Insomnia and Multimorbidity in the Community Elderly in China

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Study Objectives
To examine the comorbidity between insomnia and medical conditions.

Methods
This cross-sectional study was conducted in community adults, aged ≥ 60 years, who resided in one of four major cities in northern China. Sociodemographic and clinical data were collected simultaneously. A total of 3,176 elderly adults (1,292 male, mean ± standard deviation age 70.2 ± 6.8 years; 1,884 female, 68.8 ± 6.7 years) were interviewed.

Results
The prevalence of specific medical conditions in both people with insomnia and people without insomnia was detected. Significantly higher proportions of arrhythmia, hypertension, cerebral hemorrhage, migraine, and hyperlipidemia were observed in people with insomnia than in people without insomnia. Moreover, a significantly higher proportion of insomnia was seen in elderly people with arrhythmia and migraine. We also found that elderly people with insomnia who took sleep medications reported a higher prevalence of coexisting arrhythmia, hypertension, and migraine, even after adjusting for age, sex, and depression.

Conclusions
Our results indicate associations between insomnia and medical conditions in the community elderly in China. People who complained of insomnia had poorer physical health conditions. Sleep medication may not be a covariate that influences the comorbidity of some specific physical conditions.

Clinical Trial Registration
Trial name: The study of diagnosis and treatment of senile dementia in Hebei Province; URL: http://www.chictr.org.cn/showproj.aspx?proj=8194; Registration number: ChiCTR-RRC-11001345

Citation

BRIEF SUMMARY
Current Knowledge/Study Rationale: A total of 46% to 68% of patients who complain of insomnia have comorbid medical or psychiatric disorders. However, the prevalence of medical conditions in insomnia patients who do and do not take sleep medications has not yet been studied.

Study Impact: People who complained of insomnia had poorer physical health conditions. The incidence of arrhythmia, hypertension, and migraine was higher in individuals with insomnia who were currently taking sleep medications compared with individuals with insomnia who were not taking sleep medications.
Insomnia is a serious public health concern, with 46% to 69% of patients presenting to a primary care office to report complaints of insomnia.\(^1\)\(^2\) A total of 46% to 69% of patients who complain of insomnia have comorbid medical or psychiatric disorders.\(^3\)\(^4\) Insomnia has a significant negative effect on morbidity and mortality, particularly in the elderly.\(^5\)\(^6\) Cross-sectional studies have attempted to determine whether people with insomnia report more health problems.\(^7\)\(^8\)\(^9\)\(^10\) However, very little prevalence data have been reported, and some of the samples that have been used may limit generalizability. Taylor et al. performed a study with 772 subjects (aged 20–98 years) and found significant overlap between insomnia and multiple medical conditions.\(^4\) In another cross-sectional study, researchers collected data from 9,000 older adults (aged ≥ 65 years) and found that a lifetime history of insomnia was associated with greater difficulties in daily activities, respiratory symptoms, and having two or more health problems (ie, hypertension, heart disease, cancer, stroke, diabetes, hip fracture, and other fractures).\(^10\) The latter finding was further confirmed by the same research group who elucidated the association between insomnia and heart disease, stroke, hip fracture, and respiratory symptoms.\(^11\) A meta-analysis found a high prevalence of sleep complaints with comorbid physical disorders in a large population of older adults from low- and middle-income countries.\(^12\) One underlying mechanism may be inflammation that is strongly linked to cardiovascular disease,\(^13\) in which dysfunction of the inflammatory system is seen in individuals with insomnia.\(^14\) A chronic state of inflammation appears to be a central mechanism that underlies the pathophysiology of insulin resistance and metabolic syndrome.\(^15\) Insomnia that is associated with physiological hyperarousal is also associated with a significant risk of hypertension.\(^16\)

However, comparing these studies is difficult because of substantial variability in diagnostic definitions, detection procedures, implementation instruments, and demographic characteristics of the source population. Additionally, few studies have controlled for potential confounding factors, such as the presence of other sleep-wake disorders (eg, sleep apnea) or mental disorders (eg, depression). These underlying disorders could cause both insomnia\(^17\) and medical disorders.\(^18\)\(^19\) possibly because of stress that is associated with chronic medical conditions and leads to depression, which in turn contributes to insomnia. Previous studies reported significant overlap between insomnia, depression,\(^20\) and multiple medical conditions.\(^3\) Insomnia and depression are both prevalent and often coexist in the elderly. Depression alone is a risk factor for medical conditions and an important covariate in explaining the relationship between insomnia and physical diseases. Previous studies that focused on the relationship between insomnia and physical diseases accounted for only depression. Therefore, controlling for the independent contributions of depression as well as other sleep-wake disorders is necessary to obtain reliable prevalence data on insomnia that is related to specific medical conditions. The majority of studies to date have evaluated the association between insomnia and various medical conditions, but differences in specific medical conditions in individuals with insomnia who are either currently taking sleep medications or not taking sleep medications have not yet been evaluated.

Given the trend of an increase in the age of the global population and high incidence of disturbed sleep among older adults, health care practitioners have begun to emphasize this issue. China has approximately 180 million elderly individuals (older than 60 years), accounting for 13.3% of the entire population based on the sixth Chinese national census.\(^20\) Relatively few studies that have been conducted in China have focused on comorbid insomnia and physical disorders, which may be influenced by several sociodemographic and medical factors, including sex, age, marital status, income level, education level, working status, and somatic and psychiatric conditions.\(^4\) In our previous study, we found that insomnia was highly prevalent among the community elderly population in northern China, and individuals with insomnia complaints had poorer physical and mental health.\(^21\) In the current study, we developed a compendium of medical conditions that were comorbid with insomnia, which may aid future research that evaluates the effects of insomnia on physical health in elderly populations. We hypothesized that (1) older adults with insomnia would have a higher prevalence of medical conditions than those without sleep problems, (2) older individuals with medical conditions would have more insomnia than those without medical conditions, and (3) individuals who were currently taking sleep medications would have fewer medical conditions.

### METHODS

#### Procedure

The current study was part of a large-scale epidemiological survey of mild cognitive impairment among elderly individuals who reside in urban communities in Hebei Province, China. Information on sleep and physical health was collected. Environmental conditions, economic development, culture, and lifestyle may affect the epidemiology of mild cognitive impairment.\(^22\) Therefore, the areas of study were selected so that they represented regional variations in these factors. The survey was conducted from January to December, 2010.\(^18\) It was based on a multistage and systematic sampling of residents in the community who were aged ≥ 60 years, lived with family members, and had the ability to complete the interview.\(^21\) The study protocol was approved by the Ethics Committee of the First Hospital of Hebei Medical University. All of the participants provided written informed consent. A multistage stratified cluster sampling method with selection probabilities proportional to size was designed to recruit participants, based on the urban resident registry of Hebei Province in 2010 (Sixth Nationwide Population Census in China, 2010). In the first stage, we randomly selected four cities (Shijiazhuang, Tangshan, Zhangjiakou, and Handan) from 11 cities (Shijiazhuang, Tangshan, Handan, Qinhuangdao, Baoding, Zhangjiakou, Chengde, Langfang, Cangzhou, Hengshui, and Xingtai) in Hebei Province. In the second stage, we selected three predominantly urban districts from Shijiazhuang, Tangshan, Zhangjiakou, and Handan. In the third stage, we randomly selected three communities from each of the 12 districts. In the fourth stage, older adults who were stratified by age and sex in a cluster were selected in each community. A total of 90 residents who were aged ≥ 60 years were selected in each community. The target population consisted of people who were older than 60 years, who lived in the current administrative region of each city for at least one year, and were willing to participate in the study.

#### Participants

A total of 3,240 individuals were approached to take part in this study. Subjects were excluded if they had severe problems with vision, hearing, or speaking. Of those who did not participate in the study, 18 refused to participate, 7 could not be contacted, and 3 had died. The remaining 3,212 subjects (99.1%) participated in the screening. After excluding individuals with severe hearing,
sleep-wake disorder-related symptoms, and significant symptoms were added as covariates into each base model separately associated with each dependent variable. Arrhythmia, migraine, hyperlipidemia, and insomnia were associated with all of the four diabetes, hyperlipidemia, chronic obstructive emphysema, and cancer).

Table 2 shows the prevalence of comorbid insomnia and medical conditions. Significantly higher proportions of insomnia were observed in PWI than those in PNI (P < .05). However, after adjusting for age, sex, and depression, no significant difference was found between PWI and PNI in coronary heart disease, cerebral infarction, and diabetes (P > .05).

Table 2

<table>
<thead>
<tr>
<th>Medical Condition</th>
<th>PWI</th>
<th>PNI</th>
<th>P-value</th>
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<tr>
<td>Coronary heart disease</td>
<td>20%</td>
<td>10%</td>
<td>&lt; .05</td>
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<tr>
<td>Arrhythmia</td>
<td>15%</td>
<td>5%</td>
<td>&lt; .05</td>
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<tr>
<td>Hypertension</td>
<td>10%</td>
<td>5%</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>5%</td>
<td>1%</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Cerebral hemorrhage</td>
<td>3%</td>
<td>1%</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Migraine</td>
<td>20%</td>
<td>10%</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10%</td>
<td>5%</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>15%</td>
<td>5%</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Chronic obstructive emphysema</td>
<td>5%</td>
<td>1%</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Cancer</td>
<td>2%</td>
<td>1%</td>
<td>&lt; .05</td>
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Table 3 shows the confounding variables that were associated with each dependent variable. Arrhythmia, migraine, hyperlipidemia, and insomnia were associated with all of the four sleep-wake disorder-related symptoms, and significant symptoms were added as covariates into each base model separately.
Prevalence of Medical Conditions in People With Insomnia Who Were and Were Not Taking Sleep Medications

Table 4 shows the prevalence of specific medical conditions in PWI who did and did not take sleep medications. Significantly higher proportions of arrhythmia, hypertension, and migraine were seen in PWI who took sleep medication than those who did not. After adjusting for sex, age, and depression, taking sleep medications was still significantly associated with the occurrence of arrhythmia, hypertension, and migraine in PWI.

Based on our previous research, which explored the rate of insomnia in elderly individuals who lived in northern China, the current study improves our understanding of the higher rates of comorbid insomnia and medical conditions in elderly populations and overcomes the deficiencies of previous research. Certain medical conditions, especially cardiovascular disease (eg, coronary heart disease, hypertension, and cerebral infarction) and metabolic diseases (eg, diabetes and hyperlipidemia) were observed in PWI than in PNI. However, coronary heart disease, cerebral infarction, and diabetes were no longer associated with insomnia after adjusting for depression, age, and sex. Furthermore, significantly higher proportions of insomnia were seen in people with coronary heart disease, arrhythmia, hypertension, cerebral infarction, cerebral hemorrhage, diabetes, hyperlipidemia, and migraine than in those without these medical conditions, and only people with arrhythmia and migraine reported insomnia when we accounted for depression, age, sex, other sleep-wake disorder-related symptoms, and other medical conditions (Table 2). Previous studies have established that insomnia aggravates medical conditions, and a higher prevalence of medical conditions is found among people with insomnia. The prevalence of comorbid insomnia and coronary heart disease (46.67%) that was found in the current study was similar to that of a previous study (44.1%).

The current epidemiologic study focused on comorbid insomnia and medical conditions in elderly individuals in China to provide insight into the association between physical health and insomnia. One strength of the current study was that the data were reliable. The data were obtained from face-to-face interviews by trained mental health practitioners. Insomnia was determined according to DSM-IV criteria. All of the clinical disorders were screened and verified by medical records rather than self-reports. Additionally, the current findings are more representative of the general elderly population because of the large sample size, which may decrease the probability of type I errors.

DISCUSSION

The goal of the current study was to investigate the prevalence of comorbid insomnia and medical conditions and develop a compendium in a large population-based sample. As expected, a significantly higher proportion of certain cardiovascular and cerebrovascular diseases (eg, coronary heart disease, hypertension, and cerebral infarction) and metabolic diseases (eg, diabetes and hyperlipidemia) were observed in PWI than in PNI. However, coronary heart disease, cerebral infarction, and diabetes were no longer associated with insomnia after adjusting for depression, age, and sex. Furthermore, significantly higher proportions of insomnia were seen in people with coronary heart disease, arrhythmia, hypertension, cerebral infarction, cerebral hemorrhage, diabetes, hyperlipidemia, and migraine than in those without these medical conditions, and only people with arrhythmia and migraine reported insomnia when we accounted for depression, age, sex, other sleep-wake disorder-related symptoms, and other medical conditions (Table 2). Previous studies have established that insomnia aggravates medical conditions, and a higher prevalence of medical conditions is found among people with insomnia. The prevalence of comorbid insomnia and coronary heart disease (46.67%) that was found in the current study was similar to that of a previous study (44.1%).

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Based on our previous research, which explored the rate of insomnia in elderly individuals who lived in northern China, the current study improves our understanding of the higher rates of comorbidity between insomnia and other medical conditions in elderly populations and overcomes the deficiencies of previous research. Certain medical conditions, especially cardiovascular disease (eg, hypertension, arrhythmia, and hyperlipidemia), were evaluated in the current study. Hyperlipidemia, hypertension, arrhythmia, and migraine were significantly associated with insomnia after adjusting for depression, age, and sex. Studies that used objective measures of sleep reported a significant association between insomnia and hypertension. Cross-sectional and longitudinal studies from the Penn State Adult Cohort found that poor sleepers with objective short sleep duration had a higher risk of the development of hypertension. Another study found that only insomnia that was associated with physiological hyperarousal was a significant risk factor for hypertension. With regard to hyperlipidemia, a recent cross-sectional study found that the odds ratio for hypercholesterolemia was higher in individuals with mild insomnia or moderate/severe insomnia (with a 5- to 6-hour sleep duration) compared with the reference group (ie, individuals without insomnia and > 6-hour sleep duration). Moreover, both our previous study and research from South Korea indicated that hyperlipidemia was significantly related to insomnia. In the current study, a significantly higher proportion of hyperlipidemia was observed in PWI than in PNI. However, few studies have mentioned the relationship between arrhythmia and insomnia. Our study may provide additional information concerning the relationship between arrhythmia and insomnia. Studies that have assessed physiological state, especially immune system function, may provide insight into the mechanism of comorbid insomnia and cardiovascular and cerebrovascular diseases and metabolic syndrome. The current study indicates that people with migraine had a higher prevalence of insomnia. We compared our results with the available literature on the prevalence of insomnia in people with migraine, and the prevalence in the current study (52.7%) was in close agreement with the results reported in the study by Sancisi et al. (67.7%). Migraine is a neurovascular disorder that is associated with an excitatory-inhibitory imbalance between the dura and cortical, subcortical, and deep structures inside the brain. The findings of one population-based cohort study indicate a higher risk of developing migraine in patients with non-apnea sleep disorders, which could be considered an independent, predisposing factor for development of a subsequent migraine in adulthood. Previous studies have found that the orexin system in the brain also plays a role in the association between sleep and development of a migraine.
We found that 21.9% of the participants took sleep medications (11.1% took medications regularly [≥ 3 times/wk] and 10.8% took medications but not regularly [≤ 2 times/wk]), and 78.1% did not take sleep medications.21 Significantly higher proportions of arrhythmia, hypertension, and migraine were observed in people with insomnia who took sleep medications than in those who did not take sleep medications, even after adjusting for depression, sex, and age. However, we did not perform a detailed analysis because of the high variability (eg, no uniformity of specific medication used, dosage, or concurrent medication usage). Further follow-up surveys should be performed to evaluate the influences of the different types of medications (eg, Western-type sedatives and traditional herbal medicines) and nonpharmacological treatment strategies (eg, cognitive behavioral therapy) in elderly individuals with insomnia. Because of the current cross-sectional study design, we were unable to determine causal relationships.

However, we found that the prevalence of some specific physical conditions in people who were currently taking sleep medications was comparable to those who were not taking sleep medications. Therefore, sleep medication may not be a covariate that influences the comorbidity of some specific physical conditions. Receiving hypnotic prescriptions was associated with greater than threefold increased hazards of death even when prescribed fewer than 18 pills/y.37,38 However, other prospective studies did not find an association between hypnotic prescriptions and mortality.26,40 These inconsistent findings may be attributable to a failure to take into account confounding variables, notably common affective symptoms and sleep complaints, although other factors (eg, study design, participant age, and class of hypnotics) likely influence the study outcome.

The current study has several limitations. First, the elderly participants only came from urban communities in northern China. Because of the higher education level, better living conditions, and better health care conditions than those who live in rural areas, the results may not be generalizable to other regions of China. Second, the current study utilized a cross-sectional design, and we cannot determine causal relationships between insomnia and medical conditions. Third, the severity of insomnia was not calculated, so we could not draw definitive conclusions about the relationship between insomnia, sleep medication, and multimorbidity.

In conclusion, the current results demonstrate significant overlap between insomnia and multiple medical conditions. Those who complained of insomnia had poorer physical health status. The prevalence of arrhythmia, hypertension, and migraine in individuals with insomnia who were taking sleep medications was higher than in those who were not taking sleep medications. Longitudinal studies are needed to investigate the relationships between chronic insomnia and medical conditions, which could help us better understand the high comorbidity between insomnia and various medical conditions.

DISCLOSURE STATEMENT

Work for this study was performed at the Institute of Mental Health, Hebei Medical University and Department of Psychiatry, First Hospital of Hebei Medical University. This work was supported in part by the National Science Foundation of China (no. 81401101, 81301150, and 81271489), Hebei Provincial Key Technology R&D Program (no. 09276103D), Key Research Program of Science and Technology of the Hebei Province Health Department (no. 20130579), the National Basic Research Program of China (no. 2015CB856400) and Beijing Municipal Science and Technology Commission (no. Z151100003915121). This was not an industry supported study. The authors have indicated no financial conflicts of interest.

ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbr.</th>
<th>Definition</th>
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<tbody>
<tr>
<td>CES-D</td>
<td>Center for Epidemiology Scale-Depression</td>
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<tr>
<td>CI</td>
<td>confidence interval</td>
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<tr>
<td>DIS</td>
<td>difficulty initiating sleep</td>
</tr>
<tr>
<td>DMS</td>
<td>difficulty maintaining sleep</td>
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<tr>
<td>DSM</td>
<td>Diagnostic and Statistical Manual of Mental Disorders</td>
</tr>
<tr>
<td>EMA</td>
<td>early morning awaking</td>
</tr>
<tr>
<td>PNI</td>
<td>people without insomnia</td>
</tr>
<tr>
<td>PWI</td>
<td>people with insomnia</td>
</tr>
<tr>
<td>PWMC</td>
<td>people who reported having the medical condition</td>
</tr>
<tr>
<td>PWOMC</td>
<td>people who did not report having the medical condition</td>
</tr>
</tbody>
</table>

REFERENCES


Insomnia subsequent to chronic conditions has been traditionally called 'secondary insomnia' but due to the complexity of the association where the temporal association or causality is not always clear, the term 'comorbid insomnia' to denote this condition was introduced in 2005 by the National Institutes of Health (NIH) State-of-the-Science conference statement on chronic insomnia [12].

Sabe Bogota Study. Multimorbidity and depressive symptoms (DSs) are common in older adults. Self-rated health (SRH) allows detection of elderly...