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# Association between sleep quality and bone mineral density in Chinese women vary by age and menopausal status

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**Abstract**

*Objective*: Sleep quality is closely related to bone health. Aging and estrogen deficiency are known determinants of poor sleep quality and osteoporosis. However, the impact of aging and menopause on the associations between sleep quality and bone mineral density (BMD) remains unclear. This study aimed to examine the association between sleep quality and BMD in Chinese women vary by age groups and menopausal status.

*Methods*: A total of 2067 women aged 18–80 years were included. Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI) and the score >7 was indicative of poor sleep quality. BMD was determined using the dual-energy X-ray absorptiometry. Participants were categorized into three age groups. Multiple linear regression models were conducted to evaluate the associations between sleep quality and BMD. Covariates included in the models were age, menopausal status, weight, height, percent body fat, physical activity, alcohol drinking, calcium supplement use, marital status, education and metabolic diseases.

*Results*: We observed that poor sleep quality was correlated to low total BMD and legs BMD in middle-aged women after adjusting for potential confounders. When we further reran the regression models based on menopausal status in middle-aged women, significant associations between BMD and sleep quality were observed in premenopausal and early postmenopausal groups.

*Conclusion*: Our findings showed a more robust association between sleep quality and

BMD in premenopausal and early menopausal groups. Further studies should be conducted to explore whether sleep quality intervention would improve bone health of women in this period and prevent osteoporosis in their late life.

*Keywords*:

Bone mineral density

Sleep quality

Middle age

Menopause

Osteoporosis

## 1. Introduction

Osteoporosis, characterized by reduced bone mass and bone tissue, has been listed as one of the National Health Priorities in China since 2011 because of its high disease and economic burden [1]. The prevalence of osteoporosis in China is approximately 13% [2]. Women have a three-fold higher risk of developing osteoporosis than men [2,3]. It is widely accepted that aging and menopause are strong determinants of bone mineral density (BMD) [4]. BMD starts to decrease sharply around middle age, particularly in the first 5 years after menopause [4]. BMD measured by dual X-ray absorptiometry (DXA), has been widely accepted as a gold standard to diagnose osteoporosis [5].

Nutrition, physical activity, and other lifestyle factors play important roles in maintaining bone health [6,7]. Sleep quality has been found to closely relate to several endocrine and metabolic dysfunctions, that are involved in bone metabolism [8]. Previous studies suggested an inverted U-shaped relationship between sleep duration and BMD [9,10]. Several other studies showed that self-reported sleep quality [11] and sleep disturbance [12] were associated with osteoporosis. However, since sleep evaluation involves both quantitative and qualitative aspects, measuring only one aspect like sleep duration or self-reported sleep quality is insufficient. Recently, the Pittsburgh Sleep Quality Index (PSQI) including self-reported sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, sleep medicine and

daytime dysfunction was widely used in evaluating sleep [13–15]. In 2016, the Hiroshima Sleep and Healthcare study reported that PSQI score was negatively associated with bone stiffness index [13]. In 2017, the Netherlands Epidemiology of Obesity study pointed out that decreased PSQI score was related to increased risk of osteoporosis in middle-aged, overweight men and women [14]. Compared to single factor measurements, PSQI score is more comprehensive and has been proven to have excellent reliability and validity [16,17].

Similar to osteoporosis, sleep quality is also influenced by aging and menopause. Sleep quality decreases from early adulthood to middle age but without further decline in the transition from middle age to late life [18]. In addition, symptoms of menopause, such as hot flashes, irritability, and depressed mood, make women more likely to have worse sleep quality [19]. However, it is still unclear whether the associations between sleep quality and BMD are affected by age or menopausal status. Therefore, the aim of this study was to investigate whether the associations between sleep quality and BMD differed across age groups and menopausal status in Chinese women.

## 2. Material and methods

### 2.1 Participants

A total of 2067 women, aged 18–80 years, were included from the baseline survey of a cohort study conducted in an urban area of Lanxi, Zhejiang, China in 2015. Participants without information on DXA (*N*=35), sleeping (*N*=54) or menopause (*N*=40) were excluded from the analyses. Other exclusion criteria included malignant tumor (*N*=84), anti-osteoporosis medication (*N*=9). A final size of 1845 participants was included in the analyses. This study was approved by the Ethics Committee of the School of Public Health at Zhejiang University. Written informed consents were obtained from participants.

### 2.2 Sleep measurement

The PSQI was adopted to measure sleep quality [16,17,20]. The questionnaire consisted of 19 questions in seven components. These seven components were weighed equally using an ordinal scale ranged from 0 to 3. A PSQI score ranging from 0 to 21 was summed, with higher score indicating worse sleep quality. A PSQI score ≤7 and >7 was defined as ‘good sleep quality’ and ‘poor sleep quality’, respectively [17]. The Chinese version of the PSQI has been validated in mainland China as a reliable evaluating measure, and a global PSQI score over 7 (equal to PSQI ≥8) has been recommended in Chinese clinical practice and research [17,21–24].

### 2.3 Bone mineral measurements

Total and regional BMD and percent body fat were measured using the DXA (GE-lunar Prodigy, WI, USA) through whole-body scans. Regional BMD referred to the mean bone density in head, arms, ribs, trunk, spine, pelvis, and legs. DXA was calibrated daily with a standard phantom provided by the manufacturer. Measurements were maintained within the manufacturer's precision standard of 0.8%.

### 2.4 Age group and menopausal status

Age was divided into three groups: 18–44 years old, 45–64 years old, and ≥65 years old. Menopause was defined when there had been a complete natural cessation of menses for more than 12 months. Postmenopausal women were further divided into early postmenopausal and late postmenopausal according to the stages of reproductive aging workshop. Early postmenopausal was defined as absence of menstrual periods for at least 12 months and less than 5 years. Late postmenopausal was defined as absence of menstrual periods for 5 years or more [25].

### 2.5 Covariates measurements

Weight and height were measured with participants wearing light clothing and without shoes and were recorded to the nearest 0.1 kg (SECA704, USA) and 0.1 cm, respectively. All values were recorded as the average of three measures. Physical

activity, calcium supplement use, alcohol drinking, education, marital status and medical history (disease history, drug history) were collected through face-to-face interview. Physical activity was measured by the International Physical Activity Questionnaire short form [26], and was classified as low, moderate, or high. Education was leveled as primary, middle and college or above. In the present study, education level was selected as an indicator of socioeconomic status considering the following distinctive features of education level: (1) it is a determinant of future occupation and income; (2) it hardly changes during life; and (3) it is relatively easier to measure educational level than to measure other socioeconomic status indicators using a questionnaire [27,28]. Marital status was classified as never, married, and divorced or widowed. Participants who had a fasting serum glucose ≥7.0 mmol/L or a history of diagnosed type 2 diabetes were defined as having type 2 diabetes [29]. Hypertension was diagnosed according to the Seventh Joint National Commission recommendation: systolic blood pressure of 140 mmHg or greater or diastolic blood pressure of 90 mmHg or greater or a history of diagnosed hypertension [30]. Dyslipidemia was defined as self-reported dyslipidemia or meeting any of the following criteria: total cholesterol of 6.2 mmol/L or greater, triglycerides greater than 2.25 mmol/L, low-density lipoprotein cholesterol greater than 4.13mmol/L, high-density lipoprotein cholesterol lower than 1.03 mmol/L [31]. Participants with any diseases mentioned above were defined as having metabolic diseases.

**2.6 Statistical analyses**

The characteristics of the participants were summarized as mean ± standard deviation (SD) for continuous variables and as frequency (percentages) for the categorical variables by age groups. The differences among age groups were tested using analyses of variance (ANOVA) for continuous variables and chi-squared tests for categorical variables. The differences of BMD between sleep quality groups in different age groups were tested using Student's *t*-test. Multiple linear regression models were conducted to examine the associations between sleep quality and BMD in different age groups. The relationships between sleep quality and total and regional BMD were tested after adjusting for age, menopausal status, weight, height, percent body fat, physical activity, supplementation use, alcohol drinking, education, marital status, and metabolic diseases. We further divided middle-aged women into three groups according to menopausal status and reran the models. A value of $p<0.05$ (two sided) was considered statistically significant. Stata version 13 was used for data analyses (Stata Corporation, College Station, TX).

## 3. Results

The characteristics of participants are shown in Table 1. Participants with older age were more likely to have lower total and regional BMD (all $p<0.05$). Compared to participants in the young group (18–44 years old), participants in middle-aged group (45–64 years old) and elder group (age ≥65 years old) were more likely to have poor sleep quality ($p<0.05$). Significant differences were found in height, weight, percent body fat, marital status, and metabolic diseases across all the age categories (all $p<0.001$). Participants in the middle-aged group had the highest height and were more likely to be married (both $p<0.05$). Participants in the elder age group had lower education levels and were more likely to have metabolic disease (both $p<0.05$). There were no significant differences in the rate of drinkers across age groups ($p>0.05$).

**Table 1**. Descriptive characteristics of study participants.

| Variables | Total | Age (years) | | | |
|---|---|---|---|---|---|
| *N* (%) or mean (SD) | (*N*=1845) | <45 (*N*=511) | 45–64 (*N*=1004) | ≥65 (*N*=330) | *p* |
| Age, y | 51.80 ± 12.76 | 35.93 ± 6.58[§] | 53.97 ± 5.67[#] | 69.79± 4.19[†] | **0.000** |
| Height, cm | 156.25 ± 5.23 | 157.84 ± 4.85[§] | 156.49 ± 4.96[#] | 153.05 ± 5.23[†] | **0.000** |
| Weight, kg | 56.45 ± 8.56 | 55.53 ± 8.82[§] | 57.31 ± 8.44[#] | 55.23 ± 8.24 | **0.000** |
| % Body fat | 33.14± 5.67 | 31.94 ± 5.94[§] | 33.61 ± 5.27 | 33.54 ± 6.11[†] | **0.000** |
| Postmenopausal, *N* (%) | 1008 (54.63) | 14 (2.74)[§] | 664 (66.14)[#] | 330 (100.00)[†] | **0.000** |
| Married, *N* (%) | 1630 (88.35) | 444 (86.89)[§] | 938 (93.43)[#] | 248 (75.15)[†] | **0.000** |
| Education, *N* (%) | | | | | |
| Primary or below | 649 (35.20) | 28 (5.49)[§] | 389 (38.75)[#] | 232 (70.30)[†] | **0.000** |
| Calcium supplement, *N* (%) | 142 (7.70) | 30 (5.87) | 71 (7.07)[#] | 41 (12.42)[†] | **0.001** |
| Lifestyle factors, *N* (%) | | | | | |
| Alcohol drinking | 589 (31.94) | 163 (31.90) | 336 (33.47) | 90 (27.36) | 0.119 |
| Low activity | 498 (26.99) | 171 (33.46)[§] | 246 (24.50) | 81 (24.55) | **0.002** |
| Metabolic diseases, *N* (%) | 900 (48.78) | 105 (20.55)[§] | 542 (53.98)[#] | 253 (76.67)[†] | **0.000** |
| Good sleep quality, *N* (%) | 1570 (85.09) | 468 (91.59)[§] | 836 (83.27) | 266 (80.61)[†] | **0.000** |
| Total BMD, g/cm$^2$ | 1.06 ± 0.10 | 1.11 ± 0.07[§] | 1.06 ± 0.10[#] | 0.96 ± 0.09[†] | **0.000** |
| Head BMD, g/cm$^2$ | 2.11 ± 0.31 | 2.27 ±0.24[§] | 2.10 ± 0.31[#] | 1.86 ± 0.28[†] | **0.000** |
| Arms BMD, g/cm$^2$ | 0.77 ± 0.08 | 0.81 ± 0.06[§] | 0.78 ± 0.08[#] | 0.69 ± 0.07[†] | **0.000** |
| Ribs BMD, g/cm$^2$ | 0.60 ± 0.06 | 0.63 ± 0.05[§] | 0.60 ± 0.05[#] | 0.56 ± 0.05[†] | **0.000** |
| Trunk BMD, g/cm$^2$ | 0.83 ± 0.09 | 0.88 ± 0.07[§] | 0.83 ± 0.08[#] | 0.76 ± 0.07[†] | **0.000** |

| | | | | | |
|---|---|---|---|---|---|
| Spine BMD, g/cm$^2$ | 0.97 ± 0.14 | 1.05 ± 0.11$^{\S}$ | 0.97 ± 0.13$^{\#}$ | 0.86 ± 0.11$^{\dagger}$ | **0.000** |
| Pelvis BMD, g/cm$^2$ | 1.01 ± 0.11 | 1.07 ± 0.09$^{\S}$ | 1.01 ± 0.11$^{\#}$ | 0.91 ± 0.10$^{\dagger}$ | **0.000** |
| Legs BMD, g/cm$^2$ | 1.12 ± 0.12 | 1.16 ± 0.09$^{\S}$ | 1.13 ± 0.11$^{\#}$ | 1.00 ± 0.11$^{\dagger}$ | **0.000** |

Analysis of variance (ANOVA) for continuous variables and $\chi^2$test for categorical. BMD, bone mineral density; SD, standard deviation.

$^{\S}p<0.05$ Significant difference between participants in 18–44 years old group and 45–64 years old group.

$^{\#}p<0.05$ Significant difference between participants in 45–64 years old group and ≥65 years old group.

$^{\dagger}p<0.05$ Significant difference between participants in 18–44 years old group and ≥65 years old group.

The differences of total and regional BMD between sleep quality groups in total and by age group are shown in Table 2. In total women, compared to participants with good sleep quality, participants with poor sleep quality have significantly lower total and regional BMD. When participants were further divided into three age groups, the results remained statistically significant in middle-aged group.

**Table 2**. Total and regional bone mineral density in Chinese women across sleep quality and age groups

| BMD | Total (*N*=1845) | | Age <45 years (*N* =511) | | Age 45–64 years (*N*=1004) | | Aged ≥65 years (*N*=330) | |
|---|---|---|---|---|---|---|---|---|
| | Good | Poor | Good | Poor | Good | Poor | Good | Poor |
| Total | **1.06 ± 0.10*** ** | 1.03 ± 0.10 | 1.11 ± 0.07 | 1.11 ± 0.08 | **1.07 ± 0.10*** ** | 1.04 ± 0.09 | 0.96 ± 0.09 | 0.95 ± 0.08 |
| Head | **2.12 ± 0.31*** ** | 2.04 ± 0.31 | 2.27 ± 0.24 | 2.26 ± 0.22 | **2.11 ±0.31*** | 2.05 ± 0.30 | 1.87 ± 0.28 | 1.85 ± 0.27 |
| Arms | **0.78 ± 0.08*** ** | 0.75± 0.08 | 0.81 ± 0.06 | 0.82 ± 0.07 | **0.78 ± 0.08*** ** | 0.76 ± 0.07 | 0.70 ± 0.07 | 0.68 ± 0.07 |
| Ribs | **0.60 ± 0.06*** ** | 0.59 ± 0.00 | 0.63 ± 0.05 | 0.62 ± 0.05 | **0.60 ± 0.05** ** | 0.59 ± 0.05 | 0.56 ± 0.05 | 0.56 ± 0.04 |
| Trunk | **0.83 ± 0.09*** ** | 0.81 ± 0.08 | 0.88 ± 0.07 | 0.87 ± 0.08 | **0.83 ± 0.08*** ** | 0.81 ± 0.08 | 0.76 ± 0.07 | 0.76 ± 0.07 |
| Spine | **0.98 ± 0.14*** ** | 0.94 ± 0.13 | 1.05 ± 0.11 | 1.05 ± 0.12 | **0.97 ± 0.13** ** | 0.94 ± 0.13 | 0.86 ± 0.12 | 0.86 ± 0.10 |
| Pelvis | **1.01 ± 0.11*** ** | 0.98 ± 0.11 | 1.07 ± 0.09 | 1.06 ± 0.10 | **1.01 ± 0.11*** ** | 0.98 ± 0.10 | 0.91 ± 0.10 | 0.90 ± 0.09 |
| Legs | **1.12 ±0.12*** ** | 1.09 ± 0.12 | 1.16 ± 0.09 | 1.17 ± 0.09 | **1.14 ± 0.11*** ** | 1.10 ± 0.11 | 1.00 ± 0.11 | 1.00 ± 0.10 |

BMD, bone mineral density. Student's t-test by sleep quality across different age groups.

*$p$<0.05.
**$p$<0.01.
***$p$<0.001.

Associations between sleep quality and total and regional BMD in total women and in three different age groups are shown in Table 3. After adjusting for age, menopausal status, weight, height, percent body fat, physical activities, alcohol drinking, calcium supplement use, marital status, education, and metabolic disease, poor sleep quality was correlated with low arms BMD in total women and with low total and legs BMD in the middle-aged group ($p<0.05$). However, no significant association between sleep quality and total or regional BMD was found in young and elder groups (all $p>0.05$).

**Table 3**. The associations between sleep quality and total and regional bone mineral density in Chinese women by age group.

| | Total (*N*=1845) | Aged <45 years (*N*=511) | Age 45–64 years (*N*=1004) | Aged ≥65 years (*N*=330) |
|---|---|---|---|---|
| BMD | COEF (95%CI) | COEF (95% CI) | COEF (95% CI) | COEF (95% CI) |
| Total | -0.008 (-0.018, 0.001) | -0.003 (-0.022, 0.016) | **-0.013 (-0.025, -0.001)** | -0.007 (-0.028, 0.013) |
| Head | -0.023 (-0.056, 0.011) | -0.016 (-0.087, 0.055) | -0.028 (-0.072, 0.016) | -0.026 (-0.100, 0.048) |
| Arms | **-0.008 (-0.015, -0.000)** | 0.003 (-0.012, 0.019) | -0.009 (-0.019, 0.001) | -0.015 (-0.031, 0.001) |
| Ribs | -0.002 (-0.007, 0.003) | -0.003 (-0.015, 0.008) | -0.002 (-0.008, 0.004) | -0.003 (-0.012, 0.006) |
| Trunk | -0.006 (-0.013, 0.001) | -0.005 (-0.022, 0.012) | -0.008 (-0.018, 0.002) | -0.009 (-0.024, 0.006) |
| Spine | -0.008 (-0.020, 0.005) | 0.000 (-0.029, 0.030) | -0.012 (-0.029, 0.005) | -0.011 (-0.037, 0.014) |
| Pelvis | -0.009 (-0.020, 0.001) | -0.011 (-0.036, 0.014) | -0.012 (-0.026, 0.002) | -0.010 (-0.032, 0.012) |
| Legs | -0.007 (-0.018, 0.005) | 0.004 (-0.020, 0.028) | **-0.017 (-0.033, -0.002)** | 0.003 (-0.023, 0.029) |

Covariates included in the regression model were age, menopausal status, weight, height, percent body fat, alcohol drinking, physical activity, calcium supplement use, marital status, education and metabolic diseases. BMD, bone mineral density; CI, confidence interval; COEF, ???

Table 4 shows the associations between sleep quality and total or regional BMD stratified by menopausal status (premenopausal, early postmenopausal or late postmenopausal) in the middle-aged group. Poor sleep quality was shown to be associated with low total, arms, trunk, pelvis and legs BMD in the premenopausal group and with low total, arms and legs BMD in the early postmenopausal group (all $p<0.05$). However, in the late postmenopausal group, sleep quality showed no significant associations with BMD.

**Table 4**. The associations between sleep quality and total and regional bone mineral density in Chinese middle-aged women by menopausal status.

| | Premenopausal (*N*=340) | | Early postmenopausal (*N*=268) | | Late postmenopausal (*N*=396) | |
|---|---|---|---|---|---|---|
| BMD | COEF (95% CI) | *p* | COEF (95% CI) | *p* | COEF (95% CI) | *p* |
| Total | **-0.025 (-0.046, -0.004)** | **0.020** | **-0.030 (-0.056, -0.005)** | **0.021** | 0.002 (-0.018, 0.021) | 0.848 |
| Head | -0.068 (-0.142, 0.006) | 0.072 | -0.073 (-0.169, 0.024) | 0.141 | 0.008 (-0.059, 0.075) | 0.811 |
| Arms | **-0.021 (-0.039, -0.004)** | **0.018** | **-0.024 (-0.043, -0.004)** | **0.018** | 0.006 (-0.010, 0.022) | 0.437 |
| Ribs | -0.010 (-0.021, 0.002) | 0.099 | -0.009 (-0.021, 0.004) | 0.186 | 0.006 (-0.002, 0.015) | 0.147 |
| Trunk | **-0.022 (-0.040, -0.003)** | **0.022** | -0.018 (-0.039, 0.002) | 0.079 | 0.007 (-0.008, 0.022) | 0.363 |
| Spine | -0.028 (-0.059, 0.003) | 0.079 | -0.034 (-0.071, 0.002) | 0.061 | 0.009 (-0.015, 0.033) | 0.450 |
| Pelvis | **-0.033 (-0.059, -0.007)** | **0.014** | -0.020 (-0.046, 0.007) | 0.151 | 0.005 (-0.016, 0.026) | 0.618 |
| Legs | **-0.025 (-0.051, -0.000)** | **0.049** | **-0.041 (-0.073, -0.010)** | **0.011** | -0.002 (-0.027, 0.023) | 0.891 |

Covariates included in the regression model were age, weight, height, percent body fat, alcohol drinking, physical activity, calcium supplement

use, marital status, education and metabolic diseases. BMD, bone mineral density; CI, confidence interval; COEF, ???

## 4. Discussion

In the present study, we found associations between sleep quality and total and regional BMD varied by age groups and menopausal status after adjusting for various potential confounders in Chinese women. Middle-aged women who had poor sleep quality rated by PSQI score had significantly lower total and legs BMD compared with those who had good sleep quality. The associations were especially prominent in premenopausal and early postmenopausal middle-aged women.

We found that there was a significant association between sleep quality and BMD even after adjusting potential covariates including age, weight, height, percent body fat, alcohol drinking, physical activity, calcium supplement use, marital status, education level and metabolic disease, indicating that the association between poor sleep quality and low BMD is independent of those potential confounders. Evidence that linked sleep quality to bone health suggested that endocrine dysfunction is an underlying mechanism [32–34]. Although the relationship among sleep quality, endocrine, and bone might change with aging [35], only few studies about sleep quality and bone health have taken the age factor into account. In the present study, we found significant associations between poor sleep quality and lower BMD in the middle-aged group. Our results are consistent with previous age-specific studies that found increased PSQI score was associated with osteopenia in middle-aged, overweight participants [14]. Another epidemiological study found no significant

difference for PSQI score among normal, osteopenia and osteoporosis groups in the elderly [15]. Data on sleep quality and BMD is limited in young adults. However, several studies observed no association between sleep duration and BMD in young participants [9]. It is partly because young adults are healthier and less likely to have sleep problems or bone loss. However, it is still not clear why the associations between sleep quality and BMD were also weaker in the elderly. Eve Van Cauter et al. found an inverse interaction between sleep quality and aging on endocrine in 149 healthy participants aged 16–83 years [18], indicating that the relationship between sleep quality and BMD may weaken with aging.

Another possible explanation for the difference across age groups is estrogen [10,36], which is a potential mechanism underlying the associations between sleep quality and BMD. It has been well documented that bone loss and poor sleep quality in women often coincides with the onset of menopause and estrogen deficiency [4]. Estrogen decline begins with the perimenopause, generally around 45 years old [37,38], and accelerates in early menopause [39]. To further assess the effect of menopause on the associations between sleep quality and BMD, we divided participants into three different menopausal groups. Associations between sleep quality and BMD varied across menopausal status. Significant associations presented in premenopausal and early postmenopausal groups but not in late menopausal in the middle-aged group (45–64 years old). Consistent with our results, significant associations between PSQI-rated sleep quality and osteoporosis were only observed in perimenopause,

overweight women in the Netherlands Epidemiology of Obesity study [14]. However, it is still not clear why the associations between sleep quality and BMD were only observed in premenopausal and early postmenopausal women in our study. A study in naturally menopausal cynomolgus monkeys found that serum estradiol, a main form of estrogen, was significantly lower in late postmenopausal than perimenopausal and early postmenopausal females [40], indicating that the association between sleep quality and BMD might be diluted in late postmenopausal women. Moreover, the association between estradiol and BMD in late postmenopausal women is weaker than perimenopausal or early postmenopausal participants [41,42]. In addition, estrogen alteration is more intense in perimenopausal and early menopausal participants, making endocrine more likely to be affected by sleep quality in these periods [43].

The present study has several strengths. First, a series of important confounders such as percent body fat [9], calcium supplement use [10], social economic factors and medical history which may impact both sleep quality and BMD were taken into consideration in the analysis. Second, we collapsed age into three categories separately and further analyzed by menopausal status which enabled us to have a better understanding on the associations between sleep quality and BMD stratified by menopausal status and age among women.

However, limitations should also be noted. Firstly, because of the cross-sectional

design, a causal relationship between sleep quality and BMD may not be inferred. Secondly, perimenopause was defined as women 45–55 years of age who had irregular cycles during the previous months, or amenorrhea for 3–11 months, and might or might not present with vasomotor symptoms [41]. However, women during perimenopause cannot be distinguished in our study. Taking premenopausal middle-aged women as perimenopausal women may underestimate the association between sleep quality and BMD. Thirdly, hormonal changes such as estrogen should be measured in the future to explore the potential mechanism underlying the association between BMD and sleep quality. In addition, we did not collected data on food intake frequency. The effect of diet on the association between sleep quality and BMD is unclear. However, we used diet types (meat-based diet, balanced diet, and vegetable-based diet) as an additional covariate in our models. The associations between poor sleep quality and low BMD mainly remained unchanged after additionally adjusting for diet type in our study (data not shown). Lastly, our study used self-reported measures as indicators of sleep, which may cause a potential recall bias. However, it is reported that PSQI score over 7 had a diagnostic sensitivity of 98.3% and specificity of 90.2% in distinguishing normal subjects from patients with sleep quality problems [17].

## 5. Conclusion

In conclusion, poor sleep quality is associated with low BMD in middle-aged women, especially in premenopausal and early menopausal middle-aged women. These findings add to the current understanding regarding osteoporosis prevention. Future studies should be conducted to explore whether sleep quality intervention would improve bone health of middle-aged women in premenopausal and early menopausal stages and to verify whether prevention in this period would prevent osteoporosis in later life.

## Conflict of interest

The authors have no conflicts of interest to declare.

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## Author contributions

J.L. and S.K.Z. designed the study. J.L. and L.J.C. drafted the manuscript. L.J.C., S.L.N., Y.R., S.S.Y., X.H.F., D.G., J.Y.L., L.Z., S.H. and S.K.Z. provided comments and suggestions, and revised the manuscript. S.K.Z. accepts responsibility for the integrity of the data analysis. All authors read and approved the final manuscript.

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**Association between Sleep Quality and Bone Mineral Density in Chinese Women Vary by Age and Menopausal Status**

**Highlights**

- Poor sleep quality was associated with low total and regional bone mineral density in middle-aged women
- The association was more robust in pre- and early menopausal women
- Sleep quality intervention in the pre- and early menopausal period might improve bone health of women and prevent osteoporosis in later life