Obstructive Sleep Apnea: Diagnosis, Epidemiology, and Economics

Vishesh K Kapur MD MPH

Obstructive sleep apnea (OSA) is a disorder characterized by intermittent upper-airway collapse, which impairs ventilation and disrupts sleep. Factors that contribute to upper-airway collapse include reduced upper-airway dilator muscle activity during sleep, specific upper-airway anatomical features, decreased end-expiratory lung volume, ventilatory control instability, sleep-state instability, and rostral fluid shifts in the recumbent position. The relative contributions of these factors vary between individuals with OSA, and this may have implications as to which treatments are efficacious for an individual. OSA is common in adults; males, older individuals, and the obese are at higher risk. There is uncertainty in how to measure severity of sleep-disordered breathing, what cut-off to use to demarcate abnormal, and how to define the clinical syndrome. Identifying patients at higher risk who should have a sleep study is relatively simple, involving assessment of several factors, such as snoring, witnessed apnea/self-reported gasping, hypertension, body mass index, and neck circumference. As would be expected from a disorder that causes morbidity, OSA is associated with substantial economic costs to society, including increased medical costs. A reduction in medical costs in a diverse adult patient population with OSA after therapy has not been convincingly demonstrated. Nevertheless, the results of cost-effectiveness analyses strongly

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support the cost-effectiveness of continuous positive airway pressure therapy in patients with moderate to severe OSA, relative to other standard medical therapies that society is willing to pay for. *Key words: obstructive sleep apnea; OSA; sleep; sleep-disordered breathing; polysomnography.* [Respir Care 2010;55(9): 1155–1164. © 2010 Daedalus Enterprises]

Introduction

Obstructive sleep apnea (OSA) is a disorder characterized by repetitive collapse and reopening of the upper airway during sleep. The collapse of the airway impairs ventilation and can result in intermittent hypoxemia and hypercapnia. During airway collapse, the resistance to air flow results in increased respiratory effort and intrathoracic pressure swings. Eventually, the increased work of breathing results in disruption of sleep (arousal) and activation of upper-airway muscles that causes reopening of the airway (Fig. 1).[1,2] The repetitive acute physiologic stress of OSA noted above can result in symptoms (sleepiness, awakenings) and/or cardiovascular disease via intermediary mechanisms (Fig. 2).[3]

The presence and severity of OSA is usually determined using polysomnography, a test that measures neurologic (electroencephalogram) and cardio-respiratory parameters during sleep. Respiratory sensors detect decrements in ventilation that are classified as apneas (near complete cessation of air flow for ≥10 s), hypopneas (partial decrease in air flow for ≥10 s), or respiratory-effort-related arousals (subtle changes in air flow due to increased upper-airway resistance that result in arousals). The apnea-hypopnea index (AHI) is the commonly used metric of sleep-disordered breathing (SDB). It is defined as the sum of apneas and hypopneas during sleep divided by the sleep time in hours. The following are the cut-offs for severity of SDB when using the definition for hypopnea recommended by the American Academy of Sleep Medicine:

Mild: ≥ 5 and < 15 events/hour
Moderate ≥ 15 and < 30 events/hour
Severe ≥ 30 events/hour

Pathogenesis

This topic has been recently reviewed nicely in detail by Eckert et al.[4] A number of factors are known to contribute to the pathogenesis of OSA, including upper-airway dilator muscle activity during sleep, upper-airway anatomy, lung volume, ventilatory control stability, sleep state stability, and rostral fluid shifts. The relative contributions of each factor vary between individuals with OSA, and this may have implications as to which treatments are most efficacious for an individual.[4]

Dilator Muscle Activity

Dilator muscles stiffen and dilate various regions of the upper airway, keeping it patent. Activity is reduced during sleep, leading to narrowing of the upper airway (Fig. 3).[5,6] The largest of the dilator muscles is the genioglossus, the muscle that forms the majority of the body of the tongue. The genioglossus receives input from the sleep/wake centers of the brain, respiratory-pattern-generating neurons, chemoreceptors, and negative pressure receptors in the airway that can modify its activity.[4] Though genioglossus activity is reduced during sleep, its function can be augmented in response to heightened airway resistance and hypercapnia through inputs from these centers.[7] Other muscles may not have a similar ability to augment their activity, and as a result the patency of the upper airway becomes compromised during sleep.[4]

Anatomy

Anatomical factors, including increased airway length, lateral wall thickness, and tongue volume, as well as skel-

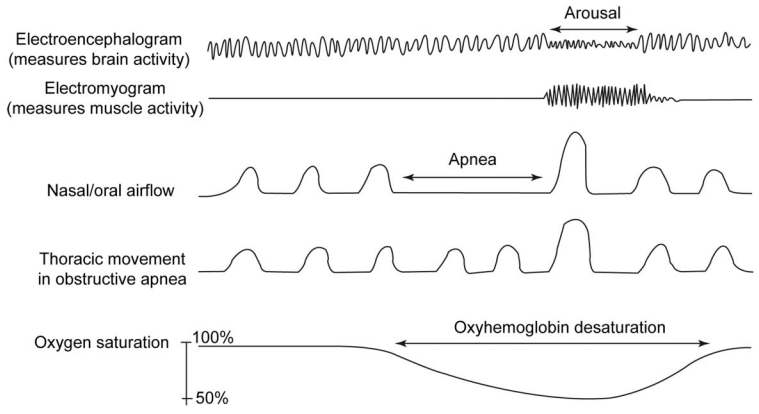

Fig. 1. Schematic tracing from polysomnography showing an obstructive apnea event. (Adapted from Reference 2.)

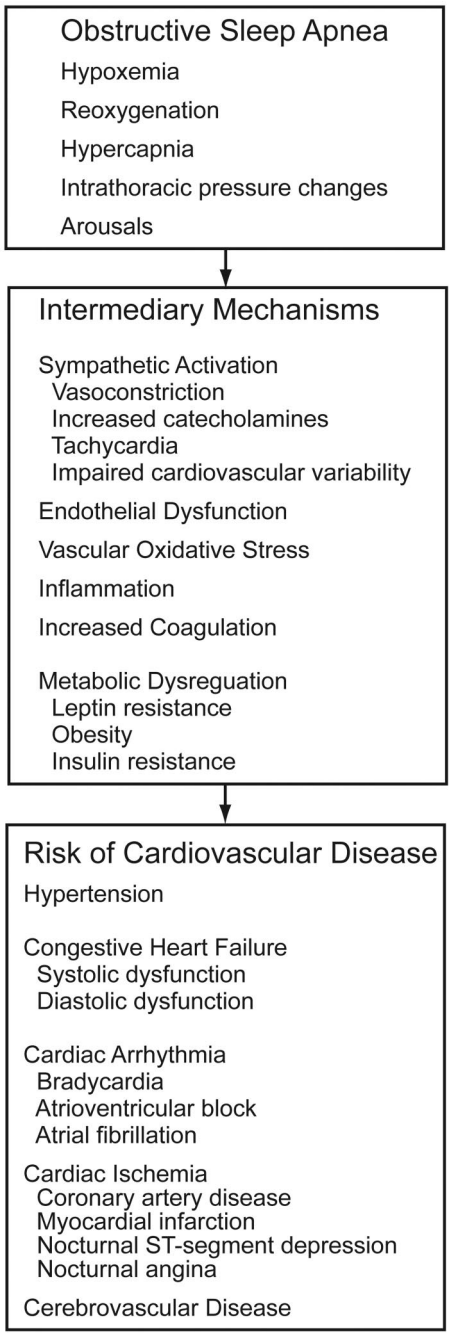

Fig. 2. Acute and intermediary mechanisms of obstructive sleep apnea that contribute to risk of cardiovascular disease. (Adapted from Reference 3.)

etal structure, are associated with the presence of OSA. The role of enlarged soft tissue structures as a risk factor for OSA has been elegantly demonstrated using sophisticated volumetric analysis techniques with magnetic resonance imaging (Fig. 4).[8] The bony enclosure (skull) interacts with soft tissue structures to determine upper-airway collapsibility.[9] A small maxilla and mandible or increased soft tissue as is found in obesity each can result in a reduced airway size; the combination will result in an even smaller lumen size (Fig. 5).[9]

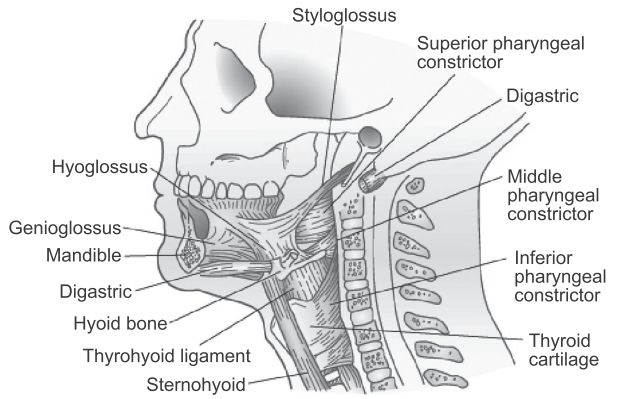

Fig. 3. Schematic diagram of upper-airway muscles (From Reference 6, with permission.)

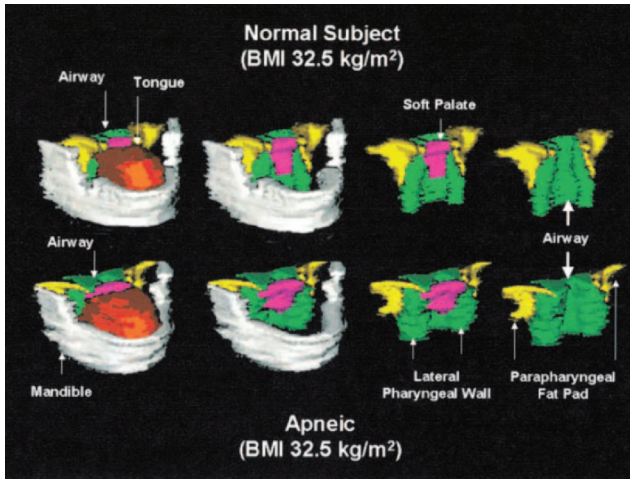

Fig. 4. Volumetric reconstructions of the mandible and soft tissue structures from magnetic resonance imaging. Volumetric reconstructions from a series of 3-mm contiguous axial magnetic resonance images of the mandible (gray), tongue (orange/rust), soft palate (purple), lateral parapharyngeal fat pads (yellow), and lateral/posterior pharyngeal walls (green) in a weight-matched normal subject (top) and a patient with sleep apnea (bottom), both with an elevated body mass index (BMI, 32.5 kg/m^2). Note that the airway is larger in the normal subject than in the apneic subject. The tongue, soft palate, and lateral pharyngeal walls are larger in the patient with sleep apnea. (From Reference 8, with permission.)

Lung Volume

Lower end-expiratory lung volume, as occurs in the setting of obesity, increases the tendency of the upper airway to collapse. Lower end-expiratory volumes have been shown to increase airway collapsibility, the continuous positive airway pressure (CPAP) level needed to maintain airway patency, and the severity of OSA.[10-12] This effect is thought to be mediated by the decreased "tug" of the trachea, which stiffens and dilates the upper airway as lung volumes increase.

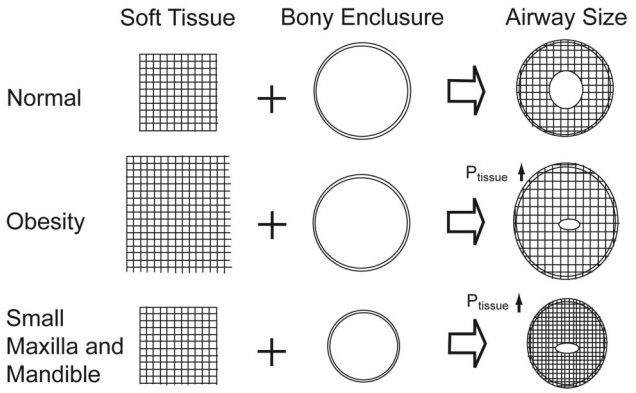

Fig. 5. Interaction of soft tissue and bony enclosure determines airway size. Schematic explanations for the mechanical model of the pharyngeal airway. P_{tissue} is the pressure surrounding the collapsible tube. (From Reference 9, with permission.)

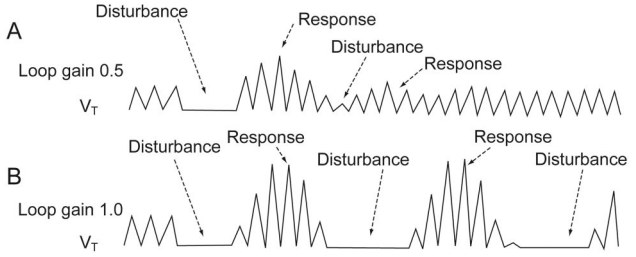

Fig. 6. Loop gain and the perpetuation of respiratory disturbance. The ventilatory response to an apnea (first disturbance in both curves) is demonstrated for (A) an individual with a loop gain of 0.5 and (B) an individual with a loop gain of 1.0. In A, ventilation quickly returns to a regular pattern, whereas in B a sustained oscillation is established. (From Reference 13, with permission.)

Ventilatory Control Stability

During sleep the respiratory system is under automatic control; P_{aCO_2} is maintained at a stable level by negative feedback control. Loop gain, a measure of the stability of a negative-feedback control system, is defined as the magnitude of response elicited by a stimulus divided by the magnitude of the perturbing stimulus. High loop gain in the ventilatory control system is synonymous with unstable ventilatory control. A system with high loop gain will tend to perpetuate the effects of a perturbation, while a low loop gain system will quickly dampen the effects (Fig. 6).[13]

Persons with OSA generally have greater instability of ventilatory control and higher loop gain than control subjects.[14] Since upper-airway muscles receive input from respiratory control centers, unstable ventilatory drive will cause greater fluctuation in the activity of these muscles and promote upper-airway collapse when ventilatory drive is at its nadir.[15] If respiratory drive is eliminated, as in a central apnea, the upper-airway muscles also turn off, resulting in airway narrowing. It has been demonstrated that airway collapse (partial or complete) is common during a central apnea.[16]

Stability of Sleep

Arousal from sleep in OSA is caused by increasing ventilatory effort.[1] While arousal can play a rescue role by opening the blocked airway and resuming ventilation, if it occurs prematurely it may abort compensatory mechanisms such as increased pharyngeal dilator activity, which could open the airway without sleep disruption.[13] Arousal from sleep can engender ventilatory instability by stimulating hyperventilation. As noted earlier, ventilatory instability can in turn promote upper-airway collapse, thereby worsening OSA.[17]

Rostral Fluid Shifts

Fluid shifts from the legs to the neck appear to play a role in the pathogenesis of OSA.[18-21] Fluid displacement from the legs caused by lower body positive pressure has been shown to reduce upper-airway size and increase collapsibility in healthy awake subjects.[18-20] Further, overnight rostral fluid displacement from the legs was found to be correlated strongly with AHI, change in neck circumference, and time spent sitting, in non-obese, healthy men suspected of having OSA.[21] This mechanism may explain findings that lack of exercise is associated with increased severity of SDB, independent of measures of body habitus.[22] Greater time spent in sedentary activity may increase lower leg edema and result in more sleep-related fluid shift to the upper airway.

Genetics

Evidence from racial, familial, and twin studies indicates that OSA has a strong genetic basis, with 35–40% of variance attributed to genetic factors.[23] There is evidence that genetic determinants of upper-airway muscle activity, craniofacial structure, obesity, fat distribution, and respiratory control may interact to cause OSA.[23] The role of specific genes in the pathogenesis of OSA remains to be elucidated, and further studies are needed.[23]

Implications for Therapy

CPAP is highly efficacious, but a significant proportion of patients have poor adherence to therapy.[24] There is a need for other therapeutic options for the non-adherent patient. Unfortunately, alternative therapies are not efficacious for significant proportions of patients with OSA.[25-27] There is variation between individuals as to the relative importance of specific pathogenetic mechanisms to the development of OSA. The identification of the predominant cause(s) for each patient would allow targeted treatment for that individual. Personalized treatment tailored to the underlying cause(s) can result in better efficacy for alternative treatments for OSA.[28] OSA caused by a well defined anatomic abnormality, such as enlarged tonsils, in the absence of other anatomic factors responds better to uvulopalatopharyngoplasty with tonsillectomy than OSA in the setting of more typical anatomic findings.[29] Oxygen, which reduces loop gain by reducing

Table 1. Studies on the Prevalence of Obstructive Sleep Apnea

Country	First Author	*N*	Ethnicity	Diagnostic Method	Prevalence (%)	
					Men	Women
United States	Young[32]	602	White	Polysomnography	4.0	2.0
United States	Bixler[33]	1,741	White	Polysomnography	3.9	1.2
Australia	Bearpark[34]	485	White	MESAM IV*	3.1	ND
India	Udwadia[35]	250	Indian	Polysomnography	7.5	4.5
China	Ip[36]	258	Chinese	Polysomnography	4.1	ND
China	Ip[37]	ND	Chinese	Polysomnography	ND	2.1
Korea	Kim[38]	457	Korean	Polysomnography	4.5	2.3

* MESAM IV (Madaus, Marburg, Germany) is a portable sleep monitoring system.
ND = no data available
(Adapted from Reference 39.)

respiratory drive, improves AHI in OSA patients with high loop gain more significantly than in patients with low loop gain.[30] Theoretically, individuals with defects in airway tone may respond more favorably to medications that augment dilator muscle activity.[31] Hypnotics may improve OSA in patients with a low arousal threshold that causes premature sleep disruption, by allowing time for compensatory airway muscle activity to increase.

Epidemiology

Prevalence

OSA, when defined physiologically as increased obstructive breathing events during sleep, is very common in adults. In the Wisconsin Sleep Cohort, a stratified random sample of Wisconsin state employees ages 30–60 years, the prevalence of OSA defined by an AHI ≥ 5 events/hour was 9% in women and 24% in men.[32] When defined as a clinical syndrome (the combination of AHI ≥ 5 events/hour and significant self-reported sleepiness), OSA was still relatively common in that cohort, with a prevalence of 2% in women and 4% in men. A number of other studies in diverse populations have provided similar prevalence estimates for the clinical syndrome (Table 1).[33-39]

Despite concordance between studies, there remains uncertainty as to what is the true prevalence of the clinical syndrome. This stems from a lack of clarity on the best metric of SDB, what cut-off distinguishes normal from a pathologic frequency of SDB, and the appropriate definition of the clinical syndrome.

There is heterogeneity in the definition of AHI, particularly the definition of hypopnea. The American Academy of Sleep Medicine scoring manual provides 2 acceptable definitions: a recommended one that requires a ≥ 30% decline in nasal-pressure-transducer signal excursions with a ≥ 4% desaturation from pre-event baseline, and an alternative option that requires a ≥ 50% decline in nasal-pressure-transducer signal excursions with a ≥ 3% desaturation or arousal.[40] Using different definitions for hypopnea can produce widely different prevalence estimates. In the Sleep Heart Health Study the median AHI was approximately 3-fold higher and the prevalence of moderate to severe OSA was 2-fold higher when hypopneas with ≥ 3% desaturations or arousals were scored than when a ≥ 4% oxygen desaturation was required for hypopnea scoring.[41]

Choosing a single best metric is complicated by the fact that no single polysomnography index is best associated with all the various negative outcomes of OSA. There is also discordance between research studies as to the relationship between specific metrics of SDB and specific outcomes. For example, results from the Cleveland Family Study indicated that the arousal index was more strongly associated with hypertension than was the AHI. In contrast, analyses from the Sleep Heart Health Study found the frequency of hypopneas with ≥ 4% desaturations (not hypopneas defined using arousals or lesser degrees of oxygen desaturation) was significantly associated with self-reported cardiovascular disease.[42,43] Analyses from the Sleep Heart Health Study and Cleveland Family Study concur that sleep-related hypoxemia is associated with impaired glucose tolerance.[42,44]

Though an AHI cut-off of 5 events/hour has traditionally been used to demarcate abnormal, this cut-off does not have a strong evidence basis to support its use. In the Wisconsin Sleep Cohort, subjects with AHI values between 0.1 and 4.9 events/hour had 1.4 times the odds of incident hypertension, relative to subjects with AHI equal to zero in fully adjusted models.[45] Cross-sectional analyses from the Sleep Heart Health Study indicate that 54% of subjects with AHI ≥ 15 events/hour did not have subjective complaints of sleepiness or being unrested.[46] SDB may lead to certain outcomes at different levels of severity, based on individual susceptibility.

An evidence-based metric and cut-off of SDB would allow a better estimation of the true prevalence of OSA. The estimation of the prevalence of the clinical syndrome

caused by OSA necessitates the identification of individuals with a negative outcome caused by OSA. The Wisconsin Sleep Cohort used subjective sleepiness as the sole outcome.[32] It is known that OSA is associated with a range of negative outcomes, including sleepiness, sleep disruption, cognitive dysfunction, and cardiovascular disease.[39] It is reasonable to label individuals with OSA and any of these outcomes as having the clinical syndrome if it can be ascertained that OSA is the cause. The difficulty arises in determining whether the outcome was caused by OSA. Further research addressing the factors that introduce ambiguity into establishing the true prevalence of the syndrome is needed, including the exploration of novel metrics of SDB and biomarkers to define the clinical syndrome.

Sex

Most population based-studies have found a 2–3-fold higher prevalence of OSA in males than in females.[39] The male predominance in population studies may be related to sex-related differences in upper-airway anatomy and function, obesity and fat distribution, ventilatory control, and hormonal status.[47] The ratio of men to women diagnosed in sleep centers is even more skewed toward men, with reported ratios of 8:1 and higher.[47] There is a tendency to under-diagnose women in clinical practice, despite the presence of key OSA symptoms.[48] Also sex differences in clinical manifestation, including less severe OSA, more frequent report of non-specific symptoms, and presentation with more coexisting problems in women, may lead clinicians to consider other diagnoses.[47] The impact of sex on outcomes associated with OSA and response to therapy remains to be answered.[47]

Obesity

Obesity is a strong risk factor for OSA. In the Sleep Heart Health Study the prevalence of moderate to severe OSA was 3-fold higher in the highest quartile of body mass index (BMI), relative to the lowest.[49] The causative role of obesity is highlighted by epidemiologic studies that have correlated changes in OSA with changes in weight over time. The Wisconsin Sleep Cohort found an approximately 3% change in OSA severity for every 1% change in weight over a 4-year period.[50] The Sleep Heart Health Study found AHI was changed with weight change over a 5-year period, but the slope of change was greater in men than in women, and the slope of change was greater with weight increase than with weight decrease (Fig. 7).[51] Obesity is postulated to cause OSA via mechanical effects on airway size and lung volume, and may also have neural effects that blunt the neuromuscular response.[52,53]

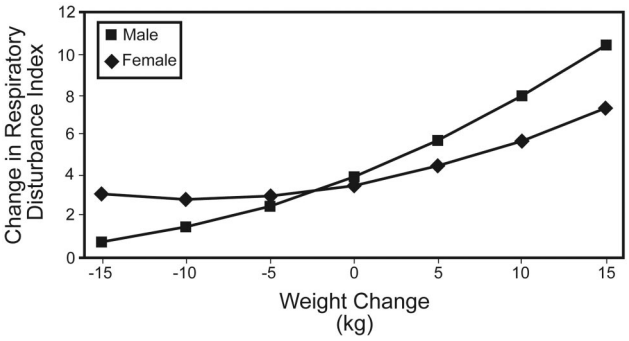

Fig. 7. Change in respiratory disturbance index by change in weight in the Sleep Heart Health Study. (Adapted from Reference 51.)

Age

The prevalence of OSA has been shown to increase with age in adults, up to the age 65.[39,49] This age-related increase has been attributed to parapharyngeal fat deposition, soft palate-lengthening, and changes in other parapharyngeal structures.[39] Some authors have suggested that the clinical presentation of OSA in the elderly is different and that the cardiovascular consequences may be less severe. In the Sleep Heart Health Study, SDB in older people was poorly predicted by obesity, neck circumference, and self-reported apneas.[49] There has been heterogeneity in the results of studies examining the relationship between morbidity and mortality and OSA in older adults. More study is needed, as some researchers report little or no association, while others report increased risk.[39]

Identifying Persons at Higher Risk for Obstructive Sleep Apnea

Persons at higher risk for OSA can be identified by considering demographic characteristics as well as body measurements, and bed partner observations (Table 2).[49] Men and older individuals are more likely to have OSA. Increased BMI and neck circumference (measured just below the thyroid cartilage) are measurements that identify individuals with obesity and fat deposition around the upper airway who are at increased risk of having OSA. Snoring, when habitual (occurring most nights), and especially when loud, is a very useful sign. Breathing pauses witnessed by a bed partner are a very specific indicator. A number of studies have developed clinical prediction rules to indentify individuals with OSA[54-57] Clinical prediction rules that incorporate features such as snoring, witnessed apnea/self reported gasping, hypertension, BMI or neck circumference, and sex have moderate to high sensitivity and specificity in identifying individuals at risk for moderate to severe OSA.[55] Individuals with several of these features, as well as others who are suspected of having OSA on the basis of less classic findings, should undergo polysomnography to confirm the presence and severity of SDB.

Table 2. Odds Ratios for Moderate to Severe Obstructive Sleep Apnea, From the Sleep Heart Health Study

Feature	Odds Ratio*
Male	1.51
Age (10-y increment)	1.52
BMI (5.3-kg/m^2 increment)	1.55
Neck girth (1.7-inch increment)	1.42
Snoring frequency	
Moderate (< 3 nights/wk)	1.02
Habitual (3–7 nights/wk)	1.75
Snoring loudness	
Somewhat loud	1.42
Extremely loud	2.21
Breathing pauses	
Sometimes	1.43
Often	2.47

* Adjusted for all features listed plus race and waist to hip ratio.
(Data from Reference 49.)

In addition to the key predictive symptoms mentioned above, patients with OSA often complain of a host of other symptoms. These include nighttime symptoms such as dyspnea, restless sleep, nocturia, diaphoresis, and reflux, and daytime complaints such as sleepiness, fatigue, morning headaches, impaired concentration, decreased libido, and depression. Findings frequently noted on examination of the upper airway include posterior lateral wall narrowing; enlarged tonsils, tongue, and/or uvula; low-lying soft palate; and retrognathia.[58] Particularly in patients with coexisting cardiopulmonary disease or hypoventilation, lower extremity-edema may be present.

Economics

Costs of Obstructive Sleep Apnea

OSA has a substantial economic impact on society. Potential costs attributable to OSA include the costs of diagnosis and treatment, the decrement in quality of life, the medical consequences, motor vehicle accidents, and occupational losses (Fig. 8). Studies have estimated some of these costs to be in the billions. OSA-related motor vehicle collisions in 2000 were estimated to cost $15.9 billion.[59] OSA is hypothesized to increase medical costs, since the disorder can have harmful and costly multi-organ consequences. Studies have documented an approximately 2-fold increase in medical costs prior to diagnosis in patients identified clinically with OSA, relative to control groups matched for age, sex, residence, and in some cases, family physician and obesity.[60] For example, in a consecutive series of 238 cases identified in a health-maintenance organization (HMO), in the year prior to the diagnosis of OSA, mean annual medical cost per patient was $2,720, versus $1,384 for age and sex matched controls ($P < .01$).[61] Regression analysis showed that the AHI among cases was significantly related to annual medical costs after adjusting for age, sex, and BMI. This study estimated the annual cost of treating the medical consequences of OSA at $3.4 billion in the United States.[61]

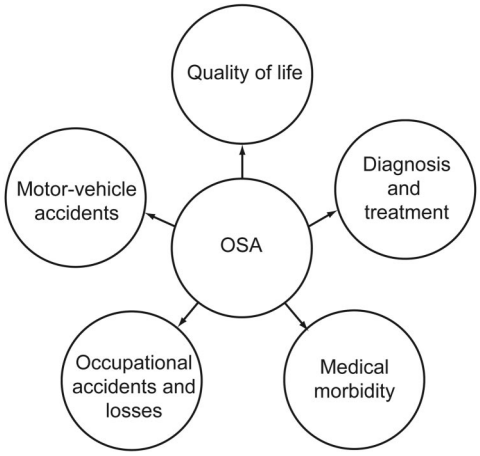

Fig. 8. Economic costs of obstructive sleep apnea (OSA).

Does Treatment Reduce Medical Costs?

Investigators have used quasi-experimental designs (subjects not randomized with respect to treatment) to answer this question.[62-64] When using this type of study design, it is important that the intervention group be compared to an untreated OSA group identified similarly to avoid threats to validity such as regression to the mean. High healthcare use may predispose to the identification of OSA and invalidate findings.[60] Appropriately designed and analyzed studies on this topic are rare. One such study included 54 patients with cardiopulmonary disease and OSA.[64] In the 2 years following treatment, hospitalizations were decreased in patients using CPAP and increased in patients who did not use CPAP (Fig. 9).[65] In adults, a reduction in healthcare costs after treatment has not been demonstrated in a less restricted OSA group (without requirement for comorbid illness), in comparison to an untreated OSA control group, though cost reduction has been shown in a pediatric population.[60]

A longitudinal, case-control study conducted at a health maintenance organization in Israel compared children who had OSA and were treated with tonsillectomy and adenoidectomy, to children who had OSA and did not undergo surgery, and to control subjects who were matched by age, sex, and area of residency.[66] Healthcare utilization was compared between one year before and one year after tonsillectomy and adenoidectomy. Total annual health care costs were reduced by one third in children who underwent tonsillectomy and adenoidectomy, whereas there was

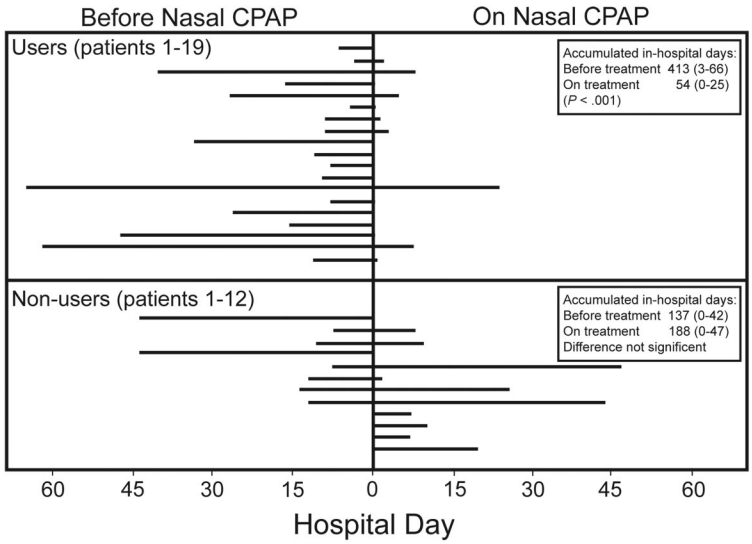

Fig. 9. In-hospital days in patients with obstructive sleep apnea (OSA) and cardiopulmonary diseases 2 years before and after prescription of continuous positive expiratory pressure (CPAP). The total number of in-hospital days for patients with obstructive sleep apnea syndrome and cardiovascular or pulmonary diseases during 2 years prior to treatment with nasal CPAP, as compared to 2 years after the nasal CPAP prescription. Shown are data from nasal CPAP users and patients non-adherent to treatment (non-users) with acute hospitalization due to cardiovascular pulmonary disease. Statistics by Wilcoxon signed-rank test. (Adapted from Reference 65, with permission.)

no change in the control and untreated OSA groups.[66] A greater reduction in costs was noted in children with moderate to severe OSA than in those with mild to moderate OSA. The treated group showed decreases in otolaryngology and pulmonary specialty visits and 25% reduction in medication costs, while costs for these items were unchanged or increased in other groups.[66] These results can not be generalized to adults, given the differences in pathogenesis and pathophysiology between OSA in adults and children, as well as the differences in the therapies that are commonly used (CPAP vs tonsillectomy) and the effectiveness of those therapies. Appropriately designed and analyzed studies on this topic in adults are needed.

Cost-Effectiveness Analysis

Cost-effectiveness analysis is an analytic method that is used to identify interventions that offer the maximum health benefit per dollar spent.[60,67] Cost-effectiveness analysis compares interventions on the differences in costs needed to provide an additional unit of a quality-adjusted life year gained, to allow comparisons across different diseases and health states.[60] The results of cost-effectiveness analysis studies have provided estimates, from a payer perspective, ranging from $2,000–11,000 per quality-adjusted life year over 5 years for treating moderate to severe OSA in a sleep clinic population.[60] These values compare favorably to other generally accepted medical interventions such as comprehensive diabetes care (Table 3).[67,68]

Summary

OSA is a disorder characterized by intermittent impairment of ventilation during sleep due to upper-airway collapse. A number of factors are known to contribute to upper-airway collapse, including reduced upper-airway dilator muscle activity during sleep, upper-airway anatomy, decreased end-expiratory lung volume, ventilatory control instability, sleep state instability, and rostral fluid shifts. There is evidence that some of these factors are genetically controlled. The relative contributions of these factors vary between individuals with OSA, and this may have implications as to which treatments are efficacious for an individual.

OSA is common in adults, with men, older individuals, and the obese being at higher risk. Identification of patients needing evaluation by sleep study is relatively simple and involves assessment of several factors such as snoring, witnessed apnea/self reported-gasping, hypertension, BMI, and neck circumference.

OSA is associated with a substantial economic burden, including increased medical costs. In adults, a reduction in

Table 3. Cost-Effectiveness of a Variety of Clinical Interventions

Intervention	$/QALY
CPAP therapy for moderate to severe OSA	$2,000–11,000
Pediatric immunization	$1,000–3,000
Breast cancer screening	$5,000–19,000
Hypertension control	$10,000–57,000
Comprehensive diabetes care	Cost saving—$34,000
Anti-depressant medication	Cost saving—$23,600

QALY = quality-adjusted life year
OSA = obstructive sleep apnea
CPAP = continuous positive airway pressure
(Adapted from Reference 68.)

medical costs in a diverse patient population with OSA after therapy has not been convincingly demonstrated. However, the results of cost-effectiveness analyses strongly support the value to society of CPAP therapy in patients with moderate to severe OSA relative to other commonly accepted treatments for other conditions.

REFERENCES

1. Gleeson K, Zwillich CW, White DP. The influence of increasing ventilatory effort on arousal from sleep. Am Rev Respir Dis 1990; 142(2):295-300.
2. Kapur V. Control of breathing in the respiratory system. Seattle: ASUW Press, 2008.
3. Shamsuzzaman AS, Gersh BJ, Somers VK. Obstructive sleep apnea: implications for cardiac and vascular disease. JAMA 2003;290(14): 1906-1914.
4. Eckert DJ, Malhotra A, Jordan A. Mechanisms of apnea. Prog Cardiovasc Dis 2009;5(4):313-323.
5. Kubin L, Davies RO. Mechanisms of airway hypotonia. In: Pack AI, editor. Sleep apnea: pathogenesis, diagnosis and treatment. New York: Marcel Dekker; 2002:99-154.
6. Schwab RJ, Kuna ST, Remmers JE. Anatomy and physiology of upper airway obstruction. In: Kryger MH, Roth T, Dement WC. Principles and practice of sleep medicine, 4th edition. Philadelphia: Elsevier Saunders; 2005:988.
7. Worsnop C, Kay A, Pierce R, Kim Y, Trinder J. Activity of respiratory pump and upper airway muscles during sleep onset. J Appl Physiol 1998;85(3):908-920.
8. Schwab RJ, Pasirstein M, Pierson R, Mackley A, Hachadoorian R, Arens R, et al. Identification of upper airway anatomic risk factors for obstructive sleep apnea with volumetric magnetic resonance imaging. Am J Respir Crit Care Med 2003;168(5):522-530.
9. Watanabe T, Isono S, Tanaka A, Tanzawa H, Nishino T. Contribution of body habitus and craniofacial characteristics to segmental closing pressures of the passive pharynx in patients with sleep-disordered breathing. Am J Respir Crit Care Med 2002;165(2):260-265.
10. Owens RL, Malhotra A, Eckert DJ, White DP, Jordan AS. The influence of lung volume on measurement of pharyngeal collapsibility. Appl Physiol 2010;108(2):445-451.
11. Heinzer RC, Stanchina ML, Malhotra A, et al. Effect of increased lung volume on sleep disordered breathing in sleep apnoea patients. Thorax 2006;61(5):435-439.
12. Heinzer RC, Stanchina ML, Malhotra A, Jordan AS, Patel SR, et al. Lung volume and continuous positive airway pressure requirements in obstructive sleep apnea. Am J Respir Crit Care Med 2005;172(1): 114-117.
13. White DP. Pathogenesis of obstructive and central sleep apnea. Am J Respir Crit Care Med 2005;172(11):1363-1370.
14. Hudgel DW, Gordon EA, Thanakitcharu S, Bruce EN. Instability of ventilatory control in patients with obstructive sleep apnea. Am J Respir Crit Care Med 1998;158(4):1142-1149.
15. Hudgel DW, Chapman KR, Faulks C, Hendricks C. Changes in inspiratory muscle electrical activity and upper airway resistance during periodic breathing induced by hypoxia during sleep. Am Rev Respir Dis 1987;135(4):899-906.
16. Badr MS, Roiber F, Skatrud JB, Dempsey J. Pharyngeal narrowing/ occlusion during central sleep apnea. J Appl Physiol 1995;78(5): 1806-1815.
17. Younes M. Role of arousals in the pathogenesis of obstructive sleep apnea. Am J Respir Crit Care Med 2004;169(5):623-633.
18. Shiota S, Ryan CM, Chiu KL, Ruttanaumpawan P, Haight J, Arzt M, et al. Alterations in upper airway cross sectional area in response to lower body positive pressure in healthy subjects. Thorax 2007;62(10): 868-872.
19. Chiu KL, Ryan CM, Shiota S, Ruttanaumpawan P, Arzt M, Haight JS, et al. Fluid shift by lower body positive pressure increases pharyngeal resistance in healthy subjects. Am J Respir Crit Care Med 2006;174(12):1378-1383.
20. Su MC, Chiu KL, Ruttanaumpawan P, Shiota S, Yumino D, Redolfi S, et al. Lower body positive pressure increases upper airway collapsibility in healthy subjects. Respir Physiol Neurobiol 2008;161(3):306-312.
21. Redolfi S, Yumino D, Ruttanaumpawan P, Yau B, Su MC, Lam J, Bradley TD. Relationship between overnight rostral fluid shift and obstructive sleep apnea in nonobese men. Am J Respir Crit Care Med 2009;179(3):241-246.
22. Peppard PE, Young T. Exercise and sleep disordered breathing: an association independent of body habitus. Sleep 2004;27(3):480-484.
23. Casale M, Pappacena M, Rinaldi V, Bressi F, Baptista P, Salvinelli F. Obstructive sleep apnea syndrome: from phenotype to genetic basis. Curr Genomics 2009;10(2):119-126.
24. Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. Proc Am Thorac Soc 2008;5(2):173-178.
25. Ferguson KA, Cartwright R, Rogers R, Schmidt-Nowara W. Oral appliances for snoring and obstructive sleep apnea: a review. Sleep 2006;29(2):244-262.
26. Elshaug AG, Moss JR, Southcott AM, Hiller JE. Redefining success in airway surgery for obstructive sleep apnea: a meta analysis and synthesis of the evidence. Sleep 2007;30(4):461-467.
27. Veasey SC, Guilleminault C, Strohl KP, Sanders MH, Ballard RD, Magalang UJ. Medical therapy for obstructive sleep apnea: a review by the Medical Therapy for Obstructive Sleep Apnea Task Force of the Standards of Practice Committee of the American Academy of Sleep Medicine. Sleep 2006;29(8):1036-1044.
28. Owens R, Wellman A, Malhotra A. The chicken-or-egg debate in OSA pathogenesis. Sleep 2009;32(10):1255-1256.
29. Friedman M, Ibrahim H, Joseph NJ. Staging of obstructive sleep apnea/hypopnea syndrome: a guide to appropriate treatment. Laryngoscope 2004;114(3):454-459.
30. Wellman A, Malhotra A, Jordan AS, Stevenson KE, Gautam S, White DP. Effect of oxygen in obstructive sleep apnea: role of loop gain. Respir Physiol Neurobiol 2008;162(2):144-151.
31. Veasey SC. Serotonin agonists and antagonists in obstructive sleep apnea: therapeutic potential. Am J Respir Med 2003;2(1):21-29.
32. 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 29;328(17):1230-1235.
33. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, Vela-Bueno A, Kales A. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med 2001;163(3 Pt 1):608-613.
34. Bearpark H, Elliott L, Grunstein R, Cullen S, Schneider H, Althaus W, Sullivan C. Snoring and sleep apnea: a population study in Australian men. Am J Respir Crit Care Med 1995;151(5):1459-1465.
35. Udwadia ZF, Doshi AV, Lonkar SG, Singh CI. Prevalence of sleep-disordered breathing and sleep apnea in middle-aged urban Indian men. Am J Respir Crit Care Med 2004;169(2):168-173.
36. Ip MS, Lam B, Lauder IJ, Tsang KW, Chung KF, Mok YW, Lam WK. A community study of sleep-disordered breathing in middle-aged Chinese men in Hong Kong. Chest 2001;119(1):62-69.
37. Ip MS, Lam B, Tang LC, Lauder IJ, Ip TY, Lam WK. A community study of sleep-disordered breathing in middle-aged Chinese women in Hong Kong: prevalence and sex differences. Chest 2004;125(1):127-134
38. Kim J, In K, Kim J, You S, Kang K, Shim J, Lee S, Lee J, Lee S, Park C, Shin C. Prevalence of sleep-disordered breathing in middle-

aged Korean men and women. Am J Respir Crit Care Med 2004; 170(10):1108-1113.
39. Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc 2008;5(2):136-143.
40. Iber C, Ancoli-Israel S, Chesson A, Quan SF. The AASM manual for the scoring of sleep and associated events: rules, terminology, and technical specifications, 1st edition. Westchester, Illinois: American Academy of Sleep Medicine; 2007.
41. Redline S, Kapur V, Sanders MH, Quan SF, Gottlieb DJ, Rapoport DM, et al. Effects of varying approaches for identifying respiratory disturbances on sleep apnea assessment. Am J Respir Crit Care Med 2000;161(2):369-374.
42. Sulit L, Storfer-Isser A, Kirchner HL, Redline S. Differences in polysomnography predictors for hypertension and impaired glucose tolerance. Sleep 2006;29(6):777-783.
43. Punjabi NM, Newman AB, Young TB, Resnick HE, Sanders MH. Sleep-disordered breathing and cardiovascular disease: an outcome-based definition of hypopneas. Am J Respir Crit Care Med 2008; 177(10):1150-1155.
44. Punjabi NM, Shahar E, Redline S, Gottlieb DJ, Givelber R, Resnick HE; Sleep Heart Health Study Investigators. Am J Epidemiol 2004; 160(6):521-530.
45. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342(19):1378-1384.
46. Kapur VK, Baldwin CM, Resnick HE, Gottlieb DJ, Nieto FJ. Sleepiness in patients with moderate to severe sleep-disordered breathing. Sleep 2005;28(4):472-477.
47. Ye L, Pien GW, Weaver TE. Gender differences in the clinical manifestation of obstructive sleep apnea. Sleep Med 2009;10(10): 1075-1084.
48. Kapur V, Strohl KP, Redline S, Iber C, O'Connor G, Nieto J. Underdiagnosis of sleep apnea syndrome in US communities. Sleep Breath 2002;6(2):49-54.
49. Young T, Shahar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ, et al. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. Arch Intern Med 2002;162(8):893-900.
50. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA 2000;84(23):3015-3021.
51. Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T. Progression and regression of sleep-disordered breathing with changes in weight: the Sleep Heart Health Study. Arch Intern Med 2005; 165(20):2408-2413.
52. Babb TG, Wyrick BL, DeLorey DS, Chase PJ, Feng MY. Fat distribution and end-expiratory lung volume in lean and obese men and women. Chest 2008;134(4):704-711.
53. Schwartz AR, Patil SP, Laffan AM, Polotsky V, Schneider H, Smith PL. Obesity and obstructive sleep apnea: pathogenic mechanisms and therapeutic approaches. Am Thorac Soc 2008;5(2):185-192.
54. Flemons WW, Whitelaw WA, Brant R, Remmers JE. Likelihood ratios for a sleep apnea clinical prediction rule. Am J Respir Crit Care Med 1994;150(5):1279-1285.
55. Takegami M, Hayashino Y, Chin K, Sokejima S, Kadotani H, Akashiba T, et al. Simple four-variable screening tool for identification of patients with sleep-disordered breathing. Sleep 2009;32(7): 939-948.
56. Maislin G, Pack AI, Kribbs NB, Smith PL, Schwartz AR, Kline LR, et al. A survey screen for prediction of apnea. Sleep 1995;18(3):158-166.
57. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med 1999;131(7):485-491.
58. Schellenburg JB, Maislin G, Schwab RJ. Physical findings and the risk for obstructive sleep apnea. Am J Respir Crit Care 2000;162(2): 740-748.
59. Sassani A, Findley LJ, Kryger M, Goldlust E, George C, Davidson TM. Reducing motor-vehicle collisions, costs, and fatalities by treating obstructive sleep apnea syndrome. Sleep 2004;27(3):453-458.
60. Kapur VK, Alfonso-Cristancho R. Just a good deal or truly a steal? Medical cost savings and the impact on the cost-effectiveness of treating sleep apnea. Sleep 2009;32(2):135-136.
61. Kapur V, Blough DK, Sandblom RE, Hert R, de Maine JB, Sullivan SD, Psaty BM. The medical cost of undiagnosed sleep apnea. Sleep 1999;22(6):749-755.
62. Bahammam A, Delaive K, Ronald J, Manfreda J, Roos L, Kryger MH. Health care utilization in males with obstructive sleep apnea syndrome two years after diagnosis and treatment. Sleep 1999;22(6):740-747.
63. Banno K, Manfreda J, Walld R, Delaive K, Kryger MH. Healthcare utilization in women with obstructive sleep apnea syndrome 2 years after diagnosis and treatment. Sleep 2006;29(10):1307-1311.
64. Peker Y, Hedner J, Norum J, Kraiczi H, Carlson J. Increased incidence of cardiovascular disease in middle-aged men with obstructive sleep apnea: a 7-year follow-up. Am J Respir Crit Care Med 2002; 166(2):159-165.
65. Peker Y, Hedner J, Johansson A, Bende M. Reduced hospitalization with cardiovascular and pulmonary disease in obstructive sleep apnea patients on nasal CPAP treatment. Sleep 1997;20(8):645-653.
66. Tarasiuk A, Simon T, Tal A, Reuveni H. Adenotonsillectomy in children with obstructive sleep apnea syndrome reduces health care utilization. Pediatrics 2004;113(2):351-356.
67. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Methods for the economic evaluation of health care programmes, 3rd edition. Oxford: Oxford University Press; 2005.
68. Neumann PJ, Levine BS. Do HEDIS measures reflect cost-effective practices? Am J Prev Med 2002;23(4):276-289.

Discussion

Parthasarathy: Looking at it from a physiological standpoint, in terms of the metric for OSA, we try to quantify the insult due to upper-airway collapse as the frequency or the number of events per hour, but someone could have a 110-second-long apnea, such as a patient with a neuromuscular disorder, wherein counting the number of events per hour doesn't do justice to the duration of every event. You could have 10-second events, as opposed to 110-second events, and the numbers in terms of index would actually tell the opposite of what the physiological insult is. It's probably pretty late in the game to think about that, but since you're talking about metrics, I'm wondering whether we can derive a composite index that quantifies not only the number of events but also the duration. Is that feasible?

Kapur: I'm not aware whether that's been looked at, but I think it would befeasible. I think the issue is that there are different insults happening with sleep-disordered breathing, whether it's intrathoracic pressure changes, fluctuations in saturation, arousal, or

sympathetic nervous system activation. We may not have one best metric to assess all those things.

My bias in terms of the AASM [American Academy of Sleep Medicine] standard scoring criteria for hypopnea is that it's a terrible criteria when you're dealing with people with sleepiness, because in clinical practice we see individuals all the time who have minimal or no desaturations, lots of events, and are sleepy. So those criteria really fall short from the perspective of a clinician who is trying to improve quality of life. On the other hand, a lot of the cardiovascular data come from studies that used 4% desaturation to qualify hypopnea. The strength of using the AASM standard criteria is that when I talk to a patient I can say, "Well, from the studies, this is what your cardiovascular risk might be."

Quan: One big issue from a clinician's perspective and a research perspective is that many individuals with sleep apnea are not sleepy.[1] In the Sleep Heart Health Study[2] approximately 50% of the people who had at least a moderately elevated respiratory disturbance index [RDI] were not sleepy. We see these people all the time in clinic; people get referred to you and they somehow get a sleep study. Then you'll have someone with an elevated RDI of 50 and you talk to them and they say, "I don't fall asleep and I'm definitely not sleepy; the only reason I'm here is because my wife dragged me here."

We really don't know what to do with these people. To someone with an RDI of 50 you will probably tell them they need to wear CPAP because they're at increased risk for heart disease. But with many people with lower RDIs we really don't know what to do because they don't want to wear CPAP, they don't want to get an oral appliance, and they certainly don't want surgery. We don't know what the health or economic implications are for these people. I think that's a major issue.

1. Kapur VK, Baldwin CM, Resnick HE, Gottlieb DJ, Nieto FJ. Sleepiness in patients with moderate to severe sleep-disordered breathing. Sleep 2005; 28(4):472-477.
2. Kapur VK, Resnick HE, Gottlieb DJ; Sleep Heart Health Study Group. Sleep-disordered breathing and hypertension: does self-reported sleepiness modify the association? Sleep 2008;31(8):1127-1132.

Kuna: I was thinking about the pathophysiology of the upper airway and remembering that we used to think of it as a donut. Initially, everybody (including myself) was looking at the hole of the donut and analyzing the size of the hole. Eventually we realized that the volume of the soft tissues surrounding walls of the airway was an important determinant of airway size. I think the direction the field is taking now is to combine those concepts and model the pharynx as a box. The soft tissues and the airway are encased within the mandible, the maxilla, and the hard palate. It's a fixed box. With this model the ratio of soft tissue volume to the box size dictates the size of the airway. Recent evidence indicates that the size of these upper airway bony and soft tissue structures is based on genetics and obesity. The size of the box relative to the size of the tongue and lateral walls dictates the size of the airway and determines the OSA risk.

Kapur: Yes, I think genetics is a big player in pathogenesis. What do you think about the notion that, beyond genetics, the patterns set up in childhood, in terms of obstruction due to congestion and mouth breathing versus nasal breathing, may influence development of sleep apnea?

Kuna: The pediatricians may be able to help us out here, but in listening to those lectures it seemed to me that those events early in childhood alter upper airway structure and bone structure. Do the bilateral tonsil or adenoid hypertrophy in childhood lead to changes in upper airway structure that perhaps predisposes them to OSA later in life?

Pierson:* I also have a comment on the upper airway. I was intrigued by your pointing out the relationship between upper airway volume and lung volume. I have a hard time seeing how mechanically the two could be related very much, and I wonder if you have any further comments. For example, are there studies of any aspect of neural activity related to different lung volumes? I'm interested in this because of the potential implications for why CPAP might help, and at a relative low CPAP level with a compliant respiratory system.

Kapur: Classically, the explanation that's been given is that tracheal tug is the mechanism; when you have higher lung volumes, you're tugging on your trachea and making the upper airways stiffer.

Pierson: But is there evidence that the configuration of the upper airway, other than just the upper trachea, is affected by changes in lung volume?

Quan: David, I believe that David White and Atul have studied the mechanics of the upper airway with changes in lung volume.[1,2] Bob, did you do a study as well?

1. Stanchina ML, Malhotra A, Fogel RB, Trinder J, Edwards JK, Schory K, White DP. The influence of lung volume on pharyngeal mechanics, collapsibility, and genioglossus muscle activation during sleep. Sleep 2003; 26(7):851-856.
2. Heinzer RC, Stanchina ML, Malhotra A, Fogel RB, Patel SR, Jordan AS, et al. Lung volume and continuous positive airway pressure requirements in obstructive sleep ap-

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nea. Am J Respir Crit Care Med 2005;172(1): 114-117.

Owens: Yes, we looked at the impact of lung volumes on the upper airway.[1] Exactly as you said, the hypothesis is that as lung volume expands, tracheal traction is exerted on the upper airway. This may cause unfolding of the upper airway, or stiffen the walls, and improve the mechanics of the upper airway. There may be neurological inputs, but that's not been well studied. The direct mechanical effect is pretty large in terms of measurements such as the pharyngeal critical pressure. A change in lung volume of about 500 mL will improve the pharyngeal critical pressure by 3 or 4 cm H_2O, so you can move somebody who's a snorer or has mild OSA into just a pure snorer or not a snorer at all.

1. Owens RL, Malhotra A, Eckert DJ, White DP, Jordan AS. The influence of end-expiratory lung volume on measurements of pharyngeal collapsibility. J Appl Physiol 2010;108(2):445-451.

Pierson: I was thinking of the reflexes between the various aspects of the upper airway and cough and various neurally mediated things in the airways.

Owens: We are looking at that in an ongoing trial of asthma and OSA patients. At least in animals, repetitive irritation of the upper airway increased the lower airway resistance.[1]

1. Nadel JA, Widdicombe JG. Reflex effects of upper airway irritation on total lung resistance and blood pressure. J Appl Physiol 1962;17:861-865.

Patil: Regarding Dr Pierson's comment on why a low level of CPAP may be effective in some patients with substantial sleep apnea, it may be in that particular situation less of an issue of lung volume, but perhaps just stabilizing the airway to some degree in certain patients who have a rather excessive response to disturbances in airflow, individuals with a high loop gain—if you're able to just stabilize the airway sufficiently, these individuals may require a relatively low CPAP pressure to prevent a series of apneas and hypopneas.

Kuna: Moving on to epidemiology, I wonder if it's time to do another epidemiologic study in the United States? The data we are quoting are a quarter century old, and during that time we've had an epidemic of obesity. Sleep apnea is already recognized as a major public health issue, but I think if another epidemiologic study were done today, it's importance would move up.

Kapur: I agree. The prevalence would be higher. We have some data on the incidence of OSA from the Sleep Heart Health Study[1] and from Susan Redline's group,[2] and they're finding that people go from having an AHI of 5 to 15 events per hour, and it might be as high as 10% of the population over several years. On the other hand there are individuals whose AHI regresses; there may be 8% who go the other way. Over time there is a net increase in prevalence. But I agree; if you did the same study now, we'd find a higher prevalence.

1. Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T. Progression and regression of sleep-disordered breathing with changes in weight: the Sleep Heart Health Study. Arch Intern Med 2005;165(20):2408-2413.
2. Tishler PV, Larkin EK, Schluchter MD, Redline S. Incidence of sleep-disordered breathing in an urban adult population: the relative importance of risk factors in the development of sleep-disordered breathing. JAMA 2003;289(17):2230-2237.

Gozal: Regarding the prevalence of obesity, at least in pediatrics, we did a study that found that one of the major contributors to AHI was BMI in children. In the pediatric sleep clinic almost 50% of our patients are obese, not just overweight. So it has been very problematic for our field, because we see either overweight or severely obese kids, and it's very unfortunate because it comes with different consequences adding to the OSA prevalence. So the question is whether OSA is causing the obesity or is obesity helping the OSA to get worse? We're still battling between the two.

1. Dayyat E, Kheirandish-Gozal L, Sans Capdevila O, Maarafeya MM, Gozal D. Obstructive sleep apnea in children: relative contributions of BMI and adenotonsillar hypertrophy. Chest 2009;136(1):137-144.

Quan: I'd like to reinforce what Leila said. In a longitudinal follow-up of our Tucson Children's Assessment of Sleep Apnea Study[1] we found that one of the big factors in determining prevalent OSA when we initially studied children in the 6–12-year age group and subsequently when they become adolescents 5 years later was increase in BMI.

Vishesh, you mentioned how obesity predisposes to sleep apnea. It is possible that sleep apnea may actually beget obesity. We have some data[2] from the Sleep Heart Health Study that was presented at last year's Associated Professional Sleep Societies meeting suggesting this. So I do think it's a two-way street here.

1. Goodwin JL Vasquez, MM, Silva GE, Quan SF. Incidence and remission of sleep-disordered breathing and related symptoms in 6- to 17-year-old children. The Tucson Children's Assessment of Sleep Apnea Study. J Pediatr 2010:157(1):57–61.
2. Brown MA, Goodwin JL, Silva E, Behari A, Newman AB, Punjabi NM, et al. Sleep-disordered breathing and weight gain: the Sleep Heart Health Study (abstract). Sleep 2009; 32(Suppl):A170.

Carlin: In dealing with primary care providers we need to disseminate the information that the overall incidence of OSA is 3–4% in the general population. We also need to educate providers that patients who have an AHI of less than 5 but who have important symptoms, such as daytime sleepiness,

may be candidates for a trial of positive airway pressure therapy, to see if it improves their symptoms. We need to link the clinical evaluation with the sleep study results. Does anyone have any recommendations regarding such a "guideline?"

Kheirandish-Gozal: I will tackle that in my lecture tomorrow, for the pediatric population.

Parthasarathy: Regarding the sleepy versus the non-sleepy apneic, didn't the Sleep Heart Health longitudinal analysis[1] suggest that it was only the sleepy apneics who had cardiovascular mobility?

1. Punjabi NM, Caffo BS, Goodwin JL, Gottlieb DJ, Newman AB, O'Connor GT, et al. Sleep-disordered breathing and mortality: a prospective cohort study. PLoS Med 2009; 6(8):e1000132.

Kapur: I did a cross-sectional study[1] on the Sleep Heart Health Study cohort and found a difference between prevalent hypertension in sleepy and non-sleepy subjects with sleep apnea. But I think the subsequent longitudinal analyses did not show a difference in incident hypertension between the sleepy and the non-sleepy apneics.[2]

1. Kapur VK, Resnick HE, Gottlieb DJ; Sleep Heart Health Study Group. Sleep-disordered breathing and hypertension: does self-reported sleepiness modify the association? Sleep 2008;31(8):1127-1132.
2. O'Connor GT, Caffo B, Newman AB, Quan SF, Rapoport DM, Redline S, et al. Prospective study of sleep-disordered breathing and hypertension: the Sleep Heart Health Study. Am J Respir Crit Care Med 2009;179(12): 1159-1164.

Parthasarathy: So were there some non-sleepy patients who transitioned into the sleepy category over the longitudinal period? At the World Congress of Sleep Apnea, Naresh Punjabi explained the possible reasons for negative trials when considering the effect of CPAP treatment on glycemic control in patients suffering from both OSA and diabetes mellitus. His concern was that by the time they manifest overt diabetes it is too late in the disease process to do anything about it. So he is talking about treating prediabetics with sleep apnea and preventing the occurrence of overt diabetes. In the same fashion, the question could be raised as to whether some of these non-sleepy apneics could transition into being sleepy apneics from sequential progression of the disease? And could early disease modification or intervention affect the disease progression?

Quan: I don't think the Sleep Heart Health Study[1] or other trials[2,3] answer whether it's a natural progression in non-sleepy people. Certainly the issue of early intervention is important, and tomorrow I'll talk about an intervention trial, HeartBEAT,[4] in which early intervention is one of the issues.

1. Quan SF, Howard BV, Iber C, Kiley JP, Nieto FJ, O'Connor GT, et al. The Sleep Heart Health Study: design, rationale, and methods. Sleep 1997;20(12):1077-1085.
2. Tishler PV, Larkin EK, Schluchter MD, Redline S. Incidence of sleep-disordered breathing in an urban adult population: the relative importance of risk factors in the development of sleep-disordered breathing. JAMA 2003;289(17):2230-2237.
3. Young T, Finn L, Peppard PE, Szklo-Coxe M, Austin D, Nieto FJ, et al. Sleep-disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. Sleep 2008;31(8):1071-1078.
4. Redline S. Phase II trial of sleep apnea treatment to reduce cardiovascular morbidity. ClinicalTrials.gov identifier: NCT01086800. http://projectreporter.nih.gov/project_info_description.cfm?aid=7853407. *Accessed June 24, 2010.*

Minkley:† Regarding the measurement of sleepiness, it's pretty well accepted that we aren't very good judges of sleepiness, and we have some different objective and subjective measurements available. When you look at societal economics, one of the high costs of sleepiness is occupational accidents. I'm wondering about the integration of more performance-based measurements. It is my understanding that there isn't a great correlation between our current measurements of sleepiness and performance. In the future do you see more discrete measures, such as performance and vigilance tests correlated to specific job-performance tasks so there is better correlation into daily life and how that correlation might help us target treatment and control the economic costs?

Kapur: To expand on your comments, one frustration is when people believe that sleepiness equals an abnormal Epworth sleepiness score. We all know that sleepiness has many facets to it, and even the subjective component has different facets. It could be that you're falling asleep unintentionally and recognizing it or not recognizing it, or it could be you're just feeling sleepy and fatigued. I want to get the word out to our trainees and others not to misuse the Epworth scale. Also, getting some functional measures, as you suggest, would be useful to get a more complete picture of how the sleepiness is affecting daily activities.

Minkley: I think that's really key. In the sleep center patients often tell us things they don't tell their doctor, because they don't think it's important enough to use the doctor's time. They'll tell us stories of falling asleep on the way to work and having people call them to keep them awake, but they didn't mention it to their doctor because they thought it was just because they work hard. Capturing these stories and creating a partnership between the different groups who work with the patients to be sure there's good information flow is, I think, a key to capturing the true impact of untreated OSA.

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