### Association between sleep-related disorders and hypertension in postmenopausal women from the United States

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#### Abstract

Objective: A notable research gap persists regarding the association between sleep-related disorders and hypertension risk in postmenopausal women in the United States, which this study aimed to address.

Methods: Data from 3,560 naturally postmenopausal women were analyzed using 6 cycles of the National Health and Nutrition Examination Survey from 2007 to 2018. Logistic regression models were employed to assess the relationships between sleep duration, trouble sleeping, and obstructive sleep apnea (OSA) symptoms with hypertension. Restricted cubic splines were used to identify nonlinear associations between sleep duration and hypertension. Finally, stratified analyses were taken to explore the associations between sleep-related disorders and hypertension across various subgroups based on healthrelated factors.

Results: Trouble sleeping and OSA were associated with an increased odds of hypertension in postmenopausal women (trouble sleeping: odds ratio = 1.61, 95% CI, 1.28-2.02; OSA: odds ratio = 1.63, 95% CI, 1.13-2.37). In addition, a U-shaped relationship between sleep duration and hypertension was identified (P for overall = 0.0007, P for nonlinear = 0.0002), indicating that both insufficient and excessive sleep increased the odds of hypertension. Subgroup analysis revealed that body mass

Received for publication February 19, 2025; accepted June 24, 2025.

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Funding/support: None reported.

Financial disclosure/conflicts of interest: None reported.

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.menopause.org.

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DOI: 10.1097/GME.0000000000002650

index moderated these associations (trouble sleeping: P for interaction = 0.038; OSA: P for interaction = 0.044), with stronger effects observed in obese women.

Conclusion: Sleep-related disorders are significantly associated with hypertension in postmenopausal women in the United States. Our findings emphasized the importance of sleep health and weight management in the management of hypertension in this population.

Key Words: Body mass index, Hypertension, Menopause, National Health and Nutrition Examination Survey, Sleep.

(Menopause 2026;33:000–000)

As a prominent cardiovascular risk factor, hypertension poses a significant threat to global health, exacerbating the burden of disease and mortality.1 Among the various demographic groups, postmenopausal women are particularly vulnerable, with a pronounced increase in hypertension prevalence and a concerning tendency towards suboptimal blood pressure (BP) management.<sup>2</sup> Furthermore, postmenopausal women tend to have poorer BP control compared with men in the same age group.<sup>3</sup> Menopause, a significant transition in a woman's life, is characterized by the loss of ovarian function and the permanent cessation of menstruation, typically diagnosed after 12 consecutive months of amenorrhea.<sup>4</sup> The decline in estrogen levels following menopause is widely believed to contribute to the increased risk of hypertension in postmenopausal women.<sup>5</sup> Against the backdrop of an aging global population and the prospect of a third of women's lives being spent in the postmenopausal phase, the urgency to safeguard the health of this cohort is paramount. By 2025, it is estimated that 1.1 billion women will be in postmenopause worldwide. Therefore, ensuring the health of this substantial population group is a critical public health priority.

In the spectrum of hypertension etiology, sleep disturbances have risen to prominence as a substantial, albeit often undervalued, risk factor. 7 Sleep is a fundamental physiological necessity for the sustenance of cardiovascular integrity. The American Academy of Sleep Medicine and the Sleep Research Society endorsed a sleep duration of 7-9 hours within a 24-hour cycle for adults.<sup>8</sup> Importantly, the constellation of sleep-related disorders can serve as precursors to hypertension, with their influence being modulated by individual characteristics such as chronological age, sex, racial/ethnic background, and menopausal status.<sup>9-12</sup> Women, particularly those undergoing menopause transition or in the postmenopausal phase, exhibited a higher propensity to report sleep disturbances compared with their male counterparts. These sleep-related disorders, which were prevalent manifestations of menopause, were posited to augment the predisposition to hypertension in postmenopausal women.<sup>12</sup>

Hypertension is a leading contributor to cardiovascular diseases (CVDs) and premature mortality among women worldwide, with risk exacerbated by factors such as age, ethnicity, and socioeconomic status. Despite this, the specific challenges faced by women have often been overlooked in research, resulting in a body of evidence that frequently applies predominantly to men or is indiscriminately generalized across sexes.<sup>3</sup> A significant gap in the data pertains to particular subgroups, especially postmenopausal women, who remain underrepresented in hypertension research. Studies that explore the link between sleep-related disorders and hypertension risk in postmenopausal women are scarce. Given the high prevalence of sleep-related disorders in this demographic and their potential to increase the risk of hypertension, there is an urgent need to investigate and understand the potential interplay between sleep-related disorders and hypertension in postmenopausal women. Such understanding is essential for developing a more comprehensive approach to managing cardiovascular risk and enhancing sleep quality in this population.

This study aims to examine the association between sleep-related disorders and the odds of hypertension, specifically in naturally postmenopausal women, utilizing data from 6 cycles of the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2018. By elucidating this potential relationship, tailored interventions can be devised to ameliorate sleep quality and mitigate cardiovascular risk in this demographic.

#### **METHODS**

### Data sources and participants

The data used in this study were sourced from the NHANES, a nationwide, continuously representative cross-sectional study that investigates the health conditions, nutritional status, and risk factors of the United States (US) population. The survey is conducted biennially by the National Center for Health Statistics, a division of the Centers for Disease Control and Prevention. Participants were invited to partake in phone interviews and health assessments conducted in professionally equipped medical mobile centers. Ethical approval for NHANES is provided by the National Center for Health Statistics Ethics Review Board. Additional details are available on

the NHANES website (https://www.cdc.gov/nchs/index.htm).

For this study, we selected survey data from 6 cycles of NHANES, spanning from 2007 to 2018. Out of a total of 59,842 participants, 21,280 were excluded due to missing sleep survey information, and 19,572 were excluded for missing reproductive health data. In addition, 1,169 participants who lacked BP-related information were also excluded. Ultimately, we recruited 14,662 naturally postmenopausal participants, after excluding 2,897 women who had undergone oophorectomy or hysterectomy before or at the time of their last menstrual period and 262 women who were younger than 45 years at the time of the survey. We further excluded participants with missing data on key covariates for multivariable analysis, including those missing information on age at menarche and menopause (n = 10,010), those lacking 2 complete 24-hour dietary recall interviews (n = 633), those without body mass index (BMI) data (n = 48), those missing family poverty-to-income ratio (PIR) data (n = 406), and those missing marital status (n = 2), education level (n = 2), and alcohol consumption data (n = 1). Given that information related to obstructive sleep apnea (OSA) symptoms was only collected during the 2007-2008, 2015-2016, and 2017-2018 cycles, our final analysis included 3,560 participants for sleep duration and selfreported trouble sleeping, and 1,770 participants for OSA symptoms (Fig. 1).

### Sleep-related disorder assessment

The NHANES program collected sleep health data through home visits and a computer-assisted personal interview system. This study primarily focuses on 3 aspects of sleep health: sleep duration, trouble sleeping, and OSA symptoms. Definitions are based on self-reported information provided by participants as follows:

- Sleep duration: Participants reported their sleep duration, which was categorized into insufficient sleep (<7 h/night), mid-range sleep (7-9 h/night), and excessive sleep (>9 h/night).<sup>13</sup>
- Trouble sleeping: Defined by participants answering "Yes" to either of the following questions: (1) "Have you ever been told by a doctor that you have trouble sleeping?" or (2) "Have you ever been told by a doctor that you have a sleep disorder?" 14
- OSA: Defined as the presence of one or more of the following: (1) snoring 3 or more nights per week, (2) snorting, gasping, or stopping breathing 3 or more nights per week, (3) feeling excessively sleepy during the day 16-30 times per month despite sleeping ~7 or more hours per night on weekdays or work nights, or (4) being diagnosed with sleep apnea by a doctor. 15

### Assessment of hypertension

The definition of hypertension used in this study is consistent with previous research.<sup>16,17</sup> Specifically, BP

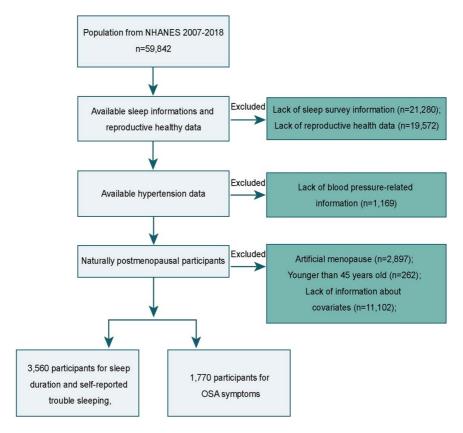


FIG. 1. Flowchart of the inclusion of the study population. OSA, obstructive sleep apnea.

measurements were collected in the Mobile Examination Center. After resting in a seated position for at least 5 minutes, each participant underwent 3 consecutive BP readings at maximum cuff inflation, and these readings were averaged. Participants were classified as having hypertension if they met one or more of the following criteria: (1) an average systolic BP  $\geq$ 140 mm Hg or diastolic BP  $\geq$ 90 mm Hg, (2) a history of being diagnosed or informed of having hypertension, and (3) self-reported use of antihypertensive medications.

### Covariates

A minimal set of covariates was determined for the multivariable analysis by constructing a Directed Acyclic Graph (Supplemental Figure S1, Supplemental Digital Content 1, http://links.lww.com/MENO/B425). Covariate information includes: age (years), ethnicity, education level, marital status, PIR, self-reported reproductive lifespan (years), BMI, presence of diabetes, CVD, smoking status, alcohol consumption, physical activity, and self-reported total energy intake (Kcal). Detailed descriptions of these covariates are provided in Supplemental Table S1 (Supplemental Digital Content 1, http://links.lww.com/MENO/B425).

### Statistical analysis

All analyses were conducted following the NHANES analysis guidelines, including the use of sample

weights (WTDR2D) and adjustments for clustering and stratification. For further details on sample weights and other considerations, refer to the "NHANES Analytic Guidelines" and the NHANES online tutorials (https://wwwn.cdc.gov/nchs/nhanes/analyticguidelines.aspx).

Categorical variables were expressed as unweighted sample sizes (N) and weighted percentages (%), with comparisons made using  $\chi^2$  or Fisher exact tests as appropriate. Variables with skewed distributions were presented as medians (first quartile [P25] and third quartile [P75]), and the nonparametric Wilcoxon rank-sum test was used for comparisons.

To systematically assess the association between sleep-related disorders and hypertension while accounting for potential confounders, we developed several sets of multivariable logistic regression models, each with incremental covariate adjustment. The rationale for this approach was to observe how the association changed with progressive adjustment for different groups of confounding variables (demographic, clinical, and lifestyle factors), and to enhance the robustness of our findings. Specifically, the crude model was unadjusted. Model 1 adjusted for demographic characteristics (age group, ethnicity, education level, marital status, and PIR). Model 2, in addition, adjusted for health conditions (BMI, diabetes, CVD, and reproductive lifespan). Model 3 further adjusted for lifestyle factors (physical activity, smoking, alcohol consumption, and total energy intake). This stepwise modeling approach provides transparency regarding the influence of different groups of covariates on the association of interest. Restricted cubic spline (RCS) functions were used to identify potential nonlinear relationships between sleep duration and hypertension, with the sleep duration corresponding to the lowest odds ratio (OR) used as the reference. The Akaike Information Criterion guided knot selection, and the likelihood ratio test was used to assess nonlinearity. Subgroup analyses, stratified by age, ethnicity, BMI, diabetes, CVD, smoking, alcohol consumption, and physical activity, were conducted to explore the association between sleep-related disorders and hypertension in postmenopausal women across various subgroups. The Wald test was used to assess interaction effects. All statistical analyses were performed using R software (version 4.3.2). A 2-tailed *P*-value of < 0.05 was considered statistically significant.

#### **RESULTS**

# Baseline characteristics of the study population stratified by hypertension status

In the analysis of the NHANES 2007-2018 survey data, a cohort of 3,560 postmenopausal women with complete data on sleep duration and self-reported sleep-related disorders was examined. The baseline characteristics of this population were detailed in Table 1. The median age of the study population was 61 (55, 69) years, with 2,250 participants diagnosed with hypertension, resulting in a prevalence rate of 63.2%. Hypertensive participants had a median age of 64 (57, 73) years, which was significantly higher than that of nonhypertensive participants (58 [53,64] y; P < 0.001). Participants were classified according to sleep duration: 26.4% were identified as having short sleep duration, 68.2% as having moderate sleep duration, and 5.4% as having long sleep duration. In addition, 39.4% of participants reported trouble sleeping. A statistical analysis revealed significant differences in sleep duration and symptoms of trouble sleeping between hypertensive and nonhypertensive women (P <0.001). A higher proportion of hypertensive women reported short or long sleep duration compared with nonhypertensive women. Similarly, 43.7% of hypertensive women reported trouble sleeping, which was higher than the 33.9% observed among nonhypertensive women. Furthermore, significant differences were observed between the hypertensive and nonhypertensive groups in terms of ethnicity, educational level, PIR, alcohol consumption, diabetes status, CVD, BMI, and reproductive lifespan (all P < 0.05).

Supplementary baseline data were obtained for 1,770 participants from 3 NHANES cycles (2007-2008, 2015-2018) with complete records on OSA symptoms, as delineated in Supplemental Table S2 (Supplemental Digital Content 1, http://links.lww.com/MENO/B425). Within this subgroup, 1,143 participants were identified with hypertension, yielding a prevalence rate of 64.6%. The median age of this subgroup was 61 (55, 70) years, aligning with the median age of the entire 6-cycle cohort. The median age for hypertensive participants within this subgroup was 65 (57, 73) years, which was significantly higher than that of

their nonhypertensive counterparts at 58 (53, 64) years (P < 0.001). Among the 915 participants diagnosed with OSA (50.1%), 55.2% also had hypertension, a proportion that was significantly higher than the 43.4% of nonhypertensive participants with OSA (P = 0.006). Furthermore, significant disparities were noted between the hypertensive and nonhypertensive groups in terms of ethnicity, educational attainment, PIR, diabetes status, CVD, BMI, and reproductive lifespan (all P < 0.05).

# The relationship between trouble sleeping and hypertension in postmenopausal women

A weighted logistic regression model was used to assess the association between self-reported trouble sleeping and hypertension in postmenopausal women (Table 2). In the unadjusted crude model, postmenopausal women who reported trouble sleeping were more likely to have hypertension than those without trouble sleeping (OR = 1.51, 95% CI, 1.21-1.89). After adjusting for demographic characteristics (age group, ethnicity, education, marital status, and PIR), health conditions (BMI, diabetes, CVD, and reproductive lifespan), and lifestyle factors (physical activity, smoking, alcohol consumption, and total energy intake), trouble sleeping remained associated with an increased odds of hypertension (OR = 1.61, 95% CI, 1.28-2.02).

# The relationship between sleep duration and hypertension in postmenopausal women

To explore the relationship between sleep duration and hypertension in postmenopausal women, self-reported sleep duration was first included as a continuous variable in the logistic regression model (Supplemental Table S3, Supplemental Digital Content 1, http://links.lww.com/ MENO/B425). The results indicated no association between sleep duration and hypertension prevalence, regardless of covariate adjustments. Next, sleep duration was categorized into insufficient sleep (<7 h/night), mid-range sleep (7-9 h/night), and excessive sleep (>9 h/night), with mid-range sleep as the reference category (Table 2). In all models, insufficient sleep was not associated with hypertension (crude model: OR = 1.24, 95% CI, 0.96-1.60; fully adjusted model: OR = 1.11, 95% CI, 0.85-1.46). However, excessive sleep was associated with a higher prevalence of hypertension (crude model: OR = 2.70, 95% CI, 1.73-4.22; fully adjusted model: OR = 1.99, 95% CI, 1.10-3.60).

RCS functions were used to further investigate the nonlinear relationship between sleep duration and hypertension in postmenopausal women. Figure 2A illustrates the RCS regression results, which showed a U-shaped curve. The lowest likelihood of hypertension was observed at 7 hours of sleep, corresponding to the mid-range sleep category. Both insufficient and excessive sleep were associated with higher odds of hypertension (*P* for overall = 0.0007, *P* for nonlinear = 0.0002).

# The relationship between obstructive sleep apnea and hypertension in postmenopausal women

The association between OSA symptoms and hypertension was examined in a subgroup of postmenopausal

TABLE 1. General characteristics of included participants according to the presence or absence of hypertension in the NHANES 2007-2018

Variable	Overall <sup>a</sup>	No hypertension	Hypertension	P
N (%)	3,560	1,310 (36.8)	2,250 (63.2)	_
Age (y)	61 (55, 69)	58 (53, 64)	64 (57, 73)	< 0.001
Age group (y)	01 (33, 07)	30 (33, 01)	01 (37, 73)	(0.001
45-55	1,081 (25.5)	425 (34.8)	656 (18.3)	< 0.001
56-65	1,550 (39.5)	433 (45.2)	1,117 (35.1)	₹0.001
66-75	749 (22.1)	433 (43.2)	328 (28.3)	_
				_
≥76	1,371 (12.8)	557 (5.7)	814 (18.3)	_
BMI (kg/m²)				
< 25	915 (29.3)	288 (38.3)	627 (22.3)	< 0.001
25-<30	1,790 (29.5)	683 (31.2)	1,107 (28.2)	_
≥30	929 (41.2)	452 (30.4)	477 (49.6)	_
Ethnicity (%)				
Mexican American	483 (5.1)	187 (5.3)	296 (5.0)	0.001
Other Hispanic	434 (5.1)	177 (5.4)	257 (4.9)	_
Non-Hispanic White	1,660 (74.9)	656 (78.1)	1,004 (72.5)	_
Non-Hispanic Black	673 (8.4)	159 (5.2)	514 (10.9)	_
Other race <sup>b</sup>	310 (6.4)	131 (6.0)	179 (6.7)	_
Education	310 (0.4)	131 (0.0)	177 (0.7)	
	416 (5.5)	122 (4.0)	204 (6.7)	< 0.001
<9th grade	416 (5.5)	122 (4.0)	294 (6.7)	< 0.001
9-11th grade	462 (9.1)	139 (7.0)	323 (10.8)	_
High school graduate	837 (24.7)	267 (20.9)	570 (27.5)	_
Some college or AA degree <sup>c</sup>	1,036 (30.7)	378 (28.8)	658 (32.1)	_
College graduate or above	809 (30.0)	404 (39.2)	405 (22.9)	_
Marital status				
Married	1,704 (56.8)	694 (61.9)	1,010 (52.9)	< 0.001
Widowed	690 (15.4)	151 (7.8)	539 (21.3)	_
Divorced	640 (16.9)	265 (20.0)	375 (14.5)	_
Separated	150 (2.4)	58 (2.4)	92 (2.3)	
Never married	` /		· · · · · · · · · · · · · · · · · · ·	_
	278 (5.4)	102 (5.0)	176 (5.7)	_
Living with partner	98 (3.1)	40 (2.9)	58 (3.2)	_
Poverty-to-income ratio				
< 1.3	1,086 (17.8)	328 (13.2)	758 (21.4)	< 0.001
1.3-3.5	1,278 (32.2)	426 (26.6)	852 (36.4)	_
> 3.5	1,196 (50.0)	556 (60.2)	640 (42.2)	_
Sleep duration				
Insufficient sleep	1,120 (26.4)	401 (24.8)	719 (27.7)	< 0.001
Mid-range sleep	2,227 (68.2)	857 (72.2)	1,370 (65.0)	_
Excessive sleep	213 (5.4)	52 (3.0)	161 (7.3)	_
Trouble sleeping	=== (===)	()	()	
No	2,289 (60.6)	908 (66.1)	1,381 (56.3)	< 0.001
Yes			869 (43.7)	₹0.001
	1,271 (39.4)	402 (33.9)	809 (43.7)	_
Diabetes	2 (52) (00 0)	4.484 (00.4)	1.505 (50.4)	0.004
No	2,658 (80.8)	1,131 (90.4)	1,527 (73.4)	< 0.001
Yes	902 (19.2)	179 (9.6)	723 (26.6)	_
Physical activity				
Inactive	1,278 (30.6)	352 (23.4)	926 (36.2)	< 0.001
Insufficiently active	607 (17.1)	242 (17.2)	365 (17.1)	_
Sufficiently active	1,675 (52.3)	716 (59.5)	959 (46.7)	_
CVD	-, ()	((	, , , , , , , , , , , , , , , , , , , ,	
No	3,203 (91.5)	1,254 (96.9)	1,949 (87.2)	< 0.001
Yes	· · · · · · · · · · · · · · · · · · ·			< 0.001
	357 (8.5)	56 (3.1)	301 (12.8)	_
Smoking	2.452 (50.5)	555 (50.2)	1.255 (50.2)	
Never	2,153 (58.7)	777 (59.3)	1,376 (58.3)	0.914
Ever	932 (28.0)	347 (27.4)	585 (28.4)	_
Now	475 (13.3)	186 (13.3)	289 (13.3)	_
Alcohol consumption				
Never	1,554 (33.1)	501 (28.2)	1,053 (36.8)	0.012
Moderate	1,247 (40.6)	491 (43.3)	756 (38.5)	_
Heavy	759 (26.3)	318 (28.4)	441 (24.7)	_
Reproductive lifespan (v)	37(33,40)	37(33,40)	37(33,41)	0.003
Total energy intake (Kcal)			1,641.50 (1315.00, 2034.50)	
	1,665.46 (1,339.35, 2,039.00)	1,694.95 (1,352.63, 2,041.14)	1,041.50 (1515.00, 2054.50)	0.252
Cycle	555 (42.0)	202 (22.5)	252 (22.4)	0.0-
2007-2008	575 (13.0)	202 (12.5)	373 (13.4)	0.99
2009-2010	626 (15.4)	218 (15.6)	408 (15.3)	_
2011-2012	530 (14.3)	209 (14.7)	321 (14.0)	_
	634 (17.9)	256 (18.0)	378 (17.8)	_
2013-2014				
2013-2014 2015-2016	594 (19.8)	212 (20.0)	382 (19.7)	_

BMI, body mass index; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey.

<sup>\*\*</sup>Post a represented as N (%) or median (P25, P75).

\*In NHANES, "other race" refers to other races or ethnicities, including multiracial.

\*Some college or AA degree means a person has either: attended university without completing a degree (Some college), or earned a 2-year college degree (AA/AS degree).

TABLE 2. Association of sleep-related disorders (categorical variable) with hypertension in postmenopausal women

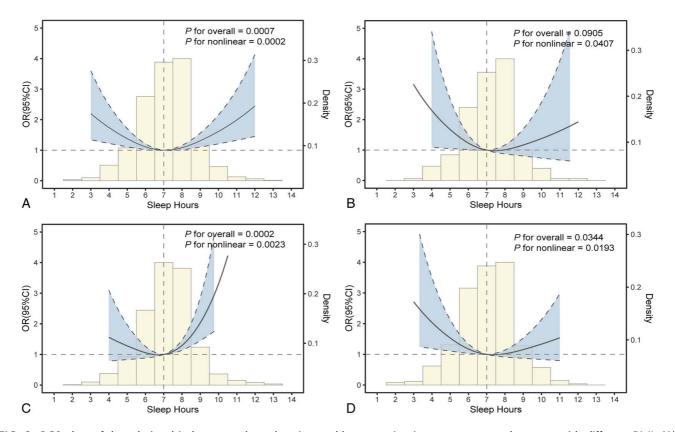
	Crude model <sup>a</sup> ;		Model 1 <sup>b</sup> ;		Model 2 <sup>c</sup> ;		Model 3 <sup>d</sup> ;	
Variables	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Trouble sleeping								
No	Ref	_	Ref	_	Ref	_	Ref	
Yes	1.51 (1.21-1.89)	< 0.001	1.74 (1.36-2.24)	< 0.001	1.61 (1.27-2.04)	< 0.001	1.61 (1.28-2.02)	< 0.001
Sleep duration								
Insufficient sleep	1.24 (0.96-1.60)	0.2	1.19 (0.89-1.59)	0.2	1.10 (0.84-1.45)	0.5	1.11 (0.85-1.46)	0.4
Mid-range sleep	Ref	_	Ref	_	Ref	_	Ref	
Excessive sleep	2.70 (1.73-4.22)	< 0.001	2.00 (1.18-3.39)	0.011	1.99 (1.12-3.54)	0.019	1.99 (1.10-3.60)	0.024
OSA								
No	Ref	_	Ref	_	Ref	_	Ref	_
Yes	1.61 (1.15-2.25)	0.007	1.88 (1.30-2.72)	0.002	1.66 (1.14-2.42)	0.01	1.63 (1.13-2.37)	0.013

OR, odds ratio; OSA, obstructive sleep apnea.

women reporting OSA symptoms (Table 2). Compared with participants without OSA, those with OSA-related symptoms had a higher prevalence of hypertension (crude model: OR = 1.61, 95% CI, 1.15-2.25), and this association remained in the fully adjusted model (OR = 1.63, 95% CI, 1.13-2.37).

### Subgroup analysis

The relationship between sleep-related disorders and hypertension in postmenopausal women was analyzed based on health-related factors. Interactions were found between BMI and the associations of trouble sleeping (P for interaction = 0.038) and sleep duration (P for interaction)



**FIG. 2.** RCS plots of the relationship between sleep duration and hypertension in postmenopausal women with different BMI. (A) Total participants. (B) Participants with a BMI  $< 25 \text{ kg/m}^2$ . (C) Participants with a BMI  $\ge 25 \text{ kg/m}^2$  and  $< 30 \text{ kg/m}^2$ . (D) Participants with a BMI  $\ge 30 \text{ kg/m}^2$ . Model adjusted for age group, ethnicity, education, marital status, poverty-to-income ratio, diabetes, CVD, physical activity, smoking, alcohol drinking, reproductive lifespan and total energy intake. BMI, body mass index; CVD, cardiovascular disease; RCS, restricted cubic spline.

<sup>&</sup>lt;sup>a</sup>Crude model: Without adjusted for any covariates.

<sup>&</sup>lt;sup>b</sup>Model 1: Adjusted for age group, ethnicity, education, marital status and poverty-to-income ratio.

Model 2: Further adjusted for body mass index, diabetes, cardiovascular disease, and reproductive lifespan based on model 1.

<sup>&</sup>lt;sup>d</sup>Model 3: Further adjusted for physical activity, smoking, alcohol drinking, and total energy intake based on model 2.

Sleep duration<sup>a</sup> **BMI** status OR (95% CI) P P for interaction Mid-range sleep  $<25 \text{ kg/m}^2$ Ref 0.044 Insufficient sleep  $<25 \text{ kg/m}^2$ 1.20 (0.78-1.86) 0.409 Excessive sleep  $<25 \text{ kg/m}^2$ 3.84 (1.29-11.45) 0.0191 Mid-range sleep  $25 - <30 \text{ kg/m}^2$ 1.63 (1.13-2.37) 0.012  $25 - <30 \text{ kg/m}^2$ 1.15 (0.73-1.80) 0.5539 Insufficient sleep  $25 - <30 \text{ kg/m}^2$ 3.80 (1.42-10.20) Excessive sleep 0.0102 Mid-range sleep  $\geq$ 30 kg/m<sup>2</sup> 2.28 (1.62-3.22) < 0.0001 Insufficient sleep  $\geq$ 30 kg/m<sup>2</sup> 3.32 (2.15-5.13) < 0.0001 Excessive sleep  $\geq$ 30 kg/m2 2.95 (1.32-6.58) 0.0107 0 12

TABLE 3. Association between sleep duration and hypertension in postmenopausal women with different BMI status

BMI, body mass index; OR, odds ratio.

"Model adjusted for age group, ethnicity, education, marital status, poverty-to-income ratio, diabetes, cardiovascular disease, physical activity, smoking, alcohol drinking, reproductive lifespan and total energy intake.

interaction = 0.044) with hypertension. No other interactions were observed (P for interaction > 0.05, Supplemental Table S4, Supplemental Digital Content 1, http://links.lww.com/MENO/B425). Thus, a stratified analysis based on BMI was conducted. Table 3 displays the relationship between sleep duration and hypertension stratified by BMI. Participants with a BMI of < 25 kg/m<sup>2</sup> and mid-range sleep were the reference group. In the fully adjusted model, participants with excessive sleep and a BMI of <25 kg/m<sup>2</sup> had a higher prevalence of hypertension (OR = 3.84, 95% CI, 1.29-11.45). Similarly, participants with a BMI of 25 to <30 kg/m<sup>2</sup> showed higher odds of hypertension with both mid-range and excessive sleep (mid-range sleep: OR = 1.63, 95% CI, 1.13-2.37; excessive sleep: OR = 3.80, 95% CI, 1.42-10.20). For participants with a BMI of 30 kg/m<sup>2</sup> or higher, all sleep durations were associated with a higher prevalence of hypertension (mid-range sleep: OR = 2.28, 95% CI, 1.62-3.22; insufficient sleep: OR = 3.32, 95% CI, 2.15-5.13; excessive sleep: OR = 2.95, 95% CI, 1.32-6.58). RCS analysis within BMI strata revealed no association between sleep duration and hypertension for participants with a BMI of  $\langle 25 \text{ kg/m}^2 \text{ } (P \text{ for overall } = 0.095).$ However, a U-shaped relationship was observed for participants with a BMI of 25 to  $< 30 \text{ kg/m}^2$  and those with a BMI of 30 kg/m<sup>2</sup> or higher (P for overall < 0.05, P for nonlinear < 0.05; Fig. 2B-D).

Table 4 presents the relationship between trouble sleeping and hypertension stratified by BMI. In the fully adjusted model, the following subgroups had an increased odds of hypertension compared with participants without trouble sleeping and a BMI of <25 kg/m<sup>2</sup>: those with

trouble sleeping and a BMI between 25 and  $< 30 \text{ kg/m}^2$  (OR = 2.21, 95% CI, 1.35-3.61), those without trouble sleeping and a BMI of 30 kg/m<sup>2</sup> or higher (OR = 1.72, 95% CI, 1.15-2.57), and those with trouble sleeping and a BMI of 30 kg/m<sup>2</sup> or higher (OR = 3.40, 95% CI, 2.22-5.22).

### **DISCUSSION**

In this study, we explored the relationship between sleep-related disorders and hypertension among postmenopausal women in the US. Our findings reveal several key insights: First, self-reported trouble sleeping and the presence of OSA symptoms are associated with elevated odds of hypertension. Second, a U-shaped relationship between sleep duration and hypertension was identified, with both insufficient and excessive sleep linked to a higher likelihood of hypertension. Lastly, we discovered an interaction between BMI and sleep duration and trouble sleeping, suggesting that the variations in hypertension prevalence across different BMI categories merit further investigation.

The prevalence of hypertension exhibits sex-specific variations, with both men and women experiencing an age-related rise in incidence rates. 18 However, the perimenopausal period is a critical time for the onset of hypertension in women. Prior study has indicated that premenopausal women exhibit a lower incidence of hypertension compared with age-matched men, whereas postmenopausal women tend to have a comparable or elevated prevalence. In this study, we observed a hypertension prevalence of 63.2% among postmenopausal women, aligning with existing literature. 19

Troubel sleeping<sup>a</sup> **BMI** status OR (95%CI) P for interaction No  $<25 \text{ kg/m}^2$ Ref 0.038 Yes  $<25 \text{ kg/m}^2$ 0.92 (0.58-1.45) 0.7268 No  $25 - <30 \text{ kg/m}^2$ 1.04 (0.68-1.61) 0.8491  $25 - <30 \text{ kg/m}^2$ 2.21 (1.35-3.61) Yes 0.0025 No  $\geq$ 30 kg/m<sup>2</sup> 1.72 (1.15-2.57) 0.0103  $\geq$ 30 kg/m<sup>2</sup> 3.40 (2.22-5.22) Yes < 0.0001

TABLE 4. Association between trouble sleeping and hypertension in postmenopausal women with different BMI status

BMI, body mass index; OR, odds ratio.

<sup>a</sup>Model adjusted for age group, ethnicity, education, marital status, poverty-to-income ratio, diabetes, cardiovascular disease, physical activity, smoking, alcohol drinking, reproductive lifespan and total energy intake.

Menopause is commonly accompanied by an increased risk of CVD and sleep disturbances.<sup>20,21</sup> Postmenopausal women commonly experience insomnia, with 53.3%-65.8% reporting difficulty during the transition.<sup>22</sup> Insomnia was tied to factors such as heightened sympathetic activity and impaired glucose metabolism, which raised hypertension risk. Despite this, the relationship between sleep duration and hypertension remains debated. While most studies have shown an association between short sleep duration and hypertension,<sup>23-25</sup> some of them suggested that long sleep duration may also increase the risk. For example, the Nurses' Health Study demonstrated that longer sleep duration ( $\geq 9$  h) was associated with a higher prevalence of hypertension,<sup>26</sup> and similar findings were observed in a study of over 50,000 adults in rural southwest China.<sup>24</sup> Our study also identified a U-shaped association between sleep duration and hypertension, aligning with previous studies like the United Kingdom (UK) Biobank that also report elevated BP among those with short and long sleep durations.<sup>27</sup> However, our logistic regression model did not detect an association between insufficient sleep (<7 h) and hypertension, possibly due to the underestimation of nonlinear effects. Similarly, no association was seen between sleep durations of 6 to < 7 hours and hypertension in women,<sup>28</sup> indicating potential sex differences in short sleep's impact. Despite this, short sleepers are more common than long sleepers, emphasizing short sleep's potential influence in real-world scenarios.<sup>29</sup> Further large-scale, rigorous studies are needed to clarify these relationships.

Our study also showed that postmenopausal women with self-reported trouble sleeping were more likely to have hypertension. Current research pointed to several potential mechanisms linking trouble sleeping and hypertension, including dysregulation of the hypothalamic-pituitary-adrenal axis, sympathetic nervous

system activation, and systemic inflammation. These factors contribute to sodium retention, increased cardiac output, arterial stiffness, and endothelial dysfunction, all of which promote hypertension.<sup>23</sup> A previous study also revealed that postmenopausal women with sleep disturbances exhibited heightened sympathetic responses during stress tests, further demonstrating the link between sleep troubles and sympathetic overactivity.<sup>20</sup> Similarly, a metaanalysis assessing sleep quality through the Pittsburgh Sleep Quality Index questionnaire also demonstrated that lower sleep quality was associated with a hypertension diagnosis.<sup>22</sup> Our study emphasized this relationship in postmenopausal women, highlighting the importance of considering sleep quality as a critical factor in assessing hypertension risk in this population. Furthermore, it is important to consider that some unmeasured factors, such as vasomotor symptoms (VMS)30 common during the perimenopausal period and depressive symptoms,<sup>31</sup> may play mediating or confounding roles. Recent evidence suggests that VMS may not only trigger and exacerbate sleep problems but also directly impact cardiovascular health, including the risk of hypertension.<sup>32</sup> Similarly, depression and sleep problems often coexist during perimenopause and may intensify sympathetic nervous system activation<sup>33</sup> and hypothalamic-pituitary-adrenal axis dysfunction,<sup>34</sup> thereby increasing cardiometabolic risk. Although this study was unable to adjust for these variables due to data limitations, their potential impact underscores the need for comprehensive assessment in future investigations to better elucidate the multifactorial pathways linking sleep-related disorders and hypertension in perimenopausal women.

Another important sleep-related disorder influencing hypertension in postmenopausal women is OSA. OSA is characterized by recurrent upper airway obstruction during sleep, leading to intermittent hypoxia, sleep

fragmentation, and BP fluctuations.<sup>35</sup> Hormonal changes during menopause, particularly increased abdominal fat and reduced upper airway muscle tone, elevate the risk of OSA in postmenopausal women.<sup>36</sup> Studies have shown that intermittent hypoxia and sleep fragmentation in OSA patients activate the sympathetic nervous system, trigger inflammatory pathways, and increase oxidative stress, all of which contribute to hypertension.<sup>37</sup> In this study, postmenopausal women with OSA symptoms had a higher likelihood of hypertension, consistent with previous findings.<sup>38</sup> Study in Brazil has shown that the prevalence of resistant hypertension is twice as high in OSA patients compared with those with primary hypertension.<sup>39</sup>

Obesity is another common condition among postmenopausal women, particularly in developed countries, and is closely associated with hypertension. Obese individuals exhibit higher sympathetic nervous activity, especially in the kidneys, which activates the reninangiotensin system and leads to hypertension.<sup>40</sup> We hypothesized that BMI played a moderating role in the relationship between sleep-related disorders and hypertension. Our stratified analysis revealed that postmenopausal women with higher BMI levels exhibited a stronger association between sleep disorders and hypertension. Specifically, among women with a BMI of  $\geq$  30 kg/m<sup>2</sup>, the odds of hypertension increased, regardless of sleep duration or trouble sleeping. Even among participants with a BMI < 25 kg/m<sup>2</sup>, excessive sleep was associated with increased odds of hypertension, suggesting that excessive sleep should be monitored in nonobese individuals as well. Although our findings did not reveal differences in the association between OSA symptoms and hypertension across different BMI levels, the well-established links between OSA, obesity, and hypertension suggest that further investigation is needed. 41 These results highlight the importance of managing body weight and sleep health as part of a comprehensive strategy to reduce hypertension risk in postmenopausal women.

This study has several limitations. First, the assessment of "trouble sleeping" was based on participants' selfreports from the NHANES database, specifically whether they have ever been diagnosed with or informed by a physician of having a sleep disorder. This assessment method has inherent limitations, as it primarily relies on participants proactively communicating their sleep problems to physicians and on physicians' timely recognition and confirmation. Consequently, sleep disorders in some menopausal women may not have been accurately captured or may have been underestimated. Sleep disturbances during menopause typically manifest as sleep fragmentation and frequent nighttime awakenings (such as increased wake after sleep onset),<sup>42</sup> which differ from the classic insomnia presentation characterized by difficulty initiating sleep or prolonged sleep latency. This discrepancy may lead to insufficient recognition of related sleep disorders by clinicians. Furthermore, this measurement method does not reflect participants' subjective perceptions of sleep quality. Future study should employ

approaches that combine subjective questionnaire assessments with objective sleep monitoring methods to more comprehensively evaluate sleep conditions in menopausal women. Second, the lack of data on VMS (eg, hot flashes and night sweats) in NHANES prevented us from examining their potential mediating role. Emerging evidence suggests that VMS may exacerbate both sleep problems<sup>34,43</sup> and cardiovascular risk in postmenopausal women.<sup>32</sup> Future studies incorporating VMS assessment are needed to clarify these relationships. In addition, the number of participants with excessive sleep duration was small in our sample, resulting in wide CIs for the associated ORs. This indicates that the estimates are statistically unstable and should be interpreted with caution. Further studies with larger sample sizes in this subgroup are needed to confirm these findings. Moreover, all subgroup analyses performed in this study were exploratory and not based on prior hypotheses. Therefore, the findings from these analyses should be interpreted with caution, as the conduct of multiple subgroup comparisons increases the likelihood of chance findings and type I errors. These results should be viewed as hypothesisgenerating rather than confirmatory. Last, due to the cross-sectional design of this study, causality and the temporal sequence between sleep disorders and hypertension cannot be established. It is possible that hypertension preceded the development of sleep-related disorders, rather than the other way around. Therefore, our findings should be interpreted as preliminary and primarily descriptive of associations at the population level. Longitudinal and experimental studies are needed to further clarify the directionality and underlying mechanisms of the observed associations.

#### CONCLUSIONS

Using cross-sectional data from NHANES 2007-2018, this study described the associations between sleep-related disorders (sleep duration, trouble sleeping, and OSA) and the odds of hypertension in postmenopausal women. The findings underscore the importance of improving sleep quality and managing BMI as key strategies for preventing hypertension in postmenopausal women.

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