Chapter 14
Health Disparities in Sleep-Related Breathing Disorders

Jose S. Loredo

Key Points

- The prevalence of snoring and obstructive sleep apnea increases with age.
- The upper airway resistance syndrome is more commonly diagnosed in younger, thinner women.
- Obstructive sleep apnea is strongly associated with male sex, older age, and obesity.
- Race/ethnicity may matter: obstructive sleep apnea is more prevalent in African Americans than in whites, and African Americans are younger, heavier, and sleepier at diagnosis. However, based on the available literature, the prevalence of obstructive sleep apnea is probably not different between Hispanics and whites, but the prevalence of snoring is higher among Hispanics as compared to non-Hispanic whites.
- Gender matters: during evaluation for sleep-disordered breathing, women complain more of insomnia, fatigue, and depression rather than sleepiness.
- Men are at a higher risk of stroke at every level of obstructive sleep apnea severity compared to women.
- Weight changes and exercise produce a larger beneficial effect in the sleep apnea of men compared to women.
- Obstructive sleep apnea may have greater cognitive impact in Hispanic children than in their white counterparts.
- Physicians may be underdiagnosing or slow to make the diagnosis of obstructive sleep apnea in women and in lean individuals who present with sleep-related complaints.
- Lower CPAP compliance is seen in patients of lower socioeconomic status, in African Americans, and in women.

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Introduction: The Significance of Sleep

Sleep or a sleep-like state is almost ubiquitous, occurring in animals ranging from fruit flies to humans [1, 2]. However, the purpose of sleep is still a question that has not been fully answered. The need for sleep appears counterintuitive to natural selection; however, it is obvious that sleep has physical and mental restorative properties that are essential for survival and health [3, 4]. Sleep produces a transitory state of cardiovascular relaxation that is thought to be important for cardiovascular health [5, 6]. Sleep has been associated with the ability to learn and memory consolidation [7, 8], and more recently sleep has been associated with the turning on of genes that repair neural tissue [9]. Above all, sleep is the ultimate cure for sleepiness.

Most of what is known about the physiology of sleep has been gained in the last 64 years since the discovery of REM sleep in 1951 [10]. From ancient times, sleep was viewed as a completely passive phenomenon, akin to the brain turning off. In fact, the Bible uses sleep as a metaphor for death [11]. However, far from being an inactive time, sleep is a dynamic state, controlled by elaborate and precise sleep stages that have physiological significance. Sleep systematically progress from light sleep (N1 and N2 sleep) to deep sleep (N3) and REM sleep (R). REM sleep is also known as paradoxical sleep for producing profound somatic atonia while maintaining wake-like brain activity. A good night's sleep is characterized by three major factors: sleep schedule, sleep duration, and sleep quality. Disturbance of any of these factors results in negative health outcomes including excessive daytime somnolence [12], fatigue and mood disorders [13, 14], cognitive impairment [15], metabolic disorders [16], cardiovascular disease [17, 18], and increased susceptibility to other disease [19–21].

Since the description of obstructive sleep apnea (OSA) in 1965 [22], sleep-disordered breathing has emerged as the most common sleep disorder evaluated in the sleep laboratory. And because of its strong association with metabolic disease, cardiovascular disease, and mortality [23–25], the public knowledge about OSA has increased dramatically since the 1990s. Yet, OSA is still unknown to many, and there is growing evidence to suggest significant health disparities with respect to OSA diagnosis and management [26]. This chapter will review the available literature on disparities in obstructive sleep-disordered breathing in the U.S. and highlight important gaps in knowledge that may be the focus of future research.

Physiological Changes during Sleep That Predispose to Sleep-Disordered Breathing

Withdrawal of the wakefulness respiratory drive during the transition from wake to sleep results in transient instability of respiratory control that predisposes the individual to sleep-disordered breathing [27]. In normal individuals, the transition from wake to sleep may result in transient episodes of central sleep apnea and Cheyne–Stokes respiration. In the obese or those who have an anatomically compromised upper airway, snoring and/or OSA may be seen during the transition from wake to

sleep. The sleep fragmentation that results from central or obstructive respiratory events at sleep onset may perpetuate the respiratory control instability and predispose the individual to more protracted sleep-disordered breathing during light sleep [27–29].

Falling asleep also promotes sleep-disordered breathing by unmasking the tendency of peripheral chemoreceptors in some individuals to overreact to a disturbance in PCO_2 levels, often described as high loop gain. High loop gain is an engineering term that describes the propensity of a feedback system to overreact to a disturbance [28, 30]. In situations that result in chronic low PCO_2 levels such as congestive heart failure or sleeping at high altitude, falling asleep results in central apnea due to PCO_2 levels dropping below the apnea threshold. High loop gain will promote overshoot of ventilation as the PCO_2 levels rise during the apnea. The hyperventilation then drives the PCO_2 below the apnea threshold again, resulting in a vicious cycle that promotes the recurrence of central apneas (Fig. 14.1) [31]. This is known as periodic breathing. Loop gain appears to play an important role in the development of OSA in those individuals with a tendency to upper airway collapse [32].

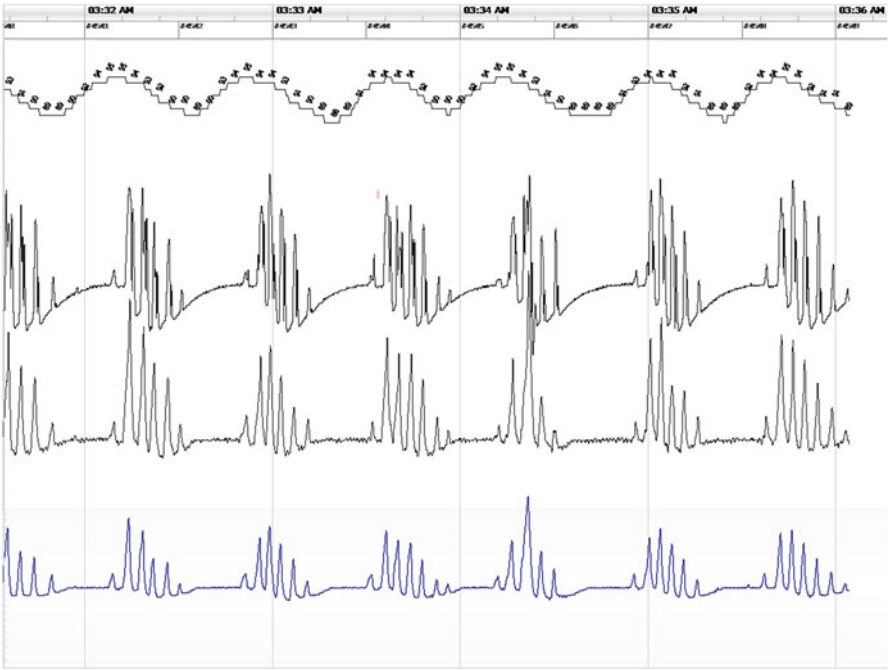

Fig. 14.1 Home sleep recording showing ventilatory response to a disturbance (central apnea) in the setting of high loop gain chemoreceptor response. Notice how high loop gain results in overreaction to the disturbance and promotion of recurrent central apneas. A low loop gain response would result in progressive dampening of the subsequent respiratory event until normal respiration is recovered. From *top* to *bottom*: SpO_2 (channels 1). Nasal airflow (channel 2). Thoracic effort (channel 3). Abdominal effort (channel 4)

Arousals from sleep also promote respiratory instability by producing hyperventilation, which in turn drives the PCO_2 level below the apnea threshold. In the setting of high chemoreceptor sensitivity, this perpetuates respiratory instability and periodic breathing [30].

Normal sleep produces a relative state of hypoventilation, as noted by a 2–3 % reduction in SaO_2 and by a 2–3 mmHg increase in PCO_2 [33]. This degree of hypoventilation has no clinical relevance in normal individuals. However, in persons prone to having low lung volumes due to obesity, respiratory muscle weakness, or in those with intrinsic lung disease, this sleep-related hypoventilation may significantly contribute to central hypopneas and obstructive apneas, especially when sleeping in the supine position [34].

Sleep more than doubles upper airway resistance which can promote sleep-disordered breathing. This is the result of dramatic loss of inspiratory genioglossus motor unit activity at sleep onset resulting in the relaxation of the tongue and pharyngeal dilator muscles, causing a partial collapse of the upper airway [35]. Upper airway resistance is also greatly enhanced by gravity when sleeping in the supine position [36]. This effect can be most marked during the generalized muscle hypotonia of REM sleep. Clinically, it is common for snoring, which is a sign of increased upper airway resistance, to be most severe or present only when sleeping in the spine position.

Importance of Health Disparities in the Practice of Respiratory Sleep Medicine

The importance of sleep in overall health has only recently been recognized [23–25, 37–39]. Sleep-disordered breathing such as snoring and sleep apnea are widespread conditions [37, 40, 41] and are associated with adverse outcomes such as hypertension, diabetes, obesity, myocardial ischemia, stroke, arrhythmia, renal failure, increased healthcare use, and all-cause mortality [23–25]. Most of what is known about the epidemiology and pathophysiology of sleep-disordered breathing has come from research performed in predominantly male non-Hispanic white populations, with limited research in African Americans [37, 42–44]. Therefore, it is difficult to generalize the results to other ethnic minorities or to women. Differences in sleep architecture, duration, and sleep disorders have been reported between various racial groups [44–48]. In a study by Profant et al., African Americans had longer total sleep time, longer REM sleep, and lower deep sleep than whites [44]. In a more recent study from the same laboratory, African Americans had more N2 sleep (light sleep) and less deep sleep than whites, which was associated with a greater personal experience of discrimination as assessed using The Scale of Ethnic Experience [46]. In a review of the literature, children in racial/ethnic and socioeconomic minority groups had a higher prevalence and greater risk for sleep-disordered breathing [48]. This suggests significant environmental or cultural effects on sleep quality and

sleep disorders that may impact the prevalence of cardiovascular disease and affect their evaluation and management [47, 48]. For example, children with health insurance who had OSA were more likely to undergo tonsillectomy to correct the problem than those without health insurance [48]. In 2003, the National Institutes of Health National Sleep Disorders Research Plan (NSDRP) stressed that there were major sleep health disparities in racial and ethnic minorities and in the socioeconomically disadvantaged, who are more likely to sleep in crowded, noisy, or otherwise less than optimal environments [49].

According to data from the 2010 US Census, minority groups in the US are rapidly growing, and by 2043, whites may become the minority. For example, Hispanics or Latinos are now the largest US minority group at 16.3 %; by 2050, it is estimated that Hispanics will make up 29 % of the US population [50]. These great shifts in demographics further stress the need to better understand health disparities and develop policies to help eliminate them.

Sleep-Disordered Breathing

Sleep-disordered breathing can be divided into obstructive (Fig. 14.2), central (Fig. 14.3), and mixed apneas (Fig. 14.4) and hypopneas. Apneas are characterized by complete or nearly complete cessation of airflow for at least 10 s in the adult and for two or more respiratory cycles in the child. Hypopneas are characterized by a 30 % to <90 % decrement in airflow for at least 10 s associated with oxyhemoglobin desaturation of ≥4 %. Alternatively, hypopneas can also be defined as a reduction in airflow of ≥50 % associated with an oxygen desaturation of ≥3 % and/or an arousal from sleep (Fig. 14.5) [51]. The severity of sleep apnea is characterized using the apnea–hypopnea index (AHI), which describes the number of these events per hour of sleep.

Obstructive sleep-disordered breathing is by far the most common of all the three forms. Obstructive events are characterized by complete or partial collapse of the upper airway and persistent respiratory efforts usually in a crescendo pattern terminated by an arousal (Fig. 14.2). Snoring is a sign of partial obstruction and occurs during hypopneas or after termination of an apnea (Fig. 14.5), but it is typically absent during an apnea due to complete obstruction of the upper airway. Snoring is also a prominent feature of the upper airway resistance syndrome (UARS). This is a variant of sleep-disordered breathing that has no apneas, hypopneas, or desaturations. The UARS is characterized by episodes of crescendo snoring and increasingly more negative esophageal and pharyngeal pressure due to crescendo respiratory effort that terminate in an arousal (Fig. 14.6) [52]. These episodes are also known as respiratory effort-related arousals. Clinically, the UARS will present with similar symptoms as OSA [53–55].

Central apneas and hypopneas are the consequence of the cessation or partial reduction of the central respiratory drive, thereby resulting in the absence or reduction of respiratory efforts. Typically, snoring is absent, but gasping and some snoring

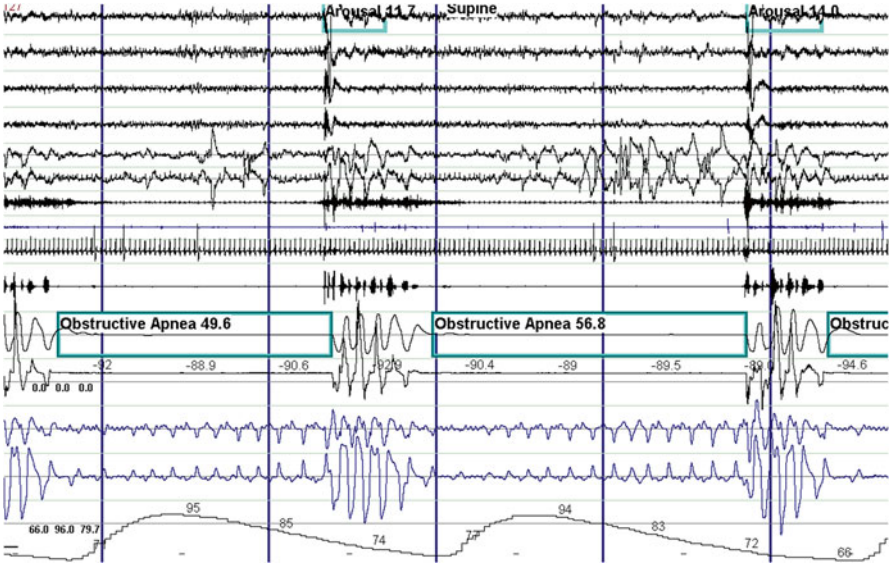

Fig. 14.2 Polysomnographic example of obstructive sleep apnea. These events are characterized by complete obstruction of the upper airway resulting in the absence of airflow while respiratory efforts persist. Gasping for air and snoring is seen when the airway opens during a resulting arousal from sleep. Oxygen desaturation can be severe as in this case. From *top* to *bottom*: EEG channels 1–4. EOG channels 5–6. Chin EMG channel 7. Tibialis anterior EMG channel 8. ECG channel 9. Snoring microphone channel 10. Thermistor and pressure transducer airflow channels 11–12. Chest and abdominal respiratory effort channels 13–14. Oxygen saturation channel 15

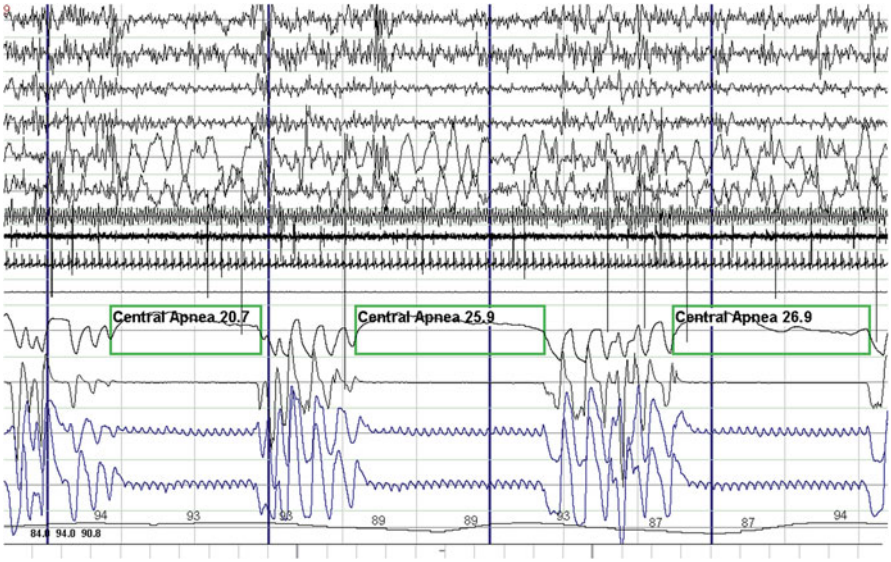

Fig. 14.3 Polysomnographic example of central sleep apnea. These events are characterized by complete cessation of airflow due to lack of respiratory efforts. Waves forms noted in the respiratory effort channels are due to sensor detecting heart pulsations. From *top* to *bottom*: EEG channels 1–4. EOG channels 5–6. Chin EMG channel 7. Tibialis anterior EMG channel 8. ECG channel 9. Snoring microphone channel 10. Thermistor and pressure transducer airflow channels 11–12. Chest and abdominal respiratory effort channels 13–14. Oxygen saturation channel 15

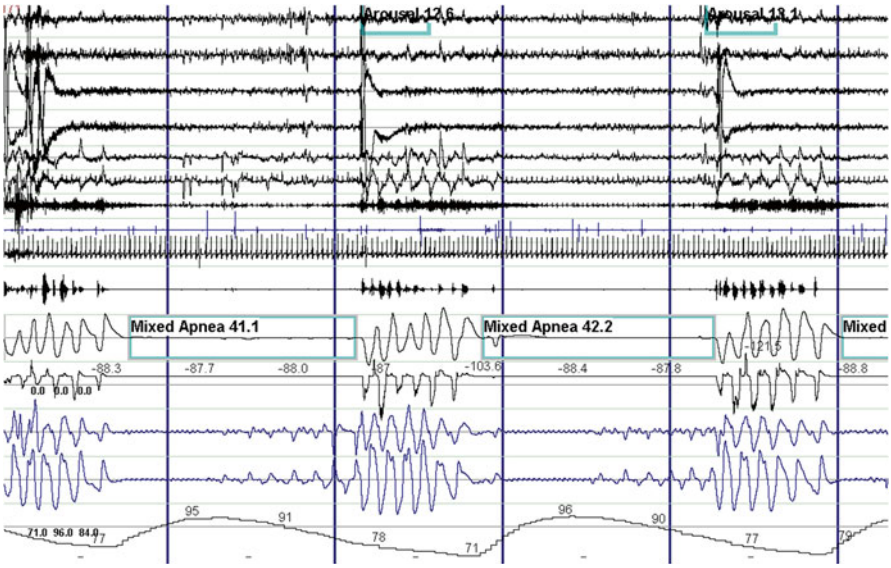

Fig. 14.4 Polysomnographic example of mixed sleep apnea. These events are characterized by complete cessation of airflow and respiratory effort in the first half of the event (central component). Then respiratory efforts start with persistent lack of airflow (obstructive component) in the second half of the event. From *top* to *bottom*: EEG channels 1–4. EOG channels 5–6. Chin EMG channel 7. Tibialis anterior EMG channel 8. ECG channel 9. Snoring microphone channel 10. Thermistor and pressure transducer airflow channels 11–12. Chest and abdominal respiratory effort channels 13–14. Oxygen saturation channel 15

sounds may be heard when respiratory efforts resume after a central apnea or during hyperventilation at the end of a central hypopnea (Fig. 14.3).

Mixed sleep-disordered breathing events have features of both central and obstructive events (Fig. 14.4). Clinically, pure mixed sleep apnea is rare. Mixed apneas and hypopneas generally appear as part of either central or OSA. The type of sleep apnea is determined by the predominant type of event in an individual (i.e., whether more than 50 % of the events are obstructive or central). During such designation, mixed apnea or hypopneas are usually counted as obstructive events since they will respond to CPAP therapy, unlike central sleep apnea.

Except in a few clinical situations, central sleep apnea and Cheyne–Stokes respiration (also known as "periodic breathing" for its waxing and waning airflow pattern (Fig. 14.7)) do not generally occur in the absence of other sleep disorders. Both can be seen transiently during the transition from wake to sleep and in the setting of sleeping at high altitude [30], but these presentations are rarely considered clinically relevant. Central sleep apnea and Cheyne–Stokes respiration disorders can also be seen in the setting of congestive heart failure, use of narcotic pain medications, obesity hypoventilation syndrome, severe central nervous system disease, and idiopathic central sleep apnea [30].

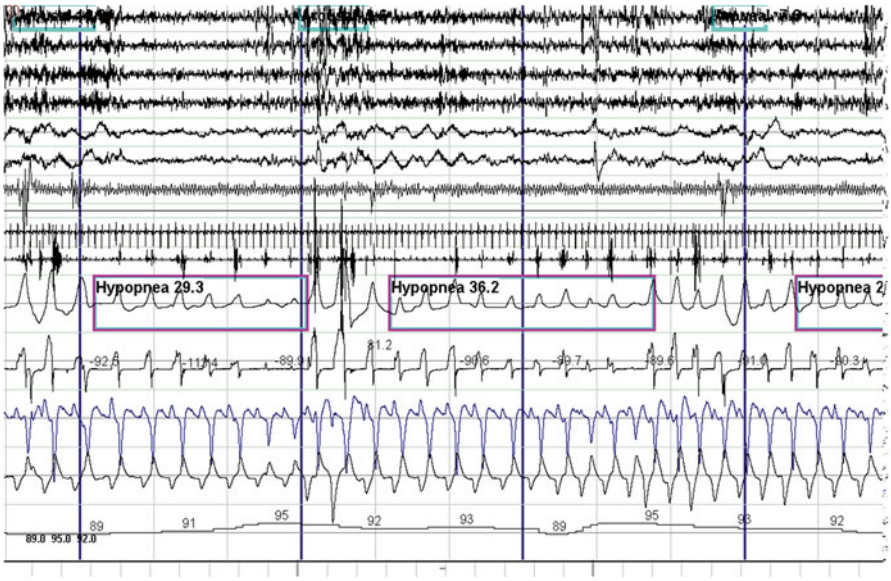

Fig. 14.5 Polysomnographic example of obstructive hypopneas. These events are characterized by partial reduction of airflow. Notice the crescendo snoring during the hypopnea with paradoxical chest and abdominal respiratory movements consistent with partial upper airway obstruction that terminates in an arousal and oxygen desaturation. From *top* to *bottom*: EEG channels 1–4. EOG channels 5–6. Chin EMG channel 7. Tibialis anterior EMG channel 8. ECG channel 9. Snoring microphone channel 10. Thermistor and pressure transducer airflow channels 11–12. Chest and abdominal respiratory effort channels 13–14. Oxygen saturation channel 15

The immediate clinical consequence of central and obstructive sleep-disordered breathing is sleep fragmentation that results in excessive daytime somnolence. Long-term complications of untreated obstructive sleep-disordered breathing syndromes include hypertension, cardiovascular disease, fatigue, depressive mood disorders, and insomnia [24, 25, 56, 57]. In addition, the untreated patient with OSA often complains of a number of psychosocial problems including reduced vigilance, excessive daytime sleepiness, reduced concentration, and deficits of memory and executive function [58], which can result in an increased rate of accidents [59].

Disparities in Obstructive Sleep-Related Breathing Disorders

Snoring

In the 1980s, the self-reported prevalence of snoring was evaluated in a 1222 adult Hispanics living in New Mexico. The prevalence of snoring was greater in men (27.8 %) than in women (15.3 %) and increased with age and obesity for both

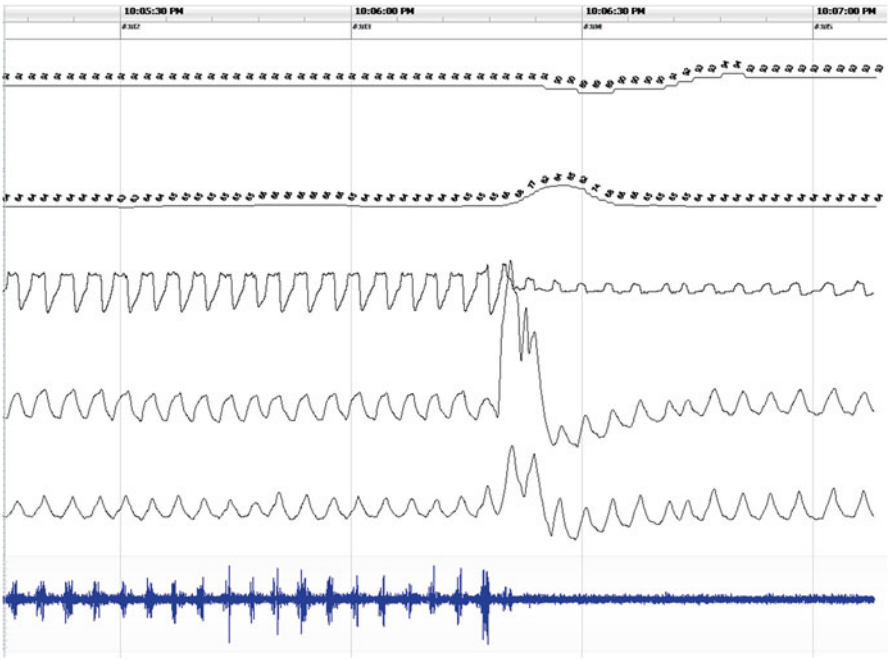

Fig. 14.6 Example of the upper airway resistance during home sleep recording. From *top* to *bottom*: SpO_2 (channels 1). Heart rate (channel 2). Nasal airflow (channel 3). Thoracic effort (channel 4). Abdominal effort (channel 5). Snoring microphone (channel 6). Notice the airflow limitation or flattening on channel 3 associated with snoring (channel 6) and a minor oxyhemoglobin desaturation of <3 % (channel 1) that resolve after an arousal as measured by a transient rise in heart rate (channel 2)

groups, but the prevalence of snoring leveled off after age 59 for men and women. In this study, snoring was associated with myocardial infarction (odds ratio 1.8; 95 % CI 0.9, 3.6) but not with hypertension after controlling for age, gender, obesity, and smoking. Snorers were also sleepier than nonsnorers, suggesting that snorers may have had a higher prevalence of OSA, which was not directly evaluated in this study [60].

The prevalence of snoring has been evaluated in representative samples from the general US population. In the 2005–2006 National Health and Nutrition Examination Survey, the prevalence of snoring was high at 48 % among 6139 individuals older than 16 years [61]. Results from the National Sleep Foundation Sleep in America 2005 poll of 1506 adults (mean age of 49 years, 51.6 % women) showed that the prevalence of snoring was 59 % and habitual nightly snoring was 40 %. Habitual snoring was more common in men [62]. In the 2007–2008 National Health and Nutrition Examination Survey, sleep symptoms were evaluated by race/ethnicity and socioeconomic position in 4081 non-Hispanic whites, African Americans, Mexican Americans, other-Hispanics/Latinos, and Asians. Non-Hispanic whites

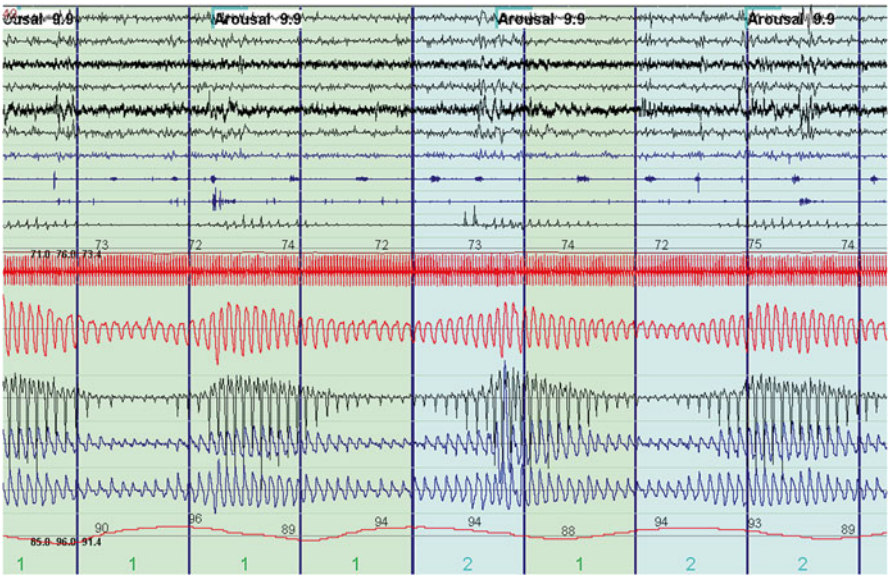

Fig. 14.7 Polysomnogram depicting Cheyne–Stokes ventilation. Notice the waxing and waning airflow pattern (Channels 13–14 from the *top*). Snoring is absent during the hypopnea but can be seen during the hyperventilation portion of the event (Channel 10). Cheyne–Stokes can result in sleep fragmentation as noted by arousals from sleep (EES channels 1–4) and transient desaturations (Channel 16) that predisposes to periodic breathing through high loop gain physiology

represented 72.81 % of the sample, followed by African Americans at 10.29 % and Mexican Americans at 7.55 %. Snoring was more common among males (odds ratio 1.93, 95 % CI 1.66–2.24), other-Hispanics/Latinos (odds ratio 1.37, 95 % CI 1.03–1.83), and those with less than a college education. In this study, African Americans reported more nonrestorative sleep (odds ratio 1.59, 95 % CI 1.25, 2.01) [63].

The Sleep Heart Health Study (1995–2006) is the largest prospective cohort study to assess sleep-disordered breathing and OSA as risk factors for major cardiovascular events, including myocardial infarction and stroke [64]. It evaluated the variations in symptoms of sleep-disordered breathing in 13,194 men and women 40 years of age and older in five major racial/ethnic groups. Snoring was more frequently reported by Hispanic men (odds ratio 2.30, 95 % CI 1.43, 3.69), Hispanic women (odds ratio 2.25, 95 % CI 1.48, 3.42), and Black women (odds ratio 1.55, 95 % CI 1.13, 2.13), compared with the white, American Indian, and Asian Pacific Islander counterparts after adjusting for age, presence of a bed partner, and body mass index [65]. The overall prevalence of self-reported snoring in whites, Hispanics, and African Americans participating in the Sleep Heart Health Study was 34 %. However, the prevalence of self-reported snoring was higher in Hispanics (41 %) compared to whites (34 %), and African Americans (30 %) ($p < 0.05$) [66].

The Northern Manhattan Study examined a cohort of 1605 older adults (mean age 65 ± 8 years) that included predominantly Hispanics (61 %) but also whites

(20 %) and African Americans (19 %). The investigators found the overall prevalence of self-reported habitual snoring was 29 %, but it was much higher in Hispanics (84 %) compared to both African Americans (9 %) and whites (7 %) [67]. In a related study focused on the more elderly participants (mean age 75 ± 9 years, 37 % men), Hispanics more frequently reported habitual snoring (odds ratio 2.8, 95 % CI 1.7–4.5) compared to African Americans and whites. They were also more likely to report long sleep (≥9 h, odds ratio 1.8, 95 % CI 1.1–3.1). There were no differences in sleep complaints between African Americans and whites [68].

The Tucson Children's Assessment of Sleep Apnea study (TuCASA) examined 1494 questionnaires for children 4–11 years old living in Tucson, Arizona. Parents of male Hispanic children were more likely to report that their boys snore frequently (11.4 % vs. 7.4 %, respectively; $p < 0.02$) and were more likely to report excessive daytime sleepiness (9.6 % vs. 5.8 %, respectively; $p < 0.01$) than their white counterparts. There was no difference between Hispanic or white girls with regard to snoring or excessive daytime sleepiness [69]. In children of age 2–6 years attending well-child care visits, the overall prevalence of reported snoring was 13.9 % (95 % CI 10.2, 17.5). However, snoring was found in 18.7 % (95 % CI 13.2, 25.7) of African American children ($n = 150$), 17.5 % (95 % CI 8.6, 32.4) of Hispanic children ($n = 40$), and 8.3 % (95 % CI 4.7, 14.4) of white children ($n = 132$) ($p = 0.031$). The odds ratio of snoring was 2.5 (95 % CI 1.2, 5.5) for African American children and 2.3 (95 % CI 0.8, 6.4) for Hispanic children as compared to their white counterparts [70].

In summary, it appears that the prevalence of habitual snoring in the general adult US population is high, ranging from 27 to 48 %, and as high as 84 % in the elderly, with the higher estimates coming from studies in more recent years [60–62, 67]. Snoring in general is more prevalent in men than in women and increases with age, but its prevalence plateaus after age 59 [60, 62, 63]. In all the studies that have evaluated snoring and ethnicity, the findings are consistent, showing that habitual snoring is more prevalent in Hispanic men and women, in African American women [63, 65–68], and in Hispanic male children [69] and African American children [70] as compared to their white counterparts.

These studies are limited by the self-reported nature of the snoring data, which can hide significant biases. These studies also do not explain why men, Hispanics, and African Americans snore more frequently than other population groups. Clearly more investigation is needed as to the epidemiology of snoring in the US population.

Upper Airway Resistance Syndrome

The diagnosis of the upper airway resistance syndrome (UARS) is difficult to make using the standard polysomnographic montage, especially when a thermistor is used to measure airflow. Guilleminault used an esophageal manometer to confirm the increasingly negative intrathoracic pressure resulting in an arousal, and this technique is currently the gold standard to make the diagnosis of UARS [53, 54]. Others

have used a combination of crescendo snoring associated with increased respiratory effort in the setting of sleep fragmentation to make the diagnosis of UARS [71]. With the advent of the nasal cannula pressure transducers to measure airflow, inspiratory airflow limitation can be determined and used as a measure of increased upper airway resistance to aid in UARS diagnosis [72, 73]. However, noninvasive methods for determining UARS are not yet well validated [54, 74]. The lack of diagnostic consensus has hampered research of UARS in the general population.

In clinical practice, UARS is rarely seen in isolation from OSA [75]. There are very few studies that have addressed the epidemiology of UARS, and all have focused on very specific populations. Kristo et al. reported on 527 patients who underwent evaluation for excessive somnolence in a US military sleep disorders center in 2000 using esophageal manometry during polysomnography. OSA was diagnosed in 72.6 % of these patients as compared to 8.4 % who were found to have pure UARS [76]. In a population of 41 morbidly obese patients (mean BMI 47 kg/m^2, 83 % women) referred for bariatric surgery, the prevalence of UARS based on polysomnographic criteria was 17 % as compared to 71 % who were diagnosed with OSA [71].

Stoohs et al. performed a retrospective evaluation of the characteristics of 2753 patients with sleep-disordered breathing seen in two sleep clinics in Germany from 1996 to 2006. They compared patients with primary snoring ($n=157$), UARS ($n=424$), OSA without sleepiness ($n=562$), and OSA with sleepiness ($n=1610$). Patients with UARS were significantly younger (45.3 ± 12.3 years) than those with primary snoring (48.7 ± 11.8 years), OSA without sleepiness (53.0 ± 12.3 years), and OSA with sleepiness (OSAS) (51.5 ± 11.7 years) ($p<0.02$). Patients with primary snoring and UARS had a lower body mass index than those with OSA and OSAS ($p<0.001$). Also of note, patients with UARS were more likely to be women [77]. No data currently exist examining racial/ethnic or socioeconomic disparities in UARS prevalence.

In summary, the prevalence of UARS in the general population is not known. The current estimates range from 8.4 to 17 % [74, 76], but these figures are based on small research populations with widely different demographic characteristics. However, those with UARS tend to be younger, less overweight, and more frequently female than patients with OSA [71, 77].

The UARS literature is limited by the retrospective nature of the available evidence, the dearth of research in the epidemiology of UARS, the differences in diagnostic methodology used in various studies, and the lack of consensus on UARS as an independent syndrome. Also, the literature has not adequately addressed risk factors related to the prevalence of UARS. Clearly more research is needed to better understand UARS with respect to its epidemiology and potential health disparities.

Obstructive Sleep Apnea

Among all sleep-related breathing disorders, OSA has been the most extensively studied due to its high prevalence and clinical relevance to cardiovascular disease [78]. Epidemiological studies and experimental work in animals support the

assertion that OSA, if left untreated, results in activation of the sympathetic nervous system and eventually systemic hypertension [79–81]. Untreated OSA is also strongly associated with other disease states, including coronary artery disease, congestive heart failure and stroke [78, 82], nocturnal arrhythmias [83], diabetes type 2 [84, 85], obesity [86], inflammation [87], hypercogulable state [88], the metabolic syndrome [89], and increased mortality [90]. Since its initial polysomnographic description in 1965 [22], the prevalence of OSA in the US has been increasing in close association with the obesity epidemic [86, 91].

In 1993, Young and colleagues first reported the prevalence of OSA in a random sample of 602 men and women recruited from the general working population ages 30–60 years (Wisconsin Cohort). Based on an AHI ≥ 5/h, the overall prevalence of OSA was 21.3 %. The prevalence of OSA was 24 % for men and 9 % for women. The prevalence of OSA syndrome (OSA plus Epworth Sleepiness Scale score [ESS] > 10) was 4 % for men and 2 % for women [37]. Since then, the prevalence of OSA has been consistently reported as 2:1 to 3:1 male predominance in the premenopausal years and a nearly 1:1 ratio after menopause [92–94]. Peppard et al. reevaluated the Wisconsin Cohort sample from 1988 to 1994 and 2007 to 2010 and adjusted for age, sex, and BMI using sampling weights provided by the respective US National Health and Nutrition Examination Survey (NHANES) for subjects 30–70 years old. The sample consisted of 1520 study participants (96 % non-Hispanic white) who were assessed for sleep-disordered breathing between 1988 and 2011. Women made up 45 % of the sample. They estimated an overall prevalence of OSA (AHI ≥ 5/h) 20 years later at 26 % (95 % CI 24,28). The overall prevalence of OSA syndrome (AHI ≥ 5/h and ESS >10) was not reported. However, the prevalence of OSA (Table 14.1) and OSA syndrome (Table 14.2) was greater for men and women in 2007–2010 as compared to 1988–1994 [91].

Aging is a major risk factor for the development of OSA and increased prevalence of OSA is found in men and women with increasing age. Ancoli-Israel and colleagues reported that 62 % of community-dwelling older adults (>65 years of age) had significant OSA (AHI ≥ 10/h) based on unattended cardiorespiratory home sleep recordings [95]. The Sleep Heart Health Study also showed the average prevalence of OSA (AHI ≥ 15/h) increased stepwise until approximately age 60, after which it leveled off at a prevalence of about 20 % in a community-dwelling popula-

Table 14.1 Wisconsin Cohort study

	1988–1994 data		2007–2013 data	
Gender	%	95 % CI	%	95 % CI
Men	26.4	23.9, 28.9	33.9	30.8, 37.0
Women	13.2	11.4, 15.3	17.4	15.2, 20.0

Prevalence estimates of obstructive sleep apnea (AHI ≥ 5/h) adjusted for age, gender, and BMI using weights provided by the NHANES for men and women ages 30–70 years. Reprinted with permission from Oxford University Press [91]

AHI apnea hypopnea index, *NHANES* US National Health and Nutrition Examination Survey, *BMI* body mass index, *CI* confidence interval

Table 14.2 Wisconsin Cohort study

	1988–1994 data		2007–2013 data	
Gender	%	95 % CI	%	95 % CI
Men	10.8	9.0, 12.6	14.3	12.0, 16.4
Women	3.8	2.9, 4.9	5.0	3.9, 6.3

Comparison of prevalence estimates of obstructive sleep apnea syndrome (AHI ≥ 5/h, ESS score > 10) adjusted for age, gender, and BMI using weights provided by the NHANES for men and women ages 30–70 years. Reprinted with permission from Oxford University Press [91]
AHI apnea hypopnea index, *NHANES* US National Health and Nutrition Examination Survey, *BMI* body mass index, *CI* confidence interval, *ESS* Epworth Sleepiness Scale

tion of 5615 men and women ages 40–98 years [92]. This is very similar to the plateau effect after age 59 seen in the prevalence of snoring described by Schmidt-Nowara et al. [60].

Comparison of the prevalence of OSA by race or ethnicity has been directly evaluated only in a few studies. In the 1990s, Kripke et al. performed overnight oximetry in 190 women and 165 men (age 40–64 years) in southern California, where there is a high proportion of Hispanics of Mexican descent. Based on these data, the authors estimated that 16.3 % of Hispanics had ≥20 episodes of transient oxyhemoglobin desaturation (≥4 %) per hour of sleep, akin to having moderate OSA, compared to only 4.9 % of non-Hispanic Whites [96]. The Hispanic Community Health Study/Study of Latinos (2008–2013) is a multicenter community-based cohort study that evaluated the prevalence of risk factors for sleep disorders and as well as for heart, lung, blood, kidney, liver, endocrine, and cognitive disorders [97]. This study performed unattended home sleep recordings and recently reported the prevalence of OSA for 14,400 participants. The age-adjusted prevalence of OSA for AHI ≥ 5/h, ≥15/h, and ≥30/h was 25.8 %, 9.8 %, and 3.9 %, respectively [41]. Consistent with prior studies, OSA was associated with male sex, obesity, and older age and the prevalence for OSA (AHI ≥ 5/h) was similar to the most recent prevalence estimates in whites [91]. Ancoli-Israel et al. evaluated the prevalence of OSA in elderly African Americans ($n = 54$) and whites ($n = 346$) older than 65 years of age. African-Americans had significantly greater AHI than whites (72.1/h vs. 43.3/h; $p = 0.014$), and there were more African Americans (17 %) with severe OSA (AHI ≥ 30/h) than whites (8 %) ($p = 0.034$; relative risk = 2.13; 95 % CI 15–19 %). This association remained significant after controlling for age, gender, and body mass index [98]. Redline et al. evaluated 225 African Americans and 622 whites using a cardiorespiratory home sleep recordings and reported that African Americans ≤25 years old had higher AHI and higher prevalence of increased apneic activity (odds ratio 1.88, 95 % CI 1.03–3.52) after adjusting for obesity, sex, proband sampling, and familial clustering. The authors concluded that young African Americans may be at increased risk for sleep apnea [99]. There are no studies directly comparing the prevalence of OSA between Asians and whites. However, in middle-aged Asian men and women the prevalence of symptomatic OSA diagnosed by polysomnography (AHI ≥ 5/h plus ESS >10) has been reported as similar to that in whites (4.1–7.5 % for men and 2.1–3.2 % for women) [37, 100–103].

In summary, OSA is strongly associated with male gender [37, 92–94], obesity [86], and increasing age [92, 96], but there appears to be a plateau effect on prevalence after age 60 [92]. There are very few studies that have directly examined differences in the prevalence of OSA by race or ethnicity, and those only compared African Americans with whites. However, from the available literature, it appears that both younger and older African Americans are more likely to have OSA compared to whites [98, 99]. In Hispanics, the prevalence of OSA was estimated to be higher than that of whites based on overnight oximetry [96]. However, based on unattended home sleep studies the prevalence of OSA in US Hispanics was similar to that of whites [41]. The prevalence of symptomatic OSA in Asians has been reported similar to that of whites [37, 100–103]. There is a temporal trend of increasing OSA prevalence over time. The OSA prevalence in the general population that was described by Young et al. in 1993 (4 % for men and 2 % for women) is still quite commonly cited by sleep researchers and clinicians today [37]. However, with the obesity epidemic [86, 91] and the aging of the population, it is highly likely that the prevalence of OSA in the US has increased. Our most recent estimates of OSA prevalence come from the mostly white population of the Wisconsin Cohort Study in 2013 (Tables 14.1 and 14.2) and the direct measurements in the Hispanics Community Health Study/Study of Latinos in 2014, showing a definite increase in the prevalence of OSA over time [41, 91, 98].

Methodological differences make it challenging to compare earlier and later studies of OSA prevalence because of changes in measurement of hypopneas. Earlier sleep recordings utilized primarily the thermistor to evaluated airflow [37], which is notable for underestimating hypopneas, while later studies have used primarily the nasal cannula pressure transducer which is a better detector of hypopneas and airflow limitation [104, 105]. Also, earlier studies used "discernible" reductions in flow to identify hypopneas [37], while later studies have used more precise airflow decrements of 30 and 50 % detected by nasal cannula pressure transducers [51]. Moreover, earlier studies generally utilized a ≥4 % oxyhemoglobin desaturation to designate hypopneas [37], while later studies have also used the 2007 American Academy of Sleep Medicine alternate definitions of hypopneas that included a ≥3 % desaturation and/or a resultant arousal [51]. In all, the prevalence of OSA in the US population is probably significantly greater now than that reported in 1993 due to a true increase in OSA severity caused by the obesity epidemic and the aging of the population, as well by more accurate detection of hypopneas due to advances in technology.

Disparities in the Clinical Presentation of OSA

The clinical presentation of OSA differs significantly by sex. In a retrospective study, Shepertycky et al. evaluated 130 men and 130 women with OSA who were matched for age, BMI, AHI, and the ESS score. Both men and women presented similarly with respect to snoring and excessive daytime sleepiness. However, women were more likely to have a main presenting complaint of insomnia (odds

ratio 4.20; 95 % CI 1.54–14.26). Women were also more likely to endorse a history of depression (odds ratio 4.60; 95 % CI 1.71–15.49) and hypothyroidism (odds ratio 5.60; 95 % CI 2.14–18.57). Compared to their male counterparts, women were less likely to present with witnessed apnea and consumed less caffeine per day [106].

In the Sleep Heart Health Study, the severity of sleepiness increased with increasing OSA severity and with increasing frequency of snoring for both men and women, regardless of age or BMI [107, 108]. In a study that evaluated complaints of insomnia in men and women with OSA, women reported sleep onset insomnia more frequently than men (62 % vs. 53 %, $p=0.03$) as well as psychophysiologic insomnia (53 % vs. 45 %, $p=0.03$) more frequently than men [109].

In a more recent study of 384 African American and white adults that were evaluated with the Berlin Questionnaire [110], women with OSA reported fatigue more frequently than men with OSA (75 % vs. 46 %, $p<0.001$). In multivariate analysis that adjusted for potential confounders, men with OSA were sleepier than women, and African American men were significantly sleepier than white men (Average ESS 12.8 ± 5.2 for African American men as compared to 10.6 ± 5.3 for white men, $p=0.05$) [111]. In a retrospective study of 383 women and 661 men diagnosed with OSA, women were older and had a greater BMI and waist-to-hip ratio than men at the time of diagnosis. OSA severity based on respiratory disturbance index (RDI) was higher in men than women (41.2 ± 27.9 vs. 30.0 ± 26.7, $p<0.001$) despite a greater BMI in women [112]. In a population of 300 OSA patients (AHI > 10/h), the same investigative team again noted that women with OSA were older, had greater BMI, and had lower AHI at diagnosis compared to men [109].

Simpson et al. evaluated the relevance of fat distribution in men and women with OSA by measuring fat with dual-energy X-ray absorptiometry. The proportion of obese men and women did not differ (68 %, BMI > 30), and in evaluation of the upper airway, there was no difference in the proportion with a Mallampati score of III or IV by sex. In women, the combination of percentage of fat in the neck region and body mass index together explained 33 % of the AHI variance. In men, percentage of fat in the abdominal region and neck-to-waist ratio together accounted for 37 % of the AHI variance [113].

There are few studies directly evaluating ethnic/racial differences with respect to the clinical presentation of OSA. In a study by Scharf et al., African American OSA patients were younger at the time of diagnosis (44.9 ± 14.1 vs. 49.2 ± 14.5 years; $P=0.022$) and had greater BMI than whites (39.7 ± 10.7 vs. 33.4 ± 9.2 kg/m^2; $p<0.0001$). However, there was no difference in the severity of OSA between whites and African Americans after controlling for BMI and median household income [114]. Subramanian et al. evaluated the gender and ethnic differences in the prevalence of insomnia in 300 patients with OSA (AHI > 10/h) that included white, African American, and Hispanic men and women. White women were more likely to complain of sleep maintenance insomnia and Hispanic women were more likely to complain of psychophysiologic insomnia [109].

In summary, there are significant gender and racial/ethnic differences in the clinical presentation of OSA that could have diagnostic and therapeutic implications.

Like men, women with OSA present with snoring and excessive daytime somnolence [106–108]. However, women tend to be older, have a greater BMI [94, 109, 112], and demonstrate greater importance of neck fat in upper airway patency [113]. Women also present more frequently with a chief complaint of insomnia, fatigue, or depression, which can lead to a misdiagnosis or delayed diagnosis of OSA [109, 111]. Less data exist regarding the racial/ethnic differences in the clinical presentation of OSA. However, African Americans tend to be younger and more overweight at the time of diagnosis than whites. There does not appear to be a racial/ethnic difference in OSA severity at presentation [114]. More research is needed, especially comparing racial/ethnic differences in the clinical presentation of sleep-disordered breathing.

Disparities in the Clinical Effects of OSA

In epidemiological studies of the general population, African Americans have consistently higher ESS scores than non-Hispanic whites [65, 115, 116]. However, it is unclear if OSA has a differential effect based on gender or race/ethnicity. In multivariate analyses of subjects at high risk for OSA based on the Berlin Questionnaire, men were more sleepy than women, and African American men were significantly sleepier than white men ($p = 0.05$) [111]. In the same study, women at high risk for OSA reported fatigue more commonly than their male counterparts [111].

In the Sleep Heart Health Study, the health-related quality of life of white, African American, and Hispanic participants was compared using the Short Form-36 (SF-36) physical composite and mental composite scales. There were no ethnic/racial differences in the mental or physical health-related quality of life of subjects with moderate or more severe OSA (AHI > 15/h), suggesting that OSA may not have a differential effect on quality of life based on race or ethnicity in adults [66]. However, in the population-based TuCASA study, Hispanic children with sleep-disordered breathing experienced more frequent symptoms such as snoring, excessive daytime somnolence, witnessed apneas, and learning problems than did white children, suggesting a potential differential effect by ethnicity of OSA on symptoms among children [69].

The current literature suggests that changes in weight and exercise differentially affect the severity of OSA by sex. In the Sleep Heart Health Study, weight gain and weight loss affected the severity of OSA more dramatically in men after controlling for age, OSA severity, neck circumference, BMI, ethnicity, and waist-hip ratio [117]. In the same study population, vigorous physical activity of a least 3 h a week was protective against OSA primarily in men and in those who were obese as compared to women and subjects who were not obese [118].

With respect to cardiovascular risk related to OSA, this was also examined in the Sleep Heart Health Study, which followed 5422 participants for a median of 8.7 years. Men with OSA were at a higher risk of an ischemic stroke at all levels of OSA severity compared to women with OSA. Men had an estimated increase in stroke risk of 6 % for each unit increase in AHI, whereas in women, increased

risk of stroke was only observed in the setting of moderate to severe OSA (AHI > 25/h) [119].

In summary, there appear to be gender and racial differences in the clinical effects of OSA. In the general population, African Americans have consistently been shown to be sleepier than whites [65, 115, 116]. In the setting of OSA, men are significantly sleepier than women, and African American men are more sleepy than whites, while women complain of fatigue more often than men [111]. OSA does not appear to affect health-related quality of life scores differentially based on race/ethnicity in adults [66]. However, Hispanic children with OSA were more likely to have learning problems as compared to their white counterparts [69]. The literature also suggests that men with OSA are better protected by weight loss and exercise [117, 118], but they are also more affected by weight gain and have a higher risk for stroke than women [119].

Disparities in Diagnosis and Treatment of OSA

OSA is a common condition [37, 41, 62, 91]; however, it is suspected to be widely underdiagnosed. Moreover, disparities in the recognition and diagnosis of OSA are suspected. Young et al. examined the proportion of OSA underdiagnosis in the Wisconsin cohort ($n = 4925$), which is a population without significant barriers to sleep disorders healthcare. They estimated that only 7 % of women and 18 % of men with moderate to severe OSA had received a clinical diagnosis. The diagnosed proportion for those with mild OSA was even lower at 2 % for women and 10 % for men [120].

The Sleep Heart Health Study investigators evaluated the factors that drive clinical recognition rates and treatment of OSA. Male gender and BMI were the only factors that were associated with increased likelihood of physician diagnosis and OSA treatment. The investigators concluded that disparities existed in the diagnosis and treatment of OSA, especially in women and individuals with lower BMI [121]. The Hispanic Community Health Study/Study of Latinos recently reported that only 1.3 % of participants ($n = 14{,}400$) that underwent an unattended home sleep study had a prior diagnosis of OSA [41]. Of note, the prevalence of OSA (AHI ≥ 5/h) in this sample population was 25.8 % [41], suggesting an extremely low level of evaluation and diagnosis for OSA in Hispanics living in the US. The 2010 Sleep in America Poll was a national survey of 1007 Americans who identified themselves as white, African American, Asian, or Hispanic to compare the sleep health, attitudes, and knowledge about sleep across different racial/ethnic groups [39]. In this study, African-Americans reported a prior diagnosis of OSA (14 %) much more often than Hispanics (8 %), whites (6 %), or Asians (4 %) [122].

With respect to OSA treatment adherence, some studies have identified differences by gender and socioeconomic status. In a study of 507 patients with OSA (77 % African Americans), women were 2.49 (95 % CI 1.39–4.46) times more likely to be noncompliant with CPAP than men after adjusting for race, marital status, and age [123]. In a population of 266 veterans with OSA, daily CPAP use ≥4 h ranged

from 34.1 % (95 % CI, 26.4, 42.7) for subjects from a low socioeconomic neighborhood to 62.3 % (95 % CI 53.8, 70.1) for subjects from a high socioeconomic neighborhood, suggesting that noncompliance with CPAP was related to socioeconomic status [124]. Others have reported that patients with low socioeconomic status are less receptive to CPAP treatment after a 2-week trial [125] and less compliant with CPAP [126] than patients with higher socioeconomic status.

Race/ethnicity has also been evaluated as a factor in CPAP compliance. Scharf and colleagues reported no difference in the acceptance and long-term compliance of CPAP therapy between African Americans and whites [114]. However, Billings et al. reported that African Americans and those in lower socioeconomic residential areas demonstrated poorer adherence to CPAP as compared to whites and Hispanics after 1 and 3 months of follow-up, despite provision of standardized access to care and treatment in a clinical trial setting [126]. The mechanisms of such disparity were not evaluated.

In summary, it appears that men and obese individuals are more likely to be evaluated for OSA compared to women and individuals of lower BMI [121]. This disparity may be explained in part by poor awareness on the part of medical providers of the gender differences in the clinical presentation of OSA. Hispanics appear to have a high prevalence of underdiagnosed OSA, which may be explained by low access to medical care [41]. Women appear to be less adherent to CPAP than men. African Americans and those in lower socioeconomic groups appear to accept CPAP less readily and are less compliant with CPAP therapy than other ethnic or higher socioeconomic groups [123–126].

Mechanisms for Disparities in Sleep-Disordered Breathing

Few have attempted to determine the mechanisms for disparities in sleep-disordered breathing with respect to gender, age, socioeconomic status, or race/ethnicity. Most of the available literature on sleep-disordered disparities is based on retrospective or observational studies. Therefore, the available literature does not lend itself to mechanistic hypotheses testing.

With respect to potential biological mechanisms, gender differences in snoring and OSA in the premenopausal years have been attributed to the protective effects of estrogen [93, 127, 128]. Indeed, in animal and in vitro studies, estrogen upregulates genioglossus estrogen receptors and has a protective effect in the fatigability of genioglossus tissue exposed to intermittent hypoxia [129]. Also, women with a history of ovarihysterectomy who have OSA demonstrated significant AHI reduction after just 1 week of combination therapy of medroxyprogesterone acetate and conjugated estrogens [128]. The results have not been as dramatic in other studies, which have only shown a slight reduction of REM-related AHI with hormonal replacement therapy [130]. However, there is sufficient evidence to suggest that estrogen has a protective effect on sleep-disordered breathing that partially explains the lower prevalence of OSA in premenopausal women as compared to men of

comparable age and BMI [93, 127]. The sleep-disordered breathing protective effect of estrogen is lost during pregnancy, probably due to multiple factors that reduce oropharyngeal caliber, such as estrogen-induced upper airway edema, weight gain, and reduced lung volume [131, 132].

Testosterone is thought to play a role in the pathogenesis of OSA in men, and this may at least partially contribute to the gender disparity. Exogenous testosterone has been shown to mildly increase OSA in obese men with severe OSA [133]. A potential mechanism is increased upper airway collapsibility [134]. However, the evidence connecting testosterone and OSA in men is weak and based primarily on case reports [135].

Less is known about the mechanisms for the sleep-disordered breathing disparity observed among racial/ethnic groups. Proposed mechanisms include differences in genetics, cultural and environmental factors, patterns of obesity, and cephalometric differences. In the US, minority and low-socioeconomic-status groups are disproportionately affected by overweight and obesity at all ages, especially African Americans and Mexican Americans, which could predispose them to higher rates of sleep-disordered breathing [136]. However, the relationship of BMI to OSA in African Americans is of similar magnitude as that of whites, suggesting that obesity patterns alone do not explain the racial/ethnic disparities in OSA [99].

Craniofacial morphology has been primarily studied in whites, Chinese, and Japanese subjects. Among patients with OSA, craniofacial abnormality findings appear to be similar in all racial/ethnic groups, primarily showing low position of the hyoid bone [137], retrognathia [138], smaller cranial base [139], and increase in the craniocervical extension angle [140]. A few studies have compared craniofacial measurements associated with OSA directly between racial/ethnic groups. Between whites and African Americans, Cakirer et al. found that brachycephaly (head shape with wider lateral and shorter anterior–posterior dimensions) is associated with an increased AHI in whites but not in African-Americans [141]. Also, in whites both skeletal craniofacial restriction and soft tissue enlargement of the tongue and soft palate are associated with OSA, while in African Americans only soft tissue enlargement is a significant factor [99]. In contrast, Chinese with OSA show greater skeletal restriction, including micrognathia and retrognathia, and a shorter and steeper anterior cranial base than whites [142, 143]. Also, Chinese subjects have more severe OSA at lower BMI as compared to whites, suggesting that skeletal restriction factors may be more important for OSA risk in Asians [142–144].

Almost no work has been reported on nonbiological factors for sleep-disordered breathing, in spite of the fact that the environment is a strong risk factor for health [145]. Only one study in the literature has evaluated the environment and the risk of sleep-disordered breathing. Ansarin et al. analyzed data from the National Health and Nutrition Examination Survey (NHANES) survey of 5545 individuals 16 years of age and older. The sample consisted of 22.5 % Mexican Americans, 44.5 % whites, 22.5 % African Americans, and 7.2 % other Hispanics and multiracial participants. OSA was assessed by using questions on habitual snoring, witnessed apneas, and daytime sleepiness, and study investigators found that never repeating a school grade and separated marital status were each associated with less risk of

OSA. In contrast, having pets in the home or living in a home with mildew or musty smell was associated with a higher risk of OSA. Factors such as the type of home, number of persons living in the home, or the presence of pests such as cockroaches did not predict OSA [146].

In summary, in the premenopausal years, the disparity in OSA prevalence between men and women may be due to the protective effects of estrogen in women and potentially the deleterious effect of testosterone in men [93, 127–130, 135]. Greater rates of obesity are found in Mexican Americans, African Americans, and patients from low socioeconomic groups as compared to whites [136]. However, at least in the case of African Americans, obesity alone does not explain the higher prevalence of OSA as compared to whites [94]. Although the data are limited, the craniofacial differences existing between Asians, African Americans, and whites may explain some of the disparities in OSA prevalence and severity [137–143]. However, the available literature is not sufficient to determine the exact contribution of these factors to the observed gender and racial/ethnic differences in the prevalence and severity of OSA [147]. Very little information exists on nonbiological factors and the risk of OSA [145]. More research is needed before a firm conclusion can be made.

Conclusion

There are significant age, gender, racial/ethnic, and socioeconomic disparities in the prevalence, presentation, diagnosis, morbidity, and therapy of sleep-disordered breathing that may contribute to disparities in the health of the U.S. population. The prevalence of snoring is very common, increases with age, and is higher in Hispanics. OSA is strongly associated with being male, increasing age, and obesity, and it is more prevalent in African Americans than in whites, Asians, or Hispanics. African Americans are also younger, heavier, and more sleepy at diagnosis, which may predispose them to greater cardiovascular complications. Women complain more of insomnia, fatigue, and depression rather than sleepiness at presentation, which may lead to misdiagnosis or delay diagnosis of OSA, especially in those with lower BMI. The literature supports significant disparities in the morbidity of sleep-disordered breathing. Men with OSA are sleepier than women, and men are at a higher risk of stroke for every level of OSA severity. Also Hispanic children may be at a higher risk of cognitive impairment when they suffer from OSA. There are also disparities in the response to therapy for OSA. Weight changes and exercise produce a larger beneficial effect in the AHI of men as compared to women. Also lower CPAP compliance is seen in patients of lower socioeconomic status, African Americans, and women. Most of the research in sleep-disordered breathing disparities is observational and does not lend itself to mechanistic hypothesis testing. However, a protective effect of estrogen and deleterious effect of testosterone may partially explain the higher prevalence of OSA in men as compared to women. The racial/ethnic differences in OSA are more difficult to explain due to the scarcity of research in

this area. Higher BMI in minorities and subjects of lower socioeconomic status has been proposed as a contributing factor for OSA, but more research is needed before a firm conclusion can be reached. Also, craniofacial differences may contribute to OSA in Asians as compared to whites. Much more research is needed to fully elucidate and understand the observed disparities in the prevalence, presentation, diagnosis, morbidity, and therapy of sleep-disordered breathing.

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