Health Technology Assessment Clinical Committee Meeting Program Update

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Health Technology Assessment
March 16, 2012

Presentation Overview

- **HTA Program Overview**
- **HTA Program Updates**
  - Topics

- **Today's Topics**
  - Sleep Apnea Diagnosis and Treatment
  - Bone Morphogenetic Proteins

Governor Gregoire's strategy : Improve quality in health care

- **Five point plan to improve health care (2005)**
  - *Emphasize evidence based health care*
    - Create more transparency in the health care system
    - Promote prevention, healthy lifestyles, and healthy choices
    - Better managed chronic care
    - Make better use of information technology
- **Collaboration of Programs across State purchasing –**
  - Health Care Authority – Public Employees and subsidized low income (Basic Health, **Uniform Medical Plan**, PEB)
  - **Medicaid** Purchasing Agency – federal/state low income health care program with **fee for service** and managed care plans
  - Labor and Industries – **Worker's compensation** program
  - Department of Corrections – Correctional health care

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Why Health Technology Assessment?

Medical Technology is a primary driver of cost:

The development and diffusion of **medical technology are primary factors** in explaining the persistent difference between health spending and overall economic growth.

New medical technology may account for about **one-half or more of real long-term spending growth**.

Kaiser Family Foundation, March 2007: **How Changes in Medical Technology Affect Health Care Costs**

Since **technological change is the biggest contributor**, an effective long-term strategy for controlling health care spending will probably **have to address the health care system's way** of incorporating new technologies into practice.

U.S. Congressional Budget Office, *Technological Change and the Growth in Health Care Spending*, 2008. Report available at www.cbo.gov.

Medical Technology has quality gaps:

Medical technology diffusing without evidence of improving quality. Highly correlated with misuses, overutilization, underutilization.

Cathy Schoen, Karen Davis, Sabrina K.H. How, and Stephen C. Schoenbaum, "U.S. Health System Performance: A National Scorecard," *Health Affairs*, Web Exclusive (September 20, 2006): w459

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WA HTA Program Purpose

Primary purpose:

To ensure medical treatments and services paid for with state health care dollars are safe and proven to work.

- Provide resources for state agencies purchasing health care.
- Develop scientific, evidence-based reports on medical devices, procedures, and tests.
- Facilitate an independent clinical committee of health care practitioners to determine which medical devices, procedures, or tests meet safety, efficacy, and cost tests.

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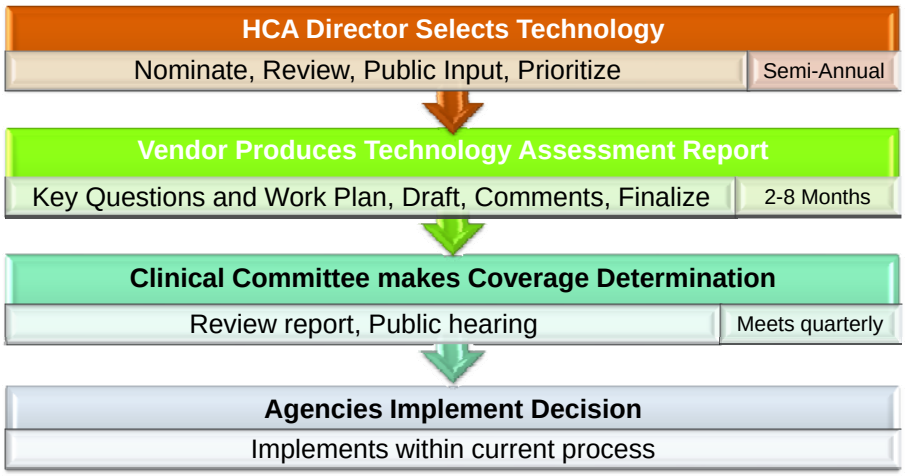
WA HTA Process

Overview



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KEY HTA Products

Pay for What Works: Better Information is Better health

Transparency: Publish topics, criteria, reports, open meeting

Technology Assessment Report: Formal, systematic process to review appropriate healthcare technologies.

Independent Coverage decision: Committee of practicing clinicians make decisions that are scientifically based, transparent, and consistent across state health care purchasing agencies.

Key focus questions:

- Is it safe?
- Is it effective?
- Does it provide value (improve health outcomes)?

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Washington State Health Care Authority
Health Technology Assessment

HTCC Decision Basis

Clinical Committee Decision must give greatest weight to most valid and reliable evidence

- Objective Factors for evidence consideration
  - Nature and Source of evidence
  - Empirical characteristics of the studies or trials upon which evidence is based
  - Consistency of outcomes with comparable studies
- Additional evaluation factors
  - Recency (date of information)
  - Relevance (applicability of the information to the key questions presented or participating agency programs and clients)
  - Bias (presence of conflict of interest or political considerations)

WAC 182-55-030: Committee coverage determination process

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Washington State Health Care Authority
Health Technology Assessment

Technology Topics Underway

- Sleep Apnea Diagnosis and Treatment
- Bone Morphogenetic Proteins
- Upper Endoscopy for GERD and GI Symptoms
- Robotic Assisted Surgery
- Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy
- Intensity Modulated Radiation Therapy
- Vitamin D Testing
- Prostate-specific Antigen Testing
- Ablation Procedures for Supraventricular Tachycardia
- Carotid Artery Stenting
- Cervical Level Fusion for Degenerative Disk Disease
- Cochlear Implants (bi- or unilateral)
- Hyperbaric Oxygen Therapy for wound care and brain injury
- Cardiac Nuclear Imaging

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Washington State Health Care Authority
Health Technology Assessment

Email distribution list: shtap@hca.wa.gov

HTA Web Pages: http://www.hta.hca.wa.gov/

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Washington State Health Care Authority, HTA Program
Final Key Questions and Background
Sleep Apnea Diagnosis and Treatment

Introduction

HTA selected Sleep Apnea Diagnosis and Treatment to undergo a health technology assessment where an independent vendor will systematically review the evidence available on the safety, efficacy, and cost-effectiveness. HTA posted the topic and gathered public input on all available evidence. HTA posted the key questions for public comment and 3 responses were received. Disposition of the comments is included at the bottom of this document.

This topic is scheduled for review in March 2012.

In this case, a federal research agency, AHRQ, also selected this topic. AHRQ has posted key Questions. HTA strives to make economical use of state resources and to not duplicate other systematic reviews where current reports meet our statutory mandate and are timely.

Key Questions *(As specified in AHRQ report)*

Diagnosis

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

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?

KQ2: In adults being screened for obstructive sleep apnea, what are the relationships between apnea-hypopnea index (AHI) or oxygen desaturation index (ODI) and other patient characteristics with long term clinical and functional outcomes?

KQ3: How does phased testing (screening tests or battery followed by full test) compare to full testing alone?

KQ4: What is the effect of pre-operative screening for sleep apnea on surgical outcomes?

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?

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

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

Additional Key Question:

Cost

KQ8: What evidence exists of the cost and cost-effectiveness for the identified strategies of sleep apnea diagnosis and treatment?

Technology Background (*from AHRQ Background- see below for link to this report*)

Sleep apnea is a common disorder that affects all ages. The American College of Chest Physicians estimates the prevalence of obstructive sleep apnea (OSA) in the United States to be between 5-10 percent and asserts that as many as one in four American adults could benefit from evaluation for OSA. The condition is characterized by periods of disturbed airflow patterns during sleep time, namely reduced airflow (hypopnea) or airflow cessation (apnea). It is postulated that both types of airflow disturbance have similar pathophysiology and bear the same clinical significance. OSA is by far the most common type of the condition; apneas and hypopneas of central and mixed central and obstructive etiology comprise the other forms. OSA has been associated with a variety of adverse clinical outcomes, such as mortality secondary to cardiovascular disease, decreased quality of life, cardiac disease and stroke, hypertension, and noninsulin-dependent diabetes and other metabolic abnormalities. It also is associated with an increased likelihood for motor vehicle and other accidents.

Diagnosis

The severity of sleep apnea is typically quantified by the number of apneas and hypopneas per hour of sleep, a quantity that has been termed the apnea-hypopnea index (AHI). The symptom of excessive daytime sleepiness is quite variable and is not always present in patients with OSA; thus, in most patients, the condition remains undiagnosed and untreated.

There is a large amount of clinical uncertainty surrounding this condition, including inconsistencies in the definition of the disease. While in-laboratory polysomnography is considered the gold standard in clinical practice to diagnose obstructive sleep apnea, it is not without constraints such as cost, interlaboratory variation in hardware and assessment methods. The standard measurement of AHI (and by extension, the diagnosis of sleep apnea) requires a comprehensive, technologist-attended sleep study with multichannel polysomnography, which is performed in specialized sleep laboratories. Laboratory-based polysomnography records a variety of neurophysiologic and cardiorespiratory signals and is interpreted by trained technologists and sleep physicians after the sleep study has been completed.

However, it is acknowledged that it is not a definitive test to either diagnose or rule out obstructive sleep apnea. In part, this is due to a lack of robust standardized criteria as to the test parameters measured and the thresholds of the parameters used to make the diagnosis.

Since in-laboratory polysomnography is costly, resource intensive, and burdensome to the patient, other diagnostic tools have been developed, including portable tests and questionnaires for pre-screening patients. There are different types of portable monitors, which gather different neurophysiologic and respiratory information and may synthesize the accumulated data differently. Different screening questionnaires exist to pre-screen patients for further testing or treatment. The value of the different tests and of the questionnaires and other screening tools remains unclear. There is also lack of clarity as to whether the tests can be accurately used to predict the clinical severity of patients' sleep apnea and their likelihood of clinically important sequelae.

Treatment

Continuous positive airway pressure (CPAP) is the standard 1st-line therapy for most patients diagnosed with obstructive sleep apnea. Obstructive sleep apnea occurs when the upper airway closes or becomes overly narrow as the muscles in the oropharynx (mouth and throat) relax during sleep. This results in inadequate or stopped breathing, which reduces oxygen in the blood and causes arousal from sleep. The CPAP machine counteracts this sequence of events by delivering compressed air to the oropharynx, splinting the airway (keeping it open with increased air pressure) so that unobstructed breathing becomes possible, reducing and/or preventing apneas and hypopneas.

For many patients, using CPAP results in immediate improvement in sleep and improvement in quality of life largely related to decreased daytime somnolence. However, it has been suggested that approximately one-quarter to one-half of patients with obstructive sleep apnea will either refuse the offer of CPAP therapy, will not tolerate it, fail to use the machine properly, or for other reasons do not comply with CPAP use. These patients are essentially untreated and receive little or no benefit from the device.

When CPAP is refused or not tolerated, a number of 2nd-line treatments are available including, uvulopalatopharyngoplasty (UPPP), radiofrequency ablation, jaw surgery, and bariatric surgery, for eligible candidates. UPPP, radiofrequency ablation, and jaw surgery are surgical techniques to remove or shrink and scar redundant tissue that is causing the obstruction or to otherwise minimize the obstruction. The goal of bariatric surgery is to reduce body weight and fat, which may shrink the oropharyngeal tissue causing the obstruction. However, life-threatening complications have been associated with sleep apnea surgery. Fatalities have been related to upper airway collapse or obstruction secondary to pharmacological sedation and surgical edema.

Other less invasive techniques include oral appliances, which are worn overnight and aim to mechanically splint the oropharynx open; positional therapy, devices to prevent lying supine during sleep, a position that for many patients exacerbates the obstruction; pharyngeal or laryngeal exercises to improve muscle tone; non-surgical weight loss programs; and physical-exercise programs.

Another management approach is to provide interventions that will increase compliance with CPAP use. These include structured education about the value of CPAP and how to use and adjust the CPAP; structured individual follow-up to correct any problems; group support; and relieving nasal congestion or dryness caused by the CPAP machine.

Public comment and Response

HTA received 3 timely public comments; one comment included evidence. All comments, references and evidence have been forwarded to the technology assessment center for consideration in the assessment of this topic. A summary of the comments follows:

One commenter provided evidence in the form of references relevant to each key question and written response to address/answer each key question. Response: No change to key questions. Commenter did not provide recommendations or comments on the key questions.

One commenter noted the need for varied approach in the diagnosis and treatment of sleep apnea due to the broad spectrum of potential patients and felt a "common guideline" would be helpful to establish diagnostic and surgical criteria. Response: No change to key questions. Commenter did not provide recommendations or comments on the key questions.

One commenter asked if cost-effectiveness analysis will include consideration of morbidities associated with different treatments for sleep apnea. Response: No change to key questions. All cost-effectiveness analyses that meet report inclusion criteria will be included in the assessment.

AHRQ Report Reference and Link

Balk EM, Moorthy D, Obadan NO, Patel K, Ip S, Chung M, Bannuru RR, Kitsios GD, Sen S, Iovin RC, Gaylor JM, D'Ambrosio C, Lau J. Diagnosis and Treatment of Obstructive Sleep Apnea in Adults. Comparative Effectiveness Review No. 32. AHRQ Publication No. 11-EHC052-EF. Rockville, MD: Agency for Healthcare Research and Quality. July 2011. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Original Draft KQ Published 2/2011

Washington State Health Care Authority, HTA Program
DRAFT Key Questions and Background
Sleep Apnea Diagnosis and Treatment

Introduction

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In this case, a federal research agency, AHRQ, also selected this topic. AHRQ has posted key Questions. HTA strives to make economical use of state resources and to not duplicate other systematic reviews where current reports meet our statutory mandate and are timely.

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When CPAP is refused or not tolerated, a number of 2nd-line treatments are available including, uvulopalatopharyngoplasty (UPPP), radiofrequency ablation, jaw surgery, and bariatric surgery, for eligible candidates. UPPP, radiofrequency ablation, and jaw surgery are surgical techniques to remove or shrink and scar redundant tissue that is causing the obstruction or to otherwise minimize the obstruction. The goal of bariatric surgery is to reduce body weight and fat, which may shrink the oropharyngeal tissue causing the obstruction. However, life-threatening complications have been associated with sleep apnea surgery. Fatalities have been related to upper airway collapse or obstruction secondary to pharmacological sedation and surgical edema.[21]

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Submitted By	Cited Evidence
Bruce Blehart **American Academy of Sleep Medicine (AASM)**	9 studies cited [Adeseun GA, Rosas SE. The impact of obstructive sleep apnea on chronic kidney disease. *Curr Hypertens Rep.* 2010 Jul 31.] [Schahin SP, Nechanitzky T, Dittel C, Fuchs FS, Hahn EG, Konturek PC, Ficker JH, Harsch IA. Long-term improvement of insulin sensitivity during CPAP therapy in the obstructive sleep apnoea syndrome**.** *Med Sci Monit*. 2008 Mar;14(3):CR117-21.] [Aihara K, Chin K, Oga T, et al. Long-term nasal continuous positive airway pressure treatment lowers blood pressure in patients with obstructive sleep apnea regardless of age. *Hypertens Res.* Oct 2010;33(10): 1025-1031.] [Abe H, Takahashi M, Yaegashi H, et al. Efficacy of continuous positive airway pressure on arrhythmias in obstructive sleep apnea patients. *Heart Vessels.* Jan 2010;25(1):63-69.] [Lettieri CJ, Eliasson AH, et al. Obstructive sleep apnea syndrome: are we missing an at-risk population? *J Clin Sleep Med.* Oct 15 2005;1(4):381-385.] [Campos-Rodriguez F, Pena-Grinan N, Reyes-Nunez N, et al. Mortality in obstructive sleep apnea-hypopnea patients treated with positive airway pressure. *Chest.* Aug 2005;128(2):624-633.] [Punjabi NM, Caffo BS, Goodwin JL, et al. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Med.* Aug 2009;6(8):e1000132.] [Young T, Finn L, Peppard PE, et al. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. *Sleep.* Aug 1 2008;31(8):1071-1078.] [Tregear S, Reston J, Schoelles K, Phillips B. Continuous positive airway pressure reduces risk of motor vehicle crash among drivers with obstructive sleep apnea: systematic review and meta-analysis. *Sleep.* Oct 1 2010;33(10): 1373-1380.]
David P. White, MD Chief Medical Officer Philips Respironics Clinical professor of Medicine	**References:** 1. Alan Mulgrew et al., Annals of Internal Medicine, (2007) 2. Skomro RP , Gjevre J , Reid J , et al . Outcomes of home-based diagnosis and treatment of obstructive sleep apnea . *Chest* .2010 ; 138 (2):257-263 3. Berry RB , Hill G , Thompson L , McLaurin V . Portable monitoring and autotitration versus polysomnography for

Harvard Medical School **Philips Healthcare**	the diagnosis and treatment of sleep apnea . *Sleep* . 2008 ; 31 (10): 1423 – 1431 4. Peppard, P.E.et.al., *Prospective Study of the Association between Sleep-Disorderd Breathing and Hypertension.* NEJM 2000. **342**(19) p. 1378-1384. 5. Yaggi, H.K., et.al*. Obstructive Sleep Apnea as a Risk Factor for Stroke and Death*. NEJM 2005. **353**: p. 2034-2041. 6. Reichmuth, K.J., et.al., *Association of Sleep Apnea and Type II Diabetes. A Population Based Study*. AJRCCM 2005. **172**: p. 1590-1595. 7. Resnick, H.E., et.al. *Diabetes and Sleep Disturbances: Findings from the Sleep Heart Health Study.* Diabetes Care 2003: **26:** p. 702-709. 8. Barbe, F., et al., *Effect of continuous positive airway pressure on the risk of road accidents in sleep apnea patients.* Respiration, 2007. **74**(1): p. 44-9. 9. George, C.F., *Reduction in motor vehicle collisions following treatment of sleep apnoea with nasal CPAP.* Thorax, 2001. **56**(7): p. 508-12. 10. Mulgrew, A.T., et al., *Risk and severity of motor vehicle crashes in patients with obstructive sleep apnoea/hypopnoea.* Thorax, 2008. **63**(6): p. 536-41. 11. Sassani, A., et al., *Reducing motor-vehicle collisions, costs, and fatalities by treating obstructive sleep apnea syndrome.* Sleep, 2004. **27**(3): p. 453-8. 12. Mehra R, et.al. *Association of Nocturnal Arrhythmia's with Sleep Disordered Breathing. The Sleep Heart Heath Study*. AJRCCM 2006. **17**: p. 910-916. 13. Gami, AS., et al., *Association of Atrial Fibrillation and Obstructive Sleep Apnea.* Circulation 2004. **110**: p. 364-367. 14. Kanagala,R., et.al. *Obstructive Sleep Apnea and the Recurrence of Atrial Fibrillation.* Circulation 2003. **107**: p. 2589-2594. 15. Bazzano, L.A., et al., *Effect of nocturnal nasal continuous positive airway pressure on blood pressure in*

	obstructive sleep apnea. Hypertension, 2007. **50**(2): p. 417-23. 16. Haentjens, P., et al., *The impact of continuous positive airway pressure on blood pressure in patients with obstructive sleep apnea syndrome: evidence from a meta-analysis of placebo-controlled randomized trials.* Arch Intern Med, 2007. **167**(8): p. 757-64. 17. Becker FH., et al., *Effect of Nasal Continuous Positive Airway Pressure treatment on Blood Pressure in Patients with Obstructive Sleep Apnea*. Circulation 2003. **107**: p.68-73. 18. Logan AG., et al., *Refractory Hypertension & Sleep Apnea : Effect of CPAP on Blood Pressure and Baroreflex*. Eur Respir J 2000. 21: p. 241-247. 19. Campos-Rodriquez, F. et.al. *Mortality in Obstructive Sleep Apnea-Hypopnea Patients with Positive Airway Pressure.* Chest 2005;128;624-633**.** 20. Marin, J. et al., *Long Term Cardiovascular Outcomes in Men With Obstructive Sleep Apnoea-Hypopnea with or without Continuous Positive Airway Pressure: An Observational Study*. Lancet, 2005. 365: p. 1046-105. 21. Arzt, M., et al*. Suppression of Central Apnea by Continuous Positive Airway Pressure and Transplant-Free Survival in Heart Failure. A Post Hoc Analysis of the Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure Trial (CANPAP)*. Circulation 2007. 115; p. 3173-3180. 22. Guest, J.F., et al., *Cost-effectiveness of using continuous positive airway pressure in the treatment of severe obstructive sleep apnoea/hypopnoea syndrome in the UK.* Thorax, 2008. **63**(10): p. 860-5. 23. Tan, M.C., et al., *Cost-effectiveness of continuous positive airway pressure therapy in patients with obstructive sleep apnea-hypopnea in British Columbia.* Can Respir J, 2008. **15**(3): p. 159-65. 24. Weatherly, H.L., et al., *An economic analysis of continuous positive airway pressure for the treatment of obstructive sleep apnea-hypopnea syndrome.* Int J Technol Assess Health Care, 2009. **25**(1): p. 26-34. 25. McDaid, C., et al., *Continuous positive airway pressure devices for the treatment of obstructive sleep apnoeahypopnoea syndrome: a systematic review and economic analysis.* Health Technol Assess, 2009. **13**(4): p. 1-142.

	26. Massie, C.A., et al., *Effects of Humidification on Nasal Symptoms and Compliance in sleep Apnea Patients Using Continuous Positive Airway pressure.* CHEST, 1999. 116:403–408. 27. Hoy, C.J, et al., *Can Intensive Support Improve Continuous Positive Airway Pressure Use in Patients with the Sleep Apnea / Hypopnea Syndrome?* AM J RESPIR CRIT CARE MED 1999;159:1096–1100. 28. Aloia, M.S., et al., *Time Series analysis of Treatment Adherence Patterns in Individuals with Obstructive Sleep Apnea.* Ann Behav Med, 2008. 29. Aloia, M.S., et al., *The Local Coverage Determination Criteria for Adherence to positive Airway Pressure Treatment: Testing the Limits?* Chest, 2010. 138;p. 875-879. 30. McEvoy, R.D., et al., *A Randomized Controlled Trial of Nurse-Led Care for Symptomatic Moderate – Severe Obstructive Sleep Apnea.* Am J Respir Crit Care Med, 2009. 179; p 501-508. 31. Weaver, T.E., et al., *Relationship Between Hours of CPAP Use and Achieving Normal Levels of Sleepiness and Daily Functioning.* SLEEP 2007; 30(6):711-719. 32. Grunstein, R.R., et al., *Increased Adherence to CPAP with a Group Cognitive Behavioral treatment Intervention: A Randomized Trial.* Sleep, 2007. 30(5), p. 635-640. 33. Aloia, M.S. et al., *Predicting Treatment Adherence in obstructive Sleep Apnea Using Principals of Behavior Change* J of Clin Sleep Med, 2005. 1(4), p. 346-353. 34. Chervin, R.D., et al., *Compliance with Nasal CPAP Can Be Improved by Simple Interventions.* SLEEP 1997; 20(4):284-289. 35. Likar, L.L., et al., *Group Education Sessions and Compliance with Nasal CPAP Therapy*. CHEST 1997; 111: 1273-1277. 36. Engleman, H.M., Wild, M.R., *Improving CPAP Use by Patients with the Sleep Apnoea / Hypopnoea Syndrome (SAHS)* Sleep Medicine Reviews 2003: 7(1); 81-99. 37. Ballard, R.D., Gay, P.C., Strollo, P.J. *Interventions to Improve Compliance in Sleep Apnea Patients Previously*

	Non-Compliant with Continuous Positive Airway Pressure. J Clin Sleep Med 2007; 3(7); 706-712. 38. Gentina, T., et al., *Auto bi-level with pressure relief during exhalation as a rescue therapy for optimally treated obstructive sleep apnoea patients with poor compliance to continuous positive airways pressure therapy – a pilot study.* Sleep Breath 2010. 39. Babu, A.R., et al., *Type 2 Diabetes, Glycemic Control, and Continuous Positive Airway Pressure in Obstructive Sleep Apnea.* Arch Intern Med. 205; 165: 447-452.
John H. Mathias II, President **Sleep Services of America, Inc.** **A GE Healthcare Company**	Same as AASM letter above
Sean Muilenburg **U.S. Sleep Diagnostics**	Outcomes of PSG vs Portable Testing and In Lab Titration vs Auto Titration Device Therapy: Chest, August, 2010; 138: 257-263 Stepanowsky et al, *Nightly variability of sleep-disordered breathing measured over 3 nights*,Otolaryngol Head Neck Surg 2004;131:837-43.

American Academy of Sleep Medicine

February 28, 2011

Leah Hole-Curry, JD
Program Director
Health Care Authority Health Technology Assessment Program
P.O. Box 42712
Olympia, WA 98504-2712

Re: Washington State Health Care Authority Health Technology Assessment Program: Sleep Apnea Diagnosis and Treatment.

Dear Ms. Hole-Curry:

The American Academy of Sleep Medicine (AASM) is pleased to provide this information in response to the Washington State Health Care Authority Health Technology Assessment Program on Sleep Apnea Diagnosis and Treatment. The AASM is the leader in setting standards and promoting excellence in sleep medicine health care, education and research. The Academy represents over 9,700 sleep care professions, including 7,219 physicians and 1,081 other health care professionals with doctoral degrees. In addition, the AASM has developed rigorous accreditation standards relating to sleep care and sleep care facilities, with 2,209 facilities currently accredited. Based on our members' scientifically based work in providing care for patients with obstructive sleep apnea (OSA), the conclusion is undeniable: there is an essential patient care benefit in identifying those with OSA and providing the related treatment for this chronic medical condition.

The questions you are asking have been addressed by the Medicare program in its action to expand coverage for diagnostic sleep care testing for Medicare beneficiaries and in providing treatment coverage for these patients. The Centers for Medicare and Medicaid Services (CMS) issued its Decision Memo (click here) for Sleep Testing for Obstructive Sleep Apnea (CAG-00405N) in 2009 and summarized its conclusion as follows:

> The evidence is sufficient to determine that the results of the sleep tests identified below can be used by a beneficiary's treating physician to diagnose OSA, that the use of such sleep testing technologies demonstrates improved health outcomes in Medicare beneficiaries who have OSA and receive the appropriate treatment, and that these tests are thus reasonable and necessary under section 1862(a)(1)(A) of the Social Security Act.

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1. Type I Polysomnography (PSG) is covered when used to aid the diagnosis of obstructive sleep apnea (OSA) in beneficiaries who have clinical signs and symptoms indicative of OSA if performed attended in a sleep lab facility.
2. A Type II or a Type III sleep testing device is covered when used to aid the diagnosis of obstructive sleep apnea (OSA) in beneficiaries who have clinical signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility.
3. A Type IV sleep testing device measuring three or more channels, one of which is airflow, is covered when used to aid the diagnosis of obstructive sleep apnea (OSA) in beneficiaries who have signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility.
4. A sleep testing device measuring three or more channels that include actigraphy, oximetry, and peripheral arterial tone is covered when used to aid the diagnosis of obstructive sleep apnea (OSA) in beneficiaries who have signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility.

In reaching this determination, CMS made the following finding that clearly identifies why Medicare coverage for diagnostic testing to ascertain whether patients have the chronic disease of OSA is reasonable and necessary:

> OSA, sometimes referred to as Obstructive Sleep Apnea Hypopnea Syndrome-(OSAHS), is associated with significant morbidity and mortality. It is a commonly underdiagnosed condition that occurs in 4% of men and 2% of women (Young et al. 1993). The prevalence increases with age (up to 10% in persons 65 and older), as well as with increased weight. Complications associated with OSA include excessive daytime sleepiness, concentration difficulty, coronary artery disease, and stroke (Kokturk et al. 2005). It is estimated that 10% of patients with congestive heart failure (CHF) have OSA, which is independently associated with systemic arterial hypertension (Caples et al. 2005). Untreated OSA is associated with a ten-fold increased risk of motor vehicle accidents (Tiran-Santos et al. 1999). The most common clinical presentation of patients with OSA is obesity accompanied by excessive daytime drowsiness (20% of adults with BMI > 30 have OSA), although other clinical findings associated with OSA include nocturnal choking or gasping, witnessed apneas during sleep, large neck circumference and daytime fatigue.

Multiple studies, some of which are set out in the Appendix, highlight the need and value for sleep care diagnostic testing and subsequent treatment.

For purposes of Medicare coverage for the durable medical equipment (DME) provided in the treatment for patients with OSA, baseline physiologic criteria are identified for making an OSA diagnosis. The sleep physician has an essential role in these determinations. This is identified in the associated Local Coverage Determinations for Washington: Local Coverage Determination (LCD) for Positive Airway Pressure (PAP) Devices for the Treatment of Obstructive Sleep Apnea (L171- click here), and Oral Appliances for Obstructive Sleep Apnea (L28606 - click here).

The AASM has published a Clinical Guideline on care for patients with OSA: *Clinical Guideline for the Evaluation, Management and Long-term Care of Obstructive Sleep Apnea in Adults* (here). This Guideline provides a comprehensive strategy for the evaluation, management and long-term care of adult patients with OSA.

The AASM has recognized the expansion of sleep diagnostic testing capability through the use of portable diagnostic sleep equipment used in testing of patients outside of the sleep care facility. Like other diagnostic tools, there is a potential for improper and over-utilization. In response to this reality, the AASM promulgated accreditation standards earlier this month on the appropriate use of this medical equipment: *Standards for Accreditation of Out of Center Sleep Testing (OCST) in Adult Patients* (here).

The AASM stands ready to provide further information to assist the Washington State Health Care Authority in addressing this and other matters relating to caring for patients with sleep disorders. Please contact Bruce Blehart at the AASM or via e-mail at @aasmnet.org for further assistance. In addition, for questions on caring for patients with sleep disorders, please do not hesitate to contact Dr. Nathaniel F. Watson and Dr. Vishesh K. Kapur. Their contact information is:

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Sincerely,

Patrick J. Strollo Jr., MD
President

cc: Jerome A. Barrett, Executive Director

Appendix

The following provides just some of the connections between OSA and comorbid conditions:

> Obstructive sleep apnea (OSA) is an important clinical problem in the chronic kidney disease (CKD) population. OSA is associated with hypoxemia and sleep fragmentation, which activates the sympathetic nervous system, the renin-angiotensin-aldosterone system, alters cardiovascular hemodynamics, and results in free radical generation. In turn, a variety of deleterious processes such as endothelial dysfunction, inflammation, platelet aggregation, atherosclerosis, and fibrosis are triggered, predisposing individuals to adverse cardiovascular events and likely renal damage. Independent of obesity, OSA is associated with glomerular hyperfiltration and may be an independent predictor of proteinuria, a risk factor for CKD progression. OSA is also associated with hypertension, another important risk factor for CKD progression, particularly proteinuric CKD. OSA may mediate renal damage via several mechanisms, and there is a need to better elucidate the impact of OSA on incident renal disease and CKD progression.
> [Adeseun GA, Rosas SE. The impact of obstructive sleep apnea on chronic kidney disease. *Curr Hypertens Rep.* 2010 Jul 31.]

> We recently demonstrated that continuous positive airway pressure (CPAP) therapy rapidly improves insulin sensitivity within 2 days in non-diabetic patients with obstructive sleep apnea syndrome. In these very patients we investigated whether this improvement of insulin sensitivity is maintained during long-term CPAP therapy. After a mean of 2.9 years (963+/-98 days) of CPAP treatment, these patients were reevaluated and hyperinsulinemic euglycemic clamp studies were performed in those with regular and effective CPAP treatment. RESULTS: From the initial 31 patients 16 could be reevaluated. 4 patients did not use their devices regularly (CPAP usage <2.5 h/night), 2 patients had insufficient CPAP treatment (AHI > or =10/h). One patient had developed type 2 diabetes mellitus. In the remaining 9 patients who used their devices regularly and effective (mean CPAP usage 5.2+/-1.6 h/night, mean AHI 3.3+/-2.6/h), mean insulin sensitivity index (ISI) was significantly higher than the baseline ISI established 2.9 years before (10.6+/-7.0 vs. 6.3+/-5.6 micromol/kg x min; p=0.008). At baseline 7 out of 9 patients had an impaired fasting glucose, after 2.9 years of treatment 3 out of 9 patients still had an impaired fasting glucose. The mean body mass index (BMI) had remained unchanged (31.4+/-7.8 vs. 31.4+/-7.6 kg/m2; mean individual difference -0.02+/-1.9 kg/m2). CONCLUSIONS: OSA is a risk factor for impaired insulin sensitivity. CPAP treatment, when used regularly and with effective pressure, may improve insulin sensitivity over long time.
> [Schahin SP, Nechanitzky T, Dittel C, Fuchs FS, Hahn EG, Konturek PC, Ficker JH, Harsch IA. Long-term improvement of insulin sensitivity during CPAP therapy in the obstructive sleep apnoea syndrome**.** *Med Sci Monit*. 2008 Mar;14(3):CR117-21.]

> Effective treatment with nasal continuous positive airway pressure (nCPAP) lowers blood pressure (BP) in patients with obstructive sleep apnea (OSA). It was reported that OSA might influence BP in middle-aged but not in elderly patients. However, effects of nCPAP treatment in elderly hypertensive OSA patients are not well known. We investigated long-

term compliance with nCPAP and its effects on BP in elderly and middle-aged OSA patients. This observational study involved 92 OSA patients (81 men, 11 women; 46 middle-aged, 46 elderly; body mass index (BMI), 27.7 (27.0-28.7) kg m(-2); apnea hypopnea index, 43.0 (39.4-46.6) per h; 95% confidence intervals). BP and BMI were measured before the study and at two checkpoints after usage of nCPAP (616 (553-679) and 1048 (985-1114) days). Diastolic BP decreased by 5.69 (3.09-8.29) mm Hg after 600 days of nCPAP treatment and by 4.50 (1.80-7.19) mm Hg after 1000 days (P=0.003). There were no significant changes in systolic BP, BMI or usage time of nCPAP. With a daily average of 3 h or more of nCPAP treatment, diastolic BP decreased significantly in subject groups >/= 60 and <60 years of age. Even in the elderly, a daily average use of nCPAP for 3 h would lower diastolic BP in OSA patients.
[Aihara K, Chin K, Oga T, et al. Long-term nasal continuous positive airway pressure treatment lowers blood pressure in patients with obstructive sleep apnea regardless of age. *Hypertens Res.* Oct 2010;33(10): 1025-1031.]

The purpose of this study was to determine the relationship between obstructive sleep apnea (OSA) and cardiovascular disorders in a large Japanese population, and to assess the efficacy of continuous positive airway pressure (CPAP) in the treatment of OSA-associated arrhythmias. The study population comprised 1394 Japanese subjects (1086 men and 308 women) who were divided into four groups on the basis of polysomnography (PSG) analysis as follows: the no sleep apnea (N-SA) group (n = 44, apnea-hypopnea index [AHI] < 5), the mild OSA (Mi-OSA) group (n = 197, 5 < AHI < 15), the moderate OSA (Mo) group (n = 368, 15 < AHI < 30), and severe OSA (SOSA) group (n = 785, AHI < 30). The following baseline characteristics were significantly associated with OSA: age (P < 0.001), gender (P < 0.001), body mass index (P < 0.001), hypertension (P < 0.001), diabetes (P = 0.009), and hyperlipidemia (P = 0.013). In the OSA group, PSG revealed the predominance of paroxysmal atrial fibrillation (PAF) (P = 0.051), premature atrial complex short run (P < 0.005), premature ventricular complex (PVC, P = 0.004), sinus bradycardia (P = 0.036), and sinus pause (arrest >2 s, P < 0.001) during the PSG recording. A total of 316 patients from the group underwent CPAP titration and were then re-evaluated. Continuous positive airway pressure therapy significantly reduced the occurrences of PAF (P < 0.001), PVC (P = 0.016), sinus bradycardia (P = 0.001), and sinus pause (P = 0.004). The results of this study demonstrate a significant relationship between OSA and several cardiac disorders, and also demonstrate the efficacy of CPAP in preventing OSA-associated arrhythmias in a large population of Japanese patients.
[Abe H, Takahashi M, Yaegashi H, et al. Efficacy of continuous positive airway pressure on arrhythmias in obstructive sleep apnea patients. *Heart Vessels.* Jan 2010;25(1):63-69.]

While age and body-mass index (BMI) are well-established risk factors for obstructive sleep apnea syndrome (OSAS), this disorder occurs across a wide spectrum of ages and weights. Preconceptions regarding “classic” patients with OSAS may lead to underdiagnosis in at-risk populations, particularly younger nonoverweight individuals. We hypothesized that the severity of OSAS is independent of age and BMI in a younger less-obese population. METHODS: Prospective study of consecutive patients diagnosed with OSAS. Active-duty military, National Guardsmen, and civilians were compared to determine if age and BMI correlated with disease severity. RESULTS: Two hundred seventy subjects (120 active-duty, 80 National Guardsmen, 70 civilians) were included. Active-duty military members were

significantly younger and less overweight than both National Guardsmen and civilians. Of the civilians, 64.3% and, of National Guardsmen, 48.8% were obese, whereas only 19.2% of active-duty had a BMI > or = 30 kg/m2 (p < .001). However, the prevalence of severe disease did not differ between groups. Disease severity showed no correlation with BMI among active-duty subjects (r = 0.09, p = .33). Of the active-duty subjects, 37.5% had severe disease, as compared with 42.5% of National Guard and 45.7% of civilian subjects (p = .18 and .09, respectively). BMI did not differ between active-duty subjects with severe disease and those with mild to moderate OSAS (26.7 kg/m2 versus 26.9 kg/m2, p = .40). There was a low but significant correlation between age and AHI (r = 0.21, p = .02) among all subjects. CONCLUSIONS: OSAS occurs in young nonobese individuals and should be considered in patients reporting excessive daytime sleepiness, regardless of age or BMI.
[Lettieri CJ, Eliasson AH, et al. Obstructive sleep apnea syndrome: are we missing an at-risk population? *J Clin Sleep Med.* Oct 15 2005;1(4):381-385.]

Untreated OSA clearly is connected to premature patient death:

The aims of this study were to analyze mortality in patients with obstructive sleep apnea-hypopnea syndrome (OSAHS) treated with positive airway pressure (PAP) and to know whether PAP compliance affects survival, as well as to investigate the prognostic value of several pretreatment variables. DESIGN AND PATIENTS: A study was made of an historical cohort of 871 patients in whom OSAHS had been diagnosed by sleep study between January 1994 and December 2000 and who had been treated with PAP. Patients were followed up until December 2001. The mean (+/- SD) age of the group was 55.4 +/- 10.6 years, the mean apnea-hypopnea index (AHI) 55.1 +/- 28.7, and 80.9% were men. To assess whether mortality was influenced by PAP therapy compliance, patients were assigned to one of the following compliance categories: < 1 h/d; 1 to 6 h/d; or > 6 h/d. Survival rates were calculated according to the Kaplan-Meier method. Survival curves were compared with the log-rank test and the trend test, when necessary. Univariate and multivariate analyses using a time-dependent Cox model were performed to elicit which variables correlated with mortality. SETTING: Outpatient sleep disorders unit. RESULTS: By the end of the follow-up period (mean duration, 48.5 +/- 22.7 months), 46 patients had died. The 5-year cumulative survival rates were significantly lower in patients who did not use PAP (compliance < 1 h) than in those who used the device for > 6 h/d (85.5% [95% confidence interval (CI), 0.78 to 0.92] vs 96.4% [95% CI, 0.94 to 0.98; p < 0.00005]) and 1 to 6 h/d (85.5% [95% CI, 0.78 to 0.92] vs 91.3% [95% CI, 0.88 to 0.94; p = 0.01]), respectively. A trend in survival rates across the groups was identified (p = 0.0004). The main cause of death in 19 cases was cardiovascular disease (CVD). Variables that independently correlated with mortality in the multivariate analysis were the following PAP use categories: compliance for > 6 h/d (odds ratio [OR], 0.10; 95% CI, 0.04 to 0.29); compliance for 1 to 6 h/d (OR, 0.28; 95% CI, 0.11 to 0.69); arterial hypertension (AHT) [OR, 3.25; 95% CI, 1.24 to 8.54]; age (OR, 1.06; 95% CI, 1.01 to 1.10); and FEV1 percent predicted (OR, 0.96; 95% CI, 0.94 to 0.98). CONCLUSION: Mortality rates in OSAHS patients who did not receive PAP therapy were higher compared with those treated with PAP and were moderately or highly compliant with therapy. A trend in survival across compliance categories was found. Patients died mainly from CVD. Categories of PAP compliance, AHT, age, and FEV1 percent predicted were the variables that independently predicted mortality.

[Campos-Rodriguez F, Pena-Grinan N, Reyes-Nunez N, et al. Mortality in obstructive sleep apnea-hypopnea patients treated with positive airway pressure. *Chest.* Aug 2005;128(2):624-633.]

Sleep-disordered breathing is a common condition associated with adverse health outcomes including hypertension and cardiovascular disease. The overall objective of this study was to determine whether sleep-disordered breathing and its sequelae of intermittent hypoxemia and recurrent arousals are associated with mortality in a community sample of adults aged 40 years or older. METHODS AND FINDINGS: We prospectively examined whether sleep-disordered breathing was associated with an increased risk of death from any cause in 6,441 men and women participating in the Sleep Heart Health Study. Sleep-disordered breathing was assessed with the apnea-hypopnea index (AHI) based on an in-home polysomnogram. Survival analysis and proportional hazards regression models were used to calculate hazard ratios for mortality after adjusting for age, sex, race, smoking status, body mass index, and prevalent medical conditions. The average follow-up period for the cohort was 8.2 y during which 1,047 participants (587 men and 460 women) died. Compared to those without sleep-disordered breathing (AHI: <5 events/h), the fully adjusted hazard ratios for all-cause mortality in those with mild (AHI: 5.0-14.9 events/h), moderate (AHI: 15.0-29.9 events/h), and severe (AHI: >or=30.0 events/h) sleep-disordered breathing were 0.93 (95% CI: 0.80-1.08), 1.17 (95% CI: 0.97-1.42), and 1.46 (95% CI: 1.14-1.86), respectively. Stratified analyses by sex and age showed that the increased risk of death associated with severe sleep-disordered breathing was statistically significant in men aged 40-70 y (hazard ratio: 2.09; 95% CI: 1.31-3.33). Measures of sleep-related intermittent hypoxemia, but not sleep fragmentation, were independently associated with all-cause mortality. Coronary artery disease-related mortality associated with sleep-disordered breathing showed a pattern of association similar to all-cause mortality. CONCLUSIONS: Sleep-disordered breathing is associated with all-cause mortality and specifically that due to coronary artery disease, particularly in men aged 40-70 y with severe sleep-disordered breathing.
[Punjabi NM, Caffo BS, Goodwin JL, et al. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Med.* Aug 2009;6(8):e1000132.]

Sleep-disordered breathing (SDB) is a treatable but markedly under-diagnosed condition of frequent breathing pauses during sleep. SDB is linked to incident cardiovascular disease, stroke, and other morbidity. However, the risk of mortality with untreated SDB, determined by polysomnography screening, in the general population has not been established. METHODS: An 18-year mortality follow-up was conducted on the population-based Wisconsin Sleep Cohort sample (n = 1522), assessed at baseline for SDB with polysomnography, the clinical diagnostic standard. SDB was described by the number of apnea and hypopnea episodes/hour of sleep; cutpoints at 5, 15 and 30 identified mild, moderate, and severe SDB, respectively. Cox proportional hazards regression was used to estimate all-cause and cardiovascular mortality risks, adjusted for potential confounding factors, associated with SDB severity levels. RESULTS: All-cause mortality risk, adjusted for age, sex, BMI, and other factors was significantly increased with SDB severity. The adjusted hazard ratio (HR, 95% CI) for all-cause mortality with severe versus no SDB was 3.0 (1.4,6.3). After excluding persons who had used CPAP treatment (n = 126), the adjusted HR (95% CI) for all-cause mortality with severe versus no SDB was 3.8 (1.6,9.0); the adjusted HR (95% CI) for cardiovascular mortality was 5.2 (1.4,19.2). Results were

unchanged after accounting for daytime sleepiness. CONCLUSIONS: Our findings of a significant, high mortality risk with untreated SDB, independent of age, sex, and BMI underscore the need for heightened clinical recognition and treatment of SDB, indicated by frequent episodes of apnea and hypopnea, irrespective of symptoms of sleepiness.
[Young T, Finn L, Peppard PE, et al. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. *Sleep.* Aug 1 2008;31(8):1071-1078.]

There is a public health connection between untreated OSA as evidenced by transportation related accidents where operator fatigue is identified as an accident cause. According to the AAA Foundation for Traffic Safety (here), "an estimated 16.5% (one in six) of fatal crashes, 13.1% (one in eight) of crashes resulting in hospitalization, and 7% (one in fourteen) of all crashes in which a passenger vehicle is towed involve a drowsy driver." For drivers with OSA, treatment reduces the risk of such accidents:

Obstructive sleep apnea (OSA) is associated with an increased risk of motor vehicle crash. OBJECTIVE: We performed a systematic review of the literature concerning the impact of continuous positive airway pressure (CPAP) treatment on motor vehicle crash risk among drivers with OSA. The primary objective was to determine whether CPAP use could reduce the risk of motor vehicle crash among drivers with OSA. A secondary objective involved determining the time on treatment required for CPAP to improve driver safety. DATA SOURCES: We searched seven electronic databases (MEDLINE, PubMed (PreMEDLINE), EMBASE, PsycINFO, CINAHL, TRIS, and the Cochrane library) and the reference lists of all obtained articles. STUDY SELECTION: We included studies (before-after, case-control, or cohort) that addressed the stated objectives. We evaluated the quality of each study and the interplay between the quality, quantity, robustness, and consistency of the evidence. We also tested for publication bias. DATA EXTRACTION: Data were extracted by two independent analysts. When appropriate, data were combined in a fixed or random effects meta-analysis. RESULTS: A meta-analysis of 9 observational studies examining crash risk of drivers with OSA pre- vs. post-CPAP found a significant risk reduction following treatment (risk ratio = 0.278, 95% CI: 0.22 to 0.35; $P < 0.001$). Although crash data are not available to assess the time course of change, daytime sleepiness improves significantly following a single night of treatment, and simulated driving performance improves significantly within 2 to 7 days of CPAP treatment. CONCLUSIONS: Observational studies indicate that CPAP reduces motor vehicle crash risk among drivers with OSA.
[Tregear S, Reston J, Schoelles K, Phillips B. Continuous positive airway pressure reduces risk of motor vehicle crash among drivers with obstructive sleep apnea: systematic review and meta-analysis. *Sleep.* Oct 1 2010;33(10): 1373-1380.]

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Dear Ms. Hole-Curry:

I would like to provide comments related to some of the draft key questions contained in the technology assessment on Obstructive Sleep Apnea (OSA) diagnosis and treatment. While the review by the AHRQ is, in general, quite thorough, there are a few key points that must be made to supplement this review.

Diagnostics

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

The AHRQ results are based on the assumption that in-lab polysomnography (PSG) is the gold standard for diagnosis of OSA. Home-based diagnostic approaches are an important new addition to sleep apnea testing and have been documented to yield similar results to in-lab PSG and PAP therapy adherence outcomes both in short and long term treatment [1-3].

When comparing the use of questionnaires versus PSG, it is agreed that the questionnaires do not effectively identify patients with OSA when compared to PSG. This would apply to all of the questionnaires mentioned in the AHRQ review as well as the Epworth Sleepiness Scale which is commonly used but not mentioned in the AHRQ document.

KQ3: What is the effect of pre-operative screening for sleep apnea on surgical outcomes?

There are several professional society statements/recommendations regarding the management of patients with OSA or suspected of having OSA pre or post operatively. In 2005, The American Society of Anesthesia recommends putting into place some form of management for patients suspected of sleep apnea as well as management of patients post operatively who have sleep apnea. The American Academy of Sleep Medicine (AASM) recommends patients with a high suspicion or likelihood of OSA be tested prior to surgery. Additionally, the American Association of Clinical Endocrinologists, the Obesity Society, and the American Society for Metabolic and Bariatric Surgery published in 2008 their *Medical Guidelines for Clinical Practice for the Perioperative Nutritional, Metabolic, and Non-Surgical Support of the Bariatric Surgery Patient.* This Guideline recommends patients suspected of OSA be screened with an in-lab study prior to surgery. In addition post operatively they also recommend the patients continue to utilize their PAP equipment both in and outside of the hospital. [26].

KQ4: In adults being screened for obstructive sleep apnea, what are the relationships between apnea-hypopnea index (AHI) or oxygen desaturation index (ODI) and other patient characteristics with long term clinical and functional outcomes?

There are many studies highlighting the impact of sleep fragmentation and recurrent arousal on a variety of outcomes. These studies show OSA to be associated with neurocognitive dysfunction including daytime sleepiness, decreased performance, increased automobile accidents and decreased quality of life [8-11]. In addition, untreated sleep apnea with chronic intermittent hypoxia has been associated with adverse cardiovascular and cerebrovascular outcomes including hypertension, type 2 diabetes, stroke, myocardial infarction, and congestive heart failure [4-7], [12-14].

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

There are a number of prospective studies that have demonstrated significant changes in adherence to CPAP therapy with interventions. Patients initiating therapy for OSA have a variety of ways in which they will adhere to therapy [28-29.] There are several studies that evaluated the impact of device features or procedures that may improve adherence to PAP therapy. Options to improve adherence include heated humidification [26], patient education via phone call or group setting [27, 34-36,] monitoring therapy usage [35] and offering bi-level therapy for patients who are non-complaint to traditional CPAP therapy 37-38. Lastly, there were several articles outlining totally new approaches to patient management from what is commonly found today. In 2009, McEvoy et.al. demonstrated that nurse- led care is not inferior to the traditional physician-led model of care for patients with moderate to severe OSA[30]. In addition, Cognitive Behavioral therapy for patients prescribed CPAP for OSA are showing significant promise in improving adherence [31-33].

Treatment of patients with sleep apnea with continuous positive airway pressure (CPAP) has been definitively shown to reduce symptoms of sleepiness, and reduces the risk of motor vehicle accidents [15-18], better regulation of blood glucose levels [39] and may lower arterial blood pressure. The data also strongly suggest that treatment of sleep apnea will reduce the risk of adverse cardiovascular outcomes although randomized clinical trials are not completed [19-21]. Existing data also conclude that CPAP treatment is cost effective when compared to treatment of other chronic diseases. Thus all indications are that sleep apnea should be treated [22-25].

Regards,

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February 28, 2011

Leah Hole-Curry, JD
Program Director
Health Care Authority Health Technology Assessment Program
P.O. Box 42712
Olympia, WA 98504-2712

Re: Washington State Health Care Authority Health Technology Assessment Program: Sleep Apnea Diagnosis and Treatment.

Dear Ms. Hole-Curry:

Sleep Services of America Inc., a GE Healthcare Company (SSA) greatly appreciates this opportunity to submit comments to the Washington State Health Care Authority Health Technology Assessment Program on Sleep Apnea Diagnosis and Treatment. SSA represent allied health professionals dedicated to providing public and professional education in sleep disorders and sleep medicine, promoting the advancement of sleep medicine and quality patient care, and insuring its employees have a voice in sleep policy development.

Based on the American Sleep Apnea Associations'(The AASM) scientifically based work in providing care for patients with obstructive sleep apnea (OSA), the conclusion is undeniable: there is an essential patient care benefit in identifying those with OSA and providing the related treatment for this chronic medical condition.

The questions you are asking have been addressed by the Medicare program in its action to expand coverage for diagnostic sleep care testing for Medicare beneficiaries and in providing treatment coverage for these patients. The Centers for Medicare and Medicaid Services (CMS) issued its Decision Memo (click here) for Sleep Testing for Obstructive Sleep Apnea (CAG-00405N) in 2009 and summarized its conclusion as follows:

> The evidence is sufficient to determine that the results of the sleep tests identified below can be used by a beneficiary's treating physician to diagnose OSA, that the use of such sleep testing technologies demonstrates improved health outcomes in Medicare beneficiaries who have OSA and receive the appropriate treatment, and that these tests are thus reasonable and necessary under section 1862(a) (1) (A) of the Social Security Act.
>
> 1. Type I Polysomnography (PSG) is covered when used to aid the diagnosis of obstructive sleep apnea (OSA) in beneficiaries who have clinical signs and symptoms indicative of OSA if performed attended in a sleep lab facility.
> 2. A Type II or a Type III sleep testing device is covered when used to aid the diagnosis of obstructive sleep apnea (OSA) in beneficiaries who have clinical signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility.
> 3. A Type IV sleep testing device measuring three or more channels, one of which is airflow, is covered when used to aid the diagnosis of obstructive sleep apnea (OSA) in

beneficiaries who have signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility.

4. A sleep testing device measuring three or more channels that include actigraphy, oximetry, and peripheral arterial tone is covered when used to aid the diagnosis of obstructive sleep apnea (OSA) in beneficiaries who have signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility.

In reaching this determination, CMS made the following finding that clearly identifies why Medicare coverage for diagnostic testing to ascertain whether patients have the chronic disease of OSA is reasonable and necessary:

> OSA, sometimes referred to as Obstructive Sleep Apnea Hypopnea Syndrome-(OSAHS), is associated with significant morbidity and mortality. It is a commonly underdiagnosed condition that occurs in 4% of men and 2% of women (Young et al. 1993). The prevalence increases with age (up to 10% in persons 65 and older), as well as with increased weight. Complications associated with OSA include excessive daytime sleepiness, concentration difficulty, coronary artery disease, and stroke (Kokturk et al. 2005). It is estimated that 10% of patients with congestive heart failure (CHF) have OSA, which is independently associated with systemic arterial hypertension (Caples et al. 2005). Untreated OSA is associated with a ten-fold increased risk of motor vehicle accidents (Tiran-Santos et al. 1999). The most common clinical presentation of patients with OSA is obesity accompanied by excessive daytime drowsiness (20% of adults with BMI > 30 have OSA), although other clinical findings associated with OSA include nocturnal choking or gasping, witnessed apneas during sleep, large neck circumference and daytime fatigue.

Multiple studies, some of which are set out in the Appendix, highlight the need and value for sleep care diagnostic testing and subsequent treatment.

For purposes of Medicare coverage for the durable medical equipment (DME) provided in the treatment for patients with OSA, baseline physiologic criteria are identified for making an OSA diagnosis. The sleep physician has an essential role in these determinations. This is identified in the associated Local Coverage Determinations for Washington: Local Coverage Determination (LCD) for Positive Airway Pressure (PAP) Devices for the Treatment of Obstructive Sleep Apnea (L171- click here), and Oral Appliances for Obstructive Sleep Apnea (L28606 - click here).

The AASM has published a Clinical Guideline on care for patients with OSA: *Clinical Guideline for the Evaluation, Management and Long-term Care of Obstructive Sleep Apnea in Adults* (click here). This Guideline provides a comprehensive strategy for the evaluation, management and long-term care of adult patients with OSA.

The AASM has recognized the expansion of sleep diagnostic testing capability through the use of portable diagnostic sleep equipment used in testing of patients outside of the sleep care facility. Like other diagnostic tools, there is a potential for improper and over-utilization. In response to this reality, the AASM promulgated accreditation standards earlier this month on the

appropriate use of this medical equipment: *Standards for Accreditation of Out of Center Sleep Testing (OCST) in Adult Patients* (click here).

The AASM stands ready to provide further information to assist the Washington State Health Care Authority in addressing this and other matters relating to caring for patients with sleep disorders. Please contact Bruce Blehart at the AASM or via e-mail at BBlehart@aasmnet.org for further assistance.

Sincerely,

John H. Mathias II
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GE Healthcare

SSA is America's Sleep Company
If you know someone who snores or has trouble sleeping
Please have them visit **www.sleepservices.net**

Appendix

The following provides just some of the connections between OSA and comorbid conditions:

> Obstructive sleep apnea (OSA) is an important clinical problem in the chronic kidney disease (CKD) population. OSA is associated with hypoxemia and sleep fragmentation, which activates the sympathetic nervous system, the renin-angiotensin-aldosterone system, alters cardiovascular hemodynamics, and results in free radical generation. In turn, a variety of deleterious processes such as endothelial dysfunction, inflammation, platelet aggregation, atherosclerosis, and fibrosis are triggered, predisposing individuals to adverse cardiovascular events and likely renal damage. Independent of obesity, OSA is associated with glomerular hyperfiltration and may be an independent predictor of proteinuria, a risk factor for CKD progression. OSA is also associated with hypertension, another important risk factor for CKD progression, particularly proteinuric CKD. OSA may mediate renal damage via several mechanisms, and there is a need to better elucidate the impact of OSA on incident renal disease and CKD progression.
> [Adeseun GA, Rosas SE. The impact of obstructive sleep apnea on chronic kidney disease. *Curr Hypertens Rep.* 2010 Jul 31.]

> We recently demonstrated that continuous positive airway pressure (CPAP) therapy rapidly improves insulin sensitivity within 2 days in non-diabetic patients with obstructive sleep apnea syndrome. In these very patients we investigated whether this improvement of insulin sensitivity is maintained during long-term CPAP therapy. After a mean of 2.9 years (963+/-98 days) of CPAP treatment, these patients were reevaluated and hyperinsulinemic euglycemic clamp studies were performed in those with regular and effective CPAP treatment. RESULTS: From the initial 31 patients 16 could be reevaluated. 4 patients did not use their devices regularly (CPAP usage <2.5 h/night), 2 patients had insufficient CPAP treatment (AHI > or =10/h). One patient had developed type 2 diabetes mellitus. In the remaining 9 patients who used their devices regularly and effective (mean CPAP usage 5.2+/-1.6 h/night, mean AHI 3.3+/-2.6/h), mean insulin sensitivity index (ISI) was significantly higher than the baseline ISI established 2.9 years before (10.6+/-7.0 vs. 6.3+/-5.6 micromol/kg x min; p=0.008). At baseline 7 out of 9 patients had an impaired fasting glucose, after 2.9 years of treatment 3 out of 9 patients still had an impaired fasting glucose. The mean body mass index (BMI) had remained unchanged (31.4+/-7.8 vs. 31.4+/-7.6 kg/m2; mean individual difference -0.02+/-1.9 kg/m2). CONCLUSIONS: OSA is a risk factor for impaired insulin sensitivity. CPAP treatment, when used regularly and with effective pressure, may improve insulin sensitivity over long time.
> [Schahin SP, Nechanitzky T, Dittel C, Fuchs FS, Hahn EG, Konturek PC, Ficker JH, Harsch IA. Long-term improvement of insulin sensitivity during CPAP therapy in the obstructive sleep apnoea syndrome**.** *Med Sci Monit*. 2008 Mar;14(3):CR117-21.]

> Effective treatment with nasal continuous positive airway pressure (nCPAP) lowers blood pressure (BP) in patients with obstructive sleep apnea (OSA). It was reported that OSA might influence BP in middle-aged but not in elderly patients. However, effects of nCPAP treatment in elderly hypertensive OSA patients are not well known. We investigated long-

term compliance with nCPAP and its effects on BP in elderly and middle-aged OSA patients. This observational study involved 92 OSA patients (81 men, 11 women; 46 middle-aged, 46 elderly; body mass index (BMI), 27.7 (27.0-28.7) kg m(-2); apnea hypopnea index, 43.0 (39.4-46.6) per h; 95% confidence intervals). BP and BMI were measured before the study and at two checkpoints after usage of nCPAP (616 (553-679) and 1048 (985-1114) days). Diastolic BP decreased by 5.69 (3.09-8.29) mm Hg after 600 days of nCPAP treatment and by 4.50 (1.80-7.19) mm Hg after 1000 days (P=0.003). There were no significant changes in systolic BP, BMI or usage time of nCPAP. With a daily average of 3 h or more of nCPAP treatment, diastolic BP decreased significantly in subject groups >/= 60 and <60 years of age. Even in the elderly, a daily average use of nCPAP for 3 h would lower diastolic BP in OSA patients.
[Aihara K, Chin K, Oga T, et al. Long-term nasal continuous positive airway pressure treatment lowers blood pressure in patients with obstructive sleep apnea regardless of age. *Hypertens Res.* Oct 2010;33(10): 1025-1031.]

The purpose of this study was to determine the relationship between obstructive sleep apnea (OSA) and cardiovascular disorders in a large Japanese population, and to assess the efficacy of continuous positive airway pressure (CPAP) in the treatment of OSA-associated arrhythmias. The study population comprised 1394 Japanese subjects (1086 men and 308 women) who were divided into four groups on the basis of polysomnography (PSG) analysis as follows: the no sleep apnea (N-SA) group (n = 44, apnea-hypopnea index [AHI] < 5), the mild OSA (Mi-OSA) group (n = 197, 5 < AHI < 15), the moderate OSA (Mo) group (n = 368, 15 < AHI < 30), and severe OSA (SOSA) group (n = 785, AHI < 30). The following baseline characteristics were significantly associated with OSA: age (P < 0.001), gender (P < 0.001), body mass index (P < 0.001), hypertension (P < 0.001), diabetes (P = 0.009), and hyperlipidemia (P = 0.013). In the OSA group, PSG revealed the predominance of paroxysmal atrial fibrillation (PAF) (P = 0.051), premature atrial complex short run (P < 0.005), premature ventricular complex (PVC, P = 0.004), sinus bradycardia (P = 0.036), and sinus pause (arrest >2 s, P < 0.001) during the PSG recording. A total of 316 patients from the group underwent CPAP titration and were then re-evaluated. Continuous positive airway pressure therapy significantly reduced the occurrences of PAF (P < 0.001), PVC (P = 0.016), sinus bradycardia (P = 0.001), and sinus pause (P = 0.004). The results of this study demonstrate a significant relationship between OSA and several cardiac disorders, and also demonstrate the efficacy of CPAP in preventing OSA-associated arrhythmias in a large population of Japanese patients.
[Abe H, Takahashi M, Yaegashi H, et al. Efficacy of continuous positive airway pressure on arrhythmias in obstructive sleep apnea patients. *Heart Vessels.* Jan 2010;25(1):63-69.]

While age and body-mass index (BMI) are well-established risk factors for obstructive sleep apnea syndrome (OSAS), this disorder occurs across a wide spectrum of ages and weights. Preconceptions regarding “classic” patients with OSAS may lead to underdiagnosis in at-risk populations, particularly younger nonoverweight individuals. We hypothesized that the severity of OSAS is independent of age and BMI in a younger less-obese population. METHODS: Prospective study of consecutive patients diagnosed with OSAS. Active-duty military, National Guardsmen, and civilians were compared to determine if age and BMI correlated with disease severity. RESULTS: Two hundred seventy subjects (120 active-duty,

80 National Guardsmen, 70 civilians) were included. Active-duty military members were significantly younger and less overweight than both National Guardsmen and civilians. Of the civilians, 64.3% and, of National Guardsmen, 48.8% were obese, whereas only 19.2% of active-duty had a BMI > or = 30 kg/m2 (p < .001). However, the prevalence of severe disease did not differ between groups. Disease severity showed no correlation with BMI among active-duty subjects (r = 0.09, p = .33). Of the active-duty subjects, 37.5% had severe disease, as compared with 42.5% of National Guard and 45.7% of civilian subjects (p = .18 and .09, respectively). BMI did not differ between active-duty subjects with severe disease and those with mild to moderate OSAS (26.7 kg/m2 versus 26.9 kg/m2, p = .40). There was a low but significant correlation between age and AHI (r = 0.21, p = .02) among all subjects. CONCLUSIONS: OSAS occurs in young nonobese individuals and should be considered in patients reporting excessive daytime sleepiness, regardless of age or BMI.
[Lettieri CJ, Eliasson AH, et al. Obstructive sleep apnea syndrome: are we missing an at-risk population? *J Clin Sleep Med.* Oct 15 2005;1(4):381-385.]

Untreated OSA clearly is connected to premature patient death:

The aims of this study were to analyze mortality in patients with obstructive sleep apnea-hypopnea syndrome (OSAHS) treated with positive airway pressure (PAP) and to know whether PAP compliance affects survival, as well as to investigate the prognostic value of several pretreatment variables. DESIGN AND PATIENTS: A study was made of an historical cohort of 871 patients in whom OSAHS had been diagnosed by sleep study between January 1994 and December 2000 and who had been treated with PAP. Patients were followed up until December 2001. The mean (+/- SD) age of the group was 55.4 +/- 10.6 years, the mean apnea-hypopnea index (AHI) 55.1 +/- 28.7, and 80.9% were men. To assess whether mortality was influenced by PAP therapy compliance, patients were assigned to one of the following compliance categories: < 1 h/d; 1 to 6 h/d; or > 6 h/d. Survival rates were calculated according to the Kaplan-Meier method. Survival curves were compared with the log-rank test and the trend test, when necessary. Univariate and multivariate analyses using a time-dependent Cox model were performed to elicit which variables correlated with mortality. SETTING: Outpatient sleep disorders unit. RESULTS: By the end of the follow-up period (mean duration, 48.5 +/- 22.7 months), 46 patients had died. The 5-year cumulative survival rates were significantly lower in patients who did not use PAP (compliance < 1 h) than in those who used the device for > 6 h/d (85.5% [95% confidence interval (CI), 0.78 to 0.92] vs 96.4% [95% CI, 0.94 to 0.98; p < 0.00005]) and 1 to 6 h/d (85.5% [95% CI, 0.78 to 0.92] vs 91.3% [95% CI, 0.88 to 0.94; p = 0.01]), respectively. A trend in survival rates across the groups was identified (p = 0.0004). The main cause of death in 19 cases was cardiovascular disease (CVD). Variables that independently correlated with mortality in the multivariate analysis were the following PAP use categories: compliance for > 6 h/d (odds ratio [OR], 0.10; 95% CI, 0.04 to 0.29); compliance for 1 to 6 h/d (OR, 0.28; 95% CI, 0.11 to 0.69); arterial hypertension (AHT) [OR, 3.25; 95% CI, 1.24 to 8.54]; age (OR, 1.06; 95% CI, 1.01 to 1.10); and FEV1 percent predicted (OR, 0.96; 95% CI, 0.94 to 0.98). CONCLUSION: Mortality rates in OSAHS patients who did not receive PAP therapy were higher compared with those treated with PAP and were moderately or highly compliant with therapy. A trend in survival across compliance categories was found. Patients died mainly

from CVD. Categories of PAP compliance, AHT, age, and FEV1 percent predicted were the variables that independently predicted mortality.
[Campos-Rodriguez F, Pena-Grinan N, Reyes-Nunez N, et al. Mortality in obstructive sleep apnea-hypopnea patients treated with positive airway pressure. *Chest.* Aug 2005;128(2):624-633.]

Sleep-disordered breathing is a common condition associated with adverse health outcomes including hypertension and cardiovascular disease. The overall objective of this study was to determine whether sleep-disordered breathing and its sequelae of intermittent hypoxemia and recurrent arousals are associated with mortality in a community sample of adults aged 40 years or older. METHODS AND FINDINGS: We prospectively examined whether sleep-disordered breathing was associated with an increased risk of death from any cause in 6,441 men and women participating in the Sleep Heart Health Study. Sleep-disordered breathing was assessed with the apnea-hypopnea index (AHI) based on an in-home polysomnogram. Survival analysis and proportional hazards regression models were used to calculate hazard ratios for mortality after adjusting for age, sex, race, smoking status, body mass index, and prevalent medical conditions. The average follow-up period for the cohort was 8.2 y during which 1,047 participants (587 men and 460 women) died. Compared to those without sleep-disordered breathing (AHI: <5 events/h), the fully adjusted hazard ratios for all-cause mortality in those with mild (AHI: 5.0-14.9 events/h), moderate (AHI: 15.0-29.9 events/h), and severe (AHI: >or=30.0 events/h) sleep-disordered breathing were 0.93 (95% CI: 0.80-1.08), 1.17 (95% CI: 0.97-1.42), and 1.46 (95% CI: 1.14-1.86), respectively. Stratified analyses by sex and age showed that the increased risk of death associated with severe sleep-disordered breathing was statistically significant in men aged 40-70 y (hazard ratio: 2.09; 95% CI: 1.31-3.33). Measures of sleep-related intermittent hypoxemia, but not sleep fragmentation, were independently associated with all-cause mortality. Coronary artery disease-related mortality associated with sleep-disordered breathing showed a pattern of association similar to all-cause mortality. CONCLUSIONS: Sleep-disordered breathing is associated with all-cause mortality and specifically that due to coronary artery disease, particularly in men aged 40-70 y with severe sleep-disordered breathing.
[Punjabi NM, Caffo BS, Goodwin JL, et al. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Med.* Aug 2009;6(8):e1000132.]

Sleep-disordered breathing (SDB) is a treatable but markedly under-diagnosed condition of frequent breathing pauses during sleep. SDB is linked to incident cardiovascular disease, stroke, and other morbidity. However, the risk of mortality with untreated SDB, determined by polysomnography screening, in the general population has not been established. METHODS: An 18-year mortality follow-up was conducted on the population-based Wisconsin Sleep Cohort sample (n = 1522), assessed at baseline for SDB with polysomnography, the clinical diagnostic standard. SDB was described by the number of apnea and hypopnea episodes/hour of sleep; cutpoints at 5, 15 and 30 identified mild, moderate, and severe SDB, respectively. Cox proportional hazards regression was used to estimate all-cause and cardiovascular mortality risks, adjusted for potential confounding factors, associated with SDB severity levels. RESULTS: All-cause mortality risk, adjusted for age, sex, BMI, and other factors was significantly increased with SDB severity. The adjusted hazard ratio (HR, 95% CI) for all-cause mortality with severe versus no SDB was

3.0 (1.4,6.3). After excluding persons who had used CPAP treatment (n = 126), the adjusted HR (95% CI) for all-cause mortality with severe versus no SDB was 3.8 (1.6,9.0); the adjusted HR (95% CI) for cardiovascular mortality was 5.2 (1.4,19.2). Results were unchanged after accounting for daytime sleepiness. CONCLUSIONS: Our findings of a significant, high mortality risk with untreated SDB, independent of age, sex, and BMI underscore the need for heightened clinical recognition and treatment of SDB, indicated by frequent episodes of apnea and hypopnea, irrespective of symptoms of sleepiness.
[Young T, Finn L, Peppard PE, et al. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. *Sleep.* Aug 1 2008;31(8):1071-1078.]

There is a public health connection between untreated OSA as evidenced by transportation related accidents where operator fatigue is identified as an accident cause. According to the AAA Foundation for Traffic Safety (click here), "an estimated 16.5% (one in six) of fatal crashes, 13.1% (one in eight) of crashes resulting in hospitalization, and 7% (one in fourteen) of all crashes in which a passenger vehicle is towed involve a drowsy driver." For drivers with OSA, treatment reduces the risk of such accidents:

Obstructive sleep apnea (OSA) is associated with an increased risk of motor vehicle crash. OBJECTIVE: We performed a systematic review of the literature concerning the impact of continuous positive airway pressure (CPAP) treatment on motor vehicle crash risk among drivers with OSA. The primary objective was to determine whether CPAP use could reduce the risk of motor vehicle crash among drivers with OSA. A secondary objective involved determining the time on treatment required for CPAP to improve driver safety. DATA SOURCES: We searched seven electronic databases (MEDLINE, PubMed (PreMEDLINE), EMBASE, PsycINFO, CINAHL, TRIS, and the Cochrane library) and the reference lists of all obtained articles. STUDY SELECTION: We included studies (before-after, case-control, or cohort) that addressed the stated objectives. We evaluated the quality of each study and the interplay between the quality, quantity, robustness, and consistency of the evidence. We also tested for publication bias. DATA EXTRACTION: Data were extracted by two independent analysts. When appropriate, data were combined in a fixed or random effects meta-analysis. RESULTS: A meta-analysis of 9 observational studies examining crash risk of drivers with OSA pre- vs. post-CPAP found a significant risk reduction following treatment (risk ratio = 0.278, 95% CI: 0.22 to 0.35; $P < 0.001$). Although crash data are not available to assess the time course of change, daytime sleepiness improves significantly following a single night of treatment, and simulated driving performance improves significantly within 2 to 7 days of CPAP treatment. CONCLUSIONS: Observational studies indicate that CPAP reduces motor vehicle crash risk among drivers with OSA.
[Tregear S, Reston J, Schoelles K, Phillips B. Continuous positive airway pressure reduces risk of motor vehicle crash among drivers with obstructive sleep apnea: systematic review and meta-analysis. *Sleep.* Oct 1 2010;33(10): 1373-1380.]

Dennis, Margaret (HCA)

From: seanm@ussleepdiagnostics.com
Sent: Wednesday, February 16, 2011 8:48 PM
Subject: OSA Open Forum Questions
Attachments: Prooflink_outcomesof_home-based_dx_&_tx_of_OSA[1].pdf; Brochure_PDx.pdf; AASM_Device_Recommendations-Product_Comparisons[1].pdf; Hypertension, Obesity, Diabetes Sleep Disorder Report.pdf; Nightly_variability_of _sleepdisordered _breathing.pdf

HTA
Attached is hopefully some information which will help in your decision making process, as it relates to safety, efficacy, effectiveness and cost, and cost effectiveness.

Attachements Brief:
1. Prooflink to a Study published in Chest August 2010 issue: Outcomes of PSG vs Portable Testing and In Lab Titration vs Auto Titration Device Therapy: Conclusion prooved that the In Lab was not a superior solution to Portable Testing with Auto Titration Therapy

2. Brochure on Alice PDx...detail on the Technology (works on the same software platform as the In Lab Diagnostic) with appropiate sensors...actually able to connect diagnostic device to therapy device and perform a simultaneous therapy-diagnostic evaluation.

3. AASM Device Recomendations and Device Comparisons (Only the Alice PDx meets the requirements of the AASM...which really means portable technology has caught up to the In lab technology)
The Embletta by Embla also meets these requirements but runs only on older Operating Systems (Windows XP) The other devices can be in some cases easier to use, however, do not possess sensors directly sampling from the appropriate physiological position and infer through algorythyms sleep disorder breathing, (Ares device is contraindicated for patients who take Hypertension Meds and Erectile Dysfunction meds)

4. Report done by Ralph Pascually on Hypertension, Diabetes, and Obesity as it relates to Sleep Disorders also addressing numerous studies, that compliance reduces substantially Health Care Cost in Individuals compliant to therapy

5. Night to Night Variability: really important in patients as the progress from Mild-Severe OSA to understand that early diagnosis and treatment can prevent Severe OSA, certainly is missed a lot of the times in the Lab setting patient doesnt sleep really well...but only a device which can collect multiple nights of data can help evaluate a patients likelyhood of developing from Mild-Sever Sleep Disorder Breathing.

Quick Experience with nearly 1000 patients

1. Manual Scoring: Sensors temporarily fall off, you need a trained Tech to identify this in Portable Testing

2. RIP Belts: As mentioned before if Sensors fall off (i.e. Pulse Oximeter or Canual we can still identify AHI because of the RIP Belt) Also for recognizing Central Apneas: Important with patients whome have a high probability for CA's (i.e. pain medicated patients)

3. Multiple Night Capabilities: Variability of Night to Night including sensor loss, patient variabiltiy night to night

4. Quality and Quantity of Data Sampling: Collection is the same as in lab setting

5. Quality of DME provider and interaction with Referring MD: Therapy options, the appropriate use of Auto CPAP, Titration identifying patients for In-Lab Titration needs...

Cost: The Devices range in price from $2500-$6500...(The Alice PDx as a Type 3 SRP $4500, a simple addition for additional $1500 makes it a Type 2 collecting EEG and EKG

EEG is more important in the evaluation for other sleep disorders: Unfortunately, Medicare has made a mistake of incentifying for the measurement of a diagnostic test including sleep time instead as a measurement of time...sleep time is important if a patient wants to "fake a Apnea" not a lot of motivation and difficult to pull off.

EKG: Technology is able to pick up irregular heartbeats, the EKG is excessive in the evaluation of OSA,

Let me know if you have any other questions, conserns, references etc....

Thanks,

Sean Muilenburg
www.ussleepdiagnostics.com
Cell 206-551-3323

PHILIPS

Outcomes of home-based Dx and Tx of OSA
Chest, 2010
Skomro et al

ProofLink Update

Outcomes of home-based diagnosis and treatment of Obstructive Sleep Apnea, Skromo et al.

- ***Find this study***
  - Chest, August, 2010; 138: 257-263
  - PN 1079760

- ***Study Objective***
  - To compare a home-based diagnostic and therapeutic strategy for OSA with the current standard of practice, the in-lab PSG in Saskatchewan, Canada.
    - Hypothesis was that the in-lab would be superior to the home-based diagnostic strategy.

- ***Study Methods***
  - 102 subjects were randomized to either home-based or in-lab PSG.
    - Home-based subjects underwent a level III test followed by an in-lab PSG, autoPAP for 1 week and then CPAP for 3 weeks based on 95% pressure derived from the autoPAP.
    - In-lab subjects underwent an overnight PSG, followed by 1 night of home monitoring, with either a split night titration or a second titration night.
  - Home monitoring of at least 4 hours included:
    - Airflow (nasal pressure)
    - Respiratory effort
    - Oxygen saturation
    - Heart rate
    - Body position
  - Baseline and 4 week assessment included:
    - History and physical exam
    - Arterial blood gas
    - Height, weight, BMI
    - Sleep quality (PSQI)
    - Epworth sleepiness scale (ESS)
    - Calgary Sleep Apnea Quality of Life Index (SAQLI)

- **Results**
  - After 4 weeks of CPAP therapy there was no difference between the home-based or in-lab arm for:
    - ESS
    - SAQLI
    - PSQI
    - SF-36 scores
    - Blood pressure
    - CPAP compliance

- ***Bottom Line***
  - In-lab diagnosis and titration did not lead to superior 4 week outcomes when compared to home-based testing.
  - HST approach may be useful in the management of subjects when access to PSG is limited.

AASM TECHNOLOGY for PORTABLE MONITORS - RECOMMENDATIONS

	Level III	BioSensor Detection				Methodology		
HST PRODUCT	**Minimum Channels** (Airflow, Effort, Blood Oxygen)	**Apnea Detection** (Oronasal thermal sensor)	**Hypopnea Detection** (Nasal Pressure Transducer)	**Respiratory Effort** (RIP)	**Blood Oxygen** (Pulse Ox)	**Manual Scoring**	**Sample Rate**	**Raw Data**
Alice PDx	Y	Y	Y	Y	Y	Y	Y	Y
Stardust II	Y		Y		Y	Y	Y	Y
ApneaLink Plus	Y		Y		Y		?	Y
Watch-PAT	Y				Y	Y	?	Y
NovaSom QSG	Y				Y		?	
ARES	Y		Y		Y	?	?	?
Embletta Gold	Y	Y	Y	Y	Y	Y	Y	Y

Y = MEETS AASM, ? = information not available

Section 2.1

At a minimum, the PMs must **record airflow, repiratory effort, and blood oxygenation.**

The type of biosensors used to monitor these parameters for in-laboratory PSG are recommended for use in PMs.

Section 2.2

The sensor to detect apnea is an oronasal thermal sensor and to detect hypopnea is a nasal pressure transducer

IDEALLY, PMs should use both sensor types.

Section 2.3

IDEALLY, the sensor for identification of respiratory effort is either calibrated or uncalibrated inductance plethysmography (RIP).

Section 2.4

The sensor for the detection of blood oxygen is pulse oximetry with the appropiate signal averaging time and accomadation for motion artifact.

(Minimum signal averaging time of ≤ 3 seconds at a heart rate of 80 beats per minute or more)

Section 3.3

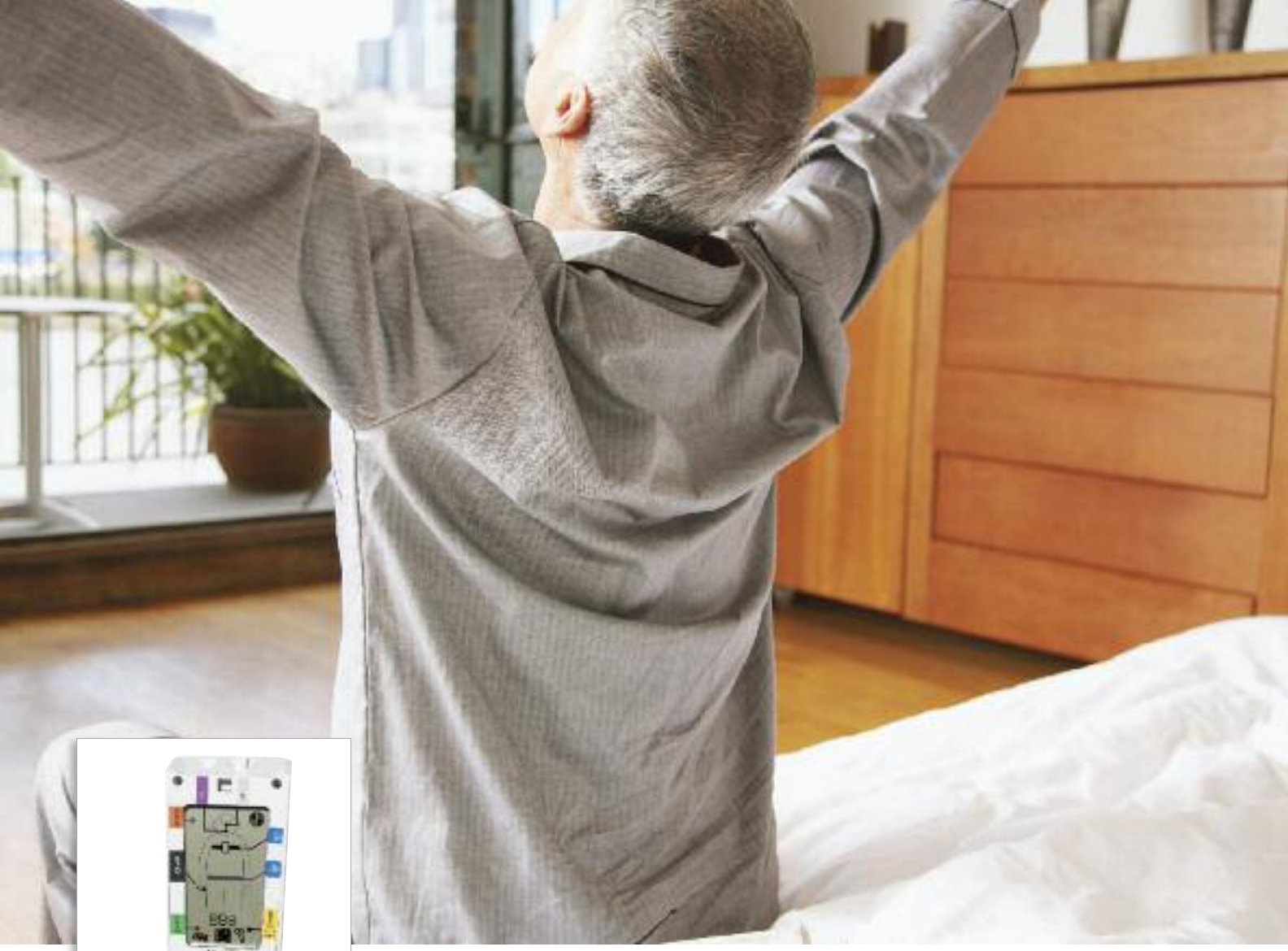
PM devices must allow for the display of raw data for manual scoring or editing of automated scoring by a trained and qualified sleep technician.

Section 3.4

Scoring criteria should be consistent with the current published AASM standards for scoring of Apneas and Hypopneas.

JCSM Journal of Clinical Sleep Medicine, Vol. 3, No. 7, 2007

Device data from manufacturer published specifications



Good study results, better night's sleep

Alice PDx Diagnostic System

PHILIPS

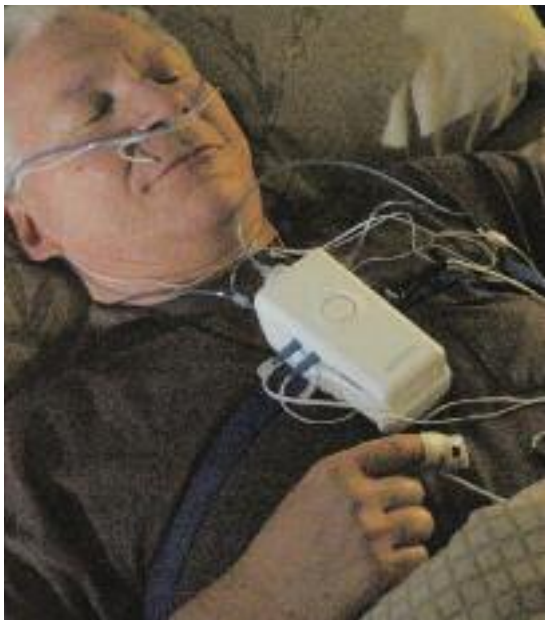
RESPIRONICS

sense and simplicity

Convenient for patients

Portable testing made easy

The Alice PDx is a portable, diagnostic recording device for Obstructive Sleep Apnea (OSA) screening, follow-up and diagnostic assessment of cardio-respiratory sleep disorders. This flexible and portable sleep system incorporates the advanced features required to meet today's industry needs. It satisfies the portable testing requirements for levels II, III and IV and offers a variety of capabilities, from basic screening to advanced diagnostic evaluation. The Alice PDx enables you to test your patients outside of the lab without compromising study results, helping you to avoid the costs associated with re-testing.



Alice PDx on patient

Flexible

The Alice PDx can be used in a sleep lab, alternative care site or a patient's home. The device is convenient for patients who are uncomfortable with, or have limited access to, a lab facility. It also increases the flexibility that facilities need for in- or out-of-lab services. Rather than having patients in need of sleep testing go untested and lose revenue because of patients who cancel or never show, the Alice PDx provides you with an opportunity to retain patients who meet the criteria for portable testing.

The Alice PDx is field upgradeable, so as new features are added, firmware upgrades will be made available, without having to return your device for service. As updates become available, you will be able to access them via web downloading.

User friendly

The Alice PDx device interface is easy to use, easy to understand and informative. Color-coded labels, located around the perimeter of the device, indicate where to connect the various sensor leads. The display shows the patient only the sensors that need to be connected. The sensor information and indicators help your patients place the sensors correctly and reduce the need for re-testing due to application errors.

Easy reference diagram

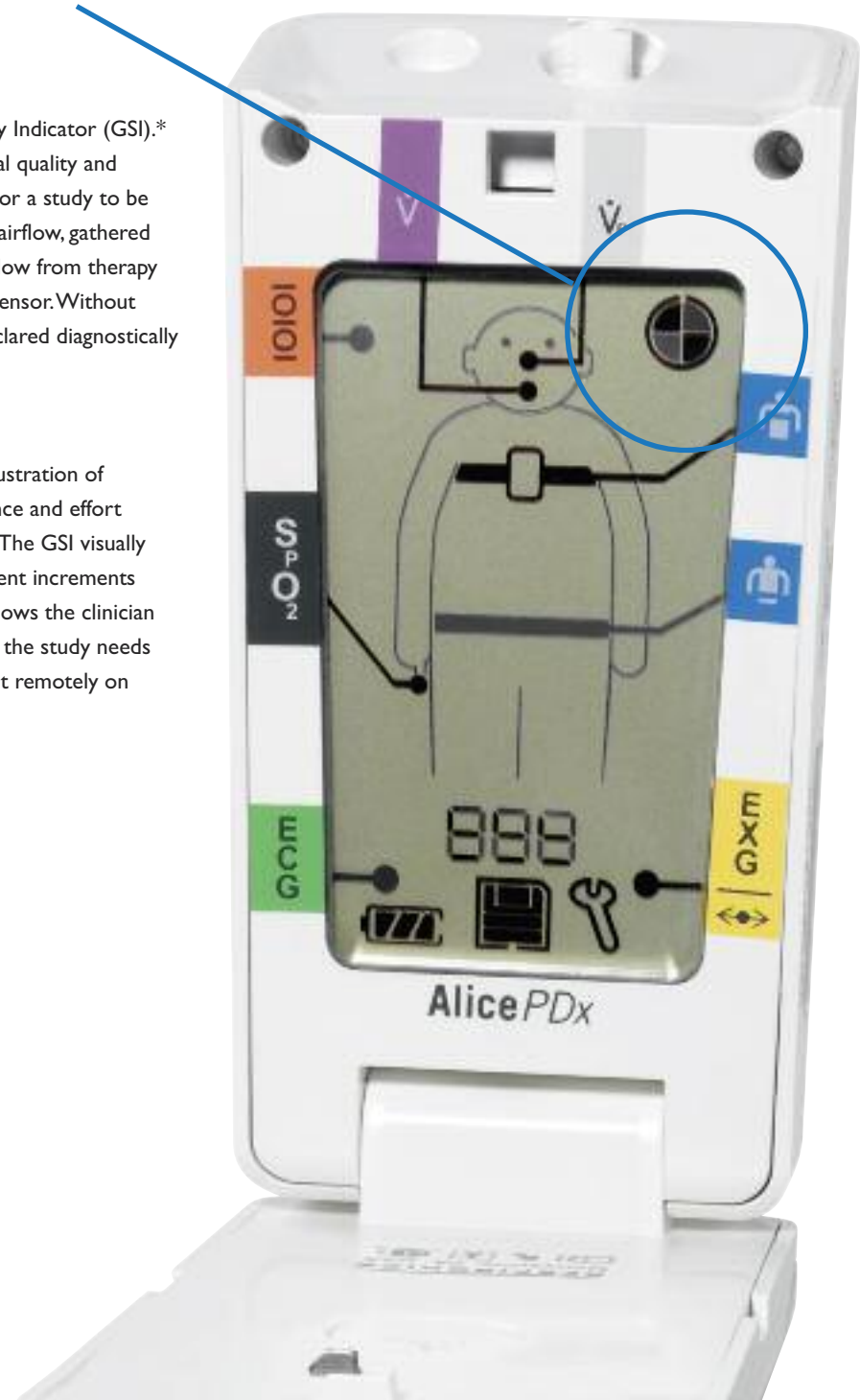
A helpful, color-coded, step-by-step diagram is included with the Alice PDx system to walk patients through the appropriate application process.

The Alice PDx is compact and can accommodate side sleepers. The wires have been specifically designed to minimize excess length to make it easier for patients to manage the wires.

Accommodates side sleepers

Flexible for you

Good study indicator
Configurable for the number of hours required for a valid study.



Minimize re-testing
The Alice PDx incorporates our unique Good Study Indicator (GSI).* The GSI is predicated on airflow and oximeter signal quality and displays the amount of "good quality data" needed for a study to be complete and valid. The indicator measures patient airflow, gathered by the nasal cannula and/or the oral thermistor, airflow from therapy devices, and pulse oximetry, gathered by the SpO_2 sensor. Without either of these signals, the sleep study would be declared diagnostically invalid because of insufficient data.

Maximize study quality
The Good Study Indicator helps to eliminate the frustration of receiving insufficient study data and the inconvenience and effort involved in rescheduling patients for a repeat study. The GSI visually displays the amount of good quality data in 25-percent increments on the Alice PDx display screen. This information allows the clinician to decide if the patient needs to repeat the study. If the study needs to be repeated, the provider can educate the patient remotely on how to apply the sensors better.

*Patent pending.

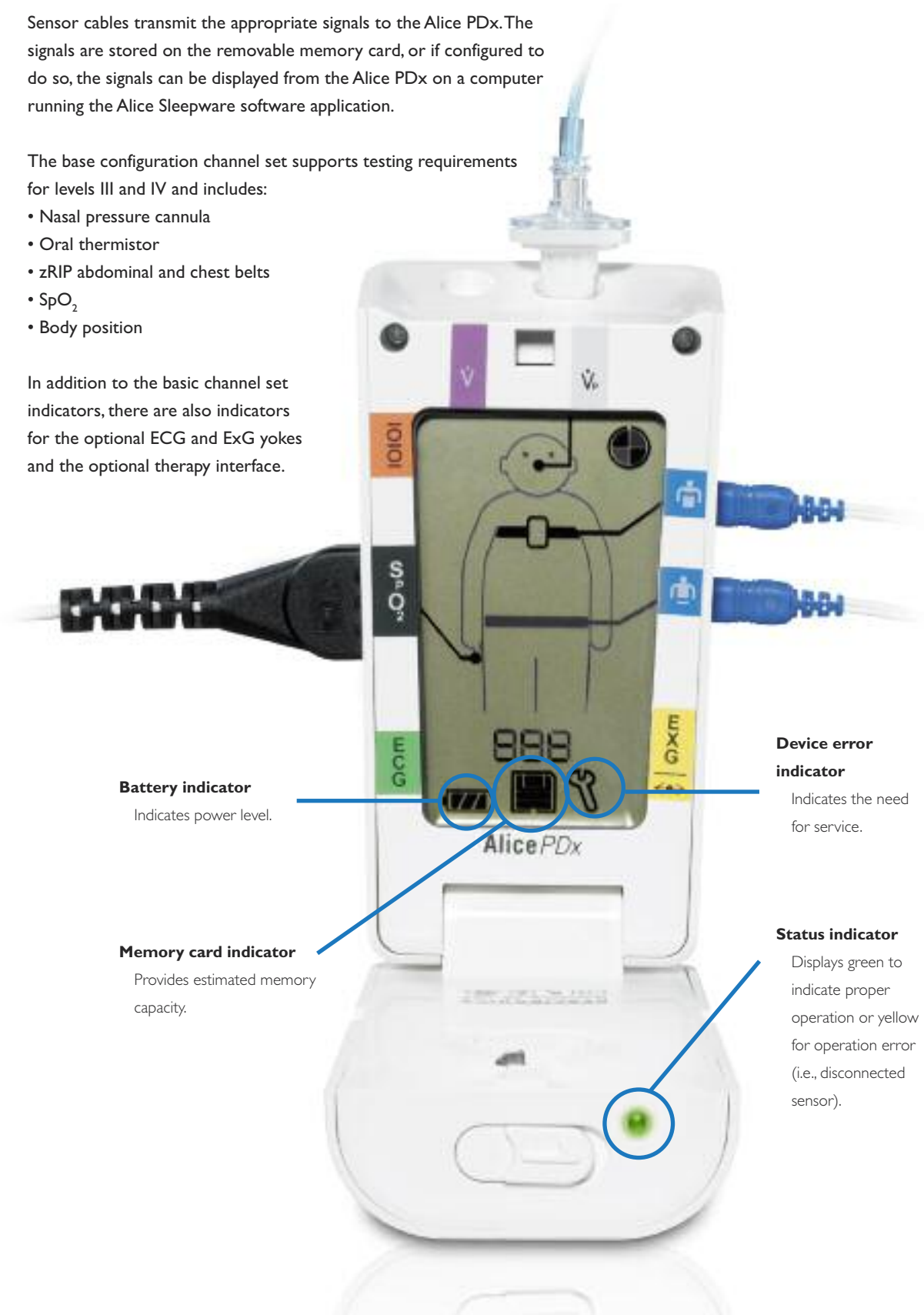
System overview

Sensor cables transmit the appropriate signals to the Alice PDx. The signals are stored on the removable memory card, or if configured to do so, the signals can be displayed from the Alice PDx on a computer running the Alice Sleepware software application.

The base configuration channel set supports testing requirements for levels III and IV and includes:

- Nasal pressure cannula
- Oral thermistor
- zRIP abdominal and chest belts
- SpO_2
- Body position

In addition to the basic channel set indicators, there are also indicators for the optional ECG and ExG yokes and the optional therapy interface.



Battery indicator
Indicates power level.

Memory card indicator
Provides estimated memory capacity.

Device error indicator
Indicates the need for service.

Status indicator
Displays green to indicate proper operation or yellow for operation error (i.e., disconnected sensor).

Connecting the Alice PDx to a therapy device

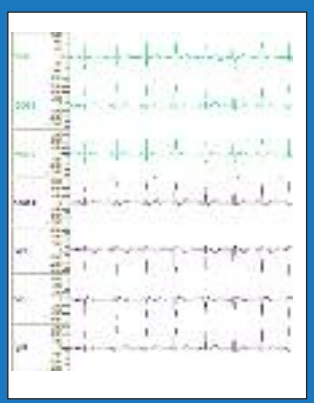
The Alice PDx interfaces with, and fully supports, certain therapy devices with serial or SmartCard connections. When using the Alice PDx, a provider can specify which treatment data to capture along with the appropriate diagnostic channel data. Depending on the Alice PDx configuration selected, it will record up to eight channels such as:

- Patient airflow
- Pressure
- Leak
- Tidal volume
- Event flags (from auto-titrating devices)

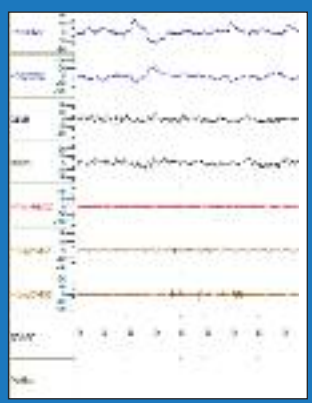
This data allows the provider to confirm the therapeutic benefit of the prescribed therapy device for the patient. Once connected to the therapy device, the Alice PDx will record data from the device during the sleep study. Using the pressure cannula port, the Alice PDx can be connected to other therapy devices, however more limited patient airflow and pressure data will be collected.

Connecting a memory card reader to a computer

After recording, the memory card is removed from the Alice PDx and placed into the provided "plug-and-play" SD card reader. The patient's data is then imported from the SD card to a computer for quick review and analysis.



Seven-channel ECG



ExG channels

Optional ECG and ExG yokes

When level II testing is needed, the Alice PDx can be interfaced to optional ECG and ExG sensor interface yokes. The ECG yoke consists of five electrode inputs, considered in cardiology to be a three-lead ECG. This provides three measured and four derived ECG channels to help assess sleep apnea in patients with possible cardiac comorbidities. The Alice PDx optional ECG yoke can provide one-, six- and seven-channel configurations.

The optional ExG yoke provides 13 inputs to provide four EEG/EOG channels and three EMG channels, including ground and references. This enables level II application for advanced sleep analysis.

Multi-night recordings

With the SD card memory and two- to three-night battery life, the Alice PDx can collect information from multi-night recordings when needed. The Alice PDx can be set to start and stop recording automatically to minimize the risk of the patient forgetting to set it.

Single software application

The Alice PDx system is provided with our proven Sleepware software, which has accommodated our Alice in-lab diagnostic systems for years. Sleepware can display live or pre-recorded data in a resolution consistent with your computer hardware specifications. As the need for your lab operation services changes or grows, Sleepware can accommodate your equipment software needs.

- Sleepware provides a single software application for lab and portable testing.
- A single software application helps to avoid confusion and additional training needed for adapting to multiple device-specific software.
- Sleepware allows you to manage your data across larger networks and remote locations, enabling you to perform remote scoring or data access.
- Sleepware software is a computerized process of analyzing polysomnographic data in order to aid a qualified healthcare provider in diagnosing sleep disorders.

  Note: The Alice PDx device is not intended to replace a qualified healthcare provider or his/her interpretation of data.

Other diagnostic products and tools available

In-lab sleep systems

For in-lab systems to cover your needs from primary to full-featured PSG capabilities, we offer the Alice family of sleep systems. The Alice 5 full-featured PSG system records, displays and prints physiological information. It offers standard functions expected in today's high-end evaluation platforms, accommodates facility expansion and supports greater analysis. For an in-lab system that can satisfy professional sleep testing standards without sacrificing usability, there's the Alice LE. The system enables you to meet AASM standards while incorporating simplicity and affordability into your facility.

Sensors and accessories

We offer a complete line of sensors and accessories including Pro-Tech sensors, zRIP effort technology, PTAF Pressure Flow, electrodes, oximeter sensors and probes. Our sensors help you meet AASM standards.

Leading the way in sleep diagnostics

Well known for innovation in advanced sleep therapy systems and technologies, we also equip sleep technicians with a full range of products and support to handle their patient monitoring needs in or out of the lab. With in-home screening and portable and full-featured PSG diagnostic devices, a dedicated sales force and 24/7 technical specialists, we are committed to helping sleep professionals lead the way in facilitating an appropriate diagnosis and healthy night's sleep for patients.

Patient and clinician training tools

- A video (on DVD) that guides the patient through how to use the PDx and correctly apply the sensors.
- A CD-ROM that guides the clinician through how to configure the Alice PDx and score the data.

  Part number information for these training tools is listed under the Ordering Information section of this brochure.

We are a past Frost & Sullivan award winner.

The base Alice PDx system includes

Alice PDx device
Alice PDx professional and user guides
Carrying case
Patient setup carrying case overlay
Serial USB Alice PDx to PC communication cable
USB SD card reader w/extension cable
1 GB SD card
Alice PDx holster (chest holder for device)
Neck lanyard for Alice PDx holster
2 ea. Pro-Tech zRIP effort belts with wireset
5-pack starter pack pressure cannulas
Oral thermal sensor
Nonin SpO_2 sensor extension cable
4 ea. AA batteries (packaged separately)
Choice of Nonin SpO_2 probe (packaged separately)

Ordering information

Item No.	Description
Optional components	
1043941	Alice PDx device kit, domestic/US
1043844	Alice PDx device kit, international
1047990	Alice PDx device kit, Japan
Optional components	
1040808	ExG yoke, Alice PDx, domestic
1048415	ExG yoke, Alice PDx, international
1040809	ECG yoke, Alice PDx, domestic
1040810	ECG yoke, Alice PDx, international
1048916	ECG yoke, Alice PDx, Japan
Accessories	
1040807	Alice PDx to MobileLink cable (PC cable)
1040806	Alice PDx to SleepLink cable
1040805	Alice PDx to RS-232 sleep therapy cable
1053280	Alice PDx holster
1053194	Alice PDx holster neck lanyard
P1328-60	Pro-Flow nasal cannula, adult qty. 60
P1343	Pro-Flow nasal-oral cannula, adult qty. 30
P1379	Oral thermistor, Alice PDx
P1388	Nasal-oral thermistor, Alice PDx
P1391	CPAP titration kit (for non-Respironics therapy devices)
P1837	zRIP adult sensor kit (belts and wiresets), Alice PDx
P1806	zRIP effort sensor, adult (24" to 75") / (61 cm to 190 cm)
P1170	zRIP wireset, Alice PDx
1053952	2-pack SD cards (secure digital card, 1GB ea.)
1053948	Alice PDx quick start guide (carry case overlay) 4-pack
936	SpO_2 reuseable sensor, adult finger clip
953	SpO_2 resueable flex sensor, adult
954A	Adult flex sensor wrap (25-pack)
Training tools	
1055905	Patient instructions video (DVD)
1055918	Clinician interactive tutorial (CD-ROM)

Basic PC recommendations:

- Windows®-compatible personal computer running Windows Vista Business, Windows XP Professional or 2000 with a CD-RW drive. A DVD drive is recommended if you will be saving audio/video files onto removable storage media.
- Intel® Pentium® 3 processor (500 MHz) or greater, 32-bit (x86) processor (1 GHz) required for Windows Vista computers
- 512 MB system memory, 1 GB or higher for Windows Vista computers

Specifications

Total channels:	Up to 21 with optional ECG and ExG yokes
Base channels:	10 channels: pressure-based flow (w/snore) and thermal airflow, zRIP effort (2), body position, SpO_2 (also pleth and pulse rate) and patient marker. Up to eight parameters from Respironics therapy devices may be acquired, including pressure, flow and leak.
Optional yokes/ channels:	ECG yoke; 7 channels: 3-lead ECG providing 3 measured and 4 derived channels
	ExG yoke; 7 channels: 4 neuro channels (EEG or EOG) and 3 differential EMG, plus references and ground
Input impedance:	ECG: 10MΩ per electrode 20MΩ differential EEG: 2MΩ per electrode 4MΩ differential EMG: 2MΩ per Electrode 4MΩ differential
Bandwidth:	ECG: 0.318Hz to 81Hz EEG: 0.318Hz to 35Hz EMG: 9.7Hz to 86Hz
Input signal range:	ECG: +/- 4mV EEG: +/- 500uV EEG: +/- 150uV
Digital resolution:	Up to 16 bits
Initial sample rate:	Up to 1,000 Hz
Max storage rate:	200 Hz for ECG/ExG, 100 Hz for effort and thermal flow, pressure flow 200 Hz, snore 500 Hz, body position 1 Hz
Communication interfaces:	Serial protocol USB PC cable, SleepLink and serial communication cables for Respironics therapy devices

System physical characteristics

Alice PDx unit:	
Size:	5" L x 3" W x 2" H (12.7 cm x 7.62 cm x 5.08 cm)
Weight:	approximately 8 oz (230 grams), (weight does not include batteries)
System power requirements:	Three AA (1.5V) alkaline batteries, 0.43 watts (typical)

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For more information about the Alice PDx, visit: www.philips.com/alicepdx

The Alice PDx and Sleepware are prescription devices that are restricted to sale by or on the order of a physician.

Hoech SB 8/27/08 MCI 4101845 PN 1055892

Diabetes, Hypertension, Obesity, and Sleep Disorders

a report by
Dr Ralph Pascualy

Medical Director, Swedish Sleep Medicine Institute, Swedish Medical Center

Dr Ralph Pascualy is Medical Director of the Swedish Sleep Medicine Institute, Swedish Medical Center. He specializes in Sleep-Disorders Medicine and has been accredited by the American Board of Sleep Medicine. Dr Pascualy is also a clinical assistant professor for the Department of Psychiatry at the University of Washington School of Medicine. He holds board certifications from the American Board of Neurology and Psychiatry as well as the National Board of Medical Examiners. Prior to this, he was medical director of Providence Seattle Medical Center's Sleep Disorders Center from 1984. Dr Pascualy is a former recipient of the distinguished William C. Dement Award in Sleep-Disorders Medicine and has spoken and written widely on the topic of sleep disorders. He completed a Sleep Disorders Fellowship from the Stanford University Sleep Lab and did an internship and residency through the University of Washington School of Medicine. While in medical school, he completed two National Institute of Mental Health Fellowships – one in consultation/liaison psychiatry at Stanford University School of Medicine and the other in epidemiology through Mental Health Services at Stony Brook School of Medicine. He earned his medical degree from Stony Brook University School of Medicine after passing his bachelor's degree at Columbia University. Dr Pascualy is a member of numerous professional organizations, including the American Sleep Disorders Association and the American Medical Association.

Diabetes, hypertension, and obesity are among the most costly and intractable public health problems. A number of syndromes have been described – cardiometabolic syndrome, Syndrome X, and the Insulin Dysmetabolic Syndrome – to characterize the overlap of these three diseases (see *Table 1*). A common denominator would be welcome that could effectively aid the management of this constellation of dysfunctions. This factor has now been discovered: disturbed sleep. In particular, obstructive sleep apnoea (OSA) is known to contribute to the morbidity of diabetes, hypertension, and obesity. Treatment of OSA may limit the cardiovascular (CV) effects and end-organ damage resulting from the other three members of the syndrome.

Recent work suggests that disordered breathing during sleep exerts its multi-organ, pathological effects through the mechanism of sympathetic stimulation caused by arousal from sleep. Thus, in the link between OSA and hypertension, the emphasis is on the repeated arousals rather than the breathing abnormality.

Repeated arousals from sleep cause bursts of sympathetic activation and increases in heart rate as well as in both systolic and diastolic blood pressure. Animal models and human studies also suggest that heart afterload is reduced and preload is increased with every apnoeic event, providing another likely mechanism for CV morbidity. Hyperinsulinemia, a consequence of diabetes and obesity, also leads to increased sympathetic activity and hypertension (see *Figure 1*). An examination of the mechanisms reveals how treating OSA can ameliorate the course of diabetes and reduce blood pressure. Two decades ago, observers noted the comorbidity of hypertension and lack of breathing during sleep. The prevalence of OSA in hypertensives is between 30% and 50%. More than half of sleep apneics are hypertensive, compared with a prevalence of 24% in the general adult population.

OSA shares many of the features of the cardiometabolic syndrome (see *Table 1*). The causal relationships between OSA, CV disease, and related metabolic disorders are complex and may be multidirectional. Two recent large research projects have reported a dose-response relationship between OSA and hypertension. One elegant study (N=1060) revealed a dose-response association between the severity of OSA and the magnitude of blood pressure elevation. Even mildly sleep-disordered breathing was associated with elevated blood pressure. The investigators adjusted for age, gender, body mass index (BMI – the weight in kilograms divided by the square of the height in meters), smoking, alcohol, education, physical activity, and antihypertensive medication.

Supporting these results is another study (N=2677) in which both blood pressure and the number of patients with hypertension increased linearly with the severity of OSA. Each additional apnoea event per hour of sleep added 1% to the risk of hypertension and each 10% decrease in the oxygen saturation nadir increased the risk of hypertension by 13%. Lavie also adjusted for confounding variables (age, level of obesity, and sex) and hypertensive medication. The chronic effects of obstructive sleep apnoea may include an increase in sympathetic tone and an elevation of nocturnal, daytime, and pulmonary blood pressure. Also associated with OSA are alterations in chemoreceptor function and morphologic changes in vessel walls.

The prevalence of obesity, diabetes, and OSA in the US is alarming – estimated at 9% of women and 24% of men. The prevalence of insulin resistance in a supposedly normal, healthy middle-aged population was found to be 37%. OSA, obesity, and hypertension are all risk factors for diabetes. Half of hypertensive patients display insulin resistance, as do the majority of patients with non-insulin-dependent diabetes. The fact that obesity contributes to OSA is not news. Obesity exacerbates OSA through upper airway obstruction and alteration of the breathing drive. BMI is the best predictor of OSA.

The humoral links between OSA, obesity, and diabetes are still being elucidated, but several clear relationships have been shown between sleep deprivation and metabolic abnormalities. Sleep debt strongly affects glucose utilization as well as circadian cycles of thyrotropin, cortisol, growth hormone, and other physiological variables. Sleep debt alone is reported to result in impaired glucose effectiveness similar to that found in non-insulin-dependent diabetics. Severe OSA

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Table 1. Diabetes, Hypertension, and Obesity Syndromes and OSA

	Cardio-metabolic syndrome Sowers 2001	Insulin dysmetabolic syndrome Groop 2001 Isomaa 2001 Golay 1994	Syndrome X (metabolic) Reaven 1994	Common in OSA
Hypertension	x	x	x	x
Diabetes (type 2)	x	x	x	x
Obesity (abdominal)	x	x	x	x
Glucose intolerance	x	x	x	x
Insulin resistance	x	x	x	x
Hyperinsulinemia	x	x	x	x
Dyslipidemia	x	x	x	~
Microalbuminuria	x	x	x	~
Coagulation abnormalities	x	?	x	~
Accelerated CV disease	x	x	x	x
Plus...	Endothelial dysfunction, diabetic cardiomyopathy, renin-angiotensin abnormalities	Hyperuricemia	Endothelial dysfunction, hyperuricemia	Renin-angiotensin abnormalities

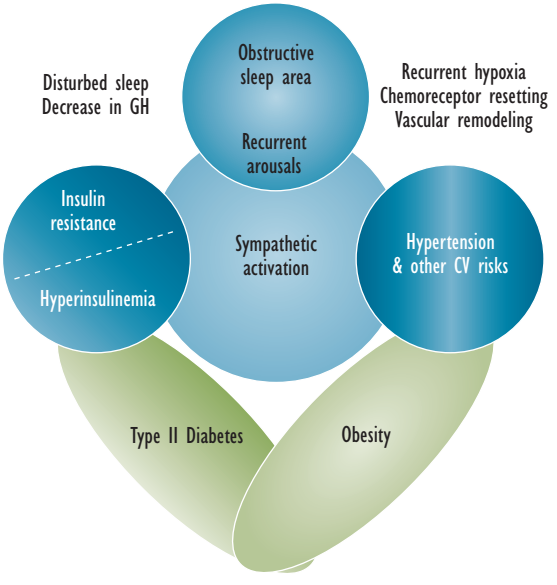
significantly influences plasma insulin and glycemia and may increase the risk of diabetes independently of obesity.

Insulin resistance is found in both obese and non-obese OSA patients. Blood pressure and fasting insulin correlate closely with both BMI and the severity of OSA. Thus, both the sleep debt and the sympathetic activation that accompany OSA may speed the deterioration of glucose tolerance. Insulin resistance and hyperinsulinemia lead to further sympathetic activation, thus completing the circle of obesity, diabetes, hypertension, and the related metabolic abnormalities.

Clearly, it is important to manage all the risk factors for diabetes and hypertension. Patients with diabetes, obesity, and hypertension have about a 70% chance of having significant OSA. Thus, OSA must be included in the differential diagnosis for hypertension. Treatment of OSA in the obese, diabetics, and hypertensives may improve insulin responsiveness (~32%), reduce blood pressure, and normalize the abnormal growth hormone cycle – and may possibly improve the impaired lipid metabolism seen in OSA. Patients with hypertension and diabetes should be asked specific questions that can reveal undiagnosed OSA. A positive answer to the following two questions provides a 90% predictability for identifying a sleep disorder:

- Do you snore?
- Have you ever been told that you stop breathing during sleep?

Figure 1: Sympathetic Activation is the Common Denominator among Obstructive Sleep Apnoea, Hypertension, Diabetes, and Obesity



Physicians who ask these questions can expect an eightfold increase in OSA patients in their office. After treatment of OSA, they can also expect improvement in the management of both hypertension and diabetes. ■

A version of this article including bibliographical references can be found in the Reference Section on the CD-ROM accompanying this business briefing.

Nightly variability of sleep-disordered breathing measured over 3 nights

CARL J. STEPNOWSKY, Jr, PHD, WILLIAM C. ORR, PHD, and **TERENCE M. DAVIDSON, MD,** San Diego, California, and Oklahoma City, Oklahoma

OBJECTIVE: **To examine the nightly variability of sleep-disordered breathing (SDB) as measured by the apnea-hypopnea index (AHI).**

STUDY DESIGN AND SETTING: **Retrospective comparison of 3 sequential nights of testing performed in the home in 1091 patients who were referred for diagnostic testing of SDB.**

RESULTS: **The Pearson and Intraclass correlation coefficients ranged between 0.88 and 0.90 for each pair of nights. Based on night 1, approximately 90% of patients were classified consistently with "AHI-high" (the highest AHI measured across the 3 nights) using an AHI threshold of 5. However, 10% were misclassified on night 1 relative to the highest AHI level.**

CONCLUSION AND SIGNIFICANCE: **These findings suggest that (1) 1 night of diagnostic testing for SDB is not sufficient to diagnosis SDB in approximately 1 of every 10 cases, and (2) there is little, if any, significant nightly change in SDB in the home environment. EBM rating: D.** (Otolaryngol Head Neck Surg 2004;131:837-43.)

The amount of nightly variability that occurs in sleep-disordered breathing (SDB) has generated considerable controversy in the diagnosis of sleep apnea. When nightly variability is small, one can have greater confidence in the results of 1 night of diagnostic sleep testing. However, when nightly variability is large, the confidence in any result is reduced and the probability of a misdiagnosis and the attendant cost and risk of a misdiagnosis in increased. Because the costs of both diagnostic testing for SDB and undiagnosed SDB are so great,[1,2] better understanding of the variability in SDB can help determine the minimal amount of diagnostic testing necessary to improve diagnostic accuracy and reduce the high costs of SDB testing.

Studies have focused on the variability of SDB across 2 nights, commonly referred to as night-to-night variability. The research on night-to-night variability has provided conflicting results with misclassifications occurring in 6% to 54.5% of patients when using an apnea-hypopnea index (AHI) threshold of 5,[3-10] and in 12% to 16% of patients when using a threshold of 10.[9,11] Table 1 provides a summary of these studies, including a brief description of each study's sample and their key findings.

One study showed that the gain in detection by adding a second night when the results of testing on the first night were negative was between 15% and 25%.[12] Data from the Sleep Heart Health Study examined nightly variability during unattended nonlaboratory polysomnography in 91 subjects over a mean time period of 2.5 months. Using an AHI based on hypopneas that were accompanied by oxygen desaturation $\geq$4% ($AHI_{Hyp4\%}$), 80.2% and 83.5% had the same classification for thresholds of 5 and 10, respectively. Because of the conflicting results in the literature, recommendations on the optimal number of nights for diagnostic testing are not clear, and the cost of more than a single night of polysomnography is prohibitive. Further, our ability to extrapolate meaningful clinical conclusions is restricted by low sample sizes in most of these studies with the exception of 2.[11,12]

Limited data exist on the variability across 3 nights. One study examined 7 healthy men over 3 nights and found that 28.5% crossed the AHI threshold of 5 one or more times.[3] Another study showed that in a sample of 46 community-dwelling elderly patients, 19.6% were misclassified on night 1 based on either night 2 or night 3 when using an AHI threshold of 5.[10] Most recently, a study examined 20 SDB patients over 4 consecutive

From the Health Services Research & Development Service, Veteran Affairs San Diego Healthcare System, San Diego, and the Department of Psychiatry, University of California, San Diego (Dr Stepnowsky); Lynn Health Research Institute, Oklahoma City, OK (Dr Orr), and the Department of Surgery, University of California, San Diego and the Division of Otolaryngology–Head and Neck Surgery, Veteran Affairs San Diego Healthcare System, San Diego (Dr Davidson), San Diego, CA.

An abstract based on these data was presented at the American Professional Sleep Society's annual scientific meeting in June 2004, in Philadelphia, PA.

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Note: Potential Conflict of Interest: The first author was provided with a small honorarium to cover partial travel costs to present the results of this study.

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Table 1. Summary table of previous research on SDB nightly variability

Study	Participants	Ages (y)	Mean AHI night 1	Mean AHI night 2	Results
Lee & Giblin, 1982[4]	7 healthy men	49-72	—	—	2 out of 7 (28.6%) sbjs crossed AHI threshold of 5 over 3 nights
Bliwise et al, 1983[5]	71 healthy adults	67.2 (11.2); 44-88	13.2 (17.6)	11.5 (15.1)	9 out of 71 (12.6%) sbjs crossed AHI threshold of 5 over 2 nights
Mosko et al, 1988[6]	46 community dwelling elderly	68.7 (6.7); 60-95	—	—	9 out of 46 (19.6%) crossed AHI = 5 threshold from night 1 to either night 2 or 3
Aber et al, 1989[7]	14 healthy older men	66.1 (5.7); 61-83	6.6 (6.6)	7.7 (9.4)	5 out of 14 (35.7%) sbjs crossed AHI threshold of 5 over 2 nights
Lord et al, 1991[8]	24 older adults	78 (5)	—	—	33% of sbjs crossed AHI threshold of 5 over 2 nights
Meyer et al, 1993[9]	11 SDB pts with negative (AHI < 5) initial PSG	44.9 (4.2)	3.1 (1.0)	19.8 (4.7)	6 of 11 (54.5%) sbjs selected for negative night crossed AHI threshold of 5 over 2 nights
Mendelson, 1994[10]	50 SDB pts	50.2 (2.3)	4 (2)	25 (5)	3 out of 50 (6%) crossed AHI threshold of 5 over 2 nights; 12% crossed AHI threshold of 10 over 2 nights
Masaquel et al, 1997[11]	60 healthy older adults	74.2 (6.6); 65-92	—	—	8 out of 60 (14%) sbjs crossed AHI threshold of 5
Quan et al, 2002[12]	91 SDB pts	Range: 40-87			Using $RDI_{4\%}$ threshold of ≤5, ≤10, & ≤15 showed that 79%, 86%, & 88% of subjects, respectively, were classified consistently across 77 ± 18 days
Le Bon et al, 2000[13]	243 suspected SDB pts	Final sample of 169: 47.2 (12.1)	12.3 (14.7)	15.5 (17.4)	Gain in detection by 2nd night when first was negative was between 15% and 25%
Bittencourt et al, 2001[14]	20 SDB pts	50 (14)	—	—	10 out of 20 sbjs changed classification (0-15, 15-30 & >30) across the 4 nights

SDB, sleep-disordered breathing; *AHI*, apnea-hypopnea index.

nights and found that 50% of subjects crossed the AHI = 15 threshold from the first to subsequent nights.[13]

Though much has been published about nightly variability of SDB measured in the laboratory, little has been reported on nightly variability measured in the home. It is well known that sleep recorded in the laboratory is confounded by the "first night effect",[14] which is characterized by lower sleep efficiency, increased wakefulness, reduction in rapid eye movement sleep (REM), and longer latencies to sleep. Evidence suggests this phenomenon is not seen in the home.[15,16] Given what is known about first night effect, it would be hypothesized that night-to-night variability would be less in studies conducted in the home environment.

We had the opportunity to examine a large clinic sample across a wide range of ages that had SDB measured on 3 nights in the home using level III cardiorespiratory monitoring.

METHODS

Participants

Adult clinical patients referred for sleep apnea diagnostic testing to Sleep Solutions (n = 1220) had their breathing monitored up to 4 nights using the NovaSom QSG™ sleep apnea diagnostic system (Palo Alto, CA). Of those patients, 1091 had valid data on 3 sequential nights and were included in the analyses. Patients were referred from a variety of physician specialties for evaluation of SDB. All patients were studied within the continental United States. None of the patients were using supplemental oxygen or continuous positive airway pressure during the diagnostic testing. Consent was obtained from the University of California, San Diego Institutional Review Board for retrospective chart review. No identifying information of any kind was obtained for the purposes of this study.

Materials and Procedure

The NovaSom QSG™ is a level III cardiorespiratory device designed to evaluate patients with possible sleep apnea (Sleep Solutions, Inc.). Sleep Solutions provides SDB diagnostic services directly to the patient based on a physician prescription. The manufacturer states that the NovaSom QSG measures airflow, oxygen saturation, pulse rate, respiration effort, and snoring sound intensity. The NovaSom QSG consists of 3 sensors: (1) a respiration airflow sensor containing 2 microphones, which detect nasal/oral airflow, snoring sound intensity (proprietary audio digital signal processing converts the respiration sound into airflow); (2) a respiration effort sensor made of Tygon® tubing, which is attached to a pressure transducer; and (3) a pulse oximeter that measures oxygen

Table 2. Study participant characteristics (valid N = 1091)

Variable		Mean (SD)	Range
Age		52.5 (12.9)	18-100
Body Mass Index		33.0 (6.8)	17.7-63.6
Epworth Sleepiness Scale		10.7 (6.1)	0-24
$AHI_{Hyp4\%}$	Night 1	17.9 (20.6)	0-113.6
	Night 2	18.2 (20.5)	0-126.9
	Night 3	18.2 (20.9)	0-108.3
Study Duration	Night 1	6.4 (1.2)	3.0-7.8
	Night 2	6.4 (1.2)	3.0-7.8
	Night 3	6.1 (1.3)	3.0-7.8

Apnea-Hypopnea Index (AHI) is based on the hypopnea definition that includes a 4% oxygen desaturation.

Table 3. Percentage of referrals for SDB testing by self-identified medical specialty area

	Frequency	Percent
Pulmonary Medicine	478	43.8
Otolaryngology (ENT)	217	19.9
Sleep Medicine	139	12.7
Other	69	6.3
Neurology	62	5.7
General Practice	60	5.5
Internal Medicine	62	5.7
Psychiatry	2	.2
Dental Medicine	1	.1
Total	1091	100.0

saturation level and pulse rate. The NovaSom QSG is attached by the patient and used to record up to 3 nights of data. The NovaSom QSG software analysis algorithm defines apnea as cessation of airflow for at least 10 seconds regardless of oxygen saturation. Two definitions of hypopnea are generated by the NovaSom QSG: ≥50% reduction in airflow for 10 seconds or more linked to either a ≥2% oxygen desaturation or a ≥4% oxygen desaturation. The total number of hypopneas and apneas are divided by total hours of recording time to yield the AHI. The AHI reported in this study is based on the hypopnea definition that utilizes the ≥4% oxygen desaturation, and for consistency with the literature is represented by $AHI_{Hyp4\%}$.

The NovaSom QSG does not record traditional polysomnographic measures of sleep. The potential for overestimation or underestimation of sleep time in the calculation of the AHI was minimized to the extent possible in the following ways. To indicate bedtime, patients were instructed to press the "start recording" button when turning out the lights and lying down to go to sleep. The scoring algorithm excluded the first 10 minutes of recording time to account for sleep onset latency. To indicate uptime, patients were instructed to remove the sensor immediately upon awakening. Once the signals were no longer being received, the recording unit shows that no data was recorded, which the scoring algorithm treats as the end of recording time. In these ways, total recording duration approximated total sleep time and provided the denominator value in the calculation of the AHI.

The NovaSom QSG has been shown to provide accurate measurement of the AHI when measured simultaneously with full polysomnography in 42 patients, with correlation coefficient = 0.96, a positive predictive value of 94%, a negative predictive value of 87.5%, a positive likelihood ratio (LR) of 17.2, and a negative LR of 0.15.[17] Using a clinical threshold of AHI = 15, a second validation study found that when both the NovaSom and polysomnography were measured simultaneously in the lab, sensitivity and specificity were 95% and 91%, respectively; for home NovaSom measurement versus in-lab polysomnography, the sensitivity was 91% and specificity was 83%.[18] The kappa coefficient was 0.734 and the intraclass correlation coefficient was 0.88. The positive LR was 11 and the negative LR was 0.06. The NovaSom was linearly related to pneumotachography, the recognized standard airflow monitoring technique, using both an automated bellows system to produce airflow[19] and in 9 human subjects measured during a daytime resting condition.[20]

Statistical Analysis

SDB variability was evaluated across the 3 nights in a variety of ways in an attempt to be comparable with reports in the literature. Cross-tabulations provide a way to measure cross-classifications across the 3 nights for a given AHI threshold level. The correlation between AHI obtained on each night was calculated using the Pearson correlation coefficient, whereas the intraclass correlation coefficient, together with its 95% confidence interval, provided a measure of consistency across the nights.[21] The Bland Altman plot[22] was generated to graphically illustrate the observed test-retest variability of the measures between the nights. SPSS was used for all statistical analyses (SPSS, Inc., version 11.0, Chicago, IL).

RESULTS

Of the original 1220 subjects for whom data were collected, 1091 had data from 3 nights of monitored sleep and breathing, recording duration greater than or equal to 3 hours on each of the 3 nights, and who were greater than or equal to 18 years of age. The mean age of the participants was 52.5 ± 12.9 years. The sample included 947 (86.8%) men and 144 (13.2%) women.

Table 4. Changes in $AHI_{Hyp4\%}$ classification from night to night (n = 1091)

$AHI_{Hyp4\%}$ Threshold	No Change (n (%))	Increased Above Threshold (n (%))	Decreased Below Threshold (n (%))
	Night 1 to Night 2		
5	939 (86.1)	88 (7.9)	64 (5.9)
10	947 (86.8)	74 (6.8)	70 (6.4)
15	955 (87.5)	75 (6.9)	61 (5.6)
	Night 1 to Night 3		
5	931 (85.3)	83 (7.6)	77 (7.0)
10	946 (86.7)	65 (5.9)	80 (7.3)
15	944 (86.5)	82 (7.5)	65 (5.9)
	Night 2 to Night 3		
5	949 (87.0)	62 (5.7)	80 (7.3)
10	938 (86.0)	67 (6.1)	86 (7.9)
15	946 (86.7)	74 (6.8)	71 (6.5)

Table 2 shows the demographic and SDB characteristics of the 1091 participants. Table 3 shows the self-identified medical specialties from which referrals for SDB testing were made. Just over 75% of all referrals came from 3 medical specialty areas: Pulmonary, ENT, and Sleep Medicine. AHI was not significantly correlated with recording duration ($r = -0.023$; $P = 0.156$).

The Pearson correlation coefficient for $AHI_{Hyp4\%}$ showed a positive correlation between nights 1 and 2 ($r = 0.896$, $P < 0.001$), nights 1 and 3 ($r = 0.887$, $P < 0.001$), and nights 2 and 3 ($r = 0.904$, $P < 0.001$). The intraclass correlation coefficient is more appropriate for determining measurement consistency than the Pearson correlation coefficient. The intraclass correlation coefficient for $AHI_{Hyp4\%}$ across the 3 nights was 0.90, with a 95% confidence interval (CI) ranging from 0.89 to 0.91, indicating very high consistency across the 3 nights of measurement. The intraclass correlation coefficient and its associated 95% CI for each pair of nights is as follows: night 1 vs. night 2: 0.90 (95% CI = 0.88-0.91), night 1 vs. night 3: 0.89 (95% CI = 0.87-0.90), and night 2 vs. night 3: 0.90 (95% CI = 0.89-0.91).

Table 4 shows the number and percentage of participants that increased above a defined threshold, decreased below that threshold and did not change classification from night to night for 3 different AHI levels (5, 10, and 15). The table shows that between 85.4% and 87.5% of the participants did not change classification from night 1 to either night 2 or 3 for each of the threshold levels. This means that between 12.5% and 14.6% changed classification from night 1 to either night 2 or 3. Specifically, between 5.6% and 7.3% of the patients decreased below the threshold and between 5.9% and 7.9% increased above the threshold.

Another way to examine the data is to assume that the highest AHI of the 3 nights represents the "true" diagnosis.[23] "AHI-high" will represent this designation. Table 5 provides the cross-tabulation data on AHI measured on night 1 compared with AHI-high. The table shows that 977 (89.4%) participants were classified consistently (i.e., did not change classification) using an AHI threshold of 5 and that 10.6% of the sample were classified inconsistently. Similar results were seen when thresholds of 10 and 15 were used: 90.1% and 89.4% are classified consistently based on night 1, respectively, and 9.9% and 10.6% were classified inconsistently. The following is not reported in Table 5, but represents a central question when studying nightly variability and is related to the analysis in the table. How many of the cases had an $AHI_{Hyp4\%}$ less than 5 on night 1, but greater than 10 on either night 2 or 3? In this sample, 33 of the 1091 (3.0%) met this criterion. Of those 33, 26 had an $AHI_{Hyp4\%}$ that was no higher than 20 on either night 2 or night 3.

The Bland Altman plot is based on the relation between the mean of 2 individual values and the difference between those values. For example, the mean $AHI_{Hyp4\%}$ for each of the first 2 nights are calculated, and then plotted against the difference in $AHI_{Hyp4\%}$ across the 2 nights. The reference lines on each plot give the 95% CI limits (e.g., $\pm$ 2 SD). Figures 1 and 2 show the Bland Altman plots for nights 1 and 2 and nights 1 and 3, respectively. Visual inspection of the data (n = 1091) reveals a low percentage of data points outside of the 95% CI. Specifically, 68 (6.2%) and 72 (6.5%) were outside the 95% CI in Figures 1 and 2, respectively.

DISCUSSION

Better understanding of the natural variability in SDB can help determine the minimal amount of diagnostic testing necessary to improve diagnostic accuracy and reduce the high costs of SDB testing. The results of

Table 5. Changes in $AHI_{Hyp4\%}$ classification from night 1 compared to highest $AHI_{Hyp4\%}$ across three nights (n = 1091)

$AHI_{Hyp4\%}$ Threshold	No Change (n (%))	Night 1 AHI less than AHI-High (n (%))
5	975 (89.4)	116 (10.6)
10	983 (90.1)	108 (9.9)
15	975 (89.4)	116 (10.6)

this study suggest that the AHI measured by the NovaSom QSG in the home environment is relatively consistent over 3 nights of testing. Approximately 90% of patients were classified consistently with the highest $AHI_{Hyp4\%}$ measured across the 3 nights whether using an AHI threshold of 5, 10, or 15. These results help to begin to clarify the discrepant findings of the literature on nightly variability studies, which have found misclassifications ranging from 12.6% to 54.5% using various threshold levels. Despite the high consistency of the measurement of SDB in the home environment, approximately 10% of cases will be misdiagnosed based on only 1 night of testing.

The present study is most comparable to the study by Le Bon et al[12] in terms of the large sample sizes and moderate mean AHI levels. However, because of the adaptation to the laboratory environment, Le Bon et al found a classic first night effect with the AHI measured on night 1 being significantly lower than the AHI measured on night 2. No measured factors accounted for the difference in AHI across the 2 nights in the laboratory, including change in sleep position or low sleep quality on night 1. It may be that differences in AHI are minimized if patients are allowed to sleep in a familiar environment. There is substantial support for the lack of a first night effect for sleep quality variables (e.g., sleep stages, arousals, sleep efficiency) when patients undergo sleep testing in the home environment.[15,16] The current study measured SDB in the home over 3 nights and is certainly also consistent with data showing very little first night effect as well as minimal variability in the night-to-night measurement of SDB.

Because of the diagnostic implications, 1 of the main goals of nightly variability studies is to explicitly examine the change in classification given a particular AHI threshold. It can be informative to take a closer look at the nightly variability literature listed in Table 1. It is clear that sample size differs across studies (range, 7-243), and it is known that sample size is directly related to measurement variability (the smaller the sample size, the larger the variability). Though it is acknowledged that the studies listed in Table 1 differed in a number of ways, including in the sample selection criteria and the measures of airflow and effort utilized, it is informative nonetheless to calculate the percentage of patients who crossed the AHI threshold of 5 in those studies that specifically report this data.[3-10] This is easily done by counting the number of patients whose AHI crossed the threshold of 5 (n = 50) and dividing by the total number of patients studied (n = 283), which results in 18% (50/283). This means that 18% percent of patients crossed the AHI threshold of 5 in 9 nightly variability studies over 20 years of research. Stated another way, 82% of patients studied on the first night were classified consistently (either AHI $<$ 5 or AHI $>$ 5) with their second night of study. This is not very different to the 86.1% (night 1 compared to night 2) and 85.4% (night 1 compared to night 3) rates found in the current study. In fact, when the data from this study are included, 1174 patients of 1376 (85.4%), are classified consistently between night 1 and night 2.

The consistency of AHI measured across 3 nights has implications for the diagnostic testing of SDB, which predominantly takes place in a traditional sleep laboratory. Traditional monitored sleep testing provides a wealth of information that informs the diagnosis and management of SDB. However, significant costs are associated with this healthcare delivery method, including not only direct financial costs, but the cost of time and disease burden to the patient who may need to wait for a substantial length of time to obtain appropriate testing. To the extent that home studies can provide equally important diagnostic data compared with traditional in-laboratory sleep studies and to the extent that the data can be shown to be reliable and valid, sleep professionals can more efficiently test the burgeoning sleep-disordered patient load with minimal increase in healthcare costs. Population SDB testing is an increasingly important public health issue.

The NovaSom is a relatively new SDB diagnostic tool that utilizes (1) total recording duration in lieu of total sleep time, and (2) an automated scoring algorithm rather than manual scoring. Using recording duration in the denominator of the AHI can underestimate the severity of SDB. For example, if the mean sleep efficiency is 85%, the AHI can be statistically erroneous by this amount. The current study does support the objectives that the home sleep study method showed little variability in night-to-night testing.

The AHI measured in the studies described in Table 1 were scored manually from polysomnography, whereas the AHI was automatically scored for the NovaSom in the current study. Automated scoring algorithms have been difficult to program to accurately

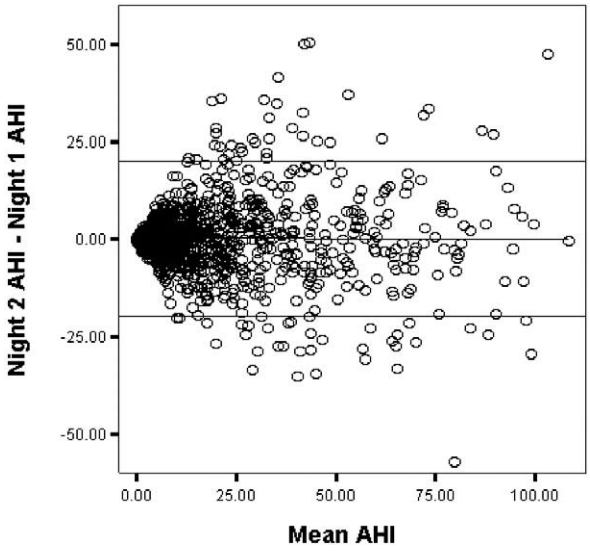

Fig 1. Bland Altman plot between nights 1 and 2 for AHI. Plot of the difference between AHI on nights 1 and 2 by the mean of the 2 nights.

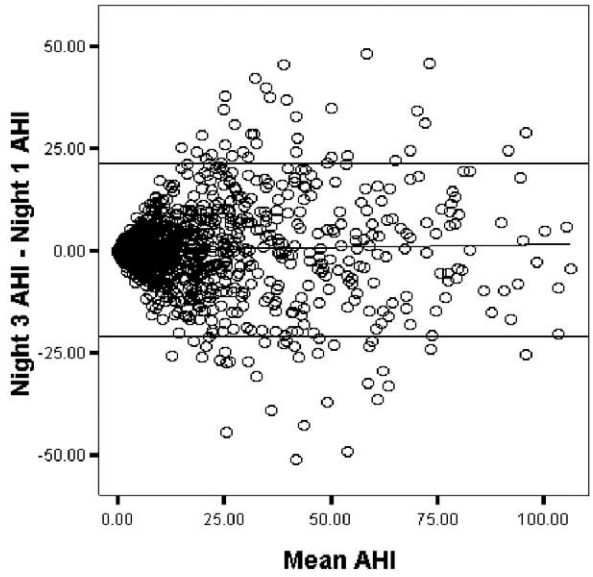

Fig 2. Bland Altman plot between nights 1 and 3 for AHI. Plot of the difference between AHI on nights 1 and 3 by the mean of the 2 nights.

and reliably classify many sleep-related events.[26] There is strong support in the medical literature for manual scoring, and this represents the current standard of care for the practice of sleep medicine. That said, no scoring method is without its challenges. There can be large variability in the manual scoring,[24,25,27] particularly in sleep centers with less than optimal training and oversight, and the reported polysomnography studies in Table 1 are limited by the lack of report of interrater reliability indices relative to a gold standard. One advantage to automated scoring is the removal of inconsistencies in human judgment. How well (or poor) automated scoring can perform is an empirical question that requires validation studies. That said, automated scoring will always require manual review, which was done for the current study, and it should not be inferred from this discussion that automatic scoring alone will ever be superior to manual scoring or review. The NovaSom scoring algorithm has been shown to be reliable and valid in clinic populations.[17,18] Its reliability and validity need to be assessed in nonclinic populations as well.

Finally, this study was not designed to examine whether the variability that was observed is clinically important from a health risk perspective because independent assessment of any adverse outcomes to make that determination were not measured. It may be that intermittent SDB occurring on different nights might signify a greater tendency to ventilatory instability on the basis of daily activity level, medication usage, or other unknown or unappreciated environmental factors. Conversely, nightly variability might constitute greater morbidity by facilitating less long-term adaptation to autonomic arousal by the cardiovascular system. Whether these speculations are borne out will take future research. Until such data are collected, the health risk of the variability in SDB remains unknown. Even though the data from this study cannot address these issues, the data do shed some light on nightly variability as it relates to diagnostic testing.

In summary, this study shows that there is little, if any, significant nightly change in SDB in the home environment and that the nightly variability of SDB measured in the home is not large. However, this study does show that at least 10% of SDB cases will be misclassified based on only 1 night of testing, which further validates the concept and practice of multiple testing nights particularly when the results of the first night are negative.

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Washington State Health Care Authority

Participant Conflict of Interest Guideline

Introduction

The HTCC Workgroup is a public service workgroup established to safeguard the public interest by identifying medical tests and treatments where evidence shows they are safe, effective, and cost-effective. Balance, independence, objectivity and scientific rigor are a basis for public trust and crucial to the credibility and integrity of decisions.

Guiding Principle

Conflict of Interest decisions must be disclosed and balanced to ensure the integrity of decisions while acknowledging the reality that interests, and sometimes even conflicting interests, do exist. Individuals that stand to gain or lose financially or professionally, or have a strong intellectual bias need to disclose such conflicts.

> *For example,* the fact that a member or stakeholder is a health care provider that may use a service under review creates a potential conflict. However, clinical and practical knowledge about a service is also useful, and may be needed in the decision making.

Procedure

Declaration of real or potential conflicts of interest, professional, intellectual, or financial is required prior to membership or provision of written or verbal commentary. Participants must sign a conflict of interest form; stakeholders providing comment must disclose conflicts.

The HTCC Chair or HCA Administrator shall make a decision, in his/her sole discretion, as to whether a conflict of interest rises to the level that participation by the conflicted participant could result in a loss of public trust or would significantly damage the integrity of the decision.

HCA defines conflict of interest as any situation in which a voting member or anyone who provides written or verbal testimony regarding products, services, or technologies discussed or voted on during the workgroup meeting, has a relationship with a manufacturer of any commercial products and / or provider of services discussed or voted on during the meeting. Relationship extends to include immediate family member(s) and / or any entity in which the member or person testifying may have an interest.

A relationship is considered as:

1. Receipt or potential receipt of anything of monetary value, including but not limited to, salary or other payments for services such as consulting fees or honoraria in excess of $10,000.
2. Equity interests such as stocks, stock options or other ownership interests in excess of $10,000 or 5% ownership, excluding mutual funds and blinded trusts.
3. Status of position as an officer, board member, trustee, owner or employee of a company or organization representing a company, association or interest group.
4. Loan or debt interest; or intellectual property rights such as patents, copyrights and royalties from such rights.
5. Manufacturer or industry support of research in which you are participating.
6. Any other relationship that could reasonably be considered a financial, intellectual, or professional conflict of interest.
7. Representation: if representing a person or organization, include the organization's name, purpose, and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).
8. Travel: if an organization or company has financially paid your travel accommodations (e.g. airfare, hotel, meals, private vehicle mileage, etc).

Washington State Health Care Authority

Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000		X
2.	Equity interests such as stocks, stock options or other ownership interests		X
3.	Status of position as an officer, board member, trustee, owner		X
4.	Loan or intellectual property rights		X
5.	Research funding	X	
6.	Any other relationship		X

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

I have research wondering through OHSU with United therapeutics to fund trials on pulmonary artery hypertension. Funding is received by OHSU.

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		X

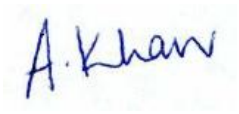
7. If yes, Provide Name and Funding Sources: _____

	Potential Conflict Type	Yes	No
8.	Travel: if an organization or company has financially paid your travel accommodations (e.g. airfare, hotel, meals, private vehicle mileage, etc).		X

8. If yes, Provide Name of Organization / Company and Disclose Travel Accommodations:

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may ***attach additional sheets*** explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

X  2/16/12 Akram Khan

Signature *Date* *Print Name*

FOR QUESTIONS: Denise Santoyo, Health Care Authority, 360-923-2742,
PO Box 42712, Olympia, WA 98504-2712

Akram Khan, MD

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Work History

Nov 2008- Present	**Assistant Professor: Pulmonary Critical Care & Sleep Medicine, Co-Director Sleep Disorders Center, Program Director Pulmonary Artery HTN Program. Oregon Health & Science University.** UHN-67 3181 SW Sam Jackson Park Road, Portland OR 97239
Jul 07 – Oct 08	**Assistant Professor: Pulmonary Critical Care & Sleep Medicine, Co-Director Sleep Disorders Center. University of Florida College Of Medicine Jacksonville.** Shands Jacksonville 655 West Eighth Street, Jacksonville, FL 32209
Oct 01-Jun 04	**Medical Director, Emergency Department**: **EmCare Inc,** Midwest Region 533 W. North Ave Suite 102 Elmhurst, IL 60126 Worked at St. Alexius Hospital, St. Louis, MO. Successfully implemented a transition from 14K to 28K annual ED visits with significant improvement in patient turnaround time, staff morale and physician satisfaction.
Jul 01-Jun 04	**Emergency Room Physician: St. Alexius Hospital**; St. Louis MO. Worked as an emergency room physician in a 200 bed medical & psychiatric facility in a medically underserved area.
Aug 01-Apr 03	**Intensivist: Critical Care Services Inc.**, 1066 Executive Parkway, Suite 105 St. Louis, MO 63141. Critical Care physician working part time in a 14 bed ICU at Saint Joseph's Hospital of Kirkwood, St. Louis, MO & a 20 bed ICU at DePaul Hospital, St. Louis, MO

Fellowship Training

Jul 06-Jun 07	**Sleep Medicine: Mayo Clinic**, 200 1st Street SW, Rochester MN 55905 Department of Sleep Medicine. Program Director: Michael Silber, MD
Jul 04-Jun 06	**Pulmonary Medicine: Oklahoma University Health Sciences Center**, Div. of Pulmonary & Critical Care Medicine, WP 1310, Oklahoma City, OK 73190. Program Director: Paul Carlile, MD
Jul 00-Jun 01	**Critical Care Medicine: Saint John's Mercy Medical Center (St. Louis University)**, 615 S. New Ballas Road, St. Louis, MO 63141. Program Director: Robert Taylor, MD

Residency Training

Jul 97-Jun 00	**Internal Medicine: Saint Louis University School of Medicine**, Dept of Internal Medicine, 1402 S Grand Blvd. St Louis, MO 63104. Program Director: Douglas, Miller, MD
Jul 95-Jun 97	**Prelim Surgery: Beth Israel Medical Center**, Department of Surgery, First Ave at 16th St, New York,, NY 10003 Prelim Surgery Residency (PGY I and II) Program Director: Moses Naussbaum, MD

Medical School

Apr 94-Jun 95	**Surgery Internship: MAMC and LNJPN Hospital,** Delhi University, New Delhi, India
Aug 88-Dec 93	**MAMC and Affiliated Hospitals, Delhi University**, New Delhi, India. Bachelor of Medicine & Bachelor of Surgery (M.B.B.S)

Journal Publications

Chacon G, Nguyen T, Khan A, Sinha A, Maddirala S. Warfarin-induced skin necrosis mimicking calciphylaxis: a case report and review of the literature. J Drugs Dermatol. 2010 Jul;9(7):859-63. (PMID: 20677545)

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Khan A, Auger RR, Kushida CA, Ramar K Rhythmic movement disorder. Sleep Med. 2008 Mar;9(3):329-30 (PMID: 18036973)

Khan A, Latif F, Hawkins B, Tawk M, Sivaram CA, Kinasewitz G Effects of obstructive sleep apnea treatment on left atrial volume and left atrial volume index. Sleep Breath. 2008 May;12(2):141-7 (PMID: 17992552)

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RJ Rosenthal, RL Friedman, A Chidambram, M. Akram Khan, et al "Effects of Hyperventilation and Hypoventilation on PaCO2 and Intracranial Pressure During Acute Elevations of Intraabdominal Pressure With CO2 Pneumoperitonium: Large Animal Observations." Journal of the American College of Surgery 1998; 187: 32-38 (PMID: 9660022)

R. J. Rosenthal, R. Friedman, M. Akram Khan, et al "Reasons for Intracranial Hypertension and Hemodynamic Instability During Acute Elevations Of Intraabdominal Pressure. Observations In A Large Animal Model." Journal of Gastrointestinal Surgery 1998; 2: 415-425 (PMID: 9843600)

Avisar E, Khan MA, Axelrod D, Oza K "Pure mucinous carcinoma of the breast: a clinicopathologic correlation study." Ann Surg Oncol. 1998 Jul-Aug;5(5):447-51 (PMID: 9718175)

Book Chapters

Akram Khan & Peter C. Gay. "Complex Sleep Apnea". AASM Nosology Casebook

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Presentations/Abstracts

Khan A, Maddirala S, Rajput N, Youssef D, Warule M, Puslavidyasagar S, Griffith K, Karamooz E, Stecker E Risk Of Obstructive Sleep Apnea In Patients With Pacemakers And Implantable Cardioverter Defibrillators. Sleep, Volume 34, Abstract Supplement A235, 2011 *Presented* 25th Annual Meeting of the Associated Professional Sleep Societies, LLC (SLEEP 2011),

Akram Khan, Wendy C. King, Emma J. Patterson, Jamie Laut, William Raum, Anita P. Courcoulas, Charles W. Atwood, Jr., Jr., and Bruce Wolfe Obstructive Sleep Apnea Prior To Bariatric Surgery: Diagnostic Testing, Prevalence And Predictive Value Of The Berlin Sleep Questionnaire In The Longitudinal Assessment Of Bariatric Surgery-2 (LABS-2) Cohort Am. J. Respir. Crit. Care Med., May 2011; 183: A6315 *Presented* ATS May 2011

Susanna Gonzales, and Akram Khan An Unexpected Aortic Mass Found During The Work-Up Of Syncope And Atrial Fibrillation Am. J. Respir. Crit. Care Med. 183: A5870. *Presented* ATS May 2011

Mohammed I, Maddirala S, Khan A Evaluating Clinical Predictors of Complications of Thoracentesis *Presented* Chest October 2010 vol. 138 no. 4 supp 348A

Ramar K, Khan A, Gay P. Positive Airway Pressure Treatment In Patients With Obstructive Sleep Apnoea And Diaphragmatic Dysfunction. *Presented* Sleep and Biological Rhythms. 2007; 5(s1):A141

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Khan A, Dernaika T, Haugland K, et al. Clinical Utility Of Bispectral Index Monitoring In The ICU: A Pilot Study. *Presented* Chest 2006; 130:225S-c-226.

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Avisar, M. Akram Khan, K Oza and D. Axelrod, "Pure Mucinous Carcinoma Of The Breast, A Clinico-Pathological Correlation Study." *Presented* (P29) at the Society of Surgical Oncology's 50th Annual Meeting, March 1997.

Invited Lectures

Endobronchial Ultrasound. Sept 2010, 19th Annual Trends in Respiratory and Acute Care McMenamins Edgfield, Troutdale, OR

Preoperative Care Of Obstructive Sleep Apnea. Sept 2011 20th Annual Trends in Respiratory and Acute Care McMenamins Edgfield, Troutdale, OR

Research

Effect of rapamycin on rat stellate cell proliferation with Robert Britton, Ph.D. and Bruce Bacon, MD, Division of Gastroenterology, Saint Louis University, Saint Louis, Missouri 1999

Evaluation of the role of percutaneous ethanol injection in the management of solitary thyroid nodules with A K Kakar, MD and V Choudhry, MD. Accepted as protocol by Delhi University for postgraduate thesis, March 1995

Board Certification

Sleep Medicine (ABIM, expires 2017)
Pulmonary Medicine (ABIM, expires 2016)
Critical Care Medicine (ABIM, expires 2017)

Professional Associations

American Academy of Sleep Medicine (Member)
American College of Chest Physicians (Fellow)
American Thoracic Society (Member)

Institutional representative, Sleep Research Network 2008-Present
Governor for the state of Oregon for American College of Chest Physicians 2010-2012

Honors / Awards

Critical Care Conundrums: Best Case Report — Chest 2007, Chicago IL

Research Support
Ongoing research support

RIN-PH-403 — Khan, A (PI) — Sponsor: United Therapeutics
A Post marketing Observational Study to Assess Respiratory Tract Adverse Events in Pulmonary Arterial Hypertension Patients Treated With Tyvaso® (Treprostinil) Inhalation Solution (ASPIRE)

TDE-PH-304 — Khan A (PI) — Sponsor: United Therapeutics
An Open-Label Extension Trial of UT-15C SR in Subjects With Pulmonary Arterial Hypertension

Completed research support

TDE-PH-308 — Khan A (PI) — Sponsor: United Therapeutics
A 16-Week, International, Multicenter, Double-Blind, Randomized, Placebo-Controlled Study of the Efficacy and Safety of Oral UT-15C Sustained Release Tablets in Subjects With Pulmonary Arterial Hypertension (FREEDOM-C2)

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TDE-PH-302 Khan A (PI) Sponsor: United Therapeutics

A 12-Week, International, Multicenter, Double-Blind, Randomized, Placebo-Controlled Comparison of the Efficacy and Safety of Oral UT-15C Sustained Release Tablets in Subjects with Pulmonary Arterial Hypertension

Washington State Health Care Authority

Agency Medical Director Comments
Health Technology Clinical Committee

Sleep Apnea Diagnosis and Treatment in Adults

Dr. G. Steven Hammond
Chief Medical Officer
Department of Corrections
3/16/2012

Sleep Apnea Background

Sleep apnea, in particular obstructive sleep apnea (OSA) has been increasingly recognized, diagnosed, and treated over the past 20-30 years.

Prevalence estimates

Adults 2-7% Adults over 60 20%

Diagnosis

- Usually polysomnography
- Diagnostic procedures and criteria are not standardized
  - Severe OSA is independently predictive of increased risk of cardiovascular morbidity and all-cause mortality

Treatment

- CPAP is the most commonly prescribed treatment for OSA
  - Improves some measures of disordered breathing during sleep
  - Not demonstrated to decrease major morbidity or mortality
  - It is not tolerated by a significant proportion of patients

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Sleep Apnea Background

AMDG Perspective

At time of topic selection, concerns about sleep apnea diagnosis and treatment were rated:

Safety - Medium

Efficacy – High

Cost – Medium

In light of subsequent literature review and agency utilization data, concerns are currently rated:

Safety – Low/Medium

Efficacy – High

Cost – Medium/High

- $12-15 million per year and rising; given high prevalence, potential for continued increase in utilization is high

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Washington State Health Care Authority

Sleep Apnea
Current State Agency Policy

PEB – covers diagnosis and treatment of sleep apnea without limitations

Medicaid – covers diagnosis and CPAP treatment of sleep apnea under conditions, including:

- polysomnography in approved sleep center
- chronic sleep apnea

L&I – covers diagnosis and treatment of sleep apnea related to occupational illness or injury without limitations

DOC – covers diagnosis and treatment of sleep apnea as deemed medically necessary in individual cases

- infrequently authorized in DOC

Washington State Health Care Authority

Sleep Apnea

State Agencies Questions

Safety:

- Sleep studies and treatment with CPAP and oral appliances appear safe
- Surgical treatment carries risk related to surgery
- Safety must be judged in relation to health benefits, which are uncertain

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Washington State Health Care Authority

Sleep Apnea

State Agencies Questions

Effectiveness

- Improvement in sleep measures and daytime sleepiness has been demonstrated
- Relation of these improvements to major health outcomes (e.g., reduction in mortality or cardiovascular morbidity) is unproven

Cost

- Cost is significant
- Cost effectiveness is indeterminate because effectiveness for major health outcomes is unproven
- Potential for increased utilization is high

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Washington State Health Care Authority

Sleep Apnea
State Agency Utilization

All Agency Sleep Apnea Summary, 2006-2010

PEB	2006	2007	2008	2009	2010	5 Year Overall*
SA Members	4846	5799	7855	9175	9987	17,739
SA Payments	$5.0M	$6.2M	$8.5M	$10.1M	$9.7M	$39.4M
Medicaid						
SA Patients	2632	3367	3924	4492	3118	11,391
SA Payments	$4.1M	$4.8M	$5.1M	$5.6M	$4.8M	$24.3M
L&I						
SA Patients	21	33	47	45	30	126
SA Payments	$38,369	$56,909	$70,362	$75,865	$76,965	$318,470

*5 year overall figures consider all years' data together, counting members once

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Washington State Health Care Authority

Sleep Apnea
State Agency Utilization

Medicaid Sleep Apnea, All Patients vs Adult only Patients, 2006-2010

Medicaid Overall	2006	2007	2008	2009	2010	5 Year Overall*
SA Patients	2632	3367	3924	4492	3118	11,391
SA Payments	$4.1M	$4.8M	$5.1M	$5.6M	$4.8M	$24.3M
Medicaid Adults						
SA Patients	2255	2913	3422	3936	2666	9816
SA Payments	$3.5M	$4.0M	$4.4M	$4.8M	$4.0M	$20.7M

*5 year overall figures consider all years' data together, counting members once

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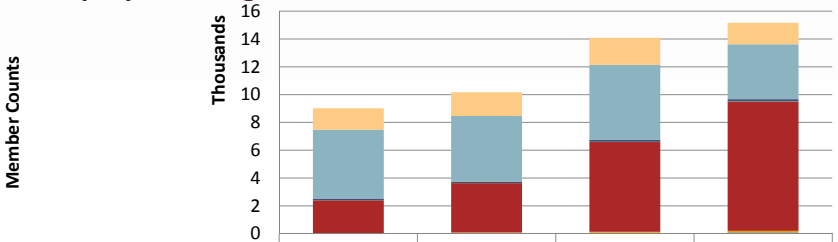
Washington State Health Care Authority

Sleep Apnea
State Agency Utilization

PEB Sleep Apnea Diagnoses Trends, 2006-2009



	2006	2007	2008	2009
SLEEP APNEA NOS	1545	1698	1944	1538
HYPERSOM W SLP APNEA NOS	4940	4711	5375	3951
INSOMN W SLEEP APNEA NOS	131	108	142	164
ORGANIC SLEEP APNEA NEC	3	5	6	10
CNTRL SLEEP APNEA OT DIS	3	10	22	25
OBSTRUCTIVE SLEEP APNEA	2365	3545	6451	9268
PRIM CENTRAL SLEEP APNEA	6	30	70	110
ORGANIC SLEEP APNEA NOS	23	57	69	96

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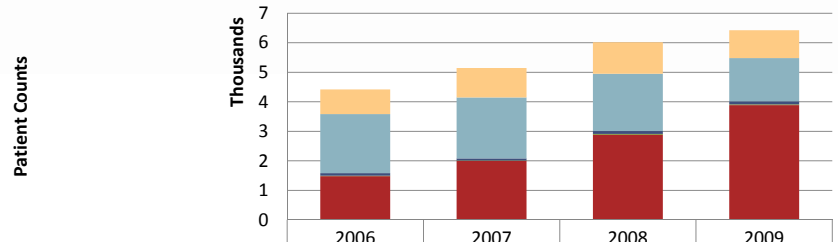
Washington State Health Care Authority

Sleep Apnea
State Agency Utilization

Medicaid Sleep Apnea Diagnoses Trends, 2006-2009



	2006	2007	2008	2009
SLEEP APNEA NOS	833	1001	1066	942
HYPERSOM W SLP APNEA NOS	2004	2064	1944	1465
INSOMN W SLEEP APNEA NOS	87	73	94	101
ORGANIC SLEEP APNEA NEC	5	2	2	4
CNTRL SLEEP APNEA OT DIS	8	12	27	21
OBSTRUCTIVE SLEEP APNEA	1457	1975	2861	3875
PRIM CENTRAL SLEEP APNEA	0	0	0	0
ORGANIC SLEEP APNEA NOS	24	21	24	15

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Washington State Health Care Authority

Sleep Apnea
State Agency Utilization

All Agency Payment Category Totals, 2006-2009

Payment Category*	Four year total Paid			% of 4 year total		
	PEB	Medicaid	L&I	PEB	Mcaid	L&I
Total Paid	$29,743,841	$19,548,369	$241,505			
Sleep Studies	$13,357,206	$7,699,131	$141,885	44.9%	39.4%	58.8%
Office Visits	$2,401,010	$1,110,995	$25,453	8.1%	5.7%	10.5%
Treatment	$13,985,625	$10,738,243	$74,167	47.0%	54.9%	30.7%
Treatment Subcategories*						
CPAP	$13,069,271	$10,194,095	$74,167	43.9%	52.1%	30.7%
Surgery	$381,434	$534,390	$0	1.3%	2.7%	0.0%
Orthotics	$9,979	$0	$0	0.0%	0.0%	0.0%

* Major categories and sub-categories only

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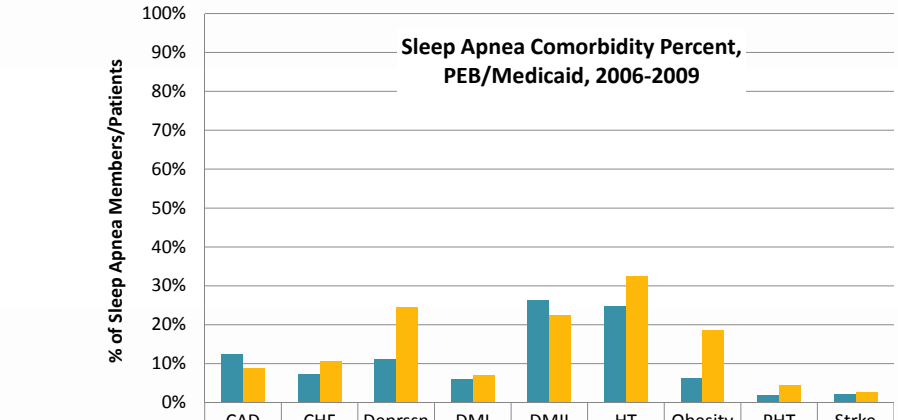
Washington State Health Care Authority

Sleep Apnea
State Agency Utilization

PEB/Medicaid Sleep Apnea Comorbidities, 2006-2009



	CAD	CHF	Deprssn	DMI	DMII	HT	Obesity	PHT	Strke
PEB SA Members	12.5%	7.2%	11.3%	5.9%	26.3%	24.9%	6.2%	2.0%	2.3%
Medicaid SA Paitients	8.9%	10.6%	24.6%	7.0%	22.6%	32.6%	18.6%	4.6%	2.7%

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Washington State Health Care Authority

Sleep Apnea Summary

State Agencies Summary View

After over 20 years of widespread clinical use and voluminous research:

Diagnostic evaluation lacks standardization in:

- instrumentation
- measurement methodology
- diagnostic criteria

We know:

- Severe OSA (AHI>30) predicts higher mortality
- CPAP improves AHI, arousal, oxygen saturation, ESS scores

We don't know if treatment improves:

- quality of life
- neurocognitive function
- mortality
- other major objective health outcomes

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Washington State Health Care Authority

Sleep Apnea

State Agencies Recommendation

Cover with conditions:

- Agency-approved diagnostic evaluation
- Treatment for AHI>30
- When medically necessary per agency policy

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Washington State Health Care Authority

Questions?

OREGON HEALTH & SCIENCE UNIVERSITY

Sleep Apnea Diagnosis and Treatment in Adults

Presented by : Ken Gleitsmann MD MPH
Center for Evidence-based Policy
Date: March 16, 2012

Introduction

- Background
- Key Questions
- Methods
- Findings
- Policy
- Summary

Background – *Clinical Overview*

- Obstructive Sleep Apnea (OSA) refers to sleep-disordered breathing
  - Associated with significant morbidity and mortality (e.g., hypertension, stroke, CVD, diabetes, neuropsychological impairment)
  - Prevalent in 2 to 7% of general adult population
  - Prevalence increases with age (e.g., ~20% at age > 60yrs)

Background – *Diagnosis*

- Polysomnography (PSG) in a sleep study facility is current "gold" standard
- During sleep, the PSG records:
  - The frequency of obstructed breathing events (e.g., apnea-hypopnea index (AHI), per hour)
- Diagnosis of OSA made when AHI is ≥15, or >5 with noticeable daytime symptoms

Background – *Diagnosis*

- Portable PSG monitors, various questionnaires (e.g., Epworth Sleepiness Scale, STOP, etc), and predictive models developed to aid in screening candidates for formal PSG studies
- Portable monitors, used at home or in sleep labs, record multiple channels of information, classified into 4 categories:
  - Type I: PSG in sleep facility
  - Type II: Portable recording same info as Type I (3 sleep arousal channels, min. of 2 respiratory channels)
  - Type III: Portable record min. of 2 respiratory channels not detecting sleeping or waking status
  - Type IV: Portable monitors that fail Type III criteria

Background – *Treatment*

- Continuous-positive-airway-pressure (CPAP
- Mandibular/oral devices
- Surgery (e.g., oropharyngeal airway, bariatric surgery)
- Other interventions
  - weight loss regimens, smoking cessation, caffeine and alcohol avoidance, positional therapy, oropharyngeal physical therapy, arrhythmia treatment, complementary and alternative medicine, various pharmacologic agents

Key Questions

- **KQ1**. Diagnostic Ability (including subgroups of pts)
- **KQ2.** Phased vs Full Testing
- **KQ3.** Pre-Operative Screening
- **KQ4**. Long Term Outcomes
- **KQ5.** Treatment Effectiveness
- **KQ6.** Treatment Compliance
- **KQ7**. Interventions to Improve Compliance
- **KQ8.** Cost-Effectiveness

Methods – Search Strategy

- AHRQ systematic review *Comparative Effectiveness of Diagnosis and Treatment of Obstructive Sleep Apnea in Adults* (Balk 2011) main evidence source
  - Updates 2007 AHRQ systematic review
- CEbP updated Balk (2011) search through November 2011
- Added KQ #8 (cost and cost-effectiveness)
  - Studies published after 2001

Methods – Quality Assessment

- Balk [AHRQ] (2011) study methodological quality grading system:
  - A (good) Least amount of bias, results considered valid
  - B (fair/moderate) - Susceptible to some bias, not sufficient to invalidate results
  - C (poor) - Carry a substantial risk of bias, may invalidate report findings
- Methodological quality of the KQ #8 studies was assessed
  - Instrument developed and adapted by CEbP
    - Studies rated as “good”, “fair”, or “poor”

Findings – *KQ 1 Diagnostic Ability*

Table 1. Comparison of Portable Devices and PSG

Monitor Type	Evidence	Strength of Evidence
Type II	3 comparative studies (3 quality B) • -36 to 36 events/hr; sensitivity 81%; specificity 97%	Low
Type III	29 studies (18 different Type III monitors) • 7 newer studies(3 quality A; 4 quality B) • Sensitivity 64-100%; specificity 41-100% • Mean AHI baseline:15.0 to 39.9 events/hr • MA diff -39 to 54 events/hr	Moderate
Type IV	70 studies (23 different Type IV monitors) (Quality: B) • 24 newer studies (7 quality A, 11 quality B, 6 quality C) • Sensitivity 75-92%; specificity 50-100% • Mean AHI baseline: 14 to 44 events/hr	Moderate

Findings – *KQ 1 Diagnostic Ability*

Comparison of Questionnaires and PSG

- 6 studies (N = 744) compared various questionnaires to PSG (1 quality A, 1 quality B, and 4 quality C)
- Berlin questionnaire, STOP,STOP-Bang, American Society Anesthesiologists Checklist (ASAC), and Epworth Sleepiness Scale (ESS) for screening of OSA

Comparison of Clinical Prediction Rules (CPRs) and PSG

- 7 studies included (10 different CPRs)
- No CPR has been independently validated, variable accuracy for predicting OSA, and not accurate for diagnosis of severe OSA

Findings – *KQ 1 Diagnostic Ability*

Table 2. Comparison of Questionnaires and PSG

Questionnaire	# of Studies	Risk Prediction Scale	Question Categories	Sensitivity & Specificity*
Berlin	4	High or Low	Snoring, tiredness, blood pressure	Sen. 54-79% Spec.51-97%
STOP	1	High or Low	Snoring, tiredness, witnessed apneas, blood pressure	Sen. 74% Spec. 53%
STOP – Bang	1	High or Low	4 STOP categories, plus BMI, age, neck circumference, gender	Sen. 93% Spec. 43%
ASAC	1	High or Low	Physical characteristics, history of sleep ion, history of somnolence	Sen. 79% Spec. 51%

* The Questionnaires used AHI>15 with the exception of Hawaii (AHI>10) and ESS (AHI>5).

Findings – *KQ 1 Diagnostic Ability*

KQ1 Overall Summary

- *Moderate strength of evidence*
  - Portable monitors (Type III and IV)
- *Low strength of evidence*
  - Portable monitors (Type II); Berlin Questionnaire; clinical prediction rules
- *Insufficient evidence*
  - Comparison of portable monitors; STOP, STOP-Bang, ASAC, ESS, and Hawaii questionnaires

Findings – *KQ 2 Phased vs. Full Testing*

- Single prospective study of commercial drivers diagnosed with OSA (quality C)

KQ2 Overall Summary

- *Insufficient evidence*
  - utility of phased testing (i.e., using a screening test result to determine the next test to be performed in a series), as compared to PSG

Findings – *KQ 3 Pre-operative Screening*

- Two prospective studies (2 quality C)
- Both studies had methodological limitations and their restricted eligibility criteria limit their applicability to the general population

KQ3 Overall Summary

– *Insufficient evidence*

- Utility of preoperative screening for OSA

Findings – *KQ 4 Long Term Outcomes*

Table 3. AHI as a Predictor for Long Term Outcomes for OSA

Outcome	# of Studies (Quality)	F/U Yrs	AHI as an Outcome Predictor
All-Cause Mortality	4 (3 A, 1 B)	2-14	• Higher baseline AHI predicted increased mortality (4 studies) • Higher AHI (>30 events/hr) had elevated mortality risk (3 studies)
CV Mortality	1 (A)	10	Increased risk of CV death with baseline AHI >30 events/hr in those not treated with CPAP
	1 (A)	14	No association
Nonfatal	1 (A)	10	Increased risk of nonfatal CVD with AHI baseline >30 events/hr in those not treated with CPAP

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Findings – *KQ 4 Long Term Outcomes*

Table 3. AHI as a Predictor for Long Term Outcomes for OSA (cont.)

Outcome	# of Studies (Quality)	F/U yrs	AHI as an Outcome Predictor
Stroke	1 (B)	12	No association, low event rate and wide CIs suggest study lacks power
HTN	1 (A)	5	AHI > 15-30 events/hr was significantly associated with incident HTN
	1 (B)	4 & 8	Any AHI > 0 events/hr was statistically significant predictor
Type 2 Diabetes	1 (B)	14	After adjusting for waist girth, strong association for AHI 5-15 events/hr (OR 2.81) and AHI >15 events/hr (OR 4.06)
	1	2.7	After adjusting for BMI, AHI >8 events/hr was

Findings – *KQ 4 Long Term Outcomes*

KQ 4 Overall Summary

- *High strength of evidence*
  - Using AHI greater than 30 events/hour can be an independent predictor of all-cause mortality
- *Low strength of evidence*
  - A higher AHI was associated with incident diabetes (Association may be confounded by obesity)
- *Insufficient evidence*
  - To determine an association of AHI with other long term clinical outcomes (e.g., cardiovascular mortality, non fatal cardiovascular mortality, hypertension)

Findings – *KQ 5 Treatment Effectiveness*

- 155 eligible studies addressed this KQ
  - 132 RCTs
- This section is organized by comparison between categories of interventions and a focus on adverse events

Findings – *KQ 5 Treatment Effectiveness*

Comparison of CPAP and "Sham" CPAP

- 24 trials (N = 1076)
  - 5 (quality A), 13 (quality B), 6 (quality C)
- Mean AHI baseline ranged from ≥5 to ≥30 events/hr
- Follow-up 1 week to 3 months
- Generally, studies had small sample sizes
- No objective clinical outcomes were reported
- Many of the meta-analysis results had significant heterogeneity
- Compliance data was not reported

Findings – *KQ 5 Treatment Effectiveness*

Table 4. Comparison of CPAP and Sham CPAP

Outcome	# of Studies	Results
AHI	9	MA stat. sig. Difference in AHI, favoring CPAP group (diff = -46 events/hr; 95%CI -57, -36)
ESS	16	MA showed stat. sig. difference favoring CPAP (diff -2.5; 95%CI -57, -36)
Other Sleep Measures	3	*Arousal index* – MA showed arousals stat. sig. reduced favoring CPAP (diff = -27 events/hr; 95%CI -42, -12)
	1	*REM Sleep* –sig. increased REM sleep time with CPAP (diff 7.5% of total sleep time; 95%CI 3.5, 11.5)
Objective Sleepiness and	4	*MWT* – no sig. difference (2 studies); stat. sig. difference favoring CPAP (2 studies)

Findings – *KQ 5 Treatment Effectiveness*

Table 4. Comparison of CPAP and Sham CPAP (cont)

Outcome	# of Studies	Results
Neurocognitive and Psychological Tests	7	1 of 26 comparisons noted a sig. difference in one parameter tested, favoring CPAP
Blood Pressure	12	Compared day or night BP, inconsistent results (~half of studies favored reduction with CPAP, and ~half reported no sig. differences)

- No significant difference between groups
  - Objective Clinical Outcomes
  - Other Sleep Measures (e.g., Minimum Oxygen Saturation; Sleep Efficiency; Slow Wave Sleep)
  - Objective Sleepiness and Wakefulness Test (MSLT)
  - QoL (FOSQ instrument)

Findings – *KQ 5 Treatment Effectiveness*

Comparison of CPAP and Control

- 22 studies (N=1116)
  - 11 studies (quality B), 11 studies (quality C)
- Controls: treatment, placebo (lactose tablets), or conservative measures (i.e., weight loss counseling)
- Mean baseline AHI ranged 10 to 65 events/hr
- Methodological concerns: small sample sizes, multiple comparisons, lack of power calculation, high dropout rates, incomplete reporting, lack of washout in some crossover trials

Findings – *KQ 5 Treatment Effectiveness*

Table 5. Comparison of CPAP and Control

Outcome	# of Studies	Results
Objective Clinical Outcomes	1	No stat. sig. improvement for CHF symptoms after 3 months with CPAP
AHI	7	MA found stat. sig. difference in AHI between groups favoring CPAP (diff = -20 events/hr; 95%CI -26, -14)
Change in ESS	14	MA (12 trials with data) noted stat. sig. difference between groups favoring CPAP (diff = -2.4; 95%CI -3.2, -1.5)
	6	*Arousal Index* – MA found stat. sig. difference in arousal index between groups favoring CPAP (diff = -15 events/hr; 95%CI -22, -7)

Findings – *KQ 5 Treatment Effectiveness*

Table 5. Comparison of CPAP and Control (cont)

Outcome	# of Studies	Results
Objective Sleepiness	6	*Multiple Sleep Latency Test (MLST)* – MA found no stat. sig. difference in MLST between groups (diff = 0.78; 95%CI -0.07, 1.63; p=0.072)
Quality of Life	14	29 comparisons using 7 QoL instruments, inconsistent findings across studies
Neurocognitive and Psychological Tests	8	56 comparisons between groups, sig. differences in favor of CPAP noted in 10 comparisons across 4 studies
Blood Pressure	7	Comparisons of day and night BP, no stat. sig. differences reported
Hemoglobin A1c	1	No difference between groups

Findings – *KQ 5 Treatment Effectiveness*

Comparison of Various CPAP devices

- 40 trials compared different types of CPAP devices
- No studies evaluated clinical outcomes
- No studies reported consistent statistically and clinically significant differences between different or modified CPAP devices

Findings – *KQ 5 Treatment Effectiveness*

Comparison of Mandibular Advancement Devices (MAD) and No Treatment or Inactive (Sham) Oral Devices

- 5 trials compared these interventions with controls (N = 264)
  - 4 (quality B), 1 (quality C)
  - Mean AHI baseline: 19 to 34 events/hr
  - Follow-up: 1 week to 3 months
- 5 trials compared MADs to sham MADs (N = 186)
  - 4 (quality B), 1 (quality C)
  - Mean AHI baseline: 25 to 36 events/hr
  - Follow-up: 1 to 6 weeks
- No studies report on objective clinical outcomes

Findings – *KQ 5 Treatment Effectiveness*

Table 6. Comparison of Mandibular Advancement Devices (MAD) and No Treatment or Inactive (Sham) Oral Devices

Outcome	# of Studies	Results
AHI	5	MA reported stat. sig. difference favoring MAD groups (similar results for MAD vs sham-MAD) (diff = -14 events/hr; 95%CI -20, -8)
ESS	4	MA reported stat. sig. difference in daytime sleepiness, favoring MAD groups (similar results for MAD vs sham-MAD) (diff = -1.9; 95%CI -2.9, -1.0)
Various Oral Devices	5	Generally, sleep study measures were not different between devices

Findings – *KQ 5 Treatment Effectiveness*

Comparison of MADs and CPAP

- 10 trials (N=385)
  - 9 (quality B), 1 (quality C)
- Mean baseline AHI: 18 to 40 events/hr
- Sample sizes generally small
- Large clinical heterogeneity due to different devices
- No studies reported objective clinical outcomes

Findings – *KQ 5 Treatment Effectiveness*

Table 7. Comparison of MAD and CPAP

Outcome	# of Studies	Results
AHI	9	MA found stat. sig. difference between MAD and CPAP, favoring CPAP (diff = 7.7 events/hr; 95%CI 5.3, 10.1)
ESS	7	MA found no sig. difference between MAD and CPAP
Other Sleep Study Measures	5	MA found arousals sig. more common while using MAD (diff = 3.5 events/hr; 95%CI 1.5, 5.5)
Quality of Life	3	Inconsistent findings
Neurocognitive	2	No sig. difference between MAD and CPAP

Findings – *KQ 5 Treatment Effectiveness*

Comparison of Surgery and Control Treatments

- 6 trials (N = 284) compared various surgical interventions to sham surgery, conservative therapy, or no treatment
  - 3 (quality A), 1 (quality B), 2 (quality C)
- Surgical interventions
  - UPPP, LAUP, RFA, combinations of various other surgeries
- Mean baseline AHI: 5 to 40 events/hr
- All patients had relatively less severe OSA (AHI <30-50)

Findings – *KQ 5 Treatment Effectiveness*

Comparison of Surgery and CPAP Treatments

- 12 studies (N = 24,215) compared surgical modalities with CPAP; 2 were RCTs
  - 1 (quality A), 11 (quality C)
- Mean AHI baseline: 5 to 80 events/hr
- Both RCTs found no difference in outcomes between
  - RFA and CPAP at 2 months
  - Mandibular advancement surgery and CPAP at 12 months

Findings – *KQ 5 Treatment Effectiveness*

Comparison of Surgery and MADs

- One RCT compared UPPP and MAD treatment (N=95)
  - 1 (quality B)
- Mean AHI baseline: 19 events/hr
- Follow-up: 4 years
- No clinical outcomes were evaluated
- Significantly more patients using MAD achieved 50% reduction in AHI at 12 months than those who had UPPP (80% vs 60%; p<0.05)
  - Similar results noted at 4 year follow-up

Findings – *KQ 5 Treatment Effectiveness*

Adverse Events in the Treatment of OSA

- RCTs were not powered to compare adverse events
- Adverse event data not collected from control or sham treatments
- **CPAP devices**
  - Generally 5 to 15% of patients report major problems when using CPAP (e.g., claustrophobia, discomfort, epistaxis)
  - All severe events resolved with discontinued CPAP use

Findings – *KQ 5 Treatment Effectiveness*

- **MADs**
  - Overall, about 2 to 4% of patients complained of jaw or TMJ pain
  - Dental crown damage occurred in 6% of patients in 1 study
- **Surgical Interventions**
  - Serious adverse events occurred among patients undergoing UPPP or bariatric surgery (perioperative mortality 0.2% for each category in largest eligible cohorts reporting)
  - Other major postsurgical complications and long-term adverse events were reported qualitatively

Findings – *KQ 5 Treatment Effectiveness*

KQ 5 Overall Summary

- *Moderate strength of evidence*
  - Treatment of OSA with CPAP (versus sham or control)
  - Use of CPAP is superior to MAD with regard to improved sleep study measures (no clinical outcomes were studied)
  - MAD is an effective treatment for OSA (versus sham or control)
- *Low strength of evidence*
  - Intensive weight loss programs is an effective treatment in obese patients with OSA

Findings – *KQ 5 Treatment Effectiveness*

KQ 5 Overall Summary (cont)

- *Insufficient evidence*
  - Which patients with CPAP or MAD benefit the most
  - Comparison of various different CPAP devices, delivery methods, and regimens
  - Comparison of different oral devices, other than MAD
  - Efficacy of surgical interventions for OSA (versus control, CPAP, or MAD)
  - Relative merits of surgical and MAD compared to CPAP
  - Management modalities (except intensive weight loss programs) effects on OSA treatment

Findings – *KQ 6 Treatment Compliance*

- 5 evaluated compliance with CPAP (N = 2160)
  - 1 (quality A), 1 (quality B), 3 (quality C)
  - Mean AHI baseline: 44 to 50 events/hr
  - Follow-up: 3 months to 4 year
- 1 evaluated compliance with MAD (N = 144)
  - 1 (quality C)
  - Mean AHI baseline: 23 events/hr
  - Follow-up: 31 months
  - Results not clearly reported

Findings – *KQ 6 Treatment Compliance*

Compliance with CPAP

- Most studies found higher AHI at baseline predicted greater compliance with CPAP; similar association noted with higher baseline ESS
- The only quality A rated study was also the largest trial (N=1103; 88% male; mean baseline AHI 50; follow-up 4 yrs)
- In the largest study, 16% of patients discontinued CPAP at 1 yr and 32% at 2 yrs

Findings – *KQ 6 Treatment Compliance*

KQ6 Overall Summary

- *Moderate strength of evidence*
  - Usage compliance is greater in patients with more severe OSA (higher AHI), for OSA patients prescribed CPAP
  - Higher ESS associated with higher compliance with CPAP
- *Insufficient evidence*
  - Potential predictors of compliance for MAD, and all other treatments

Findings – *KQ 7 Interventions to Improve Compliance*

- 18 RCTs (2 quality A, 8 quality B, 8 quality C)
  - All evaluated interventions to improve CPAP compliance

KQ7 Overall Summary

- *Low strength of evidence*
  - Interventions do not improve CPAP compliance among overweight patients with more severe OSA
- No intervention type (e.g., education, telemonitoring, behavioral interventions) was more promising than others

Findings – *KQ 8 Cost and Cost-effectiveness*

- **Economic evaluations of OSA treatment options (1 SR, 1 individual study)** (both rated as good quality)
- **SR developed an economic (York) model to evaluate the cost-effectiveness of CPAP for treating OSA**
  - 3 clinical endpoints were related to QALYs (ESS, BP, RTAs)
  - Base-case analysis: male aged 50 with specified CV risks
  - Base-case analysis compared costs and QALYs of CPAP vs. MADs vs. conservative management
  - Model characterizes the patient's lifetime prognosis in terms of 4 health states: OSA; OSA post coronary heart disease; OSA post stroke; and death

Findings – *KQ 8 Cost and Cost-effectiveness*

- Findings of York model (hypothetical cohort of men aged 50 with specified CV risk factors):
  - CPAP associated with both higher costs and higher QALYs compared with dental devices or conservative management
  - CPAP incremental cost-effectiveness compared with dental devices ~£ 4000 per QALY (CPAP may be considered cost-effective at a threshold per QALY of £ 20,000)
  - The effect of CPAP on ESS has an ICER below a cost-effectiveness threshold of £ 20,000 for moderate and severe OSA
  - Not possible to estimate differential effect of baseline severity of OSA on CVD and RTA risks

Findings – *KQ 8 Cost and Cost-effectiveness*

- **Cost-Effectiveness of Oral devices in OSA Treatment(1 study)**
  - One cost-utility analysis of the cost-effectiveness of oral appliances in the treatment of OSA
  - Markov model simulated costs and benefits of OSA treatment with MADs or CPAP based on their effects on QOL, RTAs, and CV effects
  - Many assumptions, including using AHI as a surrogate for effectiveness in reducing all adverse events related to OSA
  - ICERs (per additional QALY) $2,984 for MADs and $13,698 for CPAP were reported

Findings – *KQ8 Cost and Cost-effectiveness*

KQ 8 Overall Summary

- Not true cost-effectiveness studies
- Modeling studies only available
- Quality of modeling studies is **moderate**
- Long term outcomes no known
- Intermediate surrogate outcomes extrapolated based on assumptions
- Overall strength of evidence is **insufficient** or **low** for cost-effectiveness of CPAP treatment

Policy – *CMS National Coverage Determinations*

2009 NCD covering sleep tests to dx OSA

- Type I PSG in facility;
- Type II or III at home or facility; or
- Type IV measuring 3+ channels; devices measuring 3+ channels including actigraphy, oximetry, and peripheral arterial tone.
- Evidence
  - 2 AHRQ Reports: “Home Diagnosis of OSA-Hypopnea Syndrome,” and “OSA-Hypopnea Syndrome”
  - 33 individual studies
  - 5 guidelines
  - 4 professional society position statements

Policy – *CMS National Coverage Determinations*

2008 NCD covering CPAP for OSA therapy

- 12 week trial period if API or RDI ≥ 15/hr or 5-14 with additional symptoms;
- patient education; and
- positive diagnosis through PSG or HST.
- Evidence
  - 2 AHRQ Reports: "Home Diagnosis of OSA-Hypopnea Syndrome," and "OSA-Hypopnea Syndrome"
  - 29 individual studies
  - 6 guidelines
  - 4 professional society position statements

Overall Summary

- *High strength of evidence*
  - Using AHI greater than 30 events/hour can be an independent predictor of all-cause mortality
- *Moderate strength of evidence*
  - Portable monitors (Type III and IV)
  - Treatment of OSA with CPAP (versus sham or control)
  - Use of CPAP is superior to MAD with regard to improved sleep study measures (no clinical outcomes were studied)
  - MAD is an effective treatment for OSA (versus sham or control)
  - Usage compliance is greater in patients with more severe OSA (higher AHI), for OSA patients prescribed CPAP
  - Higher ESS associated with higher compliance with CPAP

Overall Summary

- *Low strength of evidence*
  - Portable monitors (Type II); Berlin Questionnaire; clinical prediction rules
  - A higher AHI was associated with incident diabetes (Association may be confounded by obesity)
  - Intensive weight loss programs is an effective treatment in obese patients with OSA
  - Interventions do not improve CPAP compliance among overweight patients with more severe OSA
  - **insufficient** or **low** for cost-effectiveness of CPAP treatment

Overall Summary

- *Insufficient evidence*
  - Comparison of portable monitors; STOP, STOP-Bang, ASAC, ESS, and Hawaii questionnaires
  - utility of phased testing (i.e., using a screening test result to determine the next test to be performed in a series), as compared to PSG
  - Utility of preoperative screening for OSA
  - To determine an association of AHI with other long term clinical outcomes (e.g., cardiovascular mortality, non fatal cardiovascular mortality, hypertension)
  - Which patients with CPAP or MAD benefit the most
  - Comparison of various different CPAP devices, delivery methods, and regimens

Overall Summary

- *Insufficient evidence*
  - Comparison of different oral devices, other than MAD
  - Efficacy of surgical interventions for OSA (versus control, CPAP, or MAD)
  - Relative merits of surgical and MAD compared to CPAP
  - Management modalities (except intensive weight loss programs) effects on OSA treatment
  - Potential predictors of compliance for MAD, and all other treatments

Questions or comments?

HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on these questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are Evidence based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective[1] as expressed by the following standards. [2]

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms.[3]

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

[1] Based on Legislative mandate: See RCW 70.14.100(2).

[2] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

[3] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

Using Evidence as the basis for a Coverage Decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. Availability of Evidence:

Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. Sufficiency of the Evidence:

Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence[4] using characteristics such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- the amount of evidence (sparse to many number of evidence or events or individuals studied);
- consistency of evidence (results vary or largely similar);
- recency (timeliness of information);
- directness of evidence (link between technology and outcome);
- relevance of evidence (applicability to agency program and clients);
- bias (likelihood of conflict of interest or lack of safeguards).

Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

3. Factors for Consideration - Importance

At the end of discussion at vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- risk of event occurring;
- the degree of harm associated with risk;
- the number of risks; the burden of the condition;
- burden untreated or treated with alternatives;
- the importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- the degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- value variation based on patient preference.

[4] Based on GRADE recommendation: http://www.gradeworkinggroup.org/FAQ/index.htm

Medicare Coverage and Guidelines

Payer	Coverage summary
Medicare Effective: 3/13/2008	**Medicare National Coverage Determinations Manual Chapter 1, Part 4** ***240.4 – Continuous positive Airway Pressure CPAP Therapy for Obstructive Sleep Apnea (OSA) (Various Effective Dates)*** *(Rev. 96, Issued: 10-15-08, Effective: 03-13-08. Implementation: 08-04-08)* https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=226&ncdver=3&NCAId=204&NcaName=Continuous+Positive+Airway+Pressure+(CPAP)+Therapy+for+Obstructive+Sleep+Apnea+(OSA)&IsPopup=y&bc=AAAAAAAAIAAA& **Nationally Covered Indications** B. Nationally Covered Indications Effective for claims with dates of service on and after March 13, 2008, the Centers for Medicare & Medicaid Services (CMS) determines that **CPAP therapy when used in adult patients with OSA is considered reasonable and necessary under the following situations**: 1. The use of CPAP is covered under Medicare when used in adult patients with OSA. Coverage of CPAP is initially limited to a 12-week period to identify beneficiaries diagnosed with OSA as subsequently described who benefit from CPAP. CPAP is subsequently covered only for those beneficiaries diagnosed with OSA who benefit from CPAP during this 12-week period. 2. The provider of CPAP must conduct education of the beneficiary prior to the use of the CPAP device to ensure that the beneficiary has been educated in the proper use of the device. A caregiver, for example a family member, may be compensatory, if consistently available in the beneficiary's home and willing and able to safely operate the CPAP device. 3. A positive diagnosis of OSA for the coverage of CPAP must include a clinical evaluation and a positive: a. attended PSG performed in a sleep laboratory; or b. unattended HST with a Type II home sleep monitoring device; or c. unattended HST with a Type III home sleep monitoring device; or d. unattended HST with a Type IV home sleep monitoring device that measures at least 3 channels. 4. The sleep test must have been previously ordered by the beneficiary's treating physician and furnished under appropriate physician supervision. 5. An initial 12-week period of CPAP is covered in adult patients with OSA if either of the following criterion using the AHI or RDI are met: a. AHI or RDI greater than or equal to 15 events per hour, or b. AHI or RDI greater than or equal to 5 events and less than or equal to 14 events per hour with documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders or insomnia, or documented hypertension, ischemic heart disease, or history of stroke. 6. The AHI or RDI is calculated on the average number of events of per hour. If the AHI or RDI is calculated based on less than 2 hours of continuous recorded sleep, the total number of recorded events to calculate the AHI or RDI during sleep testing must be at a minimum the number of events that would have been required in a 2-hour period. 7. Apnea is defined as a cessation of airflow for at least 10 seconds. Hypopnea is defined as an abnormal respiratory event lasting at least 10 seconds with at least a 30% reduction in thoracoabdominal movement or airflow as compared to baseline, and with at

least a 4% oxygen desaturation.8. Coverage with Evidence Development (CED): Medicare provides the following limited coverage for CPAP in adult beneficiaries who do not qualify for CPAP coverage based on criteria 1-7 above. A clinical study seeking Medicare payment for CPAP provided to a beneficiary who is an enrolled subject in that study must address one or more of the following questions:

a. In Medicare-aged subjects with clinically identified risk factors for OSA, how does the diagnostic accuracy of a clinical trial of CPAP compare with PSG and Type II, III & IV HST in identifying subjects with OSA who will respond to CPAP?

b. In Medicare-aged subjects with clinically identified risk factors for OSA who have not undergone confirmatory testing with PSG or Type II, III & IV HST, does CPAP cause clinically meaningful harm?

c. The study must meet the following additional standards:

d. The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.

e. The research study is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.

f. The research study does not unjustifiably duplicate existing studies.

g. The research study design is appropriate to answer the research question being asked in the study.

h. The research study is sponsored by an organization or individual capable of executing the proposed study successfully.

i. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is Food and Drug Administration-regulated, it also must be in compliance with 21 CFR Parts 50 and 56.

j. All aspects of the research study are conducted according to the appropriate standards of scientific integrity.

k. The research study has a written protocol that clearly addresses, or incorporates by reference, the Medicare standards.

l. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life-threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.

m. The clinical research study is registered on the ClinicalTrials.gov Web site by the principal sponsor/investigator prior to the enrollment of the first study subject.

n. The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured, including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned for publication in a peer-reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors. However, a full report of the outcomes must be made public no later than 3 years after the end of data collection.

o. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.

p. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability, or Medicaid eligibility.

C. Nationally Non-covered Indications

	Effective for claims with dates of services on and after March 13, 2008, other diagnostic tests for the diagnosis of OSA, other than those noted above for prescribing CPAP, are not sufficient for the coverage of CPAP. **240.4.1 – Sleep Testing for Obstructive Sleep Apnea (OSA) (Effective March 3, 2009)** *(Rev. 103, Issued: 07-10-09, Effective: 03-03-09, Implementation: 08-10-09)* http://www.cmms.hhs.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=330&ncdver=1&NCAId=227&NcaName=Sleep+Testing+for+Obstructive+Sleep+Apnea+(OSA)&IsPopup=y&bc=AAAAAAAAIAAA& B. Nationally Covered Indications Effective for claims with dates of service on and after March 3, 2009, the Centers for Medicare & Medicaid Services finds that the evidence is sufficient to determine that the results of the sleep tests identified below can be used by a beneficiary's treating physician to diagnose OSA, that the use of such sleep testing technologies demonstrates improved health outcomes in Medicare beneficiaries who have OSA and receive the appropriate treatment, and that these tests are thus reasonable and necessary under section 1862(a)(1)(A) of the Social Security Act. 1. Type I PSG is covered when used to aid the diagnosis of OSA in beneficiaries who have clinical signs and symptoms indicative of OSA if performed attended in a sleep lab facility. Type II or Type III sleep testing devices are covered when used to aid the diagnosis of OSA in beneficiaries who have clinical signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility. 2. Type IV sleep testing devices measuring three or more channels, one of which is airflow, are covered when used to aid the diagnosis of OSA in beneficiaries who have signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility. 3. Sleep testing devices measuring three or more channels that include actigraphy, oximetry, and peripheral arterial tone, are covered when used to aid the diagnosis of OSA in beneficiaries who have signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility. C. Nationally Non-Covered Indications Effective for claims with dates of services on and after March 3, 2009, other diagnostic sleep tests for the diagnosis of OSA, other than those noted above for prescribing CPAP, are not sufficient for the coverage of CPAP and are not covered.

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
National Institute for Health and Clinical Excellence (NICE), 2007	1.1 Current evidence on soft-palate implants for obstructive sleep apnoea (OSA) raises no major safety concerns, but there is inadequate evidence that the procedure is efficacious in the treatment of this potentially serious condition for which other treatments exist. Therefore, soft-palate implants should not be used in the treatment of this condition.	Literature review and expert consensus	Good

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
National Institute for Health and Clinical Excellence (NICE), 2008	1. Continuous positive airway pressure (CPAP) is recommended as a treatment option for adults with moderate or severe symptomatic obstructive sleep apnoea/hypopnoea syndrome (OSAHS). 2. CPAP is only recommended as a treatment option for adults with mild OSAHS if: a. They have symptoms that affect their quality of life and ability to go about their daily activities, and b. Lifestyle advice and any other relevant treatment options have been unsuccessful or are considered inappropriate. 3. The diagnosis and treatment of OSAHS, and the monitoring of the response, should be carried out by a specialist service with appropriately trained medical and support staff.	Literature review and expert consensus	Good
American Academy of Sleep Medicine, 2009	1. High risk patients with nocturnal symptoms of OSA should undergo sleep testing, including those who are obese and those with coronary heart disease, or significant tachyarrhythmias. 2. To ensure satisfactory therapeutic benefit from oral appliances (OA), patient with OSA should undergo PSG or an attended cardiorespiratory (type 3 PM) sleep study with the OA in place after final adjustments of fit have been performed.	Literature review and expert consensus	Fair
American Society of Anesthesiologists Task Force on Perioperative Management of Patients with OSA, 2006	1. **Preoperative evaluation:** A perioperative evaluation should include a comprehensive review of previous medical record, an interview with the patient and/or family, and a physical examination. The severity of the patient's OSA, the invasiveness of the diagnostic or therapeutic procedure, and the requirement for postoperative analgesics should be taken into account in determining whether a patient is at increased perioperative risk from OSA. The patient and patient's family should be informed of the potential implications of OSA on the patient's perioperative course. 2. **Preoperative preparation:** Preoperative initiation of continuous positive airway pressure should be considered, particularly is OSA is severe. For patients who do not respond adequately to CPAP noninvasive positive-pressure ventilation (NIPPV) should be considered. In addition, the preoperative use of mandibular advancement devices or oral appliances and preoperative weight loss should be considered when feasible. In patients at risk of perioperative complications from OSA, a preoperative determination must be made regarding whether surgery should be performed on an inpatient or outpatient basis.	Meta-analysis, systematic review and expert consensus	Good
American Academy of Sleep Medicine , 2010	**Diagnosis** 1. The presence and severity of obstructive sleep apnea (OSA) must be determined before initiating surgical therapy **(Standard)**. 2. The patient should be advised about potential surgical success rates and complications, the availability of alternative treatment options such as nasal positive airway pressure and oral appliances, and the levels of effectiveness and success rates of these alternative treatments **(Standard)**. **Treatment Objective** 1. The desired outcomes of treatment include resolution of the clinical signs and symptoms of obstructive sleep apnea and the normalization of sleep quality, the apnea-hypopnea index (AHI), and oxyhemoglobin saturation levels **(Standard)**.	Meta-analysis, review of published meta-analyses, systematic review, and expert consensus	Fair

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	Surgical Procedures 1. Tracheostomy: Tracheostomy has been shown to be an effective single intervention to treat obstructive sleep apnea. This operation should be considered only when other options do not exist, have failed, are refused, or when this operation is deemed necessary by clinical urgency **(Option)**. 2. Maxillo-Mandibular Advancement (MMA): MMA is indicated for surgical treatment of severe OSA in patients who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances, which are more often appropriate in mild and moderate OSA patients, have been considered and found ineffective or undesirable **(Option)**. 3. Uvulopalatopharyngoplasty (UPPP) as a single surgical procedure: UPPP as a sole procedure, with or without a tonsillectomy, does not reliably normalize the apnea-hypopnea index (AHI) when treating moderate to severe obstructive sleep apnea syndrome. Therefore, patients with severe OSA should initially be offered positive airway pressure therapy, while those with moderate OSA should initially be offered either positive airway pressure (PAP) therapy or oral appliances **(Option)**. 4. Multi-Level of Stepwise Surgery (MLS): Use of MLS, as a combined procedure or as stepwise multiple operations, is acceptable in patients with narrowing of multiple sites in the upper airway, particularly if they have failed uvulopalatopharyngoplasty as a sole treatment **(Option)**. 5. Laser Assisted Uvulopalatoplasty (LAUP): LAUP is not routinely recommended as a treatment for obstructive sleep apnea syndrome **(Standard)**. 6. Radiofrequency Ablation (RFA): RFA can be considered as a treatment in patients with mild to moderate obstructive sleep apnea who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances have been considered and found ineffective or undesirable **(Option)**. 7. Palatal Implants: Palatal implants may be effective in some patients with mild obstructive sleep apnea who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances have been considered and found ineffective or undesirable **(Option)**.		
American Academy of Sleep Medicine, 2006	**Weight Reduction** Successful dietary weight loss may improve the apnea-hypopnea index (AHI) in obese obstructive sleep apnea (OSA) patients. **(Guideline)** *This parameter is based on one Level I, one Level II, and 2 Level III papers.* Dietary weight loss should be combined with a primary treatment for OSA. (Kushida 2005; Kushida 2006; American Sleep Disorders Association, 1996) **(Option)** Bariatric surgery may be adjunctive in the treatment of OSA in obese patients. **(Option)** **Pharmacologic Agents** Selective serotonergic uptake inhibitors (SSRIs) are not recommended for treatment of OSA. **(Standard)** *The above recommendation is derived from 2 Level II publications and one level V using paroxetine and fluoxetine.*	Systematic review, expert consensus	Good

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	Protriptyline is not recommended as a primary treatment for OSA. **(Guideline)** *Three Level II and one Level V papers form the basis of this recommendation.* Methylxanthine derivatives (aminophylline and theophylline) are not recommended for treatment of OSA. **(Standard)** *For this recommendation, there are 3 Level II publications, all of which report similar negative findings.* Estrogen therapy (estrogen preparations with or without progesterone) is not indicated for the treatment of OSA. **(Standard)** *This recommendation is based on the results of 4 Level I, 3 Level II, and one Level V publications.* Modafinil is recommended for the treatment of residual excessive daytime sleepiness in OSA patients who have sleepiness despite effective positive airway pressure (PAP) treatment and who are lacking any other identifiable cause for their sleepiness. **(Standard)**		
American Academy of Sleep Medicine, 2007	**Indications for Portable Monitoring (PM)** "…PM may be used as an alternative to polysomnography (PSG) for the diagnosis of OSA in patients with a high pretest probability of moderate to severe OSA. PM should not be used in the patient groups with comorbidities, other sleep disorders, or for screening, as follows: • PM is not appropriate for the diagnosis of OSA in patients with significant comorbid medical conditions that may degrade the accuracy of PM, including, but not limited to, moderate to severe pulmonary disease, neuromuscular disease, or congestive heart failure. • PM is not appropriate for the diagnostic evaluation of OSA in patients suspected of having other sleep disorders, including central sleep apnea, periodic limb movement disorder (PLMD), insomnia, parasomnias, circadian rhythm disorders, or narcolepsy. • PM is not appropriate for general screening of asymptomatic populations. PM may be indicated for the diagnosis of OSA in patients for whom in-laboratory PSG is not possible by virtue of immobility, safety, or critical illness. PM may be indicated to monitor the response to noncontinuous positive airway pressure (CPAP) treatments for OSA, including oral appliances, upper airway surgery, and weight loss. **Conclusions** PM use should be integrated into a comprehensive program of patient evaluation and treatment under the direction of a sleep specialist board certified in sleep medicine. PM should only be used in populations with substantive published data on specificity and sensitivity. PM should be regulated by policies and procedures that maximize the reliability and validity of the diagnostic process.	Systematic review, expert consensus	Fair

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
University of Texas at Austin, School of Nursing, 2006	**Objective Assessment/Physical Examination** • Vital signs, including blood pressure, pulse, respirations: OSA is a leading cause of hypertension (The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure [JNC-7], 2003) **(Strength of Recommendation: B; Quality of Evidence: Fair)** • Height, weight, body mass index (BMI) calculation; BMI 25-30 indicates overweight, BMI >30 indicates obesity **(Strength of Recommendation: B; Quality of Evidence: Fair)** • HEENT: assess upper airway airflow obstruction, nasal polyps, septal deviation, mucosal congestion, turbinate hypertrophy, enlarged tonsils, large tongue volume, small jaw (micrognathia) • Measurement of neck circumference: >16 (women), >17 (men) • Neck exam: assess for thyroid enlargement **(Strength of Recommendation: B; Quality of Evidence: Fair)** • Cardiovascular exam: assess for rhythm regularity, bruits, murmurs (high prevalence with cardiovascular disease [CVD], CHF, arrhythmias, and hypertension (Hamilton, Solin, & Naughton, 2004; American Heart Association, 2005; JNC-7, 2003; Shahar 2001 **(Strength of Recommendation: B; Quality of Evidence: Fair)** • Pulmonary exam: assess breath sounds and quality of respirations • Abdominal exam: waist-hip ratio to determine body fat distribution: >0.72 = abnormal • Musculoskeletal: deformities, swelling, or pain with movement • Neurological exam: sensory function, balance, deep tendon reflexes • Psychiatric exam: administration of depression screening form (Netzer 2003; Schroder, 2005; Elliot, 2001; Mansfield & Naughton, 2005; Hamilton, Solin, & Naughton, 2004; Stevenson, 2003) **(Strength of Recommendation: B; Quality of Evidence: Fair)** **Diagnostic Procedures** 1. Laboratory studies • Sleep questionnaire (e.g., Epworth Sleepiness Scale), screen for sleep abnormalities (Elliott, 2001) **(Strength of Recommendation: A; Quality of Evidence: Good)** 2. Diagnostic tests • NPSG Sleep Study: Nocturnal polysomnographic diagnostic testing (Netzer 2003; Schroder, 2005; Elliot, 2001; Mansfield & Naughton, 2005; Hamilton, Solin, & Naughton, 2004; Rodsutti 2004) **(Strength of Recommendation: A; Quality of Evidence: Good)**	Systematic review	Poor

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
American Academy of Sleep Medicine, 2007	Auto-titrating continuous positive airway pressure (APAP) is not recommended to diagnose obstructive sleep apnea (OSA). (**Standard**) Patients with congestive heart failure, significant lung disease such as chronic obstructive pulmonary disease, patients expected to have nocturnal arterial oxyhemoglobin desaturation due to conditions other than OSA (e.g., obesity hypoventilation syndrome), patients who do not snore (either naturally or as a result of palate surgery), and patients who have central sleep apnea syndromes are not currently candidates for APAP titration or treatment. (**Standard**) APAP devices are not currently recommended for split-night titration. (**Standard**) Certain APAP devices may be used during attended titration with polysomnography to identify a single pressure for use with standard continuous positive airway pressure (CPAP) for treatment of moderate to severe OSA (**Guideline**) Certain APAP devices may be initiated and used in the self-adjusting mode for unattended treatment of patients with moderate to severe OSA without significant comorbidities (congestive heart failure [CHF], chronic obstructive pulmonary disease [COPD], central sleep apnea syndromes, or hypoventilation syndromes). (**Option**) Certain APAP devices may be used in an unattended way to determine a fixed CPAP treatment pressure for patients with moderate to severe OSA without significant comorbidities (CHF, COPD, central sleep apnea syndromes, or hypoventilation syndromes). (**Option**) Patients being treated with fixed CPAP on the basis of APAP titration or being treated with APAP must have close clinical follow-up to determine treatment effectiveness and safety. This is especially important during the first few weeks of positive airway pressure (PAP) use. (**Standard**) A reevaluation and, if necessary, a standard attended CPAP titration should be performed if symptoms do not resolve or if the APAP treatment otherwise appears to lack efficacy. (**Standard**)	Systematic review and expert consensus	Fair
American Academy of Sleep Medicine (2008)	**General Recommendations for Conducting Positive Airway Pressure (PAP) Titration Studies in Pediatric or Adult Patients with Obstructive** Sleep Apnea **(OSA)** All potential PAP titration candidates (including those candidates prior to a diagnostic study where the clinical suspicion of OSA is high and a split-night study is a possibility) should receive adequate PAP education, hands-on demonstration, careful mask fitting, and acclimatization prior to titration. **(Standard)** Recording the airflow signal generated by the PAP device or estimating airflow by measurement of the	Systematic review, expert consensus	Good

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	pressure difference between the mask and the outlet of the machine using a pressure transducer, with or without square root transformation of the signal, are acceptable methods for detecting apneas or hypopneas. **(Consensus)** Nasal airflow obtained from a thermistor or thermocouple placed under the PAP mask is not an acceptable method for detecting apneas or hypopneas. **(Consensus)** Respiratory effort–related arousals (RERAs) may be estimated by flattening of the inspiratory airflow profile associated with an arousal when airflow changes do not meet criteria for apneas or hypopneas. **(Consensus)** Sawtooth patterns in the unfiltered airflow or mask pressure tracings and/or detection of vibration by piezoelectric transducers or microphones applied to the neck are acceptable methods for detecting snoring. **(Consensus)** **<u>Recommendations for Conducting Continuous Positive Airway Pressure (CPAP) Titration Studies in Pediatric or Adult Patients with OSA</u>** **General Recommendations for CPAP Titration Studies** CPAP should be increased until the following obstructive respiratory events are eliminated (no specific order) or the recommended maximum CPAP is reached: apneas, hypopneas, RERAs, and snoring. **(Consensus)** The recommended minimum starting CPAP should be 4 cm H_2O in pediatric and adult patients. **(Consensus)** The recommended maximum CPAP should be 15 cm H_2O for patients <12 years and 20 cm H_2O for patients ≥12 years. **(Consensus)** Methodology to determine CPAP a priori has insufficient evidence, although a higher starting CPAP may be selected for patients with an elevated body mass index (BMI) and for retitration studies. **(Consensus)** **Full-night CPAP Titration Studies** CPAP should be increased by at least 1 cm H_2O with an interval no shorter than 5 min, with the goal of eliminating obstructive respiratory events. **(Consensus)** CPAP should be increased (according to the criterion in previous recommendation) if at least 1 obstructive apnea is observed for patients <12 years or if at least 2 obstructive apneas are observed for patients ≥12		

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	years. **(Consensus)** CPAP should be increased if at least 1 hypopnea is observed for patients <12 years or if at least 3 hypopneas are observed for patients ≥12 years. **(Consensus)** CPAP should be increased if at least 3 RERAs are observed for patients <12 years or if at least 5 RERAs are observed for patients ≥12 years. **(Consensus)** CPAP may be increased if at least 1 min of loud or unambiguous snoring is observed for patients <12 years or if at least 3 min of loud or unambiguous snoring are observed for patients ≥12 years. **(Consensus)** "Exploration" of CPAP above the pressure at which control of abnormalities in respiratory parameters is achieved should not exceed 5 cm H_2O. **(Consensus)** If the patient awakens and complains that the pressure is too high, the pressure should be restarted at a lower pressure, chosen as one that the patient reports is comfortable enough to allow return to sleep. **(Consensus)** "Down" titration is not required but may be considered as an option. **(Consensus)** **Split-night CPAP Titration Studies** The titration algorithm for split-night CPAP titration studies should be identical to that of full-night CPAP titration studies. **(Guideline)** Of note, there are insufficient data to make any recommendations for split-night CPAP titration studies in children <12 years. **<u>Recommendations for Conducting Bilevel PAP (BPAP) Titration Studies in Pediatric or Adult Patients with OSA</u>** **General Recommendations for BPAP Titration Studies** If the patient is uncomfortable or intolerant of high pressures on CPAP, the patient may be tried on BPAP. If there are continued obstructive respiratory events at 15 cm H2O of CPAP during the titration study, the patient may be switched to BPAP. **(Consensus)** BPAP (inspiratory positive airway pressure [IPAP] and/or expiratory positive airway pressure [EPAP], depending on the type of obstructive respiratory event) should be increased until the following events are eliminated (no specific order) or the recommended maximum IPAP is reached: apneas, hypopneas, RERAs,		

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	and snoring. **(Consensus)** The recommended minimum starting IPAP and EPAP should be 8 cm H_2O and 4 cm H_2O, respectively, in pediatric and adult patients **(Consensus)**. In addition, when switching from CPAP to BPAP, the Task Force recommends that the minimum starting EPAP should be set at 4 cm H_2O or the CPAP level at which obstructive apneas were eliminated. The recommended maximum IPAP should be 20 cm H_2O for patients <12 years or 30 cm H_2O for patients ≥12 years. **(Consensus)** Methodology to determine IPAP or EPAP a priori has insufficient evidence, although a higher starting IPAP or EPAP may be selected for patients with an elevated BMI and for retitration studies. **(Consensus)** The recommended minimum IPAP-EPAP differential is 4 cm H_2O and the recommended maximum IPAP-EPAP differential is 10 cm H_2O. **(Consensus)** **Full-night BPAP Titration Studies** IPAP and/or EPAP (depending on the type of obstructive respiratory event) should be increased by at least 1 cm H_2O apiece with an interval no shorter than 5 min, with the goal of eliminating obstructive respiratory events. **(Consensus)** IPAP and EPAP should be increased (according to the criterion in the previous recommendation) if at least 1 obstructive apnea is observed for patients <12 years or if at least 2 obstructive apneas are observed for patients ≥12 years. **(Consensus)** IPAP should be increased if at least 1 hypopnea is observed for patients <12 years or if at least 3 hypopneas are observed for patients ≥12 years. **(Consensus)** IPAP should be increased if at least 3 RERAs are observed for patients <12 years or if at least 5 RERAs are observed for patients ≥12 years. **(Consensus)** IPAP may be increased if at least 1 min of loud or unambiguous snoring is observed for patients <12 years or if at least 3 min of loud or unambiguous snoring are observed for patients ≥12 years. **(Consensus)** "Exploration" of IPAP above the pressure at which control of abnormalities in respiratory parameters is achieved should not exceed 5 cm H_2O. **(Consensus)** If the patient awakens and complains that the pressure is too high, the pressure should be restarted at a		

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	lower IPAP, chosen as one that the patient reports is comfortable enough to allow return to sleep. **(Consensus)** A decrease in IPAP or setting BPAP in spontaneous-timed (ST) mode with backup rate may be helpful if treatment-emergent central apneas (i.e., complex sleep apnea) are observed during the titration study. **(Consensus)** "Down" titration is not required but may be considered as an option. **(Consensus)** **Split-night BPAP Titration Studies** The titration algorithm for split-night BPAP titration studies should be identical to that of full-night BPAP titration studies. **(Consensus)** Of note, there are insufficient data to make any recommendations for split-night BPAP titration studies in children <12 years. **<u>Important Considerations for PAP Titration Studies in Pediatric or Adult Patients with OSA</u>** **Acceptable PAP Titration Study** The CPAP or BPAP selected for patient use following the titration study should reflect control of the patient's obstructive respiration by a low (preferably <5 per hour) RDI at the selected pressure, a minimum sea level oxygen saturation (SpO_2) above 90% at the pressure, and with a leak within acceptable parameters at the pressure. **(Consensus)** Grading system: An optimal titration reduces RDI <5 per hour for at least a 15-min duration and should include supine rapid-eye-movement (REM) sleep at the selected pressure that is not continually interrupted by spontaneous arousals or awakenings. **(Consensus)** Grading system: A good titration reduces the overnight RDI ≤10 per hour or by 50% if the baseline RDI <15 per hour and should include supine REM sleep that is not continually interrupted by spontaneous arousals or awakenings at the selected pressure. **(Consensus)** Grading system: An adequate titration is one that does not reduce the overnight RDI ≤10 per hour but does reduce the RDI by 75% from baseline (especially in severe OSA patients), or one in which the titration grading criteria for optimal or good are met with the exception that supine REM sleep did not occur at the selected pressure. **(Consensus)** **Repeat PAP Titration Study**		

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	A repeat PAP titration study should be considered if the initial titration does not achieve a grade of optimal or good and, if it is a split-night polysomnography (PSG) study, it fails to meet American Academy of Sleep Medicine (AASM) criteria. **(Consensus)** **Leak and Comfort** PAP mask refit or readjustment should be performed whenever any significant unintentional leak is observed. **(Consensus)** There is insufficient evidence for what constitutes a clinically significant leak given mask fit and other factors; however, in general, an unacceptable leak for PAP is one that is substantially higher than the leak recorded at a given pressure from a well-fitted, applied, and secured interface. The acceptable leak will always exceed the intentional leak, which depends on the applied pressure and interface type. The intentional leak vs. pressure relationship is usually supplied by the manufacturer of each interface. **(Consensus)** Pressure waveform modification technologies may improve patient comfort and adherence with PAP. **(Consensus)** **Positional and Sleep Stage Factors** Ideally, the patient should be recorded in supine REM sleep for at least 15 min at the designated optimal pressure during the PAP titration study. If the patient is in REM sleep but not in the supine position while at the designated optimal pressure, the patient may be awakened and instructed to lie in the supine position. **(Consensus)** **Supplemental Oxygen** Supplemental O_2 should be added during the PAP titration when, prior to the PAP titration, the patient's awake supine SpO_2 while breathing room air is ≤88%. Supplemental O_2 may also be added during the PAP titration when SpO_2 is ≤88% for ≥5 minutes in the absence of obstructive respiratory events. In both instances, supplemental O_2 should be introduced at 1 L/min and titrated upwards to achieve a target SpO_2 between 88% and 94%. **(Consensus)** The minimum starting O_2 rate should be 1 L/min (both pediatric and adult patients). **(Consensus)** O_2 rate should be increased by 1 L/min, with an interval no shorter than 15 min, until SpO_2 is between 88% and 94%. **(Consensus)** Optimally, supplemental O_2 should be connected to the PAP device outlet (using a T-connector).		

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	(Consensus) "Weaning" down of O_2 supplementation by employing BPAP or by further increasing IPAP (if BPAP was already instituted and if the patient tolerates the higher inspiratory pressures) can be attempted. **(Consensus)** **Adaptive Servoventilation** Adaptive servoventilation may be considered if the patient is observed to have Cheyne-Stokes respiration or if treatment emergent central sleep apnea (i.e., complex sleep apnea) during the titration study is not eliminated by down titration of pressure. **(Consensus)** **Follow-up After the PAP Titration Study** PAP usage should be objectively monitored to help assure utilization. **(Standard)** Troubleshooting of problems encountered while on PAP, management of side effects, and methods to increase adherence should be a part of the close follow-up of the patient on PAP. **(Standard)**		
American Society of Plastic Surgeons, 2009	Recommendations Supporting Evidence Grade Obstructive Sleep Apnea (OSA) Patient Selection **Patient selection** The physical examination should include an evaluation of the airway, nasopharyngeal characteristics, tonsil and tongue size, neck circumference, and body mass index (BMI). (Liistro 2003; Kheterpal 2006) Grade: B **Preoperative** Continuous positive airway pressure (CPAP) has been shown to be effective at treating OSA; preoperative CPAP may be beneficial, especially in patients who are already using home CPAP (Gupta 2001; Rennotte 1995; Ballester 1999; Jenkinson 1999; Spicuzza 2006) Grade: A, B If premedication, such as benzodiazepines, will be administered, patients must be monitored continuously for any signs of respiratory compromise; CPAP should be available for use if the patient becomes sleepy and cannot control his or her own airway. (Gupta 2001; Rennotte 1995; Hoijer 1994; Dolly & Block, 1982) Grade: B **Patient Selection** The medical history should include questions about current symptoms (e.g., cough, dyspnea, wheezing) and frequency of symptoms; intensity of treatment (did patient require therapy at a medical facility?); current medications; recent use of rescue medications; tolerance to aspirin, cold air, dust, or smoke; smoking history; and previous exposures to general anesthesia and endotracheal intubation. (Warner, 2000) Grade: D**	Systematic review, expert consensus	Fair

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	A complete physical examination should be performed, including chest auscultation, assessment of skin coloration, and chest radiography when indicated. Patients should be free of symptoms and have optimal lung function. If a patient presents with symptoms, elective surgery should be postponed, if possible, pending resolution of symptoms. Patients with severe or uncontrolled disease, or those in which pulmonary status is uncertain, should be referred to a pulmonologist for assessment of pulmonary function. If patients have been on steroid therapy during the past 6 mo before surgery, additional steroid support may be necessary. **Preoperative** If endotracheal intubation is required, consider preoperative prophylaxis (corticosteroids, topical lidocaine, $beta_2$-adrenergic agonists). (Groeben 2000; Maslow 2000; Groeben "Both local anesthetics and salbutamol," 2002; Silvanus, Groeben, & Peters, 2004) Grade: A Consider preoperative sedation with benzodiazepines. (Expert opinion) Grade: D		
American Academy of Sleep Medicine, 2006	Treatment with continuous positive airway pressure (CPAP) must be based on a prior diagnosis of obstructive sleep apnea (OSA) established using an acceptable method **(Standard**). ***This recommendation is based on previous American Academy of* Sleep *Medicine (AASM) practice parameters for the indications for polysomnography and related procedures (2005 update).*** CPAP is indicated for the treatment of moderate to severe OSA **(Standard)**. ***This recommendation is based on 24 randomized controlled trials meeting Level I or II evidence-based medicine criteria.*** CPAP is recommended for the treatment of mild OSA **(Option)**. ***This recommendation as an option is based on mixed results in 2 Level I and 3 Level II outcome studies in patients with mild OSA.*** CPAP is indicated for improving self-reported sleepiness in patients with OSA **(Standard)**. ***This recommendation is based on 10 randomized controlled trials in which CPAP reduced* sleep*iness more than control procedures in patients with OSA.*** CPAP is recommended for improving quality of life in patients with OSA **(Option)**. ***This recommendation***	Systematic review and expert consensus	Good

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	as an option is based on inconsistent results from 2 Level I studies and 4 Level II studies with placebo control, and 1 Level II study with conservative therapy as the control. CPAP is recommended as an adjunctive therapy to lower blood pressure in hypertensive patients with OSA **(Option)**. ***This recommendation as an option is based on 9 clinical trials, 6 of which did not find changes in mean arterial pressure compared to placebo.*** Full-night, attended polysomnography performed in the laboratory is the preferred approach for titration to determine optimal positive airway pressure; however, split-night, diagnostic-titration studies are usually adequate **(Guideline)**. ***This recommendation is based on 1 Level II and 6 Level IV studies.*** CPAP Usage should be objectively monitored to help assure utilization **(Standard)**. ***This recommendation is based on overwhelming evidence at all levels indicating patients with OSA overestimate their positive airway pressure. Level I and Level II studies indicate that objectively-measured nightly CPAP "time on" ranges from 3.5 hours/night in minimally symptomatic new patients to 7.1 hours/night in established users.*** Close follow-up for positive airway pressure (PAP) usage and problems in patients with OSA by appropriately trained health care providers is indicated to establish effective utilization patterns and remediate problems, if needed. This is especially important during the first few weeks of PAP use **(Standard)**. ***This recommendation is based on 61 studies that examined management paradigms and collected acceptance, utilization, and adverse events; 17 of these studies qualified as Level I.*** The addition of heated humidification is indicated to improve CPAP utilization **(Standard)**.***This recommendation is based on 3 Level I studies. There was 1 Level II study that did not find increased utilization with heated humidification. Three additional studies favored heated humidification over unheated or non-humidified CPAP.*** The addition of a systematic educational program is indicated to improve PAP utilization **(Standard)**. ***This recommendation is based on 4 Level I studies, 1 Level II study, and 1 Level III study.*** After initial CPAP setup, long-term follow-up for CPAP-treated patients with OSA by appropriately trained health care providers is indicated yearly and as needed to troubleshoot PAP mask, machine, or usage problems **(Option)**. ***This recommendation as an option is based on task force and SPC member consensus.*** CPAP and bi-level positive airway pressure (BPAP) therapy are safe; side effects and adverse events are		

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	mainly minor and reversible **(Standard)**. ***This recommendation is based on more than 23 published reports.*** While the literature mainly supports CPAP therapy, BPAP is an optional therapy in some cases where high pressure is needed and the patient experiences difficulty exhaling against a fixed pressure or coexisting central hypoventilation is present **(Guideline)**. ***This recommendation is based on 2 Level I studies which yielded no evidence that BPAP improves efficacy or adherence in the management of OSA compared to CPAP.*** BPAP may be useful in treating some forms of restrictive lung disease or hypoventilation syndromes associated with daytime hypercapnia **(Option)**. ***This recommendation as an option is based on 11 studies all graded at Level III or better that overall found improvement associated with BPAP therapy.***		
European Federation of Neurological Societies, 2007	1. Patients with neurologic diseases often have significant sleep disorders which may affect both nocturnal sleep and daytime function with increased morbidity and even mortality. Many of these disorders are potentially treatable. Therefore, increased awareness should be directed toward sleep disorders in patient with neurodegenerative, cerebrovascular and neuromuscular diseases. Despite that, there are practically no grade A or B studies in this area. 2. A polysomnography (PSG) is usually a diagnostic minimum for the diagnoses of the most commonly reported sleep disorders in patients with neurologic diseases. 3. In patients with nocturnal motor and/behavior manifestations, a full video-PSG/video-electroencephalography (EEG)-PSG should be considered. 4. Respiratory polygraphy has a moderate sensitivity and specificity in the diagnosis of obstructive sleep apnea syndrome (OSAS) without neurologic diseases, but its value for diagnosis of other sleep-related breathing disorder (SBD) or in patients with OSAS with neurologic diseases has not been evaluated compared to gold standard PSG. 5. Limited channel polygraphy oximetry has a poor to moderate sensitivity-specificity for the identification of OSAS in patients without neurologic diseases. Oximetry cannot differentiate between obstructive and central sleep apnea or is insufficient to identify stridor. It is possible that oximetry has a role for the screening of hypoventilation in patients with neuromuscular weakness. Furthermore, oximetry may be useful for the control of continuous positive airway pressure (CPAP) treatment. 6. Patients with sleep-disordered breathing and muscle weakness and/or cardiac or pulmonary co-morbidity may present a sleep hypoventilation syndrome (SHVS), which manifests early as increased CO_2, hence $PaCO_2$ should be considered and controlled in such cases during sleep recordings. 7. Fixed pressure CPAP/auto-adjusted CPAP is the most effective treatment of OSAS. This probably also includes patients with OSAS and neurologic diseases. However, there is a need for further evaluation of the effect of CPAP in patients with OSAS and neurologic diseases.	Meta-analyses review, systematic review, and expert consensus	Fair

Recommending Body, Year Published	Guideline(s)	Evidence Base	Overall Quality
	8. Bi-level PAP/variable PAP, noninvasive positive pressure ventilation (NIPPV) and volumetric ventilation is useful for SBD-like central apneas, Cheyne-Stokes breathing, and alveolar hypoventilation. 9. There is a clear need for further studies focusing on the diagnostic procedures and treatment modalities in patients with sleep disorders and neurologic diseases.		

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document: What are the key factors and health outcomes and what evidence is there?

Sleep Apnea Diagnosis	
Safety Outcomes	**Safety Evidence**
Morbidity	
Mortality	
Efficacy – Effectiveness Outcomes	**Efficacy / Effectiveness Evidence**
Sensitivity/specificity	
Validity	
Clinical utility	
Repeatability/reproducibility	
Special Population / Considerations Outcomes	**Special Population Evidence**
Gender	
BMI	
Age	
Diabetes	

Cardiovascular disease	
Hypertension	
Clinical symptoms	
Prior stroke	
Airway characteristics	
Cost	**Cost Evidence**
Total Health Care Costs / Societal Costs	
Cost Effectiveness	

Clinical Committee Evidence Votes - Diagnosis

First voting question - Diagnosis
The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Is there sufficient evidence under some or all situations that the technology is:

	Unproven (no)	**Equivalent** (yes)	**Less** (yes)	**More** (yes)
Effective				
Safe				
Cost-effective				

Discussion - Diagnosis
Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second vote - Diagnosis
Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

_____Not Covered. _____ Covered Unconditionally. _____ Covered Under Certain Conditions.

Discussion Item - Diagnosis

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Sleep Apnea Treatment	
Safety Outcomes	**Safety Evidence**
Morbidity	
Mortality	
Surgical complications	
Speech/voice changes	
Dental complications	
Claustrophobia	
Discomfort	
Epistaxis	
Efficacy – Effectiveness Outcomes	**Efficacy / Effectiveness Evidence**
All Cause Mortality	
Cardiovascular Mortality	
Nonfatal cardiovascular mortality	
Stroke	
Hypertension	

Diabetes/ HbA1c	
QOL	
Apnea Hypopnea Index (AHI)	
Epworth Sleepiness Scale (ESS)	
Other measures	
Compliance	
Special Population / Considerations Outcomes	**Special Population Evidence**
Gender	
Race	
BMI	
Age	
Diabetes	
Cardiovascular disease	
Hypertension	
OSA Severity	
Prior stroke	
Airway characteristics	
Cost	**Cost Evidence**
Total Health Care Costs / Societal Costs	
Cost Effectiveness	

Clinical Committee Evidence Votes - Treatment

First voting question - Treatment

The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the

public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Is there sufficient evidence under some or all situations that the technology is:

	Unproven (no)	**Equivalent** (yes)	**Less** (yes)	**More** (yes)
Effective				
Safe				
Cost-effective				

Discussion - Treatment
Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second vote - Treatment
Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

_____Not Covered. _____ Covered Unconditionally. _____ Covered Under Certain Conditions.

Discussion Item - Treatment

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Clinical Committee Findings and Decisions

Next Step: Cover or No Cover
If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions
If covered with conditions, the Committee will continue discussion.

1) Does the committee have enough information to identify conditions or criteria?
   - Refer to evidence identification document and discussion.
   - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
   - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.

2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
   - What are the known conditions/criteria and evidence state
   - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff ; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Efficacy Considerations:

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
  - Direct outcome or surrogate measure
  - Short term or long term effect
  - Magnitude of effect
  - Impact on pain, functional restoration, quality of life
  - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests' accuracy
  - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
    - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
    - Adverse effect on health that can result in lasting harm or can be life-threatening.
- Other morbidity concerns
- Short term or direct complication versus long term complications
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

Overall

- What is the evidence about alternatives and comparisons to the alternatives
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?