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Short Sleep Is Associated With Low Bone Mineral Density and Osteoporosis in the Women's Health Initiative

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ABSTRACT

Short sleep duration, recognized as a public health epidemic, is associated with adverse health conditions, yet little is known about the association between sleep and bone health. We tested the associations of usual sleep behavior and bone mineral density (BMD) and osteoporosis. In a sample of 11,084 postmenopausal women from the Women's Health Initiative (WHI; mean age 63.3 years, SD = 7.4), we performed a cross-sectional study of the association of self-reported usual hours of sleep and sleep quality (WHI Insomnia Rating Score) with whole body, total hip, femoral neck, and spine BMD using linear regression models. We also studied the association of sleep duration and quality with dual-energy X-ray absorptiometry (DXA)-defined low bone mass (*T*-score < −2.5 to <−1) and osteoporosis (*T*-score ≤ −2.5) using multinomial regression models. We adjusted for age, DXA machine, race, menopausal symptoms, education, smoking, physical activity, body mass index, alcohol use, physical function, and sleep medication use. In adjusted linear regression models, women who reported sleeping 5 hours or less per night had on average 0.012 to 0.018 g/cm^2 significantly lower BMD at all four sites compared with women who reported sleeping 7 hours per night (reference). In adjusted multinomial models, women reporting 5 hours or less per night had higher odds of low bone mass and osteoporosis of the hip (odds ratio [OR] = 1.22; 95% confidence interval [CI] 1.03–1.45, and 1.63; 1.15–2.31, respectively). We observed a similar pattern for spine BMD, where women with 5 hours or less per night had higher odds of osteoporosis (adjusted OR = 1.28; 95% CI 1.02–1.60). Associations of sleep quality and DXA BMD failed to reach statistical significance. Short sleep duration was associated with lower BMD and higher risk of osteoporosis. Longitudinal studies are needed to confirm the cross-sectional effects of sleep duration on bone health and explore associated mechanisms. © 2019 American Society for Bone and Mineral Research.

KEY WORDS: SLEEP; SLEEP DURATION; BONE; DUAL-ENERGY X-RAY ABSORPTIOMETRY; BONE DENSITY; OSTEOPOROSIS

Introduction

Sleep is a fundamental biological process that plays a key role in a variety of metabolic and endocrine functions.[1] Poor sleep is linked to a broad range of adverse health conditions, including obesity,[2] diabetes, hypertension, cardiovascular disease,[3] and mortality.[4]

Low bone density and osteoporotic fractures are common manifestations of aging and associated with both greater risks of morbidity and mortality. Approximately one in three women

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age 50 years or older will experience a fracture in her lifetime.[5] To our knowledge, there are few large studies on the association between sleep health and bone health, including measurements of bone mineral density and osteoporosis risk. Since aging is associated with changes in bone resorption and bone formation,[6] it is prudent to conduct larger epidemiologic studies in postmenopausal women who are at highest fracture risk.

Here, we build on our prior work where we identified an association of short, long, and disturbed sleep with recurrent falls and fractures[7] to evaluate whether sleep behavior is also associated with bone mineral density (BMD). The goal of our study was to examine the association of sleep duration and quality with BMD at multiple body sites and prevalence of osteopenia and osteoporosis. We hypothesized that women with short sleep duration, long sleep duration, and poor sleep quality have lower BMD and are more likely to have low bone mass and osteoporosis.

Materials and Methods

Study population

The Women's Health Initiative (WHI) enrolled 161,808 postmenopausal women between the ages of 50 and 79 years at baseline at 40 clinical centers for clinical trials and an observational study. Here, we focused on the WHI DXA cohort, a group of women for whom dual-energy X-ray absorptiometry (DXA) was measured at one of three clinical centers (Pittsburgh, PA; Birmingham, AL; Tucson/Phoenix, AZ).[8] Approximately 11,323 women had a complete DXA scan at the WHI baseline visit. After excluding 239 women with incomplete sleep data, we had a final sample of 11,084 women.

DXA measurement

Hip, spine, and whole body DXA scans were performed using the Hologic QDR scanners (QDR 2000, 2000+, or 4500 W; Hologic, Waltham, MA, USA) by certified and trained operators. Scanners were calibrated daily with body mass phantoms according to the manufacturer's protocol. The WHI DXA coordinating center at the University of California at San Francisco monitored scans as a part of the WHI DXA Quality Assurance plan. Random samples of non-flagged scans as well as checks for outliers were also conducted as a part of the ongoing quality assurance program. Specific bone measures of interest include BMD of the total body, total hip, femoral neck, and spine (L_2 to L_4), all measured in g/cm^2. Women were further classified as having low bone mass (*T*-score between −2.5 and − 1) and osteoporosis (*T*-score ≤ −2.5) compared to normal (*T*-score ≥ −1).

Sleep variables

Sleep behavior was assessed at WHI baseline using self-administered questionnaires. The question on sleep duration asked, "About how many hours of sleep did you get on a typical night during the past 4 weeks? (≤5 hours, 6 hours, 7 hours, 8 hours, 9 hours, and ≥10 hours)." Sleep quality was assessed using the WHI Insomnia Rating Scale (WHIIRS), a composite index of sleep disturbance ranging from 0–20 with higher numbers indicating greater insomnia.[9] The score is calculated based on responses to five questions as part of a self-reported questionnaire focused on the past 4 weeks: "Did you have trouble falling asleep? Did you wake up several times at night? Did you wake up earlier than you planned to? Did you have trouble getting back to sleep after you woke too early? Overall, how was your typical night's sleep?"[9] This score was validated in two independent clinical trials and was sensitive to detect changes in sleep behavior associated with hormone therapy use.[10] For this analysis, the WHIIRS score was analyzed as a continuous variable with values ranging from 0 to 20 as well as using the cut-off of 9, which signifies insomnia.

Statistical analysis

For this cross-sectional study, we first performed descriptive and bivariate analyses to characterize the sample. We used multivariable-adjusted linear regression models to examine the associations of usual sleep duration and the WHIIRS with anatomic site-specific BMD measures (whole body, total hip, femoral neck, and spine). We classified the DXA measurements into *T*-scores (using the reference database of the Third National Health and Nutrition Examination Survey[11] for hip; Hologic reference databases were used for spine and whole body), which enabled us to evaluate the associations of sleep with risk of low bone mass (*T*-score between −2.5 and −1) and osteoporosis (*T*-score ≤ −2.5) compared with normal (*T*-score > −1) using multinomial logistic regression.

Using linear regression and multinomial logistic models, we estimated both crude (adjusted for age, scanner, menopausal symptoms, and race) and adjusted models. Race was classified into five categories (American Indian/Alaskan Native, Asian or Pacific Islander, black or African American, Hispanic/Latino, white [non-Hispanic], or other). Other covariates that we considered were measured via WHI baseline questionnaires and selected a priori based on published literature and include education, smoking, physical activity, and body mass index (BMI), alcohol use, physical function score, and sleep medication use. Menopausal symptoms were classified as none/mild or moderate/severe if women answered "yes" to having hot flashes or night sweats in the past 4 weeks. Education was coded as ≤high school, some college or vocational training, college graduate or more. Smoking status was categorical and women were classified as never, former, or current smokers. Physical activity was represented using MET-hours/week (<2.5, 2.5 to <5, 5 to <12, ≥12). BMI in kg/m^2 was modeled as a continuous variable. For alcohol use, women were classified as non-drinkers, past drinkers, or current drinkers (<1 drink per week, ≥1 drinks per week). The physical function score was measured by the 10-item Rand-36 physical function score[12] and dichotomized as <70, ≥70. Current sleep medication use was categorical and either yes or no.

We selected 7 hours of sleep per night as the reference group because this is the amount recommended for adults.[13] Sleep duration was recoded for the multinomial models where we analyzed sleep duration, collapsing 9 and 10 or more hours per night because of low numbers. Analyses were completed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

In a priori power calculations for linear regression, we assumed a mean BMD (femoral neck) of 0.72 g/cm^2 (SD = 0.12), alpha = 0.05, and used a two-sided test. We assumed the above parameters and an estimated sleep duration SD of 1.36 and found that we could detect a beta as small as 0.002. For sleep quality (WHIIRS), we assumed a SD of 4.5 and found that we could detect a beta coefficient as small as 0.001.

Results

With a mean age of 63.3 years (SD = 7.4), our postmenopausal sample is 78% non-Hispanic white. Approximately 10% of our sample reported sleeping 5 hours or less per night, and 4.5%

reported sleeping 9 or more hours per night. Approximately 33% of women met the threshold for insomnia, defined using the WHI insomnia rating score (Table 1). {TBL 1}

In covariate-adjusted linear regression models for total hip, femoral neck, spine and whole body BMD, women sleeping 5 hours or less per night had BMD values that were approximately 0.015, 0.012, 0.018, and 0.018 g/cm^2 lower compared with women who slept 7 hours per night (reference group; Table 2). {TBL 2} The spine and whole body BMD values were also lower on average for women who slept 6 hours per night, for a difference of approximately 0.01 g/cm^2 compared with women sleeping 7 hours/night.

In multinomial logistic models, women sleeping 5 hours or less per night had significantly higher odds of low bone mass of the total hip and whole body compared with women sleeping 7 hours per night; hip and total body odds ratios (ORs) were 1.22 and 1.37, respectively (Table 3). {TBL 3} Similarly, women sleeping 5 hours or less per night had higher odds of osteoporosis of the total hip, spine, and whole body; ORs were 1.63, 1.28, and 1.94, respectively. Women sleeping 6 hours per night had higher but slightly attenuated odds of spine and whole body osteoporosis (versus 7 hours per night), with ORs of 1.17 and 1.27, respectively. For femoral neck BMD, we failed to observe statistically significant associations with low bone mass or osteoporosis and sleep duration.

With regard to sleep quality and BMD, we found a mild protective effect for women in the 7–10 WHIIRS category versus the no insomnia group (0–3 score), where women in this category had 0.01 g/cm^2 higher hip and femoral neck BMD (95% CI_{hip} 0.001–0.014 and 95% $CI_{femoral\ neck}$ 0.001–0.013) compared with women with no insomnia; however, when adjusted for the full set of covariates, these associations became nonsignificant (data not shown).

In multinomial models, we observed a protective effect of insomnia on both femoral neck and spine low bone mass; women in the 7–10 and ≥11 WHI insomnia rating score category were less likely to have low bone mass at the femoral neck (crude OR_{7-10} 0.86, 95% CI 0.77–0.97; data not shown); however, these became nonsignificant with covariate adjustment. When we evaluated risk for low bone mass and osteoporosis according to the insomnia cut-off (WHIIRS <9 versus ≥9), we observed no statistically significant associations (data not shown).

Discussion

In the largest study of sleep and BMD to date in a US postmenopausal female sample, our findings indicate that short sleep in older adult women is associated with lower BMD at multiple body sites, albeit with modest clinical significance. Specifically, women who slept 5 hours or less had higher odds of low bone mass and osteoporosis of the total hip and whole body. The associations we identified are modest in terms of the continuous BMD measures when comparing across the different sleep duration categories. The difference we observed between the ≤5 hour per night group compared with the reference group was approximately −0.012 to −0.017 g/cm^2 (approximately 1.7% to 1.9%), which is roughly equivalent to 1 year of aging.[14,15]

Currently, the scant literature on the association of sleep and bone mineral density is limited to small cross-sectional studies, many of which are outside of the U.S. The largest US study, The South Dakota Rural Bone Health Study, showed that short sleep (<6.5 h/night) was associated with lower cortical volumetric BMD (vBMD) at the 20% distal radius in a sample of 348 women.[16] These findings of lower BMD with short sleep were supported by a Chinese study (n = 602 women); women older than 45 years who slept ≤6 hours per night (versus 8 h/night) had lower total and regional BMD.[17] The authors observed no significant associations in the <45-year-old women, which is not surprising given that bone loss begins during perimenopause. In a more recent study of 512 women aged 45 to 65 years by Lucassen and colleagues, the authors reported a smaller and nonsignificant effect size for sleep duration and hip BMD (beta = −0.004) than we did (−0.016 for hip BMD).[18] Our study, which was larger and had better representation of women older than 65 years, may have had more power to detect the association of short sleep and a higher prevalence of low BMD.

Conversely, long sleep has also been associated with lower BMD.[19–21] A Korean study that included 1274 women older than 60 years found a significant trend of lower BMD of the total hip and femoral neck with increasing sleep duration.[19] The covariate-adjusted betas were − 0.007 and − 0.005 for total hip and femoral neck, respectively. In a French sample that included 290 women, long sleepers (≥8 hours) were more likely to have osteoporosis at the femoral neck (OR = 6.29, 95% CI 1.51–15.92).[21] Two other studies were null for sleep duration and BMD; one in Iceland that analyzed vBMD of the femur, and the other was a study of Puerto Rican women that analyzed total and regional BMD.[20] Although our current analysis did not show an association between long sleeping and BMD, this may be due to low power and the fact that few women in our sample (<1%) reported sleeping 10 or more hours/night. The negative coefficients we observed for the ≥10-hour group was suggestive of lower BMD in that group, similar to our odds ratio estimates for osteoporosis, which were suggestive of higher odds.

Short sleep duration (<6 hours) was associated with osteoporosis in a sample of women aged 50 years or older in NHANES.[22] Results from a large Japanese study indicate that long sleep duration (>8 hours) is associated with higher risk of osteoporosis.[23] Findings from a Chinese study suggest that short sleep, long sleep, and daytime napping is associated with higher odds of osteoporosis; these findings were limited to postmenopausal women.[24]

The prior literature shows only few studies focused on the association of sleep quality and DXA. Lucassen and colleagues reported an inverse association of the Pittsburgh Sleep Quality Index (PSQI) and BMD in a sample of 512 Dutch women, where a one-unit-higher PSQI score (higher values represent poorer sleep quality) was associated with reduced hip and spine BMD of approximately 0.003 g/m^2. This study also reported that a one-unit increase in PSQI was associated with higher osteopenia risk (OR = 1.08, 95% CI 1.00–1.17). The PSQI includes a dimension of sleep duration, while our questionnaire does not. Therefore, their significant findings may in part be driven by the influence of sleep duration. The protective effect of insomnia on femoral neck and spine BMD that we observed for the low bone mass outcome may be due to women being out of bed more often. We adjusted for physical activity; however, this does not represent the activity occurring in the early morning hours resulting from lack of sleep. This finding may also be due to chance. Studies including objective assessments of sleep are needed.

This large cohort of postmenopausal women supported the in-depth examination of the associations of bone health with sleep duration and quality. Our analysis focused on postmenopausal women who are at highest risk for low bone mass and osteoporosis. Our results were unchanged when we added comorbidities and hormone therapy use to the models (data

Table 1. Characteristics in Women's Health Initiative (WHI) Bone Mineral Density (BMD) Cohort by Hours of Sleeping Per Night

		Self-reported usual sleep duration (*n* [%] or mean [SD])						
	Total 11,084	≤5 hours 1080	6 3157	7 4025	8 2320	9 405	≥10 hours 97	*p* Value
Age (years)	63.3 (7.4)	63.2 (7.9)	63.2 (7.4)	63.3 (7.3)	63.4 (7.2)	63.9 (7.5)	61.8 (7.4)	0.137
Race/ethnicity (*n* = 11,066)								
White, non-Hispanic	8624 (77.9)	689 (63.8)	2384 (75.6)	3300 (82.1)	1897 (82.1)	306 (75.7)	48 (49.5)	
African American	1534 (13.9)	287 (26.6)	518 (16.4)	416 (10.3)	228 (9.9)	58 (14.4)	27 (27.8)	
Hispanic/Latino	676 (6.1)	71 (6.6)	192 (6.1)	220 (5.5)	141 (6.1)	31 (7.7)	21 (21.6)	
American Indian or Alaskan Native	139 (1.3)	16 (1.5)	32 (1.0)	56 (1.4)	29 (1.3)	5 (1.2)	1 (1.0)	<0.001
Asian or Pacific Islander	36 (0.3)	8 (0.7)	10 (0.3)	13 (0.3)	5 (0.2)	0 (0.0)	0 (0.0)	
Other	57 (0.5)	9 (0.8)	18 (0.6)	15 (0.4)	11 (0.5)	4 (1.0)	0 (0.0)	
Education (*n* = 11,007)								
≤High school	3451 (31.4)	420 (39.2)	992 (31.6)	1168 (29.2)	706 (30.7)	125 (31.2)	40 (42.1)	<0.001
Some college or vocational training	4173 (37.9)	408 (38.1)	1200 (38.2)	1523 (38.1)	856 (37.2)	149 (37.2)	37 (38.9)	
College graduate	3383 (30.7)	244 (22.8)	947 (30.2)	1306 (32.7)	741 (32.2)	127 (31.7)	18 (18.9)	
Body mass index (kg/m^2) (*n* = 11,014)	28.2 (5.9)	29.5 (6.5)	28.5 (5.9)	27.7 (5.6)	27.9 (5.7)	28.8 (6.0)	30.0 (6.7)	<0.001
Recreational physical activity (*n* = 9883)								
<2.5 MET h/week	2919 (29.5)	369 (37.6)	864 (30.5)	959 (26.8)	572 (27.9)	117 (32.5)	38 (44.2)	<0.001
2.5 to <5 MET h/week	1209 (12.2)	149 (15.2)	357 (12.6)	414 (11.6)	245 (12.0)	34 (9.4)	10 (11.6)	
5 to <12 MET h/week	2280 (23.1)	198 (20.2)	668 (23.6)	874 (24.4)	452 (22.1)	76 (21.1)	12 (14.0)	
≥12 MET h/week	3475 (35.2)	266 (27.1)	942 (33.3)	1,328 (37.1)	780 (38.1)	133 (36.9)	26 (30.2)	
Alcohol intake (*n* = 10,994)								
Non-drinker	1852 (16.8)	234 (21.8)	519 (16.6)	637 (15.9)	384 (16.7)	60 (15.0)	18 (18.9)	<0.001
Past drinker	2442 (22.2)	287 (26.8)	725 (23.2)	815 (20.4)	479 (20.8)	99 (24.7)	37 (38.9)	
<1 drink per month	1432 (13.0)	140 (13.1)	412 (13.2)	525 (13.1)	282 (12.3)	65 (16.2)	8 (8.4)	
<1 drink per week	2139 (19.5)	190 (17.7)	622 (19.9)	813 (20.3)	436 (19.0)	65 (16.2)	13 (13.7)	
1 to <7 drinks per week	2229 (20.3)	162 (15.1)	616 (19.7)	870 (21.8)	496 (21.6)	73 (18.2)	12 (12.6)	
≥7 drinks per week	900 (8.2)	58 (5.4)	235 (7.5)	339 (8.5)	222 (9.7)	39 (9.7)	7 (7.4)	
Smoking status (*n* = 10,937)								
Never	5948 (54.4)	602 (56.3)	1710 (55.0)	2158 (54.2)	1232 (53.9)	204 (51.4)	42 (44.2)	<0.001
Former	4100 (37.5)	369 (34.5)	1112 (35.8)	1524 (38.3)	898 (39.3)	159 (40.1)	38 (40.0)	
Current	889 (8.1)	98 (9.2)	288 (9.3)	298 (7.5)	156 (6.8)	34 (8.6)	15 (15.8)	
Age at menopause								
Mean (SD)	47.5 (6.9)	46.1 (7.5)	47.5 (7.0)	47.7 (6.8)	47.7 (6.6)	48.0 (6.6)	47.3 (6.8)	<0.001
Missing	1124	116	309	399	245	44	11	
Hormone therapy use (*n* = 1079)								
Never used	5257 (47.5)	566 (52.4)	1518 (48.1)	1838 (45.7)	1097 (47.3)	182 (44.9)	56 (57.7)	<0.001
Past user	1762 (15.9)	189 (17.5)	490 (15.5)	656 (16.3)	343 (14.8)	68 (16.8)	16 (16.5)	
Current user	4060 (36.6)	325 (30.1)	1145 (36.3)	1531 (38.0)	879 (37.9)	155 (38.3)	25 (25.8)	

(Continues)

Table 1. Continued

	Total	Self-reported usual sleep duration (*n* [%] or mean [SD])						
	Total 11,084	≤5 hours 1080	6 3157	7 4025	8 2320	9 405	≥10 hours 97	*p* Value
Hot flash or night sweats in past 4 weeks								
No/mild	9787 (88.8)	827 (77.3)	2776 (88.4)	3652 (91.3)	2104 (91.0)	354 (88.7)	74 (77.1)	<0.001
Moderate/severe	1231 (11.2)	243 (22.7)	365 (11.6)	349 (8.7)	207 (9.0)	45 (11.3)	22 (22.9)	
Missing	66	10	16	24	9	6	1	
Diet and supplemental calcium intake	1113 (719)	1018 (682)	1073 (717)	1147 (714)	1158 (742)	1122 (728)	945 (669)	<0.001
Missing	28	1	6	9	11	1	0	
Diet and supplemental vitamin D intake	8.1 (6.6)	7.3 (6.2)	7.9 (6.7)	8.4 (6.5)	8.4 (6.9)	8.3 (6.6)	6.9 (6.4)	<0.001
Missing	29	1	6	10	11	1	0	
Hypnotics								
No	10,963 (98.9)	1052 (97.4)	3126 (99.0)	3988 (99.1)	2303 (99.3)	400 (98.8)	94 (96.9)	<0.001
Yes	121 (1.1)	28 (2.6)	31 (1.0)	37 (0.9)	17 (0.7)	5 (1.2)	3 (3.1)	
WHI Insomnia Rating Score								
0–3	2956 (26.7)	102 (9.4)	628 (19.9)	1194 (29.7)	852 (36.7)	153 (37.8)	27 (27.8)	<0.001
4–6	2927 (26.4)	106 (9.8)	700 (22.2)	1197 (29.7)	762 (32.8)	136 (33.6)	26 (26.8)	
7–10	2849 (25.7)	217 (20.1)	885 (28.0)	1115 (27.7)	526 (22.7)	84 (20.7)	22 (22.7)	
≥11	2352 (21.2)	655 (60.6)	944 (29.9)	519 (12.9)	180 (7.8)	32 (7.9)	22 (22.7)	
Insomnia Rating Score cut-off								
<9	7457 (67.3)	303 (28.1)	1790 (56.7)	3019 (75.0)	1942 (83.7)	342 (84.4)	61 (62.9)	<0.001
≥9	3627 (32.7)	777 (71.9)	1367 (43.3)	1006 (25.0)	378 (16.3)	63 (15.6)	36 (37.1)	
Total hip BMD (g/cm^2)	0.852 (0.139)	0.860 (0.149)	0.856 (0.142)	0.848 (0.133)	0.847 (0.138)	0.853 (0.144)	0.884 (0.163)	0.005
Femoral neck BMD (g/cm^2)	0.724 (0.127)	0.737 (0.141)	0.728 (0.129)	0.719 (0.122)	0.718 (0.126)	0.730 (0.129)	0.757 (0.142)	<0.001
Anterior-posterior spine BMD (g/cm^2)	0.980 (0.168)	0.983 (0.171)	0.979 (0.172)	0.980 (0.165)	0.979 (0.168)	0.995 (0.173)	0.991 (0.161)	0.533
Whole body BMD (g/cm^2)	1.013 (0.106)	1.007 (0.109)	1.013 (0.105)	1.014 (0.105)	1.013 (0.109)	1.017 (0.102)	1.017 (0.112)	0.460

The *p* value is ANOVA or chi-square.

Table 2. Linear Regression Models for Bone Mineral Density (BMD; g/cm^2) and Usual Sleep Duration

		Model 1	Model 2
	n	Beta (95% CI)	Beta (95% CI)
Total hip BMD			
≤5 hours	1080	−0.007 (−0.016, 0.001)	−0.015 (−0.024, −0.006)
6 hours	3157	0.001 (−0.005, 0.007)	−0.002 (−0.008, 0.004)
7 hours	4025	Reference	Reference
8 hours	2320	0.0001 (−0.006, 0.006)	−0.002 (−0.008, 0.005)
9 hours	405	0.005 (−0.008, 0.018)	−0.002 (−0.015, 0.011)
≥10 hours	97	0.008 (−0.018, 0.033)	−0.007 (−0.034, 0.020)
Overall *F*-test		0.428	0.033
Femoral neck BMD			
≤5 hours	1080	−0.004 (−0.011, 0.004)	-0.012 (−0.019, −0.004)
6 hours	3157	0.001 (−0.005, 0.006)	−0.002 (−0.007, 0.003)
7 hours	4025	Reference	Reference
8 hours	2320	0.001 (−0.005, 0.006)	−0.001 (−0.007, 0.005)
9 hours	405	0.010 (−0.001, 0.022)	0.001 (−0.011, 0.013)
≥10 hours	97	0.008 (−0.015, 0.030)	−0.008 (−0.032, 0.016)
Overall *F*-test		0.421	0.078
Spine BMD			
≤5 hours	1080	−0.010 (−0.021, 0.002)	−0.018 (−0.029, −0.006)
6 hours	3157	−0.005 (−0.012, 0.003)	−0.008 (−0.016, −0.001)
7 hours	4025	Reference	Reference
8 hours	2320	0.000 (−0.008, 0.009)	−0.001 (−0.010, 0.008)
9 hours	405	0.014 (−0.003, 0.031)	0.006 (−0.012, 0.023)
≥10 hours	97	−0.007 (−0.041, 0.026)	−0.031 (−0.068, 0.005)
Overall *F*-test		0.156	0.010
Whole body BMD			
≤5 hours	1080	−0.015 (−0.021, −0.008)	−0.018 (−0.025, −0.011)
6 hours	3157	−0.004 (−0.008, 0.001)	−0.005 (−0.010, −0.0001)
7 hours	4025	Reference	Reference
8 hours	2320	−0.000 (−0.005, 0.005)	−0.001 (−0.006, 0.005)
9 hours	405	0.002 (−0.008, 0.012)	−0.005 (−0.015, 0.006)
≥10 hours	97	−0.013 (−0.033, 0.007)	−0.022 (−0.044, 0.001)
Overall *F*-test		<0.001	<0.001

Model 1 adjusted for DXA serial number, age, menopausal symptoms, and race.
Model 2 adjusted for model 1 plus education, smoking, physical activity, body mass index, alcohol use, physical function score, and sleep medication use.

not shown). It is important to consider the possibility of reverse causality on the sleep-BMD hypothesis, since lower BMD may be associated with factors that influence sleep behavior. Here, we focused on the WHI baseline visit, where postmenopausal women were generally healthy and free of chronic conditions. Although our analysis is limited by its cross-sectional nature and self-reported sleep behavior, we found clear evidence to justify further investigations of the associations of sleep with bone health and the underlying mechanisms. However, because we evaluated multiple DXA sites, we conducted multiple statistical tests and some significant findings may be attributable to chance. Future studies may use more objective measures of sleep, such as waist-wearing actigraphy device to improve quality of sleep data, and should include the additional consideration of bone microarchitecture. While the mechanisms for the association of sleep duration and BMD are not known, inadequate sleep duration is thought to impact hormone levels, sympathetic activation,[25,26] inflammatory processes,[27,28] and involve metabolic derangement. In a meta-analysis, short sleep duration was associated with higher levels of C-reactive protein, supporting a role of inflammation.[28] Further support for a biological explanation for sleep and bone associations comes from the ability of insufficient sleep to disrupt the circadian rhythm of bone turnover markers.[6,29,30]

In sensitivity analyses, we stratified by race in linear regression models given the differences in sleep duration; African Americans in our sample had a higher frequency of short sleep duration and are known to have higher BMD compared with whites.[31] For whites, the sleep-BMD associations in whites are unchanged. For African Americans, although none of the sleep duration-BMD associations reached statistical significance, the coefficients were in a similar direction, suggesting that short sleep is associated with lower BMD. It is difficult to discern whether the lack of significance is due to low power, given the sample size. Nonetheless, it is important for future studies to evaluate these associations in larger samples, given the higher prevalence of short sleep in African Americans.[32]

In summary, we have provided epidemiologic evidence into sleep as a partially modifiable risk factor for BMD that is deserving of further replication and mechanistic studies. Prospective studies are needed to evaluate whether sleep duration is associated with BMD loss and the short- and long-term effects of

Table 3. Multinomial Logistic Regression of Sleep Duration and Odds of Low Bone Mass or Osteoporosis Compared With Normal Bone Mass

	Low bone mass versus normal			Osteoporosis versus normal			
	n	Model 1[1] OR (95% CI)	Model 2[2] OR (95% CI)	*n*	Model 1[1] OR (95% CI)	Model 2[2] OR (95% CI)	*p* Value*
Total hip							
≤5 hours	419	1.07 (0.92, 1.25)	1.22 (1.03, 1.45)	67	1.45 (1.07, 1.97)	1.63 (1.15, 2.31)	0.135
6 hours	1239	1.01 (0.91, 1.11)	1.01 (0.90, 1.14)	161	1.04 (0.84, 1.31)	1.10 (0.86, 1.42)	
7 hours	1595	Reference	Reference	207	Reference	Reference	
8 hours	947	1.03 (0.92, 1.14)	1.02 (0.90, 1.15)	111	0.94 (0.73, 1.20)	0.99 (0.74, 1.31)	
9+ hours	188	0.92 (0.75, 1.13)	1.03 (0.81, 1.30)	30	1.17 (0.76, 1.78)	1.45 (0.91, 2.32)	
Femoral neck							
≤5 hours	534	0.97 (0.84, 1.13)	1.07 (0.90, 1.27)	111	1.12 (0.87, 1.44)	1.30 (0.97, 1.74)	0.657
6 hours	1584	0.94 (0.85, 1.04)	0.97 (0.86, 1.09)	326	1.01 (0.85, 1.20)	1.11 (0.91, 1.35)	
7 hours	2100	Reference	Reference	415	Reference	Reference	
8 hours	1202	0.96 (0.86, 1.08)	0.96 (0.85, 1.09)	243	0.99 (0.82, 1.20)	1.05 (0.84, 1.30)	
9+ hours	259	0.95 (0.77, 1.16)	1.11 (0.87, 1.41)	45	0.82 (0.57, 1.18)	1.11 (0.74, 1.68)	
Spine							
≤5 hours	416	1.07 (0.92, 1.24)	1.07 (0.90, 1.26)	186	1.13 (0.93, 1.38)	1.28 (1.02, 1.60)	0.264
6 hours	1193	1.04 (0.94, 1.15)	1.06 (0.94, 1.19)	537	1.13 (0.99, 1.30)	1.17 (1.00, 1.37)	
7 hours	1513	Reference	Reference	610	Reference	Reference	
8 hours	833	0.94 (0.84, 1.05)	0.94 (0.83, 1.07)	373	1.03 (0.89, 1.20)	1.08 (0.91, 1.28)	
9+ hours	180	0.87 (0.71, 1.07)	0.91 (0.73, 1.15)	71	0.81 (0.60, 1.08)	1.03 (0.75, 1.41)	
Whole body							
≤5 hours	466	1.31 (1.13, 1.52)	1.37 (1.17, 1.62)	82	1.82 (1.37, 2.43)	1.94 (1.42, 2.67)	<0.001
6 hours	1310	1.08 (0.97, 1.19)	1.08 (0.96, 1.20)	195	1.22 (0.99, 1.50)	1.27 (1.00, 1.60)	
7 hours	1657	Reference	Reference	224	Reference	Reference	
8 hours	927	0.96 (0.86, 1.08)	0.95 (0.85, 1.08)	160	1.25 (1.00, 1.56)	1.27 (0.99, 1.63)	
9+ hours	185	0.88 (0.72, 1.08)	0.97 (0.78, 1.22)	34	1.18 (0.79, 1.77)	1.29 (0.82, 2.03)	

[1] Model 1 adjusted for DXA serial number, age, menopausal symptoms, and race.
[2] Model 2 adjusted for model 1 plus education, smoking, physical activity, body mass index, alcohol use, physical function score, and sleep medication use.
*p value is overall type 3 Wald test for multinomial logistic model 2.

unhealthy sleep patterns on bone health. If studies show that sleep duration has a causal link with bone density, sleep promotion interventions may serve as a way to mitigate bone loss in individuals at high risk of osteoporosis.

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