Sleep Duration and Risk for Hypertension in Women: Results from The Nurses' Health Study

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BACKGROUND
Acute sleep restriction has been shown to increase blood pressure and sympathetic nervous system activity.

METHODS
We investigated the relationships between sleep duration and hypertension among women whose sleep durations were self-reported in 1986 (n = 82,130) and 2000 (n = 71,658) in the Nurses' Health Study I (NHS-I) and in 2001 (n = 84,674) in the Nurses' Health Study II (NHS-II).

RESULTS
After controlling for multiple risk factors in logistic regression models, the prevalence of hypertension was significantly higher among women in all 3 groups who slept ≤5 hours (odds ratio = 1.19, 95% confidence interval [CI] = 1.14–1.25) per night compared with 7 hours. In prospective analyses using Cox regression shorter sleep duration of ≤5 hours per night was significantly associated with a higher incidence of hypertension only in younger women (hazard ratio [HR] =1.20, 95% CI = 1.09–1.31 for those aged <50 years; HR = 1.11, 95% CI = 1.00–1.23 for those aged 50–59 years). In both prevalent and incident analyses, results were consistent with obesity acting as a partial mediator. Results were not consistent with diabetes or hypercholesterolemia acting as mediators or with shift work, snoring, menopause, or postmenopausal hormone therapy acting as effect modifiers.

CONCLUSIONS
Sufficient sleep could represent a lifestyle practice worthy of investigation as an approach to reduce hypertension incidence and prevalence.

Keywords: blood pressure; circadian rhythm; epidemiology; hypertension; obesity; sleep.

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Cardiovascular diseases (CVDs) are the leading causes of death in women worldwide. In the United States, more women than men die every year from CVDs,[1] and over half of the yearly health-care costs related to CVDs are incurred by women.[2] Hypertension is one of the most important modifiable risk factors for CVDs.

There is growing evidence that short sleep duration is a significant etiological factor for hypertension. Acute sleep restriction has been shown to increase blood pressure and sympathetic nervous system activity.[3,4] Over time, the increased hemodynamic load from short sleep duration can lead to hypertropic remodeling and the elevation of the cardiovascular pressure equilibrium.[5]

The effects of short sleep duration on hypertension in women could be modified by other factors, including shift work, snoring, menopause, postmenopausal hormone therapy, and age. Shift work, and in particular rotating night shift work, disrupts circadian rhythmicity and autonomic balance and has been found to be associated with CVDs.[6] Snoring, a cardinal symptom of sleep apnea, has been theorized to lead to hypertension by causing hypoxia and hypercapnia, resulting in chronic stimulation of the sympathetic nervous system.[7] Estrogen deficiency during menopause is thought to induce endothelial and vascular dysfunction through reduced compliance of the large arteries, resulting in increased age-related increases in systolic blood pressure,[8] raising the question of whether hormone therapy could affect hypertension incidence in postmenopausal women. Sleep complaints also increase after menopause, and estrogen therapy has been shown to improve objective sleep quality.[9] Advanced age is associated with changes in sleep architecture, with increased difficulties initiating and maintaining sleep.[10]

Obesity, diabetes, and hypercholesterolemia could lie along the causal pathway between short sleep duration and hypertension and therefore act as partial mediators of the relationship. Sleep deprivation has been shown to increase appetite,[11] compromise insulin sensitivity,[12] and increase total and low-density lipoprotein cholesterol levels.[13] Short sleep duration is associated with obesity,[14] type 2 diabetes,[15] and high cholesterol.[16]

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In this study, we examined the relationships between sleep duration and hypertension prevalence and incidence among women in the Nurses' Health Study I (NHS-I) and the Nurses' Health Study II (NHS-II). We hypothesized that short sleep duration would be associated with increased risk for hypertension. We theorized that shift work, snoring, menopause, postmenopausal hormone therapy, and age would act as effect modifiers and that obesity, diabetes, and hypercholesterolemia would act as mediators of the relationship between sleep duration and hypertension.

METHODS

Study population

The NHS-I cohort was established in 1976 and initially included 121,700 female, married, registered nurses aged 30 to 55 years old who resided in 11 large US states. The NHS-II cohort was established in 1989 and initially included 116,686 female registered nurses aged 25–42 years who resided in 14 US states. Sleep duration was assessed on the questionnaires in 1986 and 2000 in NHS-I and in 2001 in NHS-II. Cross-sectional analyses included all women who reported their sleep duration on these questionnaires (n = 82,130, 71,658, and 84,674, respectively). In analyses of incident hypertension, the study populations were smaller (n = 60,009, 32,105, and 68,784, respectively) because of the exclusions of the prevalent hypertension cases reported on a previous or the same questionnaire as sleep duration. This study was approved by the institutional review boards at Brigham and Women's Hospital and Columbia University/New York State Psychiatric Institute; women in this study provided implied consent by virtue of their voluntary return of mailed questionnaires.

Ascertainment of sleep duration

Participants in NHS-I and NHS-II were asked to report the number of hours that they typically sleep per night, ranging from <5 to ≥11. Because of small sample sizes in the extreme responses, sleep duration was categorized as ≤5, 6, 7, 8, and ≥9 hours in this analysis, with 7 hours as the reference group. The validity of the sleep duration question was explored previously for the NHS-I, with a Spearman correlation of 0.79 ($P < 0.0001$) between average sleep time reported on sleep diaries and time reported on the sleep duration question. Individuals who reported 7 hours of sleep on the questionnaire also averaged 7.0 hours according to sleep diaries. Individuals who reported 5 and 6 hours of sleep on the questionnaire had slightly more sleep based upon their diaries, averaging 5.2 and 6.2 hours, respectively, whereas those who reported 8 and 9 hours had slightly less sleep according to their diaries (7.7 and 8.5 hours, respectively).[17]

Ascertainment of hypertension

Every 2 years, participants were asked to report whether or not a physician had diagnosed them with hypertension. The validity of self-reported hypertension in these cohorts was assessed in 1982[18] (in NHS-I) and 2005 (in NHS-II).[19]

Covariables

Covariables in the analyses included age (continuous variable); race (white, black, Asian, missing/other); Hispanic ethnicity; family history of hypertension; diabetes; hypercholesterolemia; body mass index (BMI) (<20, 20–24.9, 25–29.9, 30–34.9, ≥35 kg/m2, missing); menopausal status (premenopausal, postmenopausal, unsure, missing); postmenopausal hormone therapy (never, past, current, unknown); snoring (every night, most nights, a few nights per week, occasionally, almost never, missing); lifetime rotating night-shift work (never, 1–11, 12–23, 24–59, 60–95, ≥96 months, missing); physical activity (<3, 3–8.9, 9–17.9, 18–26.9, 27–41.9, ≥42 metabolic equivalent hour/week, missing); caffeine intake (<150, 150–249, 250–349, 350–449, ≥450 mg/day, missing); smoking status (never, past (>20, >10–20, >5–10, ≤5 years since quitting), current (1–14, 15–24, ≥25 cigarettes/day), missing); alcohol intake (none, <10, 10–19, 20–29, ≥30 g/day, missing); Dietary Approaches to Stop Hypertension (DASH) diet score (quintiles); aspirin use (nonuser, current user, missing); other nonsteroidal anti-inflammatory drug use (nonuser, current user, missing); and acetaminophen use (nonuser, current user, missing).

Statistical analyses

We performed analyses in separate study populations based on the 3 reports of sleep duration. Chi-square tests for categorical variables and Wald-F tests for continuous variables were used to explore differences by sleep duration. Multivariable logistic regression was used to calculate odds ratios (ORs) to examine the cross-sectional relationship between sleep duration and hypertension prevalence.

Cox proportional hazard was used to calculate hazard ratios (HRs) for hypertension incidence in longitudinal analyses. Women were censored upon first report of hypertension, failure to respond to questionnaires for reporting hypertension, date of death, or end of the 6-year follow-up period. We decided to restrict follow-up to a consistent 6 years in all 3 analyses (which was limited to 6 years in NHS-II) because sleep duration is not stable over time and results would attenuate for long follow-up periods. For example, in NHS-I participants who answered both the 1986 and 2000 sleep questions, only 42% reported the same duration category. In addition, only 32% of women who reported ≤5 hours in 1986 also reported ≤5 hours in 2000, whereas 96% of those who reported >5 hours in 1986 also reported >5 hours in 2000.

Diabetes, hypercholesterolemia, and BMI were added to age-adjusted Cox models to explore whether these variables acted as partial mediators of the relationship between sleep duration and hypertension. We considered an attenuation of ≥10% in the β coefficients of the main exposure term (sleep duration) after the introduction of the hypothesized mediating variables as a cutoff sufficient to be consistent with mediation. All other assessed covariables were then added to the multivariable model. Because BMI resulted in an attenuation in the β coefficients of sleep duration of >10%, we excluded BMI from the final model to determine the association if BMI acted as a mediator. We used the log

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likelihood ratio test to evaluate multiplicative interaction with analyses stratified by shift work (yes/no), snoring (yes/no), menopausal status (pre/post), postmenopausal hormone therapy (yes/no), and age (≤59 years vs. ≥60 years) to examine whether these variables acted as effect modifiers of the relationship between short sleep duration and hypertension.

To obtain summary measures, a random effects model was used to combine the OR and HR results from the 3 study populations and to test for heterogeneity ($P < 0.05$).[20] All statistical analyses were conducted using SAS statistical software version 9.1 (SAS Institute, Cary, NC).

RESULTS

The baseline characteristics for NHS-I in 1986, NHS-I in 2000, and NHS-II in 2001 after exclusion of those with prevalent hypertension according to their sleep duration categories are shown in Table 1. Because of large sample sizes, all of the bivariable analyses between sleep duration and the covariables were highly statistically significant. Women with short sleep duration were more likely to have diabetes, have a BMI ≥ 30, and be a shift worker. Ages ranged 37–54 years in 2001 in NHS-II, 40–65 years in 1986 in NHS-I, and 54–79 years in 2000 in NHS-I.

Table 2 shows the results from the cross-sectional analyses. At each of the 3 baselines, participants with sleep durations of ≤5 hours and 6 hours had significantly increased age-adjusted odds of prevalent hypertension. The inclusion of diabetes and hypercholesterolemia in models 2 and 3 only moderately attenuated the associations, which is inconsistent with these variables acting as mediators. Consistent with our hypothesis that BMI would act as a partial mediator, the addition of BMI in model 4 appreciably attenuated the odds ratios. After controlling for all the covariables (model 5), sleep durations of ≤5 hours were associated with significantly increased odds of hypertension prevalence at each baseline. The association was stronger if BMI was considered a mediator and excluded from the model (model 6).

In results from meta-analyses combining data from all 3 baseline years and controlling for all of the covariables, sleep durations of ≤5 hours were associated with significantly increased odds of hypertension prevalence (OR = 1.19, 95% CI = 1.14–1.25). If BMI was considered a mediator and removed from the multivariable model, the odds of hypertension prevalence were higher (OR = 1.30, 95% CI = 1.17–1.45). Sleep durations of ≥9 hours were also associated with increased prevalence of hypertension at each of the 3 baseline years.

Results of the longitudinal multivariable analyses are shown in Table 3 using Cox proportional hazards models to examine the relationship between sleep duration at baseline and hypertension incidence over follow-up. In both the 2001 NHS-II and 1986 NHS-I populations, participants who reported sleep durations of ≤5 hours had significantly increased age-adjusted HRs of hypertension compared with participants who reported sleep durations of 7 hours (HR = 1.40, 95% CI = 1.30–1.52 in 2001 in NHS-II; HR = 1.20, 95% CI = 1.08–1.35 in 1986 in NHS-I). The addition to the models of diabetes (model 2) and hypercholesterolemia (model 3) did not appreciably attenuate the HRs, suggesting that these variables did not act as partial mediators of the relationship between sleep duration and hypertension incidence. Consistent with BMI acting as a partial mediator, the inclusion of BMI in model 4 appreciably attenuated the HRs, and results for ≤5 hours remained statistically significant only in NHS-II (HR = 1.23, 95% CI = 1.13–1.33). The associations were attenuated further with the inclusion of all the covariables in model 5, but the HR for hypertension in the category for ≤5 hours remained significant in women from NHS-II (HR = 1.18, 95% CI = 1.09–1.28 in 2001 in NHS-II; HR = 1.10, 95% CI = 0.98–1.23 in 1986 in NHS-I). Short sleep duration was not significantly associated with hypertension incidence in 2000 in NHS-I participants (HR = 1.01, 95% CI = 0.91–1.12). When BMI was considered a mediator and therefore excluded from the model, the association between sleep duration and hypertension incidence strengthened (model 6).

As we anticipated, results attenuated with longer follow-up after the baseline sleep assessment. For example, with 10 years of follow-up after the 1986 sleep assessment in NHS-I, the multivariable HR associated with ≤5 hours of sleep was 1.07 (95% CI = 1.01–1.14).

We stratified each population into 4 age categories (aged <50, 50–59, 60–69, and ≥70 years) and used meta-analysis to combine the results for each strata (Table 4). Sleep durations of ≤5 hours were associated with an increased incidence of hypertension in those aged <60 years (HR = 1.20, 95% CI = 1.09–1.31 for those aged <50 years; HR = 1.11, 95% CI = 1.00–1.23 for those aged 50–59 years), whereas no association was observed in the older age categories. However, the tests for multiplicative interaction were not significant ($P = 0.63$ at 1986 baseline; $P = 0.58$ at 2000 baseline). We also did not find significant interactions in analyses stratified by shift work, snoring, menopause, or postmenopausal hormone therapy (data not shown), refuting the contention that these variables acted as effect modifiers of the relationship between sleep duration and hypertension incidence.

DISCUSSION

We observed an association between short sleep duration and hypertension incidence in women aged <60 years but not in women aged ≥60 years. The differences we found between the younger and older age groups are in agreement with results from previous longitudinal studies that showed associations between short sleep duration and hypertension incidence in younger cohorts[21,22,23] but not in older cohorts.[21,24] There are plausible explanations for the differences in results between younger and older age groups. First, increased sympathetic activation from short sleep duration could influence systolic and diastolic hypertension, which is common in middle-aged populations, but not isolated systolic hypertension resulting from age-related loss of arterial compliance, which accounts for nearly 60% of hypertension in elderly populations.[25] Second, hypertension is a common disease that becomes more prevalent as age increases. By excluding prevalent cases of hypertension at baseline, longitudinal analyses with older cohorts are limited to those individuals at an age when difficulties initiating and maintaining sleep are common.

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Table 1. Bivariable relationships between sleep duration and covariables in the Nurses' Health Study I (NHS-I) at baseline year 1986, NHS-I at baseline year 2000, and Nurses' Health Study II (NHS-II) study populations

	Self-reported sleep duration in hours per night				
	≤5	6	7	8	≥9
NHS-I 1986, No. (%)	2,546 (4.2)	15,268 (25.2)	25,674 (42.4)	14,408 (23.8)	2,687 (4.4)
NHS-I 2000, No. (%)	1,705 (4.9)	8,035 (22.9)	13,992 (39.9)	9,111 (26.0)	2,235 (6.4)
NHS-II, No. (%)	3,689 (5.4)	16,053 (23.3)	29,359 (42.7)	16,130 (23.4)	3,553 (5.2)
Covariables			**Mean**		
Age					
NHS-I 1986	52.9	52.2	51.9	52.3	52.5
NHS-I 2000	65.3	64.9	64.8	65.8	66.6
NHS-II	46.9	46.5	46.4	46.1	46.0
			%		
Race					
White					
NHS-I 1986	90.1	93.8	95.6	95.3	95.0
NHS-I 2000	91.3	94.6	95.7	95.6	95.7
NHS-II	87.4	91.8	94.2	94.9	94.6
Black					
NHS-I 1986	2.9	1.5	0.6	0.5	0.5
NHS-I 2000	2.1	0.8	0.5	0.4	0.4
NHS-II	3.3	1.7	0.7	0.4	0.7
Other					
NHS-I 1986	7.0	4.7	3.8	4.2	4.5
NHS-I 2000	6.6	4.6	3.8	4.0	3.9
NHS-II	9.3	6.6	5.1	4.7	4.7
Hispanic ethnicity					
NHS-I 1986	1.1	0.9	0.7	0.9	0.9
NHS-I 2000	1.3	0.9	0.7	0.8	0.9
NHS-II	1.9	1.6	1.3	1.2	1.5
Family history of hypertension					
NHS-I 1986	43.4	44.8	45.6	43.5	41.4
NHS-I 2000	43.1	42.4	42.1	41.0	38.5
NHS-II	50.9	49.8	47.1	46.8	45.5
Diabetes					
NHS-I 1986	3.1	2.1	1.7	2.1	2.8
NHS-I 2000	4.5	3.8	3.5	3.7	5.5
NHS-II	2.5	1.5	1.3	1.3	1.9
Hypercholesterolemia					
NHS-I 1986	10.8	9.3	8.7	9.8	9.6
NHS-I 2000	55.0	52.2	50.6	52.5	55.5
NHS-II	32.6	28.0	25.7	26.3	31.6
Body mass index ≥ 30					
NHS-I 1986	14.6	11.6	8.8	9.1	11.1
NHS-I 2000	18.2	15.3	13.1	12.8	17.6
NHS-II	24.5	20.4	16.2	15.7	19.7

(*Continued*)

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Table 1. Continued

	Self-reported sleep duration in hours per night				
	≤5	6	7	8	≥9
			%		
Snore regularly					
NHS-I 1986	9.4	8.3	7.4	8.4	10.5
NHS-I 2000	15.5	14.1	13.6	13.8	16.4
NHS-II	14.8	13.8	12.9	12.9	15.3
Postmenopausal					
NHS-I 1986	59.1	54.3	51.2	52.8	52.0
NHS-I 2000	96.9	96.9	97.3	97.9	98.3
NHS-II	27.2	24.0	21.3	18.8	20.0
Current shift worker					
NHS-I 1986	19.0	12.6	8.4	8.2	9.2
NHS-I 2000	14.8	10.2	8.6	8.2	8.6
NHS-II	32.2	24.9	19.8	18.4	20.3
Total activity < 9 MET hours per week[a]					
NHS-I 1986	57.0	54.2	52.4	53.6	59.0
NHS-I 2000	42.5	38.3	36.2	36.7	44.7
NHS-II	43.3	39.9	37.3	37.4	45.5
Current postmenopausal hormone therapy					
NHS-I 1986	19.1	25.0	27.8	25.9	25.3
NHS-I 2000	29.3	26.7	25.3	25.6	27.6
NHS-II	18.6	17.6	16.2	14.1	16.2
Current smoker					
NHS-I 1986	24.9	25.5	23.1	22.4	25.7
NHS-I 2000	10.7	10.9	9.7	9.4	11.6
NHS-II	14.1	10.5	7.6	6.9	7.8
Caffeine ≥ 245 mg/d					
NHS-I 1986	45.1	47.6	46.4	44.1	40.1
NHS-I 2000	32.4	35.8	36.6	36.9	34.8
NHS-II	30.9	33.8	33.9	33.3	31.8
Alcohol > 28 g/day					
NHS-I 1986	3.3	3.9	4.4	5.7	7.8
NHS-I 2000	2.7	2.6	3.1	3.6	5.9
NHS-II	1.5	1.6	1.8	2.2	2.5
DASH score in bottom quintile					
NHS-I 1986	18.1	16.2	14.8	14.8	17.6
NHS-I 2000	16.3	14.1	11.8	12.6	13.5
NHS-II	17.8	15.7	13.5	13.5	15.6
Current aspirin					
NHS-I 1986	60.5	65.8	67.6	65.7	63.2
NHS-I 2000	36.1	38.7	39.4	40.2	40.0
NHS-II	87.0	88.7	89.8	90.1	89.6

(*Continued*)

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Table 1. Continued

	Self-reported sleep duration in hours per night				
	≤5	6	7	8	≥9
	%				
Current acetaminophen					
NHS-I 1986	37.8	38.2	37.3	36.0	36.1
NHS-I 2000	63.2	61.5	59.0	57.7	59.7
NHS-II	72.7	77.2	80.0	81.1	78.6
Current nonaspirin NSAIDs					
NHS-I 1986	53.7	54.7	56.5	58.8	57.1
NHS-I 2000	30.3	32.7	34.2	37.6	36.6
NHS-II	59.3	59.2	61.2	63.4	63.7

Because of large sample sizes, all of the bivariable analyses between sleep duration and the covariables were highly statistically significant.
Abbreviations: DASH, Dietary Approaches to Stop Hypertension; MET, Metabolic Equivalent; NSAID, Non-Steroidal Anti-Inflammatory Drug.
[a]Nine MET hours per week is equivalent to 3 hours per week of walking at a moderate pace.

Table 2. Cross-sectional multivariable analyses using logistic regression to explore the relationship between sleep duration and hypertension prevalence at baseline

Sleep duration in hours	Prevalent HTN cases, No.	Prevalent hypertension at baseline OR (95% CI)					
		Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	Model 5[e]	Model 6[f]
NHS-II, 2001, ages 37–54 years							
≤5	1,304	1.63 (1.52–1.75)	1.57 (1.46–1.69)	1.55 (1.44–1.66)	1.35 (1.25–1.45)	1.20 (1.11–1.30)	1.31 (1.22–1.42)
6	4,217	1.25 (1.19–1.30)	1.24 (1.19–1.30)	1.22 (1.17–1.28)	1.14 (1.08–1.19)	1.09 (1.04–1.15)	1.14 (1.09–1.20)
7	6,102	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
8	3,306	1.01 (0.96–1.05)	1.00 (0.96–1.05)	1.00 (0.95–1.04)	1.02 (0.97–1.07)	1.01 (0.96–1.06)	1.00 (0.95–1.05)
≥9	961	1.33 (1.23–1.44)	1.28 (1.18–1.38)	1.24 (1.15–1.34)	1.19 (1.10–1.30)	1.07 (0.98–1.17)	1.10 (1.01–1.19)
NHS-I, 1986, ages 40–65 years							
≤5	1,260	1.48 (1.38–1.59)	1.43 (1.32–1.55)	1.45 (1.35–1.57)	1.31 (1.21–1.41)	1.25 (1.15–1.35)	1.32 (1.23–1.43)
6	5,777	1.17 (1.13–1.22)	1.16 (1.12–1.21)	1.17 (1.12–1.22)	1.10 (1.06–1.15)	1.09 (1.05–1.14)	1.13 (1.09–1.18)
7	8,170	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
8	5,133	1.08 (1.04–1.12)	1.07 (1.02–1.11)	1.07 (1.03–1.12)	1.06 (1.01–1.11)	1.05 (1.00–1.09)	1.05 (1.01–1.10)
≥9	1,207	1.34 (1.24–1.44)	1.30 (1.20–1.40)	1.32 (1.25–1.43)	1.26 (1.17–1.36)	1.21 (1.12–1.31)	1.25 (1.16–1.35)
NHS-I, 2000, ages 54–79 years							
≤5	2,259	1.37 (1.28–1.47)	1.32 (1.23–1.41)	1.33 (1.24–1.43)	1.26 (1.18–1.35)	1.14 (1.06–1.23)	1.17 (1.09–1.26)
6	8,591	1.14 (1.09–1.18)	1.13 (1.08–1.17)	1.12 (1.08–1.17)	1.10 (1.05–1.14)	1.06 (1.01–1.10)	1.07 (1.03–1.12)
7	13,191	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
8	9,571	1.06 (1.02–1.11)	1.05 (1.01–1.10)	1.06 (1.02–1.10)	1.04 (1.00–1.08)	1.04 (1.00–1.08)	1.05 (1.01–1.10)
≥9	2,968	1.30 (1.22–1.38)	1.24 (1.17–1.32)	1.27 (1.19–1.35)	1.20 (1.13–1.28)	1.12 (1.05–1.20)	1.17 (1.09–1.25)

Abbreviations: CI, confidence interval; HTN, Hypertension; OR, odds ratio; NSH-I, Nurses' Health Survey I; NHS-II, Nurses' Health Survey II.
[a]Model 1: Controlling for age.
[b]Model 2: Controlling for age and diabetes.
[c]Model 3: Controlling for age and hypercholesterolemia.
[d]Model 4: Controlling for age and body mass index.
[e]Model 5: Controlling for age, diabetes, hypercholesterolemia, body mass index, race, Hispanic ethnicity, menopause, smoking, physical activity, alcohol, caffeine, Dietary Approaches to Stop Hypertension diet, aspirin, acetaminophen, nonaspirin Non-Steroidal Anti-Inflammatory Drugs, family hypertension history, snoring, and shift work.
[f]Model 6: Controlling for variables in model 5 except body mass index.

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Table 3. Longitudinal multivariable analyses using Cox proportional hazards models to explore the relationship between sleep duration at baseline and hypertension incidence over follow-up

Sleep duration in hours	Incident HTN cases, No.	Incident hypertension over follow-up HR (95% CI)					
		Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	Model 5[e]	Model 6[f]
NHS-II, 2001, ages 37–54 years							
≤ 5	701	1.40 (1.30–1.52)	1.38 (1.27–1.50)	1.37 (1.26–1.48)	1.23 (1.13–1.33)	1.18 (1.09–1.28)	1.26 (1.16–1.37)
6	2,493	1.14 (1.09–1.21)	1.14 (1.09–1.20)	1.14 (1.08–1.19)	1.07 (1.02–1.13)	1.05 (1.00–1.11)	1.09 (1.04–1.15)
7	3,981	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
8	2,097	0.97 (0.92–1.03)	0.97 (0.92–1.03)	0.97 (0.92–1.02)	0.98 (0.93–1.03)	0.98 (0.93–1.03)	0.97 (0.92–1.02)
≥9	520	1.11 (1.01–1.21)	1.09 (1.00–1.20)	1.07 (0.98–1.18)	1.05 (0.96–1.15)	1.01 (0.92–1.11)	1.02 (0.93–1.12)
NHS-I, 1986, ages 40–65 years							
≤5	346	1.20 (1.08–1.35)	1.20 (1.07–1.34)	1.20 (1.07–1.34)	1.11 (0.99–1.24)	1.10 (0.98–1.23)	1.15 (1.02–1.29)
6	1,965	1.14 (1.08–1.21)	1.14 (1.08–1.21)	1.14 (1.08–1.21)	1.10 (1.04–1.16)	1.09 (1.03–1.16)	1.12 (1.05–1.18)
7	2,864	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
8	1,671	1.03 (0.97–1.10)	1.03 (0.97–1.09)	1.03 (0.97–1.09)	1.02 (0.96–1.09)	1.04 (0.97–1.10)	1.04 (0.97–1.10)
≥9	276	1.06 (0.94–1.20)	1.06 (0.93–1.20)	1.06 (0.94–1.20)	1.03 (0.91–1.17)	1.03 (0.91–1.17)	1.05 (0.93–1.19)
NHS-I, 2000, ages 54–79 years							
≤5	262	1.03 (0.94–1.14)	1.03 (0.93–1.14)	1.03 (0.93–1.14)	1.02 (0.92–1.12)	1.01 (0.91–1.12)	1.01 (0.91–1.12)
6	1,043	1.02 (0.97–1.08)	1.02 (0.97–1.08)	1.02 (0.97–1.08)	1.01 (0.96–1.07)	1.01 (0.96–1.07)	1.01 (0.96–1.07)
7	2,506	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
8	3,031	0.96 (0.91–1.01)	0.96 (0.91–1.01)	0.96 (0.91–1.01)	0.96 (0.91–1.01)	0.96 (0.91–1.01)	0.97 (0.92–1.02)
≥9	2,119	0.97 (0.89–1.06)	0.96 (0.88–1.05)	0.97 (0.88–1.06)	0.93 (0.85–1.02)	0.92 (0.84–1.01)	0.94 (0.86–1.03)

Abbreviations: CI, confidence interval; HR, hazard ratio; HTN, Hypertension; NHS-I, Nurses' Health Study I; NHS-II, Nurses' Health Study II.
[a]Model 1: Controlling for age.
[b]Model 2: Controlling for age and diabetes.
[c]Model 3: Controlling for age and hypercholesterolemia.
[d]Model 4: Controlling for age and body mass index.
[e]Model 5: Controlling for age, diabetes, hypercholesterolemia, body mass index, race, Hispanic ethnicity, menopause, smoking, physical activity, alcohol, caffeine, Dietary Approaches to Stop Hypertension diet, aspirin, acetaminophen, nonaspirin Non-Steroidal Anti-Inflammatory Drugs, family history of hypertension, snoring, and shift work.
[f]Model 6: Controlling for all variables in model 5 except for body mass index.

Our results are consistent with obesity acting as a partial mediator in the relationship between short sleep duration and hypertension incidence. Sleep deprivation has been shown to result in insulin resistance,[12] which on a chronic basis can facilitate fat deposition. Short sleep has also been shown to alter the appetite hormones leptin and ghrelin, resulting in increased appetite,[11] which could lead to increased caloric consumption and weight gain. We did not find diabetes or hypercholesterolemia to act as mediators of the relationship.

The results from this epidemiological study are consistent with interventional studies that have shown that shortened sleep increases blood pressure.[3,4] Blood pressure follows a diurnal pattern, dropping by 10%–20% during sleep, so less sleep increases average 24-hour blood pressure.[26] Short sleep also prolongs exposure to stress, which has been shown to promote salt appetite and suppress renal salt-fluid excretion.[27] Chronic exposure to elevated hemodynamic load resulting from short sleep duration can lead to structural adaptations, such as arterial and left ventricular hypertrophic remodeling, that gradually entrain the cardiovascular system to operate at an elevated pressure equilibrium.[5]

We observed associations between short sleep duration and hypertension prevalence in younger and older participants in cross-sectional analyses. Our results with younger participants are consistent with previous studies with younger samples,[22,23,28,29,30] whereas our results with older participants differed from 2 previous studies that showed no association between short sleep duration and hypertension prevalence.[31,32]

In older subjects, we found sleep durations ≥9 hours to be associated with hypertension prevalence in cross-sectional analyses but not with hypertension incidence in longitudinal analyses, and we are not aware of any previous longitudinal studies that have shown such an association. Given that there is little evidence to suggest that sleeping >8 hours has adverse health effects,[33] it is likely that long sleep duration is more of an epiphenomenon of hypertension as opposed to a cause. The inflammatory process has been shown to play a key role in the pathogenesis and pathophysiology of metabolic disorders such as cardiovascular disease.[34] Proinflammatory cytokines contribute toward sleepiness and fatigue[35] and have been shown to be elevated in those suffering from hypertension.[36]

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Table 4. Age-stratified meta-analyses combining multivariable results for incident hypertension from the Nurses' Health Study II, Nurses' Health Study I 1986 baseline, and Nurses' Health Study I 2000 baseline

	Aged <50 years	Aged 50–59 years	Aged 60–69 years	Aged >70 years
No. of participants	**76,737**	**51,534**	**26,366**	**9,808**
Sleep duration in hours	**Incident hypertension**	**Incident hypertension**	**Incident hypertension**	**Incident hypertension**
≤5 hours				
No. of cases	577	531	257	162
HR (95% CI)	1.20 (1.09–1.31)	1.11 (1.00–1.23)	1.00 (0.88–1.15)	1.05 (0.89–1.25)
6 hours				
No. of cases	2,406	2,264	1,303	657
HR (95% CI)	1.10 (0.99–1.22)	1.04 (0.99–1.10)	1.05 (0.97–1.12)	0.99 (0.90–1.09)
7 hours				
No. of cases	3,713	3,447	2,235	1,125
HR (95% CI)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
8 hours				
No. of cases	2,013	1,849	1,495	798
HR (95% CI)	1.02 (0.94–1.10)	1.01 (0.95–1.07)	0.99 (0.91–1.09)	0.90 (0.82–0.99)
≥9 hours				
No. of cases	459	401	368	213
HR (95% CI)	1.00 (0.91–1.11)	1.00 (0.86–1.16)	0.98 (0.87–1.09)	0.89 (0.77–1.04)

Controlling for age, diabetes, hypercholesterolemia, body mass index, race, Hispanic ethnicity, menopause, smoking, physical activity, alcohol, caffeine, Dietary Approaches to Stop Hypertension diet, aspirin, acetaminophen, nonaspirin Non-Steroidal Anti-Inflammatory Drugs, family history of hypertension, snoring, and shift work.

Abbreviations: CI, confidence interval; HR, hazard ratio.

Our findings from cross-sectional and longitudinal analyses of large and well-characterized samples of health professionals must be considered in light of the limitations of these analyses. First, we were not able to control for the presence of sleep apnea, which has been shown to increase the risk for hypertension incidence, but we were able to control for snoring and body weight, which are closely related to sleep-disordered breathing. We did not find snoring to act as an effect modifier of the relationship between sleep duration and hypertension incidence. Second, our study lacked repeated and objective measures of sleep duration. Sleep duration often varies over time, so when answering the sleep question, respondents were likely to experience recall bias whereby their most recent sleep durations were remembered more clearly. The wide age range of the study population could also have affected the reported sleep duration. The measure of self-reported sleep duration is likely to result in some misclassification, but because the outcome is assessed prospectively, any misclassification is likely to be nondifferential with respect to hypertension. Third, hypertension frequently goes undiagnosed, and we have no way of knowing whether participants with different sleep durations were more or less likely to seek or receive treatment and therefore be diagnosed with hypertension. The fact that the participants in this study were health professionals should have helped minimize this potential bias. Fourth, the potential exists for confounding from unmeasured variables, such as anxiety. Our sample was made up exclusively of female registered nurses, making it difficult to generalize our results to men or to individuals with other socioeconomic statuses.

The results from this study lend support to the hypothesis that short sleep duration plays a role in the etiology of hypertension in some young women. Sufficient sleep could represent a lifestyle practice worthy of investigation as an approach to reduce hypertension incidence and prevalence. One recent pilot study found that behavioral strategies to extend sleep in individuals with prehypertension or type 1 hypertension significantly increased sleep duration and reduced systolic and diastolic blood pressure over a 6-week intervention period.[37] When sleep disturbances are secondary to mood and anxiety disorders, then the treatment of those disorders is often necessary to materially affect sleep. Other interesting lines of inquiry are whether getting adequate sleep could help individuals follow other commonly recommended lifestyle practices that are protective against hypertension, such as engaging in regular physical activity and eating a healthy diet.

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DISCLOSURE

The authors declared no conflict of interest.

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