Obstructive Sleep Apnea Case Study Facilitator Guide

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August 2014

What are important components of a good sleep history?

In addition to a comprehensive medical history, a focused sleep history involves asking about bed time, how long it takes to fall asleep on average (sleep latency), the number of awakenings during the night (or major sleep portion, in person who sleeps during the day), the reasons for these awakenings, how long does it take to fall asleep after these awakenings, final wake up time, and average sleep duration. A distinction should be made between weekday and weekend sleep routine. Patient should be asked about snoring, gasping and choking during sleep, and witnessed apneas. Questions should be asked about bedtime routine prior to falling asleep, including the use of medication (prescribed or over the counter) to fall asleep, the bedroom environment, the use of alcohol and caffeinated beverages during the day. The patient's satisfaction with their sleep, whether they feel refreshed when they wake up and/or whether there is daytime hypersomnolence should be addressed. Problems with memory or concentration should be explored. Inquiries should be made about sleep walking, unusual movements during sleep, sleep paralysis (sensation of being awake but paralyzed just as you are falling asleep or just as you are waking up), and falling out of bed. Ideally, the sleep history would include input from the sleep partner.

An evaluation of health conditions affected by sleep apnea including hypertension, stroke, myocardial infarction, memory and concentration issues, and motor vehicle accidents should be considered.

Elements of a comprehensive screening sleep history can be found here:

http://www.aasmnet.org/Resources/MedSleep/(Harding)questions.pdf

Epstein LJ; Kristo D; Strollo PJ; Friedman N; Malhotra A; Patil SP; Ramar K; Rogers R; Schwab RJ; Weaver EM; Weinstein MD. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 2009;5(3):263-276.

What is the differential diagnosis of daytime hypersomnolence?

Excessive sleepiness is undesired sleepiness that occurs when an individual would usually be expected to be awake and alert. Excessive daytime sleepiness (EDS) is a clinical syndrome with a varied underlying etiology. It has been associated with sleep apnea and may indeed be the presenting complaint, but its correlation with objectively diagnosed sleep apnea is not strong. Young et al. reported in their study of middle aged adults, that only 22% of women and 17% of the men who had objectively sleep apnea also reported EDS. Thus, it is important to consider all possible causes when evaluating a patient with EDS. Causes of EDS include insufficient sleep duration/sleep deprivation, sleep disorders such as OSA, narcolepsy, idiopathic hypersomnia, and periodic limb movement disorder, a variety of medical conditions (e.g. diabetes, cancer, obesity), neurological conditions (e.g. Parkinson Disease), psychiatric conditions (e.g. depression), and side effects of many medications (e.g. Alpha-adrenergic blocking agents). Table 1, summarizes many of the important causes of EDS.

Differential Diagnosis of EDS

Insufficient Sleep
Sleep deprivation
Environmental causes of poor sleep
Sleep Disorders
OSA
Central sleep apnea
Insomnia
Restless Legs Syndrome
Periodic Limb Movement Disorder
Circadian Rhythm Disorders
Hypersomnia
Narcolepsy
Idiopathic Hypersomnia
Kleine-Levin Syndrome
Neurologic Disorders
Parkinson Disease
Alzheimer Disease
Dementia with Lewy bodies
Post traumatic
Myotonic Dystrophy
Encephalitis lethargica
Medical Disorders
Hypothyroidism
Obesity
End-stage renal disease
Adrenal insufficiency
Hepatic encephalopathy

Prader-Willi syndrome

Psychiatric Disorders
Depression
Anxiety
Substance abuse
  Alcohol
  Narcotics
  Opioid abuse
  Stimulant withdrawal
Psychogenic sleepiness

Medication Antipsychotics Benzodiazepines Nonbenzodiazepine sedatives Barbiturates Opioid analgesics Beta blockers (lipophilic) Antihistamines Anticonvulsants Sedative antidepressants

Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230-5.

Bixler EO, Vgontzas AN, Lin HM, Calhoun SL, Vela-Bueno A, Kales A. Excessive daytime sleepiness in a general population sample: the role of sleep apnea, age, obesity, diabetes, and depression. The Journal of clinical endocrinology and metabolism 2005;90:4510-5.

What clinical tools are available to measure daytime hypersomnolence?

Symptoms of EDS warrant a careful medical and sleep history, to determine medical conditions that contribute to sleepiness, sleep habits, sleep duration, and presence of risks for sleep disorders.

A commonly used, validated screening tool to evaluate subjective symptoms of EDS is the **Epworth sleepiness scale (ESS)**. ESS measures self-rated average sleep propensity (chance of dozing) over common situations that almost everyone encounters. Eight items are rated on a scale of 0–3, total scores range 0–24, with higher scores indicating a greater propensity to fall asleep in different situations. In samples of sleep apnea patients, it shows high internal consistency and correlates with objective measures of sleep latency. Normal is assumed to be 10 or less. ESS scores of 16 or greater are associated with severe sleepiness.

http://www.thoracic.org/assemblies/srn/questionaires/ess.php

STANFORD SLEEPINESS SCALE (SSS): The SSS is another validated subjective measure of sleepiness. It is typically used as a research tool to measure the impact of short-term acute sleep loss on subjective sleepiness. During the SSS, one of seven statements is chosen that best describes an individual's level of sleepiness:

1 = feeling active, vital, alert, wide awake

2 = functioning at a high level, not at peak, able to concentrate

3 = relaxed, awake, not at full alertness, responsive

4 = a little foggy, not at peak, let down

5 = fogginess, losing interest in remaining awake, slowed

6 = sleepiness, prefer to be lying down, fighting sleep, woozy

7 = almost in reverie, sleep onset soon, losing struggle to remain awake

Individuals, who choose the fourth to seventh statement at a time when they should be feeling alert, may have excessive sleepiness.

http://www.thoracic.org/assemblies/srn/questionaires/sss.php

Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14:540-5.

Johns MW. Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth Sleepiness Scale. Chest 1993;103:30-6.

Hoddes E, Zarcone V, Smythe H, Phillips R, Dement WC. Quantification of sleepiness: a new approach. Psychophysiology. 1973 Jul;10(4):431-6

What are important components of a good sleep physical examination?

The physical exam can suggest increased risk and determine co-morbidities, and potential consequences of sleep apnea. It should include an evaluation of the cardiac respiratory and neurological systems. Anthropometric measures (neck circumference, height, and weight) should be included. Signs of upper airway narrowing (nose, hard, and soft palate, neck size, chin, jaw, and facial structure) that can increase risk for sleep apnea should be evaluated.

Physical exam findings that suggest increased risk of sleep apnea include neck circumference > 17 inches (> 43.2 cm) in men, > 16 inches (> 40.6 cm) in women, body mass index (BMI) > 30 kg/m^2, a Modified Mallampati score of 3 or 4, the presence of retrognathia, overjet, lateral peritonsillar narrowing, macroglossia, tonsillar hypertrophy, elongated/enlarged uvula, high arched/narrow hard palate, and nasal abnormalities (polyps, deviation, valve abnormalities, turbinate hypertrophy).

Epstein LJ; Kristo D; Strollo PJ; Friedman N; Malhotra A; Patil SP; Ramar K; Rogers R; Schwab RJ; Weaver EM; Weinstein MD. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 2009;5(3):263-276

Mallampati Score

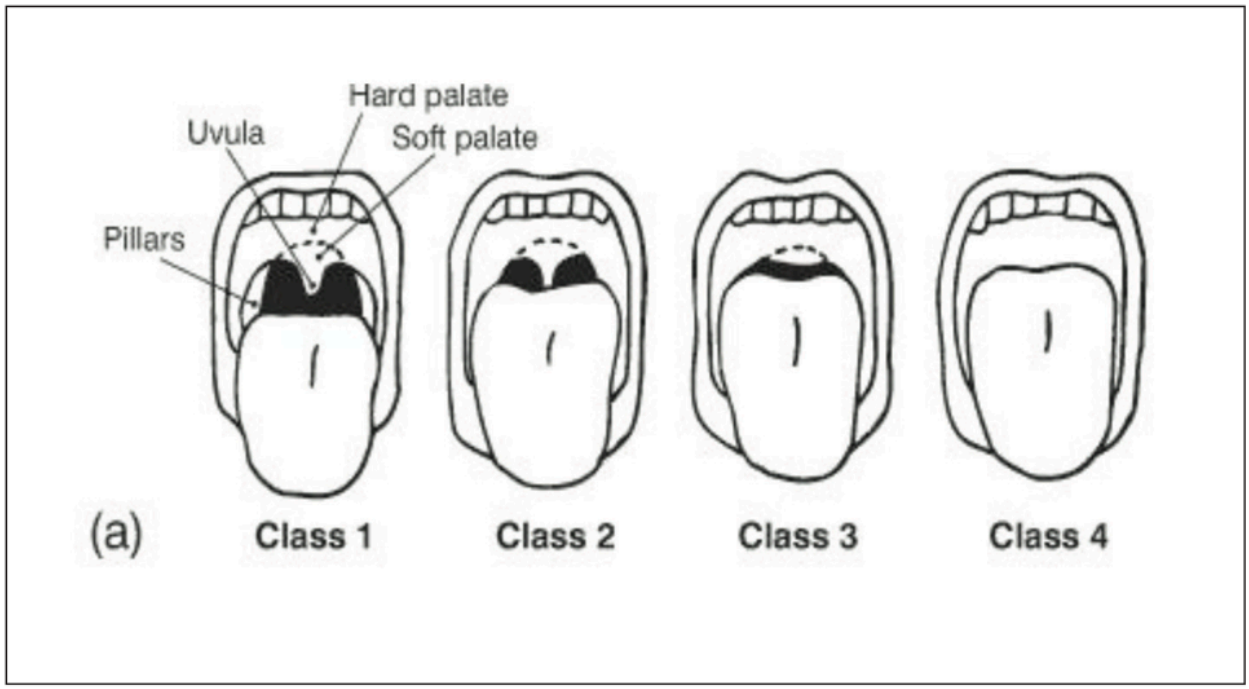


Figure 1. The Mallampati score:
Class 1. Complete visualization of the soft palate
Class 2. Complete visualization of the uvula
Class 3. Visualization of only the base of the uvula
Class 4. Soft palate is not visible at all

The modified Mallampati score is similar to above except the patient is asked to keep the tongue inside the mouth.

Mallampati S, Gatt S, Gugino L, Desai S, Waraksa B, Freiberger D, Liu P. A clinical sign to predict difficult tracheal intubation: a prospective study. Can Anaesth Soc J 1985; 32(4): 429-434.

Myers KA, Mrkobrada, M, Simel, D. Does This Patient Have Obstructive Sleep Apnea? The Rational Clinical Examination Systematic Review. JAMA. 2013;310(7):731-741.

What are risk factors for obstructive sleep apnea (OSA), in general, and this patient in particular?

Risk factors noted on physical exam include obesity (BMI >30), an increased neck circumference (>17 inches for men or >16 inches for women), and the presence of craniofacial abnormalities that cause narrowing of the upper airway including retrognathia, large tonsils, high arched palate, nasal polyps, turbinate hypertrophy, and Mallampati score of three or four.

Gender is an important risk factor. Population based studies suggest that men have a two to three fold increased risk of sleep apnea compared with women. Men and women may also differ in their presenting symptoms as well. Whereas a typical male patient with sleep apnea tends to report excessive daytime sleepiness and loud snoring, women are less likely to endorse these classic symptoms and more likely to report symptoms of daytime fatigue, morning headache, and mood disturbance.[9] Interestingly, women's risk for OSA increases post menopause and may improve with hormonal replacement therapy, suggesting a hormonal role in development of sleep apnea in women.

This risk factors in this patient include "*male gender*, *body mass index of 35 kg/m^2, Mallampati score III, high arched palate, and neck size 17.5 inches (44.5 cm)."*

Video: Review of Sleep Apnea Pathophysiology

https://www.youtube.com/watch?v=NZszF7OaDVE

Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. JAMA 2004; 291:2013-6.

Bixler EO, Vgontzas AN, Lin HM, et al. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med 2001;163:608-13.

Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002;165:1217-39.

Collop NA, Adkins D, Phillips BA. Gender differences in sleep and sleep-disordered breathing. Clinics in chest medicine 2004;25:257-68.

Young T, Rabago D, Zgierska A, Austin D, Laurel F. Objective and subjective sleep quality in premenopausal, perimenopausal, and postmenopausal women in the Wisconsin Sleep Cohort Study. Sleep 2003;26:667-72.

What are symptoms of OSA?

The most common complaints in individuals with sleep apnea are loud snoring, fatigue and daytime sleepiness. Some people, however, have no symptoms, or do not have a bed partner to provide a collaborative history. Other symptoms include restless sleep, nocturia, awakening with choking or gasping, morning headaches, dry mouth or sore throat on awakening, feeling unrested or groggy in the morning with difficulty concentrating throughout the day.

What questionnaires can be used to better quantify risk for OSA (pre-test probability)?

There are several validated questionnaires available. The most commonly used in clinical and research settings are Berlin Questionnaire and STOP BANG questionnaire. The links below provide more information about these questionnaires.

http://www.thoracic.org/assemblies/srn/questionaires/berlin-questionnaire.php

http://www.thoracic.org/assemblies/srn/questionaires/stop-bang.php

What tests are available to diagnosis OSA?

Objective testing is required to confirm the diagnosis of OSA and determine severity. The two accepted methods of objective testing are in-laboratory attended polysomnography (PSG, gold standard) and home testing with portable monitors (PM).

In lab PSG can be done over 2 nights as a baseline monitoring study, followed by a positive airway pressure (PAP) titration several nights later.

There is a growing trend to perform “split night studies”. During a split night study, the first portion of the study is used to observe baseline sleep events and the second portion devoted to determining the amount PAP that is necessary to prevent upper airway collapse during sleep.

According to the American Academy of Sleep Medicine's (AASM) practice parameters a split night study is a valid alternative if the following three criteria are met:

AHI of ≥40 events per hour of sleep is documented during ≥2 hours of sleep. Alternatively, an AHI of 20 to 39 events per hour of sleep is acceptable during ≥2 hours of sleep when there is strong evidence of OSA.

PAP titration is conducted over ≥3 hours and adequate elimination of obstructive events is documented during rapid eye movement (REM) and non-REM (NREM) sleep. Split night study may be a cost effective approach to sleep testing while reducing sleep scheduling delays.

Kushida CA, Littner MR, Morgenthaler T, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. Sleep 2005; 28:499.

Deutsch PA, Simmons MS, Wallace JM. Cost-effectiveness of split-night polysomnography and home studies in the evaluation of obstructive sleep apnea syndrome. J Clin Sleep Med 2006; 2:145.

Types of Monitoring Devices

Type 1 devices: technician attended, overnight polysomnography (PSG), typically done in a sleep laboratory.

Type 2 devices: attended or unattended, are similar to Type 1 devices in their recording capabilities (EEG, several flow and effort measures, position, pulse oximetry, snore, limb movement or chin tone [EMG]). They differ in that they are often outside of the sleep lab and are unattended.

Type 3 devices: unattended, usually measure between four to seven variables: two respiratory variables (e.g., respiratory movement and airflow), one cardiac variable (e.g., heart rate), and pulse oximetry. Some devices may be able to monitor sleep position or snoring. EEG is usually not included with these devices and therefore unable to determine sleep stage, EEG arousal, and sleep duration. As a result, the AHI is calculated based on total recording time rather than total sleep time (as done for in lab or Type I or 2 PSG). The index derived from Type 3 devices is usually lower than an AHI derived by Type PSG. This decreases the diagnostic sensitivity of type 3 devices compared with type 1 and 2 devices.

Type 4 devices: unattended, are defined differently depending on the organization but usually refer to devices that record 1 or 2 variables (e.g., oxyhemoglobin saturation and airflow). Pulse oximetry alone can be a Type 4 device. Information obtained from these devices is limited.

Collop NA, Anderson WM, Boehlecke B, et al. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. Portable Monitoring Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med 2007; 3:737.

Collop NA, Tracy SL, Kapur V, et al. Obstructive sleep apnea devices for out-of-center (OOC) testing: technology evaluation. J Clin Sleep Med 2011; 7:531.

What are practice guideline recommendations for the use of portable sleep studies?

Portable sleep studies may be used to diagnose OSA when the pretest likelihood of moderate to severe OSA is high. It is not indicated in patients with major co-morbid conditions including moderate to severe pulmonary disease, neuro- muscular disease, or congestive heart failure, or those suspected of having a co-morbid sleep disorders (insomnia, parasomnias, REM behavior disorder, central sleep apnea, etc.).

El Shayeb M, Topfer LA, Stafinski T, Pawluk L, Menon D. Diagnostic accuracy of level 3 portable sleep tests versus level 1 polysomnography for sleep-disordered breathing: a systematic review and meta-analysis. CMAJ. 2014 Jan 7;186(1):E25-51

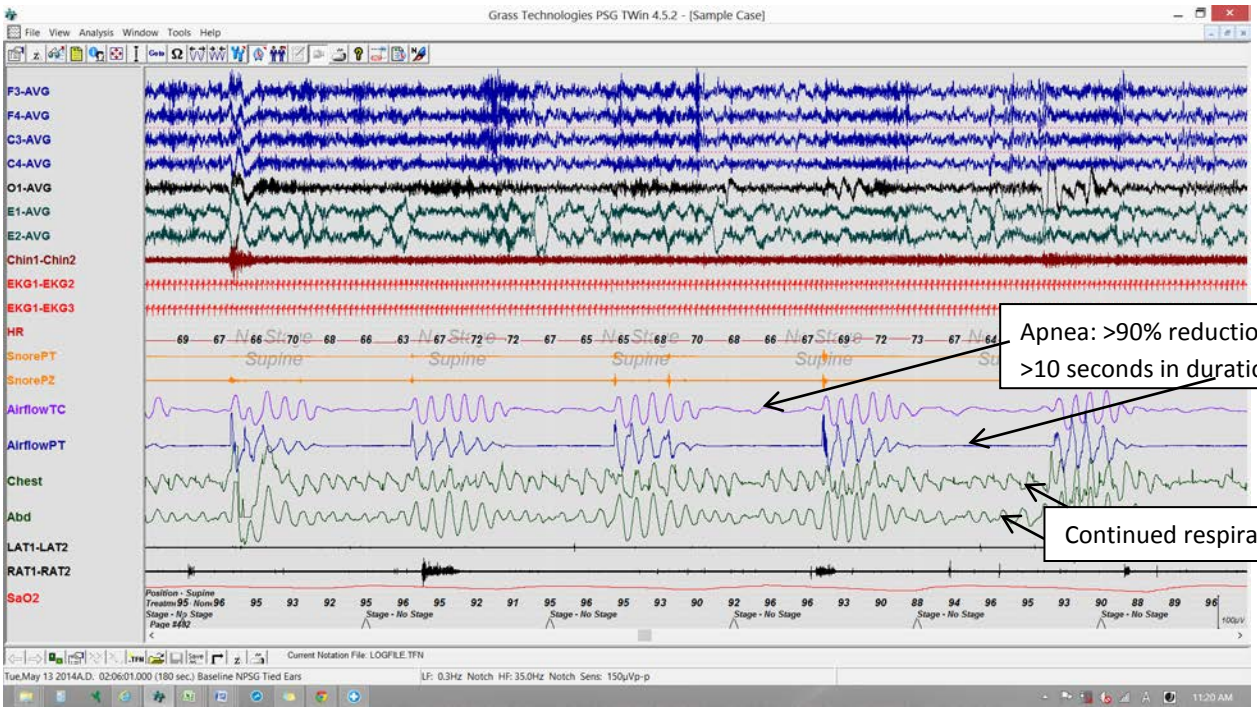
Collop NA, Anderson WM, Boehlecke B, et al. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. Portable Monitoring Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med 2007;3:737-47.

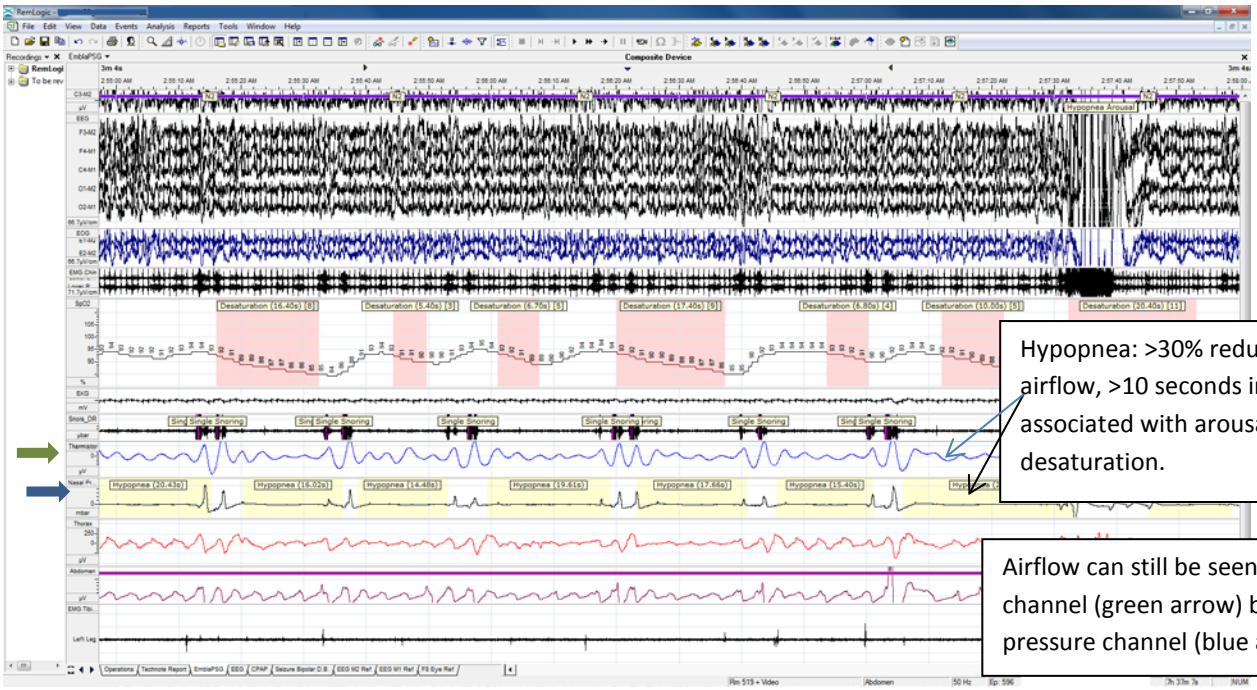
Canadian Sleep Society, Blackman A, McGregor C, Dales R, Driver HS, Dumov I, Fleming J, Fraser K, George C, Khullar A, Mink J, Moffat M, Sullivan GE; Canadian Thoracic Society, Fleetham JA, Ayas N, Bradley TD, Fitzpatrick M, Kimoff J, Morrison D, Ryan F, Skomro R, Series F. Canadian Sleep Society/Canadian Thoracic Society position paper on the use of portable monitoring for the diagnosis of obstructive sleep apnea/hypopnea in adults. Can Respir J. 2010 Sep-Oct;17(5):229-32.

How do you interpret the sleep report?

Please refer to the “Interpretation of Sleep Report” primer.

Interpretation of tracings from case





How do you calculate AHI and RDI? What is the AHI/RDI for this patient?

Apnea: ≥ 90% reduction in airflow signal (thermistor; breathing cessation) for >10 seconds in duration.
Obstructive apnea: an apnea is scored as obstructive if it meets criteria above and is associated with continued or increased inspiratory effort throughout the entire period of airflow cessation.

Hypopnea: reduced respiratory airflow ≥ 30% from baseline (usually using nasal pressure transducer, duration > 10 seconds) with a ≥ 3% decrease in oxygen saturation or associated with EEG arousal.

Respiratory effort-related arousal (RERA): A sequence of breaths lasting > 10 seconds with increasing respiratory effort or airflow limitation (flattening of the inspiratory limb of the airflow channel) not meeting criteria for apnea or hypopnea and associated with arousal from sleep.

Apnea-hypopnea index (AHI): total number of apnea and hypopnea events recorded per hour of sleep.

Respiratory Disturbance Index (RDI): sum of apnea, hypopnea, and RERA events recorded per hour of sleep.

For this patient:

Total sleep time: 404.3 minutes = 6.74 hours

Total respiratory events (apneas and hypopneas): 295 events, no RERAs noted

AHI = 295/6.74 = 43.8 events/hr. Since there were no RERAs scored the RDI is equal to AHI and 43.8 events/hr.

What is the difference between obstructive and mixed apneas and what are clinical implications of such a distinction?

Apnea: ≥ 90% reduction in airflow signal (thermistor; breathing cessation) for >10 seconds in duration

Obstructive apnea: an apnea is scored as obstructive if it meets criteria above and is associated with continued or increased inspiratory effort throughout the entire period of airflow cessation.

Mixed apnea: an apnea is scored as mixed if it meets apnea criteria and is associated with absent inspiratory effort during the first part (central component), followed by resumption of inspiratory effort during the second portion of effort (obstructive component).

Practically, mixed apneas are included in the AHI calculation as a respiratory event with an equal weight to an “obstructive apnea” or “hypopnea”, and are treated by sleep clinicians with PAP. However, recent studies suggest that patients with predominately mixed apneas may be pathophysiologically, and phenotypically different than pure obstructive apnea patients with perhaps more observed severity in oxygen desaturation and worse CPAP compliance.

Xie A, Bedekar A, Skatrud JB, et al. The heterogeneity of obstructive sleep apnea predominant obstructive vs pure obstructive apnea. Sleep.2011; 34(6): 745-750.

Yamauchi M, Tamaki S, Yoshikawa M, et al. Differences in Breathing Patterning During Wakefulness in Patients With Mixed Apnea-Dominant vs Obstructive-Dominant Sleep Apnea. Chest.2011; 140; 54-61.

Eckert DJ, White DP, Jordan AS, Malhotra A, Wellman A. Defining phenotypic causes of obstructive sleep apnea. Identification of novel therapeutic targets. Am J Respir Crit Care Med. 2013 Oct 15; 188(8): 996-1004.

How do you classify severity of sleep apnea? What is the sleep apnea severity in this case?

One measure of sleep apnea severity is AHI.

Mild OSA: AHI ≥5-15/h

Moderate OSA: AHI ≥15-30/h

Severe OSA: AHI ≥30/h

OSA syndrome: AHI ≥5 with evidence of daytime sleepiness (Usually ESS ≥ 10)

This patient has severe obstructive sleep apnea, given AHI 43.8.

What treatment options are available for sleep disordered breathing and what would you recommend for this patient?

Continuous positive airway pressure (CPAP) is the treatment of choice for patients with obstructive sleep apnea (OSA) of all severities. There are numerous other treatment options available, which include behavioral, medical (oral appliances), and surgical options.

(1) Behavioral options include weight loss, exercise, avoidance of hypnotics/sedatives and alcohol and positional therapy. (2) Several oral appliances (e.g. mandibular repositioning appliances and tongue retaining devices) are available for use in patients with OSA. They are generally indicated for use in patients with mild to moderate OSA and for those who cannot tolerate CPAP or are not appropriate candidates for CPAP therapy. (3) Primary surgical therapy for OSA is limited for mild OSA patients who have an anatomical abnormality blocking the pharyngeal airway and is surgically correctable. Surgical therapy can be a secondary treatment option for improving tolerance to other treatment modalities outlined above. Of the available surgical procedures, tracheostomy eliminates OSA and mandibular advancement procedure has a comparable effect to CPAP in reducing OSA severity. Most other surgical treatments rarely cure OSA especially laser assisted uvulopalatoplasty, which is not recommended as a treatment choice for OSA. (4) Finally, adjunctive therapies such as bariatric surgery, pharmacological therapy and oxygen therapy may be utilized in patients with OSA.

Patient SA has severe OSA and therefore the treatment of choice is continuous positive airway pressure therapy. An in-lab PAP titration study would be recommended as the next step. Behavioral therapies such as weight loss, avoidance of sedatives and alcohol and positional therapy should also be recommend in this patient.

Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD, Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5(3):263.

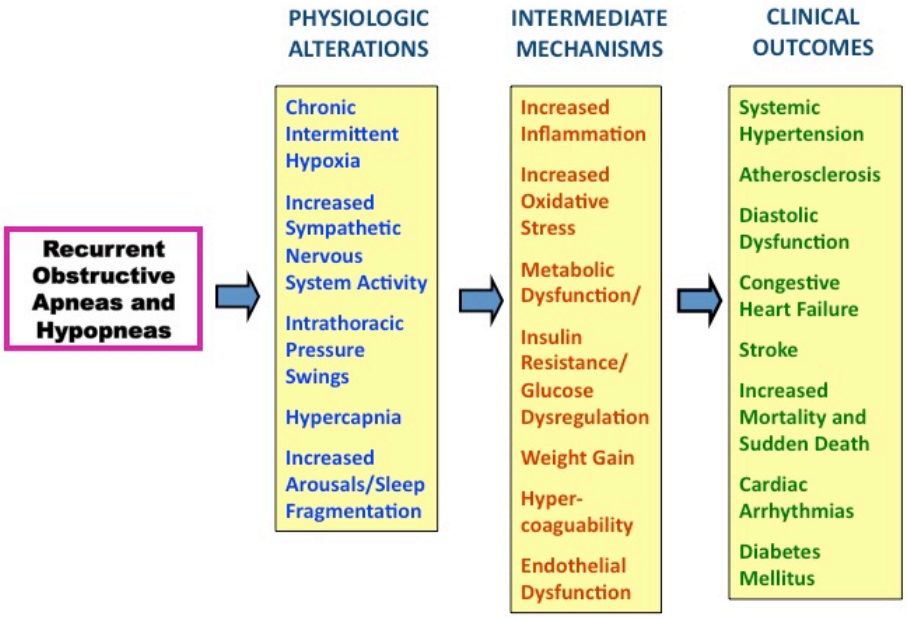
Is sleep disordered breathing associated with long term health outcomes? What is the strength of the evidence?

OSA has been associated with numerous long-term health outcomes specifically cardiovascular outcomes including hypertension, coronary heart disease, cardiac arrhythmias, heart failure, stroke and sudden death.

Marin et al. showed that untreated severe OSA significantly increased the risk of fatal (odds ratio 2.87, 95%CI 1.17-7.51) and non-fatal (3.17, 1.12-7.51) cardiovascular events compared with healthy participants over a mean period of 10 years.

Peppard P, Young T, Palta M et al. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378-84.
Peker Y, Kraiczi H, Hedner J et al. An independent association between obstructive sleep apnoea and coronary artery disease. Eur Respir J 1999;14(1):179-84.
Mehra R, Benjamin EJ, Shahar E et al. Association of nocturnal arrhythmias with sleep-disordered breathing: The Sleep Heart Health Study. Am J Respir Crit Care Med 2006;173(8):910-6.
Gottlieb DJ, Yenokyan G, Newman AB et al. Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure: the sleep heart health study. Circulation 2010;122(4):352-60.
Shahar E, Whitney C, Redline S et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med 2001;163:19-25.
Yaggi H, Brass L, Kernan W et al. Obtructive sleep apnea as a risk factor for stroke. Stroke 2004;316:365.
Gami AS, Howard DE, Olson EJ et al. Day-night pattern of sudden death in obstructive sleep apnea. N Engl J Med 2005;352(12):1206-14.
Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005 Mar 19-25;365(9464):1046-53.

What are proposed mechanisms for the association between sleep disordered breathing and cardiovascular outcomes (hypertension, MI)?



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What are potential advantages and disadvantages to using auto-PAP devices vs. in-lab PAP titration?

Advantages for Auto PAP:

- Can be used in patients who are unable to get in-lab titration studies for a number of reasons
- Can be used in patients who have inadequate/suboptimal in-lab titration studies
- Can be used in the pre-operative phase of surgery especially when adequate time to schedule in-lab titration study is not feasible
- Indicated in positional sleep apnea or more sleep stage specific (REM) sleep apnea
- Most private payors require home sleep testing followed by auto-CPAP before approval for in-lab titration
- In sixteen randomized controlled trials, autoPAPs were able to reduce the apnea-hypopnea index (AHI) to less than 10 events/hour in 80-95% of patients studied. Many were actually able to reduce the AHI to less than 5 events/hour and did show an improvement in daytime sleepiness. Therefore, APAP is an effective alternative to in-lab PAP titration.

Cons for AutoPAP:

- AutoPAPs are more expensive than standard CPAP devices, yet the insurance reimbursement is the same between the two devices
- There are contraindications to autoPAP:

- CHF (CSR)
- COPD (hyperinflation concerns)
- Central sleep apnea
- Obesity hypoventilation
- Neuromuscular weakness
- Restrictive lung disease

Strength of evidence of APAP versus CPAP

Outcomes	Number of trials	Total number	Trials with data for Meta-analysis	Meta-analysis results comparing APAP with CPAP	Favors	Strength of evidence
Clinical outcomes (death, cardiovascular events and others)	0	0	0	N/A		Insufficient
Compliance	24	1008	22	0.18 hours (95% CI 0.05 to 0.31; $P = 0.006$)	APAP	Moderate
Apnea-Hypopnea Index	16	548	16	0.25 events/hour (95% CI -0.16 to 0.66; NS)	No difference	Moderate
Epworth Sleepiness Scale	22	954	18	-0.48 (95% CI -0.81 to -0.15; $P = 0.005$)	APAP	Moderate
Arousal Index	10	356	9	-0.85 events/hour (95% CI -2.2 to 0.5; NS)	No difference	Moderate
Minimum O_2 saturation	9	258	9	-1.3% (95% CI -2.2 to -0.4; $P = 0.003$)	CPAP	Moderate
Sleep efficiency	3	126	0		No difference	Insufficient
Rapid eye movement sleep	9	273	0		No difference	Moderate
Slow wave sleep	8	243	0		No difference in seven trials; one trial favored APAP	Moderate
Quality of life	9	509	0		No difference in eight trials; one trial favored APAP	Moderate
Blood pressure	3	149	0		No difference in two trials; one trial favored CPAP (decrease in diastolic blood pressure)	Insufficient

APAP: auto-titrating CPAP; CPAP: continuous positive airway pressure; N/A: not applicable; NS: non-significant.

Ip et al. Auto-titrating versus fixed continuous positive airway pressure for the treatment of obstructive sleep apnea: a systematic review with meta-analyses. Systematic Reviews 2012; 1: 20

What is P_{crit}?

Pcrit is the transmural pressure (difference between the airway intraluminal pressure and the pressure exerted by surrounding tissues) required to collapse the upper airway.

Schwartz AR, Smith PL, Wise RA, Gold AR, Permutt S. Induction of upper airway occlusion in sleeping individuals with subatmospheric nasal pressure. J Appl Physiol. 1988;642:535-542.

What is the impact of CPAP therapy on sleep apnea health outcomes?

Summary of Key Studies on Impact of Obstructive Sleep Apnea (OSA) Treatment on Cardiovascular Diseases (CVD)				
CVD of interest	Type of Study	Sample Size	Duration of Treatment	Impact of Treatment of OSA
Hypertension	Randomized Controlled Trial	N=118	1 month	Mean BP reduced by 2.5 mm Hg (SE 0.8), in therapeutic CPAP group (p=0.0013, unpaired t test). This benefit was seen in both systolic and diastolic blood pressure, and during both sleep and wake.
Arrhythmias	Non-randomized study	N=316	One-night of CPAP	Significant reduction in occurrence of paroxysmal atrial fibrillation, sinus bradycardia and sinus pause
Arrhythmias	Randomized Controlled Trial	N=83 (males only)	One-month	No significant change in the frequency of any cardiac arrhythmias
Arrhythmias	Non-randomized study	N=29 (heart failure patients with both obstructive and central sleep apnea)	One-night of CPAP	Significant reduction in nocturnal premature ventricular contractions and couplets
Arrhythmias	Non-randomized study	N=23	14 months CPAP	Significant decrease in sinus pauses and bradycardia No significant difference in supraventricular arrhythmias
Coronary Artery Disease and Stroke	Non-randomized study	N=1347 (men only)	10 year follow-up	Significantly fewer number of non-fatal and fatal coronary and cerebrovascular events in treated OSA patients compared to untreated severe OSA patients

Despite evidence suggesting a beneficial role of treatment of OSA on cardiovascular outcomes, there has been a lack of large-scale long-term randomized studies indicating that treatment of

OSA reduces cardiovascular disease related outcomes. It is important to note that, in the last few years, there has been emergence of randomized clinical trials that are investigating the impact of OSA treatment on the risk of cardiovascular disease. One such trial is currently underway in Europe. It is a prospective randomized intervention study (n=400 patients) called "RICCADSA" (1) (Randomized Intervention with CPAP in CAD and OSA). It will assess the impact of CPAP on a composite endpoint of myocardial infarction, new revascularization, stroke and cardiovascular mortality among those with both CAD and OSA. Similarly in the United States, a multi-center study called the Heart Biomarker Evaluation in Apnea Treatment randomized patients with OSA and CAD or CAD risk factors to CPAP, nocturnal oxygen and health lifestyle instruction. The major goal of this trial is to determine whether CPAP or oxygen alter cardiac biomarkers including (not limited to) markers of systemic inflammation and oxidative stress, cardiac rhythm, impulse generation and ischemia and myocardial stress. Another clinical trial, Continuous Positive Airway Pressure Treatment of Obstructive Sleep Apnea to Prevent Cardiovascular Disease(2) (SAVE), is underway and will be the largest clinical trial to date in the sleep apnea field (anticipated completion date September 2015). "The overall aim of SAVE is to determine if CPAP can reduce the risk of heart attack, stroke or heart failure for people with OSA." This trial plans to recruit 5,000 participants. (references are from Klar paper)

Abe H, Takahashi M, Yaegashi H et al. Efficacy of continuous positive airway pressure on arrhythmias in obstructive sleep apnea patients. Heart Vessels 2010;25(1):63-9.
Craig S, Pepperell JC, Kohler M et al. Continuous positive airway pressure treatment for obstructive sleep apnoea reduces resting heart rate but does not affect dysrhythmias: a randomised controlled trial. J Sleep Res 2009;18(3):329-36.
Javaheri S. Effects of continuous positive airway pressure on sleep apnea and ventricular irritability in patients with heart failure. Circulation 2000;101(4):392-7.
Simantirakis EN, Schiza SI, Marketou ME et al. Severe bradyarrhythmias in patients with sleep apnoea: the effect of continuous positive airway pressure treatment: a long-term evaluation using an insertable loop recorder. Eur Heart J 2004;25(12):1070-6.
Marin JM, Carrizo SJ, Vicente E et al. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005;365(9464):1046-53.
Hypertension first reference Pepperell JC, Ramdassingh-Dow S, Crosthwaite N, Mullins R, Jenkinson C, Stradling JR, Davies RJ

What are predictors of short term and long term CPAP compliance?

The following factors have been identified as predictors of adherence to CPAP therapy:

- Adherence with CPAP during the first week of therapy predicts long-term compliance (study investigated mild OSA patients)
- Greater severity of sleep apnea
- Lack of claustrophobic tendencies
- Optimism regarding the benefit of CPAP therapy
- Presence of problem-solving skills

Stepnowsky CJ Jr, Marler MR, Ancoli-Israel S. Determinants of nasal CPAP compliance. Sleep Med. 2002 May;3(3):239-47.
Ye L, Pack AI, Maislin G, Dinges D, Hurley S, McCloskey S, Weaver TE. Predictors of continuous positive airway pressure use during the first week of treatment. J Sleep Res. 2012 Aug;21(4):419-26.

What are usual follow-up recommendations for newly diagnosed sleep apnea?

The usual follow-up recommendations for newly diagnosed sleep apnea includes:

a) Discussion of the findings of the sleep study and severity of disease
b) Discussion and explanation of the natural course of sleep apnea and associated conditions including both cardiovascular and non-cardiovascular
c) Identification of risk factors and discuss strategies for risk factor modification
d) Discussion of treatment options
e) Expectations from various treatments
f) Discussion of consequences of untreated disease
g) Counseling on drowsy driving/sleepiness
h) Long-term follow-up
    - Access to disease management team including sleep specialist, other specialists to manage comorbidities, nurses, sleep technologists, and support groups
    - Monitor adherence to treatment of choice for sleep apnea
    - Monitor for side effects from treatment
    - Monitor for development of complications related to sleep apnea

Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD, Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5(3):263.

What is the impact of weight loss on obstructive sleep disordered breathing?

1. Increasing weight worsens OSA
2. Weight loss affects the severity of OSA
    a. Strengthening a causal relationship between obesity and OSA
3. Peppard conducted a population based, prospective cohort study (1989-2000)
    a. Determined the independent association between weight change and change in AHI severity as outlined in table below where a 20% weight loss is associated with a nearly 50% improvement in AHI.

Peppard et al. JAMA 2000

How is CPAP compliance measured and what is considered good compliance?

CPAP compliance can be measured in several ways. The CPAP machines can display usage over the course of past 30 days. Additionally a data card is typically provided with the CPAP machine that is mailed by the patient (after using the device for 30-90 days) to the provider or the vendor. This data card can provide information on usage of the CPAP device with

appropriate software. More recently, the information cannot be transmitted continuously by wireless transmission. These can then be accessed via a cloud-based platform or reports generated from these transmissions can be provided to the provider. These reports contain information of the total number of usage birthday of the CPAP device by the patient it also contains information on last week estimated I can copy and next and how many nights in a week the patient use the machine. It's important to note that different CPAP manufacturers define mask weak and residual AHI differently. Therefore interpretation of this data should be done in the context of clinical evaluation. Overall usage of the CPAP device by the patient is generally consistent across different CPAP manufacturers.

Medicare requires 4+ hours/night of use ≥70% of the nights in 30 consecutive days for continued coverage for PAP therapy. This is generally considered to be adequate use of PAP therapy. However, a linear dose-response relationship has been reported between increased CPAP use and achieving normal levels of For objective and subjective daytime sleepiness, there was a linear dose-response relationship ($P < .01$) between increased hours of CPAP use and achieving normal levels.

Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning.Weaver TE, Maislin G, Dinges DF, Bloxham T, George CF, Greenberg H, Kader G, Mahowald M, Younger J, Pack AI. Sleep. 2007 Jun;30(6):711-9.