WAHINGTON STATE HEALTH CARE AUTHORITY

Public Comments and Responses

Health Technology Assessment

Tuesday, February 15, 2012

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Public Comments and Disposition

Sleep Apnea Diagnosis and Treatment in Adults

Washington Health Technology Assessment

February 15, 2012

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OVERVIEW OF PUBLIC COMMENTS AND DISPOSITION

The Center for Evidence-based Policy is an independent vendor contracted to produce evidence assessment reports for the WA HTA program. For transparency, all comments received during the comments process are included in this response document. Comments related to program decisions, process, or other matters not pertaining to the evidence report are acknowledged through inclusion only.

This document responds to comments from the following parties:

Key Questions

1. Eric J. Freer
2. Douglas Myers, MD
3. Kerilyn Nobuhara

Draft Report

1. Karen Anderson
2. Washington State Medical Directors

The full version of each public comment received is available in the Public Comments section, beginning on page 8.

Table 1. Overview of Public Comments on Draft Key Questions

Submitted By	Cited Evidence	Overview of Public Comment
Eric J. Freer, GE Healthcare, Respiratory & Sleep, Home Care, Sales and Marketing Leader	▪ Cited evidence from eight reviews from The Cochrane Collaboration Database of Systematic Reviews, which included: o Surgery for Obstructed Sleep Apnea in Adults; o Continuous Positive Airways Pressure for Obstructed Sleep Apnea in Adults; o Lifestyle Modification in Obstructed Sleep Apnea; o Drug Therapy for Obstructed Sleep Apnea in Adults; o Pressure Modification for Improving Usage of Continuous Positive Airway Pressure Machines in Adults with Obstructed Sleep Apnea; o Oral Appliances for Obstructed Sleep Apnea; o Continuous Positive Airways Pressure Delivery Interfaces for Obstructed Sleep Apnea; and o Educational, Supportive and Behavioral Interventions to Improve Usage of Continuous Positive Airway Pressure Machines for Adults with Obstructed Sleep Apnea. ▪ Cited comparative effectiveness reviews from the Agency for Healthcare Research and Quality	▪ *Response to Key Question #1:* The severity of sleep apnea is typically quantified by the number of apneas and hypopneas per hour of sleep, defined as the AHI, measured during overnight monitoring. The American Academy of Sleep Medicine uses a threshold to define OSA of 15 events/hr (with or without OSA symptoms) or 5 events/hr with OSA symptoms. However, they found during their review, the minimum thresholds to diagnose sleep apnea in research studies vary from 5 to 20 events per hour by PSG. ▪ Polysomnography: the current diagnostic standard used in clinical practice is PSG. The formal diagnosis of sleep apnea requires a comprehensive, technologist-attended sleep study with multichannel PSG performed in specialized sleep laboratories. Laboratory-based PSG records a variety of neurophysiologic and cardiorespiratory signals that are read by trained technologist and interpreted by sleep physicians after a diagnostic sleep study has been completed. ▪ Portable Monitors: since in-laboratory PSG is costly, resource-intensive, and potentially inconvenience for the patient, other diagnostic tools have been developed, including portable testing and questionnaires for prescreening patients. Portable monitors vary in the type of neurophysiologic and respiratory information collected, and each synthesizes the accumulated data differently. Provided the American Sleep Disorders Association's classification of the different monitors that have been used into four categories. ▪ Pretesting Questionnaires and Other Tests: Questionnaires are used to prescreen patients for further testing or treatment. The most commonly used screening questionnaire in clinical practice is the Epworth Sleepiness Scale (ESS). The ESS focuses solely on sleepiness and not other signs and symptoms of OSA, thus is not specific to OSA. Another questionnaire commonly used in practice is the STOP questionnaire from the University of Toronto. In addition, researchers

Submitted By	Cited Evidence	Overview of Public Comment
		have created models to predict OSA based on demographic features, symptoms, head and neck anatomy and other variables. The value of the various questionnaires and other screening tools remain unclear. It is also unknown whether the tests can be accurately used to predict the clinical severity of patients' sleep apnea and the likelihood of clinically important sequelae. ▪ *Response to Key Question #5:* cited systematic reviews from the Cochrane Database. ▪ *Response to Key Question #6:* Cited a comparative effectiveness review from the Agency for Healthcare Research and Quality from July 2011. ▪ *Response to Key Question #7:* Cited a comparative effectiveness review from the Agency for Healthcare Research and Quality from July 2011.
Douglas Myers, MD, Vancouver, WA	No	▪ The diagnosis and treatment of sleep apnea requires a varied approach. ▪ In some instances, sleep studies represent an unnecessary expense and surgery is most cost effective; and in the other, the surgery is an unnecessary expense and sleep studies are most cost effective. ▪ Diagnostic evaluation and treatment must be individualized. ▪ The expertise to perform both diagnosis and treatment is available in most local medical communities, so that the added cost in time and transportation to regional centers is unnecessary. ▪ A common guideline for best practices would be helpful for use in community multispecialty discussions to establish diagnostic and surgical criteria.
Kerilyn Nobuhara, Senior Medical Consultant, Health	No	▪ Question: Will the cost effectiveness analysis include consideration of the morbidities associated with the different treatments?

Submitted By	Cited Evidence	Overview of Public Comment
Care Authority, WA		

Table 2. Public Comments on Draft Report and Disposition

Reviewer	Comment	Disposition
Karen Anderson	One of the concerns I have is that there are some vulnerable populations that were not "teased out" for evaluation. Specifically, patients with Down's Syndrome are notoriously afflicted with ENT issues and I had the unfortunate experience of dealing with one who was in heart failure, was evaluated and determined to have OSA, given CPAP which, despite her severe mental retardation, she avidly wore and improved immensely. I don't know how that fits in with the EBM eval but I do think that there may be some populations that have not been separately evaluated and who may benefit from treatment.	*Thank you for your comments and concerns. This report did not address patient populations which included Down syndrome. The sole source of evidence for this report, (Balk [AHRQ] 2011, p. 12-13) specifically excluded studies in which more that 20% of the participants had Down syndrome, among many other disorders…"This threshold (20 percent) was chosen arbitrarily to avoid excluding potentially relevant small studies that included some patients with conditions not of interest to the current report. This turned out to be a moot point since no eligible studies explicitly included patients with any of these conditions."*
	I did not see CHF findings or symptoms included in the pre/post rx evals. I think that is an important deficit.	*Thank you for your question involving CHF finding or symptoms in the treatment evaluations. This relates to KQ#5 (Comparative effective of different treatment for OSA).* *Congestive heart failure was discussed in KQ#5b in the comparison of "CPAP and Control" section (KQ#5b.) included 2 studies which "which included only patients with symptomatic, stable, and optimally-treated congestive heart failure." (CEbP Report, pg.79) The conclusion in that report section stated "A single study evaluated the impact of CPAP on the severity of symptoms of congestive heart failure and reported nonsignificant results." (CEbP Report, p. 82)*

Washington State Agency Medical Directors	The significance of the association between apnea-hypopnea index (AHI) and all-cause mortality is unclear, particularly given the uncertain association between AHI and cardiovascular mortality, stroke, hypertension, diabetes and other metabolic abnormalities, and quality of life. The draft report does comment on p. 5 "Thus the association between reductions in AHI by OSA treatment and improvements in long-term clinical outcomes remains theoretical."	*Thank you for your comments. Language has been inserted to clarify this issue (CEbP Report, p. 4-5).*
	In general, the wording of the report gives unsupported credence to a putative causal relationship between obstructive sleep apnea (OSA) and major morbidity and mortality.	*Thank you for your comment. This causal relationship (OSA and morbidity/mortality) was discussed and independently referenced (i.e. other than Balk) in p.12, paragraph 3, of the CEBP Report Background section.*
	Similarly, it is not sufficiently critical of the strength of evidence supporting the proposition that continuous positive airway pressure (CPAP) and other treatments for OSA improve major clinical outcomes.	*Thanks you for your comments. Several areas of this report discuss the evidence to support CPAP as an effective method for improving sleep indices and sleepiness symptoms. This point is reinforced in the Balk (CEbP Report, p. 149) conclusions "While the relevant trials are conclusive regarding the effects of CPAP on AHI and sleepiness measures, among over 40 trials of patients treated with CPAP or no treatment, none have reported long-term clinical outcomes." Further support for this perspective is found in Balk (CEbP Report, p.151) "Notably, little evidence exists across interventions supporting any OSA treatment as improving quality of life or neurocognitive function. Although trials did report improvements in these outcomes for CPAP, MAD, and surgical intervention, overall findings were inconsistent."*
	Regarding key question 4, the "relationships between… AHI and oxygen desaturation index… and other patient characteristics with long term clinical and functional outcomes" is further elaborated in the draft report, quoting from the AHRQ comparative effectiveness review on sleep apnea diagnosis and	*Thank you for your comments. These issues are discussed above. There appears to be confusion between the sleep indices (such as AHI) which is associated with all-cause mortality when high (and has been clarified in the text as above), and OSA, which is associated with significant*

	treatment, concluding, on p. 164 [CEbP Report, p. 149], "Unfortunately, as discussed below, there are almost no trial data to support that treatment of OSA and reduction of AHI improves clinical outcomes" and, on p. 165 [CEbP Report, p. 149] "While the relevant trials are conclusive regarding the effects of CPAP on AHI and sleepiness measures, among over 40 trials of patients treated with CPAP or no treatment, none have reported long-term clinical outcomes." Thus, it is contradictory and unclear what evidence is relied on for statements such as: p. 174 [CEbP Report, p.158], "Obstructive sleep apnea is a cause of significant morbidity and mortality, and is thus an important public health issue. In addition, the diagnosis and treatment of OSA have societal cost implications, making cost-effectiveness a concern in both of these aspects."	*morbidity/mortality as above.*
	On p. 7 of the draft report it is stated: "A moderate strength of evidence was found for the treatment of OSA with CPAP", a statement that in itself says little, but presumably intends to say that a moderate strength of evidence was found to support the effectiveness of treatment of OSA with CPAP. Subsequent statements qualify the statement, noting that there is relatively strong evidence that CPAP treatment improves sleep measures such as AHI, arousal index, and minimum oxygen saturation, and subjective report of daytime sleepiness on the Epworth Sleepiness Scale. Directly quoted from the AHRQ comparative effectiveness review on sleep apnea diagnosis and treatment, the draft report says on p. 7: "There is only weak evidence that that CPAP treatment may improve quality of life or neurocognitive measures, or other intermediate outcomes" and "Despite no or weak evidence for an effect of CPAP on clinical outcomes, given the large magnitude of effect on the intermediate outcomes of AHI and ESS, the strength of evidence that CPAP is an effective treatment to alleviate sleep apnea signs and symptoms was rated moderate."	*Thank you for your comments. Language has been inserted to clarify this statement (CEbP Report, p.7)*

	The term "signs and symptoms" is not further specified, leaving it unclear exactly what beneficial effects of CPAP treatment are supported by evidence.	*"Signs and symptoms" is not further specified in the Balk report (CEbP Report, p.69).*
	It would be helpful to remind the reader at this point that any association between reductions "in AHI by OSA treatment and improvements in long-term clinical outcomes remains theoretical."	*Thank you…this language has been inserted in the draft (CEbP Report, p.7)*
	The discussion of cost effectiveness studies in both the Executive Summary and the body of the report fails to adequately emphasize that the "cost effectiveness" analysis assumes effectiveness of OSA treatment rather than basing the analysis on empirical findings of effectiveness, thus seriously undermining validity of "cost effectiveness" analyses. Such problems with the major "cost utility" study reported on (McDaid, 2009) are mentioned in the "Limitations" section on p. 174 [CEbP Report, pp. 158-9], yet the highly conjectural results of the cost utility study are reported with little in the way of caveat.	*Thank you…such language has been inserted in the Executive Summary (CEbP Report, p.8) and in the draft (CEbP Report, p. 155)*
	Similarly the cost-analysis studies of health care costs of persons with OSA compared to those without do not establish causality or evidence to support the expectation that diagnosis and treatment of OSA will reduce health care costs. Thus, in the "Policy context and cost information" discussion in the "Background" section of the draft report, on p. 17, it is surprising to see the statement "Undiagnosed OSA results in roughly a two-fold increase in health care utilization and costs, in the years preceding the diagnosis, due largely to the number of attendant comorbidities." The use of the words "results in" implies causality where it has not been established.	*Thank you…such language has been changed to reflect this comment in the draft (CEbP Report, p.17)*
	The draft report would do better to emphasize how much of the case for treatment of OSA is based on conjecture and extrapolation from associative relationships between sleep	*Thank you…such language has been inserted in the draft as above (CEbP Report, p. 155)*

	measures and clinical morbidity and the effects of OSA treatments on sleep measures and a few intermediate clinical outcome measures of uncertain clinical significance. In this context, “cost-effectiveness” studies of OSA treatment have little value other than as conjecture.	

PUBLIC COMMENTS – KEY QUESTIONS

1. Eric J. Freer

KQ1: How do different available tests compare to diagnose sleep apnea in adults with symptoms suggestive of disordered sleep?

Source:
Diagnosis and Treatment of Obstructive Sleep Apnea in Adults
Comparative Effectiveness Reviews, No. 32

Investigators: Ethan M Balk, MD, MPH, Denish Moorthy, MBBS, MS, Ndidiamaka O Obadan, MD, MS, Kamal Patel, MPH, MBA, Stanley Ip, MD, Mei Chung, PhD, MPH, Raveendhara R Bannuru, MD, Georgios D Kitsios, MD, PhD, Srila Sen, MA, Ramon C Iovin, PhD, James M Gaylor, BA, Carolyn D'Ambrosio, MD, MS, and Joseph Lau, MD.

Tufts Evidence-based Practice Center
Rockville (MD): Agency for Healthcare Research and Quality (US); July 2011.
Report No.: 11-EHC052

Diagnosis
In general, individuals with OSA experience repetitive cycles of upper airway obstruction and frequent nighttime arousals. Upper airway obstruction during sleep is most often due to anatomical anomalies of the nasopharyngeal or mandibular areas that cause narrowing of the respiratory passages, decreased pharyngeal muscle tone that reduces the cross-sectional area of the upper airway, and insufficient neuromuscular responses to airway obstruction.[5] This narrowing is often exacerbated by obesity-related peripharyngeal fat.[5] AHI, the count of the hourly apnea and hypopnea events during sleep, when combined with determinations of obstruction, is the primary measurement used for the diagnosis of OSA. It (or variations that measure oxygen desaturations or other measures of respiratory disturbance instead of apnea) can by measured by polysomnography (PSG) in a sleep laboratory or by (portable) monitors in other settings. Notably, though, AHI can vary from night-to-night or between settings and does not take into account symptoms, comorbidities, or response to treatment.[30]

The severity of sleep apnea is typically quantified by the number of apneas and hypopneas per hour of sleep, defined as the AHI, measured during overnight monitoring. The American Academy of Sleep Medicine uses a threshold to define OSA of 15 events/hr (with or without OSA symptoms) or 5 events/hr with OSA symptoms (unintentional sleep episodes during wakefulness; daytime sleepiness; unrefreshing sleep; fatigue; insomnia; waking up breath-holding, gasping, or choking; or the bed partner describing loud snoring, breathing interruptions, or both during the patient's sleep).[31,32] However, as we found during our review, the minimum thresholds to diagnose sleep apnea in research studies vary from 5 to 20 events per hour by PSG.

Polysomnography
The current diagnostic standard used in clinical practice is PSG. The formal diagnosis of sleep apnea requires a comprehensive, technologist-attended sleep study with multichannel PSG performed in specialized sleep laboratories.[4,33] Laboratory-based PSG records a variety of neurophysiologic and cardiorespiratory signals that are read by trained technologists and interpreted by sleep physicians after a diagnostic sleep study has been completed. The sleep study incorporates a number of assessments and measurements including: recordings of rapid eye movements, electroencephalogram to detect arousals, chest and abdominal wall monitors to evaluate respiratory movements, electrocardiogram, electromyogram, oximetry, and nasal and oral air flow measurements.[5] This process of diagnosing OSA by PSG in a sleep lab has some constraints including cost, inconvenience, and interlaboratory variation in hardware and assessment methods. Additionally, the current

clinical standard, which is the 16-channel, in-laboratory PSG has never been validated, and its true sensitivity and specificity in diagnosing OSA is not well documented.[26]

Portable Monitors

Since in-laboratory PSG is costly, resource-intensive, and potentially inconvenient for the patient, other diagnostic tools have been developed, including portable testing and questionnaires for prescreening patients. Portable monitors vary in the type of neurophysiologic and respiratory information collected, and each synthesizes the accumulated data differently.[34] There are different types (classes) of portable monitors. Each gathers different neurophysiologic and respiratory information and may synthesize the accumulated data differently. Portable monitors can be used in the home setting or sleep units.

The American Sleep Disorders Association has classified the different monitors that have been used in sleep studies into four categories, depending on which channels they record and evaluate.[34] As we did in the *2007 Technology Assessment of Home Diagnosis of Obstructive Sleep Apnea-Hypopnea Syndrome*,[26] we used the operational rules described in Table 1 to classify sleep monitors. Briefly:

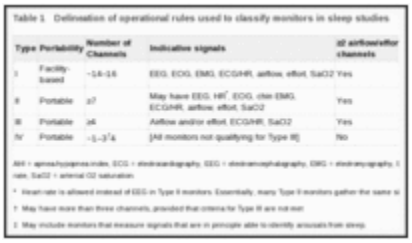

Table 1

Delineation of operational rules used to classify monitors in sleep studies.

- Type I is facility-based PSG.
- Type II monitors are portable and record the same information as Type I (perhaps with fewer channels). Type II monitors record signals that allow the reliable identification of (micro) arousals from sleep (e.g., electro-oculography, chin electromyography, electroencephalography) *and* at least two respiratory channels (two airflow channels or one airflow and one effort channel).
- Type III monitors are portable, but do not record the channels that differentiate between sleep and wake, but have at least two respiratory channels (two airflow channels or one airflow and one effort channel).
- Type IV are all other portable monitors that fail to fulfill criteria for Type III monitors. Therefore Type IV channels may include monitors that record more than two bioparameters.

Thus, portable monitors are classified as either Type II, III or IV. Please refer to our previous report for a more complete discussion of portable monitors.[26]

Pretesting Questionnaires and Other Tests

Questionnaires are used to prescreen patients for further testing or treatment. The most commonly used screening questionnaire in clinical practice is the Epworth Sleepiness Scale (ESS).[35] This questionnaire asks patients to rate how likely they are to fall asleep in certain situations, such as riding in the car on a long trip. The ESS focuses solely on sleepiness and not other signs and symptoms of OSA, thus is not specific to OSA. Another questionnaire commonly used in practice is the STOP questionnaire from the University of Toronto.[36] In addition, researchers have created models to predict OSA based on demographic features, symptoms, head and neck anatomy, and other variables.

The value of the various questionnaires and other screening tools remains unclear. It is also unknown whether the tests can be accurately used to predict the clinical severity of patients' sleep apnea and the likelihood of clinically important sequelae. If the screening tests are found to be sufficiently predictive of the results of full sleep testing, the question arises of how best to determine which patients should be prescreened (or sent directly for a sleep study), and, after screening, which should be treated for OSA, tested further, or considered to not have OSA.

References:

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35. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14:540–545. [PubMed: 1798888]

36. Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology. 2008;108:812–821. [PubMed: 18431116]

a. How do the different tests compare in different subgroups of patients, based on: race, gender, body mass index (BMI), existing non-insulin dependent diabetes mellitus (NIDDM), existing cardiovascular disease (CVD), existing hypertension (HTN), clinical symptoms, previous stroke, or airway characteristics?

Source: The Effect of Race and Sleep-Disordered Breathing on Nocturnal BP "Dipping"

*Analysis in an Older Population

1. Sonia Ancoli-Israel, PhD,
2. Carl Stepnowsky, PhD,
3. Joel Dimsdale, MD,

4. Matthew Marler, PhD,
5. Mairav Cohen-Zion, MA and
6. Sherella Johnson, AA

CHEST October 2002 vol. 122 no. 4 1148-1155

In a study of randomly selected white and African-American elderly subjects, Ancoli-Israel et al,1 found that African Americans, when compared to white subjects, had twice the relative risk of severe sleep-disordered breathing (SDB) [defined as the presence of ≥ 30 respiratory events per hour of sleep] independent of age, gender, or body mass index (BMI). In a study of African-American families, Redline et al2 observed that the apnea index differed by race and age, finding a threefold risk for SDB in African Americans < 25 years old and a twofold greater risk in middle-aged African Americans (age range, 25 to 55 years). These data suggest that there may be a high rate of undiagnosed SDB among African Americans.

There is also a high rate of undiagnosed SDB among patients with hypertension.3 Approximately one third of all hypertensive subjects have SDB, and approximately one third of all patients with SDB have hypertension.45 Peppard et al6 found a dose-response association between SDB at baseline and hypertension 4 years later, suggesting that SDB may be a risk factor of hypertension and, consequently, of cardiac morbidity. Nieto et al,7 in one of the largest cross-sectional studies, found that the prevalence of hypertension increased with increasing levels of SDB. In addition, patients with severe SDB, defined as ≥ 30 respiratory events per hour of sleep, were one and a half times more likely to have hypertension than those with no or mild SDB. This association was significant in younger and older men and women, and in all ethnic groups.

References

1. Ancoli-Israel, S, Klauber, MR, Stepnowsky, C, et al (1995) Sleep-disordered breathing in African-American elderly. Am J Respir Crit Care Med 152,1946-1949

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   CrossRef

4. Millman, RP, Redline, S, Carlisle, CC, et al Daytime hypertension in obstructive sleep apnea: prevalence and contributing risk factors. Chest 1991;99,861-866

   Abstract/FREE Full Text

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   CrossRefMedlineWeb of Science

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Treatment

KQ5: What is the comparative effect of different treatments for obstructive sleep apnea (OSA) in adults?

a. Does the comparative effect of treatments vary based on presenting patient characteristics, severity of OSA, or other pre-treatment factors? Are any of these characteristics or factors predictive of treatment success?

o Characteristics: Age, sex, race, weight, bed partner, airway and other physical characteristics, specific comorbidities

SO: Chai Ching Li, Pathinathan Anna, Smith Brian J. Continuous positive airway pressure delivery interfaces for obstructive sleep apnoea. Cochrane Database of Systematic Reviews: Reviews 2006 Issue 4

DOI: 10.1002/14651858.CD005308.pub2

CONTINUOUS POSITIVE AIRWAY PRESSURE DELIVERY INTERFACES FOR OBSTRUCTIVE SLEEP APNOEA IN ADULTS: Obstructive sleep apnoea (OSA) is a condition whereby patients experience obstruction of their airways and develop an irregular breathing pattern during their sleep. If untreated, OSA can cause a variety of health problems, including high blood pressure, heart problems, difficulty concentrating, excessive sleepiness and an increased risk of having a motor vehicle accident. One widely recommended form of treatment for OSA is CPAP (continuous positive airway pressure), which consists of a pump which blows air into a patient's nose and/or mouth during sleep to hold open the airways and stop obstructions from occurring. The pump is connected to the patient via a connecting hose and an "interface" which rests on the patient's face. There are many different types of interface available for CPAP use, including masks which cover the nose, the mouth, both the nose and mouth, and even the entire face. Unfortunately, patients will often experience side effects related to their interface, which may make them want to stop their CPAP treatment. This review compares the different interface options for CPAP in patients with OSA. Four trials involving 132 people were included. Two studies compared nasal masks with an oral mask called the Oracle, and there did not appear to any significant differences between the two in terms of compliance, sleep study recordings, sleepiness or other symptoms of OSA. One study assessing nasal masks versus nasal pillows (consisting of prongs that rest within the nostrils) showed that patients using the nasal pillows had fewer overall side effects and reported greater satisfaction. The nose mask performed better than the face mask (which covers both the nose and mouth) with one study showing greater compliance and less sleepiness, and was the preferred mask in almost all patients. The choice of interface for a particular person will need to be tailored to the individual. Further trials comparing the many interfaces for CPAP in the treatment of OSA are needed.

SO: Giles Tammie L, Lasserson Toby J, Smith Brian, White John, Wright John J, Cates Christopher J. Continuous positive airways pressure for obstructive sleep apnoea in adults. Cochrane Database of Systematic Reviews: Reviews 2006 Issue 3

DOI: 10.1002/14651858.CD001106.pub3

CONTINUOUS POSITIVE AIRWAYS PRESSURE FOR RELIEVING SIGNS AND SYMPTOMS OF OBSTRUCTIVE SLEEP APNOEA: Obstructive sleep apnoea is the term used to describe the interruption in normal breathing of individuals during sleep. It is caused by collapse of the upper airways during sleep and is strongly associated with obesity. The mainstay of medical treatment is a machine used at night to apply continuous positive airways pressure (CPAP). The machine blows air through the upper air passages via a mask on the mouth or nose to keep the throat open. We searched and reviewed all randomised controlled trials that had been undertaken to evaluate the benefit of CPAP in adult patients with sleep apnoea. Some of the trials had methodological flaws, although more recent studies have begun to use appropriate forms of control. The overall results demonstrate that in people with moderate to severe sleep apnoea CPAP can improve measures of sleepiness, quality of life and associated daytime sleepiness. CPAP leads to lower blood pressure compared with control, although the degree to which this is achieved may depend upon whether people start treatment with raised blood pressures. Oral appliances are also used to treat sleep apnoea but, whilst some people find them more convenient to use than CPAP, they do not appear to be as effective at keeping the airway open at night. Further good quality trials are needed to define who benefits, by how much and at what cost. Further

trials are also needed to evaluate the effectiveness of CPAP in comparison to other interventions, particularly those targeted at obesity.

SO: Smith Ian, Lasserson Toby J, Wright John J. Drug therapy for obstructive sleep apnoea in adults. Cochrane Database of Systematic Reviews: Reviews 2006 Issue 2

DOI: 10.1002/14651858.CD003002.pub2

DRUG THERAPY FOR OBSTRUCTIVE SLEEP APNOEA IN ADULTS: Obstructive sleep apnoea (OSA) is caused by collapse of the upper airway. The mainstay of medical treatment is continuous positive airways pressure (CPAP) delivered through a mask during sleep. Drug therapy has been proposed for patients with mild OSA and those intolerant of CPAP. Many drugs have been tested as treatments for obstructive sleep apnoea (when breathing stops during sleep). Most have not been found to be effective. A few have been shown to reduce the number of apnoeic episodes during sleep but have not yet been shown to improve well-being during wakefulness. We searched and reviewed all randomised placebo controlled trials of drugs in adult patients with OSA . Most of the trials had methodological flaws. Of 21 drugs tested, eight had some impact on the severity of OSA (in terms of either markers of sleep quality or symptoms of sleepiness) although in most people changes were only modest. Physostigmine, Mirtazipine and nasal lubricant were only trialed on single night studies and the long-term effects are therefore unknown. Topical nasal steroid was tolerated, reduced the severity of sleep apnoea and improved subjective daytime alertness in a specific sub group with both OSA and rhinitis. Acetazolamide reduced the number of respiratory events per hour of sleep but did not reduce daytime sleepiness and was poorly tolerated long term. Paroxetine had only a small effect on the amount of OSA and while it was tolerated there was no useful effect on daytime symptoms. In contrast participants reported a symptomatic benefit from protriptyline, but there was no improvement in OSA suggesting a different mechanism for their improved sense of well-being.

SO: Smith Ian, Nadig Vidya, Lasserson Toby J. Educational, supportive and behavioural interventions to improve usage of continuous positive airway pressure machines for adults with obstructive sleep apnoea. Cochrane Database of Systematic Reviews: Reviews 2009 Issue 2

DOI: 10.1002/14651858.CD007736

DO EDUCATIONAL, SUPPORTIVE AND/OR BEHAVIOURAL INTERVENTIONS INCREASE USAGE OF CONTINUOUS POSITIVE AIRWAY PRESSURE MACHINES FOR ADULTS WITH OBSTRUCTIVE SLEEP APNOEA?: Continuous positive airway pressure (CPAP) treats obstructive sleep apnoea (OSA) effectively in the majority of people. Despite its efficacy in ameliorating symptoms resulting from OSA, CPAP usage has been reported as 65-80%. This review critically appraises studies involving educational and behavioural interventions and supportive strategies aimed at improving CPAP usage. After reviewing the literature, we have found some evidence that educational interventions and cognitive behavioural therapy increased CPAP usage. Short course education did not have a statistically significant effect on CPAP usage.

SO: Shneerson John, Wright John J. Lifestyle modification for obstructive sleep apnoea. Cochrane Database of Systematic Reviews: Reviews 2001 Issue 1 UK DOI: 10.1002/14651858.CD002875

DOI: 10.1002/14651858.CD002875

LIFESTYLE MODIFICATION STRATEGIES FOR MANAGING OBSTRUCTIVE SLEEP APNOEA: Obstructive sleep apnoea happens when breathing is either stopped or reduced during sleep because of a narrowing or blockage of the upper airway (passage to the lungs). It causes loud snoring and occasional apnoea (stopping breathing). It can lead to daytime sleepiness and may cause, hypertension, stroke and road accidents. Lifestyle modification, especially weight loss, sleep hygiene and exercise, are often recommended. These could help by relieving pressure on the upper airway, and increasing muscle tone in the airway. However, the review found no trials to assess the effects of these strategies, and more research is needed.

SO: Lim Jerome, Lasserson Toby J, Fleetham John, Wright John J. Oral appliances for obstructive sleep apnoea. Cochrane Database of Systematic Reviews: Reviews 2006 Issue 1

DOI: 10.1002/14651858.CD004435.pub3

ORAL APPLIANCES FOR TREATING SLEEPINESS, QUALITY OF LIFE AND MARKERS OF SLEEP DISRUPTION IN PEOPLE WITH OBSTRUCTIVE SLEEP APNOEA/HYPOPNOEA (OSAH): OSAH is characterized by recurrent episodes of partial or complete upper airway obstruction during sleep, leading to a variety of symptoms including excessive daytime sleepiness. The current first choice therapy is CPAP that keeps the upper airway patent during sleep. However, this treatment can be difficult for some patients to tolerate and comply with on a long-term basis. OA are now widely used as an alternative to CPAP therapy. They are designed to keep the upper airway open by either advancing the lower jaw forward or by keeping the mouth open during sleep. This review found that OA should not be considered as first choice therapy for OSAH, where symptoms and sleep disruption are severe. There has not been a sufficient amount of research that examines the effects of OA compared with CPAP in terms of symptoms and quality of life. Although CPAP was clearly more effective at reducing the disruption to sleep, some people with OSAH may prefer using them if they are found to be tolerable and more convenient than CPAP. When an active OA was compared with an inactive OA , there were improvements in daytime sleepiness and apnoea/hypopnoea severity. OA may be more effective than corrective upper airway surgery. Further research should consider whether people with more distinctly severe symptoms respond in a similar way to those patients represented in the studies we have included in the review.

SO: Smith Ian, Lasserson Toby J. Pressure modification for improving usage of continuous positive airway pressure machines in adults with obstructive sleep apnoea. Cochrane Database of Systematic Reviews: Reviews 2009 Issue 4

DOI: 10.1002/14651858.CD003531.pub3

THE EFFECTS OF DIFFERENT PRESSURE DELIVERY INTERVENTIONS FOR IMPROVING USE OF CONTINUOUS POSITIVE AIRWAY PRESSURE IN THE TREATMENT OF OBSTRUCTIVE SLEEP APNOEA: Obstructive sleep apnoea (OSA) is caused by intermittent airway closure during sleep such that airflow stops despite continued efforts to breathe. Continuous positive airways pressure (CPAP) can be an effective treatment for this condition but requires regular use, and many people cannot tolerate it, or do not use it every night. Attempts to improve compliance with treatment have included changes to the mechanical devices used to deliver airway pressure, such as auto-CPAP, bi-level PAP, expiratory pressure relief and additional humidification. We examined the evidence for these different approaches. None led to large increases in hours of use, though when asked, most participants expressed a preference for the auto-CPAP machine rather than fixed pressure. When bi-level PAP and fixed CPAP were compared, initial patient acceptance was greater for bi-level PAP in one study, but long-term usage in those accepting treatment was similar for both devices. Expiratory pressure relief (C-flexTM) did not show improvement in hours of use and symptom scores. According to the evidence currently available, compliance with positive airway pressure therapy for OSA is similar, irrespective of the mode of delivery (e.g. fixed, auto-titrating or bi-level device).

SO: Sundaram Supriya, Lim Jerome, Lasserson Toby J. Surgery for obstructive sleep apnoea in adults. Cochrane Database of Systematic Reviews: Reviews 2005 Issue 4

DOI: 10.1002/14651858.CD001004.pub2

SURGERY FOR OBSTRUCTIVE SLEEP APNOEA/HYPOPNOEA SYNDROME: Surgery for obstructive sleep apnoea/hypopnoea syndrome aims to relieve obstruction by increasing the size of the airway in the throat, bypassing the airway or removing a lesion. A limited number of trials assessing diverse surgical techniques

were identified. There were inconsistent effects reported across the trials. The available evidence from these small studies does not currently support the widespread use of surgery in people with mild to moderate daytime symptoms associated with sleep apnoea.

o OSA severity or characteristics: Baseline questionnaire (etc.) results, formal testing results (including hypoxemia levels), Baseline QoL; positional dependency, REM dependency

o Other: specific symptoms

b. Does the comparative effect of treatments vary based on the definitions of OSA used by study investigators?

KQ6: In OSA patients prescribed non-surgical treatments, what are the associations of pre-treatment patient-level characteristics with treatment compliance?

Source:
Diagnosis and Treatment of Obstructive Sleep Apnea in Adults
Comparative Effectiveness Reviews, No. 32

Investigators: Ethan M Balk, MD, MPH, Denish Moorthy, MBBS, MS, Ndidiamaka O Obadan, MD, MS, Kamal Patel, MPH, MBA, Stanley Ip, MD, Mei Chung, PhD, MPH, Raveendhara R Bannuru, MD, Georgios D Kitsios, MD, PhD, Srila Sen, MA, Ramon C Iovin, PhD, James M Gaylor, BA, Carolyn D'Ambrosio, MD, MS, and Joseph Lau, MD.

Tufts Evidence-based Practice Center
Rockville (MD): Agency for Healthcare Research and Quality (US); July 2011.
Report No.: 11-EHC052

Preoperative Testing
The occurrence of both perioperative and postoperative complications in OSA patients has been documented with respect to either surgical intervention for OSA or other procedures.[37–39] In a study of patients undergoing hip or knee replacement surgery, 24 percent of 101 patients with OSA had major postoperative complications (respiratory or cardiac) compared with 9 percent of matched controls.[39] Other studies have highlighted the risk of anesthesia and analgesia-related adverse outcomes, such as perioperative airway collapse and postoperative oxygen desaturation.[37,39] Many surgical patients with OSA, however, remain undiagnosed at the time of surgery,[37–39] and may benefit from some type of preoperative assessment for OSA.[37] Finding patients with undiagnosed sleep apnea who are undergoing surgery could, in theory, allow for optimization of perioperative care to minimize problems with intubation, extubation, and other respiratory events. At present, the value of screening all or selected surgical patients, and what method of screening would be most effective and efficient, is unclear.

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39. Gupta RM, Parvizi J, Hanssen AD, et al. Postoperative complications in patients with obstructive sleep apnea syndrome undergoing hip or knee replacement: a case-control study. Mayo Clin Proc. 2001;76:897–905. [PubMed: 11560300]

KQ7: What is the effect of interventions to improve compliance with device (CPAP, oral appliances, positional therapy) use on clinical and intermediate outcomes?

Source:
Diagnosis and Treatment of Obstructive Sleep Apnea in Adults
Comparative Effectiveness Reviews, No. 32

Investigators: Ethan M Balk, MD, MPH, Denish Moorthy, MBBS, MS, Ndidiamaka O Obadan, MD, MS, Kamal Patel, MPH, MBA, Stanley Ip, MD, Mei Chung, PhD, MPH, Raveendhara R Bannuru, MD, Georgios D Kitsios, MD, PhD, Srila Sen, MA, Ramon C Iovin, PhD, James M Gaylor, BA, Carolyn D'Ambrosio, MD, MS, and Joseph Lau, MD.

Tufts Evidence-based Practice Center
Rockville (MD): Agency for Healthcare Research and Quality (US); July 2011.
Report No.: 11-EHC052

Eric J. Freer
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Sales & Marketing Leader

2. Douglas Myers

The diagnosis and treatment of sleep apnea requires a varried approach. On one end of the spectrum is the child with an oropharynx obstructed by grossly enlarged tonsils for whom no diagnostic studies are beneficial and for whom tonsillectomy results in a cure. On the other end is the obese adult individual who would be helped by weight loss, smoking and alcohol cessation, and C-PAP, who requires sleep studies for monitoring and for whom surgery holds little benefit. In one instance sleep studies represent an unnecessary expense and surgery is most cost effective, and in the other the surgery is an unnecessary expense and sleep studies are most cost effective. Diagnostic evaluation and treatment must be individualized. The expertise to perform both diagnosis and treatment is available in most local medical communities, so that the added cost in time and transportation to regional centers is unnecessary. A common guideline for best practices would be helpful for use in community multispecialty discussions to establish diagnostic and surgical criteria.

Douglas Myers, M.D.

Vancouver, WA

3. Kerilyn Nobuhara

Will the cost effectiveness analysis include consideration of the morbidities associated with the different treatments? Ie we receive a number of PA requests for UPPP surgery, which is at best only 50% successful in treatment of sleep apnea, and patients frequently require CPAP even if they have had the surgery, which essentially negates any cost benefit for the surgical intervention.

Thanks.

Kerilyn Nobuhara
Senior Medical Consultant
Healthcare Authority

PUBLIC COMMENTS – DRAFT REPORT

1. Karen Anderson

Hi, Denise.
I have just finished reviewing the summary on the OSA eval. One of the concerns I have is that there are some vulnerable populations that were not "teased out" for evaluation. Specifically, patients with Down's Syndrome are notoriously afflicted with ENT issues and I had the unfortunate experience of dealing with one who was in heart failure, was evaluated and determined to have OSA, given CPAP which, despite her severe mental retardation, she avidly wore and improved immensely. I don't know how that fits in with the EBM eval but I do think that there may be some populations that have not been separately evaluated and who may benefit from treatment. Also, I did not see CHF findings or symptoms included in the pre/post rx evals. I think that is an important deficit.
thanks
Karen Anderson

2. Washington State Agency Medical Directors

Comments on Sleep Apnea Draft Evidence Report

The significance of the association between apnea-hypopnea index (AHI) and all-cause mortality is unclear, particularly given the uncertain association between AHI and cardiovascular mortality, stroke, hypertension, diabetes and other metabolic abnormalities, and quality of life. The draft report does comment on p. 5 "Thus the association between reductions in AHI by OSA treatment and improvements in long-term clinical outcomes remains theoretical."In general, the wording of the report gives unsupported credence to a putative causal relationship between obstructive sleep apnea (OSA) and major morbidity and mortality. Similarly, it is not sufficiently critical of the strength of evidence supporting the proposition that continuous positive airway pressure (CPAP) and other treatments for OSA improve major clinical outcomes.

Regarding key question 4, the "relationships between… AHI and oxygen desaturation index… and other patient characteristics with long term clinical and functional outcomes" is further elaborated in the draft report, quoting from the AHRQ comparative effectiveness review on sleep apnea diagnosis and treatment, concluding, on p. 164, "Unfortunately, as discussed below, there are almost no trial data to support that treatment of OSA and reduction of AHI improves clinical outcomes" and, on p. 165 "While the relevant trials are conclusive regarding the effects of CPAP on AHI and sleepiness measures, among over 40 trials of patients treated with CPAP or no treatment, none have reported long-term clinical outcomes." Thus, it is contradictory and unclear what evidence is relied on for statements such as: p. 174, "Obstructive sleep apnea is a cause of significant morbidity and mortality, and is thus an important public health issue. In addition, the diagnosis and treatment of OSA have societal cost implications, making cost-effectiveness a concern in both of these aspects."

On p. 7 of the draft report it is stated: "A moderate strength of evidence was found for the treatment of OSA with CPAP", a statement that in itself says little, but presumably intends to say that a moderate strength of evidence was found to support the effectiveness of treatment of OSA with CPAP. Subsequent statements qualify the statement, noting that there is relatively strong evidence that CPAP treatment improves sleep measures such as AHI, arousal index, and minimum oxygen saturation, and subjective report of daytime sleepiness on the Epworth Sleepiness Scale. Directly quoted from the AHRQ comparative effectiveness review on sleep apnea diagnosis and treatment, the draft report says on p. 7: "There is only weak evidence that that CPAP treatment may improve quality of life or neurocognitive measures, or other intermediate outcomes" and "Despite no or weak evidence for an effect of CPAP on clinical outcomes, given the large magnitude of effect on the intermediate outcomes of AHI and ESS, the strength of evidence that CPAP is an effective treatment to alleviate sleep apnea signs and symptoms was rated moderate." The term "signs and symptoms" is not further specified, leaving it unclear exactly what beneficial effects of CPAP treatment are supported by evidence. It would be helpful to remind the reader at this point that any association between reductions "in AHI by OSA treatment and improvements in long-term clinical outcomes remains theoretical."
The discussion of cost effectiveness studies in both the Executive Summary and the body of the report fails to adequately emphasize that the "cost effectiveness" analysis assumes effectiveness of OSA treatment rather than basing the analysis on empirical findings of effectiveness, thus seriously undermining validity of "cost effectiveness" analyses. Such problems with the major "cost utility" study reported on (McDaid, 2009) are mentioned in the "Limitations" section on p. 174, yet the highly conjectural results of the cost utility study are reported with little in the way of caveat.

Similarly the cost-analysis studies of health care costs of persons with OSA compared to those without do not establish causality or evidence to support the expectation that diagnosis and treatment of OSA will reduce health care costs. Thus, in the "Policy context and cost information" discussion in the "Background" section of the draft report, on p. 17, it is surprising to see the statement "Undiagnosed OSA results in roughly a two-fold

increase in health care utilization and costs, in the years preceding the diagnosis, due largely to the number of attendant comorbidities." The use of the words "results in" implies causality where it has not been established.

The draft report would do better to emphasize how much of the case for treatment of OSA is based on conjecture and extrapolation from associative relationships between sleep measures and clinical morbidity and the effects of OSA treatments on sleep measures and a few intermediate clinical outcome measures of uncertain clinical significance. In this context, "cost-effectiveness" studies of OSA treatment have little value other than as conjecture.

Department of Corrections
Dr. Steve Hammond