Self-reported Snoring and Risk of Cardiovascular Disease among Postmenopausal Women (From the Women's Health Initiative)

Megan Sands, PhD, MPH[a,b], **Eric B. Loucks, PhD**[b], **Bing Lu, MD, DrPH**[c,d], **Mary A. Carskadon, PhD**[e,f], **Katherine Sharkey, MD, PhD**[f,g], **Marcia Stefanick, PhD**[h], **Judith Ockene, PhD, M.Ed**[i], **Neomi Shah, MD, MPH**[j], **Kristen G. Hairston, MD**[k], **Jennifer Robinson, MD, MPH**[l], **Marian Limacher, MD**[m], **Lauren Hale, PhD**[n], and **Charles B. Eaton, MD, MS**[b,c]

[a]University of Pennsylvania Perelman School of Medicine, Center for Sleep and Circadian Neurobiology

[b]Brown University, Department of Epidemiology, Program in Public Health

[c]Department of Family Medicine, Alpert Medical School of Brown University

[d]Brigham & Women's Hospital, Harvard Medical School

[e]Brown University, Center for Chronobiology and Sleep Research, E.P. Bradley Hospital

[f]Alpert Medical School of Brown University

[g]Department of Medicine, Rhode Island Hospital

[h]Stanford University School of Medicine

[i]University of Massachusetts, Worcester, Department of Medicine

[j]Montefiore Medical Center and Albert Einstein College of Medicine

[k]Wake Forest University School of Medicine, Department of Internal Medicine

[l]University of Iowa, Department of Epidemiology and Medicine

[m]University of Florida, Gainesville, Division of Cardiovascular Medicine

[n]State University of New York, Stony Brook

Abstract

Habitual snoring may be associated with cardiovascular disease (CVD); however limited evidence exists among women. We investigated whether frequent snoring is a predictor of coronary heart disease (CHD) and stroke among 42,244 postmenopausal women participating in the Women's Health Initiative Observational Study. Participants provided self-reported information regarding snoring habits at baseline (1993-1998) and were followed for outcomes through August 2009. Physician adjudicators confirmed CHD, defined as MI, CHD death, revascularization procedures,

Corresponding Author: Megan Sands, PhD, MPH, University of Pennsylvania Perelman School of Medicine, Center for Sleep and Circadian Neurobiology, 3624 Market Street, Suite 205, Philadelphia, PA 19104, Tel: 215.615.4870 Fax: 215.615.4874, Megsands@mail.med.upenn.edu.

or hospitalized angina, and confirmed ischemic stroke. Cox proportional hazards models were used to evaluate whether snoring frequency is a significant predictor of adjudicated outcomes. We observed 2,401 incident cases of CHD over 437,899 person-years of follow up. After adjusting for age and race, frequent snoring was associated with incident CHD (HR=1.54, 95% CI 1.39-1.70) and stroke (HR=1.41, 95% CI 1.19-1.66), and all CVD (HR=1.46, 95% CI 1.34-1.60). In fully adjusted models that included CVD risk factors such as obesity, hypertension, and diabetes, frequent snoring was associated with a more modest increase in incident CHD (HR=1.14 95% CI 1.01-1.28), stroke (HR=1.19, 95% CI 1.02-1.40) and CVD (HR=1.12, 95% CI 1.01-1.24). In conclusion, snoring is associated with a modest increased risk of incident CHD, stroke and CVD after adjustment for CVD risk factors. Additional studies are needed to elucidate the mechanisms in which snoring may be associated with CVD risk factors and outcomes.

Keywords

Snoring; Cardiovascular Disease; Coronary Heart Disease; Menopause

---

Snoring is a correlate and early symptom of Obstructive Sleep Apnea (OSA).[1] Snoring may also be associated with hypertension,[2] cardiovascular disease (CVD),[3,4] type II diabetes[5] and metabolic syndrome.[6] The current evidence related to snoring focuses primarily on studies in men, relies upon cross-sectional studies and underrepresents women.[4,7,8] Habitual snoring occurs among approximately 33% of the general population, and although sleep apnea is more common among men, the prevalence of sleep disturbance and snoring increases among women as they approach and pass through menopause.[9-11] Emerging evidence suggests this increase in sleep problems may be due to aging, weight gain, or menopause-induced hormonal changes, such as decreases in progesterone and estradiol, which may modulate sleep regulation and breathing.[11-14] Only 1 previous study has prospectively evaluated associations of snoring with CVD among older women,[3] and although that study also included pre- and perimenopausal women their findings suggested snoring was associated with a significant increase in CVD. The primary aim of the present study is to determine if self-reported snoring frequency among postmenopausal women is significantly associated with an increased risk for incident coronary heart disease (CHD), stroke and all CVD.

METHODS

The Women's Health Initiative (WHI) is a multi-center national study of 161,808 postmenopausal women who were enrolled in either the clinical trials (WHI-CT) or observational study (WHI-OS). Methods for recruitment, inclusion and exclusion criteria, protocols and study design have been described elsewhere.[15-17] This study was conducted using longitudinal data from the WHI-OS cohort, which included women who were unable or unwilling to participate in the WHI-CTs. The WHI-OS cohort is a multiethnic population comprised of 93,676 women aged 50-79 years at baseline from 40 sites around the United States. Women with prior CVD were excluded from the analysis (N=6,813), as well as those with 'don't know' (N=43,839) or 'missing' (N=780) responses to the snoring question. Recruitment (1993-1998) was conducted through mailings to eligible women. All participants were followed for outcomes through August 2009. All participants provided informed consent, which was approved by the Institutional Review Board for each of the participating study sites.

Snoring was evaluated based on self-report at the baseline study visit. Participants were asked, 'Over the past 4 weeks, did you snore?' Snoring was measured as: '1) No, not in the past 4 weeks 2) Yes, less than once a week 3) Yes, 1 or 2 times a week 4) Yes, 3 or 4 times a

week 5) Yes, 5 or more times a week 6) Don't know.' Individuals were classified as non-snorers, occasional snorers (<1-4 times per week), and frequent snorers (5 times per week). This variable was analyzed as a categorical variable with 'non-snoring' as the reference group.

All outcomes were adjudicated by trained physicians using medical records and death certificates. The diagnosis and adjudication of the outcomes for this study have been previously described and outlined in established protocols.[18] Our primary endpoint was incident CHD, defined as incident myocardial infarction (MI), CHD death, coronary revascularization, including coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA), and hospitalized angina. Participants were followed for first occurrence of the CHD outcome, and those individuals who did not develop CHD were censored at the date of death or last contact. We also assessed incident ischemic stroke and total CVD (CHD and ischemic stroke).

Baseline demographic characteristics were assessed by self-reported questionnaire at the initial visit. Race/ethnicity was categorized as 'White/Caucasian', 'Black/African American', 'Hispanic/Latina', 'Asian' and 'Other'. Annual household income was categorized into 3 groups, <$20,000, $20,000-<$50,000, and $50,000. Education was classified as a 4-level variable, 'less than high school', 'high school graduate', 'some college', and 'college graduate'. Marital status was categorized as a binary variable, married or marriage-like relationship and widowed, divorced, separated or single.

Behavioral risk factors measured in the baseline questionnaire included smoking, alcohol consumption and physical activity. Smoking was categorized as current smoker, former smoker or non-smoker. Alcohol consumption was measured as servings per week and physical activity was measured as MET-hours per week, estimated from 9 questions related to expenditure of energy from recreational activity (including walking, mild, occasional and strenuous activity).

Physical measurements, including height (m), weight (kg), waist circumference (cm), and systolic and diastolic blood pressure (mm Hg) were assessed at the baseline visit by trained and certified staff. Hypertension was defined as systolic blood pressure >140 mm Hg and/or diastolic blood pressure >90 mm Hg, and/or use of antihypertensive medication. Diabetes was defined by self-report of physician-diagnosed diabetes or use of diabetes medications. Hyperlipidemia was defined as use of lipid-lowering medications or having been told of high cholesterol by a physician. Depression was measured at baseline using the Burnam screening algorithm, a measure that includes 6 items from the 20-item CES-D and 2 items from the National Institute of Mental Health's Diagnostic Interview Schedule.[19] A cutpoint of 0.06 was used to identify current depressive symptomatology.

We restricted analyses to those individuals without missing data for the primary exposure and outcome. The distribution of demographic characteristics, health behaviors and cardiovascular risk factors was examined across snoring category and the corresponding associations were statistically tested using analysis of variance (ANOVA) and Chi-square tests.

Person-years of follow-up were based on time from enrollment to cardiovascular event, loss to follow-up, death or end of the study (August 2009). Crude event rates were calculated and compared across snoring categories. The Log-Rank test was used to determine if there were significant differences in survival by snoring group. Hazard Ratios (HR) were computed using Cox proportional hazards models for each outcome. Models were assessed for the proportional hazards assumption.

Covariates that were considered for the models from baseline data included age, race/ethnicity, education, income, marital status, BMI, waist-to-hip ratio (WHR), sleep duration, hypertension status, diabetes status, smoking status, alcohol consumption, physical activity, depression, hyperlipidemia and hormone medication use. The final model included only those covariates that were statistically appropriate (p<0.10) and important based on theoretical considerations. Two-way interactions for snoring and BMI were assessed and stratified analyses were conducted.

Since over 50% of participants reported 'don't know' for the primary exposure, we excluded these participants for the primary analysis or 'complete case analysis'. Recognizing that this exclusion may result in selection bias,[20] we conducted a sensitivity analysis utilizing the inverse probability weighting (IPW) method[21] in which a model for the probability of 'non-missingness' was fit, and the inverse of these probabilities were used as weights in the complete case analysis. We used SAS version 9.3 (SAS Institute, Inc., Cary, NC) to perform all statistical analyses.

RESULTS

We observed 2,401 incident cases of CHD over 437,890 person-years of follow up. At baseline, 47% of women reported no snoring, 33% reported occasional snoring and 20% reported frequent snoring (Table 1). With regards to race/ethnicity, 84.5% of participants were Caucasian, 7.5% were African American, 3.6% were Hispanic/Latino, 2.8% were Asian and 1.5% were 'other'. Compared to the overall cohort, women who reported frequent snoring had a greater BMI, a greater proportion of current smokers, a higher systolic and diastolic blood pressure, and a higher prevalence of diabetes and depression (Table 1).

Product-limit survival estimates were assessed and the log-rank test indicated significant differences in survival rate by snoring group (p<0.001). Cox proportional hazards models adjusted for age and race indicated a 54% increased risk in CHD among frequent snorers and a 27% increased risk among occasional snorers, and similar hazard ratios were observed for stroke and CVD (Table 2). In fully adjusted models, adjusted for age, race, education, BMI, WHR, smoking, alcohol consumption, physical activity, depression, hypertension, diabetes, and hyperlipidemia, the positive associations for frequent snoring and cardiovascular outcomes were attenuated but still significant with an approximate 14% increased risk for CHD, 19% increased risk for stroke and 12% increased risk for CVD (Table 2). BMI, hypertension and diabetes were key drivers of this attenuation, and models including these covariates and sociodemographics are presented in Table 3. Because BMI is a strong confounder of the association between snoring and coronary disease, we tested for an interaction by obesity status, which was significant (p=0.024). In the stratified analysis, frequent snoring was a significant predictor of CHD among overweight and obese individuals in the age- and race-adjusted models (HR=1.29, 95% CI 1.07-1.54 for overweight; HR=1.33, 95% CI 1.10-1.61 for obese), but not normal weight individuals (HR=1.19, 95% CI 0.93-1.52). These associations were attenuated and no longer statistically significant in the fully adjusted models (Figure 1).

A sensitivity analysis was conducted using IPW. The weighted method generated results that also were similar to that of the complete case for the age- and race-adjusted models and indicated a 59% increased risk of CHD, 37% increased risk of stroke and 49% increased risk of CVD among frequent snorers (Table 4).

DISCUSSION

This prospective study among postmenopausal women demonstrates that frequency of snoring is associated with modestly increased risk of incident CHD, ischemic stroke and all CVD after adjusting for age and race. This significant association persisted but was attenuated in fully adjusted models.

These findings build on previous studies among men.[4,7,8,22] Estimates from Marin et al. suggested a much weaker and non-significant association between snoring and CVD (OR=1.03, 95% CI 0.31-1.84), however the effect estimates among men with untreated mild-moderate OSA were similar to that of the postmenopausal women in our study (OR=1.15, 95% CI 0.34-2.69). Since the present study could not differentiate between simple snoring and OSA, it is likely that the snoring measure in our study included those with OSA and thus generated similar estimates. The differences between studies could also be due to power issues, as Marin and colleagues utilized a smaller sample (N=1,651) and had fewer events. Other previous studies among men reported a stronger association including a 71% increased odds of CHD, >2-fold increased risk of CVD, and >2-fold increased risk of stroke in adjusted models.[4,7] These discrepancies however could be attributed to methodological differences in study design, including lack of adjustment for sociodemographics or CVD risk markers.[4,7,8,22]

We also evaluated the issue of potential selection bias induced by excluding the 'don't know' individuals in a sensitivity analysis that used the IPW method.[21] This approach is a powerful tool that addresses selection bias by creating a pseudo-population with characteristics that are more representative of the censored individuals. Similar HRs with a slightly stronger estimate of effect was observed in the IPW analysis, which further supported our findings from the complete case analysis.

It has been previously demonstrated that habitual snoring is associated with greater BMI.[6,23] Our findings indicate that snoring is an independent predictor of increased CVD risk even after adjustment for obesity and other risk factors, and an interaction was present between snoring and BMI (p=0.02). When stratifying by obesity status, findings indicated a dose-response relationship between frequency of snoring and CHD risk, however this was present only among obese and overweight individuals and not among those with a BMI<25. These findings are not completely consistent with Hu and colleagues, where a positive association between snoring and CVD was observed across all BMI strata.[3] Given the bidirectional relationship of obesity and snoring, we cannot rule out that obesity may be the driving force of the observed association. Compared to previous reports among women,[3] our findings draw from a more diverse sample with regards to race/ethnicity and sociodemographics, and thus these results are more generalizable to the entire U.S. population. Replication of these findings is important, especially given the cardiovascular consequences of obesity and the complex relationship with snoring. Additional investigations need to evaluate the association between snoring and incident CVD and assess the relationship among obese and non-obese subjects.

Snoring may increase risk of CVD through atherosclerosis. Proposed biological mechanisms involve increased localized carotid endothelial dysfunction due to upper airway resistance and subsequent vibrations in the pharyngeal wall, a hypothesis that has been supported by animal models among rabbits.[24-26] Heavy snoring is significantly associated with increased carotid intima-media thickness (IMT) and plaque (OR=1.71, 95% CI 1.22-2.39 for IMT; OR=3.63, 95% CI 2.57-5.12 for carotid bifurcation plaque),[27] and there exists a dose response (p<0.04) between snoring frequency and atherosclerosis.[24] Lee and colleagues also suggested that frequent snoring is associated with increased carotid atherosclerosis

(OR=10.5, 95% CI, 2.1-51.8), but not with femoral atherosclerosis.[24] Findings from angiography have also supported that snoring in combination with feelings of tiredness was associated with increased atherosclerosis compared to non-snorers (0.18 mm vs. 0.07 mm change, p=0.0006).[25] Further research is needed to determine if snoring alone increases CVD risk through these mechanisms, or if it simply represents a marker for the presence of sleep apnea, an established as a risk factor for CVD.

Because the simple measure of self-reported snoring may represent early stages of the OSA continuum, it may serve as an early marker of sleep apnea and serve as a useful public health screening tool. Polysomnography (the gold standard for diagnosing OSA) is costly and time intensive, and so it is increasingly important to understand how self-reported snoring is associated with CVD outcomes. However, although snoring is considered a symptom of OSA, many individuals that snore do not have sleep apnea. Future research should strive to identify the relative impact of sleep symptoms versus true disorders on adverse disease outcomes.

Self-reported snoring is not a perfect measure of snoring frequency and the reliability of snoring data were not validated in this population. We conducted a sensitivity analysis among only those women that were partnered (71% of women) and found similar estimates of effect for age and race adjusted models. Although a similar trend was observed in fully adjusted models, the association was not significant among this subgroup. However, self-reported snoring has been previously validated against overnight sleep monitoring, and findings suggest self-report to be a reliable measure.[28] Also, self-reported snoring over 1 month represents an integrated assessment, which cannot always be achieved by a single overnight study in a controlled setting. Because this association was assessed prospectively, it is likely that the misclassification is non-differential with respect to the outcome, resulting in an underestimation of the effect estimate, which would bias the results towards the null. Future studies should consider alternative ways to measure this exposure, such as partner-reported snoring habits or alternative measures of snoring during sleep. Because over 50% of these individuals reported 'don't know' in response to the snoring question, we cannot make inferences for these individuals. It should be noted that the IPW statistical methodology does not come without some limitations, and that if the level of exposure is associated with whether snoring was reported, then the level of weights may be subject to bias.[29] The IPW sensitivity analysis did however generate similar estimates of effect, which supported our primary analysis. Lastly, because we did not assess sleep apnea using polysomnography, we are unable to determine whether simple snoring without sleep apnea may increase the risk of CVD outcomes. While sleep apnea may be driving the observed association, we noted that occasional snoring was also significantly associated with CVD, suggesting that individuals who snore but potentially do not have OSA were still at increased risk for disease.

Acknowledgments

Women's Health Initiative Memory Study: (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker

For a list of all the investigators who have contributed to WHI science, please visit: https://cleo.whi.org/researchers/ Documents%20%20Write%20a%20Paper/WHI%20Investigator%20Long%20List.pdf

References

1. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med. 2002; 165:1217–1239. [PubMed: 11991871]

2. Young T, Finn L, Hla KM, Morgan B, Palta M. Snoring as part of a dose-response relationship between sleep-disordered breathing and blood pressure. Sleep. 1996; 19(10 Suppl):S202–205. [PubMed: 9085511]

3. Hu FB, Willett WC, Manson JE, Colditz GA, Rimm EB, Speizer FE, Hennekens CH, Stamfer MJ. Snoring and risk of cardiovascular disease in women. J Am Coll Cardiol. 2000; 35:16–19.

4. Koskenvuo M, Kaprio J, Telakivi T, Partinen M, Heikkila K, Sarna S. Snoring as a risk factor for ischaemic heart disease and stroke in men. Br Med J (Clin Res Ed). 1987; 294:16–19.

5. Al-Delaimy WK, Manson JE, Willett WC, Stamfer MJ, Hu FB. Snoring as a risk factor for type II diabetes mellitus: a prospective study. Am J Epidemiol. 2002; 155:387–393. [PubMed: 11867347]

6. Leineweber C, Kecklund G, Akerstedt T, Janszky I, Orth-Gomer K. Snoring and the metabolic syndrome in women. Sleep Med. 2003; 4:531–536. [PubMed: 14607347]

7. Palomaki H. Snoring and the risk of ischemic brain infarction. Stroke. 1991; 22(8):1021–1025. [PubMed: 1866748]

8. Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005; 365:1046–1053. [PubMed: 15781100]

9. Phillips, BA.; Collop, NA.; Drake, C.; Consens, F.; Vgontzas, AN.; Weaver, TE. Sleep disorders and medical conditions in women. J Womens Health (Larchmt); Proceedings of the Women & Sleep Workshop; Washington, DC. March 5-6, 2007; National Sleep Foundation; 2008. p. 1191-1199.

10. Kapsimalis F, Kryger M. Sleep breathing disorders in the U.S. female population. J Womens Health (Larchmt). 2009; 18:1211–1219. [PubMed: 19627224]

11. Eichling PS, Sahni J. Menopause related sleep disorders. J Clin Sleep Med. 2005; 1:291–300. [PubMed: 17566192]

12. Netzer NC, Eliasson AH, Strohl KP. Women with sleep apnea have lower levels of sex hormones. Sleep Breath. 2003; 7:25–29. [PubMed: 12712394]

13. D'Ambrosio C, Stachenfeld NS, Pisani M, Mohsenin V. Sleep, breathing, and menopause: the effect of fluctuating estrogen and progesterone on sleep and breathing in women. Gend Med. 2005; 2:238–245. [PubMed: 16464735]

14. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, Vela-Bueno A, Kales A. Prevalence of sleep-disordered breathing in women: effects of gender. Am J of Resp and Crit Care Med. 2001; 163:608–613. [PubMed: 11254512]

15. Hays J, Hunt JR, Hubbell FA, Anderson GL, Limacher M, Allen C, Rossouw JE. The Women's Health Initiative recruitment methods and results. Ann Epidemiol. 2003; 13(9 suppl):S18–S77. [PubMed: 14575939]

16. Langer RD, White E, Lewis CE, Kotchen JM, Hendrix SL, Trevisan M. The Women's Health Initiative Observational Study: baseline characteristics of participants and reliability of baseline measures. Ann Epidemiol. 2003; 13(9 suppl):S107–S121. [PubMed: 14575943]

17. Rossouw JE, Hurd S. The Women's Health Initiative: recruitment complete – looking back and looking forward. J Womens Health. 1999; 8:3–5. [PubMed: 10094073]

18. Curb JD, McTiernan A, Heckbert SR, Kooperberg C, Stanford J, Nevitt M, Johnson KC, Proulx-Burns L, Pastore L, Crique M, Daugherty S. WHI Morbidity and Mortality Committee. Ann Epidemiol. 2003; 13(9 suppl):S122–S128. [PubMed: 14575944]

19. Tuunainen A, Laner RD, Klauber MR, Kripke DF. Short version of the CES-D (Burnam screen) for depression in reference to the structured psychiatric interview. Psychiatry Res. 2001; 103:261–270. [PubMed: 11549413]

20. Hernan M, Hernandez-Diaz S, Robins JM. A structural approach to selection bias. Epidemiology. 2004; 15:615–625. [PubMed: 15308962]

21. Hernan M, Lanoy E, Costagliola D, Robins J. Comparison of dynamic treatment regimes via inverse probability weighting. Basic Clinical Pharmacol Toxicol. 2005; 98:237–242.

22. Partinen M, Palomaki H. Snoring and cerebral infarction. Lancet. 1985; 2(8468):1326–1326.

23. Svensson M, Lindberg E, Naessen T, Janson C. Risk factors associated with snoring in women with special emphasis on body mass index: a population-based study. Chest. 2006; 129:933–941. [PubMed: 16608941]

24. Lee SA, Amis TC, Byth K, Larcos G, Kairaitis K, Robinson TD, Wheatley JR. Heavy snoring as a cause of carotid artery atherosclerosis. Sleep. 2008; 31:1207–1213. [PubMed: 18788645]

25. Leineweber C, Kecklund G, Janszky I, Akerstedt T, Orth-Gomer K. Snoring and progression of coronary artery disease: The Stockholm Female Coronary Angiography Study. Sleep. 2004; 27:1344–1349. [PubMed: 15586787]

26. Cho JG, Witting PK, Verma M, Wu BJ, Shanu A, Kairaitis K, Amis TC, Wheatley JR. Tissue vibration induces carotid artery endothelial dysfunction: a mechanism linking snoring and carotid atherosclerosis? Sleep. 2011; 34:751–757. [PubMed: 21629363]

27. Li Y, Liu J, Wang W, Yong Q, Zhou G, Wang M, Sun J, Zhao D. Association of self-reported snoring with carotid artery intima-media thickness and plaque. J Sleep Res. 2011; 14:1365–2869.

28. Telakivi T, Partinen M, Koskenvuo M, Salmi T, Kaprio J. Periodic breathing and hypoxia in snorers and controls: validation of snoring history and association with blood pressure and obesity. Acta Neurol Scand. 1987; 76:69–75. [PubMed: 3630648]

29. Hernan MA, Alonso A, Logan R, Grodstein F, Michels K, Willett W, Manson J, Robins J. Observational studies analyzed like randomized experiments: an application to postmenopausal hormone therapy and coronary heart disease. Epidemiology. 2008; 19:766–779. [PubMed: 18854702]

Figure 1.
a. Cox Proportional Hazards Models Snoring and Coronary Heart Disease Stratified by
Obesity Status
BMI – body mass index
HR – hazard ratio
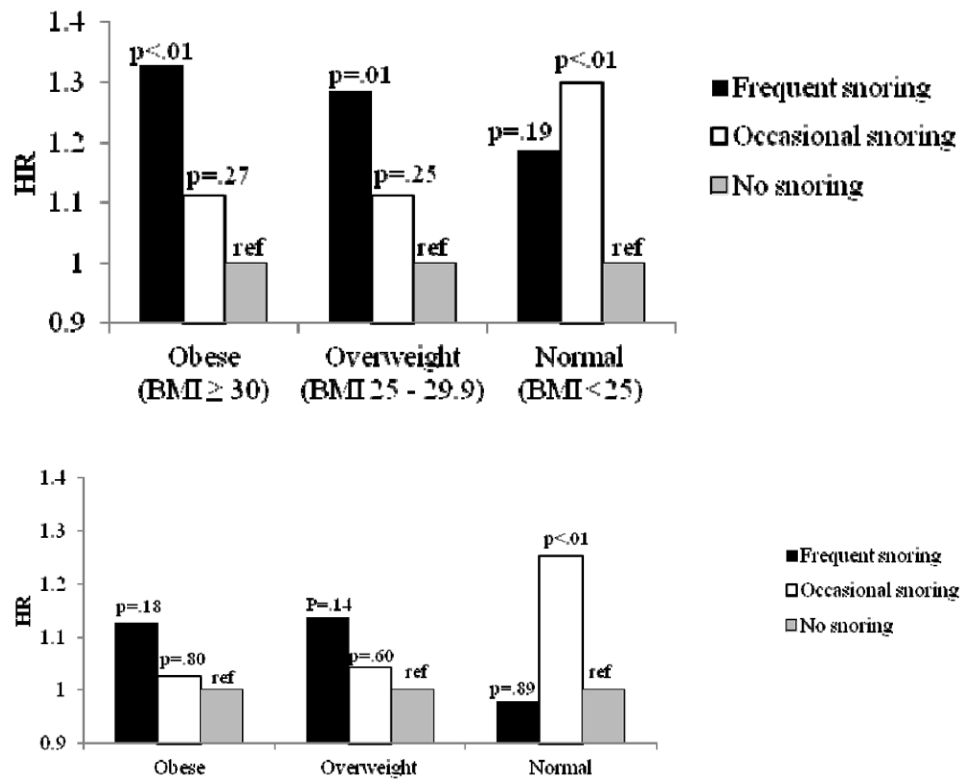REF – reference group
*Adjusted for age and race
b. Cox Proportional Hazards Models Snoring and Incident Coronary Heart Disease Stratified
by Obesity Status
BMI – body mass index
HR – hazard ratio
REF – reference group
WHR – waist to hip ratio
**Adjusted for age, race, education, income, smoking, physical activity, alcohol intake,
depression, diabetes, hyperlipidemia, BMI, WHR, hypertension

Table 1

Baseline characteristics in the Women's Health Initiative study population distributed by snoring status

Variable	Overall (N=42,244)	Frequency of snoring (times/wk)				p-value
		0 (N=19,886)	<1 - 4 (N=13,734)	5 (N=8624)		
Age (years)	62.6 (7.2)	62.8 (7.5)	62.3 (7.0)	62.5 (7.0)		<0.001
Race						
Black/African American	7.5%	6.3%	7.2%	11.0%		<0.001
Caucasian	84.5%	87.0%	84.7%	78.6%		
Hispanic/Latino	3.6%	2.5%	4.1%	5.6%		
Asian	2.8%	2.8%	2.5%	3.1%		
Other	1.5%	1.5%	1.4%	1.8%		
Education						
Less than High School Grad	4.4%	3.2%	4.5%	6.8%		<0.001
High School Graduate	15.1%	13.3%	15.9%	18.2%		
Some College	35.6%	33.9%	36.6%	37.8%		
College Graduate	44.9%	49.6%	43.0%	37.2%		
Income (% annual household)						
<$20,000	12.4%	11.1%	10.5%	18.1%		<0.001
$20,000 - $49,999	40.6%	38.6%	40.8%	44.6%		
$50,000	47.1%	50.3%	48.6%	37.3%		
Marital status						
Married or partnered	71.1%	69.5%	78.3%	63.5%		<0.001
Single/divorced/widowed	28.9%	30.5%	21.7%	36.5%		
Body Mass Index (mean kg/m2)	27.2 (5.9)	25.5 (12.1)	27.7 (5.8)	30.3 (6.8)		<0.001
Systolic blood pressure (mm Hg)	125.9 (17.7)	124.1 (17.7)	126.6 (17.4)	128.9 (17.4)		<0.001
Diastolic blood pressure (mm Hg)	74.9 (9.3)	74.0 (9.2)	75.4 (9.2)	76.3 (9.6)		<0.001
Hyperlipidemia[†]	9.4%	8.0%	10.4%	11.3%		<0.001
Diabetes Mellitus	3.1%	2.1%	3.1%	5.4%		<0.001
Smoker						
Never	52.2%	54.7%	51.1%	48.3%		<0.001
Past	42.2%	41.0%	43.1%	43.5%		

		Frequency of snoring (times/wk)			
Variable	**Overall (N=42,244)**	**0 (N=19,886)**	**<1 - 4 (N=13,734)**	**5 (N=8624)**	**p-value**
Current	5.6%	42.7%	5.8%	8.2%	
Alcohol (servings/week)	2.6 (5.3)	2.6 (5.1)	2.9 (5.4)	2.4 (5.4)	0.036
Depression (CES-D/DIS)	10.5%	8.7%	10.3%	15.0%	<0.001
Physical activity (met-hours/wk)	14.4 (14.8)	16.3 (15.7)	13.7 (13.8)	10.46 (13.0)	<0.001
WHIIRS [*]	6.6 (4.5)	6.2 (4.4)	6.6 (4.3)	7.4 (4.7)	<0.001

[*] WHI Insomnia Rating Scale - greater number indicates higher level of sleep disturbance

[†] Defined as individuals taking lipid-lowering medications and who had been told by a physician that they had high cholesterol

Table 2

Cox proportional hazards models - snoring and incident cardiovascular disease among Women's Health Initiative study participants (N=42,244)§

	Snoring frequency	Cases	Person-years	Model adjusted for age, race			Model fully adjusted†		
				HR	95% CI	P-value	HR	95% CI	P-value
CHD*	Frequent	609	86,227	1.54	1.39, 1.70	<0.001	1.14	1.01, 1.28	0.038
	Occasional	814	143,209	1.27	1.16, 1.39	<0.001	1.12	1.01, 1.24	0.032
	None (referent)	978	208,454	1.00	REF	REF	1.00	REF	REF
CVD‡	Frequent	790	84,671	1.46	1.34, 1.60	<0.001	1.12	1.01, 1.24	0.031
	Occasional	1103	141,122	1.25	1.16, 1.36	<0.001	1.11	1.01, 1.21	0.026
	None (referent)	1354	205,547	1.00	REF	REF	1.00	REF	REF
Ischemic Stroke	Frequent	232	95,307	1.41	1.19, 1.66	<0.001	1.19	1.02, 1.40	0.030
	Occasional	349	153,389	1.29	1.11, 1.50	<0.001	1.15	0.96, 1.38	0.140
	None (referent)	412	220,697	1.00	REF	REF	1.00	REF	REF

*
Total CHD outcome includes MI, CHD death, PTCA, CABG, or hospitalized angina

†
CVD outcome includes MI, CHD death, PTCA, CABG, hospitalized angina, or ischemic stroke

‡
Model adjusted for age, race, education, income, smoking, physical activity, alcohol intake, depression, diabetes, high blood pressure, BMI, WHR, hyperlipidemia

§
All analyses conducted among disease-free cohort and total N's reflect this difference by outcome

Table 3

Cox proportional hazards models - snoring and incident coronary heart disease[*]

Model	Snoring Frequency	HR	95% CI	p-value
	Frequent	1.46	1.15, 1.40	<0.001
1	Occasional	1.27	1.32, 1.63	<0.001
	None (ref)	1.00	REF	REF
	Frequent	1.28	1.14, 1.43	<0.001
2	Occasional	1.19	1.08, 1.31	<0.001
	None (ref)	1.00	REF	REF
	Frequent	1.33	1.19, 1.48	<0.001
3	Occasional	1.19	1.08, 1.31	<0.001
	None (ref)	1.00	REF	REF
	Frequent	1.41	1.27, 1.57	<0.001
4	Occasional	1.25	1.13, 1.37	<0.001
	None (ref)	1.00	REF	REF
	Frequent	1.21	1.08, 1.36	<0.001
5	Occasional	1.15	1.04, 1.27	0.008
	None (ref)	1.00	REF	REF

Model 1: adjusted for sociodemographics (age, race, education, income)

Model 2: adjusted for sociodemographics + BMI

Model 3: adjusted for sociodemographics + hypertension

Model 4: adjusted for sociodemographics + diabetes

Model 5: adjusted for age, race, education, income, BMI, hypertension, diabetes

[*] CHD outcome includes MI, CHD death, PTCA, CABG, or hospitalized angina

Table 4

Sensitivity analysis - Cox proportional hazards models of snoring and incident cardiovascular disease among Women's Health Initiative participants using inverse probability weighting (N=42,244)[§]

Snoring frequency		Cases	Person-yrs	Model adjusted for age, race			Model fully adjusted[†]		
				HR	95% CI	P-value	HR	95% CI	P-value
CHD[*]	Frequent	609	86,227	1.59	1.42, 1.78	<0.001	1.16	1.03, 1.30	0.018
	Occasional	814	143,209	1.28	1.16, 1.42	<0.001	1.12	1.00, 1.24	0.043
	None (referent)	978	208,454	1.00	REF	REF	1.00	REF	REF
CVD[‡]	Frequent	790	84,671	1.49	1.35, 1.65	<0.001	1.13	1.02, 1.25	0.018
	Occasional	1103	141,122	1.26	1.15, 1.38	<0.001	1.12	1.02, 1.23	0.026
	None (referent)	1354	205,547	1.00	REF	REF	1.00	REF	REF
Stroke	Frequent	232	95,307	1.37	1.15, 1.64	0.001	1.21	1.03, 1.43	0.020
	Occasional	349	153,389	1.30	1.11, 1.52	0.002	1.14	0.94, 1.37	0.178
	None (referent)	412	220,697	1.00	REF	REF	1.00	REF	REF

[*] CHD outcome includes MI, CHD death, PTCA, CABG, or hospitalized angina

[‡] CVD outcome includes MI, CHD death, PTCA, CABG, hospitalized angina, or ischemic stroke

[†] Model adjusted for age, race, education, income, smoking, physical activity, alcohol intake, depression, diabetes, high blood pressure, BMI, WHR, hyperlipidemia

[§] All analyses conducted among disease-free cohort and total N's reflect this difference by outcome