Effects and differences of sleep duration on the risk of new-onset chronic disease conditions in middle-aged and elderly populations

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ABSTRACT

Background: Few longitudinal cohort studies investigated the risk of the duration of nighttime sleep and naps to the new-onset common chronic disease conditions (CDCs) in middle-aged (45-60) and the elderly (age ≥ 60) populations using an age-stratified strategy.

Methods: The 7025 participants from The China Health and Retirement Longitudinal Study were screened as eligible subjects. Established 13 cohorts with CDCs, acquired their sleep records in 2011, and obtained new-onset incidents of CDCs during follow-up in 2011-2018. Performed risk association analyses between sleep duration and 13 new-onset CDCs respectively.

Results: New-onset risk of four CDCs decreased with increasing nighttime sleep (p-nonlinear > 0.05). The risk threshold was approximately 7 hours in middle-aged people and 6 hours in the elderly. For the middle-aged population, compared with > 7-hours sleep, < 7-hours sleep was associated with 1.312~1.675 times more risk of hypertension, kidney disease, diabetes or high blood sugar status, and multimorbidity. Compared with no nap, a 0-30 min nap was associated with 1.413(1.087~1.837) times the heart disease risk.

In the elderly, < 5 hours of night sleep was a significant risk factor for four CDCs including kidney disease and multimorbidity, etc. A long night’s sleep (> 9 hours) was connected with 61.2% reduction in risk of memory disease, a > 90 min nap increased 62% risk of memory disease, and a 0-30 min nap was associated with higher risks of heart disease, hypertension, and a lower kidney disease risk.

Conclusions: Nighttime sleep and daytime naps may have their own implications for the new-onset CDCs’ risk in the aging process.

1. Introduction

It is expected that by 2050 the population over 65 in China will reach 400 million [1]. A recent epidemiological study in China has demonstrated that 75.8% of residents over 60 years old suffer from at least one chronic disease [2]. According to a report from China Centers for Disease Control and Prevention in 2020, the mortality rates (1/100000) of chronic disease aged 45-60 and over 60 were 366.88, and 3504.22 respectively [3]. With the acceleration of the aging process, aging-related chronic diseases have become the top priority of disease health management.

Sleep is instrumental to the balance of metabolism, memory consolidation, and brain detoxification [4], which is crucial for the body, cognition, and mental health. However, with the increase of age, sleep problems have become increasingly prominent. About 40% of the elderly develop sleep problems [5], including insufficient and excessive sleep time [6]. Rapid eye movement sleep and slow wave sleep decrease with age, and sleep latency and wake-up times gradually increase [7].

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which may lead to excessive nap [8].

Inappropriate sleep time is associated with various chronic diseases, such as cardiovascular diseases [9], chronic kidney diseases [10], cognitive decline [11] and etc. A study based on people aged 50-75 in Europe shows that sleep 7-8.5 h is associated with less risk of chronic diseases [12]. Among women aged 18-64, there is a stronger relationship between very short or very long sleep time and chronic diseases [13]. As for daytime naps and new-onset risk of chronic diseases, some studies claim that an appropriate daytime nap will increase [14,15] or reduce [16,17] risks and some results show that there is no significant correlation between the two [18]. Additionally, evidence from longitudinal investigations is lacking with regard to exploring the relationship between sleep duration, especially napping duration, to the new-onset risk of multimorbidity.

Considering the influence of aging on sleep duration and the incidence of chronic disorders varied in different age groups, it is inappropriate to adopt the same analysis strategy to analyze the risk of sleep duration for new-onset chronic diseases in the population regardless of aging. In the current research from China Health and Retirement Longitudinal Study (CHARLS), we analyzed the risk of sleep duration (nighttime sleep and daytime nap) to 13 new-onset common chronic disease conditions (CDCs) in middle-aged (45 < age < 60) and elderly (≥60) and explored different thresholds of sleep duration on disease risk in specific age groups. To our knowledge, this is the first nationwide cohort study to explore the effects and differences of sleep duration on CDCs from a different age perspective in a longitudinal cohort.

2. Methods

2.1. Population

The China Health and Retirement Longitudinal Study (CHARLS) is a longitudinal survey of nationally representative people aged 45 and over. So far, a total of four waves 2011 (wave 1), 2013 (wave 2), 2015 (wave 3), and 2018 (wave 4) of data have been released (A.1).

The study was approved by the Ethics Committee of the Peking University Health Science Center, and informed consents were obtained from each participant prior to participation.

We selected the population data published in 2011 as the baseline. Those with qualified records to sleep questionnaires were chosen as the goal population in the study. We established a series of cohorts containing 13 CDCs by excluding those with corresponding medical histories in 2011 and tracked eligible participants until 2018 for new incidences of these diseases. The specific flow chart of the research design is shown in Fig. 1.

2.2. Ascertainment of twelve chronic diseases and multimorbidity

According to the participants’ answers to question DA007 (Have you been diagnosed with… by a doctor?) in the health status and function questionnaire, whether the patients had chronic diseases was determined. A respondent with no less than two chronic diseases was considered to have multimorbidity [19]. The time of onset was determined according to question DA009 (When was the condition first...
diagnosed or known by yourself?). The onset time of the disease (earlier than 2011) was used as the baseline history of the disease, and the disease that occurred during the follow-up period in 2011 and beyond was considered as a new-onset disease event. New-onset chronic diseases during follow-up were considered to be endpoints in this study.

2.3. Assessment of sleep duration

We evaluate subjects’ sleep duration by records in the above questionnaire.

Nighttime sleep duration(hour): Based on the answers to the question DA049 (During the past month, how many hours of actual sleep did you get at night (average hours for one night)? This may be shorter than the number of hours you spend in bed).

Daytime nap duration(minute): Based on the answers to the question DA050 (During the past month, how long did you take a nap after lunch (minutes))?

Groups of Nighttime sleep: (6.5)hours, [5,7)hours, [7,9)hours, [9,) hours [20]

Groups of Daytime nap: 0 minutes, (0,30) minutes, (30,90) minutes, (90,) minutes [21]

2.4. Covariates

Physical examination indexes (age, sex, body mass index, systolic blood pressure, diastolic blood pressure) were included in this study. The middle-aged population was defined as 45<age<60, and the elderly as age≥60. Habits of smoking (yes/no) and drinking (often/sometimes/never) were recorded in the study. According to the educational records of the interviewed population (BD001’; What is the highest level of education you have attained? ), we divided the population into four groups: illiterate, elementary school, middle school, and college. For each chronic disease cohort (except for multimorbidity defined by the number of diseases), the remaining 11 chronic disease histories at baseline were applied as confounding factors (A.1).

2.5. Statistical methods

Quantitative data of normal and non-normal distribution were expressed as mean ± SD and medians with interquartile range (IQR). Categorical data were presented as amounts with percentages, respectively. Comparisons of differences among sleep duration groups were analyzed by ANOVA and Kruskal–Wallis tests for continuous variables in line with normal and nonnormal distributions, respectively, and by chi-square tests for categorical variables. Descriptive statistics are presented for the proportion of 13 chronic diseases across age and sleep duration groups. Hazard ratios (HRs) and 95% confidence intervals (CIs) of daytime nap, daytime nap groups, nighttime sleep, and nighttime sleep groups. Hazard ratios (HRs) and 95% confidence intervals (CIs) of risk of CDCs. Produce forest plots to visualize the different new-onset square tests for categorical variables. Descriptive statistics are presented 10.11). Two-tailed p values were used throughout the study, and p<0.05 was considered statistically significant.

3. Results

3.1. Basic characteristics and differences between middle-aged and elderly people at baseline

A total of 7025 people participated in the study, including 4003 middle-aged people and 3022 elderly. Compared with the middle-aged, the elderly had less nighttime sleep duration (6.17vs.6.50 hours, p<0.001), a greater number of diseases at baseline (1.41vs.1.07, p<0.001), a higher proportion of medical history of 8 CDCs (Table 1). In addition, there are significant differences in the proportion of sex, BMI, SBP, DBP, educational level, habits of smoking, and drinking between the two age groups (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Disease Number in 2011</th>
<th>1.07 (1.17)</th>
<th>1.41 (1.37)</th>
<th>&lt;0.001</th>
<th>0.262</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical History</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart disease (%)</td>
<td>0.001</td>
<td>0.214</td>
<td>&lt;</td>
<td>0.062</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>0.001</td>
<td>0.199</td>
<td>&lt;</td>
<td>0.064</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM/Hglu (%)</td>
<td>0.009</td>
<td>0.064</td>
<td>&lt;</td>
<td>0.193</td>
</tr>
<tr>
<td>Digestive disease (%)</td>
<td>0.056</td>
<td>0.014</td>
<td>&lt;</td>
<td>0.061</td>
</tr>
<tr>
<td>Cancer (%)</td>
<td>0.36 (1.2)</td>
<td>0.36 (1.2)</td>
<td>&lt;</td>
<td>0.061</td>
</tr>
<tr>
<td>Liver disease (%)</td>
<td>0.447</td>
<td>0.02</td>
<td>&lt;</td>
<td>0.131</td>
</tr>
<tr>
<td>Kidney disease (%)</td>
<td>0.057</td>
<td>0.047</td>
<td>&lt;</td>
<td>0.193</td>
</tr>
<tr>
<td>Lung disease (%)</td>
<td>0.001</td>
<td>0.193</td>
<td>&lt;</td>
<td>0.061</td>
</tr>
<tr>
<td>Arth/Rheu (%)</td>
<td>0.001</td>
<td>0.131</td>
<td>&lt;</td>
<td>0.061</td>
</tr>
<tr>
<td>Memory disease (%)</td>
<td>0.001</td>
<td>0.131</td>
<td>&lt;</td>
<td>0.061</td>
</tr>
<tr>
<td>Asthma (%)</td>
<td>0.001</td>
<td>0.131</td>
<td>&lt;</td>
<td>0.061</td>
</tr>
</tbody>
</table>

Table 1: Basic characteristics of the participants at baseline stratified by age groups in 2011.

(A) Heart disease, (B) Hypertension, (C) Stroke, (D) DM/Hglu, (E) Digestive disease, (F) Cancer, (G) Liver disease, (H) Kidney disease, (I) Lung disease, (J) Arth/Rheu, (K) Memory disease, (L) Asthma, and (M) Multimorbidity. The vertical axis (left) represents the Hazard ratio for diseases in the restricted cubic splines; the vertical axis (right) represents the elderly’s nighttime sleep in the 2011 distribution fraction of the population in density maps. The cutoff refers to the value of their night sleep duration when hazard ratios for almost all new-onset chronic diseases equal 1.

Models were all adjusted by age, sex, BMI, SBP, DBP, PP, smoke, drink, and Education. In addition, considering the interrelationships between chronic diseases, we included 11 chronic diseases history as covariates (except for multimorbidity and cohort outcome event disease itself) in our subgroup analysis for each disease cohort to control for the effect of baseline medical history on outcome events when analyzing the risk of nighttime sleep duration on the new-onset chronic diseases. Specific covariate information for each model is available in Table A.S.

Abbreviations could be seen in Table 1.
3.2. Baseline characteristics of participants stratified by groups of nighttime sleep and daytime nap

A total of 1133, 2428, 2907, 557 participants were included in the nighttime sleep groups of <5, 5-7, 7-9, and >9 hours respectively, and 3329, 1134, 1748, 814 participants were included in the daytime nap groups of 0-30, 30-90, and >90 minutes respectively. Those with longer nighttime sleep duration had significantly longer daytime naps than those who slept less at night (Table A.1), and vice versa (Table A.2).

In terms of the proportions of medical histories, among the nighttime sleep groups, except for DM/Hglu, Cancer, and liver disease, there were significant differences in the other nine CDCs. Meanwhile, among the daytime nap groups, there were significant proportion differences in heart disease, hypertension, stroke, DM/Hglu, Arth/Rheu, and multimorbidity.

Follow up a total of 7025 participants for seven years and perform longitudinal cohort studies based on daytime sleep duration (Table A.3) and nighttime (Table A.4) to track the new onset incidents of 13 CDCs.

3.3. Cox regression analysis of daytime nap duration for new-onset risk of thirteen CDCs

The nap duration was an independent protective factor for new-onset kidney disease in the elderly (HR, 95%CI: 0.995, 0.91-0.999), but not in the middle-aged by covariate-adjusted Cox regression analysis (Table A.5). There was an overall negative linear relationship (p-non-linear > 0.05) between the increased length of daytime naps and the new-onset risk of kidney disease in the elderly by RCS regression (Fig. A.1).

3.4. Longitudinal associations between groups of daytime naps and new-onset risk of thirteen CDCs

The risk of new-onset kidney disease increased slightly and then decreased as the nap’s length increased, with a risk threshold of approximately 40 minutes. However, the duration of daytime naps was not significantly associated with the new-onset risk of the remaining 11 CDCs (Table A.5). Figs. A.1 and A.2 displayed the association between the length of the daytime nap and the new-onset risk of all diseases in middle-aged and elderly populations.

3.5. Cox regression analysis of nighttime sleep duration for new-onset risk of thirteen chronic disease status

By covariate-adjusted Cox regression analysis, the nighttime...
duration was an independent protective factor for new-onset DM/Hgлу (HR, 95%CI: 0.939, 0.887-0.994) and memory disease (HR, 95%CI: 0.875, 0.772-0.992) in the middle-aged population, but not in the elderly. Meanwhile, it significantly increased the risk of kidney disease in the elderly (HR, 95%CI: 0.895, 0.829-0.966) but not in middle-aged persons. Increased nighttime sleep duration was associated with a reduced risk of multimorbidity in both the middle-aged and elderly populations (Table A.7). As the nighttime sleep duration increased, the risk of new-onset chronic disease conditions generally decreased, with a risk threshold of approximately 7 hours in middle-aged people and 6 hours in the elderly (Figs. 3 and A.3).

3.6. Longitudinal associations between groups of nighttime sleep and new-onset risk of thirteen chronic disease status

Cox regression analyses adjusted by confounders were performed to explore the association between groups of nighttime sleep and risk of chronic disease status. Compared with a group of 7-9 nightsleep duration, a short nightsleep of <5 hours was a significant new-onset risk predictor for hypertension in the middle-aged population (HR,95%CI: 1.312,1.042-1.651), but not in the elderly. In addition, it also increased the new-onset risk of asthma only in the elderly and increased the risk for kidney disease and multimorbidity in both middle-aged and elderly populations. A 5-7 hours nightsleep was associated higher risk of DM/Hgлу (HR,95%CI: 1.456,1.155~1.837) and multimorbidity (HR,95%CI: 1.306,1.098~1.552) in the middle-aged persons. Especially, a long sleep duration at night (>9 hours) decreased the elderly’s risk of memory disease (HR,95%CI: 0.388,0.156~0.970), but not in the middle-aged population (Tables 2 and A.4; Fig. 2B).

4. Discussion

This large prospective cohort study revealed risk associations and differences in nighttime sleep and daytime nap duration for new-onset CDCs in middle-aged and elderly:

a There is a significant negative linear relationship between daytime nap duration and the new-onset risk of chronic kidney disease in the elderly. The risk of new-onset chronic diseases roughly decreases with the increase in nighttime sleep duration, and the risk threshold is 7 hours in the middle-aged and 6 hours in the elderly, respectively.

b For middle-aged and elderly people, compared with no nap, 0-30 minutes of daytime nap is an independent risk factor for new-onset heart disease; compared with 7-9 hours of nighttime sleep, <5 hours of sleep is a predictor for new-onset kidney disease.

c For middle-aged people, not the elderly, 0-30 minutes of a nap and <5 hours of nighttime sleep were risk factors for new-onset hypertension; 5-7 hours of nighttime sleep increased the new-onset risk of DM/Hgлу and multimorbidity.

d For the elderly, but not middle-aged, a 0-30 minutes nap was a protective factor for new-onset chronic kidney disease. A nap of >90 minutes significantly increased the new-onset risk of memory disease. The nighttime sleep of <5 hours was associated with a higher risk of chronic kidney disease and asthma. Nighttime sleep >9 hours significantly reduced the risk of developing memory diseases.

Sleep duration decreased with age [22,23]. Healthy elderly people are more tolerant of sleep deprivation than young elderly people [24]. The physiological mechanism may explain that: The number of ventrolateral preoptic nuclei of the hypothalamus decreases with age, resulting in a reduction in sleep time in physiological [24]. That suggested the need to separately investigate the effect of sleep duration on the risk of new-onset CDCs in middle-aged and the elderly, and the physiological basis for this risk difference. Consistently with this, we found that 7 hours and 6 hours were the risk thresholds for new-onset CDCs in the middle-aged and the elderly, respectively. Therefore, it may be unreasonable to analyze the relationship between sleep duration and CDCs by ignoring aging.

A SNAC-K survey found that sleep disturbances were associated with a faster rate of developing multimorbidity in people (age>60) [25]. A cross-sectional study from KORA revealed that short daily sleep duration was significantly associated with multimorbidity in the elderly (age

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**Fig. 3.** The combined graphs of restricted cubic splines with 3 knots to flexibly model the association between the elderly’s nighttime sleep in 2011 and HRs (95% CI) for their new-onset diseases and distribution density maps of their nighttime sleep in 2011 in each chronic disease subgroup cohort.
Table 2
Cox regression analysis of nighttime sleep groups in 2011 to the 7-year new-onset risk of thirteen chronic diseases.

<table>
<thead>
<tr>
<th>Model1</th>
<th>Liver disease</th>
<th>Kidney disease</th>
<th>Lung disease</th>
<th>Memory disease</th>
<th>Arth/Rheu</th>
<th>Asthma</th>
<th>Multimorbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart disease</td>
<td>0.969 (0.717-1.330)</td>
<td>0.120</td>
<td>0.907 (0.664-1.232)</td>
<td>0.350</td>
<td>1.016 (0.715-1.430)</td>
<td>0.916</td>
<td>0.997 (0.749-1.317)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.973 (0.726-1.323)</td>
<td>0.250</td>
<td>0.943 (0.687-1.290)</td>
<td>0.706</td>
<td>0.998 (0.706-1.440)</td>
<td>0.940</td>
<td>1.002 (0.735-1.355)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.977 (0.726-1.323)</td>
<td>0.970</td>
<td>0.943 (0.687-1.290)</td>
<td>0.706</td>
<td>0.998 (0.706-1.440)</td>
<td>0.940</td>
<td>1.002 (0.735-1.355)</td>
</tr>
<tr>
<td>DM/Hกล</td>
<td>1.149 (0.859-1.552)</td>
<td>0.378</td>
<td>1.062 (0.845-1.336)</td>
<td>0.607</td>
<td>1.114 (0.765-1.622)</td>
<td>0.574</td>
<td>0.890 (0.546-1.479)</td>
</tr>
<tr>
<td>Model2</td>
<td>Liver disease</td>
<td>Kidney disease</td>
<td>Lung disease</td>
<td>Memory disease</td>
<td>Arth/Rheu</td>
<td>Asthma</td>
<td>Multimorbidity</td>
</tr>
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</tr>
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</table>

1 No adjusted
2 Comparing the interrelationships between chronic diseases, we included 11 chronic diseases history as covariates (except for multimorbidity and cohort outcome event disease itself) in our subgroup analysis for each disease cohort to control for the effect of baseline medical history on outcome events when analyzing the risk of daytime nap duration on the new-onset chronic diseases.
range 65-93) [26]. Our study confirmed that shorter nighttime sleep duration was an independent new-onset risk factor for multimorbidity. However, the specific sleep length that manifested risk was not consistent across age groups: when sleep duration was less than 7 hours, the risk increased significantly in middle-aged, but in the elderly, a similar risk profile could be observed when sleep duration was less than 5 hours.

Multiple previous studies have shown that short sleep duration appears to increase the risk of cardiovascular-related events [15,27]. Another study (age from 18-98) found no significant association between night sleep duration and myocardial infarction [28]. The populations in these studies spanned a wide age range, which may lead to age-mediated links between shorter sleep duration and increased risk of heart disease. No association was found between the new-onset risk of heart disease and nighttime sleep duration in this study. But there is a significant association between that risk and a 0–30-minute nap among middle-aged and the elderly, which agreed with the previous study that there were adverse effects of naps on serious cardiovascular-related events [15,29].

A study of 4810 Americans (age from 48-59) found that short nighttime sleep was 60% associated with an increased hypertension risk [30]. Meanwhile, another study (participants aged 58-98) found no association between nighttime sleep and hypertension or blood pressure changes [31]. A Spanish study (age >60) reported the same conclusion [32]. In our study, this link was not observed in the elderly, either. And it was found that a short night’s sleep duration for increased hypertension risk in the middle-aged. The biological relationship between nighttime sleep and hypertension is not clear. A link between sleep apnea and hypertension only exists in middle-aged people [33] may partly explain why a significant association between short sleep duration and increased hypertension risk was found in middle-aged people only.

Japanese cohort studies reported the lowest risk of chronic kidney disease with sleep duration <6 hours [34]. A prospective cohort (age >20) from Taiwan found a “U”-shaped dose association: Both <6 and >8 hours of sleep increased the risk of kidney disease [35]. In the present study, a shorter nighttime sleep duration (<5 hours), but not a longer sleep duration (>9 hours), was an independent risk factor for new-onset kidney disease in the middle-aged and the elderly. In addition, for the first time, we found the protective effect of the nap on new-onset nephropathy in the elderly. That means that a daytime nap may act as a compensatory measure to reduce the risk of new-onset kidney disease from sleep deprivation at night.

Our study found that a long duration of sleep at night significantly reduced the risk of memory disease in the elderly, whereas prolonged daytime naps significantly increased this risk. This phenomenon has not been captured in the middle-aged population. That suggests a link between sleep, especially nighttime sleep, for memory consolidation, memory recovery, cognitive protection, and neuronal repair in the brain [36]. Long daytime naps may compete for nighttime sleep duration and counteract this physiological effect on cognitive memory protection. Several studies have confirmed that sleep helps consolidate memories, while sleep deprivation increases the formation of false memories [37]. However, large-scale cohort studies on the effects of daytime and nighttime sleep on the risk of long-term memory-related disorders are lacking.

As we know, the current study is the first to investigate the age-stratified effects of daytime and nighttime sleep duration on the new-onset risk of CDCs in the middle-aged or the elderly, respectively, and how these effects differ with aging. That provided a pragmatic theoretical basis for establishing sleep management strategies, which vary in process of aging and different disease conditions. However, all sleep features are self-reported in this study, which may lead to potential misclassifications. In addition, a long daytime nap may reduce the duration of sleep at night and compensate lack of night sleep at the same time. There was an interaction between nighttime and daytime sleep duration that is difficult to completely disentangle in the analysis, which may overestimate or underestimate the risk effect of nighttime sleep or daytime nap on diseases. Exploring the overall, rational physiological effects of a 24-hour sleep pattern is the focus of our further study.

Author contributions

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Availability of data and materials

The data that support the findings of this study are available from http://charls.pku.edu.cn/index/zh-cn.html. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of National Development Institute, Peking University.

Declaration of Competing Interest

None.

Funding

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Supplementary materials

Supplementary material associated with this article can be found, in

References


