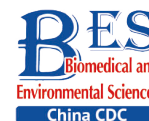


## Original Article



# Midday Napping, Nighttime Sleep, and Mortality: Prospective Cohort Evidence in China\*

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## Abstract

**Objective** In developed countries, midday napping and nighttime sleep duration have been linked to long-term survival; however, little is known about such effects in less developed regions. Therefore, this study aimed to assess the associations of midday napping and nocturnal sleep with mortality in middle-aged and older Chinese adults.

**Methods** A nationwide cohort of 15,524 adults aged  $\geq 45$  years was enrolled from 28 provincial regions across mainland China and followed up from 2011 to 2018, using data from the Chinese Health and Retirement Longitudinal Study. Midday napping and nighttime sleep duration were assessed using standardized questionnaires. Cox proportional hazards models with random intercepts for the surveyed provinces were used to estimate hazard ratios (HRs) of all-cause mortality, adjusting for sociodemographic characteristics, behavioral factors, and health status.

**Results** A total of 1,745 deaths occurred during a median follow-up of 7.1 years, and the mean (standard deviation) age was 59 (10.1) years at baseline. Compared with non-nappers, over 60 min nappers had a higher risk of all-cause mortality [HR: 1.35, 95% confidence interval (CI): 1.17–1.56], while no significant associations were observed among  $< 30$  min nappers. Compared with sleep duration of 6–8 h/night, both short ( $< 6$  h) and long ( $\geq 8$  h) sleep duration were significantly associated with increased mortality, with corresponding HR (95% CI) estimates of 1.21 (1.05–1.38) and 1.26 (1.10–1.44), respectively. We observed significant patterns for greater risks associated with longer nap duration, with a  $P_{\text{trend}}$  value  $< 0.001$  for all-cause mortality. No significant evidence of an additive interaction was identified between midday napping and nighttime sleep.

**Conclusion** Long midday napping and inappropriate nighttime sleep were independently associated with an increased risk of all-cause mortality in middle-aged and older Chinese populations. Biological studies are needed to validate our findings and clarify the mechanisms underlying this association.

**Key words:** Midday napping; All-cause mortality; Nighttime sleep; Cohort; Chinese; CHARLS

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## INTRODUCTION

Sleep is an important indicator of health and is essential for maintaining optimal health and physiological function<sup>[1]</sup>. The National Sleep Foundation from the United States recommends 7–9 h of sleep for people aged 26–64 years, and at least 7 h for older people aged > 65 years<sup>[2]</sup>. In 2022, the China Sleep Research Society pointed out that among those who slept < 6 h, participants aged 46–60 and ≥ 61 accounted for 66.3% and 59.7%, respectively<sup>[3]</sup>. Nearly half (49.7%) of the older Chinese population (> 65 years old) reported a total sleep duration < 7 h/day<sup>[4]</sup>. Given the aggravation of population aging in China and insufficient sleep duration among older adults, attention to their sleep health has become an important public health issue. Numerous epidemiological studies have observed that inappropriate sleep duration (insufficient or excessive sleepiness) is associated with a series of chronic diseases<sup>[5–11]</sup> or deaths<sup>[12–19]</sup>. A cohort study comprising 13,164 participants from South Korea found a U-shaped sleep-mortality association<sup>[13]</sup>. However, a U-shaped relationship has not been confirmed in other studies<sup>[12,14,15,17,18]</sup>. From a physiological perspective, epidemiological evidence is needed to further understand the impacts of sleep duration on health outcomes in middle-aged and older Chinese individuals.

Midday napping is fairly common and conventionally deemed a healthy behavior in several countries. The prevalence of habitual napping ranges from 30.0% to 70.0% worldwide (e.g., 60.5% in the Middle East, 48.0% in China, 35.5% in Southeast Asia, and 34.4% in South America)<sup>[19]</sup>. Especially in China, daytime napping is considered a part of the cultural norm<sup>[19,20]</sup>. In recent years, researchers have paid increased attention to the effects of midday napping on health<sup>[6,21–23]</sup>. Several studies have investigated the relationship between daytime napping and all-cause mortality in many Eastern<sup>[12,24,25]</sup> and Western countries<sup>[14,26–28]</sup>. However, heterogeneous results have been reported in these studies. Large-scale cohort studies in the United States<sup>[26]</sup>, England<sup>[28]</sup>, and Israel<sup>[27]</sup> have found that participants who took long naps (≥ 1 h) had a greater risk of death than those who took no naps. A Greek study involving 23,681 individuals found that daytime napping may play a protective role against heart-related deaths<sup>[29]</sup>, whereas midday napping had no effect on mortality among the older population in China<sup>[18]</sup>. Some previous studies may

fail to consider potential reverse causality<sup>[12,13]</sup>; however, our study paid attention to this potential issue in longitudinal cohort studies. To date, there is still a lack of large-scale cohort studies investigating the association between midday napping and mortality in middle-aged and older Chinese individuals.

To fill these knowledge gaps, we conceived a population-based cohort design based on 15,000+ participants from 150 counties in 28 provincial regions to assess the associations of midday napping and nighttime sleep with all-cause mortality among middle-aged and older adults in China. The dose–response relationship between all-cause mortality and midday napping and nighttime sleep was outlined for middle-aged and older Chinese individuals. We also conducted a range of subgroup analyses to identify potential effect modifications, particularly, we explored whether it was the independent effects of midday napping or nighttime sleep or the interaction between midday napping and nighttime sleep on overall health outcomes. Our findings may provide scientific evidence to formulate reasonable and healthy sleep time management strategies and help promote healthy lifestyle behaviors.

## METHODS

### *Study Design and Population*

The participants in this study were obtained from the Chinese Health and Retirement Longitudinal Study (CHARLS). Administered by the National School for Development (China Center for Economic Research), CHARLS is an ongoing, longitudinal, nationwide survey of Chinese community residents aged ≥ 45 years<sup>[30]</sup>. The baseline survey of CHARLS was launched in 2011 and involved approximately 17,708 individuals chosen through multistage probability sampling from 28 provinces (Figure 1). CHARLS publicly released data from the baseline and three waves of follow-up surveys to date (CHARLS-2011, -2013, -2015, and -2018), using face-to-face computer-assisted personal interviews by trained interviewers. A detailed description of the design and method of CHARLS has been reported elsewhere<sup>[31]</sup>. The Biomedical Ethics Review Committee of Peking University approved this study (approval number: IRB00001052–11015), and informed consent was obtained from each participant. Detailed data were obtained from the official website (<http://charls.pku.edu.cn/en/>,

accessed on September 24, 2021).

For the current analysis, we used data from four waves of CHARLS-2011, -2013, -2015, and -2018. We conceived a population-based cohort design regarding the association of napping duration and nighttime sleep with all-cause mortality and applied the following exclusion criteria for 17,708 CHARLS participants at baseline: 1) participants lost to follow-up during 2013–2018 ( $n = 790$ ); 2) individuals with missing or logical errors on important covariates ( $n = 1,352$ ); and 3) adults who died within 6 months after the baseline survey ( $n = 42$ ). Finally, 15,524 individuals were included in the analysis (Supplementary Figure S1, available in [www.besjournal.com](http://www.besjournal.com)). The characteristics of the participants ( $n = 15,524$ ) were highly comparable to those of the total surveyed participants ( $n = 17,708$ ) at the CHARLS baseline (Supplementary Table S1A, available in [www.besjournal.com](http://www.besjournal.com)).

### Assessment of Midday Napping and Nighttime Sleep

Information on midday napping and nighttime sleep duration at baseline was collected through a face-to-face questionnaire investigation by well-trained interviewers. Midday napping was evaluated by asking the question, “During the past month, how long did you take a nap after lunch in general?”

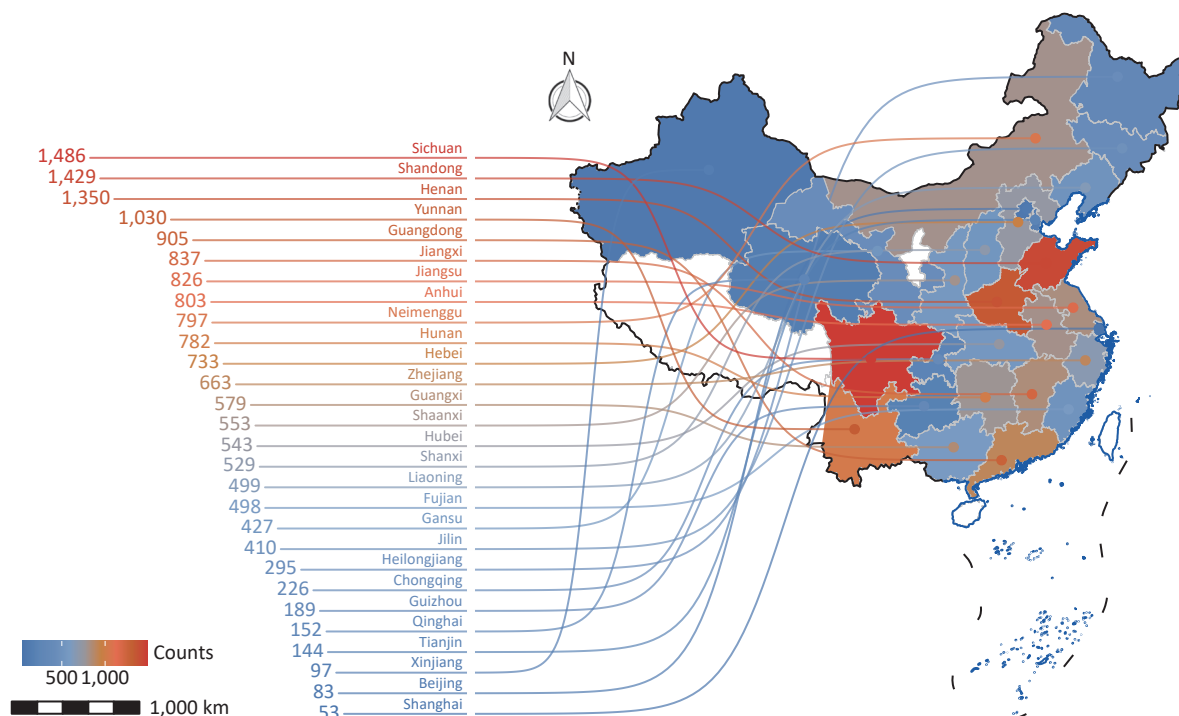
Midday napping duration was categorized into four groups: 0, 0–, 30–, and  $\geq 60$  min<sup>[32]</sup>. Nighttime sleep was ascertained using the following question: “During the past month, how many hours of actual sleep did you get at night (average hours for one night)?” We classified nighttime sleep duration into three groups:  $< 6$ ,  $6 - < 8$ , and  $\geq 8$  h<sup>[33]</sup>.

### Ascertainment of Outcome

The survival outcome of participants, including status (dead or alive), date, and cause of death, was ascertained through CHARLS interviews conducted with family members in three waves of follow-up surveys after baseline. Owing to the large number of unknown or uncertain causes of death, we used all-cause mortality as the endpoint in this study. Survival time was calculated as the interval from the date of the initial survey until the date of death, censored, or the end of CHARLS 2018, whichever came first.

### Covariates

In line with previous studies<sup>[14,19]</sup>, we included information about sociodemographic characteristics, behavioral factors, and health status in this analysis. Sociodemographic variables included sex, age, marital status (married, widowed, or single), urbanization (urban or rural areas), geographical



**Figure 1.** Map of participants' distribution in our cohort.

region (North or South), and educational attainment (illiterate, 1–6, 7–9, or > 9 years). Behavioral factors included social activity (yes or no), smoking status, and alcohol consumption (current, former, or never). Health status comprised self-reported chronic diseases (cardiovascular disease, respiratory disease, diabetes, and depression status) and body-mass index [body-mass index (BMI): < 18.5, 18.5–23.9, 24–27.9, and  $\geq 28.0$  kg/m<sup>2</sup>]. BMI was calculated by dividing weight in kilograms by height in meters squared and was grouped according to the predictive values of BMI for risk factors of certain related diseases in Chinese adults<sup>[34]</sup>. The northern and southern regions were divided according to China's geographical boundaries, namely, Qinling Mountains and Huai River. Social activities include physical exercise, helping relatives and friends, participating in community-related organizations, volunteering, and charity activities.

### Statistical Analysis

The baseline characteristics of participants were compared by category of napping duration and described as mean  $\pm$  standard deviation (SD) for continuous variables and frequency with percentages for categorical variables. We constructed survival models using the baseline covariates only, and Cox proportional hazards models with random intercepts for the surveyed provinces were applied to evaluate the associations of midday napping and nighttime sleep duration with all-cause mortality. We assessed hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) of all-cause mortality associated with daytime napping duration (0 min nap for reference) and nocturnal sleep (6 – < 8 h/night as reference), using the sex- and age-adjusted and multivariable-adjusted models (including the aforementioned various confounders). *Kaplan-Meier* survival analysis with a log-rank test was used to compare differences in survival curves between each category of midday napping and nighttime sleep duration<sup>[35]</sup>. Tests for linear trends in the HRs were performed using Wald tests by entering dummy variables for each category of midday napping and nighttime sleep duration as a single continuous variable (e.g., 1–4) in the Cox models<sup>[36]</sup>. The proportional hazards assumption was not violated, as examined by the weighted Schoenfeld residuals.

A restricted cubic spline with three knots at fixed percentiles (10%, 50%, and 90%) of the distribution was employed to smooth the dose-response (D-R) relationship of midday napping and nighttime sleep

duration with mortality<sup>[37]</sup>. Daytime napping was divided into three groups (0, 0–60, and  $\geq 60$  min) to explore the joint effects between midday napping and nighttime sleep against all-cause mortality (midday napping 0 min and nighttime sleep 6 – < 8 h as reference). To investigate the interactive effects of daytime napping and nighttime sleep, we calculated the relative excess risk due to interaction (RERI) and attributable proportion (AP) of additive effects to the total observed effects<sup>[38]</sup>. RERI > 0 indicated that the combined effects were greater than those of each exposure alone (i.e., additive interaction), and RERI < 0 indicated a negative additive joint effect. The AP of additive effects for the total observed effects was calculated by dividing RERI by total effects, with 0 indicating no interactions. In accordance with our D-R analysis, we classified midday napping into two groups (i.e., < 30 min vs.  $\geq 30$  min) and categorized nighttime sleep as < 6, 6 – < 8, and  $\geq 8$  h, with group < 30 min and 6 – < 8 h as the reference.

To address the potential effects of modification of the relationship between sleep duration and mortality, trend and subgroup analyses were performed by 1) demographic characteristics [e.g., sex, age (45–65 vs.  $\geq 65$  years)], 2) residential factors [e.g., region (urban vs. rural area) and geolocation (North vs. South)], and 3) behavioral risks [for example, smoking status and alcohol consumption (no vs. yes)]. Based on the overweight standard ( $\geq 24.0$  kg/m<sup>2</sup>) of Chinese adults<sup>[39]</sup>, we divided BMI into two groups (i.e., < 24.0 vs.  $\geq 24.0$  kg/m<sup>2</sup>). To minimize the potential influence of reverse causation, we further conducted sensitivity analyses by excluding deaths identified in the initial first year during follow-up and adding health insurance variables to the multivariable-adjusted model. *P*-values for interactions were calculated using the likelihood ratio test<sup>[40]</sup>. Associations were considered significant at *P*-values < 0.05. All statistical analyses were performed using R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria), using the package “coxme” for Cox frailty modeling, “rms” for smoothing nonlinear terms, and “epiR” for interactive analysis.

## RESULTS

### Baseline Characteristics

Table 1 describes the characteristics of the participants stratified by midday napping duration. A total of 15,524 participants were employed, with an

**Table 1.** Baseline characteristics of the participants ( $n = 15,524$ ) by daytime napping

Characteristics	Total	Midday napping duration			
		0 min	0– min	30– min	≥ 60 min
Population					
Persons, <i>n</i>	15,524	7,272	2,612	3,440	2,200
Death, <i>n</i>	1,745	618	250	357	520
Demographic characteristics					
Age (years), mean ± SD	59.0 ± 10.1	58.6 ± 9.7	59.2 ± 10.0	59.2 ± 10.0	60.0 ± 10.3
Male sex, %	47.9	40.2	46.4	54.8	57.4
Married, %	80.5	82.2	83.8	84.1	84.5
Urban residents, %	38.7	36.5	44.4	40.3	37.6
Northern provinces, %	44.3	37.1	53.2	48.4	52.5
Education attainment, %					
Illiteracy	27.6	32.0	23.7	23.0	24.7
1–6 years	39.6	39.3	38.3	41.5	41.2
7–9 years	20.6	18.7	22.6	20.7	22.5
> 9 years	12.2	10.0	15.4	14.8	11.6
Behavioral factors					
Social activity, %					
Yes	46.2	51.9	47.9	47.2	50.4
No	53.8	48.1	52.1	52.8	49.6
Smoking status, %					
Current	29.1	27.9	27.6	32.5	37.5
Former	8.3	6.9	9.3	10.8	10.5
Never	62.6	65.2	63.2	56.7	52.0
Alcohol consumption, %					
Current	25.1	21.5	23.6	28.2	31.7
Former	6.0	5.1	5.9	7.0	7.1
Never	68.9	73.3	70.5	64.8	61.2
Nighttime sleep (h/night), %					
< 6	29.3	33.5	28.5	25.5	22.4
6 – < 8	40.5	38.5	44.3	43.2	38.4
≥ 8	30.2	27.9	27.2	31.3	39.2
Health status					
BMI (kg/m²), mean ± SD	23.4 ± 3.5	23.2 ± 3.5	23.6 ± 3.6	23.6 ± 3.6	23.7 ± 3.6
Cardiovascular disease, %	34.4	31.0	39.2	37.1	37.8
Respiratory disease, %	11.6	11.4	11.2	12.4	12.5
Diabetes, %	5.6	4.3	7.2	6.8	6.4
Depression status, %	37.3	40.8	35.2	34.5	32.6

**Note.** Data are presented using mean  $\pm$  standard deviation for continuous variables and percentages for categorical variables. The sum of percentages from multiple subgroups may not equal 100% exactly due to rounding-off numbers. BMI, body-mass index.

average age of  $59.0 \pm 10.1$  years at baseline, and 47.9% were male. The BMI was  $23.4 \pm 3.5$  kg/m<sup>2</sup>, and 34.6% ( $n = 5,376$ ) were adults with BMI  $\geq 24$  kg/m<sup>2</sup>. During 107,419.5 person-years of follow-up (median 7.1 years), we observed 1,745 all-cause mortality events. A total of 46.8% of participants reported no daytime napping, and 14.1% napped for  $\geq 60$  min/day. Participants with  $< 6$  h and  $\geq 8$  h nocturnal sleep accounted for 29.3% and 30.2%, respectively. Approximately a quarter (25.1%) of the participants were alcohol drinkers, and less than one-third (29.1%) were current smokers. Regarding health status, the prevalence of cardiovascular disease and depression was 34.4% and 37.3%.

### Sleep-Mortality Associations

Table 2 illustrates the associations of midday napping and night-time sleep duration with all-cause mortality. Compared with non-nappers, the sex- and age-adjusted model revealed high risks of all-cause mortality in nappers  $\geq 30$  min, and the multivariable-adjusted model (adjusted HR: 1.30, 95% CI: 1.12–1.52) showed a high risk of death in long nappers ( $\geq 60$  min). In addition, we observed significant positive associations between long or short night-time sleep and all-cause mortality across the crude and multivariable-adjusted models. Specifically, in the multivariable-adjusted model, we found all-cause mortality HRs of 1.21 (1.05–1.38) and 1.26 (1.10–1.44) associated with nocturnal sleep durations  $< 6$  and  $\geq 8$  h/night, respectively. Trend

analyses for nap-mortality associations indicated high risks associated with long napping duration ( $P_{\text{trend}} < 0.001$ ) for all-cause mortality.

Figure 2 presents the Kaplan–Meier curves predicting survival probabilities of groups stratified by midday napping and nighttime sleep duration. We found a significant difference in the survival probability between midday napping and nighttime sleep subgroups (log-rank test,  $P < 0.001$ ). The group with  $\geq 60$  min of midday napping had the lowest predicted survival probability, with the number of participants dropping from 2200 to 1719. Compared with those who slept 6 –  $< 8$  h at night, the probability of survival for both short ( $< 6$  h/night) and long ( $\geq 8$  h/night) sleep duration decreased to  $< 90\%$  after approximately 70 months of follow-up. Similar results were also suggested in our Kaplan–Meier survival curves jointly stratified by midday napping and nighttime sleep duration, highlighting the lowest predicted survival probability at nighttime sleep duration  $< 6$  h (Supplementary Figure S2 available in [www.besjournal.com](http://www.besjournal.com)).

Figure 3 outlines the exposure–response relationships of midday napping and nighttime sleep duration with all-cause mortality. We did not detect a significant violation of the linear relationship ( $P_{\text{nonlinear}} = 0.130$ ) between midday napping and all-cause mortality over the entire exposure range. Specifically, the lowest risk of mortality occurred in the napping duration  $< 1$  h, but the risk rose sharply when the napping duration exceeded 1 h. A distinct

**Table 2.** Associations between midday napping and nighttime sleep duration with all-cause mortality

Exposures	Groups	Sex- and age-adjusted model			Multivariable-adjusted model <sup>a</sup>		
		HR	P for association	P for trend	HR	P for association	P for trend
		[95% CI]			[95% CI]		
Midday napping (min)				< 0.001			< 0.001
	0	1.00 (Ref)			1.00 (Ref)		
	0–	1.08 [0.93–1.25]	0.327		1.08 [0.92–1.26]	0.352	
	30–	1.15 [1.00–1.31]	0.048		1.14 [0.99–1.31]	0.076	
	≥ 60	1.35 [1.17–1.56]	< 0.001		1.30 [1.12–1.52]	0.001	
Nighttime sleep (h)				0.121			0.552
	< 6	1.39 [1.23–1.57]	< 0.001		1.21 [1.05–1.38]	0.007	
	6 – < 8	1.00 (Ref)			1.00 (Ref)		
	≥ 8	1.26 [1.11–1.43]	< 0.001		1.26 [1.10–1.44]	0.001	

**Note.** <sup>a</sup>Multivariable-adjusted models adjusted for sex, age, BMI, marital status, residential region, education attainment, social activity, smoking status, alcohol consumption, and chronic disease. HR, hazard ratio; CI, confidence interval; BMI, body-mass Index.

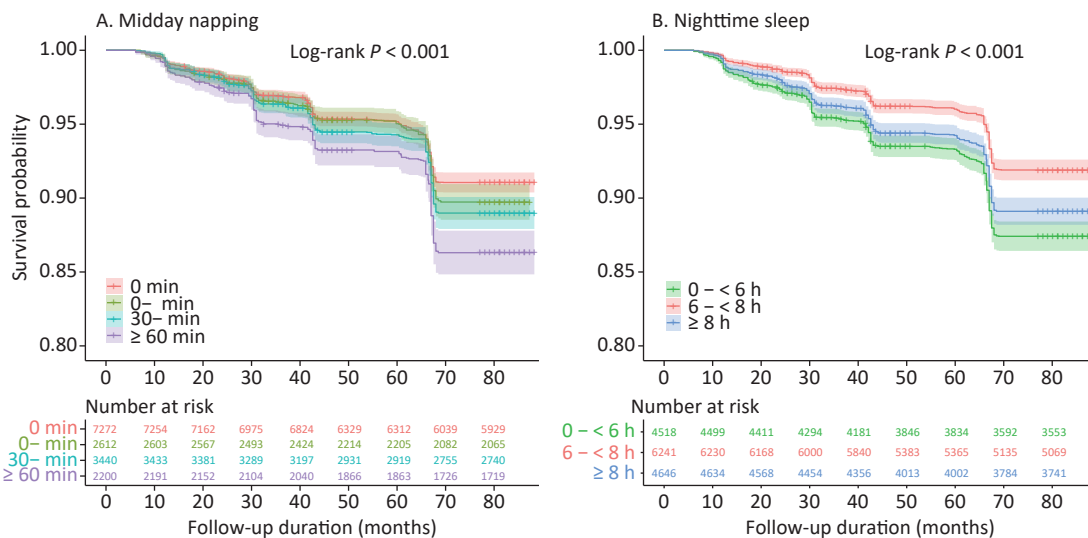
J-shaped curve was identified in the association of mortality with nighttime sleep duration, with a  $P$ -value  $< 0.001$  for potential nonlinearity. Individuals with a sleep duration of 6 – < 8 h/night had the lowest all-cause mortality; both short (< 6 h/night) and long ( $\geq 8$  h/night) sleep durations were associated with a high risk of all-cause mortality.

Figure 4 shows the joint effect of midday napping and nighttime sleep against all-cause mortality. We observed that midday napping increased the risk of death regardless of whether insufficient or extended nighttime sleep duration, compared with nighttime sleep of 6 – < 8 h and midday napping of 0 min. For instance, individuals with midday napping  $\geq 60$  min were associated with an excess mortality risk of 79%

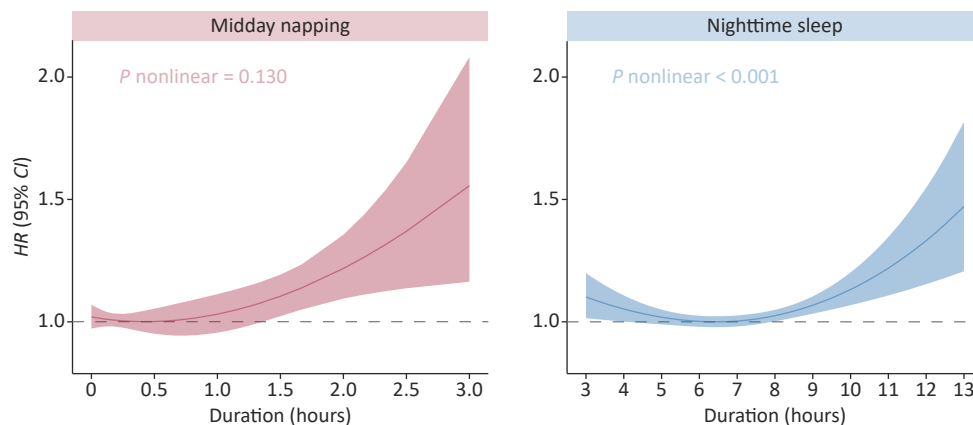
(1.79, 1.34–2.38) for nighttime sleep < 6 h and 58% (1.58, 1.22–2.03) for nighttime sleep  $\geq 8$  h. Based on the analysis using interaction (RERI) and AP, we did not identify significant evidence for an additive interaction between midday napping and nighttime sleep (Supplementary Table S2, available in [www.besjournal.com](http://www.besjournal.com)).

### Stratified Analyses

Figure 5 compares the subgroup-specific associations of mortality with daytime napping and nighttime sleep, stratified by individual characteristics (i.e., demographic, behavioral, and health) and geographical regions. In short, individuals with  $\geq 60$  min of daytime napping per day



**Figure 2.** Kaplan-Meier survival curves stratified by midday napping and nighttime sleep duration in each group.



**Figure 3.** Multivariable-adjusted spline curve for associations of all-cause mortality with midday napping and nighttime sleep duration. Models are adjusted for sex, age, BMI, marital status, residential region, education attainment, social activity, smoking status, alcohol consumption, and chronic diseases.

were significantly associated with an increased risk of mortality compared with the other groups. We found that nap-associated risks were highly profound among females (1.52 [1.17–1.97]), older adults aged  $\geq 65$  years (1.32 [1.09–1.59]), and overweight participants (1.54 [1.15–2.06]). Additionally, regional differences were highly conspicuous between midday napping and all-cause mortality, with a significant risk of mortality among rural ( $P_{\text{trend}} = 0.003$ ) and northern ( $P_{\text{trend}} = 0.007$ ) residents (Supplementary Table S3, available in [www.besjournal.com](http://www.besjournal.com)). Furthermore, stratified analyses for the association of nighttime sleep and mortality are presented in Supplementary Table S4 (available in [www.besjournal.com](http://www.besjournal.com)), wherein associations with short and long nocturnal sleep existed in females, underweight participants, and rural and southern residents.

In the sensitivity analyses, when limiting our analysis to participants with onset 1 year later (Supplementary Table S5, available in [www.besjournal.com](http://www.besjournal.com)), the significant associations of long nap duration with increased risk of all-cause mortality remained (1.30 [1.11–1.52]). Regarding mortality in relation to nighttime sleep duration, the associated *HR* estimates of short (1.35 [1.19–1.54] vs. 1.17 [1.02–1.34]) and long sleep duration (1.25 [1.10–1.43] vs. 1.23 [1.07–1.42]) changed slightly. After adding health insurance variables to the multivariable-adjusted model, the results did not change significantly (Supplementary Table S6 available in [www.besjournal.com](http://www.besjournal.com)). In addition, as suggested in our descriptive analysis of midday napping and nighttime sleep duration, no significant evidence that participants with a relatively unhealthy status may be prone to have long daytime napping and nighttime sleep (Supplementary Table

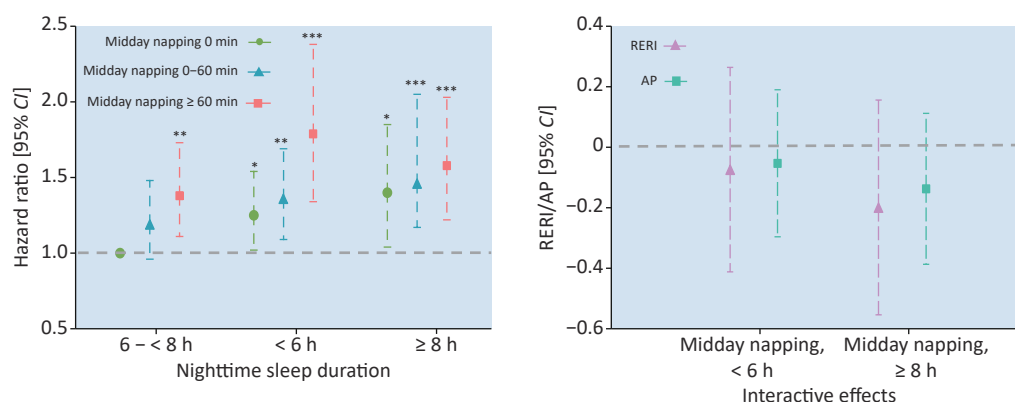
S7 available in [www.besjournal.com](http://www.besjournal.com)) was found. Thus, the potential influence of reverse causation may have been minimized in our study.

## DISCUSSION

In this large prospective cohort study among middle-aged and older Chinese populations, we observed an increased mortality risk associated with daytime naps of at least 60 min compared with non-nappers. This nationwide study also added novel cohort evidence for a J-shaped relationship between nighttime sleep duration and all-cause mortality, with durations  $< 6$  h and  $\geq 8$  h significantly elevating the risk. Currently, inappropriate sleep duration has become a critical public health issue and social problem, and mastering the beneficial effects of appropriate sleep duration is a key factor in promoting national health. According to the findings of our study, appropriate sleep duration (including nap duration  $< 60$  min and night sleep duration  $6 - < 8$  h) should be recommended in middle-aged and older people in China to reduce the adverse impact of inappropriate sleep duration on health. These findings may also have reference significance for the formulation of public health policies and provide scientific guidance for rational sleep arrangements.

### Midday Napping-Mortality Associations

In accordance with a meta-analysis involving 11 prospective cohort studies<sup>[41]</sup>, our study linked midday napping with a 15%–35% increased risk of all-cause mortality. Notably, less consistent findings have been reported in association with a short nap duration ( $< 30$  min). There was suggestive evidence

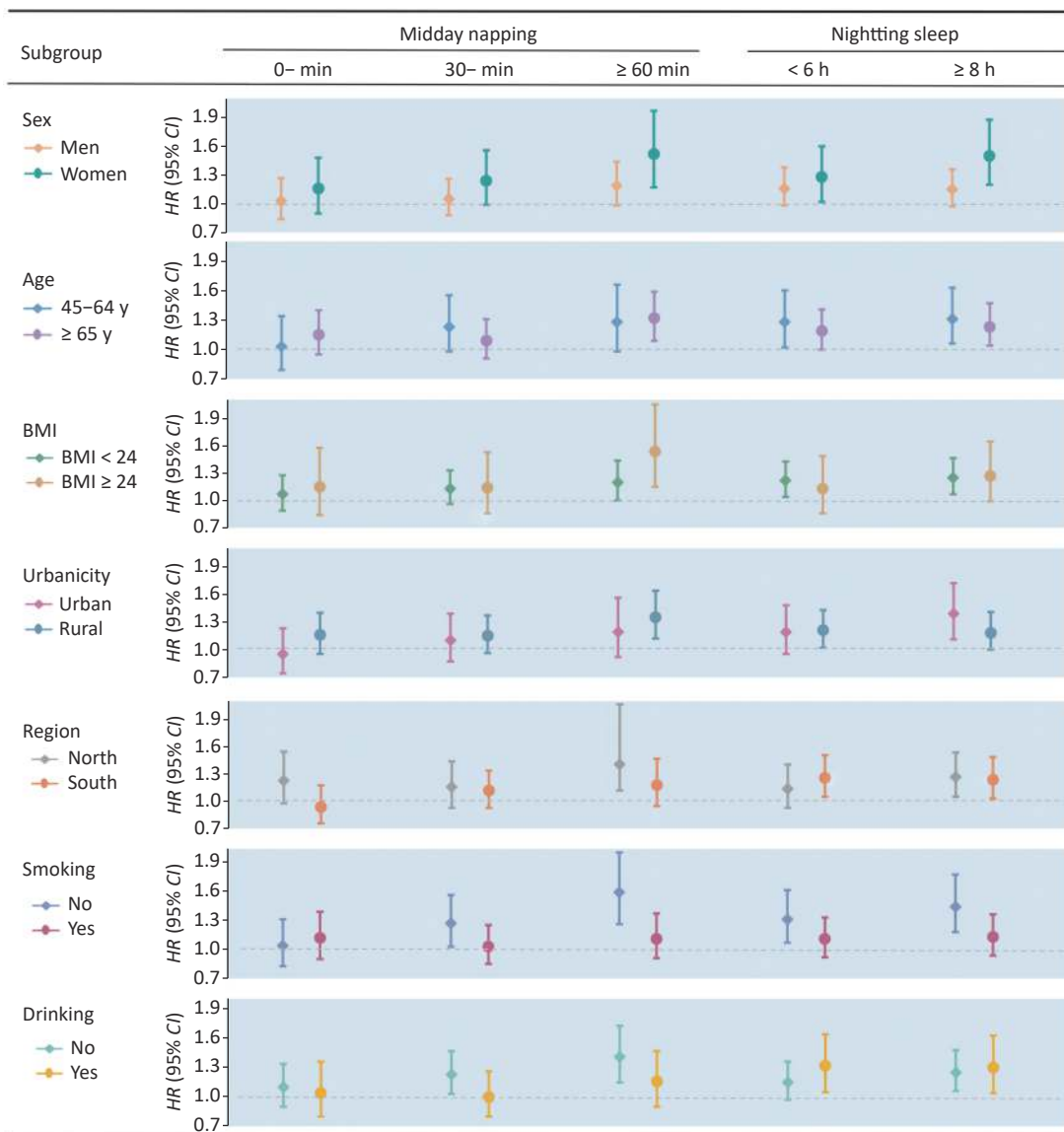


**Figure 4.** Joint effect of midday napping and nighttime sleep duration against all-cause mortality. RERI, relative excess risk due to interaction; AP, attributable proportion. \*  $P < 0.05$ ; \*\*  $P < 0.01$ ; \*\*\*  $P < 0.001$ .

for the significant effects of short nap duration (< 30 min) in triggering mortality events<sup>[14]</sup>, while some investigations showed negative<sup>[29]</sup> or null associations<sup>[18,42]</sup>. However, the increased risk of death associated with prolonged napping (≥ 60 min) remains highly consistent in most longitudinal studies, suggesting an excess risk ranging from 23% to 100% in studies from Asia<sup>[43,44]</sup>, Europe<sup>[28]</sup>, and the Americas<sup>[26]</sup>. The underlying biological mechanisms remain unclear but could be related to fluctuations in blood pressure (e.g., cardiovascular disease), basic metabolic disease (e.g., diabetes), and elevated levels of inflammatory biomarkers (e.g., C-reactive

protein and interleukin-17) due to long napping<sup>[45]</sup>.

Consistent with our prior analysis of a young cohort (mean age 46 years) based on the China Family Panel Studies<sup>[43]</sup>, this study used a sample population with a mean age of 59 years and found an increased risk of death in participants with daytime napping ≥ 60 min. By performing a joint effect analysis (Figure 4), this study provided several novel insights into the association of midday napping and nighttime sleep duration with mortality risk. First, although a significant joint effect was observed in sleeping ≥ 9 h/night and midday napping > 90 min in a regional population from the Dongfeng-Tongji



**Figure 5.** Subgroup analysis for the association of napping duration and nighttime sleep with all-cause mortality.

cohort study<sup>[6]</sup>, our nationwide analysis did not provide significant evidence of an additive interaction between midday napping and nighttime sleep. Second, we identified the lowest risk of mortality in the group with nighttime sleep of 6 – < 8 h at night and midday napping of 0 min, and midday napping was associated with an increased risk of mortality regardless of whether night sleep duration was insufficient (< 6 h) or prolonged (≥ 8 h). Third, in participants with nighttime sleep duration < 6 h, we observed a trend of increased risk with napping duration and the greatest excess mortality risk of 79% for napping ≥ 60 min. This finding challenged the generally accepted public perception that napping during the day can compensate for sleep debt if nighttime sleep is insufficient. In addition, a large cross-sectional study in China observed a high risk among participants with nighttime sleep < 7 h and midday napping ≥ 60 min<sup>[46]</sup>. Given the currently limited evidence, large-scale, well-designed cohort studies focusing on participants with insufficient nighttime sleep are urgently needed to validate this finding.

#### **Nighttime Sleep-Mortality Associations**

Our findings are consistent with most previous longitudinal studies<sup>[13,47,48]</sup> that have reported an association between nighttime sleep and mortality outcomes. For instance, the Korean Multi-center Cancer Cohort study<sup>[13]</sup>, Hawaiian Multiethnic Cohort study<sup>[48]</sup>, and American Nurses Health Study<sup>[47]</sup> showed that sleep durations ≤ 5 h and ≥ 9 or 10 h were related to a high risk of death. In contrast, our results were also incompletely echoed in some investigations, which implies that only short or long sleep durations were associated with all-cause mortality. A cohort study of working Scottish<sup>[16]</sup> revealed that the risk of death was increased for participants sleeping < 7 h compared with those sleeping 7–8 h. Moreover, nighttime sleep ≥ 9 h was independently associated with mortality after full adjustment for covariates was found in a large-scale cohort study from 21 countries<sup>[19]</sup>, Hong Kong, China<sup>[12]</sup>, the United States<sup>[15]</sup>, and Taiwan, China<sup>[17,18]</sup>. These conflicting findings might be attributable to the diverse races, ages, and lifestyles among participants in various studies.

Although the biological mechanisms underlying the joint effect of midday napping and nighttime sleep are unclear, there are several possible mechanisms. First, long sleep duration (nighttime sleep duration (≥ 9 h) and midday napping (> 1 h) may disrupt the sleep-wake cycle and lead to

imbalanced hormone secretion<sup>[49]</sup>, which might be associated with adverse health outcomes and increased odds of premature death<sup>[50]</sup>. Second, due to relatively poor sleep quality, long sleep duration may fail to compensate for insufficient nighttime sleep, allowing the body to maintain its ability to cope with stress and resist disease<sup>[51]</sup>. Third, prolonged nighttime sleep and midday napping are related to changes in hypothalamic-pituitary-adrenal system activity, which increases sympathetic activity and impairs endothelial function, which could be linked with cardiovascular disease, thus increasing the risk of mortality<sup>[52]</sup>.

#### **Potential Effect Modifiers**

In the sex-specific analysis, female nappers for ≥ 1 h had a higher mortality risk than male nappers. A consistent association was also observed in relevant studies among females<sup>[15,45]</sup>, but several studies found that males<sup>[14,27]</sup> were more vulnerable than females. This potential explanation for these findings is that sex dimorphism and different hormone levels might lead to an interaction between sex and sleep duration on the risk of all-cause mortality<sup>[53,54]</sup>. The link between sleep duration and mortality in studies involving slightly older participants may be attributable to hormonal changes around menopause in middle-aged and older women<sup>[21,55]</sup>. In addition, the social roles of men and women may vary according to different regional cultures. For example, women in China and Japan are involved in domestic chores<sup>[21,56]</sup>, which might make them susceptible to stress and anxiety from their families<sup>[57,58]</sup>, and changes in specific brain neurotransmitters may affect sleep to some extent<sup>[59]</sup>. The underlying physiological mechanisms may partially explain the increased risk of all-cause mortality in women. Our results also highlighted high risks among rural and northern residents, whether in napping or nocturnal sleep duration. However, in another Chinese cohort study, the significant effects of long daytime napping on death risk were profound in rural and southern adults<sup>[43]</sup>. Due to discrepancies in lifestyle behaviors and sociocultural environments, future prospective longitudinal studies are warranted to investigate the associations among regional residents.

#### **Strengths and Limitations**

It is worth noting that the combined effect of nighttime sleep and daytime napping on the prediction of all-cause mortality in the general population was carefully evaluated and verified in

this study. Our study found a high risk effect of short sleep duration (< 6 h/night) and long midday napping ( $\geq 60$  min) on all-cause mortality. Notably, most previous studies have observed that daytime nap duration was associated with an increased risk of mortality<sup>[19]</sup> or chronic disease<sup>[5,6,46]</sup> in those with nocturnal sleep duration of > 6 h, but not in short nocturnal sleepers. A few reasons suggest that naps may compensate for lack of sleep at night among those who stay up late for work or leisure; however, excessive naps and night sleep do not compensate for sleep loss and may also harm our bodies<sup>[60]</sup>. Therefore, our findings need to be further clarified through meta-analysis or large-scale research.

This study has several potential limitations. First, information on sleep habits was obtained from self-reported questionnaire. Self-reports are the primary method for evaluating napping in prior investigations, while recall bias is unavoidable<sup>[61]</sup>. Second, the lack of objective information on sleep duration in their life and the measurement error of self-reported sleep habits would likely have attenuated the associations of midday napping and nighttime sleep duration with mortality. Third, we included important demographic characteristics, behavioral, and health status factors in the multivariable-adjusted models to control for potential confounding factors, but the results could still have been influenced by residual confounders (e.g., diet, health insurance, doctor visiting, and occupation) or other biases arising from unmeasured factors<sup>[62]</sup>. In addition, time-varying variables (e.g., repeated measurements of sleep duration variables and other covariates) were not fully considered in our survival analysis, which may fail to sufficiently capture changes in risk factors over time. Fourth, as relevant information was not available, we did not address the contribution of other sleep features, such as sleep quality, frequency, and sleep apnea, to mortality risks, which should be studied in the future<sup>[63,64]</sup>. Fifth, owing to data unavailability, we failed to investigate the associations of cause-specific mortality with midday napping and nighttime sleep.

## CONCLUSION

Long midday napping was independently associated with a high risk of all-cause mortality in middle-aged and older Chinese individuals, and nighttime sleep duration was associated with all-cause mortality in a J-shaped pattern in Chinese adults. These associations were strong among

females and rural and northern residents. Our study might provide some significant suggestions for directing sleep behavior, especially among middle-aged and older Chinese populations. However, the potential biological mechanisms responsible for these associations have not yet been completely elucidated, and further research is required to confirm our findings in other populations.

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## AUTHORS CONTRIBUTIONS

ZHANG Yun Quan and CHENG Hong Ping conceived and designed the study; WANG Lu and YUAN Yang cleaned the data; WANG Ke and HU Lan drafted the original manuscript; SHU Hai Nan, WANG Yi Ting, CHENG Hong Ping, and ZHANG Yun Quan revised the manuscript. All authors have read and approved the final manuscript.

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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