

# Dose-response association of sleep quality with anxiety symptoms in Chinese rural population: the Henan Rural Cohort

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## Research article

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## Abstract

Objectives The epidemiological evidence on the effect of sleep quality on anxiety symptoms has been inconclusive. This study aimed at exploring the relationship between sleep quality and anxiety symptoms in rural China and investigated whether age, lifestyle and chronic diseases modified the association.

Methods A total of 27,911 participants aged 18–79 years from the Henan Rural Cohort Study were included in the study. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI). Poor sleep quality was defined as PSQI  $\geq 6$ . Anxiety symptoms were evaluated with the two-item generalized anxiety disorder scale (GAD-2). A score  $\geq 6$  was viewed as having anxiety symptoms. Logistic regression and restricted cubic spline was conducted to examine the association of sleep quality with anxiety symptoms.

Results Altogether, 6,087(21.80%) were poor sleepers and 1,557(5.58%) had anxiety symptoms. The odds of anxiety were increased with increment of PSQI score after fitting restricted cubic splines. And the poor sleep quality was associated with a higher possibility of anxiety symptoms (4.60, 3.70-5.72) in men, and (3.56, 3.10-4.09) in women on multivariable analysis. Further stratified analyses showed that the effect of sleep quality and anxiety symptoms could be modified by age, marital status, smoking status, drinking status, hypertension and type 2 diabetes mellitus.

Conclusions A dose-response association between PSQI score and anxiety symptoms was found. In addition, relationship between poor sleep quality and anxiety symptoms was observed in this rural population, especially in participants aged  $\geq 60$  years and those with unhealthy habits or had a chronic disease.

## Introduction

Anxiety is an emotion characterized by tension and restlessness, associated with mental and physical discomfort [1]. In 2010, mental and substance use disorders accounted for 7.4 % of all disability-adjusted life years (DALYs) worldwide, among which depression, anxiety, and alcohol abuse accounted for 40.5%, 14.6%, and 9.6 %, respectively [2]. According to reports, generalized anxiety disorder (GAD) was present in 8.4% of adults from the Manaus Metropolitan Region [3]. Anxiety as a kind of psychological stress, will trigger a series of physiological events and cause a decrease in immunity[4]. Sleep, considered as a fundamental operating state of the central nervous system, may be one of the most important basic dimensions of brain function and mental health[5, 6]. Good sleep quality is important for optimal health status and wellness[7]. Previous studies suggested that better sleep quality could therefore improve emotional well-being [8]. A web-based study showed that a high prevalence of GAD and poor sleep quality in the Chinese public during COVID-19 outbreak[9]. Some studies have also reported an association between sleep quality and anxiety using PSQI[7, 10-13].

Although there are findings on the association between sleep quality and anxiety symptoms, there has been little research. And the concurrence of these findings have been limited by study population and methodological variations, especially among under-developed rural populations in China [14]. China is an agricultural country with 1.3 billion people and 70% of Chinese people live in rural areas[15]. And Henan Province, which is the province with the largest rural population in China. Focusing on people living in undeveloped area might be significant. Moreover, genetics showed that genes associated with circadian rhythms have been also related to a range of mental disorders[16]. Investigating the association of sleep quality with anxiety symptoms may provide references for the neurobiological mechanisms of mental disorders. In this context, to fill in the gap and add to the evidence for adverse effect of poor sleep quality to anxiety symptoms, this study was aimed at investigating the relationship between sleep quality measured by Pittsburgh Sleep Quality Index (PSQI) and anxiety symptoms in a Chinese rural population aged 18–79 years, and examined whether age, lifestyles and chronic diseases modified the association.

## Methods

## **Study population**

The participants of the current study were included from the Henan Rural Cohort, which has been previously described in detail [17, 18]. Briefly, a multistage cluster sampling method was utilized to select samples from permanent residents. Target population aged 18-79 years was recruited in Suiping, Yuzhou, Yima, Tongxu and Xinxiang counties of Henan province from July 2015 to September 2017 and registered in Chinese Clinical Trial Register (Registration number: ChiCTR-OOC-15006699). Consequently, a total of 39,259 adults (15,490 men and 23,769 women) were obtained in the baseline of Henan rural cohort.

For the current analysis, a total of 29,995 completed the evaluation of anxiety symptoms. Furthermore, participants were excluded if they had missing data on PSQI score (n=269), Because of the impaired sleep quality in shift workers[19, 20] and cancer[21], we further excluded the participants of self-reported experience of night shift work (n=1,530), or having a history of cancer (n=285) to minimize the confounding bias. The final samples included 27,911 subjects aged 18-79 years from the Henan rural cohort.

Ethics approval was provided by the Zhengzhou University Life Science Ethics Committee. Signed informed consent was obtained for each participant.

## **Data collection**

Data collection was performed by well-trained investigators in a face-to-face interview using a structured questionnaire. Demographic variables of participants included gender, age (continuous variable), marital status (married/cohabitation, other), educational levels (primary school or below, junior high school and senior high school or above), smoking status (non-smoker, or current smoker), alcohol consumption (non-drinker, or current drinker), and personal and family history of diseases.

Physical activity levels were classified into three categories; light, moderate and vigorous referenced to the criterion in the International Physical Activity Questionnaire [22]. Additionally, the physical measurement was conducted on the basis of a standard protocol [23]. Height and weight were measured with individuals wearing light clothes and barefoot to the nearest 0.1 kg and 0.1 cm. Body mass index (BMI) was computed by body weight in kilograms divided by square of height in meters.

## **Evaluation of sleep quality**

Information on sleep was collected by PSQI [24], which consisted of 19 items. The scale which scores 0 to 21 has been widely used to evaluate sleep quality and well validated and readily completed by most participants. A previous study reported that at least a cutoff score of 5 PSQI yields a sensitivity of 89.6% and a specificity of 86.5%[24]. Thus, a participant with at least 6 PSQI score is considered as having a poor sleep quality in this study. Self-reported night sleep duration was obtained by asking the following question of the PSQI, "What time did you usually go to bed and wake up during the past month?" And the sleep onset latency was collected by the following question: "How long (in minutes) has it taken you to fall asleep each night during the past month?" The sleep initiation time was calculated as bed time plus sleep latency. The night sleep duration was computed on the basis of wake-up time and sleep initiation time [25].

## **Definition of anxiety symptoms**

The anxiety symptoms of participants were collected using the two-item generalized anxiety disorder scale (GAD-2) which included two items (feeling nervous, anxious, or on edge and not being able to stop or control worrying) yielding a sensitivity of 85% [26]. The scores of this scale ranged from 0 to 6. To examine the association between sleep quality and anxiety symptoms, we dichotomized scores of the GAD-2 scale. Participants were view as having anxiety symptoms if they scored  $\geq 3$  in the current study[27]..

## Statistical analysis

Mean  $\pm$  standard deviation (SD) and frequencies (percentages) was presented for continuous and categorical variables, respectively. Multivariable restricted cubic regression spline curves[28] with 3 knots (5th, 50th, and 95th) were fitted to observe the shape of the association between continuous PSQI score and anxiety symptoms. Furthermore, the PSQI score was dichotomized to examine the association between poor sleep quality and anxiety symptoms with good sleep quality as reference group by performing logistic regression models. In the fully adjusted model, we included age, gender, physical activity, marital status, smoking status, drinking status, educational levels, average monthly income and BMI, night sleep duration and napping duration in the model as the underlying confounder according the previous studies [29, 30]. Additionally, stratified analyses were conducted by each potential modifier to examined whether poor sleep quality and anxiety symptoms were potentially changed by age, gender, marital status, smoking status, drinking status, average monthly income , physical activity, BMI, snoring, hypertension, type 2 diabetes mellitus(T2MD). A two-tailed P value of less than 0.05 was determined the statistical significance in the current study. All analyses were run on SAS version 9.1 (SAS Institute) and R version 3.5.1.

## Results

### Demographic characteristics

Table 1 displays the demographic characteristics of participants by the presence or absence of anxiety symptoms. In total, among the 27,911 participants included in this study, the mean (SD) age was 55.96 (12.22) years, 16,743 (59.99%) were women, the mean (SD) PSQI score was 3.79 (2.73), 6,087 (21.81%) were poor sleepers, and 1,557 (5.58%) have anxiety symptom. Those with anxiety symptoms were more likely to have lower education and income, lower physical activity levels, and have poorer sleep quality. (Table 1 is on page 20)

### Dose-response association between PSQI score and anxiety symptoms

Figure 1 presents the association between PSQI score and the likelihood of anxiety symptoms. Modeling PSQI score as a continuous variable, this study observed the increased likelihood of anxiety symptoms increased with the elevated PSQI score after adjustment of potential covariates.

### Association between poor sleep quality and anxiety symptoms

Table 2 reports results sleep quality and anxiety symptoms, with less than 6 score of PSQI as reference category. Compared to the reference group, poor sleep quality ( $PSQI \geq 6$ ) was associated with a higher possibility of anxiety symptoms (3.85, 3.42-4.33) in total populations, (4.60, 3.70-5.72) in men, and (3.56, 3.10-4.09) in women on multivariable analysis.

### Stratified analysis for poor sleep quality and anxiety symptoms

The results of the stratified analysis for anxiety symptoms are shown in Figure 2. The ORs of anxiety symptoms associated with poor sleep quality were significantly higher among aged 60 or older (4.41, 3.70-5.27), married (3.99, 3.52-4.52), smokers (4.73, 3.45-6.48), participants with light level of physical activity (5.55, 4.47-6.90), those who had obesity (4.66, 3.42-6.33) and those with snoring (4.60, 3.75-5.64), T2DM (4.83, 3.30-7.06) (Figure 2).

## Discussion

This study demonstrated that in a large population in Chinese rural area, a positive association between poor sleep quality and anxiety symptoms was found in both men and women. According to the stratified analysis, this study observed stronger positive associations in aged 60 or older, smokers, light level of physical activity, obesity and chronic disease

(e.g., T2DM). The current study is the first to focus on the association between poor sleep quality and the odds of anxiety symptoms in a large Chinese rural population. This study used baseline data from a large cohort study that rigorously controlled for quality and standardized assessments of outcomes and confounders.

China is an agricultural country with 1.3 billion people and 70% of Chinese people live in rural areas[15]. However, most people in rural area with poor sleep quality were either not treated or treated inadequately. There is an obvious gap between the levels of urban and rural health, and the health level of rural residents is relatively low[15]. Previous study showed that inequality and imbalance of medical facilities were found across 203801 villages and 1609 townships in Henan Province[31]. The current study explored the associations between the sleep quality and anxiety symptoms in rural China; this had not been explored for in previously published studies. Therefore, this study is meaningful among rural residents. The study found those with anxiety symptoms were more likely to have a lower income and are exposed to unhealthy lifestyles, such as lower physical activity levels.

This study presents the association between poor sleep quality and anxiety symptoms, which is consistent with a previous study that poor sleep quality were strongly associated with anxiety symptoms among women[32]. Previous studies on patients with coronary artery bypass graft patients identified that a better quality of sleep was related to lower anxiety levels[8, 33]. Some studies have also reported an association between sleep quality and anxiety symptoms using PSQI[7, 10-13]. For example, One of the studies found that patients with an increase in preoperative state anxiety has 1.186 times the odds to have poor sleep quality (95% CI: 1.074 to 1.115), after controlling the potential confounders[7]. The fully adjusted OR in this study, poor sleep quality was associated with a higher possibility of anxiety symptoms (3.85, 3.42-4.33) in total populations. Although previous studies have reported an association between poor sleep quality and anxiety symptoms, these studies were limited to specific populations (adult women [10], Older Chinese[11], Cardiovascular patient[12], after coronary artery bypass surgery[7], T2DM [13]). No study has been sufficiently large to show a statistically significant modifying effect of sleep quality and anxiety in an overall healthy population. However, there was another study found that poor sleep quality was associated with both depression and anxiety, whereas only daytime sleepiness was associated with anxiety symptoms in older adults [34].

The mechanisms behind the association between sleep quality and anxiety are not clear. Moreover, lack of sleep can lead to a range of adverse neurobehavioral consequences and physiological changes, such as inattention, depression, impaired glucose tolerance, and sympathetic nervous system activation [35]. These changes in sleep quality may manifest as the onset of mental illness, including anxiety. Nevertheless, we should keep in mind that our findings, based on cross-sectional data, are limited to confirming a causal relationship between sleep quality and anxiety, and the exact mechanisms remain to be studied.

This study successfully demonstrated the following strength. This study thoroughly clarified the association between poor sleep quality and anxiety symptoms in a large-scale rural population from the Henan rural cohort study. This is the first analysis of this association in rural China so far. Poor sleep quality is a symptom of many health problems. It gave us a chance to understand the relationship between sleep quality and anxiety symptoms in the Chinese rural population.

The current study also has some limitations. First, this was a cross-sectional study, and there is the possibility of reverse causality. We recommend long-term longitudinal studies to characterize the overall changes in sleep quality and anxiety symptoms. Second, although the PSQI is a well-validated scale of sleep quality, the recall bias on the results cannot be excluded thoroughly. Third, the dataset we used is not a national representative one, the extrapolation of the results may be limited.

## Conclusions

A dose-response association between PSQI score and increased odds of anxiety symptoms was observed. Moreover, this study also found that poor sleep quality contributes to the increased prevalence of anxiety symptoms in a Chinese rural population, especially in those who were 60 years old or above, smokers, with light level of physical activity, obesity. In addition, these findings suggests that people should develop good sleeping habit to prevent anxiety symptoms. Governments publicize the need for exercise and guide them on how to implement appropriate activities. At the same time, the focus is on identification and early intervention in the elderly population over 60 years old. This can help lessening the incidence of poor sleep quality.

## Abbreviations

PSQI: Pittsburgh Sleep Quality Index ;

GAD: Generalized anxiety disorder;

BMI: Body mass index ;

GAD-2: The two-item generalized anxiety disorder scale;

SD: Standard deviation;

T2MD: Type 2 diabetes mellitus;

## Declarations

### Ethics approval and consent to participate

Ethical approval for this study was obtained from the “Zhengzhou University Life Science Ethics Committee”, and written informed consent was obtained from all participants. Ethics approval code: [2015] MEC (S128)

### Consent for publication

All authors made significant contributions to the manuscript and all authors have read and approved the final version as well as agreed with the publication on *BMC Public Health*.

### Availability of data and materials

The data used in this study are available and will be provided by the corresponding author on a reasonable request.

### Competing interests

The authors have declared that no competing interests exist.

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### Authors' contributions

During the research, Chongjian Wang and Zhenxing Mao designed the study. Jiali Shen, Haiqing Zhang, Yan Wang, Tanko Abdulai , Miaomiao Niu, Zhicheng Luo, Yikang Wang, Ruiying Li, Fang Wang directed the collection of the data. Jiali Shen and Haiqing Zhang analyzed the data. Jiali Shen and Haiqing Zhang wrote the manuscript. Yan Wang and Tanko Abdulai provided writing assistance. All authors read and approve this version of the article.

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## Tables

**Table 1. Demographic characteristics of participants according to anxiety symptoms stratified by gender**

Variables	Total			Men			Women		
	No-anxiety	Anxiety	P	No-anxiety	Anxiety	P	No-anxiety	Anxiety	P
N	26354	1557		10719	449		15635	1108	
Age(year), mean±SD	55.94±12.27	56.34±11.37	0.180	57.21±12.16	56.62±12.05	0.316	55.07±12.27	56.22±11.09	<0.001
Married/cohabitation, n (%)	23,697(89.92)	1,381(88.70)	0.121	9,645(89.98)	397(88.42)	0.282	14,052(89.88)	984(88.81)	0.257
Educational levels, n (%)			<0.001			0.061			<0.001
Primary school or below	11,921(45.23)	848(54.46)		3,693(34.45)	179(39.87)		8,228(52.63)	669(60.38)	
Junior high school	10,131(38.44)	547(35.13)		4,828(45.04)	187(41.65)		5,303(33.92)	360(32.49)	
Senior high school or above	4,302(16.32)	162(10.40)		2,198(20.51)	83(18.49)		2,104(13.46)	79(7.13)	
Average monthly income, n (%)			<0.001			0.067			<0.001
<500 RMB	9,654(36.63)	693(44.51)		4,059(37.87)	194(43.21)		5,595(35.79)	499(45.04)	
500- RMB	8,380(31.80)	430(27.62)		3,285(30.65)	122(27.17)		5,095(32.59)	308(27.80)	
≥1000 RMB	8,320(31.57)	434(27.87)		3,375(31.49)	133(29.62)		4,945(31.63)	301(27.17)	
Current smoker, n (%)	5,226(19.83)	215(13.81)	<0.001	5,182(48.34)	212(47.22)	0.639	44(0.28)	3(0.27)	0.948
Current drinker, n (%)	4,515(17.13)	174(11.18)	<0.001	4,215(39.32)	151(33.63)	0.015	300(1.92)	23(2.08)	0.713
Physical activity, n (%)			0.018			0.872			0.002
Light	8,353(31.70)	440(28.26)		3,697(34.49)	155(34.52)		4,656(29.78)	285(25.72)	
Moderate	9,672(36.70)	601(38.60)		2,973(27.74)	129(28.73)		6,699(42.85)	472(42.60)	
Vigorous	8,329(31.60)	516(33.14)		4,049(37.77)	165(36.75)		4,280(27.37)	351(31.68)	
BMI(kg/m <sup>2</sup> ), mean±SD	24.74±3.57	24.31±3.58	<0.001	24.45±3.45	23.90±3.40	<0.001	24.93±3.64	24.48±3.63	<0.001
Night sleep duration(h), mean±SD	7.72±1.26	7.47±1.51	<0.001	7.72±1.27	7.57±1.50	0.041	7.73±1.26	7.43±1.52	<0.001
Napping duration(min), mean±SD	58.84±50.76	56.69±53.20	0.121	64.10±50.20	62.12±52.52	0.412	55.23±50.83	54.49±53.34	0.656
PSQI score, mean±SD	3.66±2.61	6.04±3.63	<0.001	3.22±2.27	5.20±3.21	<0.001	3.96±2.77	6.38±3.74	<0.001
Poor sleep quality, n (%)	5,315(20.17)	772(49.58)	<0.001	1,556(14.52)	185(41.20)	<0.001	3759(24.04)	587(52.98)	<0.001

Abbreviation: SD, standard deviation; BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index

**Table 2. OR (95% CI) of sleep quality and anxiety symptoms stratified by gender**

Sleep quality	Cases/N	Model 1	Model 2
Total			
Good	785/21,824	1	1
Poor	772/6,087	3.89(3.51-4.32)	3.85(3.42-4.33)
Men			
Good	264/9,427	1	1
Poor	185/1741	4.13(3.39-5.02)	4.60(3.70-5.72)
Women			
Good	521/12,397	1	1
Poor	587/4,346	3.56(3.15-4.03)	3.56(3.10-4.09)

Model 1: unadjusted;

Model 2: adjusted for age, gender, physical activity, marital status, smoking status, drinking status, educational levels, average monthly income, body mass index (BMI), night sleep duration and napping duration

## Figures

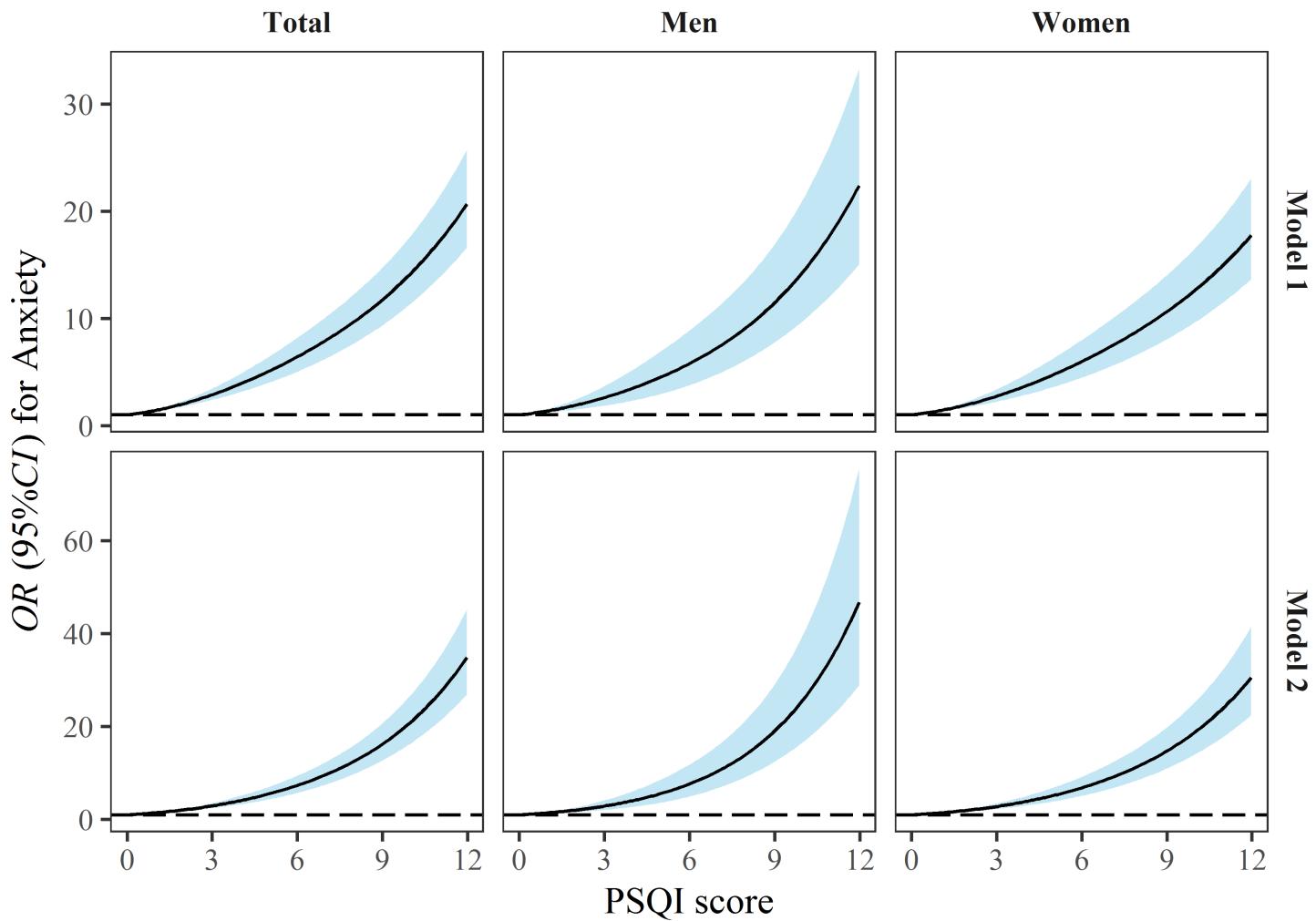
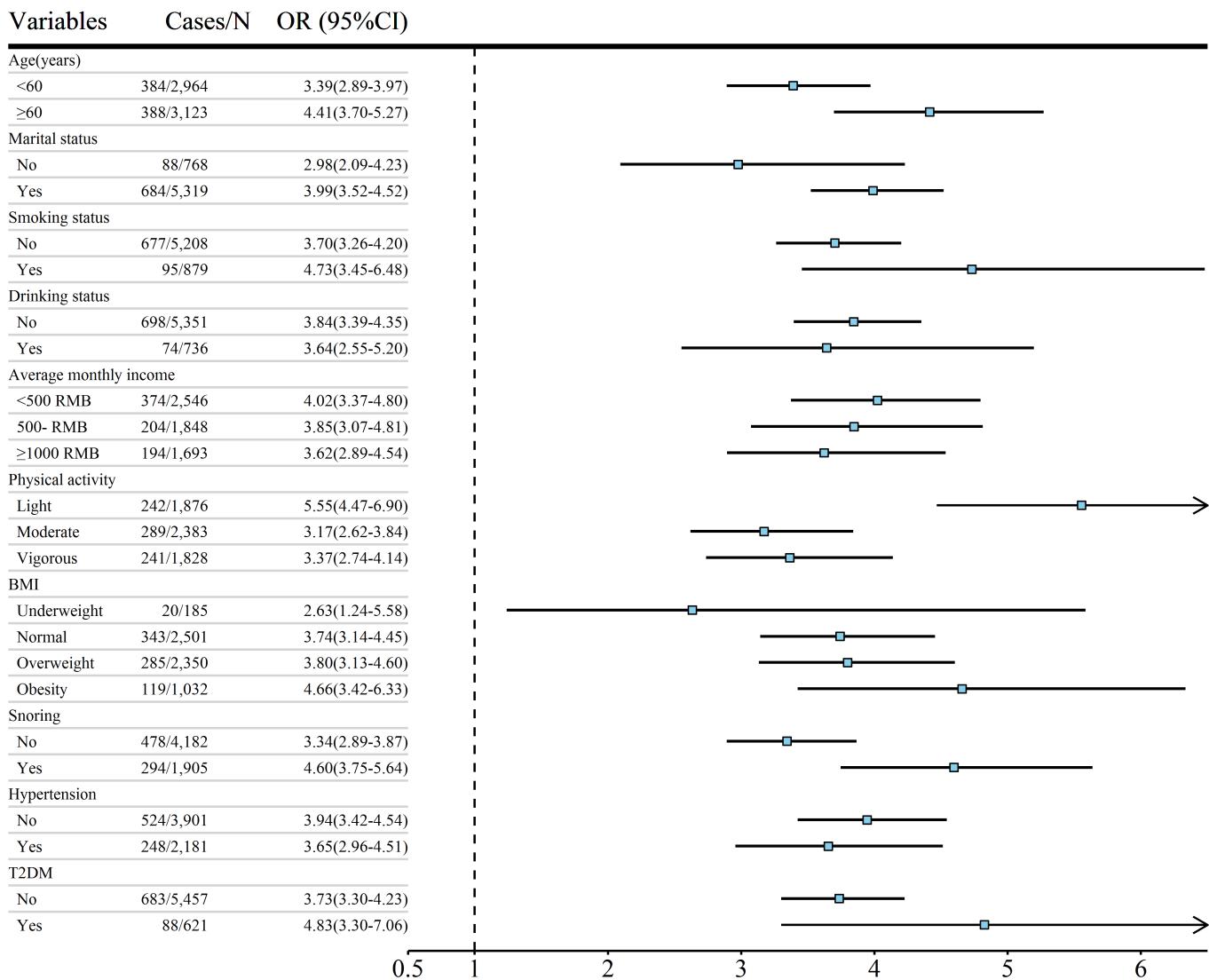


Figure 1

Restricted cubic spline plot of elevated trend of Pittsburgh Sleep Quality Index (PSQI) score with anxiety symptoms stratified by gender. Model 1: unadjusted; Model 2: adjusted for age, gender (only in total population), physical activity, marital status, smoking status, drinking status, educational levels, average monthly income, body mass index (BMI), night sleep duration and napping duration



**Figure 2**

OR (95% CI) of poor sleep quality (PSQI  $\geq 6$ ) between anxiety symptoms stratified by potential modifiers. Adjusted for age, gender (only in total population), physical activity, marital status, smoking status, drinking status, educational levels, average monthly income, body mass index (BMI), night sleep duration and napping duration Abbreviation: PSQI, Pittsburgh Sleep Quality Index

## Supplementary Files

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- [Supplementaryfile.docx](#)