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ORIGINAL CONTRIBUTIONS

Snoring as a Risk Factor for Type II Diabetes Mellitus: A Prospective Study

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To examine the association between snoring and risk of developing type II diabetes mellitus, the authors analyzed data from the Nurses' Health Study cohort. This analysis included 69,852 US female nurses aged 40–65 years without diagnosed diabetes, cardiovascular disease, or cancer at baseline in 1986. Snoring patterns were ascertained by questionnaire. During 10 years of follow-up, 1,957 women were diagnosed with type II diabetes. In analyses adjusted for age and body mass index, snoring was associated with risk of diabetes (for occasional snoring vs. nonsnoring, relative risk (RR) = 1.48 (95% confidence interval (CI): 1.29, 1.70); for regular snoring vs. nonsnoring, RR = 2.25 (95% CI: 1.91, 2.66); p for trend < 0.0001). Further adjustment for other diabetes risk factors and sleeping-related covariates only slightly attenuated the risk (for occasional snoring, RR = 1.41 (95% CI: 1.22, 1.63); for regular snoring, RR = 2.03 (95% CI: 1.71, 2.40); p for trend < 0.0001). Analyses stratified by body mass index, smoking history, or parental history of diabetes showed a consistent association between snoring and diabetes within the categories of these variables. These results suggest that snoring is independently associated with elevated risk of type II diabetes. *Am J Epidemiol* 2002;155:387–93.

diabetes mellitus, non-insulin-dependent; prospective studies; sleep; sleep apnea, obstructive; snoring

Editor's note: *An invited commentary on this article appears on page 394, and the authors' response is on page 396.*

Habitual snoring and sleep apnea are associated with increased risk of cardiovascular disease morbidity and mortality (1–4). Less is known about the relation between snoring and diabetes mellitus. Obstructive sleep apnea, which usually involves heavy snoring, is more common among glucose-intolerant and diabetic individuals than among healthy subjects (5, 6). However, earlier studies that found a higher prevalence of diabetes among snorers did not adjust for important confounding factors such as body mass index and waist:hip circumference ratio (7).

The mechanism by which snoring or sleep apnea might increase diabetes risk is the triggering of metabolic processes involving insulin action and glucose regulation (8, 9). More specifically, upper airway obstruction caused by snoring or sleep apnea can lead to oxygen desaturation, which increases catecholamine and cortisol levels, thereby increasing insulin resistance.

We investigated prospectively the relation between habitual snoring and the development of type II diabetes among women in the Nurses' Health Study cohort. The study provided us with an opportunity to adjust for variables such as body mass index, waist:hip ratio, smoking, and other factors that might confound the relation between snoring and diabetes incidence.

MATERIALS AND METHODS

Study population

The Nurses' Health Study cohort was established in 1976, when 121,700 US female registered nurses aged 30–55

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Abbreviations: CI, confidence interval; RR, relative risk.

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years and residing in one of 11 states completed a mailed questionnaire regarding medical history and lifestyle factors (3). This information has been updated every 2 years. On the 1986 detailed questionnaire, the following question about snoring was asked: "Do you snore (regularly, occasionally, or never)?" We also asked the women to indicate total hours of actual sleep in a 24-hour period (from ≤5 hours to ≥11 hours) and their usual sleeping position (on back, on side, or on front). A total of 83,476 women returned the questionnaire. Only 559 women did not answer the question on snoring and were excluded. After exclusion of women with diabetes, cancer, or cardiovascular disease prior to the 1986 baseline and those who developed stroke during follow-up, 69,852 women were included in the final analyses for the 1986–1996 follow-up period.

Assessment of diabetes

On each follow-up questionnaire, we inquired about the diagnosis of diabetes. Whenever a participant reported a diagnosis of diabetes, we mailed her a supplementary questionnaire requesting information on the details of the diagnosis (diagnostic tests, symptoms, and year of diagnosis) and treatment (insulin or oral hypoglycemic medication). In accordance with the criteria of the National Diabetes Data Group (10), diabetes was considered confirmed if the questionnaire indicated one of the following: 1) classic symptoms (excessive thirst, polyuria, weight loss, hunger) associated with an elevated plasma glucose level (fasting value of ≥7.8 mmol/liter, random value of ≥11.1 mmol/liter, or a ≥2-hour post-glucose-challenge value of ≥11.1 mmol/liter); 2) no symptoms, but at least two elevated plasma glucose values (by the above criteria) on different occasions; or 3) treatment with hypoglycemic medication (insulin or an oral hypoglycemic agent). We used the National Diabetes Data Group criteria to define diabetes because all of our cases were diagnosed prior to the release of the American Diabetes Association criteria in 1997 (11).

We depended on self-reported information from the supplementary diagnostic questionnaire for confirmation of diabetes, but we validated the reports in a random sample of women by obtaining their medical records. Among 84 women classified by the supplementary questionnaire as having type II diabetes, 71 provided permission to review their medical records and 62 had records available. An endocrinologist blinded to the information reported on the supplementary questionnaire reviewed the records according to the National Diabetes Data Group criteria (10). The diagnosis of type II diabetes was confirmed in 61 (98 percent) of the 62 women (12). Furthermore, at each 2-year follow-up, most of the nondiabetic women (an average of 86.3 percent) reported being physically examined by a doctor, and therefore it is unlikely that there was underdiagnosis in this group.

Assessment of covariates

The follow-up questionnaire included requests for information on age, current weight, smoking status, physical activity, alcohol use, history of high cholesterol, history of high blood pressure, postmenopausal hormone use, family history of diabetes, usual sleeping position, number of hours of sleep per day, and number of years of shift-work. Except for the latter three variables, for which data were recorded only in 1986, updated information on the other covariates was collected on the biennial follow-up questionnaires. A validation study was carried out for self-reported weight. In a sample of 140 women, we compared self-reported weight with actual weight as measured by a technician (mean self-reported weight = 144.2 pounds (65.5 kg), mean technician weight measurement = 147.9 pounds (67.2 kg)); the two measurements were highly correlated (r = 0.96) (13). In 1986, participants were asked to measure and report their waist circumference (measured at the umbilicus) and hip circumference by using a tape measure. This information was provided by 43,708 women included in this analysis. For validation of these measures, self-reported measurements in a sample of 140 nurses were compared with two standardized measurements taken approximately 6 months apart by technicians who visited participants in their homes; correlations were high for both measures (0.89 for waist circumference and 0.84 for hip circumference) (13). The waist:hip ratio was calculated from these two measurements.

Physical activity was measured by the amount of time per week in which the participant had engaged in 10 specified physical activities and four sedentary activities during the previous year (14). Using these activities, we calculated a weekly metabolic equivalent task score for total physical activities. The validity of the questionnaire in assessing physical activity has been described elsewhere (14). The correlation between activities reported in four 1-week diaries and those reported on the questionnaire was 0.62.

Statistical analyses

Participants contributed person-time from the date of return of the 1986 questionnaire to the date of diagnosis, the date of death, or June 1, 1996, whichever came first.

Pooled logistic regression models with 2-year time increments were used to control simultaneously for known diabetes risk factors. Most of the covariates were updated biennially, including age (<45, 45–49.9, 50–54.9, 55–59.9, and ≥60 years), smoking status (never smoking, past smoking, and current smoking of 1–14, 15–24, or ≥25 cigarettes per day), postmenopausal hormone use (premenopausal status, never use, current use, and past use), alcohol intake (0, 0.1–4.9, 5.0–14.9, and ≥15.0 g/day), body mass index (calculated as weight (kg) divided by height (m) squared and included in analyses in the categories <22, 22–23, 23–25, 25–27, 27–29, 29–31, 31–33, and >33), physical activity (quartiles of metabolic equivalents per week), history of high cholesterol (yes, no), history of high blood pressure (yes, no), parental history of diabetes (yes, no), usual sleeping position (on side, on back, on front, and mixed positions), usual number of hours of sleep (≤5, 6, 7, 8, and ≥9 hours/day), and number of years of shift-work (0, 1–5, 6–14, and ≥15). We additionally adjusted for waist:hip ratio (<0.72, 0.72–0.75, 0.76–0.78, 0.79–0.86, and >0.86) in secondary analysis of a subsample of the study population. The following covariates

TABLE 1. Age-adjusted characteristics of women in the Nurses' Health Study, according to snoring status in 1986

	Never snorers (n = 18,340)	Occasional snorers (n = 45,161)	Regular snorers (n = 6,351)
Mean age (years)	50.3 (7.1)*	52.8 (7.1)	53.3 (6.8)
Mean body mass index†	23.8 (3.7)	25.3 (4.6)	28.0 (5.9)
Mean waist:hip ratio	0.77 (0.2)	0.78 (0.1)	0.81 (0.1)
Mean waist circumference (inches)‡	29.6 (3.9)	30.9 (4.2)	33.2 (5.1)
Mean total hours of sleep per day	7 (0.9)	7 (0.9)	7 (1.0)
Mean physical activity (METs§)	15.7 (21.9)	14.1 (20.9)	11.1 (17.9)
Mean daily alcohol consumption (g)	5.8 (9.6)	6.5 (10.9)	6.7 (12.3)
History of high blood pressure (%)	18	23	31
History of high cholesterol level (%)	9	11	14
Current postmenopausal hormone use (%)	34	27	25
Ever engaging in shift-work (%)	16	18	22
Usual sleeping position (%)			
On side	80	82	81
On back	6	7	8
On front	13	11	9
Current smoker (%)	16	23	28
Parental history of diabetes (%)	15	16	18

* Numbers in parentheses, standard deviation.
† Weight (kg)/height (m)^2.
‡ 1 inch = 25.4 mm.
§ MET, metabolic equivalent task.

were also used as variables in stratified analyses for assessment of potential effect modification: parental history of diabetes (yes, no), current smoking (yes, no), and body mass index (<25, 25–29.9, and ≥30). Body mass index was collapsed to five categories (<21, 21–22.9, 23–24.9, 25–28.9, and ≥29) in analyses stratified by smoking and parental history of diabetes because of small numbers in each category. In analyses stratified by body mass index, we adjusted for body mass index in continuous form to minimize residual confounding.

Tests for trend were conducted using the categorical variable of snoring as an ordinal variable (0 = nonsnoring, 1 = occasional snoring, 2 = regular snoring). All p values were two-sided.

RESULTS

During 10 years of follow-up (1986–1996) among 69,852 nurses who had answered the question on snoring, 1,957 cases of diabetes were diagnosed during 664,280 person-years.

Table 1 shows the characteristics of this population according to their snoring status in 1986. Regular snorers had a higher mean body mass index, a higher waist:hip ratio, and a higher prevalence of high blood pressure and high cholesterol levels; they also were more likely to do shift work and were less often engaged in physical activity. Therefore, we adjusted for these variables in the multivariate analyses.

Age-adjusted relative risks of developing type II diabetes according to snoring status are shown in table 2. Compared with nonsnorers, women who snored regularly were at a five-fold higher risk of developing diabetes, while the risk was doubled among those who snored occasionally. These relative risks were substantially attenuated after adjustment for body mass index, but a significantly elevated risk of diabetes was still seen for both occasional snorers and regular snorers. Adjusting for all variables simultaneously changed the relative risks only slightly in comparison with the model that included

TABLE 2. Adjusted relative risk of type II diabetes among women in the Nurses' Health Study who were followed up between 1986 and 1996, according to snoring status in 1986

	No. of cases	Person-years of follow-up	Relative risk: Adjusted for age		Adjusted for age and body mass index*		Multivariate-adjusted†	
			RR‡	95% CI‡	RR	95% CI	RR	95% CI
No snoring	237	176,679	1.00§		1.00		1.00	
Occasional snoring	1,297	428,686	2.12	1.85, 2.44	1.48	1.29, 1.70	1.41	1.22, 1.63
Regular snoring	423	58,915	4.99	4.31, 5.96	2.25	1.91, 2.66	2.03	1.71, 2.40
p for trend			<0.0001		<0.0001		<0.0001	

* Weight (kg)/height (m)^2.
† Adjusted for age, history of high cholesterol, history of high blood pressure, time period, smoking, body mass index (eight categories), physical activity, alcohol use, postmenopausal hormone use, family history of diabetes, usual sleeping position, number of hours of sleep per day, and years of shift-work.
‡ RR, relative risk; CI, confidence interval.
§ Reference category.

TABLE 3. Adjusted relative risk of type II diabetes among women in the Nurses' Health Study who reported their waist and hip circumferences in 1986 and were followed up between 1986 and 1996, according to snoring status in 1986

	No. of cases	Person-years of follow-up	Relative risk							
			Adjusted for age		Adjusted for age and body mass index*		Multivariate-adjusted†		Multivariate-adjusted†, including waist:hip ratio	
			RR‡	95% CI‡	RR	95% CI	RR	95% CI	RR	95% CI
No snoring	129	114,400	1.00§		1.00		1.00			
Occasional snoring	644	269,384	1.95	1.61, 2.36	1.39	1.14, 1.68	1.30	1.07, 1.58	1.22	1.00, 1.48
Regular snoring	199	34,117	4.67	3.73, 5.84	2.15	1.71, 2.70	1.88	1.48, 2.37	1.63	1.29, 2.07
p for trend			<0.0001		<0.0001		<0.0001		<0.0001	

* Weight (kg)/height (m)^2.
† Adjusted for age, history of high cholesterol, history of high blood pressure, time period, smoking, body mass index (eight categories), physical activity, alcohol use, postmenopausal hormone use, family history of diabetes, usual sleeping position, number of hours of sleep per day, and years of shift-work.
‡ RR, relative risk; CI, confidence interval.
§ Reference category.

only body mass index and age (table 2). We also adjusted for body mass index as a continuous variable in a separate analysis, and there was no difference in the relative risks in comparison with the model that included body mass index in eight categories (for occasional snoring, relative risk (RR) = 1.45 (95 percent confidence interval (CI): 1.25, 1.69); for regular snoring, RR = 1.94 (95 percent CI: 1.62, 2.32)). Furthermore, we reran the analyses using baseline body mass index, smoking, and alcohol intake values; the results were slightly attenuated but nevertheless consistent with the model that adjusted for the updated covariates (for occasional snoring, RR = 1.34 (95 percent CI: 1.16, 1.55); for regular snoring, RR = 1.85 (95 percent CI: 1.56, 2.20); *p* for trend < 0.0001).

When waist:hip ratio was included in a secondary analysis of a subsample of participants (only 43,708 women reported this measurement (972 diabetes cases)), the relative risk of diabetes among snorers was slightly attenuated in comparison with the multivariate model that did not include waist:hip ratio (table 3). Substituting the waist:hip variable with the waist circumference variable (<26, 26–29.9, 30–33.9, 34–37.9, and ≥38 inches (1 inch = 25.4 mm)) in the latter model did not change the relative risks.

To assess possible effect modification by smoking, family history of diabetes, or body mass index, we conducted stratified analyses according to these variables (table 4). To adjust further for possible confounding, we also included body mass index (five categories) in the model in each of the strata of smoking and family diabetes history. We found a consistently elevated risk of developing diabetes among regular snorers in all strata.

In a separate analysis, we stratified the data by weight change over the 10 years of study follow-up. Among women whose weight had remained stable (<2 kg of weight change over time), we found relative risks for snoring and diabetes similar to those of the overall multivariate-adjusted analyses among all participants (for occasional snoring, RR = 1.49

TABLE 4. Multivariate-adjusted* relative risk of type II diabetes among women in the Nurses' Health Study who were followed up between 1986 and 1996, according to history of snoring in 1986

	No. of cases	Risk of diabetes†				*p* for trend
		Occasional snoring		Regular snoring		
		RR‡	95% CI‡	RR	95% CI	
Body mass index§						
<25	199	1.04	0.74, 1.47	1.82	1.11, 2.99	0.06
25–29.9	540	1.25	0.98, 1.59	1.91	1.41, 2.58	<0.0001
≥30	1,009	1.59	1.26, 2.00	1.98	1.53, 2.55	<0.0001
Current smoker						
No	1,560	1.54	1.32, 1.81	2.30	1.91, 2.77	<0.0001
Yes	310	1.15	0.79, 1.66	2.05	1.36, 3.09	<0.0001
Family history of diabetes						
No	1,268	1.53	1.28, 1.83	2.29	1.86, 2.82	<0.0001
Yes	607	1.35	1.05, 1.73	2.12	1.58, 2.83	<0.0001

* Adjusted for age, history of high cholesterol, history of high blood pressure, time period, smoking, body mass index (five categories), physical activity, alcohol use, family history of diabetes, usual sleeping position, number of hours of sleep per day, and years of shift-work (excluding the stratifying variable).
† Reference category: no snoring.
‡ RR, relative risk; CI, confidence interval.
§ Weight (kg)/height (m)^2. Data were further adjusted for confounding by body mass index as a continuous variable in each category.

(95 percent CI: 1.04, 2.13); for regular snoring, RR = 2.14 (95 percent CI: 1.41, 3.24)).

DISCUSSION

The results from this prospective study indicate that occasional or regular snoring is associated with increased risk of developing diabetes, even after adjustment for body mass index and waist:hip ratio. Regular snorers were at higher risk of developing diabetes than occasional snorers within the same body mass index categories, which further supports the hypothesis that there is an independent dose-response relation between severity of snoring and development of diabetes.

Confounding by obesity is a major concern with regard to our analyses. Obesity can cause breathing disturbances such as snoring and obstructive sleep apnea (15, 16). Obesity can also cause insulin resistance and diabetes (17). This has led to speculation that any relation between snoring or obstructive sleep apnea and diabetes is simply a reflection of obesity (18), because both measures of obesity, body mass index and waist:hip ratio, have been found to be strong predictors of heavy snoring (19, 20). Because body mass index was updated every 2 years in our data and we had measures of waist:hip ratio for a subset of women, we were able in our analyses to control tightly for confounding by obesity. Although some residual confounding may remain, the lack of major change in the associations after we adjusted for body mass index as a continuous variable in the main analyses, and the presence of significant risk even after we added waist:hip ratio to the secondary analysis, suggests that residual confounding is unlikely to explain the observed associations. The large number of participants in our cohort allowed us to perform stratified analyses and simultaneously adjust for body mass index and other risk factors; this showed a persistent increase in relative risk among regular snorers across the different subgroups. We were also able to stratify the analyses by weight change during the 10-year follow-up period, and we found consistently elevated risks of diabetes associated with snoring among women whose weight had not changed substantially during the follow-up period. Furthermore, recall and reporting bias was minimized because of the prospective nature of the study.

Potential weaknesses of the study include the subjective nature of self-reported snoring. However, in a previous study, self-reported snoring and snoring reported by roommates were found to be reasonably correlated (19). In an earlier analysis in the Nurses' Health Study, snoring prevalence was similar between women who were living with spouses or partners and those who were not, which suggests no obvious bias in reporting (3). Telakivi et al. (21) also suggested that self-reported snoring was a reliable measure, as validated by all-night sleep recording. Neck circumference, which was not assessed in our study, is thought to be related to snoring and possibly to obstructive sleep apnea (22–24). However, it was a weaker predictor of snoring than waist circumference in a multivariate regression analysis (25).

There have been few published studies on the relation of snoring or obstructive sleep apnea to the incidence of diabetes. In a cross-sectional study of 5,201 adults over 65 years of age (20), snoring in women (n = 2,601) was independently associated with diabetes (odds ratio = 1.34, 95 percent CI: 1.10, 1.65) after adjustment for body mass index. Obstructive sleep apnea was similarly associated with diabetes (odds ratio = 1.74, 95 percent CI: 1.12, 2.70). In another cross-sectional study of 3,034 individuals in the Swedish Obese Subjects cohort (26), investigators reported a higher frequency of diabetes among patients with obstructive sleep apnea than among those without obstructive sleep apnea (odds ratio = 1.8, 95 percent CI: 1.2, 2.7). In a cross-sectional study of 2,001 subjects in Toronto, Canada (7) who reported on snoring, descriptive analyses showed that persons above 40 years of age who snored (n = 563) did not have a higher prevalence of diabetes than nonsnorers (n = 261).

In a well-designed prospective study in Uppsala, Sweden, the investigators followed 2,668 men aged 30–69 years from 1984 to 1994 (27). By 1994, 5.4 percent (n = 19) of the snorers had developed diabetes as compared with only 2.4 percent (n = 49) of the nonsnorers. Compared with lean nonsnorers, the odds ratio for developing diabetes among obese snmorers (body mass index > 27) was 7.0 (95 percent CI: 2.9, 16.9), while it was 5.1 (95 percent CI: 2.7, 9.5) among obese nonsnorers. This study suggested an additive effect of obesity and snoring on diabetes risk.

The mechanism by which snoring leads to the development of diabetes is still not well understood. The mechanism would be similar to that of sleep apnea, because both snoring and sleep apnea are related to mechanical obstruction of the upper airway. It has been found that heavy snoring is the major manifestation of obstructive sleep apnea and a predictor of obstructive sleep apnea (19, 28). We were not able to distinguish between snoring and sleep apnea in our study, because we did not measure sleep apnea. We speculate that the observed association between snoring and diabetes is partially mediated by sleep apnea. Obstructive sleep apnea has been more extensively studied in the literature than snoring and has been found to be related to several illnesses, although snoring has also been linked to several illnesses (29–31). Increased insulin resistance (which is a precursor of type II diabetes) among individuals who snore or have obstructive sleep apnea is believed to explain the association between snoring or sleep apnea and diabetes (26, 32–34). The increased insulin resistance may result from increased sympathetic activity and increased catecholamine levels (9, 35, 36). Oxygen desaturation may play a role in the increased circulating insulin levels and risk of insulin resistance (9) through increased catecholamine (36–40) and cortisol levels (41), which can lead to increased insulin levels by stimulating glycogenolysis, gluconeogeneses, and glucose intolerance (9, 42). Catecholamine and cortisol hormone levels have been found to be elevated among subjects with documented obstructive sleep apnea as compared with controls (35, 43) and have been correlated with levels of oxygen desaturation among these patients (44). Furthermore, catecholamine levels have been found to be significantly lower after tracheostomy (36) and continuous positive airway pressure treatment (45) in patients with obstructive sleep apnea. In the latter study, Brooks et al. (45)

carried out a carefully planned intervention among 10 obese (body mass index >35) diabetes patients suffering from obstructive sleep apnea. Recordings of insulin responsiveness (by hyperinsulinemic euglycemic clamp) were taken before and after the 4-month intervention, which involved continuous positive airway pressure treatment to minimize snoring and obstructive sleep apnea among these patients. Insulin responsiveness was significantly improved after 4 months of intervention, although there was no significant change in weight during the study period.

In conclusion, our data suggest that individuals who regularly snore are at higher risk of developing type II diabetes, although we cannot completely exclude residual confounding by obesity. Lifestyle modifications that reduce the risks of snoring and diabetes, such as physical activity, smoking cessation, and weight loss, should be recommended to persons who regularly snore. Surgical interventions or direct appliances may be considered for those with a severe snoring problem.

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