 4 RCTs, one was low risk of bias[30] and 3 were medium risk of bias. Of the 4 observational studies, 3 were medium risk of bias and one was high risk of bias.[32]

Table 1. Key Question 1: Study Characteristics

Characteristic	Weighted Mean (range) *Unless otherwise noted*	Number of studies reporting
Total number enrolled/randomized	1,401 (65-403)	8
Randomized controlled trials, total n	589 (65-195)	4
Other, total n	812 (96-403)	4
Primary care, total n	564 (96-210)	4
Sleep-specialist nurse, total n	434 (65-195)	3
Other non-sleep physician provider, total n	403	1
Age of subjects (years)	52.2 (47.7-58.7)	8
Percent Male	67% (47-85.5)	8
Baseline BMI, kg/m^2	34 (30.2-36.6)	7
Baseline ESS	11.5 (8.5-15.7)	7
Baseline AHI (events/hour)	32 (21-43)	3
Percent with hypertension (%)*	54 (38-58.5)	4
Location – North America, total n	716 (103-403)	3
Location – Europe, total n	335 (65-174)	3
Location – Australia/New Zealand, total n	350 (155-195)	2
Required participants to have daytime sleepiness, total n	415 (65-195)	3

*as defined by study

Case Finding

One retrospective study reported on the ability of a primary care pulmonologist to order the proper sleep test.[32] Patients (n = 96) were referred to the primary care pulmonologist by their family physician. An SSP reviewed the sleep tests ordered by the primary care pulmonologist. There was good agreement between the primary care pulmonologist and SSP (kappa = .74) and 93% (89/96) of the referred patients were diagnosed with OSA.

Care

Seven studies reported treatment outcomes in patients being treated by providers other tha SSPs. Three of these studies compared SSP care to primary care (n = 468; 1 RCT), 3 compared SSP care to sleep specialist nurses (n = 434; 3 RCTs), and one compared SSP care to management by a variety of physicians who were not sleep specialists. The nature of care provided by different professionals was varied and often inconsistently reported. Two of the studies (n = 506) were retrospective and gave few details regarding the care given by each practitioner.[35,36] Three studies (n = 560; 2 RCTs and one cohort study) described interventions in which the SSP had much more autonomy than the non-SSP provider, who was generally giving protocol-driven care that followed clinical guidelines.[30,31,33] Two RCTs compared patients who received similar care delivered by different providers and at different locations (home versus a hospital/clinic).[29,34] Many of the articles only described the care given to patients in non-specific terms and often details were only given for one study arm.

Clinical Outcomes – Table 2; Appendix C, Tables 2-3

Clinical outcomes were only reported sporadically. The most commonly reported clinical outcome was resource utilization (k = 5). Two studies reported receipt of treatment finding no significant difference in the proportion of patients using CPAP at follow-up.[31,36] One study found that patients whose follow-up appointments were at the hospital, as opposed to at home, often needed additional help from a specialist nurse for practical problems, although the significance and impact of this finding was not reported.[34] Three studies reported provider contact. One RCT found that patients being managed by a sleep specialist nurse had significantly more scheduled nursing time than patients being managed by a SSP (153 minutes vs 103 minutes, P<.001, effect size 1.25, 95% CI 0.94, 1.56) and patients managed by SSPs had significantly more physician visits than patients receiving nurse-led care (2.4 vs 0.2; P<.001, effect size 2.24, 95% CI 1.88, 2.60).[30] A second RCT compared the time nurse-managed patients spent with a nurse to the time SSP-managed patients spent with a SSP and found groups were similar (effect size 0.32, 95% CI -0.13, 0.66).[34] A third study reported extra visits and calls required by patients but without a measure of statistical significance.[29] We had difficulty determining what would constitute *improved* resource utilization and ultimately, OSA management by a non-SSP had no significant effect on any measure of resource utilization as compared to SSP care.

Three studies reported quality of life and all found that SF-36 scores were similar for patients being managed by primary care (k = 1)[31] or sleep-specialist nurses (k = 2)[30,34] compared to SSPs. The pooled standard mean differences in change from baseline for the mental health and vitality components of the SF-36 are presented in Figure 3.

The 2 studies reporting patient satisfaction both found no significant difference in overall satisfaction between groups.[30,31] One study reported significant differences on several VSQ-9 items but cautioned that the effect sizes were all small and may not be clinically significant.[31] No study reported all-cause mortality, access to care, minimally important differences in symptom scores, cognitive outcomes, libido, or percent of patients achieving physiological targets.

Table 2. Clinical Outcomes Comparing Non-sleep Specialists to Sleep Specialists

Author, Year Enrolled/ Randomized (n) Study Design	All-cause Mortality	Normalization of AHI	MID ESS	MID Urinary Symptom Scores	Quality of Life SF-36	Quality of Life SAQLI	Patient Satisfaction VAS	Patient Satisfaction VSQ-9	Resource Utilization Hospitalization	Resource Utilization Treatment	Resource Utilization Provider Contact	Resource Utilization Referrals	Access to Care	Libido	% Achieving Target Weight Loss	% Achieving Target BMI	% Achieving Target Blood Pressure	% Achieving Target HbA1c	Cognitive Symptoms	Other
Primary Care *3 studies (n = 468)*																				
Chai-Coetzer 2013 [31] (n = 155); RCT					↔			↕		↔										
Lettieri 2011[33] (n = 210); Obs. cohort																				
Scharf 2004[36] (n = 103); Retro survey/chart review										↔										↔[a]
Nurse *3 studies (n = 434)*																				
Andreu 2012[29] (n = 65); RCT											X									
Antic 2009[30] (n = 195); RCT					↔			↔			↕									
Palmer 2004[34] (n = 174); RCT					↔						↔	X								↔[b]
Not specified *1 study (n = 403)*																				
Pamidi 2012[35] (n = 403); Retro chart review																				
Total	0	0	0	0	3↔	0	0	1↔ 1↕	0	2↔	1↔ 1↕ 1X	1X	0	0	0	0	0	0	0	2↔

[a]subjective symptom improvement, [b]HADS = Hospital Anxiety and Depression Scale

MID = minimally important difference; ESS = Epworth Sleepiness Scale; BMI = body mass index; SF-36 = 36 item short form survey; SAQLI = Calgary Sleep Apnea Quality of Life Index; VAS = visual analogue scale; VSQ-9 = Visit-Specific Satisfaction Instrument; HbA1c = hemoglobin A1c; retro = retrospective; Obs = observational

↑ = significantly better with non-SSP than with usual care SSP including less resource utilization, ↔ = non-significant difference between non-SSP and SSP care, ↓ = significantly better with SSP than non-SSP, ↕ = mixed results comparing non-SSP and SSP care, X = between provider significance not reported; number before symbol indicates number of studies

Light gray shading in a cell indicates measure of significance was calculated, not reported by the study.

Figure 3. SF 36 Mental Health and Vitality Scores, Standardized Mean Differences in Mean Change from Baseline, Non-sleep Specialist versus Sleep Specialist[a]

Mental Health

Study name	Non-specialist	Statistics for each study			Sample size		Std diff in means and 95% CI
		Std diff in means	Lower limit	Upper limit	Non-specialist	Sleep specialist	
Chai-Coetzer 2013 (31)	PCP	-0.03	-0.34	0.29	81	74	
Antic 2009 (30)	Nurse	-0.02	-0.32	0.28	89	81	
Palmer 2004 (34)	Nurse	-0.06	-0.40	0.27	68	71	
		-0.04	-0.22	0.15			

-0.50   -0.25   0.00   0.25   0.50

Favors sleep specialist   Favors non-specialist

Vitality

Study name	Comparison	Statistics for each study			Sample size		Std diff in means and 95% CI
		Std diff in means	Lower limit	Upper limit	Non-specialist	Sleep specialist	
Chai-Coetzer 2013 (31)	PCP	-0.16	-0.48	0.15	81	74	
Antic 2009 (30)	Nurse	0.04	-0.26	0.34	89	81	
Palmer 2004 (34)	Nurse	0.00	-0.33	0.33	68	71	
		-0.04	-0.22	0.14			

-0.50   -0.25   0.00   0.25   0.50

Favors sleep specialist   Favors non-specialist

[a]Lower and upper limits represent 95% confidence intervals
PCP = primary care physician

Intermediate Outcomes – Table 3; Appendix C, Tables 4-6

The most frequently reported intermediate outcome was compliance with therapy, reported by 7 studies with some reporting multiple indicators of compliance. The majority of studies reported adherence as hours of use per night (k = 6).[29-31,33-35] Several reported the proportion of patients with regular use (k = 4), defined as ≥ 4 hours of CPAP use on ≥ 70% of nights, a compliance threshold often used to define minimally acceptable compliance for payment reimbursement.[29,33,35,36] One reported the proportion of nights with any use.[33] Six of the 7 studies found no difference in compliance, regardless of measure used, when comparing patients receiving SSP care to those receiving care from non-SSPs. The pooled mean difference from the RCTs was -0.25 (95% CI -0.72, 0.22; I^2 = 21%) (Figure 4). The final study found that patients who were referred for a sleep study by non-SSPs were significantly less compliant, with fewer hours per night and less regular use, than those patients who were referred by SSPs.[35] Cost was reported, in various ways, by 4 of the studies.[29-31,34] Two did not report the significance of differences between SSP and non-SSP care for OSA.[31,34] Two studies, however, found that nurse-led OSA care was associated with significantly lower costs per patient[29] and within-trial costs.[30]

Table 3. Intermediate Outcomes Comparing Non-sleep Specialists to Sleep Specialists

Author, Year Enrolled/ randomized (n) Study design	AHI	Oxygen Saturation – Mean	Time <90%	ODI	Minimum	ESS	FOSQ	SASQ	Arousals	TST	PSQI	Snoring	Other	Weight Loss	BMI	Blood Pressure	HbA1c	Time to Initiation of Therapy	Adverse Events	Cost	Hrs/night	Proportion of Nights	Regular Use[c]	Other
Primary Care *3 studies (n = 468)*																								
Chai-Coetzer, 2013 [31] (n = 155); RCT						↔	↔	↔						↔		↔				X	↔			
Lettieri, 2011 [33] (n = 210); Obs. cohort						↔													↔		↔	↔	↔	
Scharf, 2004 [36] (n = 103); Retro survey/chart review																		↓					↔	
Nurse *3 studies (n = 434)*																								
Andreu, 2012 [29] (n = 65); RCT						↔	↕												X	↑[a]	↔		↔	
Antic, 2009 [30] (n = 195); RCT						↔	↔						↔[b]					↕		↑	↔			
Palmer, 2004 [34] (n = 174); RCT						↔							↔							X	↔			
Not specified *1 study (n = 403)*																								
Pamidi, 2012 [35] (n = 403); Retro chart review	↑																				↓		↓	
Total	1↑					5↔	2↔ 1↕	1↔					2↔	1↔		1↔		1↓ 1↕	1↔ 1X	2↑ 2X	5↔ 1↓	1↔	3↔ 1↓	

[a] decreased costs
[b] maintenance of wakefulness
[c] ≥ 4h of use on ≥ 70% of nights

AHI = apnea-hypopnea index; ODI = oxygen desaturation index; ESS = Epworth Sleepiness Scale; FOSQ = Functional Outcomes of Sleep Questionnaire; SASQ = Sleep Apnea Symptom Questionnaire;TST = total sleep time; PSQI = Pittsburgh Sleep Quality Index; BMI = body mass index; retro = retrospective; Obs = observational
↑ = significantly better with non-SSP than with usual care SSP including less resource utilization, ↔ = non-significant difference between non-SSP and SSP care, ↓ = significantly better with SSP than non-SSP, ↕ = mixed results comparing non-SSP and SSP care, X = between provider significance not reported; number before symbol indicates number of studies
Light gray shading in a cell indicates measure of significance was calculated, not reported by the study.

Figure 4. Compliance, Weighted Mean Difference for Hours per Night, Non-sleep Specialist versus Sleep Specialist[a]

Study name	Non-specialist	Statistics for each study			Sample size		Difference in means and 95% CI
		Difference in means	Lower limit	Upper limit	Non-specialist	Sleep specialist	
Chai-Coetzer 2013 (6 months) (31)	PCP	-0.60	-1.23	0.03	51	44	
Andreu 2012 vs Group B (6 months) (29)	Nurse	0.30	-0.88	1.48	22	21	
Antic 2009 (3 months) (30)	Nurse	-0.50	-1.30	0.30	94	81	
Palmer 2004 (3 months) (34)	Nurse	0.30	-0.61	1.21	63	63	
		-0.25	-0.72	0.22			

-2.00 -1.00 0.00 1.00 2.00

Favors sleep specialist Favors non-specialist
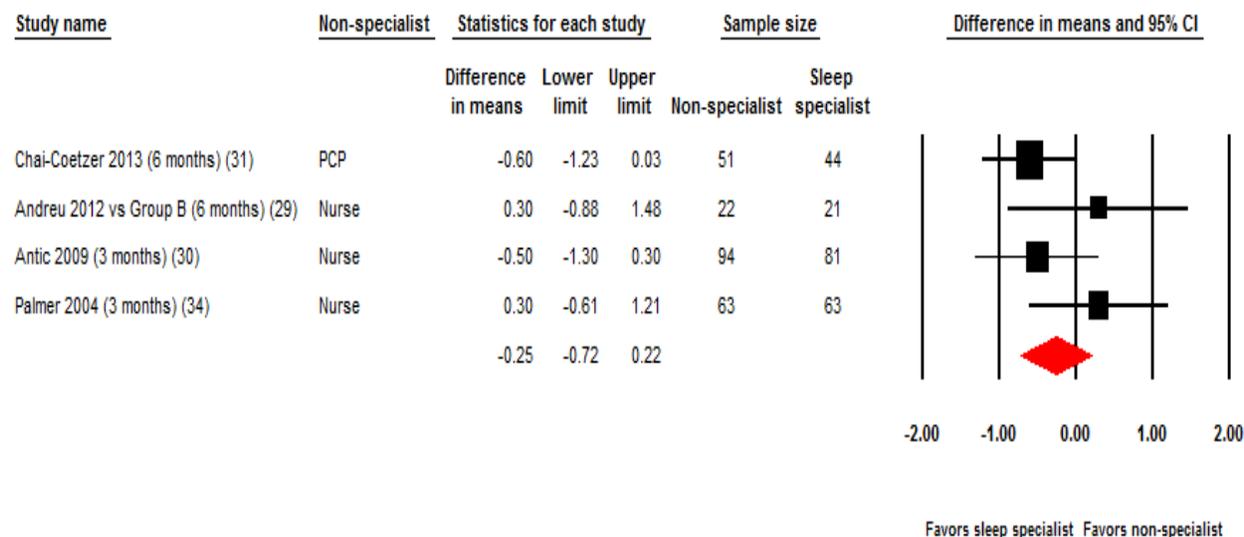
[a]Lower and upper limits represent 95% confidence intervals
PCP = primary care physician

Sleep symptom scores were reported by 5 studies.[29-31,33,34] All 5 reported ESS scores and all found similar results for groups receiving care from different providers. For the RCTs, the SMD for improvement from baseline was 0.06 (95% CI -0.11, 0.24; I^2 = 2%) (Figure 5) and the weighted mean difference (WMD) was 0.30 (95% CI -0.50, 1.10). Three studies also reported FOSQ and one reported SASQ scores; 2 reported no significant between group differences in either score.[30,31] The third study, which used a 3-arm design, found that patients with sleep unit nurse-led follow-up care had lower (*ie*, worse) FOSQ scores than one of the 2 groups of patients with sleep pulmonologist follow-up.[29] The difference was small (one point) but statistically significant. There was no difference between the nurse-followed group and the other pulmonologist group. AHI was reported by one study, which found that residual AHI on CPAP was significantly lower in patients referred for PSG by non-SSPs than in patients referred by SSPs (P<.001).[35]

One RCT reported dryness (54%), nasal congestion (40%), and abrasions (25%) but did not provide separate data for the 2 study groups.[29] An observational study reported no significant differences between groups in the percentages of patients who discontinued therapy although reasons for discontinuing were not reported.[33] In one study, changes in weight loss and blood pressure were similar with primary care management of OSA as compared to SSP care.[31] Time to initiation of therapy was reported in 2 studies. One found that significantly fewer patients in the primary care group received CPAP within one month of PSG when compared to patients in the SSP group (P = .012).[36] The other reported that while groups were similar in satisfaction with time waiting (P = .71), patients receiving nurse-led care were more satisfied with their impression of wait time (P = .004).[30] No studies reported oxygen saturation, HbA1c, or BMI.

Figure 5. Epworth Sleepiness Scores, Standardized Mean Differences for Mean Change from Baseline, Non-sleep Specialist versus Sleep Specialist[a]

Study name	Non-specialist	Std diff in means	Lower limit	Upper limit	Non-specialist	Specialist	Std diff in means and 95% CI
Chai-Coetzer 2013 (6 months) (31)	PCP	0.07	-0.25	0.38	81	74	
Andreu 2012 vs Group B (6 months) (29)	Nurse	-0.27	-0.87	0.34	22	20	
Antic 2009 (3 months) (30)	Nurse	-0.03	-0.33	0.27	90	84	
Palmer 2004 (3 months) (34)	Nurse	0.28	-0.06	0.61	68	71	
		0.06	-0.11	0.24			

-1.00   -0.50   0.00   0.50   1.00

Favors sleep specialist   Favors non-specialist
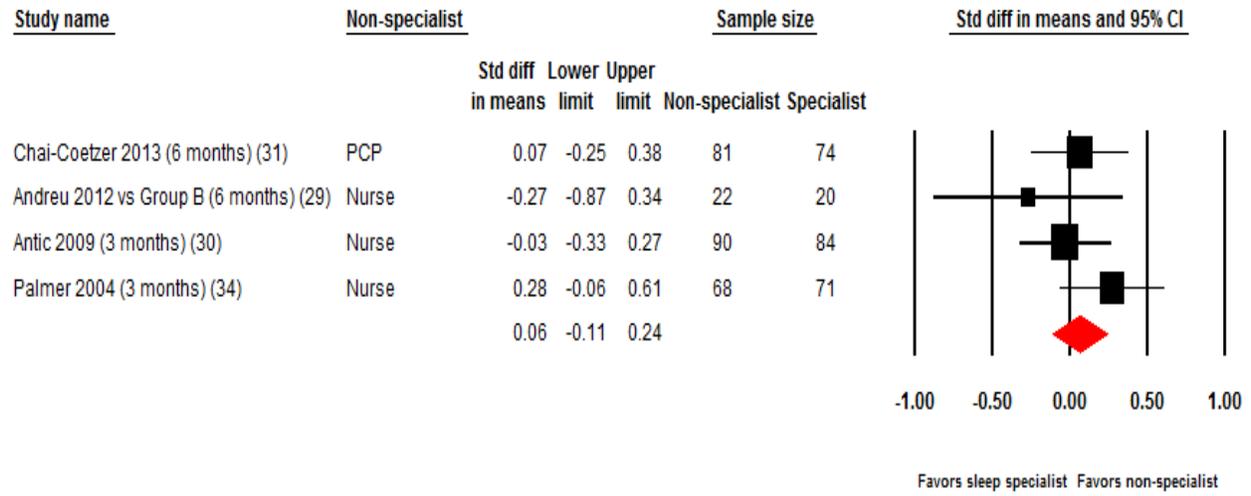
[a]Lower and upper limits represent 95% confidence intervals
PCP = primary care physician

KEY QUESTION #1A: Do effectiveness/harms/resource utilization vary by patient characteristics:

a. Unexplained daytime sleepiness/fatigue

b. AHI severity

c. Other risk factors or coexisting conditions associated with OSA (*eg*, obesity, neck circumference, treatment-resistant hypertension, diabetes, age, sex, race)

d. Symptoms (*eg*, nocturia, loss of libido, snoring, witnessed sleep "apnea")?

Few studies provided information to address KQ1A.

A. Unexplained Daytime Sleepiness/Fatigue

Of the studies eligible for KQ1, 2 required patients to have at least mild daytime sleepiness (ESS ≥ 8)[30,31] and one required an ESS ≥ 12.[29] Another study did not report ESS but noted that 68% of patients reported excessive sleepiness at baseline.[36] No study reported results for subgroups of patients based on daytime sleepiness. In addition, with sporadic outcome reporting, it was not possible to determine whether results were different in studies that required a measure of sleepiness for study inclusion versus those that did not.

B. AHI Severity

Four studies reported baseline AHI. Values ranged from 21/hour[33] to 68/hour.[30] In one of the studies, 55% were diagnosed with severe OSA (AHI ≥ 30/hour).[35] Similar to the finding for daytime sleepiness, no study reported results for subgroups of patients based on AHI and it was not possible to determine whether results were different in the studies with higher baseline AHI values.

C. Other Risk Factors or Coexisting Conditions Associated with OSA

Each of the 7 studies with newly evaluated/diagnosed patients reported BMI. Values ranged from 30 kg/m^2[33] to 36 kg/m^2.[35] One study reported neck circumference (mean of 45.5 cm).[29] No study reported treatment resistant hypertension but 4 reported percentages of study participants with hypertension ranging from 38%[32] to 58%.[35] Three reported percentages of participants with diabetes (14% to 26%).[32,35,36] As noted previously, mean age in the 8 studies was 52 years with little variation across studies (range 48 to 59 years). The mean percentage of male study participants was 67% but values ranged from 47% to 85%. No study reported results for subgroups of patients based on obesity, neck circumference, hypertension, diabetes, age, or gender.

One study from the US (Chicago) reported race with 54% African American and 46% non-African American.[35] In a model adjusted for age, sex, BMI, Medicaid insurance, AHI, ESS, Center for Epidemiologic Studies Depression Scale, and education level, African Americans

used CPAP an average of 56 minutes/day less than non-African Americans (P = .002) It was not reported whether there was an interaction with physician specialty.

D. Symptoms

Four studies addressed snoring. In 2 studies, snoring was an inclusion criterion with "habitual snoring" being a high-risk feature in one study[33] and history of snoring "most" or "every" night being a factor in patient referral in another study.[30] Two studies reported the percentage of patients with snoring at baseline: 100%[29] and 83%.[36] None of the studies reported results for subgroups of patients based on snoring as an inclusion criterion or a baseline factor.

Strength of Evidence for Key Question 1 (Table 4, Appendix D)

There was insufficient evidence for access to care and adverse events. Strength of evidence for quality of life, ESS, and CPAP compliance (hours of use per night) was rated as moderate. Quality of life, ESS, and compliance were similar for patients managed by practitioners who are not sleep physicians compared to patients managed by SSPs.

Table 4. Strength of Evidence for Outcomes, Key Question 1

Comparison	Outcome of Interest	Strength of Evidence	Direction	Findings
KQ1: Sleep physician care compared to management by primary care, sleep-specialist nurses or other non-sleep physicians	Access to care	Insufficient		We found no evidence for this outcome.
	Epworth Sleepiness Scale (ESS)	Moderate	Similar	Based on 4 RCTs (n = 568) with aggregate moderate risk of bias, we found improvement from baseline in ESS scores was similar for patients being managed by primary care/sleep-specialist nurses compared to SSPs (SMD = 0.06 [95% CI -0.11, 0.24]). One observational study also found ESS scores were similar between groups.
	Quality of life	Moderate	Similar	Based on 3 RCTs (n = 524) with aggregate moderate risk of bias, we found quality of life measures were similar for patients being managed by primary care/ sleep-specialist nurses compared to SSPs. SMDs for SF-36 Vitality and Mental Health scores were -0.04 [95% CI -0.22, 0.15]) and -0.04 [95% CI -0.22, 0.14], respectively.
	Compliance, hours per night	Moderate	Similar	Based on 4 RCTs (n = 568) with aggregate moderate risk of bias, we found compliance was similar for patients being managed by primary care/sleep-specialist nurses compared to SSPs (WMD = -0.25 [95% CI -0.72, 0.22]). One observational cohort study also found compliance was similar between groups but one study based on retrospective chart review reported compliance was greater in the SSP group compared to the non-sleep specialist group.
	Adverse events	Insufficient		Based on the findings of one RCT (n = 65) that did not report adverse events by treatment arm, the evidence is insufficient to draw conclusions.

APAP = Auto-adjusted (autoregulated) continuous positive airway pressure; CPAP = continuous positive airway pressure; RCT = randomized controlled trial; SAQLI = Sleep Apnea Quality of Life Index; SF-36 = Short Form-36; SMD = standardized mean difference; WMD = weighted mean difference.
[a]Strength of Evidence Definitions;[28] See Appendix D for more details
• High: Very confident that estimate of effect lies close to true effect. Few or no deficiencies in body of evidence, findings believed to be stable.
• Moderate: Moderately confident that estimate of effect lies close to true effect. Some deficiencies in body of evidence; findings likely to be stable, but some doubt.
• Low: Limited confidence that estimate of effect lies close to true effect; major or numerous deficiencies in body of evidence. Additional evidence necessary before concluding that findings are stable or that estimate of effect is close to true effect.
• Insufficient: No evidence, unable to estimate an effect, or no confidence in estimate of effect. No evidence is available or the body of evidence precludes judgment.

KEY QUESTION #2: For adults with suspected OSA, what are the effectiveness/harms/resource utilization of electronic consultation versus interactive (*eg*, in-person, telephone) consultation?

Key Question #2A: Do effectiveness/harms/resource utilization vary by patient characteristics:

a. Unexplained daytime sleepiness/fatigue

b. AHI severity

c. Other risk factors or coexisting conditions associated with OSA (*eg*, obesity, neck circumference, treatment-resistant hypertension, diabetes, age, sex, race)

d. Symptoms (*eg*, nocturia, loss of libido, snoring, witnessed sleep "apnea")?

We found no studies that addressed KQ2 or KQ2a.

KEY QUESTION #3: For adults diagnosed with OSA, what are the effectiveness/harms/resource utilization (including cost avoidance) of using in-home autotitrating continuous positive airway pressure (APAP) technology compared to standard continuous positive airway pressure (CPAP) titrated by in-lab PSG?

Summary of Findings for Key Question 3

Titration

- Few studies compared clinical (ie, patient-centered) outcomes between in-lab CPAP titration and at-home APAP titration. In limited reporting, study groups were generally similar on measures of quality of life (moderate strength of evidence) and cognitive symptoms. Some differences were noted for resource utilization and patient preference.

- Intermediate outcomes (ie, sleep measures, blood pressure, adverse events, and compliance/adherence) were more commonly reported and generally similar. Strength of evidence for ESS was moderate and strength of evidence for compliance was low. Strength of evidence for adverse events was insufficient.

Treatment

- Twenty-three studies compared treatment with CPAP to treatment with APAP. The studies enrolled patients with a broad range of baseline AHI values.

- Few studies reported clinical (ie, patient-centered) outcomes other than quality of life and patient preference for one treatment approach over another. Quality of life, assessed with the SF-36, was generally similar between the CPAP and APAP groups (moderate strength of evidence). Patient preference was also generally similar or favored APAP in studies reporting statistical significance. Strength of evidence was insufficient for access to care.

- Intermediate outcomes including post-treatment ESS scores were frequently reported and generally similar for the 2 treatment approaches (moderate strength of evidence). Adverse events were mild and similar for APAP and CPAP (low strength of evidence).

- Compliance, reported as either hours per night or the proportion of nights the device was used, was also similar for the CPAP and APAP treatment groups (moderate strength of evidence).

Titration

Overview of Studies – Table 5; Appendix C, Table 7

Four studies compared *titration* of positive airway pressure using in-lab CPAP versus at-home APAP to determine a final long-term CPAP pressure setting.[33,37-39] Three were RCTs conducted in Canada,[39] Australia,[38] and Spain.[37] The fourth study, a cohort study, was done in the US.[33] Follow-up periods ranged from 4 to 12 weeks. Sample sizes ranged from 68[39] to 245[37] at baseline but at least 10% of the sample was not included in the final analysis of each study. Each of the studies was rated medium risk of bias.

Table 5. Key Question 3, Titration: Study Characteristics

Characteristic	Weighted Mean (range) *Unless otherwise noted*	Number of studies reporting
Total number enrolled/randomized	622 (68-245)	4
Randomized controlled trials, total n	482 (68-245)	3
Other, total n	140	1
Age of subjects (years)	50 (46-54)	4
Percent Male	76 (67-88)	4
Baseline BMI (kg/m^2)	33 (29.3-38.5)	4
Baseline ESS	14.7 (14.0-15.6)	3
Baseline AHI (events/hour)	43 (21.2-62.3)	3
Percent with hypertension (%)*	45 (32-56)	2
Location - North America, total n	208 (68-140)	2
Location - Europe, total n	213	1
Location - Australia/New Zealand, total n	169	1

*as defined by study

In 3 of the studies, all of the study participants had a diagnostic PSG.[33,37,38] In the cohort study, those diagnosed with OSA (defined as an AHI > 5/hour with compatible symptoms) and eligible for the home sleep study program (having at least 2 high-risk features such as habitual snoring and daytime fatigue) were included.[33] The RCT from Australia required patients to have symptomatic OSA, defined as ESS ≥ 8 and AHI ≥ 15/hour.[38] The RCT from Spain also required patients to have symptomatic OSA, defined as ESS ≥ 12 and AHI ≥ 30/hour.[37]

In the remaining RCT, patients with clinical suspicion of moderate to severe OSA were evaluated using a diagnostic algorithm. Patients with ESS ≥ 10, Sleep Apnea Clinical Score (SACS) ≥ 15, and RDI ≥ 15/hour (respiratory disturbance index, a measure similar to AHI) were eligible for the study.[39] The group assigned to in-lab CPAP titration underwent PSG to evaluate the performance of the diagnostic algorithm and 34 of 36 patients had an AHI ≥ 15/hour (probability of moderate to severe OSA 0.94 (95% CI 0.81, 0.99)).

Baseline ESS scores were similar in all 4 studies, ranging from 14.0 to 15.5 with the highest score in the study requiring an AHI ≥ 30/hour.[37] Baseline AHI values ranged from 21/hour[33] to 62/hour.[37]

Clinical Outcomes - Table 6, Appendix C Tables 8-9

None of the studies reported all-cause mortality; minimally important differences in AHI, ESS, or urinary symptom scores; patient satisfaction; hospitalizations; access to care; libido; or percent achieving targets for weight loss, BMI, blood pressure, or HbA1c. Quality of life measures were most commonly reported including SF-36 (2 RCTs) and the Sleep Apnea Quality of Life (SAQLI) (1 RCT).

In the study from Spain, SF-36 scores were reported as change from baseline. There was a significant (P<.01) improvement from baseline for both groups in the physical score while the

mental score improved from baseline only for the in-lab CPAP titration group.[37] The Australian study found CPAP and APAP titration resulted in similar scores at the 4-week follow-up for both the physical and mental components of the SF-36.[38] Standard mean difference for the change from baseline in the mental and physical health components of the SF-36 are depicted in Figure 6.

One RCT reported several resource utilization outcomes.[38] During the 4-week study period, there were more humidifiers issued to the home APAP group but fewer chin straps. Technologist staff time for education was similar in the 2 groups as was the time required for follow-up clinics and telephone calls. Technologist time was significantly higher for the home APAP group compared to the in-lab titration group on titration morning. Technologist time for the home APAP group included time needed to download data from the home device. Physician time for titration study reporting was significantly higher in the in-lab titration group compared to the home APAP group as the physician analyzed the manual titration results to determine the fixed pressure for CPAP therapy. Physician time for follow-up clinics was similar.

The same study reported cognitive outcomes.[38] Baseline and 4-week scores on the Trails A and Trails B cognitive function tests were similar in the in-lab CPAP and home APAP groups.

One study reported patient preference.[39] Sixty-two percent in the in-lab study group would have preferred home management while 6% of the home groups would have preferred in-lab management.

Table 6. Clinical Outcomes Comparing APAP to CPAP, Titration Studies

Author, Year Enrolled/ Randomized (n) Study Design	All-cause Mortality	Normalization of AHI	MID		Quality of Life		Patient Satisfaction		Resource Utilization				Access to Care	Libido	% Achieving Target				Cognitive Symptoms	Patient Preference	Other
			ESS	Urinary Symptom Scores	SF-36	SAQLI	VAS	VSQ-9	Hospitalization	Treatment	Provider Contact	Referrals			Weight Loss	BMI	Blood Pressure	HbA1c			
Lettieri 2011[33] (n = 140) Obs. Cohort																					
McArdle 2010[38] (n = 169) RCT					↔					↕	↓								↔		
Mulgrew 2007[39] (n = 68) RCT						↔														X	
Masa 2004[37] (n = 245) RCT					↕																
Total *4 studies* (n = 622)	0	0	0	0	1↔ 1↕	1↔	0	0	0	1↕	1↓	0	0	0	0	0	0	0	1↔	1X	0

MID = minimally important difference; AHI = apnea-hypopnea index; ESS = Epworth Sleepiness Scale; BMI = body mass index; SF-36 = 36 item short form survey; SAQLI = Sleep Apnea Quality of Life Index; VAS = visual analogue scale; VSQ-9 = Visit-Specific Satisfaction Instrument; HbA1c = hemoglobin A1c; Obs = observational

↑ = significantly better with APAP than CPAP, ↔ = non-significant difference between APAP and CPAP, ↓ = significantly better with CPAP than APAP, ↕ = mixed results comparing APAP and CPAP, X = between group significance not reported; number before symbol indicates number of studies

Figure 6. SF 36 Scores, Standardized Mean Differences in Mean Change from Baseline, Titration Studies[a]
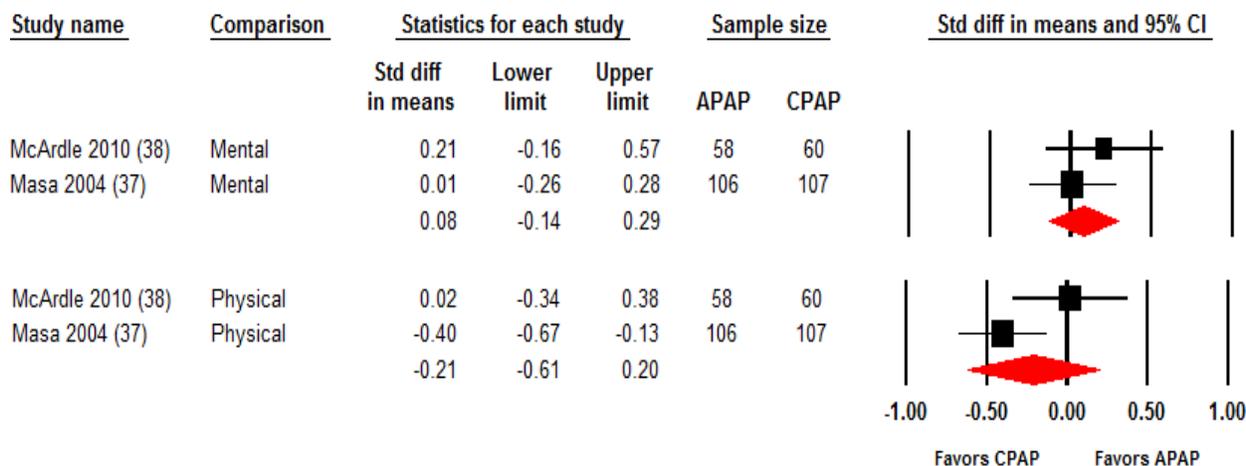
[a]Lower and upper limits represent 95% confidence intervals

Intermediate Outcomes – Table 7; Appendix C, Tables 10-12

Changes in sleep measures were commonly reported with the in-lab CPAP titration and home APAP titration groups, and found to be similar at follow-up. Three RCTs reported AHI values on PAP were similar at 4 weeks[38] and 12 weeks.[37,39] Two RCTs reported oxygen saturation outcomes finding the groups to be similar at 4 weeks[38] and 12 weeks.[37] All 4 studies reported ESS scores and found the titration groups were similar at follow-up. For the 2 RCTs reporting mean ESS scores, the SMD in change in ESS scores from baseline was 0.00 (95% CI -0.22, 0.21; $I^2 = 0\%$) (Figure 7) and the WMD was -0.01 (95% CI -1.11, 1.10).[37,38]

Other sleep symptom measures included the FOSQ,[37] Arousal Index,[37,38] and total sleep time;[38] these were also similar at follow-up for the in-lab CPAP and home APAP groups.

One study reported blood pressure.[38] At 4 weeks follow-up, the in-lab CPAP and home APAP groups had similar systolic and diastolic blood pressures. No studies reported on weight loss, BMI, or HbA1c.

The cohort study reported on discontinuation of therapy during the 4-6 week follow-up and found similar discontinuation rates – 8.6% of the in-lab CPAP group and 10% of the home APAP groups discontinued treatment.[33] The RCT from Spain reported "secondary effects" (*eg*, oral dryness, mask intolerance, noise, headache, claustrophobia, smothering sensations, bed partner intolerance) noting that there were no important differences between the in-lab CPAP and home APAP groups.[37]

One study reported staff costs per patient and capital equipment and consumable costs per patient. Both were higher for the in-lab CPAP group but the statistical significance of the findings was not reported.[38]

Each of the studies reported on PAP use (*ie*, hours per night). Three studies reported that the in-lab CPAP and home APAP groups were similar[33,37,38] while one reported significantly (P = .02) more hours per night (median 6.0 vs 5.4) in the home APAP group.[39] Mean differences from the RCTs are presented in Figure 8. The pooled mean difference was 0.02 (95% CI -0.41, 0.45).

Other reported adherence/compliance measures were similar for the 2 groups including percentage of nights used,[33] use of device for more than 4 hours per night for more than 70% of nights,[33] and percentage of patients continuing to use device at 4 week follow-up.[38]

One study reclassified participants into "adherent" and "non-adherent" groups based on use of the device for more than 4 hours per night for more than 70% of nights.[33] Age, gender, BMI, AHI, and baseline sleepiness did not influence use of the PAP device.

Table 7. Intermediate Outcomes Comparing APAP to CPAP, Titration Studies

Author, Year Enrolled/Randomized (n) Study Design	Oxygen Saturation					Sleep Symptom Scores								Weight Loss	BMI	Blood Pressure	HbA1c	Adverse Events	Costs	Compliance/Adherence			
	AHI	Mean	Time <90%	ODI	Minimum	ESS	FOSQ	SASQ	Arousals	Total Sleep Time	PSQI	Snoring	Other							Hrs/night	Proportion of Nights	Regular Use[a]	Other
Lettieri, 2011[33] (n = 140) Obs. Cohort						↔												↔		↔	↔	↔	
McArdle, 2010[38] (n = 169) RCT	↔	↔	↔			↔			↔	↔						↦			X	↔			↔[b]
Mulgrew, 2007[39] (n = 68) RCT	↔					↔														↑			
Masa, 2004[37] (n = 245) RCT	↔		↔			↔	↔		↔									↔		↔			
Total *4 studies* (n = 622)	3↔	1↔	2↔	0	0	4↔	1↔	0	2↔	1↔	0	0	0	0	0	1	0	2↔	2X	1↑ 3↔	1↔	1↔	1↔

[a]as defined by study
[b]percentage of patients continuing to use CPAP
AHI = apnea-hypopnea index; ODI = oxygen desaturation index; ESS = Epworth sleepiness scale; FOSQ = functional outcomes of sleep questionnaire; PSQI = Pittsburgh sleep quality index; BMI = body mass index
↑ = significantly better with APAP than CPAP, ↔ = non-significant difference between APAP and CPAP, ↓ = significantly better with CPAP than APAP, ↕ = mixed results comparing APAP and CPAP, X = between group significance not reported; number before symbol indicates number of studies

Figure 7. Epworth Sleep Scores, Standardized Mean Difference for Mean Change from Baseline, Titration Studies[a]

Study name	Statistics for each study			Sample size		Std diff in means and 95% CI
	Std diff in means	Lower limit	Upper limit	APAP	CPAP	
McArdle 2010 (4 weeks) (38)	-0.04	-0.39	0.32	62	61	
Masa 2004 (12 weeks) (37)	0.02	-0.25	0.29	106	107	
	-0.00	-0.22	0.21			
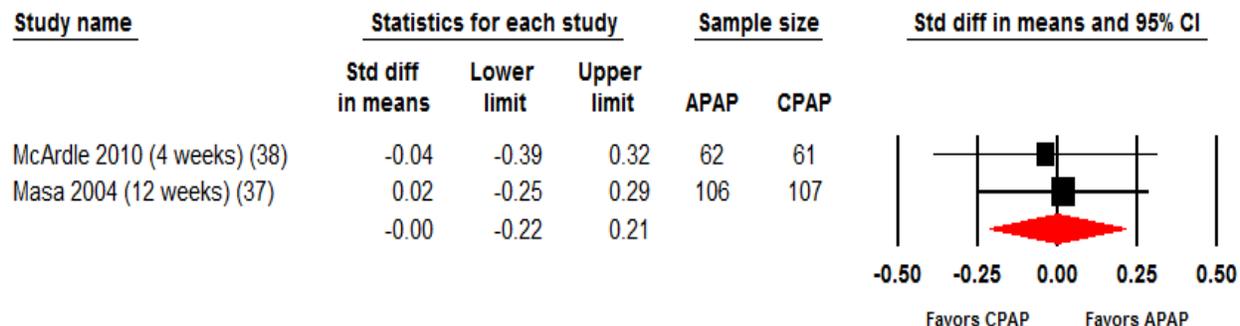
[a]Lower and upper limits represent 95% confidence intervals

Figure 8. Compliance, Weighted Mean Difference for Hours per Night, Titration Studies[a]

Study name	Statistics for each study			Sample size		Difference in means and 95% CI
	Difference in means	Lower limit	Upper limit	APAP	CPAP	
McArdle 2010 (4 weeks) (38)	-0.14	-0.87	0.59	68	70	
Masa 2004 (12 weeks) (37)	0.10	-0.42	0.62	106	107	
	0.02	-0.41	0.45			
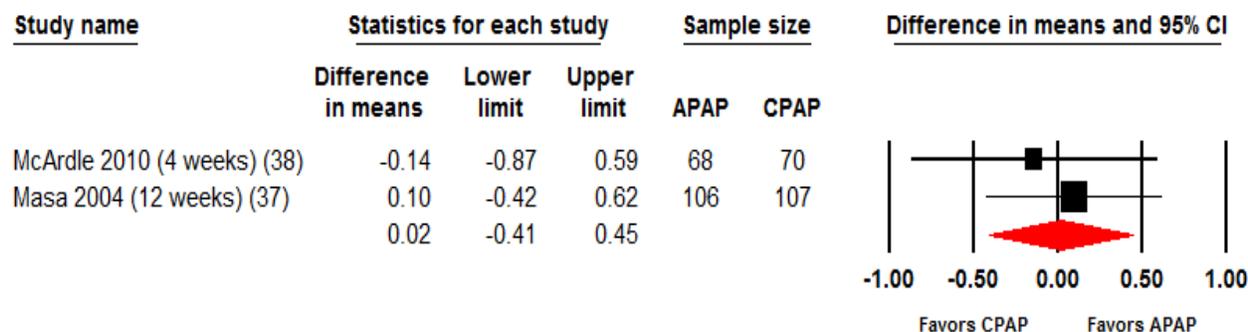
[a]Lower and upper limits represent 95% confidence intervals

Treatment

Overview of Studies –Table 8; Appendix C, Table 7

We included 23 studies (with 1,260 patients) comparing CPAP to APAP for *treatment* of OSA.[40-62] Most of the studies included an in-lab CPAP titration study, but 4 of the 23 studies put patients on APAP without a titration study.[43,56,59,62] In 2 of those 4 studies, the CPAP fixed pressure was based on a 1-week[62] or 2-week[59] adaptation period of APAP (rather than an in-lab titration study). Three studies were rated low risk of bias[52,54,61] and the remaining studies medium risk of bias.

Table 8. Key Question 3, Treatment: Study Characteristics

Characteristic	Weighted Mean (range) *Unless otherwise noted*	Number of studies reporting
Total number enrolled/randomized	1260 (10-200)	23
Randomized controlled trials, total n	486 (21-109)	7
Crossover studies, total n	600 (10-200)	15
Other, total n	174	1
Age of subjects (years)	53 (45-57)	23
Percent Male	87 (75-100)	22
Baseline BMI	33 (29.3-49.9)	22
Baseline ESS	11.8 (6.4-17.4)	20
Baseline AHI (events/hour)	44 (14.7-75.8)	19
Percent with hypertension (%)*	28 (20-55)	2
Location - North America, total n	119 (10-109)	2
Location - Europe, total n	1,018 (20-200)	17
Location - Australia/New Zealand, total n	77 (12-55)	3
Location - Multi-national, total n	46	1

*as defined by study

There were 22 RCTs (15 of which used a crossover design) and one retrospective cohort study.[58]. One study was conducted in the US with a VA population.[43] Of the remaining studies, one was conducted in Canada, 3 in Australia or New Zealand, and 17 in Europe.

Individual study sample sizes ranged from 10[47] to 200.[61] Among the non-crossover RCTs, treatment periods ranged from one[43] to 6[50,62] months. In the crossover studies, treatment phases ranged from 6 nights[40] to 2 months/8 weeks.[42,45,46,51,53,60] Several of the crossover studies reported either a washout period between study arms or exclusion of data collected during an initial period of use following a change to a different protocol.

Patient inclusion criteria varied in the 23 studies. All but 3 studies enrolled patients based on AHI. Minimum AHIs for enrollment were 5/hour,[46,51,58] 10/hour,[42,45,54,57,59] 15/hour,[40,41,47,49,61] 20/hour,[53,55,60] and 30/hour.[48,50,56] One study included patients with a home sleep test AHI above 10/hour or a laboratory PSG AHI above 20/hour.[44] Three studies did not specify a minimum AHI. In one, patients were referred for PSG based on the Berlin Questionnaire.[43] Another included patients based on excessive daytime sleepiness and an ESS above 9.[62] The third study enrolled patients who were already being treated with CPAP.[52] Of the studies specifying an AHI, 11 also required clinical symptoms: sleepiness in 4[44,54,59,61] and daytime symptoms in 2.[41,58]

Baseline values for AHI ranged from 15/hour[51] (a study that required participants to have AHI values between 5/hour to 30/hour) to 76/hour[40] (a study that required participants to have an AHI of 15/hour or higher with morbid obesity). The baseline value was below 20/hour in one study, between 31 and 40/hour in 3 studies, between 41 and 50/hour in 8 studies, and 51/hour or higher in 7 studies. No studies had baseline values between 21 and 30/hour; 4 did not report baseline AHI.

Baseline ESS scores ranged from 6.4[58] to 17.4[40] in 21 studies. Two studies did not report baseline ESS scores.

Clinical Outcomes – Table 9; Appendix C, Table 8-9

The most frequently reported clinical outcomes were patient preference (12 studies) and quality of life assessed with the SF-36 (9 studies). In 7 of the 12 studies reporting preference, patients preferred APAP over CPAP. The difference was reported to be statistically significant in 3 studies.[45,54,57] Four studies did not report statistical significance.[40,42,48,53] The percentage of patients expressing a preference for APAP or CPAP was similar in 5 studies with 2 reporting the statistical significance for the comparison.[47,61] No study reported a significantly higher patient preference for CPAP. In 4 studies reporting, between 10% and 72% of patients did not express a preference.[48,51,59,61]

Seven of the 9 studies reporting SF-36 quality of life found the APAP and CPAP groups to be similar post-intervention.[44,46,52,54,59,61,62] One study reported a significantly higher mental health composite score in the APAP group.[49] The remaining study did not report statistical significance for between group comparisons.[50] One study also reported groups were similar for the SAQLI.[62]

All-cause mortality was reported in 3 studies with no or few events.[43,58,61] One study reported that a minimally important difference in ESS scores was achieved in both study groups.[59] The minimally important difference was 2 points. Patient satisfaction (2 studies) was similar for the APAP and CPAP groups.[46,58] Four studies reported measures of resource utilization including hospitalization for chest pain,[43] seeking help from the sleep center,[61] extra calls or visits with sleep nurses,[62] or unplanned contacts and duration of unplanned contacts.[46] finding the groups were similar or not reporting statistical significance.

No study reported minimally important differences in urinary symptom scores, access to care, or diagnosis of cognitive impairment.

Table 9. Clinical Outcomes Comparing APAP to CPAP, Treatment Studies

Author, Year Enrolled/Randomized (n) Study Design	All-cause Mortality	Normalization of AHI	MID ESS	MID Urinary Symptom Scores	Quality of Life SF-36	Quality of Life SAQLI	Patient Satisfaction VAS	Patient Satisfaction VSQ-9	Resource Utilization Hospital i-zation	Resource Utilization Provider Contact	Access to Care	Diagnosis of Cognitive Impairment	Patient Preference	Other
Bakker 2011[40] (n = 12) crossover													X	
Drummond 2010[43] (n = 109) RCT	X								X					
Vennelle 2010[61] (n = 200) crossover	X				↔					↔			↔	
Damjanovic 2009[41] (n = 100) RCT														
Galetke 2008[45] (n = 20) crossover													↑	
Fietze 2007[44] (n = 21) RCT					↔									
Meurice 2007[50] (n = 83) RCT					X									
Nolan 2007[51] (n = 29) crossover													X	
Patruno 2007[55] (n = 40) RCT														
Richard 2007[58] (n = 174) retro cohort	X						↔							
Nolan 2006[52] (n = 27) crossover					↔								X	
Nussbaumer 2006[54] (n = 34) crossover					↔								↑	
West 2006[62] (n = 98) RCT					↔	↔				X				
Hukins 2004[46] (n = 55) crossover					↔		↔			↔				
Hussain 2004[47] (n = 10) crossover													↔	
Marrone 2004[48] (n = 22) crossover													X	
Noseda 2004[53] (n = 27) crossover													X	
Massie 2003[49] (n = 46) crossover					↑									
Planes 2003[56] (n = 35) RCT														↔[a]
Senn 2003[59] (n = 31) crossover			↔		↔								X	

Randerath 2001[57] (n = 52) crossover													↑	
D'Ortho 2000[42] (n = 25) crossover													X	
Teschler 2000[60] (n = 10) crossover														
Total 23 studies (n = 1,260)	3X	0	1↔	0	1↑ 7↔ 1X	1↔	2↔	0	1X	2↔ 1X	0	0	3↑ 2↔ 7X	1↔

[a]tolerance

↑ = significantly better with APAP than CPAP, ↔ = non-significant difference between APAP and CPAP, ↓ = significantly better with CPAP than APAP, ↕ = mixed results comparing APAP and CPAP, X = between group significance not reported

Intermediate Outcomes – Table 10; Appendix C, Tables 10-12

Intermediate outcomes were more frequently reported. Seventeen studies reported AHI after the treatment periods with 12 finding APAP and CPAP resulted in similar AHI values, one reporting significantly better results with CPAP compared to APAP, and 4 not reporting the significance of the findings. Oxygen saturation measures were reported in 11 studies with most finding APAP and CPAP to be similar.

Sleep symptom scores were also generally similar. The most frequently reported score was the ESS (reported in 20 of the 23 studies). Sixteen studies found the CPAP and APAP groups to be similar, 2 reported the scores were statistically significantly better for the APAP groups, and 2 did not report significance. For the 4 pooled parallel group RCTs, the SMD in improvement from baseline was 0.18 (95% CI -0.06, 0.43; $I^2 = 0\%$) (Figure 9) and the WMD was 0.85 (95% CI -0.28, 1.99). We included data from the longest follow-up time reported. Findings for other sleep measures including the FOSQ, arousals, total sleep time, PSQI, and snoring were similar between the CPAP and APAP groups.

Few studies measured changes in weight, BMI, or blood pressure with none reporting a significant difference between groups.[41,51,55,56,62] One study reported statistically significant decreases in systolic and diastolic blood pressure in the CPAP group but not the APAP group but did not report the significance of the difference between study groups.[55] No study reported changes in HbA1c.

One study reported time to initiation of therapy follow diagnosis.[56] Mean time in the APAP group was 12 days compared to 27 days in the CPAP group (P <.01). The difference was attributed to wait time for PSG.

Adverse events were reported in 6 studies. Three found similar frequency of events (dry mouth, blocked/runny nose, skin irritation, nasal irritation, pressure feeling too high, claustrophobia) in the CPAP and APAP groups.[51,57,59] One found incidence of nasal and throat/mouth symptoms was similar for different APAP devices but did not compare findings to CPAP.[52] One study reported mixed results (*ie,* no difference in nasal irritation/obstruction, pressure intolerance, or partner dislike but fewer total side effects [P = .02] in the APAP group).[46] One reported no side effects requiring alteration of treatment.[54] In this study, the incidence of nasal and mouth/throat

side effects was similar for the CPAP and APAP groups while discomfort with air pressure was significantly higher in the CPAP group.

One study reported costs during a 2-month treatment period.[56] Hospital costs were significantly lower in the APAP group while telecommunication costs (to transmit data from home to sleep laboratory) were significantly higher (both P <.001). Costs for equipment and home nurse visits were similar for the APAP and CPAP groups. Total cost per patient of the 2-month treatment was lower in the APAP group (€1,264 vs €1,720; P <.01).

Table 10. Intermediate Outcomes Comparing APAP to CPAP, Treatment Studies

Author, Year Enrolled/Randomized (n) Study Design	AHI	Oxygen Saturation: Mean	Time <90%	ODI	Minimum	Sleep Symptom Scores: ESS	FOSQ	SASQ	Arousals	Total Sleep Time	PSQI	Snoring	Other	Weight Loss	BMI	Blood Pressure	HbA1c	Time to Initiation of Therapy	Adverse Events	Costs	Compliance/Adherence: Hrs/night	Proportion of	Regular Use	Other
Bakker 2011[40] (n = 12) crossover	↔	↓	↔	↔		↔				↔											↔			
Drummond 2010[43] (n = 109) RCT						↔	↔																	
Vennelle 2010[61] (n = 200) crossover	↔					↑															↑			
Damjanovic 2009[41] (n = 100) RCT	↔			↔		↔			↔					X							↔	↔		↔[a]
Galetke 2008[45] (n = 20) crossover	↔				↔	↔			↔			↔									↔			
Fietze 2007[44] (n = 21) RCT	↔					↔															↔	↔		
Meurice 2007[50] (n = 83) RCT	X	↔	↔			↔				X											↔			
Nolan 2007[51] (n = 29) crossover	↔	↔				↔			↑	↔		↔		X		X			X		↔	↔		
Patruno 2007[55] (n = 40) RCT	↓	↔		↓										X	X						↔			
Richard 2007[58] (n = 174) retro cohort																					↔	↔	X	
Nolan 2006[52] (n = 27) crossover						↔													X		↕	↕		
Nussbaumer 2006[54] (n = 34) crossover	↔			↔		↔													↕		↔			↔
West 2006[62] (n = 98) RCT	↔					↔							↔[b]			↔					↔	↔		
Hukins 2004[46] (n = 55) crossover						↔													↑		↔	↔		
Hussain 2004[47] (n = 10) crossover	↔			↔	↓	↔			↔	↔											↔			

Study																							
Marrone 2004[48] (n = 22) crossover				↔															↔	↔		
Noseda 2004[53] (n = 27) crossover				↑		↔		↔											↔	↔		
Massie 2003[49] (n = 46) crossover	↔			↔														↑	↔			
Planes 2003[56] (n = 35) RCT	↔		↔		↔						X		↑		↑	↔			↔			
Senn 2003[59] (n = 31) crossover	↔		↔		↔										↔		↔		↔			
Randerath 2001[57] (n = 52) crossover	X			X		X	X		X						↔		X	X				
D'Ortho 2000[42] (n = 25) crossover	X	X		X												↔			X			
Teschler 2000[60] (n = 10) crossover	X														↔		↔					
Total *23 studies* *(n = 1,260)*	12↔ 1↓ 4X	3↔ 1↓ 1X	4↔	4↔ 1↓	1↓ 1←	2↑ 16↔ 2X	1↔	0	1↑ 4↔ 1X	3↔ 2X	1↔	2↔ 1X	1↔	1X	3X	1↑ 2X	0	1↑	1↑ 2↔ 1↕ 2X	1↑		

[a] hours use/sleep time
[b] maintenance of wakefulness

↑ = significantly better with APAP than CPAP, ↔ = non-significant difference between APAP and CPAP, ↓ = significantly better with CPAP than APAP, ↕ = mixed results comparing APAP and CPAP, X = between group significance not reported

Twenty-two of the 23 included studies reported hours per night of use with 19 of 22 reporting the CPAP and APAP groups were similar. Of the remaining 3 studies, 2 noted significantly higher use with APAP[49,61] and one reported mixed results for different APAP devices.[52] The differences in means for the 5 non-crossover RCTs are presented in Figure 10. Using data from the longest reported follow-up time, the pooled difference was -0.08 (95% CI -0.55, 0.38; $I^2 = 14\%$).

The results for proportion of nights used were similar; 10 of 12 studies found the CPAP and APAP groups to be similar, one reported mixed results,[52] and one did not report statistical significance.[57] "Regular use," as defined by the study, was similar in 3 of the 5 studies reporting (with 2 not reporting significance).

Figure 9. Epworth Sleepiness Scores, Standardized Mean Difference for Mean Change from Baseline from Parallel Group RCTs, Treatment Studies[a]

Study name	Statistics for each study			Sample size		Std diff in means and 95% CI
	Std diff in means	Lower limit	Upper limit	APAP	CPAP	
Damjanovic 2009 (9 months) (41)	-0.02	-0.41	0.37	50	50	
Meurice 2007 (6 months) (50)	0.07	-0.53	0.66	51	14	
Planes 2003 (2 months) (56)	0.26	-0.46	0.98	16	14	
Drummond 2010 (final, 2-6 months) (43)	0.46	0.03	0.88	42	44	
	0.18	-0.06	0.43			

-1.00   -0.50   0.00   0.50   1.00

Favors CPAP   Favors APAP
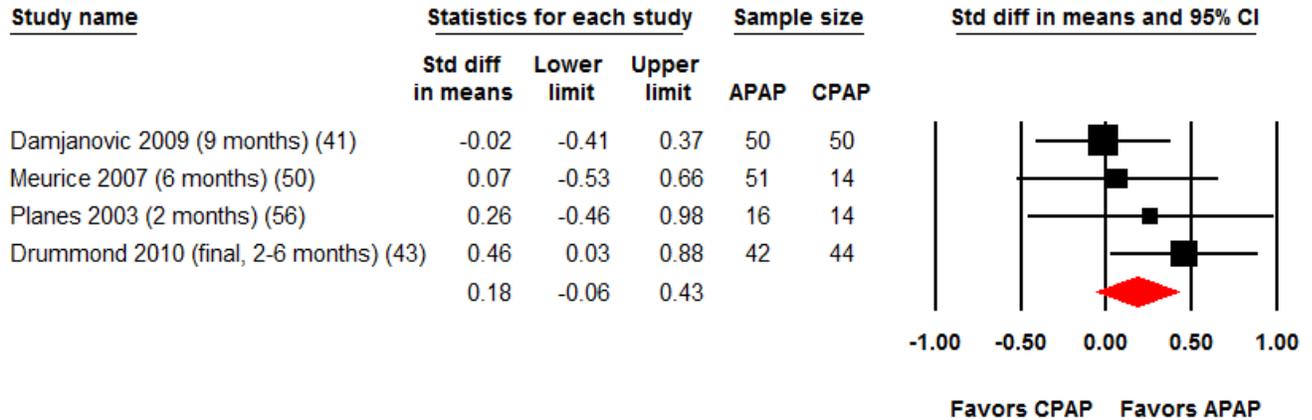
[a]Lower and upper limits represent 95% confidence intervals

Figure 10. Compliance, Weighted Mean Difference for Hours per Night from Parallel Group RCTs, Treatment Studies[a]

Study name	Statistics for each study			Sample size		Difference in means and 95% CI
	Difference in means	Lower limit	Upper limit	APAP	CPAP	
Fietze 2007 (6 weeks) (44)	0.80	-0.86	2.46	10	11	
Patruno 2007 (3 months) (55)	0.20	-0.44	0.84	15	16	
Planes 2003 (2 months) (56)	-0.80	-1.92	0.32	16	14	
Meurice 2007 (6 months) (50)	-0.60	-1.57	0.37	51	14	
Damjanovic 2009 (9 months) (41)	0.10	-0.87	1.07	50	50	
	-0.08	-0.55	0.38			

-2.00   -1.00   0.00   1.00   2.00

Favors CPAP   Favors APAP
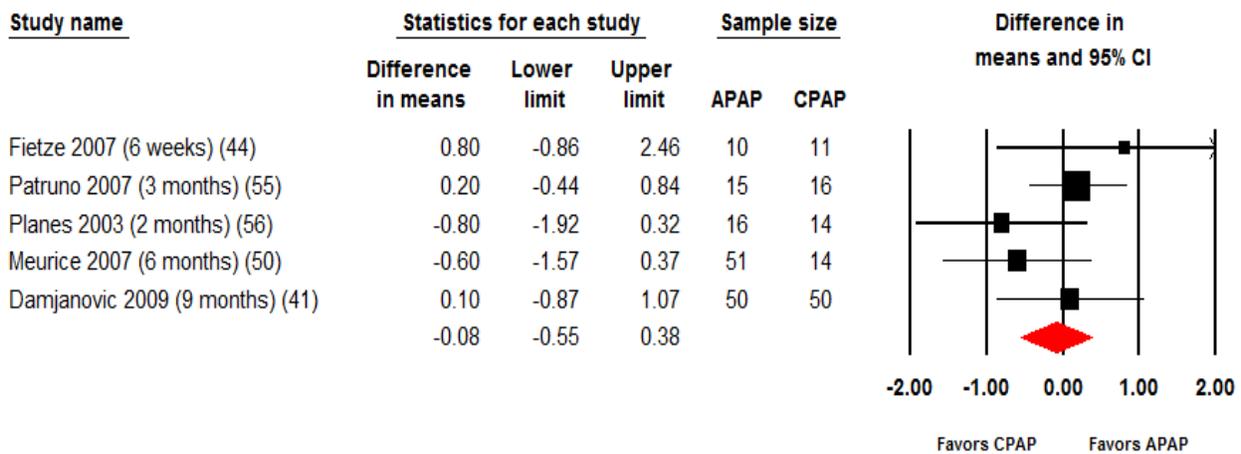
[a]Lower and upper limits represent 95% confidence intervals

KEY QUESTION #3A: Do effectiveness/harms/resource utilization vary by patient characteristics:

a. Unexplained daytime sleepiness/fatigue

b. AHI severity

c. Other risk factors or coexisting conditions associated with OSA (*eg*, obesity, neck circumference, treatment-resistant hypertension, diabetes, age, sex, race)

d. Symptoms (*eg*, nocturia, loss of libido, snoring, witnessed sleep "apnea")?

Few studies reported results by patient characteristics.

A. Unexplained Daytime Sleepiness/Fatigue

No study reported results for subgroups of patients based on unexplained daytime sleepiness or fatigue.

B. AHI Severity

One treatment study grouped patients by baseline AHI (< 60/hour or ≥ 60/hour).[42] Duration of use (hours/night) of CPAP and APAP was similar in the overall study population. There was significantly longer use of both CPAP and APAP in patients with baseline AHI ≥ 60/hour compared to those with baseline AHI <60/hour. A second study compared baseline AHI in compliant and non-compliant patients (with compliance defined as at least 4 hours per night for at least 5 days per week). AHI levels did not differ (51/hour for the compliant group, 47/hour for the non-compliant group, P = .40); results were not reported by treatment group.[58] A third study reported that compliance was similar between CPAP and APAP treatment groups in post-hoc subgroup analyses of patients with differing degrees of OSA severity.[46]

Two treatment studies compared baseline AHI in patients who expressed a preference for CPAP or APAP. One found that baseline AHI was a significant predictor of preference for CPAP or APAP.[48] Patients who preferred APAP had a higher baseline AHI than patients who preferred CPAP (73.1 vs 60.0/hour, P<.02). The other found AHI values were similar whether patients preferred APAP or CPAP (16.3 vs 14.2/hour, P = .49).[51]

C. Other Risk Factors or Coexisting Conditions Associated with OSA

One treatment study included only morbidly obese (BMI ≥ 40 kg/m^2) patients.[40] Neck circumferences was 46.5 (4.0) cm. CPAP and APAP generally produced similar results; patients were not stratified by BMI.

Two treatment studies evaluated age and compliance. In both studies, older patients tended to be more compliant with therapy but the findings were not statistically significant.[45,58] One study also reported that baseline BMI and ESS were not associated with compliance.[58] Neither study reported results by treatment group (CPAP or APAP).

Two studies reported other factors associated with preference for CPAP or APAP. One found that neither age or ESS score at baseline were significant predictors of preference.[48] Another reported that neither age, BMI, neck circumference, or ESS score were significant predictors.[51]

D. Symptoms

One titration study reported baseline percentages of patients with habitual snoring (88%), observed apneas (61%), and nocturia (27%).[37] The study did not report results for subgroups of patients based on these characteristics.

Strength of Evidence for Key Question 3 (Table 4, Appendix D)

Titration

For studies comparing in-lab CPAP *titration* to at-home APAP *titration*, there was insufficient evidence for the outcomes of access to care and adverse events. Strength of evidence was moderate for quality of life and low for compliance (hours/night) and ESS with similar findings for the 2 study groups.

Treatment

Among studies comparing CPAP to APAP for *treatment* of OSA, there was insufficient evidence for access to care. Strength of evidence was moderate for quality of life, ESS, and compliance (hours/night) and low for adverse events. These outcomes were similar in the 2 treatment groups.

Table 11. Strength of Evidence for Outcomes, Key Question 3

Comparison	Outcome of Interest	Strength of Evidence	Direction	Findings
KQ3: Home APAP technology versus standard in-center manual CPAP *titration*	Access to care	Insufficient		We found no evidence for this outcome.
	Epworth Sleepiness Scale (ESS)	Moderate	Similar	Based on 2 RCTs (n = 414) with moderate risk of bias, we found improvement from baseline in ESS scores was similar for patients allocated to home APAP titration compared to patients allocated to in-center CPAP titration (SMD = 0.0 [95% CI -0.22, 0.21]). One moderate risk of bias RCT (n = 68) found median change in EES scores from baseline was also similar between groups (MD 1 [95% CI -1, 4]). One observational cohort study also found ESS scores were similar between groups.
	Quality of life	Moderate	Similar	Based on 2 RCTs (n = 414) with moderate risk of bias, we found quality of life measures were similar for patients allocated to home APAP titration compared to patients allocated to in-center CPAP titration. The SMDs for SF-36 Mental Health and Physical Health scores were 0.08 [95% CI -0.14, 0.29] and -0.21 [95% CI -0.61, 0.20], respectively. Results for the Physical Health scores were imprecise. One moderate risk of bias RCT (n = 68) found median improvement from baseline in the SAQLI was similar between groups (median difference = 0.17 [95% CI -0.6, 0.9])
	Compliance, hours per night	Low	Similar	Based on 2 RCTs (n = 414) with moderate risk of bias, we found compliance was similar for patients allocated to home APAP titration compared to patients allocated to in-center CPAP titration (WMD = 0.02 [95% CI -0.41, 0.45]). One moderate risk of bias RCT (n = 68) found median compliance was better in the APAP group versus the CPAP group (MD -1.1 [95% CI -2.0, -0.2]). One observational cohort study found compliance was similar between groups.
	Adverse events	Insufficient		Based on the findings of one RCT (n = 245) that reported no "important differences" in adverse events between the home APAP and in-lab CPAP and groups, the evidence is insufficient to draw conclusions.
KQ3: APAP versus CPAP *treatment*	Access to care	Insufficient		We found no evidence for this outcome.
	Epworth Sleepiness Scale (ESS)	Moderate	Similar	Based on 4 parallel group RCTs (n = 327) with aggregate moderate risk of bias, we found improvement from baseline in ESS scores was similar for patients allocated to APAP treatment compared to patients allocated to CPAP treatment (SMD = 0.18 [95% CI -0.06, 0.43]). Two parallel group trials not pooled (reported as a median or data not shown) also found improvement from baseline in ESS scores similar between groups. Ten crossover RCTs (n = 269) reported similar improvements between groups and 2 (N = 227) reported greater improvement with APAP.

Comparison	Outcome of Interest	Strength of Evidence	Direction	Findings
	Quality of life	Moderate	Similar	Based on 3 parallel group RCTs (n = 202) with aggregate moderate risk of bias, we found quality of life measures (SF-36, SAQLI) were similar for patients allocated to APAP treatment compared to patients allocated to CPAP treatment (data were not pooled due to variation in reporting of results, *ie,* reported as medians). Six crossover RCTs (n = 393) also reported no differences in most of the quality of life measures between the treatment groups.
	Compliance, hours per night	Moderate	Similar	Based on 5 parallel group RCTs (n = 279) with aggregate moderate risk of bias, we found compliance was similar for patients allocated to APAP treatment compared to patients allocated to CPAP treatment (WMD = -0.08 [95% CI -0.55, 0.38]). One parallel group RCT reporting median compliance, most of the remaining crossover RCTs, and one observational study also found compliance was similar between groups.
	Adverse events	Low	Similar	Adverse events were infrequently reported. One parallel group RCT (n = 109) reported adverse events, chest pain in 12% and 9% of APAP and CPAP patients, respectively. Five crossover trials reported adverse events for both APAP and CPAP treatments. One trial (n = 55) reported a higher frequency of total number of events and another trial (n = 34) reported a higher incidence of pressure discomfort with CPAP therapy arm compared with the APAP treatment. There trials (n = 112) reported no differences in adverse events between the treatment groups.

APAP = Auto-adjusted (autoregulated) continuous positive airway pressure; CPAP = continuous positive airway pressure; RCT = randomized controlled trial; SAQLI = Sleep Apnea Quality of Life Index; SF-36 = Short Form-36; SMD = standardized mean difference; WMD = weighted mean difference.
[a]Strength of Evidence Definitions;[28] See Appendix D for more details
• High: Very confident that estimate of effect lies close to true effect. Few or no deficiencies in body of evidence, findings believed to be stable.
• Moderate: Moderately confident that estimate of effect lies close to true effect. Some deficiencies in body of evidence; findings likely to be stable, but some doubt.
• Low: Limited confidence that estimate of effect lies close to true effect; major or numerous deficiencies in body of evidence. Additional evidence necessary before concluding that findings are stable or that estimate of effect is close to true effect.
• Insufficient: No evidence, unable to estimate an effect, or no confidence in estimate of effect. No evidence is available or the body of evidence precludes judgment.

SUMMARY AND DISCUSSION

Our systematic review compared outcomes associated with 3 key questions: 1) use of non-SSP providers compared to SSPs; 2) electronic consultation compared to interactive consultation; and 3) in-home APAP compared to in-laboratory CPAP. Overall the evidence was often lacking to fully address the key questions and we found no data for Key Question 2.

For Key Question 1, we found 8 studies, of which 4 were randomized trials. Access to care was not reported in any of the studies, so we were unable to determine if use of non-SSP providers improves access to OSA diagnosis and treatment. Likewise, adverse events including overdiagnosis/overtreatment and underdiagnosis/undertreatment were not reported. We found moderate-strength evidence that care provided by non-SSP providers and SSPs resulted in similar Epworth Sleepiness Scores, quality of life, and treatment compliance.

For Key Question 3, we found 4 studies comparing at-home APAP to in-laboratory CPAP for *titration* of CPAP pressures and 23 for *treatment*. For both *titration* and *treatment*, access to care was not reported in any of the studies. Adverse events were rarely reported and therefore strength of evidence was insufficient to low to determine whether at-home APAP and in-laboratory CPAP differ for adverse events. We found moderate-strength evidence in both *titration* and *treatment* studies that at-home APAP and in-lab CPAP were similar in regards to Epworth Sleepiness Scores and quality of life outcomes. For PAP *titration*, at-home APAP and in-laboratory CPAP resulted in similar treatment compliance, though strength of evidence was low. For PAP *treatment*, at-home APAP and in-laboratory CPAP resulted in similar treatment compliance (moderate strength of evidence).

Our systematic review was not intended to determine the best OSA screening tools nor in whom OSA treatments are most effective. However, most of the included studies in our report enrolled patients who were generally older, obese, and sleepy, as determined by Epworth Sleepiness Scores. Furthermore, 2 recent evidence reports and clinical practice recommendations have addressed OSA screening and treatment.[12-15] This additional evidence may assist clinicians and policymakers when determining referral recommendations and evaluation pathways to target individuals with the greatest likelihood of benefiting while minimizing harms, as well as financial and opportunity costs associated with diagnosis and treatment of OSA. Specifically, a prior evidence report and accompanying clinical practice guideline by the ACP recommends that clinicians target their assessment of OSA to individuals with unexplained daytime sleepiness. The ACP concluded that assessment of OSA in the absence of daytime sleepiness or treatment of persons with low AHI scores is low-value care because evidence to date indicates that neither improves clinical outcomes.[14] Additionally, a draft evidence report and recommendation statement from the U.S. Preventive Services Task Force indicates that evidence is insufficient to assess the net benefit of screening for and treatment of asymptomatic OSA.[15] While good evidence has established that people with severe OSA are at increased mortality risk compared to controls, trials of CPAP and other treatments have not established whether treatment reduces mortality or improves most other health outcomes, except possibly for sleep-related quality of life. In addition to the findings included in the ACP and USPSTF reports, a recently published multi-site randomized trial showed that CPAP was not effective for secondary prevention of cardiovascular events in those with established cardiovascular disease and moderate to severe

OSA.[16] Furthermore, the USPSTF evidence report also found uncertainty about the clinical utility of screening tools and that most screening questionnaires had poor diagnostic accuracy.

When redesigning OSA care models we recommend that clinicians and policymakers consider the limited data to support some of these newer models (*eg,* hiring non-SSPs to provide sleep care) and the existing evidence used to inform clinical practice recommendations by the ACP and USPSTF. While the existing data do not suggest significant harm from these newer care models, current data are insufficient to draw firm conclusions.

LIMITATIONS

Inherent to the process of systematic review there are certain general limitations, some related to our inclusion criteria, others inherent in the available research. For example, we limited inclusion to English language studies and those performed in the United States, Canada, Western Europe, Australia, or New Zealand. We did this to target research most likely to be applicable to clinical practice in the United States and Veterans Affairs facilities. However, these search criteria also mean that our findings may not apply to the evaluation and care of OSA patients in other healthcare settings.

We also chose to exclude studies of dentists and anesthesiologists due to our uncertainty whether or not these persons truly represent "Non-Sleep-Specialist Physicians" given that many dentists and anesthesiologists have substantial practices or background in sleep medicine. Therefore, our systematic review does not address the role of these practitioners on sleep apnea care. We also did not assess the role of surgery or mandibular assist devices for OSA treatment including referral of patients who may be more interested in or better candidates for these options.

A significant limitation is the paucity of high-quality literature regarding key questions 1 and 2. For initial evaluation and treatment of OSA (Key Question 1), we identified 4 randomized trials and 4 observational studies. The non-SSP providers were primary care providers in 4 studies, nurses in 3 studies, and a pulmonologist in one study. Therefore, although we are aware of the existence of clinical care models utilizing sleep respiratory therapists to provide varying degrees of OSA care, we did not find any studies to address this particular type of practitioner. Due to small sample sizes, we were also unable to directly compare primary care-based models of OSA evaluation and treatment to sleep nurse-based models.

We also note that, importantly, the providers in many of these "primary care" studies were persons who had substantial experience in sleep medicine. For example, in the randomized trial of Chai-Coetzer and colleagues,[31] one of the 4 primary care nurses had 15 years of experience at a tertiary care sleep medicine center. In the study by Chamorro and colleagues,[32] the non-SSP provider was a 'primary care pulmonologist' – the degree of sleep training and experience of this person was unclear. Therefore, the generalizability of these findings to primary care providers with less experience in sleep medicine is not clear.

Due to the lack of studies regarding electronic consultation for persons suspected of having OSA (Key Question 2), we are unable to determine the effectiveness/harms/resource utilization of this evolving practice.

We found the most data for Key Question 3, which compared at-home autotitrating continuous positive airway pressure (APAP) to the more traditional CPAP titrated in the PSG laboratory. Several studies that compared at-home APAP to in-lab CPAP[63-65] were excluded as these studies also used different methods of diagnostic testing (*eg*, HST preceded at-home APAP, while PSG preceded in-lab CPAP) and we were concerned that the differences in diagnostic testing might confound our analysis of outcomes between APAP and CPAP. Although these studies were not included in our formal analysis, they reassuringly also further support the notion that APAP and CPAP (combined with at-home vs in-laboratory testing, respectively) result in similar outcomes in regards to: 1) 6-week ESS and PAP adherence among 106 Veterans in Florida using 2-3 nights of APAP for *titration*,[63] 3-month ESS, SF-12, and adherence among 182 Veterans in Pennsylvania using 4-5 nights of APAP for *titration*,[64] and 3-month ESS and SF-36 among 142 patients at 7 academic sleep centers in the U.S. using 5-7 nights of APAP for *titration*;[65] this last study also found higher 3-month PAP adherence in those assigned to the home study plus APAP titration arm.[65]

APPLICABILITY AND IMPLEMENTATION OF FINDINGS

Most patients enrolled in studies were obese, middle-aged men, with severe OSA based on both high AHI levels and the presence of excessive daytime sleepiness. Our findings are most applicable to these individuals. We found only one study that was performed in a VA population for Key Question 3.[43] One study was performed at Walter Reed Army Medical Center for key questions 1 and 3.[33] While most studies were not specifically conducted in VA or military populations, because the patients enrolled in these studies were generally older, overweight men with OSA, we believe the findings of our systematic review should be applicable to the population of Veterans served by VA facilities.

Many of the study providers who were not SSPs had prior sleep training and therefore the results may not be fully generalizable to all primary care providers.While data are not conclusive, because our findings indicated similar Epworth Sleepiness Scores, quality of life, and treatment compliance scores among patients evaluated and treated by non-SSPs compared to SSPs, it may be reasonable to consider expanded use of non-SSP providers who have received training in sleep medicine, especially where SSPs are in limited supply and demand for OSA services is high. Similarly, greater use of at-home APAP may lessen dependence on backlogged PSG laboratories, as most health outcomes were similar between groups.

Our report focused on methods that might improve the 'supply' side of OSA evaluation and treatment, through use of non-SSPs, electronic consultation, and at-home APAP titration and treatment. However, healthcare systems struggling to match supply to demand might also consider whether the 'demand' is truly appropriate. We found little to no data in screen-detected patients (*ie,* those found to have abnormal AHI either through direct referral to sleep laboratories or based on results of screening questionnaires such as the Berlin questionnaire but without excessive daytime sleepiness). The evidence to date indicates that the main benefit of OSA detection and treatment is improvement in patient-reported sleepiness symptoms among those with unexplained daytime somnolence. Therefore, VA healthcare providers and decision-makers could potentially achieve the highest value care, including resource use, by targeting case finding approaches and subsequent evaluation and treatment to individuals with unexplained daytime somnolence and who express interest in further evaluation and treatment. Theorectically, this referral approach could be readily be implemented by developing and using electronic medical

record templates that describe the evidence-based rationale for the referral recommendations while requesting that referring providers include information specifically about daytime somnolence and the patient's willingness for further evaluation and treatment in the consult.

RESEARCH GAPS/FUTURE RESEARCH

Comparative effectiveness trials were lacking for all key questions. Key questions 1 and 2 would particularly benefit from trials to address the outcomes resulting from non-SSP case finding and care of sleep apnea patients (Key Question 1) and outcomes resulting from electronic consultation (Key Question 2). Limited available data suggest that care led by non-SSPs may potentially provide equivalent outcomes to care led by SSPs. Comparative effectiveness trials are needed in order to determine whether such results can be achieved in routine practice, outside of controlled research settings. The available data suggest that with appropriate training, non-SSPs can potentially provide equivalent outcomes, but the operationalization of such training is unclear. Therefore, future comparative effectiveness trials should describe their training programs in detail. Such trials should also collect clinical outcomes where possible.

In regards to case finding, future studies should compare outcomes among differing strategies such as offering sleep studies and treatment to a broad set of patients (*eg,* with OSA risk factors, regardless of number of risk factors or symptoms) versus a narrow set of criteria (*eg,* high OSA risk or very symptomatic). Outcomes of interest in such studies would include consultation rates, sleep study rates, percent of sleep studies confirming OSA, severity of OSA, changes in sleepiness, and adherence to CPAP. Such studies might also compare case finding led by sleep specialists, primary care providers, nurses, or even automated through electronic medical record (EMR) systems.

As more healthcare systems implement comprehensive EMRs, we anticipate Key Question 2 will become more feasible to study. In the current climate of increasing numbers of sleep referrals, yet a declining number of SSPs, EMR-based electronic consultation holds significant promise to provide equivalent outcomes in a more cost-effective, time-efficient manner. Although many systems have already implemented electronic consultation systems,[66] evidence supporting this practice is largely lacking and further studies should be conducted. We think comparative effectiveness study designs such as stepped-wedge randomization (where sites are randomly assigned to the time point at which they implement electronic consultation) would allow the creation of good-quality evidence to quantify the risks, benefits, and economic impacts of electronic consultation for patients with known or suspected OSA.

Many studies have addressed Key Question 3 and while we found similar sleepiness, quality of life, and adherence between APAP and CPAP, future studies should include longer-term follow-up to allow better determination of long-term clinical ouctomes. Future studies should also include more rigorous collection and reporting of adverse event data.

A large gap in evidence is related to the effectiveness of treatment for individuals without excessive daytime sleepiness (screen detected or case-finding in at-risk asymptomatic individuals) and on outcomes other than daytime sleepiness. For example, a recently published multi-site randomized trial showed that CPAP was not effective for secondary prevention of cardiovascular events in those with established cardiovascular disease and moderate to severe OSA.[16] Additional information gaps include the effectiveness of treatment in those with mild

AHI regardless of symptoms. These gaps are supported by recent evidence reports and accompanying clinical practice recommendations by the ACP and USPSTF and described in greater detail in the introduction and above. There are also critically important gaps to fill due to the dramatic increase in patients with, or suspected to have, OSA and thus being referred for evaluation and treatment.

CONCLUSIONS

Among patients suspected of having OSA, evidence suggests that primary care providers and sleep-specialist nurses might provide similar outcomes to SSPs, although the strength of this evidence was only moderate and many outcomes were inconsistently reported. Likewise, among patients diagnosed with OSA, evidence suggests that at-home APAP *titration* and *treatment* provides similar outcomes to fixed pressure CPAP titrated in the PSG laboratory, although the strength of evidence was generally low to moderate.

We found no evidence addressing the topic of electronic consultation for the management of known or suspected OSA.

Future studies are needed to determine which patients derive the most benefit from treatment and should be prioritized for testing and treatment, whether newer models of care with less reliance on SSP time (either through utilization of other types of providers or electronic consultation) result in similar outcomes to traditional models, and if effective, how such models should be implemented.

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