Incidence of Sleep-Disordered Breathing in an Urban Adult Population
The Relative Importance of Risk Factors in the Development of Sleep-Disordered Breathing

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Numerous studies have demonstrated that sleep-disordered breathing (SDB) is both a prevalent phenomenon and associated with or causal of serious chronic illness. Current treatments seem to halt the progression or even reverse some deleterious effects of SDB. If these therapies are to be made available to larger liable populations, precise estimates of both prevalence and incidence rates of SDB and its sequelae must be developed. Cross-sectional studies have derived estimates of the prevalence of SDB in a number of populations, particularly of adults. Incidence data are equally important in anticipating the scale of effects of SDB and of resources to treat patients; however, no studies have examined the incidence of SDB or the influence of risk factors on the incidence of SDB.

The Cleveland Family Study was established both to examine causal factors and to document the natural history of SDB. As part of this effort, sleep studies have been carried out several times on a portion of the participants. This affords the opportunity to determine the incidence of SDB. We have also assessed the relative role of risk factors in determining the incidence of SDB. The results of these studies, previously reported in abstract form, are reported in detail herein.

Context Sleep-disordered breathing (SDB) is both prevalent and associated with serious chronic illness. The incidence of SDB and the effect of risk factors on this incidence are unknown.

Objective To determine the 5-year incidence of SDB overall and as influenced by risk factors.

Design, Setting, and Participants Of the 1149 participants in the Cleveland Family Study, those aged 18 years or older, from either case or control families, who had 2 in-home sleep studies 5 years apart. The first had to have been performed before June 30, 1997, and had to have normal results (apnea hypopnea index [AHI] <5). Data included questionnaire information on medical and family history, SDB symptoms; measurement of height, weight, blood pressure, waist and hip circumference, and serum cholesterol concentration; and overnight sleep monitoring.

Main Outcome Measure Apnea hypopnea index, defined as number of apneas and hypopneas per hour of sleep. Sleep-disordered breathing was defined by an AHI of at least 10 (mild to moderate) or of at least 15 (moderate).

Results Forty-seven (16%) of 286 eligible participants, (95% confidence interval [CI], 13%-21%) had a second-study AHI of at least 10 and 29 (10%) participants (95% CI, 7%-14%) had a second-study AHI result of at least 15. For the AHI results of at least 15, we estimate that about 2.5% may represent test variability. By ordinal logistic regression analysis, AHI was significantly associated with age (odds ratio [OR] per 10-year increase, 1.79; 95% CI, 1.41-2.27), body mass index (BMI; OR per 1-unit increase, 1.14; 95% CI, 1.10-1.19), sex (OR for men vs women, 4.12; 95% CI, 2.29-7.43), waist-hip ratio (OR per 0.1 unit increase, 1.61; 95% CI, 1.04-2.28), and serum cholesterol concentration (OR per 10-mg/dL [0.25-mmol/L] increase, 1.11; 95% CI, 1.03-1.19).

Interactions were noted between age and both sex (P = .003) and BMI (P = .05). The OR for increased AHI per 1-unit increase in BMI decreased from 1.21 (95% CI, 1.11-1.31) at age 20 years to 1.05 (95% CI, 0.96-1.15) at age 60 years.

Conclusions The 5-year incidence is about 7.5% for moderately severe SDB and 16% (or less) for mild to moderately severe SDB. Incidence of SDB is influenced independently by age, sex, BMI, waist-hip ratio, and serum cholesterol concentration. Predominance in men diminishes with increasing age, and by age 50 years, incidence rates among men and women are similar. The effect of BMI also decreases with age and may be negligible at age 60 years.

JAMA. 2003;289:2230-2237
www.jama.com

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METHODS
Population and Measures
The characteristics of the case and community control populations that reside in the greater Cleveland area have been described in detail. Of the entire population, 1149 individuals, aged 18 years or older, members of either case families with at least 1 member with polysomnographically confirmed SDB or of neighborhood control families, had at least 1 evaluation and in-home sleep study before June 30, 1997 (FIGURE 1). These family members included relatives and spouses of affected probands or neighborhood controls. A portion of these individuals also had undergone a second sleep study approximately 5 years later. From these, participants who were free of SDB on the initial polysomnogram (apnea hypopnea index [AHI] <5) were selected for this study.

Participants were studied in their homes, using nearly identical protocols at both examinations. Medical history, medication use, family history, ethnicity, and symptoms of SDB were assessed with the Sleep and Health Questionnaire. A limited physical examination was performed by the research technician, including measurement of height, weight and circumferences of waist and hips, and visual assessment of the presence and degree of tonsillar hypertrophy or upper airway obstruction. Blood pressure (Korotkoff-1 and Korotkoff-5 sounds) was measured twice in the sitting position after at least 5 minutes of rest, using a size-appropriate cuff. For discrepant results (≥4 mm Hg discordance), a third reading was obtained. Serum total cholesterol concentration was measured without regard to the last meal. Overnight in-home sleep monitoring was performed with an Edentrace I or II monitor (Eden Prairie, Minn) as described. Respiratory events were defined as cessations (apneas) or discrete reductions (hypopneas) in airflow or chest wall impedance, lasting at least 10 seconds and associated with a fall in oxygen saturation of at least 2.5%. The AHI was determined by dividing the number of respiratory events by the estimated hours of sleep.

Data on the covariates that were examined in relation to the incidence of SDB were obtained from the first examination whenever possible. The exceptions were waist and hip circumferences and serum cholesterol concentrations, which were measured at the second examination. Systemic hypertension was defined as a systolic blood pressure of at least 140 mm Hg or a diastolic blood pressure of at least 90 mm Hg by measurement, or by a self-reported use of antihypertensive medication. Cardiovascular disease or diabetes mellitus was defined by a self-reported history of heart attack, angina pectoris, stroke, heart failure, cardiac arrhythmia, or physician-diagnosed diabetes mellitus. Criteria for smoking included either ever smoking or currently smoking (≥1 cigarette daily during the month preceding the visit). Use of alcohol was defined by consuming an alcoholic beverage more than once weekly. A positive family history included multiple (≥2) relatives with AHI values of at least 15.

Incident SDB was based on 2 definitions. An AHI of at least 15 was used to identify at least moderately severe SDB, according to the definition of an American Academy of Sleep Medicine task force. An AHI of at least 10 was also examined as an indicator of mild SDB. Change in AHI from less than 5 to a level of 5 to 9.9 may indicate progression of SDB. We did not include such change in the definition of incidence, however, because small changes are likely to be in the range of night-to-night variability.

The protocol was approved by the institutional review boards of the local hospitals from which the probands were recruited. Written informed consent was obtained for all participants.

Statistics
Data were analyzed using SAS version 8.2 (SAS Inc, Cary, NC). To account for familial clustering, univariate between-group comparisons of continuous variables were made using mixed models, with family as a random effect; comparisons of binary outcomes were made using generalized estimating equation (GEE) logistic regression models. Multivariate analyses were performed using ordinal logistic regression under a proportional odds model, for which AHI at the second visit was grouped in 4 ordered categories (<5, 5-9.9, 10-14.9, ≥15). This approach simultaneously models 3 cumulative logits corresponding to using binary cut points at 5, 10, and 15, written as log Pr(AHI ≥5)/ Pr(AHI <5), log Pr(AHI ≥10)/ Pr(AHI <10), and log Pr(AHI ≥15)/ Pr(AHI <15), respectively. Preliminary analyses and model building were done ignoring the familial clustering. In the final models, we adjusted for familial clustering using the GEE approach, using the SAS macro GEECAT program of Williamson et al with an independence working correlation structure. Under this proportional odds model, 1 parameter is estimated for each predictor in the model. The parameter

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(Reprinted) JAMA, May 7, 2003—Vol 289, No. 17 2231
represents the effect of a 1-unit increase in the predictor variable on the logit (log odds), which is assumed to be the same for all 3 logits. A score test was used to verify the proportional odds assumption in the final model.18 To further verify the proportional odds model, we fit binary GEE logistic regressions using AHI cutoffs of at least 5, at least 10, and at least 15, and compared the results with those of the ordinal regressions. The modeling strategy was to first enter age, sex, and BMI. Variables were retained in the model if the likelihood ratio test was significant at P<.05. Interactions among the final covariates were then tested. Because of the smaller size of the subset in which serum cholesterol was measured (cholesterol subsample), findings were repeated both with and without cholesterol and the parameter estimates were compared.

RESULTS
Of the 1149 individuals aged 18 years or older at the time of their initial sleep study, 613 were found to have an AHI of at least 5. As noted in Figure 1, 286 of the remaining 536 participants were followed up with a second evaluation and in-home sleep study and serve as the study population for this investigation. Two hundred fifty participants met the inclusion criteria but were not followed up. Serum cholesterol concentrations were measured for 218 of these participants. Sixty-eight participants did not have their cholesterol concentrations measured because of the following reasons: refused venipuncture, were studied before we began collecting blood samples, or were evaluated at a time when the phlebotomist was unavailable.

Baseline characteristics of the participants who are studied herein (entire subsample) and those who were not followed up (eligible participants not studied) are compared in Table 1. These groups differed slightly but significantly in mean BMI and in percentage that were women but not in other comparisons. Of the 286 participants in the entire subsample, 132 (46%) were ever smokers, 77 (27%) were current smokers, 37 (13%) were currently taking antihypertensive medication, 66 (23%) used alcohol currently, 89 (31%) had large tonsils that appeared to crowd the oral airway, and 123 (43%) had a family history of SDB. A small difference in percentage of women existed in the smaller cholesterol subsample (n=218) relative to either the entire subsample or the eligible participants who were not studied (Table 1).

Comparisons of participants in case vs control families are shown in Table 2. The sample included 198 members of case families and 88 members of control families. Virtually no differences were noted between case and control groups in the incidence of AHI of at least 10 (16% vs 18%, respectively) or of at least 15 (10% vs 10%, respectively). Similar relationships were observed between sex and age incidence SDB for members of case and control families (Table 2). Thus, data from the case and control participants were combined for subsequent analyses.

At the second visit, 181 of the 286 participants (63%) retained AHI values of 5 and thus were not...
considered to have SDB (TABLE 3). Forty-seven participants were newly found to have an AHI of at least 10 on the second sleep study. Sixteen percent of participants (95% confidence interval [CI], 13%-21%) had AHI values of at least 10, and 10% (95% CI, 7%-14%) had AHI values of at least 15. These percentages represent the upper bound of the 5-year incidence of mild and/or moderately severe SDB and moderately severe SDB, respectively.

Factors that may modify the incidence rates of SDB are examined in TABLE 4 by means of univariate statistics. Incidences varied in a statistically significant manner with several factors: male sex, increasing initial age, BMI, and second-visit waist-hip ratio. A trend of increase in SDB with the higher quartiles of cholesterol levels and presence of cardiovascular disease (including diabetes mellitus) or hypertension was observed. The incidence of SDB did not appear to be influenced by race, large tonsils, smoking, alcohol intake, or family history of SDB.

The relative importance of the covariates on the incidence of SDB was examined by ordinal logistic regression analysis, deriving odds ratios (ORs) at an AHI of at least 5, less than 10, and less than 15, respectively (TABLE 5). The OR for each covariate was adjusted for the effects of the other significant covariates. In analyses of the entire subsample, age, BMI, and sex were significant covariates. Waist-hip ratio was independently associated with AHI (OR, 1.61, 95% CI, 1.04-2.48). Of note, adjusting for waist-hip ratio reduced the OR of sex from 1.04-2.48). Of note, adjusting for waist-hip ratio reduced the OR of sex from 1.04 to 2.65. In the cholesterol subsample, serum cholesterol concentration was significantly associated with AHI (OR, 1.11 for each 10-mg/dL [0.26 mmol/L] increase). The ORs for the other covariates were changed minimally with inclusion of cholesterol as a covariate. Variables that were not significant in these analyses included self-reported cardiovascular disease or diabetes, family history, race, smoking, alcohol ingestion, and tonsil size. Hyper-tension, which was marginally significant in the univariate analysis, was highly associated with age, BMI, and increased cholesterol concentration. The significance of its association with AHI was inconsistent, and it was not included in the multivariate analysis, deriving odds ratios (ORs) at each quartile of cholesterol levels and presence of cardiovascular disease (including diabetes mellitus) or hypertension was observed. The incidence of SDB did not appear to be influenced by race, large tonsils, smoking, alcohol intake, or family history of SDB.

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incurred in final models. Separate binary logistic regression analyses yielded ORs that are very similar to those of Table 5. Tests of the proportional odds assumption were not significant, indicating that the proportional odds model was appropriate for these data.

We further explored potential variation in effects across population subgroups with the use of interaction terms in the regression models. Both age and sex and age and BMI interacted in a significant manner (P = .003 and .05, respectively). No other interactions, including those involving waist-hip ratio (for example, sex-waist-hip ratio), were statistically significant. The effect of these interactions on ORs is provided in Table 6 and Figure 2. The odds for increased AHI increases by about 140% per 10-year increment in women (OR, 2.41) but by only 15% in men (OR, 1.15). This results in a curvilinear decrease in the preponderant association of male sex with SDB with increasing age, approaching unity at about age 50 years (Figure 2A). In other words, there is little or no apparent increased risk of incident SDB associated with male sex after age 50 years. The influence of BMI on AHI decreases with age, approaching unity after age 60 years (Figure 2B). Both waist-hip ratio and serum cholesterol concentration remain significant covariates.

### Table 5. Adjusted Odds Ratios Relating Incident Sleep-Disordered Breathing to Potential Risk Factors

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Entire Subsample</th>
<th>Waist-Hip Ratio Excluded (n = 283)</th>
<th>Waist-Hip Ratio Included (n = 281)</th>
<th>Cholesterol Subsample (n = 213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age per 10-year increment</td>
<td>1.79 (1.41-2.27)</td>
<td>1.76 (1.37-2.27)</td>
<td>1.51 (1.14-2.02)</td>
<td></td>
</tr>
<tr>
<td>BMI per unit increase</td>
<td>1.14 (1.10-1.19)</td>
<td>1.12 (1.07-1.17)</td>
<td>1.10 (1.05-1.16)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>4.12 (2.29-7.43)</td>
<td>2.65 (1.21-5.78)</td>
<td>2.29 (0.96-5.47)</td>
<td></td>
</tr>
<tr>
<td>Cholesterol per 10-mg/dL increase</td>
<td>1.11 (1.03-1.19)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist-hip ratio per unit increase</td>
<td>1.66 (1.04-2.48)</td>
<td>1.51 (0.87-2.63)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: BMI, body mass index, which is calculated as weight in kilograms divided by the square of height in meters.

SI conversion factor: To convert cholesterol from mg/dL to mmol/L, multiply by 0.0259.

*Adjusted odds ratios (95% confidence intervals), adjusted for each covariate for the effects of the other covariates, were derived by ordinal logistic regression analysis, as detailed in the “Methods” section. Of the entire subsample of 286 participants, 283 had measurements of BMI and 281 had measurements of both BMI and waist-hip ratio.

### Table 6. Adjusted Odds Ratios for Incident Sleep-Disordered Breathing, Including Interactions of Age With Sex and Body Mass Index

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Entire Subsample</th>
<th>Cholesterol Subsample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age per 10-year increment†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.15 (0.78-1.68)</td>
<td>1.04 (0.69-1.56)</td>
</tr>
<tr>
<td>Women</td>
<td>2.41 (1.78-3.26)</td>
<td>2.18 (1.53-3.52)</td>
</tr>
<tr>
<td>Men vs women.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>5.04 (2.19-11.6)</td>
<td>4.26 (1.68-10.7)</td>
</tr>
<tr>
<td>40</td>
<td>2.40 (1.24-5.07)</td>
<td>2.02 (0.87-4.70)</td>
</tr>
<tr>
<td>50</td>
<td>1.14 (0.45-2.93)</td>
<td>0.96 (0.33-2.80)</td>
</tr>
<tr>
<td>60</td>
<td>0.54 (0.15-1.99)</td>
<td>0.46 (0.10-1.99)</td>
</tr>
<tr>
<td>BMI per unit increase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>1.21 (1.11-1.31)</td>
<td>1.21 (1.10-1.34)</td>
</tr>
<tr>
<td>40</td>
<td>1.13 (1.07-1.18)</td>
<td>1.12 (1.05-1.19)</td>
</tr>
<tr>
<td>60</td>
<td>1.05 (0.96-1.15)</td>
<td>1.03 (0.98-1.13)</td>
</tr>
<tr>
<td>Waist-hip ratio per 0.1-unit increase</td>
<td>1.66 (1.04-2.64)</td>
<td>1.74 (0.94-3.21)</td>
</tr>
<tr>
<td>Cholesterol per 10-mg/dL increase</td>
<td>1.09 (1.01-1.18)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: BMI, body mass index, which is calculated as weight in kilograms divided by the square of height in meters.

SI conversion factor: To convert cholesterol from mg/dL to mmol/L, multiply by 0.0259.

*Adjusted odds ratios (95% confidence intervals) were derived by ordinal logistic regression analysis. ORs apply to an apnea hypopnea index of at least 10.

†Adjusted to a body mass index of 27.

### COMMENT

The Cleveland Family Study was undertaken to provide added definition of the natural history of SDB and to identify and quantify the importance of risk factors that predispose individuals to this syndrome. Although index cases with polysomnographically proven SDB were identified in local sleep laboratories, these individuals most importantly served as an entree to the proband’s family and also to control families. The members of these families represent a relatively young urban population. Our previous studies in this population have demonstrated the familial aggregation of and inherited predisposition to SDB.9,10 Except for the selection bias resulting from this familial aggregation in families of index cases, this population would appear to have no special liability for the development of SDB.

In our analyses, we have selected a subgroup from the Cleveland Family Study in which to document the incidence of SDB over a period of nominally 5 years. Adults (aged ≥18 years), selected from both case and control families, had an AHI of less than 5 at the study’s start. Despite the differences in the methods for selecting case and control families, we were unable to find any differences between them that might bias our incidence data (Table 2). We thus believed ourselves justified in combining the data from both groups for these analyses. The overall study population was slightly more obese, was predominantly white and female but was otherwise representative of the total popula-
tion that was eligible for 2 in-home sleep studies (Table 1). Participants were often cigarette smokers; consumed alcohol; or had a chronic illness, such as hypertension, cardiovascular disease, and/or diabetes mellitus.

We found that the overall 5-year incidence of SDB is 10% for those with an AHI of at least 15 and 16% for those with an AHI of at least 10 (Table 3). We know of no other studies that have directly evaluated the incidence of SDB. Data bearing on prevalence are available from a number of sources. These data are subject to variation according to the nature of the population under study, the method of ascertainment, and the definition of SDB. Most studies of sleep apnea, using a 2-tiered method of ascertainment (usually questionnaire followed by sleep monitoring), yield prevalence estimates on the order of 1% to 4% in general populations of adults.1,7,10,21

In the Cleveland Family Study of the same population of adult subjects represented in our analysis, we documented a prevalence of SDB (AHI>15) of 10.5% on an initial in-home sleep study, and 16.3% on a second study about 5 years later.22 Relatively similar prevalences were found by Peppard et al23 (7% and 10% prevalence rates in middle-aged adults studied twice at a 4-year interval), and by Duran et al24 (1.4% for men, 7% for women aged 30-70 years). In both studies, SDB was defined by an AHI of at least 15 but with a 4% oxygen desaturation threshold for identification of apneic events (as opposed to a 2.5% threshold in our study). Substantially higher prevalence rates of SDB (>25%) have been reported in populations of elderly individuals.25

One might expect that a 5-year incidence of 10% would lead to a considerably higher long-term prevalence (ie, in older individuals) than the 16% that our data document.22 Certainly the prevalence of SDB does increase with age,12 but probably not to the degree suggested by the current incidence figure. Several reasons may explain this paradox. One must consider the possibility of measurement variability or of amelioration of SDB over time. Data bearing on these concepts are meager. In a study that is of much shorter duration, Quan et al15 determined the AHI from 2 in-home sleep studies approximately 4 months apart in 91 subjects from the Sleep Heart Health Study, with the finding of a high degree of concordance in the 2 evaluations. The intraclass correlation coefficient for AHI between the 2 examinations was 0.81 (95% CI, 0.72-0.87). In 82% of subjects, the second respiratory disturbance index remained either less than 15 or 15 or higher. Further analyses of these data show that of 35 participants with an AHI of at least 15 on the first examination, none had an AHI lower than 5 on second examination (S.R., unpublished data, 2003). Similarly, in our own cohort, of the 48 adults with an initial AHI of at least 15 who underwent a repeat in-home sleep study about 5 years later, 2 subjects (4%) had second AHI values of less than 5. These results suggest that only a small proportion (approximately 2.5%) of individuals regress on second study from an AHI of at least 15 to an AHI of less than 5. Thus, the overall 5-year incidence rate of SDB is reduced from 10% to about 7.5% for an AHI of at least 15. We do not have information on which to base a similar estimate of test variability for an AHI of at least 10. Another possible explanation for any discrepancy between incidence and prevalence rates is that SDB accelerates mortality in older individuals who have SDB for prolonged periods, perhaps by facilitating the development of coronary artery disease, systemic hypertension and its sequelae, or diabetes mellitus. Although this is a controversial subject, a number of publications indicate that an acceleration in mortality may occur.26,27

Since the prevalence of SDB is influenced by either proven risk factors (obesity, sex, age, family history) or less well-established associations (cardiovascular disease, hypertension, diabetes mellitus),12,19,28,30 we postulated that incidence may be affected in a similar manner. We examined this relationship with data primarily from each participant’s initial visit, anticipating that early data may even be predictive of the development of SDB. The serum cholesterol and waist-hip ratio measurements were only available from the second visit, however. Epidemiologic experience with serum cholesterol concentrations has demonstrated a high correlation among repeat measurements over many years. For example, the product-moment correlation coefficients over 6 years of repeated serum cholesterol concentrations from more than 1000 participants in the Framingham Study were approximately 0.7.31 A similar correlation obtained for waist-hip ratio, a measure of body fat distribution particularly in the abdomen.32 In 691 male members of a Swedish birth cohort, the Spearman correlation coefficient for waist-hip ratio at age 43 vs

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age 37 years was 0.66 (K. M. Henriksson, written communication, September 27, 2002). These data suggest that measures of cholesterol and waist-hip ratio are moderately to strongly correlated over several years, supporting the use of second-visit data as surrogate predictive factors.

The initial analyses, using univariate statistics, suggested that incidence varied significantly with sex, age, BMI, and waist-hip ratio, and possibly the presence of chronic illness (cardiovascular disease, diabetes mellitus, and hypertension) and casual serum cholesterol concentration (Table 4). Examining these associations by a multivariate procedure (ordinal logistic regression), we found that age, BMI, sex, and waist-hip ratio remained significant predictors of AHI (Table 5, entire subsample). Waist-hip ratio reduced the OR for sex by about 35% (from 4.12 to 2.65), suggesting that some of the association between sex and SDB is mediated by body fat distribution. Serum cholesterol added to the regression was also significantly associated with AHI and had little effect on the ORs of the other covariates (Table 5, cholesterol subsample). Results were similar with binary logistic regression. Age, BMI, sex, waist-hip ratio, and serum cholesterol concentration are all significant predictors of AHI.

The associations of age, sex, obesity with SDB have been well documented, not only in the Cleveland Family Study but also in many other investigations. Thus, our finding strong direct associations of these covariates with the incidence of SDB is not surprising. Other factors that are associated in a possibly causal manner with the presence of SDB were not associated with the incidence of SDB in the present study. In previous reports from the Cleveland Family Study, we documented a strong association of race and family history with SDB. The effect of race was seen in black participants who were younger than 25 years. Since most members of the population in these analyses were older than 25 years, the lack of a race effect is understandable. The absence of an association of family history may be the result of our necessarily restricting the analyses to individuals who did not have SDB at their initial examination.

The effects of sex, age, and BMI on SDB are interrelated in a complex manner, resulting in major modification of the incidence in special circumstances. The incidence in men is, overall, greater than that in women (Table 4). With age, this risk in men increases only modestly, whereas that risk in women increases steadily and markedly (Table 6). The result is that by age 50 years, sex differences in the incidence of SDB essentially disappear (Table 6, Figure 2A). Changes in sex hormone economy (metabolism distribution, clearance, use) have been suggested as a cause of the increased prevalence of SDB in perimenopausal women. This suggestion has been strengthened by the recent finding in the Sleep Heart Health Study that hormone replacement therapy is associated with lower AHI levels in postmenopausal women. The AHI also increases directly with increasing BMI, a measure of overall obesity (Table 5). Interestingly, the effects of BMI diminish with increasing age (Table 6, Figure 2B), a phenomenon that has been noted previously. Perhaps other factors (change in ventilatory control, upper airway stability, etc) assume a greater relative importance with age.

The mechanism by which serum total cholesterol concentration might influence the incidence of SDB is unknown. Sleep disordered breathing is associated with a predilection for cardiovascular disease, possibly because individuals with SDB have augmented cardiovascular risk factors. For example, Newman et al recently showed that community-based subjects with AHIs in the highest population quartiles had worse cardiovascular disease risk profiles (blood pressure, serum cholesterol concentrations, and also waist-hip ratios) than those with lower AHIs. Obesity, clearly a risk factor for SDB, is associated with insulin resistance, glucose intolerance, and disordered lipid homeostasis. Possibly the lipid (cholesterol) abnormalities predispose to SDB by mechanisms that are independent of obesity. Kadotani et al have described an association between apolipoprotein E ε4 and SDB, but this association has not been confirmed by others. Given mounting evidence for a genetic basis for SDB, these data suggest that a cardiovascular disease–SDB phenotype may be a manifestation of common genetic risk factors (involving primary genes or modifier genes). If so, individuals with elevated cholesterol levels may represent a phenotype with augmented risk for progression of SDB.

We must consider how representative this population is of ambulatory communities in the United States in general in order to extrapolate our findings. The study population is well represented in black individuals proportionately to their representation in the overall population of the United States. One must still be cautious, however, in applying the overall findings to a group that comprised only about 20% of the study population. Moreover, ethnic groups other than whites and blacks were not represented in the participants. Otherwise, members of control families were not knowingly selected for any medical condition, including SDB. Our studying members of case families might bias the incidence of or the effects of risk factors for SDB. Because of the familial nature of SDB, for example, the incidence of SDB in relatives of probands with SDB may be augmented. Our detailed comparison of the data from the case vs the control populations does not identify any significant difference in incidence, however. Moreover, logistic regression analyses failed to identify family history as a risk factor for incident SDB. The fact that the population in this study was slightly weighted toward both women and individuals with higher BMI values, relative to others in this sample of family members who were not studied, may distort the general applicability of these results.

In summary, we found the 5-year incidence of SDB in a community-based

INCIDENCE OF SLEEP DISORDERED BREATHING
sample of adults aged 18 years or older to be 16% or less for mild to moderately severe SDB and to be about 7.5% for moderately severe SDB. Incidence was influenced by age, sex, BMI, waisthip ratio, and serum cholesterol concentration, either singly or (for age-sex and age-BMI) in combination. We believe that these findings are applicable to many populations and may ultimately be important in framing the public health impact of SDB. We await the results of studies by others to place our findings in proper perspective.

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**Author Contributions:** Study concept and design: Tishler, Redline. Acquisition of data: Redline. Analysis and interpretation of data: Tishler, Larkin, Redline, Schluchter.

**Reference**