

Sleep Duration and Snoring at Midlife in Relation to Healthy Aging in Women 70 Years of Age or Older

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Hongying Shi^{1,2}
Tianyi Huang^{3,4}
Yanan Ma⁵
A Heather Eliassen^{2,3}
Qi Sun²⁻⁴
Molin Wang^{2,3,6}

¹Department of Epidemiology and Health Statistics, School of Public Health and Management, Wenzhou Medical University, Wenzhou, Zhejiang, People's Republic of China; ²Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA; ³Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA; ⁴Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA; ⁵Department of Biostatistics and Epidemiology, School of Public Health, China Medical University, Shenyang, Liaoning, People's Republic of China; ⁶Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, USA

Purpose: Both short and long sleep durations are associated with higher mortality. This study examined the association between sleep duration and overall health among those who survive to older ages.

Participants and Methods: In the Nurses' Health Study, participants without major chronic diseases in 1986 and survived to age 70 years or older in 1995–2001 were included. Habitual sleep duration and snoring were self-reported in 1986. Healthy aging was defined as being free of 11 major chronic diseases and having no cognitive impairment, physical impairment, or mental health limitations. Logistic regression was used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for healthy aging.

Results: Of the 12,304 participants, 1354 (11.0%) achieved healthy aging. We observed a non-linear association between sleep duration and the odds of achieving healthy aging. Compared with women sleeping 7 hours per day, women with longer sleep duration were less likely to achieve healthy aging; there was also a suggestion of lower odds of healthy aging for shorter sleepers, although the associations did not reach statistical significance: the multivariate-adjusted ORs (95% CIs) of healthy aging for those sleeping ≤ 5 , 6, 8, and ≥ 9 hours were 0.94 (0.70, 1.27), 0.88 (0.76, 1.02), 0.83 (0.72, 0.96), and 0.60 (0.43, 0.84), respectively. Similar non-linear associations were consistently observed for individual dimensions of healthy aging. Regular snoring was associated with 31% lower odds of healthy aging (95% CI: 0.54, 0.88), which was primarily due to lower odds of having no major chronic diseases.

Conclusion: Both short and long sleep durations as well as regular snoring at midlife were associated with lower odds of healthy aging in later life.

Keywords: sleep, healthy aging, prospective studies, Nurses' Health Study, snoring

Correspondence: Molin Wang
Department of Epidemiology, Harvard T.H. Chan School of Public Health, 665
Huntington Avenue, Boston, MA, 02115,
USA
Tel +1 617 525 2202
Email mwang@hsph.harvard.edu

Qi Sun
Department of Nutrition, Harvard T.H. Chan School of Public Health, 665
Huntington Avenue, Boston, MA, 02115,
USA
Tel +1 617 432 7490
Email qisun@hsph.harvard.edu

Introduction

Life expectancy has increased over the last century, and 617 million people (8.5%) are 65 years or older worldwide.¹ By 2050, this number is projected to reach 1.6 billion (nearly 20%) of the world's population.² However, longevity does not entail good health at older ages. A major challenge that aging societies are facing today is severe financial and societal burdens caused by diseases and disabilities prevailing in older populations.³ To address this challenge, the World Health Organization has identified financial, social, and scientific preparation for population aging as a global imperative, and the US National Academy of Medicine is launching a Healthy Longevity Global Grand Challenge, an international effort

directed at improving the health for older people² that emphasizes the urgent need of multidisciplinary solutions to maximize the number of years lived in good health. All these actions highlight the importance of achieving healthy aging, including being free of diseases and having good physical, mental and cognitive health. So far, prior studies have linked several lifestyle factors,⁴ such as physical activity,^{5,6} alcohol drinking,⁷ weight change,⁸ and diet quality,⁹ to healthy aging. However, more research is needed to identify other modifiable factors that may lead to healthy aging.

Sleep is a critical health behavior and plays a central role in human health. Emerging evidence shows that sleep duration may be an important risk factor for multiple chronic diseases,^{10–12} cognitive function,^{13,14} mental health,¹⁵ and mortality.^{16–19} Evidence synthesis based on meta-analysis generally supports that both short and long sleep durations are adversely associated with a wide range of health outcomes. Further, it has been increasingly recognized that sleep health is multi-dimensional beyond sleep duration.²⁰ Snoring, which causes sleep disturbances and is a hallmark symptom of obstructive sleep apnea, has been associated with an increased risk of physical, cognitive and mental problems in adult populations.^{21–23} Thus far, to the best of our knowledge, no prospective study has considered sleep duration or snoring as potentially modifiable risk factors for healthy aging. Moreover, sleep duration and snoring are closely related to other lifestyles such as physical activity, sedentary time, and overweight/obesity,^{24,25} although few studies have explored their inter-relationship or their joint associations with overall health.

In this study, we aimed to examine the independent associations of sleep duration and snoring with healthy aging as measured by a full spectrum of health outcomes, and explore whether and how other lifestyle factors modified these associations in the Nurses' Health Study.

Participants and Methods

Study Population

The Nurses' Health Study (NHS) is a prospective cohort study of 121,701 US registered nurses aged 30–55 that was established in 1976 when a baseline questionnaire was administered to collect information of demographics, lifestyle and medical history. Follow-up questionnaires have been used to update these information and newly diagnosed diseases every 2 years since the study baseline. Women were first asked to report their sleep duration in

1986, which was treated as a baseline for the current analysis. The end of follow-up was through the year 2000 when the overall health status among survivors aged 70 years or older was evaluated, including chronic diseases, physical function, mental health, and cognitive function. The cumulative follow-up rate was over 95% in this cohort.⁶

The study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the institutional review boards of the Brigham and Women's Hospital and the Harvard T.H. Chan School of Public Health. Participants provided implied consent by returning the questionnaires and we also obtained written consent from each participant to obtain and review medical records.

Assessment of Sleep Habits

Women reported their sleep habits in 1986, including daily sleep duration and frequency of snoring. Participants were asked to specify the average total hours of sleep in 24 hours; possible choices included ≤ 5 , 6, 7, 8, 9, 10, and ≥ 11 hours. Considering the small sample size of the last two groups, we collapsed the last three categories, leaving five categories of sleep duration for data analyses: ≤ 5 , 6, 7, 8, and ≥ 9 hours. We defined regular snorers as those who reported snoring regularly and non-snorers as those who only occasionally or almost never snored.

The self-reported sleep duration strongly correlated with sleep duration recorded in sleep diaries ($r_s=0.79$, $P<0.001$), and details of the validity and reproducibility of self-reported sleep have been reported elsewhere.²⁶

Assessment of Healthy Aging

The definition of healthy aging has been described in previous publications.^{6,7} In brief, the outcome is defined based on survival status until at least age 70 years and health information from four domains including chronic diseases, cognitive function, physical function, and mental health. A description of each of the four domains is listed below.

Assessment of Cognitive Function

Beginning in 1995 through 2001, every participant who had survived to age 70 was invited to a cognitive function study and 19,415 (92% of 21,202 eligible nurses) women agreed to participate. We administered the Telephone Interview of Cognitive Status (TICS), a telephone version of the Mini-Mental State Examination (MMSE). TICS

scores range from 0 (worst) to 41 (best), and a score below 31 is considered as cognitive impairment.²⁷ Studies have shown high test–retest reliability and validity of TICS in assessing cognitive status. For example, a strong correlation ($r=0.97$) was found between TICS and MMSE assessments.²⁸ Trained study nurses who were unaware of the study hypothesis performed the assessment, and inter-interviewer reliability was high (>0.95).²⁹

Assessment of Chronic Diseases

Clinical diagnoses of major chronic diseases were queried on each biennial questionnaire since 1986, including cancer, diabetes, myocardial infarction, coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty, congestive heart failure, stroke, kidney failure, chronic obstructive pulmonary disease, Parkinson disease, multiple sclerosis, and amyotrophic lateral sclerosis. Self-reported disease diagnosis was confirmed by study physicians through medical record review, pathology report review, telephone interview, or supplementary questionnaire inquiries, and has been shown to have high validity in this cohort.⁶ Women who reported no history of these 11 diseases as of 2000 were considered being free of chronic diseases.

Assessment of Physical Function and Mental Status

Physical function and mental health were assessed by the Medical Outcomes Study Short-Form Health Survey (SF-36), which was embedded in the 1992, 1996, and 2000 follow-up questionnaires. Physical function was evaluated by 10 questions on physical limitations in performing the following activities: moderate activities; bathing and dressing yourself; walking 1 block; walking several blocks; walking more than 1 mile; vigorous activities; bending, kneeling, or stooping; climbing 1 flight of stairs; climbing several flights of stairs; and lifting or carrying groceries. Each question had 3 response choices: “Yes, limited a lot,” “Yes, limited a little,” or “No, not limited at all.” Impairment of physical function was defined as limited at least “a little” on moderate activities or limited “a lot” on more difficult physical tasks; otherwise, they were defined as no impairment of physical function.

Mental health was evaluated by five questions: “have you been a very nervous person?, have you felt so down in the dumps nothing could cheer you up?, have you felt calm and peaceful?, have you felt downhearted and

blue?, and have you been a happy person?” There were six possible responses to each question, ranging from “none of the time” to “all the time.” Based on the response to these questions, a score between 1 and 6 was assigned to each question, with the score 6 indicating the best mental status and score 1 indicating the worst. We then summed these scores and rescaled them to a range of 0–100. Good mental health was defined as a mental health score greater than 84 (the median value in this cohort).⁶ The validity and reproducibility of the SF-36 and its components have been previously established.³⁰

Covariates

The baseline and subsequent questionnaires collect information of a broad range of covariates, including demographic characteristics such as age, education, husband’s education, race, marital status; lifestyle factors, such as body mass index (BMI, kg/m^2), smoking status, physical activity, sitting time, and standing time; family history of cancer, family history of myocardial infarction, and family history of diabetes; hypertension and high cholesterol; use of supplemental multivitamin, menopausal status and postmenopausal hormone use, and aspirin use. Median annual household income and home value were estimated from the census tract of participant’s residence, geocoded to the 1994 US Census. Dietary data were collected using a validated semi-quantitative food frequency questionnaire,^{31,32} based on which, total energy intake (kJ/day), alcohol (g/day) and coffee (cups/day) consumption and the Alternate Healthy Eating Index (AHEI) were derived.³³ In addition, women were asked the total number of years working rotating night shifts (at least 3 nights per month) with 8 pre-specified categories, including never, 1–2, 3–5, 6–9, 10–14, 15–19, 20–29, and ≥ 30 years. Participants were also asked for “What is your usual sleeping position?” with three response categories: on back, on side, or on front.

Study Population for Analysis

Of the 19,415 participants who completed the assessment of cognitive function, we excluded participants who had missing year of birth ($n=20$), who reported any of the 11 chronic diseases ($n=3893$) at or before baseline. We further excluded those who skipped more than 2 items on mental health or 5 items on physical function scale in SF-36 ($n=708$), those with no questionnaire in 1986 ($n=773$), and those with missing sleep information in 1986 ($n=1737$), a total of 12,304 participants remained for this

analysis. Participants who did not answer the sleep question did not differ substantially from respondents according to age, BMI, physical activity, alcohol consumption, and other major potential confounders (Table S1). In a secondary analysis, we further included 2425 women who died before 2000 as usual agers ($n=14,729$).

Statistical Methods

First, we used logistic regression models to estimate odds ratios (OR) and 95% confidence intervals (95% CI) by sleep duration [≤ 5 , 6, 7 (reference), 8, and ≥ 9 hours per 24 hours]. An OR <1 in these models indicates decreased odds of healthy aging. In the multivariable analysis, we adjusted for possible confounding factors at baseline, including age (continuous), education, race, marital status, household income, family history of diseases (cancer, myocardial infarction, and diabetes), hypertension and high cholesterol, use of supplemental multivitamin (yes, no), menopausal status and hormone use (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users), aspirin use (regular use or not), smoking history (never, former smoker, current smoker), alcohol intake (none, 1–14.9, ≥ 15 g/d), total energy intake, diet quality, coffee consumption, physical activity (MET-hours/week), standing and sitting time (all in quintiles). Because body mass index (BMI) had a strong and positive association with risk of healthy aging,³⁴ we further adjusted for BMI (<18.5 , 18.5–24.9, 25–29.9, ≥ 30 kg/m²) in a separate model. We used restricted cubic splines with 4 knots to evaluate the possible nonlinearity of the association between sleep duration in midlife (measured in 1986) and healthy aging.³⁵ We tested nonlinearity in the dose–response relationship by comparing the model with only the linear term to the model with the linear and the cubic spline terms using the likelihood ratio test. Likewise, we examined the dose–response curves for the relationship between sleep habits and four individual components of healthy aging.

Stratified analyses were performed to evaluate whether the association with sleep duration was modified by baseline lifestyle variables, including BMI (<25 , ≥ 25 kg/m²), smoking behavior (never, smokers), alcohol consumption (none, 1–14.9, ≥ 15 g/d), physical activity ($<$ median, \geq median), diet quality ($<$ median, \geq median), total calorie intake ($<$ median, \geq median), standing and sitting time ($<$ median, \geq median). Statistical interactions were assessed by likelihood ratio tests comparing the models with and without the multiplicative interaction terms. In addition,

we examined the joint associations of sleep duration and regular snoring.

We performed several sensitivity analyses to examine the robustness of observed associations. First, we repeated all analyses including 2425 women who died before age 70 through 2000 as usual agers. Then, we restricted analyses within participants with sleep position on side and also those with no history of snoring. Because shift work status might be a substantial confounder due to its potentially strong associations with both sleep duration and overall health, we excluded women who reported having rotating shift work in 1992 (at least 3 nights/month in addition to days or evenings during the last six months), and also restricted analysis within women who reported never having shift work in 1988. And additional adjustment for shift work also was performed.

All analyses were performed with SAS, version 9.4 (SAS Institute, Inc., Cary, North Carolina). A 2-sided P value of less than 0.05 was considered statistically significant.

Results

Of the 12,304 participants included in the analysis, 8321 (67.6%) women remained free of the 11 chronic diseases included in the definition of healthy aging, 3434 (27.9%) had no impairment of physical function, 5311 (43.2%) had good mental health, and 11,079 (90.0%) reported no impairments of cognitive function during the follow-up assessment in 1995–2001. A total of 1354 (11.0%) participants met all criteria of healthy aging and therefore were healthy survivors, and the rest were usual agers. Compared with usual agers (Table 1), healthy survivors were more active, had lower BMI, and were less likely to be smokers or have hypertension and high cholesterol. Healthy agers were also less likely to be regular snorer compared with usual agers (6.0% vs 10.8%), but they had a similar mean sleep duration at baseline (7.0 ± 1.0 h vs 6.9 ± 0.9 h).

Sleep Duration and Healthy Aging

Table 2 summarizes the age- and multivariate-adjusted ORs of healthy aging associated with sleep duration. After adjustment for all covariates except for BMI, compared with women sleeping 7 hours per day, women with longer sleep duration were less likely to achieve healthy aging; there was also a suggestion of lower odds of healthy aging for shorter sleepers, although the associations did not reach statistical significance: ORs (95% CIs) for those sleeping ≤ 5 , 6, 8, and ≥ 9 hours were 0.93 (0.69, 1.24), 0.87 (0.75, 1.01), 0.83 (0.71,

Table I Baseline Characteristics of Healthy Aged and Usual Aged in the Nurses' Health Study

| Characteristics | Usual Aged (n=10,950)* | Healthy Aged (n=1354)* |
|--|------------------------|------------------------|
| Age at 1986, years [†] | 60.6 (2.5) | 60.1 (2.5) |
| Education, % | | |
| Registered nurse | 77.9 | 73.4 |
| Bachelor | 15.8 | 17.5 |
| Master or doctorate | 6.4 | 9.1 |
| Husband's education, % | | |
| ≤ High school | 52.2 | 46.1 |
| College graduate | 27.1 | 30.2 |
| Graduate school | 20.6 | 23.7 |
| Race (white), % | 98.5 | 98.3 |
| Marital status, % | | |
| Married | 92.8 | 92.9 |
| Widowed | 4.6 | 4.9 |
| Separated, divorced, or never married | 2.6 | 2.2 |
| Family annual income, 10,000\$ | 5.7 (4.5, 7.3) | 6.0 (4.7, 7.7) |
| Family home value, 10,000\$ | 12.8 (8.9, 19.5) | 13.6 (9.3, 21.2) |
| BMI, kg/m ² | 25.5 (4.4) | 23.8 (3.2) |
| Smoking status, % | | |
| Never smoker | 47.2 | 53.5 |
| Past smoker | 35.8 | 35.3 |
| Current smoker | 16.9 | 11.2 |
| Alcohol intake (g/d), % | | |
| None | 42.1 | 38.6 |
| 1–14.9 | 45.4 | 48.3 |
| ≥15 | 12.6 | 13.1 |
| AHEI (no alcohol) | 48.9 (10.7) | 51.3 (11.1) |
| Total calories, kcal | 1757.4 (520.2) | 1728.4 (527.3) |
| Total coffee, cup/d | 2.5 (1.0, 2.9) | 2.5 (1.0, 3.5) |
| Physical activity, MET-h/wk [‡] | 7.9 (2.9, 19.4) | 11.6 (4.3, 26.2) |
| Standing time, h/d | 4.4 (1.1, 7.2) | 4.4 (1.6, 7.2) |
| Sitting time, h/d | 4.4 (1.1, 4.4) | 2.2 (1.1, 4.4) |
| Family history of diabetes, % | 29.6 | 26.4 |
| Family history of myocardial infarction, % | 17.2 | 15.5 |
| Family history of cancer, % | 18.3 | 16.0 |
| History of hypertension, % | 21.0 | 13.3 |
| History of high cholesterol, % | 10.4 | 7.5 |
| Use of multivitamin, % | 43.8 | 41.3 |
| Menopausal status and hormone use, % | | |
| Pre-menopausal | 1.3 | 1.0 |
| Post and never used | 73.2 | 73.8 |
| Post and past user | 3.6 | 4.0 |
| Post and current user | 22.0 | 21.2 |
| Regular aspirin use (≥ 2 tabs/wk), % | 38.0 | 26.6 |
| Sleep habits | | |
| Sleep duration, h/d | 7.0 (1.0) | 6.9 (0.9) |
| Regular snorer, % | 10.8 | 6.0 |
| Night shift work >5 years, % | 21.4 | 16.0 |
| Sleep position, % | | |
| On back | 6.2 | 6.6 |
| On side | 84.4 | 82.6 |
| On front | 9.4 | 10.8 |

Notes: *Values are mean (SD) or median (P_{25} , P_{75}) for continuous variables and percentages for categorical variables and are standardized to the age distribution of the study population. [†]Value was not age adjusted. [‡]MET-h/wk = sum of the average time/week spent in each activity × MET value of each activity.

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); MET, metabolic-equivalent; AHEI, Alternate-Healthy Eating Index.

Table 2 Odds Ratios of Healthy Aging by Sleep Duration, Snoring at Midlife in the Nurses' Health Study*

| | Number of Participants | Healthy Aging, n (%) | Age-Adjusted | MV1-Adjusted [†] | MV2-Adjusted [‡] |
|------------------------------|------------------------|----------------------|-------------------|---------------------------|---------------------------|
| Sleep duration, hours | | | | | |
| ≤5 | 506 | 57 (11.3) | 0.91 (0.68, 1.21) | 0.93 (0.69, 1.24) | 0.94 (0.70, 1.27) |
| 6 | 3052 | 326 (10.7) | 0.85 (0.74, 0.98) | 0.87 (0.75, 1.01) | 0.88 (0.76, 1.02) |
| 7 | 5061 | 621 (12.3) | 1 (reference) | 1 (reference) | 1 (reference) |
| 8 | 3094 | 310 (10.0) | 0.81 (0.70, 0.93) | 0.83 (0.71, 0.96) | 0.83 (0.72, 0.96) |
| ≥9 | 591 | 40 (6.8) | 0.54 (0.38, 0.75) | 0.59 (0.42, 0.82) | 0.60 (0.43, 0.84) |
| Regular snoring | | | | | |
| No | 10,974 | 1259 (11.5) | 1 (reference) | 1 (reference) | 1 (reference) |
| Yes | 1254 | 81 (6.5) | 0.53 (0.42, 0.67) | 0.61 (0.49, 0.78) | 0.69 (0.54, 0.88) |

Notes: *ORs <1.00 denote lower odds of healthy aging. For sleep duration, n=13,099; for snoring: n=13,018 due to 81 participants with missing snoring; we defined regular snorers as those who reported snoring regularly and non-snorers as those who only occasionally or almost never snored; [†]MV1 was adjusted for age (continuous), education (registered nurse, bachelor, or graduate), marital status (married, widowed, or separated/divorced), household income (quintiles); family history of cancer; family history of myocardial infarction and family history of diabetes (yes or no); baseline hypertension and high cholesterol (yes or no); menopausal status and hormone use (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users), aspirin use (regular use or not); smoking history (never, former smoker, current smoker), alcohol intake (none, 1–14.9, ≥15 g/d), total energy intake (quintiles), diet quality (Alternate Healthy Eating Index score, in quintiles), physical activity (metabolic equivalent task-hours per week, in quintiles), standing and sitting time (in quintiles); [‡]MV2: MV1 + body mass index (BMI <18.5, 18.5–24.9, 25–29.9, ≥30 kg/m²).

0.96), and 0.59 (0.42, 0.82), respectively. The associations remained similar with additional adjustment for BMI. As shown in the estimated dose–response curve from a multivariate analysis (Figure 1A), there was a nonlinear association between sleep duration and healthy aging (P for nonlinearity = 0.0073), with substantially lower odds of healthy aging for long sleep duration.

When examining the association by each domain of healthy aging (Table 3), short sleep duration was associated with lower odds of no limitation of mental health (OR for ≤5 versus 7 hours: 0.73; 95% CI: 0.60, 0.88) and no impairment of cognitive function (comparable OR: 0.67; 95% CI: 0.51, 0.88), whereas long sleep duration was associated with lower odds of good physical function (OR for ≥9 versus 7 hours: 0.69; 95% CI: 0.56, 0.86), no limitation of mental health (comparable OR: 0.83; 95% CI: 0.69, 0.99) and no impairment of cognitive function (comparable OR: 0.74; 95% CI: 0.57, 0.97). The results were further supported by the significant nonlinear associations of sleep duration with no impairment of physical function (P for nonlinearity=0.0004), no mental health limitations (P for nonlinearity=0.0002), and no impairment of cognitive function (P for nonlinearity=0.0336) in the restricted cubic spline analyses (Figure 1C–E). However, no significant association was observed between sleep duration and the odds of having no major chronic disease (P for linearity=0.1064; Figure 1B).

Snoring and Healthy Aging

We found that regular snoring was associated with reduced odds of healthy aging after adjusting for potential covariates except BMI (OR: 0.61; 95% CI: 0.49, 0.78; Table 2). Further adjustment of BMI somewhat attenuated the association (OR: 0.69, 95% CI: 0.54, 0.88). The associations of snoring with each domain of healthy aging are shown in Table 3. Regular snoring was associated with 14% lower odds of being free of major chronic diseases (95% CI: 0.76, 0.97), but was not significantly associated with the other three domains of healthy aging.

When we examined sleep duration and snoring jointly, participants with long sleep (≥9 h/day) and regular snoring had the lowest odds of healthy aging compared with participants with 7 hours of sleep and no regular snoring (fully adjusted OR: 0.23; 95% CI: 0.06, 0.94; Figure 2). However, we did not observe a significant interaction between sleep duration and snoring on healthy aging (P for interaction=0.198).

Stratified Analysis by Lifestyles

In stratified analyses of sleep duration and healthy aging by lifestyle factors, including overweight, smoking status, alcohol intake, total energy intake, dietary quality, physical activity, standing and sitting time (Table S2), long sleep duration was consistently associated with lower odds of healthy aging almost in each subgroup (although some of these associations were not statistically significant due to

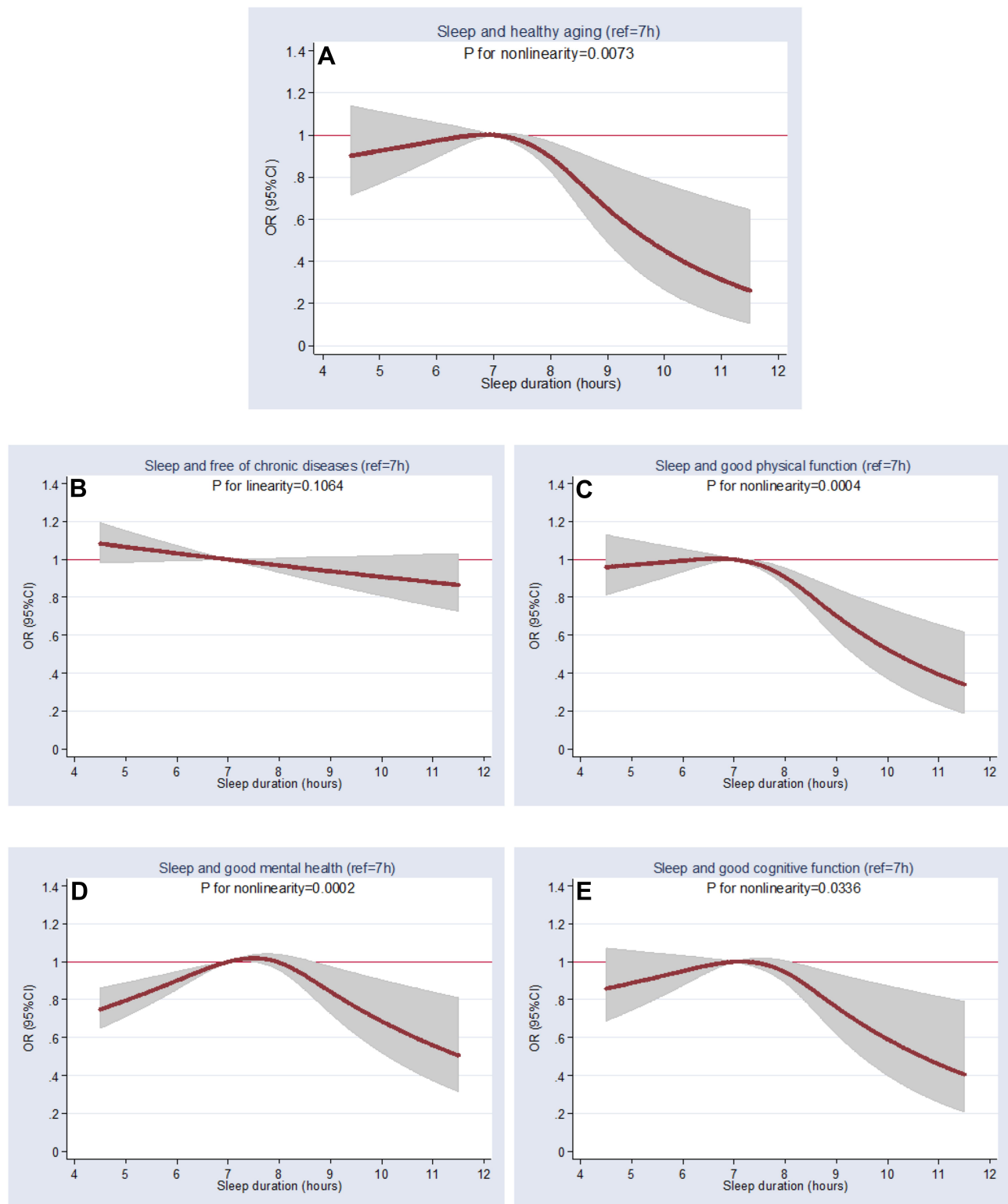


Figure 1 Association of sleep duration with healthy aging including 4 domains*: **(A)** Sleep duration and healthy aging, **(B)** sleep duration and free of chronic diseases, **(C)** sleep duration and good physical function, **(D)** sleep duration and good mental health, **(E)** sleep duration and good cognitive function. **Notes:** *ORs <1.00 denote lower odds of healthy aging. All model was adjusted for age (continuous), education (registered nurse, bachelor, or graduate), marital status (married, widowed, or separated/divorced), household income (quintiles); family history of cancer, family history of myocardial infarction and family history of diabetes (yes or no); baseline hypertension and high cholesterol (yes or no); menopausal status and hormone use (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users), aspirin use (regular use or not); smoking history (never, former smoker, current smoker), alcohol intake (none, 1–14.9, ≥15 g/d), total energy intake (quintiles), diet quality (Alternate Healthy Eating Index score, quintiles), physical activity (MET-h/wk), standing and sitting time (all in quintiles); body mass index (BMI <18.5, 18.5–24.9, 25–29.9, ≥30 kg/m²).

Table 3 Odds Ratios of Each Domain of Healthy Aging by Sleep Duration, Snoring at Midlife in the Nurses' Health Study*

| | Free of Chronic Diseases | | Good Physical Function | | No Limitation of Mental Health | | No Impairment of Cognitive Function | |
|------------------------------|--------------------------|-------------------|------------------------|-------------------|--------------------------------|-------------------|-------------------------------------|-------------------|
| | n (%) | MV2-Adjusted | n (%) | MV2-Adjusted | n (%) | MV2-Adjusted | n (%) | MV2-Adjusted |
| Sleep duration, hours | | | | | | | | |
| ≤5 | 342 (67.6) | 1.01 (0.83, 1.23) | 141 (27.9) | 0.96 (0.78, 1.19) | 189 (37.4) | 0.73 (0.60, 0.88) | 436 (86.2) | 0.67 (0.51, 0.88) |
| 6 | 2090 (68.5) | 1.05 (0.95, 1.16) | 854 (28.0) | 0.94 (0.85, 1.05) | 1268 (41.6) | 0.87 (0.79, 0.95) | 2770 (90.8) | 1.04 (0.89, 1.22) |
| 7 | 3440 (68.0) | 1 (reference) | 1516 (30.0) | 1 (reference) | 2283 (45.1) | 1 (reference) | 4592 (90.7) | 1 (reference) |
| 8 | 2075 (67.1) | 0.98 (0.89, 1.08) | 802 (25.9) | 0.86 (0.77, 0.96) | 1341 (43.3) | 0.95 (0.86, 1.04) | 2766 (89.4) | 0.89 (0.77, 1.04) |
| ≥9 | 374 (63.3) | 0.90 (0.75, 1.08) | 121 (20.5) | 0.69 (0.56, 0.86) | 230 (38.9) | 0.83 (0.69, 0.99) | 515 (87.1) | 0.74 (0.57, 0.97) |
| Regular snoring | | | | | | | | |
| No | 7502 (68.4) | 1 (reference) | 3139 (28.6) | 1 (reference) | 4764 (43.4) | 1 (reference) | 9885 (90.1) | 1 (reference) |
| Yes | 766 (61.1) | 0.86 (0.76, 0.97) | 270 (21.5) | 0.92 (0.79, 1.07) | 509 (40.6) | 0.95 (0.84, 1.08) | 1125 (89.7) | 0.95 (0.78, 1.16) |

Note: *All footnotes are same with Table 2.

small number of cases). The nonlinear association pattern between sleep duration and healthy aging appeared more apparent among those with longer sitting time (P for interaction=0.007) or standing time (P for interaction=0.044).

Sensitivity Analysis

We conducted further analyses to test the robustness of the association between sleep duration and healthy aging. In a secondary analysis, we included 2425 women who died before age 70 through 2000 as usual agers and repeated the analysis, and the results remained similar (Table S3). In

a sensitivity analysis, excluding women with a history of shift work or recent shift work did not change our results materially (Table S4). Additional adjustment for duration of shift work also resulted in similar associations. Likewise, when we restricted analyses to the participants whose sleep position was on sides, and those who did not snore regularly, results were essentially unchanged (Table S4). The results did not appreciably change in sensitivity analyses with adjustment for continuous BMI instead of categorical BMI (data not shown). When sleep duration and snoring were mutually adjusted in the same model, the results for healthy aging and individual domains also remained the same (data not shown).

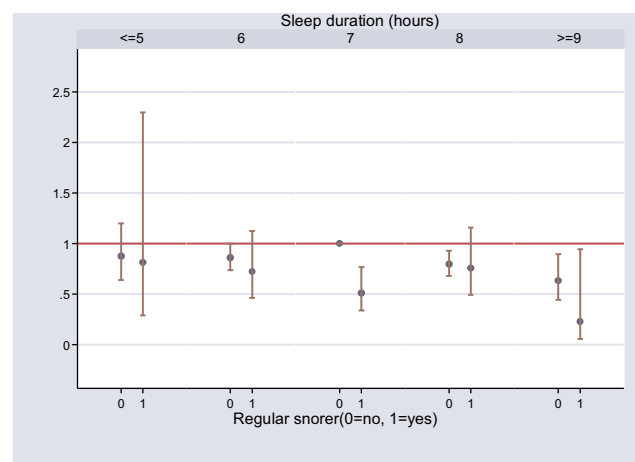


Figure 2 Joint effect of sleep duration and regular snoring on healthy aging*.

Notes: *Model was adjusted for age (continuous), education (registered nurse, bachelor, or graduate), marital status (married, widowed, or separated/divorced), household income (quintiles); family history of cancer, family history of myocardial infarction and family history of diabetes (yes or no); baseline hypertension and high cholesterol (yes or no); menopausal status and hormone use (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users), aspirin use (regular use or not), smoking history (never, former smoker, current smoker), alcohol intake (none, 1–14.9, ≥15 g/d), total energy intake (quintiles), diet quality (Alternate Healthy Eating Index score, quintiles), physical activity (MET-h/wk), standing and sitting time (all in quintiles); body mass index (BMI <18.5, 18.5–24.9, 25–29.9, ≥30 kg/m²).

Discussion

In this large, prospective cohort study, sleep durations were non-linearly associated with odds of healthy aging after adjusting for potential confounding factors: in comparison with 7 hours of sleep, long sleep duration was associated with lower odds of achieving healthy aging at age 70; there was also a suggestion of lower odds of healthy aging for shorter sleepers, although the associations did not reach statistical significance. Such nonlinear relationships were also observed for different components of healthy aging, except for the absence of chronic diseases. Regular snoring was associated with reduced odds of healthy aging (especially free of diseases), independent of sleep duration. To our knowledge, this is the first study that characterized the associations of sleep habits with overall health status among those who have survived to older ages.

Comparison with Others and Explanations

The non-linear association observed in the current analysis was consistent with those observed in most prior studies in

general documenting that both shorter and longer sleep durations were associated with increased mortality.^{16–18} For example, several meta-analyses showed a U-shaped association between sleep duration and mortality, with the lowest mortality observed among individuals with approximately 7-hour daily sleep duration.^{16–18} Studies also found U-shaped relationships between sleep duration and other health outcomes, including chronic diseases,^{10–12} mental health,¹⁵ memory or cognition decline,^{13,14} although the sleep duration was associated with the lowest risk varied from 6 to 9 hours for different disease outcomes.^{10,13,14,18,36} Interestingly, while short sleep duration has been previously associated with increased risk of diabetes,³⁷ coronary heart disease³⁸ and mortality²⁶ in our cohort, we observed no significant association especially between short sleep duration and the composite chronic disease outcome, which may be driven by the null findings for cancers.³⁹ In our study, we found self-reported sleep duration of 7 hours per night at midlife was associated with the highest odds of achieving healthy aging as well as optimal cognitive, physical, and mental health. This is consistent with recommended sleep duration of 7–8 hours per night by the American Academy of Sleep Medicine and highlights the potential benefits of adequate sleep duration on healthy aging.

There are several potential mechanisms for the non-linear association. Given that sleep is essential for repair, restoration and rejuvenation of the human body, insufficient sleep may lead to alterations in these physiologic processes that ultimately precipitate the development of physical, mental and cognitive impairment. For example, sleep has been shown to enhance clearance of neurotoxic waste products in the brain, whereas sleep deprivation results in cerebral accumulation of β -amyloid, a key biomarker for cognitive decline and Alzheimer's disease.^{40–42} This may explain the associations with short sleep duration we observed for the domains of mental and cognitive health. Long sleep duration, on the other hand, may be the consequence of poor sleep quality due to frequent awakenings, which also disrupt these sleep-facilitated processes. Further, both short and long sleep durations are associated with energy imbalance, elevated inflammation, reduced immune response and insulin resistance; these pathways are key mechanisms for a variety of adverse health outcomes. Individuals with short or long sleep duration are also more likely to be affected by circadian disruption due to night shift work or irregular sleep schedules. Previous studies have linked shift work and

irregular sleep schedules to increased risk of cardiometabolic disease and mental disorders.^{43–47} However, we cannot fully exclude the possibility that certain preclinical, unrecognized conditions for aging may result in extreme sleep duration.

Our results also suggest that, independent of sleep duration, snoring was associated with lower odds of healthy aging (especially free of chronic diseases). This was consistent with previous studies that have reported associations between snoring and chronic diseases such as hypertension, diabetes and cardiovascular events.^{48–50} Snoring is one of the cardinal manifestations of obstructive sleep apnea,⁵¹ which has been associated with chronic diseases,^{52–55} cancers,⁵⁶ depression,⁵⁷ and cognitive function.⁵⁸ Therefore, habitual snorers are more likely to experience intermittent hypoxia, which results in reduced cerebral blood flow and brain oxygen supply during sleep and may adversely influence brain regions regulating mood and memory.^{59,60} Heavy snoring may also lead to repeated arousals and fragmented sleep that disrupt sleep quality and stimulate the sympathetic nervous system.⁶¹ Increased sympathetic activity is associated with the development of a wide range of health outcomes,^{62,63} including cardiometabolic disease, cancers and psychiatric disorders. Additionally, we found that participants with long sleep duration and regular snoring had the lowest odds of healthy aging. Although replication in future studies is warranted, our findings suggest potential target populations for sleep hygiene interventions to maximize the benefits of sleep on healthy aging.

Limitation

Several limitations of this study should be considered. First, self-reported sleep duration may be subjected to measurement error. However, previous validation studies found that self-reported usual sleep duration is well correlated with that derived from sleep diaries,²⁶ and there was a moderate correlation between self-reported and actigraphy-assessed sleep duration.^{64,65} In addition, as our sleep data were prospectively collected, the measurement error was likely non-differential, biasing the association towards the null. Second, as this is an observational study, we cannot rule out the possibility of residual unmeasured confounding. For example, the observed associations may be confounded by sleep quality given its relationships with mortality⁶⁶ and cognitive function.³⁶ Third, we only assessed sleep habits once at baseline, which may not reliably reflect long-term sleep patterns. Future studies

using repeated measures to evaluate changes or trajectory of sleep duration will provide further insights into the associations with healthy aging.⁶⁷

Fourth, we could not entirely exclude the possibility of reverse causation as we did not assess impaired physical function, mental health, and subjective memory at study baseline. Thus, the study population may include individuals with these conditions that may lead to excess sleep duration or snoring. However, we excluded all people with major diseases at baseline and adjusted for common health conditions (eg, hypertension, high cholesterol) as covariates in the analysis, which often coexist with the aforementioned conditions. Finally, the participants in our study are predominantly white female nurses. Whether our results apply to men, other racial/ethnic groups, or people with heterogeneous socioeconomic backgrounds requires further study.

Conclusion

In conclusion, we found that sleep duration at midlife was nonlinearly associated with healthy aging in later life. In comparison with 7 hours of sleep, shorter and longer durations were associated with lower odds of achieving healthy aging at age 70. In addition, regular snorers had lower odds of attaining optimal health at old ages, especially for those with sleep duration ≥ 9 hours. These findings highlight the role of sleep duration and snoring in promoting healthy longevity. Future research is necessary to better understand the mechanisms by which sleep duration and snoring, as well as other sleep traits, may influence healthy aging.

Ethics Approval and Consent to Participate

The study protocol was approved by the institutional review boards of the Brigham and Women's Hospital and the Harvard T.H. Chan School of Public Health. Participants provided implied consent by returning the questionnaires and we also obtained written consent from each participant to obtain and review medical records.

IRB protocol title and number: Improving Women's Health: The Nurses' Health Study, 1999-P-011114.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. Hongying Shi and Tianyi Huang contributed equally as co-first authors and Qi Sun and Molin Wang authors contributed equally as co-corresponding authors.

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Disclosure

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