THE OCCURRENCE OF SLEEP-DISORDERED BREATHING AMONG MIDDLE-AGED ADULTS

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Abstract *Background.* Limited data have suggested that sleep-disordered breathing, a condition of repeated episodes of apnea and hypopnea during sleep, is prevalent among adults. Data from the Wisconsin Sleep Cohort Study, a longitudinal study of the natural history of cardiopulmonary disorders of sleep, were used to estimate the prevalence of undiagnosed sleep-disordered breathing among adults and address its importance to the public health.

Methods. A random sample of 602 employed men and women 30 to 60 years old were studied by overnight polysomnography to determine the frequency of episodes of apnea and hypopnea per hour of sleep (the apnea–hypopnea score). We measured the age- and sex-specific prevalence of sleep-disordered breathing in this group using three cutoff points for the apnea–hypopnea score ($\geq$5, $\geq$10, and $\geq$15); we used logistic regression to investigate risk factors.

Results. The estimated prevalence of sleep-disordered breathing, defined as an apnea–hypopnea score of 5 or higher, was 9 percent for women and 24 percent for men. We estimated that 2 percent of women and 4 percent of men in the middle-aged work force meet the minimal diagnostic criteria for the sleep apnea syndrome (an apnea–hypopnea score of 5 or higher and daytime hypersomnolence). Male sex and obesity were strongly associated with the presence of sleep-disordered breathing. Habitual snorers, both men and women, tended to have a higher prevalence of apnea–hypopnea scores of 15 or higher.

Conclusions. The prevalence of undiagnosed sleep-disordered breathing is high among men and is much higher than previously suspected among women. Undiagnosed sleep-disordered breathing is associated with daytime hypersomnolence. (N Engl J Med 1993;328: 1230-5.)

RECENT attempts to assess the public health burden attributable to sleep disorders[1,2] have underscored the need for epidemiologic data on sleep-disordered breathing. The condition is characterized by repeated pauses in breathing during sleep, which lead to the fragmentation of sleep and decreases in oxyhemoglobin saturation.[3] The physiologic spectrum of sleep-disordered breathing ranges from partial airway collapse and increased upper-airway resistance, manifested as loud snoring and episodes of hypopnea, to complete airway collapse and episodes of apnea lasting 60 seconds or more.[4] Sleep apnea syndrome, clinically defined by frequent episodes of apnea and hypopnea and symptoms of functional impairment,[5] can be life-threatening and has been associated with extreme daytime hypersomnolence, automobile accidents, and cardiovascular morbidity and mortality.[6-8] Reports that snoring is associated with myocardial infarction, stroke, and hypertension[9-12] suggest that even a mild degree of sleep-disordered breathing may have adverse health effects.

Epidemiologic investigation of sleep-disordered breathing has been hampered by difficulties in obtaining valid data from an adequate population-based sample. Polysomnography is the current standard for the evaluation of sleep-disordered breathing.[13,14] It provides detailed data on respiratory effort, airflow, oxygenation, sleep state, and other variables, but it is costly and requires subjects to sleep overnight in a laboratory. Previous studies have been limited to polysomnography in small samples of men[15,16] and, in larger samples, to home-based recordings that rely on single indicators of abnormal breathing, without an objective measure of sleep state.[17-19] In spite of limitations that made age- and sex-specific estimates of occurrence impossible, these studies concluded that sleep-disordered breathing is prevalent and drew attention to a potential public health burden.

In this report we have used data from the Wisconsin Sleep Cohort Study, initiated in 1988, to address the public impact of sleep-disordered breathing. The Sleep Cohort Study is a population-based prospective study using overnight polysomnography to investigate the epidemiologic features of sleep-disordered breathing. We estimated the age-specific prevalence of sleep-disordered breathing among middle-aged men and women, analyzed the spectrum of severity, and investigated age, sex, and obesity as risk factors.

METHODS

Sample

This investigation was based on a random sample of state employees in Wisconsin. A two-stage sampling scheme, designed to optimize the study's precision by oversampling subjects more likely to have sleep-disordered breathing, was used to construct a cohort representing a wide range of sleep-disordered breathing. In the first stage, all employees 30 to 60 years of age who worked for three large state agencies were surveyed about their sleep patterns and other characteristics by a mailed questionnaire.* In the second stage, data from six survey questions, answered by a five-point frequency scale and "do not know" category, were used to classify survey participants as habitual snorers according to whether they reported habitual (almost every night or every night) snoring, snorting, or breathing pauses, or extremely loud snoring. Given the clinic observations that most patients with sleep apnea snore and snort habitually and

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loudly,[3] we predicted that recruiting 100 percent of the habitual snorers and a 25 percent random sample of those who were not habitual snorers would yield a cohort with adequate variance in sleep-disordered breathing.

Completed questionnaires were returned by 3513 subjects (response rate, 82 percent). A comparison of respondents and nonrespondents with respect to personnel data, including sex, age, and job category, revealed no significant differences ($P>0.1$). The distribution of surveyed men and women according to sampling stratum is shown in Table 1.

Subjects were recruited by telephone. The criteria for exclusion were as follows: pregnancy; unstable or decompensated cardiopulmonary disease, including myocardial infarction; airway cancers; recent upper-airway surgery; and tracheostomy. Eight respondents were excluded. The participation rate was 43 percent. The most common reason for declining to participate was the inconvenience of sleeping away from home.

Collection of Polysomnographic Data

Studies were conducted at the University of Wisconsin General Clinical Research Center. Before bedtime, the subjects were interviewed about their sleep characteristics and health history. Measures of body habitus were recorded by standard anthropometric methods.[20] The polysomnography consisted of continuous polygraphic recording (Polygraph model 78, Grass Instruments, Quincy, Mass.) from surface leads for electroencephalography, electrooculography, electromyography, and electrocardiography, and from noninvasive sensors for nasal airflow (thermocouples), oral airflow (end-tidal carbon dioxide gauge), tracheal sounds (microphone), thoracic and abdominal respiratory effort (inductance plethysmograph [Respitrace, Ambulatory Monitoring, Ardsley, N.Y.]), and oxyhemoglobin level (finger-pulse oximeter [Ohmeda 3740, Englewood, Colo.]). The transducers and lead wires permitted normal positional changes during sleep. Bedtime and awakening time were at each subject's discretion; the polysomnography was terminated after final wakening.

Table 1. Distribution of Survey Population According to Sampling Stratum.*

Sex and Age Group	Habitual Snorers	Not Habitual Snorers	Total
	number (percent)		
Women — age in yr			
30–39	196 (25)	603 (75)	799
40–49	223 (31)	486 (69)	709
50–60	103 (31)	232 (69)	335
All	522 (28)	1321 (72)	1843
Men — age in yr			
30–39	188 (35)	348 (65)	536
40–49	313 (45)	383 (55)	696
50–60	232 (53)	206 (47)	438
All	733 (44)	937 (56)	1670

*The habitual snorers reported snoring, snorting, or breathing pauses every night or almost every night, or extremely loud snoring. The rest of the survey subjects were considered not to be habitual snorers.

The reproducibility of single-night polysomnography was investigated by conducting second studies in 40 subjects one to two weeks after the first.

Interpretation of Polysomnographic Data

Polysomnography records were scored for sleep, breathing, oxygenation, and movement in 30-second periods. Sleep data were staged (stages I, II, III, and IV and rapid-eye-movement [REM] sleep) according to the system of Rechtschaffen and Kales.[21] An abnormal breathing event during objectively measured sleep was defined according to the commonly used clinical criterion of either a complete cessation of airflow lasting 10 seconds or more (apnea) or a discernible reduction in respiratory airflow accompanied by a decrease of 4 percent or more in oxyhemoglobin saturation (hypopnea).

The average number of episodes of apnea and hypopnea per hour of sleep (the apnea–hypopnea score) was calculated as the summary measurement of sleep-disordered breathing. For categorical analysis, cutoff points of ≥ 5, ≥ 10, and ≥ 15 were used. Subjects with apnea–hypopnea scores of less than 5 were further classified according to whether they were habitual snorers or not. These cutoff points are widely used to describe sleep apnea, but it is important to note that the clinical importance of any particular cutoff point has not been adequately determined.

Assessment of Hypersomnolence

Daytime hypersomnolence was assessed before the polysomnography study with three subjective questions on sleepiness.[22] Using a five-point scale, the subjects rated how often they felt excessively sleepy during the daytime; woke up unrefreshed, regardless of how long they had slept; and had uncontrollable daytime sleepiness that interfered with daily living. Responses of "frequent" or "habitual" (≥ 2 days per week) were considered to indicate hypersomnolence.

Statistical Analysis

Data were analyzed with SAS software modules for descriptive statistics, contingency tables, and multiple logistic regression.[23] Repeated polysomnography studies were compared with use of paired t-tests. Pearson's chi-square and ordinary t-tests were used for other comparisons of means and proportions. Two-tailed P values of less than 0.05 were considered to indicate statistical significance.

We calculated age- and sex-specific prevalences of sleep apnea among the habitual snorers and those who were not habitual snorers using cutoff points of ≥ 5, ≥ 10, and ≥ 15 in the apnea–hypopnea scores. Within age and sex groups, we combined the estimates into weighted averages using the survey population proportions given in Table 1. Standard formulas for stratified sampling were used to calculate 95 percent confidence intervals.[24] This resulted in age- and sex-specific estimates of sleep-disordered breathing in middle-aged adults. The sex-specific age distribution in the survey population (Table 1) was used as a standard to estimate summary prevalences of sleep-disordered breathing in employed men and women.

The prevalence of the joint occurrence of an apnea–hypopnea score of 5 or higher and all three symptoms of hypersomnolence was calculated as the prevalence of sleep apnea syndrome meeting minimal diagnostic criteria.

The association of sleep-disordered breathing with obesity, as indicated by variables for weight, body-mass index (the weight in kilograms divided by the square of the height in meters), circumferences, and skin-fold thicknesses, was examined by multiple logistic regression. A separate model was fit for each measure of body habitus because of multicollinearity. Terms for age and sex were included in all the models. Two-way interactions of body-habitus variables, age, and sex were examined; results are reported for terms with P values of 0.1 or less.

Results

Representativeness of the Sample

Subjects who agreed to undergo polysomnography and those who refused were compared with regard to their responses to all questionnaire items on sleep characteristics, body habitus, sex, and age; no significant differences were found. The frequencies of snoring, other breathing abnormalities during sleep, and hypersomnolence did not differ significantly whether the subjects agreed to participate or not. There was no

evidence of selection bias that would compromise the representativeness of the sample.

Quality of Polysomnographic Data

The overnight polysomnographic studies of 625 subjects were analyzed. Twenty-three subjects who had insufficient total sleep time (less than 240 minutes) or no REM sleep were excluded, resulting in the final sample of 602 subjects for whom high-quality polysomnographic data were available (Table 2). The subjects slept, on average, less than the seven to eight hours considered usual. However, since the percentages of total sleep spent in each sleep stage were similar to normative values for adults[25] and since the number of REM periods indicated adequate repeated sleep cycles, we are confident that the breathing during monitored sleep was a valid indicator of breathing during usual sleep.

Data from 40 pairs of polysomnographic studies separated by 7 to 14 days showed that the subjects slept 32 minutes longer, on average, during the second study ($P<0.05$). However, there was no significant difference between study nights in the percentage of time spent in each sleep stage or in the apnea–hypopnea score. The mean (±SE) apnea–hypopnea scores for the first and second studies were 3.0±1.1 and 3.9±1.1, respectively.

Spectrum of Severity of Sleep-Disordered Breathing

A wide range of sleep-disordered breathing, ranging from apnea–hypopnea scores of zero to 89, was found (Fig. 1). Most subjects had some episodes of apnea or hypopnea; 76 percent of the habitual snorers and 64 percent of those who were not habitual snorers had apnea–hypopnea scores greater than zero. As compared with the distribution of scores among the habitual snorers, however, the distribution among the subjects who were not habitual snorers was more skewed toward scores under 5.

Prevalence of Sleep-Disordered Breathing

Table 3 shows the proportions of the habitual snorers and subjects who were not habitual snorers, according to the apnea–hypopnea score. Habitual snorers, both men and women, were more likely to have apnea–hypopnea scores of 15 or higher. The prevalence of mild sleep-disordered breathing (an apnea–hypopnea score of at least 5 but less than 15), however, was higher among habitual snorers for women only.

Table 2. Time the Study Subjects Spent in Each Sleep Stage, According to Sex.

	Women (N = 250)	Men (N = 352)
	mean (±SD)	
Total sleep time (min)	358.7±71.0	333.7±58.9
Distribution according to stage (%)		
1	8.2±4.6	11±6.3
2	60±10	63±10
3 and 4	13±8.5	8.9±7.6
REM	18±6.2	17±6.0
No. of REM periods	3.7±1.3	3.3±1.3

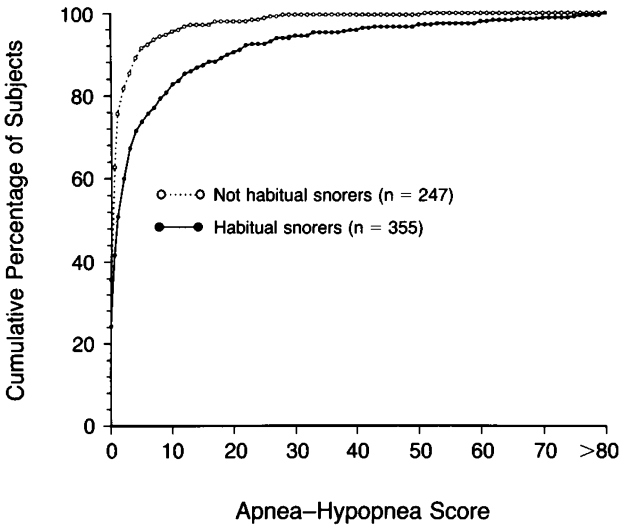

Figure 1. Cumulative Distribution of Apnea–Hypopnea Scores According to Study Stratum.

The prevalence of sleep-disordered breathing at apnea–hypopnea scores of ≥5, ≥10, and ≥15 was extrapolated from the cohort to the general population (Table 4). For men, the prevalence at all three levels was significantly higher among those 40 to 49 years old than among those 30 to 39 years old. Among women, the only statistically significant difference was that apnea–hypopnea scores of 5 or higher were more prevalent among those 50 to 60 years old than among younger women.

Men had a higher prevalence of sleep apnea than women in all age groups and at all cutoff points for the apnea–hypopnea score; all the differences were statistically significant except among subjects 30 to 39 years old who had apnea–hypopnea scores of 15 or higher. Men were 2.0 to 3.7 times as likely as women to have sleep-disordered breathing.

Occurrence of Hypersomnolence

The prevalence of hypersomnolence did not vary according to age ($P>0.1$), but it was higher among women than men ($P<0.01$) (Fig. 2). As compared with subjects with little or no sleep-disordered breathing, habitual snorers and subjects with apnea–hypopnea scores of 5 or higher were significantly ($P<0.001$) more likely to have hypersomnolence. In subjects with apnea–hypopnea scores of 5 or higher, 22.6 percent of the women and 15.5 percent of the men reported the frequent occurrence (≥2 days per week) of all three indicators of hypersomnolence. Although these indicators were based on questions used in clinical evaluations, self-reported sleepiness is not an objective measure and is believed to underestimate the physiologic state of sleepiness.[26] Thus, the actual prevalence of hypersomnolence may be higher than these data indicate.

On the basis of these data, we estimate that the

proportion of middle-aged adults who have both sleep-disordered breathing (an apnea–hypopnea score of 5 or higher) and self-reported hypersomnolence is 2 percent among women (9 percent with sleep-disordered breathing, 22.6 percent of whom have hypersomnolence) and 4 percent among men (24 percent with sleep-disordered breathing, 15.5 percent of whom have hypersomnolence).

Obesity and Sleep-Disordered Breathing

Table 5 shows the odds ratios estimating the increased risk of sleep-disordered breathing associated with an increase of 1 SD (adjusted for sampling design) in the value of the specific measure of body habitus. Obesity, as indicated by any of these measures, was a significant ($P<0.001$) risk factor for an apnea–hypopnea score of 5 or higher.

Discussion

There are three major findings from our data. First, there is a wide spectrum of undiagnosed sleep-disordered breathing among adults, ranging from a few episodes of apnea or hypopnea during sleep to 89 abnormal breathing events per hour of sleep. Second, undiagnosed sleep-disordered breathing, as indicated by five or more episodes of apnea or hypopnea per hour of sleep, is prevalent among both women (9 percent) and men (24 percent) of middle age. Finally, 4 percent of men and 2 percent of women in the middle-aged work force are likely to meet minimal diagnostic criteria for the sleep apnea syndrome.

Strengths and Limitations of the Study

Our findings use the apnea–hypopnea score as an indicator of sleep-disordered breathing and rely on the results of a single-night polysomnography study conducted in a laboratory. These definitions and methods mirror those recommended for clinical practice.[13] The apnea–hypopnea score is commonly used to describe the spectrum of severity among patients in clinics, but there has been concern about the usefulness of this measurement alone outside clinics.[27-29] Although the primary abnormal event is the apnea or hypopnea, the immediate consequences include varying degrees of increased negative intrapleural pressure, arterial hypoxemia and hypercapnia, central nervous system arousal, fragmented sleep states, and fluctuations in heart rate and blood pressure.[30] It is possible that the immediate consequences are more severe in patients in sleep clinics, even at the same apnea–hypopnea score. Thus, the relation between the apnea–hypopnea score and the immediate consequences in the asymptomatic general adult population needs investigation.

There have been some studies of the ability of a single-night laboratory study to represent usual sleep. Studies of the concordance between data obtained by laboratory polysomnography and by home monitoring have indicated that apnea–hypopnea scores are not influenced by the laboratory environment.[31] Most studies have indicated that although there may be a higher proportion of lighter sleep during the first night under laboratory conditions, abnormal breathing during sleep has less night-to-night variability. Like some[15,32,33] but not all[34] studies, our investigation found that the distribution of sleep stages and the mean apnea–hypopnea score were not significantly different between the initial and second laboratory studies conducted in 40 subjects.

The strengths of our study include the generalizability of its results to other middle-aged populations. The employed differ from the entire population in their sex and age distribution, but one can extrapolate the prevalence of sleep-disordered breathing to other populations of different composition using standard age-adjustment procedures in conjunction with our age- and sex-specific prevalences. However, since employed people are healthier than those who do not work, our findings may underestimate the prevalence of sleep-disordered breathing in the entire population.

Assessment of the Public Health Burden of Undiagnosed Sleep Apnea

Reliable and generalizable polysomnographic data, collected according to clinical standards of practice, enhance the ability to address the implications of our

Table 3. Sex-Specific Prevalence of Sleep-Disordered Breathing, According to Apnea–Hypopnea Score and Sampling Stratum.*

Group	Apnea–Hypopnea Score			Total
	<5	5–14	≥15	
	number of subjects (percent)			
Women (n = 250)				
Habitual snorers	105 (81)	16 (12)	9 (6.9)	130
Not habitual snorers	114 (95)	3 (2.5)	3 (2.5)	120
Men (n = 352)				
Habitual snorers	149 (66)	38 (17)	38 (17)	225
Not habitual snorers	106 (83)	17 (13)	4 (3.1)	127

*The habitual snorers reported snoring, snorting, or breathing pauses every night or almost every night, or extremely loud snoring. The rest of the survey subjects were considered not to be habitual snorers. Because of rounding, not all percentages total 100.

Table 4. Age-Specific Estimates of Sleep-Disordered Breathing in the General Population, According to Apnea–Hypopnea Score and Sex.

Age (yr)	Women			Men		
	Apnea–Hypopnea Score			Apnea–Hypopnea Score		
	≥5	≥10	≥15	≥5	≥10	≥15
	percent of subjects (95% confidence interval)					
30–39	6.5 (1.4–11)	4.9 (0.6–9.8)	4.4 (1.1–7.3)	17 (9.6–25)	12 (5.4–19)	6.2 (1.9–10)
40–49	8.7 (4.2–13)	4.9 (1.7–8.1)	3.7 (1.0–6.5)	25 (18–32)	18 (11–24)	11 (6.7–16)
50–60	16 (5.2–26)	5.9 (0.0–12)	4.0 (0.0–10)	31 (21–40)	14 (7.5–20)	9.1 (5.1–13)
30–60*	9.0 (5.6–12)	5.0 (2.4–7.8)	4.0 (1.5–6.6)	24 (19–28)	15 (12–19)	9.1 (6.4–11)

*Values are adjusted to the age distribution of the survey population.

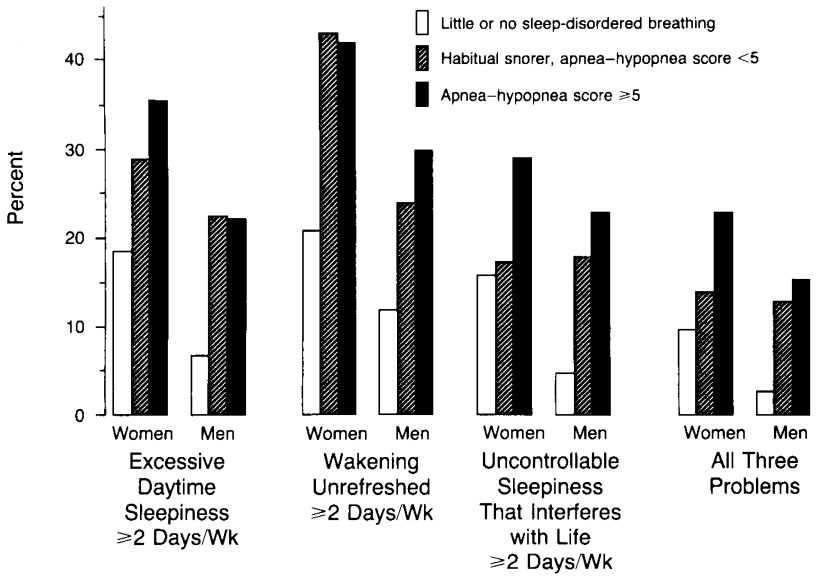

Figure 2. Proportion of Men and Women Who Reported Hypersomnolence, According to Category of Sleep-Disordered Breathing.

estimates within the context of current sleep medicine. We estimate that 2 percent of women and 4 percent of men in the middle-aged work force meet the current minimal diagnostic criteria for sleep apnea syndrome.[5] If the men and women who were found in this study to have frequent episodes of apnea and hypopnea are pathophysiologically similar to patients in sleep clinics who have similar apnea–hypopnea scores, then undiagnosed sleep-disordered breathing among adults represents a public health burden.

Health care costs arising from the diagnosis and treatment of sleep apnea syndrome are substantial. Evaluation by current standards includes full-night polysomnography, at a cost per procedure of approximately $1,100.[35] Sleep-disordered breathing can usually be eliminated by the nightly use of a nasal device that delivers continuous positive pressure to the upper airway.[36] Since patients must continue to receive this therapy throughout their lives, it is often viewed as a hardship. The demand for sleep medicine has spiraled upward over the past few years, in part because of increased awareness of sleep apnea, and current resources are barely adequate to evaluate and treat the patients who seek care.[37,38] If the condition of frequent episodes of apnea and hypopnea during sleep is indeed a sign of substantial morbidity that would be ameliorated with treatment, our findings indicate that men and women who seek evaluation for sleep-disordered breathing are merely a fraction of the total. Consequently, it is imperative that we evaluate the clinical and physiologic importance of sleep-disordered breathing at the mild end of the spectrum. Data from longitudinal studies of asymptomatic, untreated sleep-disordered breathing are needed to determine its progression, acute and chronic pathophysiologic sequelae, and other vital aspects of its natural history. Such information will be necessary to identify features that best describe the spectrum of severity of sleep-disordered breathing, and for clinical decision making about whom to treat.

Table 5. Odds Ratios for Sleep-Disordered Breathing and Measures of Body Habitus.*

Measure	SD of Covariate	Odds Ratio for a 1-SD Increment in the Covariate	95% CI
Weight (kg)	10.12	2.00	1.68–2.24
Body-mass index†	5.67	4.17	2.89–6.04
Girth (cm)			
Neck	4.49	5.00	3.29–7.61
Waist	15.29	4.12	2.91–5.83
Hip	12.65	3.86	2.71–5.53
Waist:hip ratio	0.09	3.41	2.27–5.13
Skin-fold thickness (mm)			
Bicep	6.76	2.76	2.02–3.77
Tricep	7.43	2.49	1.85–3.34
Subscapular	7.83	2.29	1.77–2.95
Suprailiac	10.40	1.87	1.53–2.48

*Sleep-disordered breathing was defined as an apnea–hypopnea score of 5 or higher. The odds ratios are for the comparison with subjects who were not habitual snorers and whose apnea–hypopnea scores were below 5. All the logistic-regression models included variables for age in years and sex. CI denotes confidence interval.

†The weight in kilograms divided by the square of the height in meters.

Risk Factors

The lack of a continuous increase in the prevalence of sleep-disordered breathing with increasing age in our study suggests that age is not a strong risk factor for sleep-disordered breathing over the middle adult years. Our results do indicate that male sex and obesity are important risk factors for sleep apnea in people 30 to 60 years old. The male:female ratio for the prevalence of sleep-disordered breathing was approximately 3:1. Although this risk ratio indicates an important difference in morbidity, it is lower than the widely cited clinic-based ratio of 8:1 or 10:1.[5,39,40] The higher ratio of diagnosed sleep apnea in clinical settings may be a result of greater self-selection and referral bias. Alternatively, the higher ratio in clinic populations may reflect sex differences in the natural history of sleep apnea, including differences in symptom response to the same frequency of apnea and hypopnea, or differences in disease progression.

In agreement with observations in clinics, our findings indicated that obesity was strongly related to undiagnosed sleep-disordered breathing. An increase of 1 SD in any measure of body habitus was related to a threefold increase in the risk of an apnea–hypopnea score of 5 or higher. Obesity clearly has an important role in sleep-disordered breathing. Because it is a modifiable risk factor, further research on its association with sleep apnea is particularly justified.

In summary, our finding is that undiagnosed sleep-disordered breathing, as measured according to clinical criteria, is prevalent and has a wide range of severity among middle-aged women and men. Consequently, further data on the natural and pathophysiologic importance of the spectrum of abnormal breathing during sleep are essential to rational health planning and clinical decisions about whom to treat.

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