# The relationship of sleep duration with premature menopause in American adults: data from the National Health and Nutrition Examination Survey (NHANES) from 2005-2018 

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## Research Article

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## Abstract <br> Objective

The correlation between sleep time and menopausal age is still unclear. This study investigated the causal relationship between sleep duration and premature menopause based on the National Health and Nutrition Survey (NHANES) database.

## Materials and methods

This study included 4055 female participants in the NHANES database from 2005 to 2018, and used a logistic regression model to evaluate the relationship between sleep duration and menopausal age. Draw RCS curve to illustrate the relationship between sleep duration and menopause age. Short term sleep was defined as $\leq 7$ hours of sleep per day, normal sleep was defined as 7.0-8.9 hours of sleep, and long-term sleep was defined a $\geq 9$ hours of sleep per day. Premature menopause was defined as menopause before the age of 40 .

## Results

The average age of 4055 female participants was $62.26 \pm 11.42$. There was a significant correlation between sleep duration and menopausal age ( $P<0.05$ ). The results of the logistic regression model showed that short-term sleep ( $\leq 7$ hours) was associated with premature menopausal age ( $\leq 40$ ) ( $\mathrm{OR}=0.80 ; 95 \% \mathrm{Cl}: 0.66-0.98 ; P=0.028$ ), and after adjusting for potential confounding factors, short-term sleep ( $\leq 7$ hours) was also associated with premature menopausal age ( $\leq 40$ ) ( $\mathrm{OR}=0.82 ; 95 \% \mathrm{Cl}: 0.67-1.99 ; P=0.049$ ). The RCS results showed a U-shaped association between sleep time and menopausal age ( $P<0.001$ ), with a threshold of 7 hours for sleep time. Whether sleep time increases or decreases, the risk ratio of premature menopause shows an increasing trend.

## Conclusion

Our cross-sectional analysis elucidated the U-shaped relationship between sleep duration and menopausal age among the American age group.

## Introduction

Menopausal period is a normal physiological process characterized by permanent cessation caused by a decrease in ovarian hormone secretion, typically occurring between the ages of $45-55^{[1]}$. The age of menopause is often influenced by genetic, biological, environmental, and socio-economic factors ${ }^{[2]}$. The age of menopause in women can affect their health in later years ${ }^{[3]}$. Premature menopause ( $<40$ years old) has potential impacts on women's health, which are associated with an increase in cardiovascular disease and hypertension, as well as an increase in overall mortality, neurological disorders, mental illness, and osteoporosis ${ }^{[4]}$. Premature Ovarian Failure (POF) refers to the loss of ovarian function before the age of 40 , and the incidence rate is about $0.5-1 \%{ }^{[5]}$. For women with premature ovarian failure, they may experience amenorrhea, unstable vasoconstriction (hot flashes, night sweats), sleep disorders, vulvovaginal atrophy, urinary system infections, and emotional disorders ${ }^{[6]}$. A study has found that the prevalence and fracture risk of osteoporosis in women with POF were twice that of the general population, and
the prevalence of osteoporosis was twice that of natural postmenopausal women ${ }^{[7]}$. Smoking, alcohol consumption, nutrition, and other environmental factors were all considered risk factors for premature menopausal age ${ }^{[8]}$.

Sleep is the main physiological process that regulates human circadian rhythms, and it is crucial for human health. People spend about one-third of their time sleeping ${ }^{[9]}$. The American Academy of Sleep Medicine (AASM) and the Sleep Research Society (SRS) recommend that the optimal sleep time for adults is 7 hours or more per night ${ }^{[10]}$. It was reported that insufficient sleep and excessive sleep were related to various health-related diseases, such as hypertension, obesity, diabetes and cardiovascular diseases ${ }^{[11]}$. Two meta-analyses found that sleep deprivation was significantly associated with increased incidence rate and mortality of the metabolic syndrome, whereas a similar association was observed with prolonged sleep. Some studies have also found that sleeping for $4-5$ hours or more was associated with most tumor mortality rates ${ }^{[12]}$. For perimenopausal women, changes in hormone levels can have an impact on sleep structure, which can easily interfere with sleep, leading to shorter and more fragmented sleep time, and fewer deep sleep and rapid eye movement sleep ${ }^{[13]}$.

The NHANES database is a representative survey that monitors the health status of the general population in the United States over the past few decades ${ }^{[14-16]}$. Epidemiological studies using the NHANES database have identified the association between sleep time and other diseases ${ }^{[17]}$. For example, Jiang et al. explored the Ushaped relationship between sleep duration and chronic kidney disease (CDK) in American adults by incorporating it into the NHANES database ${ }^{[18]}$. Di et al. conducted a correlation analysis between sleep habits, sleep disorders, and prevalence among American adults by incorporating them into the NHANES database from 2017 to 2020 ${ }^{[19]}$. So far, there has been no systematic study evaluating the impact of sleep time on menopausal age. This study utilizes data from the National Health and Nutrition Continuous Survey (NHANES) from 2005 to 2018 to explore the impact of sleep duration (short sleep duration, normal sleep duration, and long sleep duration) on menopausal age.

## Materials and Methods

## Research population

NHANES database (https://wwwn.cdc.gov/nchs/nhanes/)is a population-based cross-sectional survey conducted every two years in the United States, aimed at collecting information on the health and nutritional status of American adults and children. The survey includes interviews, physical examinations, and laboratory tests. The research protocol of NHANES has been approved by the NCHS Race Review Committee. All participants signed informed consent before participating in the study. Using information from the NHANES database, this study aims to explore the correlation analysis between sleep duration and menopausal age. This study extracted data ( $\mathrm{n}=$ 70196) from 7 NHANES cycles. Excluded males $(n=34715)$, the lack of sleep time information $(n=12606)$, women who have undergone hysterectomy ( $n=10153$ ), the lack of information on the last menstrual period ( $n=7705$ ), women who have undergone bilateral ovariectomy ( $n=62$ ), unknown menarche time ( $n=48$ ), unknown number of pregnancies ( $n=451$ ), unknown information on taking contraceptives ( $n=8$ ), female hormone ( $n=16$ ), unknown information on smoking $(\mathrm{n}=2)$, unknown information on drinking ( $\mathrm{n}=315$ ), unknown information on hypertension and diabetes ( $n=7$ ), Excluding BMI, education level and marital status were unknown ( $n=53$ ). The final analysis recruited 4055 participants. The filtering steps were shown in Fig. 1.

## Independent variable

Determine the total duration of habitual sleep by asking the following question: "How much sleep do you usually have on weekdays or weekdays at night? Sleep duration was divided into $\leq 7$ hours, 7.0-8.9 hours, and $\geq 9$ hours. Short sleep duration was defined as $\leq 7$ hours of sleep per day. Long term sleep duration was defined as sleeping for $\geq 9$ hours per day. The normal sleep duration was defined as a sleep duration of 7.0-8.9 hours. Select the following potential confounding variables from demographic, examination, laboratory test data, and questionnaire data: age, race (Mexican American, other Hispanic, Non-Hispanic White, non-Hispanic Black and other RaceIncluding Multi-Racial), marry(married, other), education(high school and below, above high school), BMI, hypertension, diabetes(yes, no, borderline), drink(1-12/year, > 12/year), smoke, menarche, pregnancy, contraceptive, hormone. Smoke (including smokers or non-smokers) was defined as an individual who smokes $\geq$ 100 cigarettes in their lifetime. BMI was obtained at the Mobility Inspection Center (MEC), and other covariates can be obtained through standardized questionnaires during the interview. The NHANES database used complex multistage sampling, and according to the NHANES database usage guidelines, weighted analysis was performed on the included data. Some of the variables included in this study were collected in MEC, so MEC check weights (WTMEC2YR) were used for analysis. The sample weight used in the final analysis was equal to $2 / 7$ of the "WTMEC2YR" value, corresponding to the MEC weights for 14 survey years.

## Outcome variables

The outcome variable was menopausal age, which defines menopause before the age of 40 years as premature menopause.

## Statistical methods

All analyses in this study were performed using Statistics 26.0 (SPSS Inc., Chicago, IL, USA) and R 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org/). Continuous variables were represented by quartiles. Categorical variables were expressed as percentages. Logistic regression analysis was used to calculate the odds ratio (OR) and $95 \%$ confidence interval ( $95 \% \mathrm{CI}$ ) of the relationship between sleep duration and menopausal age. We adjusted for age, race, marital status, education, BMI, hypertension, diabetes, alcohol consumption, smoke, age at menarche, pregnancy, use of oral contraceptives or hormone therapy, hormone. In addition, four cross-sectional restricted cubic spline curves (RCS) were used to explore the nonlinear correlation between sleep duration and menopausal age. $P<0.05$ indicated a statistically significant difference.

## Results

Short sleep ( $\leq 7$ hours), normal sleep (7-8.9 hours), and long sleep ( $\geq 9$ hours) were reported by $33.05 \%, 54.30 \%$, and $12.65 \%$ of the participants, respectively (Table 1). The proportion of long-term sleep among Mexican American participants was higher than that of normal sleep and short sleep. Compared with participants with normal and short sleep duration, subjects with longer sleep duration had an increased incidence of hypertension. In addition, we found that as age increases, sleep time prolongs. Participants with increased number of pregnancies had longer sleep times. There was a significant correlation between the duration of sleep and menopausal age ( $P=$ 0.032 ). No significant difference was observed in sleep duration by smoking status or age at menarche.

Table 1
Characteristics of NHANES participants from 2005 to 2018(weighted)

| Characteristic | Total | $\leq 7$ | 7-8.9 | $\geq 9$ | $P$ value |
| :---: | :---: | :---: | :---: | :---: | :---: |
| N\% | 4055 | 1340(33.05) | 2202(54.30) | 513(12.65) |  |
| Age (year median [IQR]) | $\begin{aligned} & 62.00[55.00, \\ & 70.00] \end{aligned}$ | $\begin{aligned} & 61.00[55.00, \\ & 69.00] \end{aligned}$ | $\begin{aligned} & 62.00 \text { [55.00, } \\ & 70.00] \end{aligned}$ | $\begin{aligned} & 65.00[57.00 \\ & 74.00] \end{aligned}$ | $\begin{aligned} & < \\ & 0.001 \end{aligned}$ |
| Race (\%) |  |  |  |  | $\begin{aligned} & < \\ & 0.001 \end{aligned}$ |
| Mexican American | 645(15.91) | 202(15.07) | 351(15.69) | 92 (17.93) |  |
| Other Hispanic | 492(12.13) | 184(13.73) | 246 (11.17) | 62 (12.09) |  |
| Non-Hispanic White | 1761(43.43) | 460(34.33) | 1069 (48.55) | 232 (45.22) |  |
| Non-Hispanic Black | 802(19.78) | 364(27.16) | 354 (16.08) | 84 (16.37) |  |
| Other Race-Including MultiRacial | 355(8.75) | 130(9.70) | 182 (8.27) | 43 (8.38) |  |
| Marital status (\%) |  |  |  |  | $\begin{gathered} < \\ 0.001 \end{gathered}$ |
| Married | 1952(48.14) | 577 (43.06) | 1157 (52.54) | 218 (42.50) |  |
| Other | 2103(51.86) | 763 (56.94) | 1045 (47.46) | 295 (57.50) |  |
| Education (\%) |  |  |  |  | $\stackrel{<}{0.001}$ |
| High School and below | 2128(52.48) | 735 (54.85) | 1087 (49.36) | 306 (59.65) |  |
| Above High school | 1927(47.52) | 605 (45.15) | 1115 (50.64) | 207 (40.35) |  |
| BMI (median [IQR]) | $\begin{aligned} & 29.00[25.00, \\ & 34.00] \end{aligned}$ | $\begin{aligned} & 29.00[25.00, \\ & 34.00] \end{aligned}$ | $\begin{aligned} & 29.00[25.00, \\ & 34.00] \end{aligned}$ | $\begin{aligned} & 29.00[25.00, \\ & 34.00] \end{aligned}$ | 0.042 |
| Hypertension (\%) |  |  |  |  | 0.003 |
| Yes | 2083(51.37) | 720 (53.73) | 1072 (48.68) | 291 (56.73) |  |
| No | 1972(48.63) | 620 (46.27) | 1130 (51.32) | 222 (43.27) |  |
| Diabetes (\%) |  |  |  |  | 0.049 |
| Yes | 751(18.52) | 261 (19.48) | 379 (17.21) | 111 (21.64) |  |
| No | 3193(78.74) | 1033 (77.09) | 1769 (80.34) | 391 (76.22) |  |
| Borderline | 111(2.74) | 46 (3.43) | 54 (2.45) | 11 (2.14) |  |
| Drink (\%) |  |  |  |  | 0.001 |
| Yes | 1977(48.75) | 648 (48.36) | 1129 (51.27) | 200 (38.99) |  |
| No | 2078(51.25) | 692 (51.64) | 1073 (48.73) | 313 (61.01) |  |
| Smoke (\%) |  |  |  |  | 0.309 |


| Characteristic | Total | $\leq 7$ | $7-8.9$ | $\geq 9$ | $P$ <br> value |
| :--- | :--- | :--- | :--- | :--- | :--- |
| Yes | $1586(39.11)$ | $540(40.30)$ | $853(38.74)$ | $193(37.62)$ |  |
| No | $2469(60.89)$ | $800(59.70)$ | $1349(61.26)$ | $320(62.38)$ |  |
| Menarche (median [IQR]) | $13.00[12.00$, | $13.00[12.00$, | $13.00[12.00$, | $13.00[12.00$, | 0.189 |
|  | $14.00]$ | $14.00]$ | $14.00]$ | $14.00]$ |  |

Model 0 included no covariate adjustments. Model 1 was adjusted for age, race, marital status and education. Model 2 adjusted for alcohol consumption, BMI, hypertension, diabetes, age at menarche, number of pregnancies, smoking status and use of oral contraceptives or hormone therapy.Model 3 adjusted for all variables in Model 2 and Model 1. We observed that compared to normal sleep time ( $7-8.9$ hours), short sleep time ( $\leq 7$ hours) was associated with premature menopause (OR: $0.80 ; 95 \% \mathrm{Cl}$ : $0.66-0.98 ; P=0.028$ ), but long sleep time ( $>9$ hours) was not negatively associated with menopausal age. After adjusting for potential confounding factors, short sleep time ( $\leq 7$ hours) was still negatively associated with premature menopause (OR: $0.82 ; 95 \% \mathrm{CI}: 0.67-1.00 ; P=0.049$ ) (Table 2).

Table 2
Application of logistic regression analysis on the relationship between sleep duration and menopausal age

| Sleep duration |  | Model 0 |  | Model 1 |  | Model 2 |  | Model 3 |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | N | $\begin{aligned} & \text { OR } \\ & (95 \% \mathrm{CI}) \end{aligned}$ | Pvalue | $\begin{aligned} & \text { OR } \\ & (95 \% \mathrm{Cl}) \end{aligned}$ | Pvalue | $\begin{aligned} & \text { OR } \\ & (95 \% \mathrm{Cl}) \end{aligned}$ | Pvalue | $\begin{aligned} & \text { OR } \\ & (95 \% \mathrm{Cl}) \end{aligned}$ | Pvalue |
| 7-8.9 | 1340 | Ref |  | Ref |  | Ref |  | Ref |  |
| $\leq 7$ | 2202 | $\begin{aligned} & 0.80(0.66- \\ & 0.98) \end{aligned}$ | 0.028 | $\begin{aligned} & 0.90(0.73- \\ & 1.12) \end{aligned}$ | 0.349 | $\begin{aligned} & 0.82(0.67- \\ & 1.00) \end{aligned}$ | 0.049 | $\begin{aligned} & 0.92(0.74- \\ & 1.14) \end{aligned}$ | 0.446 |
| $\geq 9$ | 513 | $\begin{aligned} & 1.02(0.77- \\ & 1.36) \end{aligned}$ | 0.886 | $\begin{aligned} & 0.78(0.57- \\ & 1.06) \end{aligned}$ | 0.105 | $\begin{aligned} & 0.77(0.58- \\ & 1.02) \end{aligned}$ | 0.692 | $\begin{aligned} & 0.82(0.60- \\ & 1.12) \end{aligned}$ | 0.203 |

Using the RCS model, we found a U-shaped correlation between sleep duration and menopausal age ( $P<0.001$ was non-linear). This study found that the threshold for sleep duration was 7 hours, and whether sleep duration increases or decreases, the risk of premature menopause tended to increase. In addition, the inflection points varied among different groups(Fig. 2).

## Discussion

Our results indicated a significant correlation between different sleep durations (short sleep, normal sleep, and long sleep) and menopausal age. Among them, short sleep ( $\leq 7$ hours) is more prone to premature menopause when no covariates were controlled for. When we control covariates, short sleep is still more likely to cause an early menopausal age. Perimenopause is a critical period in women's lives, marking not only the end of reproductive ability, but also the possibility of symptoms such as hot flashes, vaginal dryness, sleep pattern disorders, emotional fluctuations, headaches, lack of concentration, joint pain, etc ${ }^{[20-22]}$. Sometimes these symptoms may have a significant negative impact on the lives of at least $30 \%$ of women ${ }^{[23]}$. Premature menopause will affect the physiological state of women before menopause, which is more likely to cause an increase in cardiovascular disease (CVD), a decrease in bone density (BMD), a significant decrease in fertility, and psychological distress ${ }^{[24,}$ ${ }^{25]}$.

Insufficient sleep duration was a common problem in modern society, and it is also one of the most common health problems for perimenopausal women ${ }^{[26-28]}$. Approximately $28 \%-63 \%$ of women experience sleep problems during the perimenopausal period ${ }^{[29]}$. The negative consequences of poor sleep were multifaceted, including physical, psychological, and cognitive impairments ${ }^{[30,31]}$. Research has shown that middle-aged and elderly women are more sensitive to nighttime traffic noise than men of the same age ${ }^{[13]}$. A 6-year follow-up study by Lampio et al. found that aging and increased serum follicle stimulating hormone (S-FSH) concentrations both affect sleep structure ${ }^{[32]}$. Previous studies have found that circadian rhythm regulation plays a crucial role in tumor cell proliferation, cell death, DNA repair, and metabolic changes. These biological mechanisms suggest that sleep may be related to the etiology and development of tumors ${ }^{[33]}$. In addition, our study also observed a statistically significant U-shaped relationship between sleep duration and menopausal age, with a threshold of 7 hours for sleep duration. Regardless of whether sleep duration increased or decreased, there was an increasing trend in the risk of premature menopause. A study found that patients who slept for 7 hours had a lower risk of hemorrhagic stroke death compared to those who slept for a shorter time ( $\leq 6 \mathrm{~h})^{[33]}$. Wu et al. included 7511 adults aged $\geq 20$ years in the NHANES database from 2005 to 2008 and analyzed the association between sleep pattern changes in vitamin D status and coronary heart disease. The results showed that compared to participants with sleep time of $7-8$ hours, participants with sleep time $<7 \mathrm{~h}$ or $>8 \mathrm{~h}$ had a more significant correlation between serum $25(\mathrm{OH}) \mathrm{D}$ concentration and coronary heart disease risk ${ }^{[34]}$. A cross-sectional study of 801 adolescents found that menstrual cycle irregularity increases with a decrease in sleep duration ${ }^{[35]}$. In addition, we found that compared to normal sleep duration (7-8.9 h), sleep duration exceeding 9 hours did not affect menopausal age, which requires further research and analysis. However, a prospective cohort study involving 6090 adult women found that prolonged sleep duration was associated with an increased risk of estrogen mediated tumors ${ }^{[36]}$.

## Advantages and limitations

The advantages of the present study included the use of a large, nationally representative sample. Our research had some limitations. Our research has some limitations. Firstly, this study was an observational study and
therefore cannot prove a causal relationship; Second, although we adjusted for many confounding factors in the analysis, unmeasured covariates may still lead to confounding bias; Thirdly, information about sleep duration was not objectively measured, making it prone to recall bias. Therefore, more research was needed to determine longterm trends and further elucidate the correlation between sleep duration and menopausal age.

## Conclusion

Overall, the analysis of NHANES data from 2005 to 2018 indicates a U-shaped correlation between sleep duration and menopausal age, with 7 hours of sleep per day being the optimal sleep time for women and further prospective research should be conducted.

## Declarations

## Ethical approval and informed consent

The study was conducted according to the guidelines of the Declaration of Helsinki. The NHANES database has been approved by the National Center for Health Statistics (NCHS) Research Ethics Review Committee of the United States Centers for Disease Control and Prevention (CDC), and all participants have signed informed consent forms.

## Consent for publication

Consent for publication- Not applicable.

## Availability of data and materials

All NHANES data for this study are publicly available and can be found here: https://wwwn.cdc.gov/nchs/nhanes.

## Conflict of Interests

The authors declare no conflict of interest.

Consent for publication statement is only applicable if any identifiable information (image, face, name etc.) of participant/s is revealed in the submission.

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## Author conclusions

Conceptualization, R.L.; Methodology, M.Z..; Validation, W.L.; Writing-Original Draft Preparation,R.L.; Writing-Review \& Editing, Y.G. All authors have read and agreed to the published version of the manuscript.

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## Figures



Figure 1
Flow diagram of exclusion criteria


Figure 2

Showing the association between sleep durationand menopausal age using the 3-section RCS. (A) Sleep duration; (B) Drink; (C) Smoke;(D) Marry;(E) Hormone;(F) Hypertension.

