Sleep Medicine 95 (2022) 1–8

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Associations between self-reported sleep duration and abnormal serum lipids in eastern China: a population-based cross-sectional survey

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ARTICLE INFO

Article history:
Received 6 December 2021
Received in revised form
21 February 2022
Accepted 6 April 2022
Available online 16 April 2022

Keywords:
Sleep duration
Lipid
Dyslipidemia
Cholesterol
Triglyceride
Dose–response relationship

ABSTRACT

Objective: To evaluate the associations between sleep duration and total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C).
Methods: The present study included 60,283 adults aged ≥18 years from the Chronic Disease and Risk Factor Surveillance in Nanjing. Generalized additive model (GAM) with forward stepwise selection method was used to analyze the nonlinear relationships between sleep duration and abnormal serum lipids. The reported effective degree of freedom (EDF) values in GAM indicates the degree of smooth curvature. EDF = 1 is a sign of linear correlation between predictors and outcome. EDF >1 is the sign of a more complex relationship between sleep duration and abnormal serum lipids.
Results: The evaluation of interaction of sex and sleep duration by using multivariable GAM revealed a U-shaped correlation between sleep duration and dyslipidemia (EDF = 4.60, $P < 0.001$), high TC (EDF = 3.38, $P < 0.001$), and high LDL-C (EDF = 3.67, $P < 0.001$) in male, and a U-shaped correlation between sleep duration and dyslipidemia (EDF = 4.69, $P < 0.001$), high TC (EDF = 3.33, $P < 0.001$), and high LDL-C (EDF = 3.21, $P < 0.001$) in female. There was a U-shaped correlation between sleep duration and high TG in male (EDF = 3.84, $P < 0.001$) and semi-linear correlation in female (EDF = 1.82, $P = 0.028$). Moreover, there was a linear correlation between sleep duration and low HDL-C in men (EDF = 1.04, $P = 0.002$), but no significant correlation in women (EDF = 3.18, $P = 0.080$).
Conclusions: Both shorter and longer sleep durations were associated with abnormal serum lipid profiles in men and women.

1. Introduction

With the development of the economy and the aging of the population, the blood lipid level of the Chinese population has gradually increased and the prevalence of dyslipidemia has significantly increased, becoming a major public health problem [1]. A recent national survey indicated that the overall prevalence of dyslipidemia in Chinese adults was as high as 40.40%, which was a significant increase from 2002 [2]. Previous studies have shown that dyslipidemia was a major risk factor for cardiovascular disease (CVD) and increased the morbidity and mortality of CVD [3–5]. Effective control of dyslipidemia is important for the prevention and control of CVD in China. A variety of risk factors have been confirmed to be related to dyslipidemia [6–8], and sleep has also been reported to play an important role in the progression of dyslipidemia [9–11].

Sleep is an important physiological activity for human beings, who spend about one-third of their time in sleep [12]. In recent years, the associations between sleep duration and human health outcomes have received increasing attention from researchers [13,14]. Several studies have demonstrated that sleep duration is associated with obesity [15,16], hypertension [17], diabetes [18], metabolic syndrome [19], cardiovascular disease [20,21]. In addition to physical illnesses, sleep duration is also associated with psychological disorders such as stress perception, the incidence of depressive symptoms, and suicidal thoughts [22].

The associations between sleep duration and abnormal serum lipids are controversial. A Chinese cohort study involving 34,260 subjects reported that longer sleep duration was associated with

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https://doi.org/10.1016/j.sleep.2022.04.004
1389-9457/

low HDL-C levels [9]. A Japanese cohort study with a 6-year follow-up showed that shorter sleep duration was associated with low HDL-C and high TC levels in middle-aged men [23]. However, a meta-analysis that included 137 prospective cohort studies with 5,134,036 participants showed that long sleep duration was not associated with dyslipidemia [24], and a meta-analysis of 153 prospective cohort studies with 5,172,710 participants showed that short sleep duration was not associated with dyslipidemia [25]. This phenomenon may occur because of inconsistencies in the study population, the classification of sleep duration and the definition of dyslipidemia.

The generalized additive model objectively described the dose−response relationship between sleep duration and abnormal serum lipids, which was not affected by the categorization of sleep duration, and was more accurate compared to those of the multivariate logistic regression model [26]. Currently, there are few studies using generalized additive model to analyze sleep duration and dyslipidemia. Smiley A et al. conformed that short sleep duration was associated with low HDL-C and high TG using generalized additive model [27]. However, their survey was conducted in the United States, while our study was conducted in the Chinese population aged 18 and older. Therefore, this study used data from a cross-sectional study to further analyze the association between sleep duration and abnormal serum lipids among people aged 18 and over in eastern China.

2. Methods

2.1. Study population and sampling

Data were obtained from the Chronic Disease and Risk Factor Surveillance in Nanjing, the capital of Jiangsu Province in eastern China. This survey was a population-based cross-sectional study designed to determine the prevalence of chronic diseases and associated risk factors from January 2017 to June 2018. The sample population was permanently residents aged 18 years and above who lived in local villages/communities for at least 6 months. According to the estimated overall prevalence of diabetes among adults aged 18 years and older in China 10.4% [28], α of 0.05, allowable error of 5%, design effect of four and a non-response rate of 15%, the required sample size was approximately 62,000.

This study used a multi-stage stratified random cluster sampling method to select research objects. In the first stage, five districts in Nanjing were randomly selected. In the second stage, all streets/towns in each sampled district were covered. In the third stage, three neighborhood committees/administrative villages were selected in each street/township based on the proportional population size sampling (PPS). In the fourth stage, one residential group (at least 50 households) was randomly selected from the sampled neighborhood committee/administrative village through cluster sampling. In the fifth stage, one adult aged 18 and above was randomly selected from each household using the Kish grid.

A total of 62,000 study subjects were recruited and 61,098 subjects agreed to participate in the survey, with a response rate of 98.5%. Eight hundred and fifteen study subjects were excluded due to missing data from sleep duration and serum lipids, 60,283 participants were included in the final analyses.

2.2. Data collection and measurement

Data from face-to-face questionnaires, anthropometric measurements, and blood samples were collected by trained medical professionals.

The questionnaire included basic demographic characteristics (eg, age, gender, education.), behavioral risk factors (eg, smoking and drinking status, sleep duration.), personal and family medical history of chronic diseases (eg, diabetes, hypertension, dyslipidemia). Anthropometric measurements included height, body weight, waist circumference (WC), and blood pressure (BP). The blood pressure was measured by trained medical staff using the Omron HBP-1300 electronic blood pressure monitor. Three measurements were taken at 2-min intervals, and the average of the last two measurements was taken as the final blood pressure value. Fasting venous blood was drawn by professional medical staff. Fasting plasma glucose (FPG) was assessed with a glucose oxidase method; total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were analyzed enzymatically with commercially available reagents.

2.3. Sleep duration

Data on sleep duration was obtained through a questionnaire. Participants were asked: “What time did you usually go to bed at night and wake up in the morning over the past month (excluding the times lying on the bed but not sleeping)?”. The reference group was the sleep duration of 7-<8 h, given that previous studies have shown that 7-<8 h was the appropriate duration of sleep for Chinese adults [14]. We divided the duration of sleep into four groups: <7 h, 7-<8 h, 8-<9 h, and ≥9 h.

2.4. Diagnosis of abnormal serum lipids

According to Chinese guidelines on the prevention and treatment of dyslipidemia in adults (2016 Revised Edition) [29], high TC was defined as TC ≥ 6.2 mmol/L, high TG was defined as TG ≥ 2.3 mmol/L, high LDL-C was defined as LDL-C ≥4.1 mmol/L, low HDL-C was defined as HDL-C <1.0 mmol/L. Dyslipidemia was defined as self-reported history of dyslipidemia and/or the use of antilipemic medication, and/or having at least one of the above abnormal serum lipids.

2.5. Covariates

According to Chinese guidelines on the prevention and treatment of hypertension in adults (2018 Revised Edition) [30], hypertension was defined as self-reported current treatment with antihypertensive medication in the past two weeks, and/or an average systolic blood pressure (SBP) ≥140 mmHg and/or an average diastolic blood pressure (DBP) ≥90 mmHg. According to Chinese guidelines on the prevention and treatment of type 2 diabetes in adults (2017) [31], Diabetes was defined as self-reported current treatment with anti-diabetes medication (insulin or oral hypoglycemic agents), and/or FPG ≥7.0 mmol/L. Low intake of vegetables and fruits was defined as an intake of less than 500 g per day [32]. High intake of red meat was defined as an intake of more than 75 g per day [32]. Regular exercise was defined as exercising two or more days per week [10,14]. Current smokers were defined as participants who have smoked at least 100 cigarettes in their lifetime and currently smoke cigarettes [33]. Current drinker was defined as consuming at least one alcoholic beverage per week in the past month [34]. Body mass index (BMI) was calculated as weight (in kilograms) divided by the square of height (in meters). Overweight and obesity were defined as BMI between 24.0 and 27.9 kg/m^2 and of ≥28.0 kg/m^2, respectively [35].

2.6. Statistical analysis

Quantitative data were presented as means ± SD, and qualitative data as proportions. Differences in quantitative and qualitative

variables were compared by independent *t* test and Chi-square test, respectively. Standardized values (means, prevalence) were calculated using the weight coefficients to represent the total Nanjing adult population aged ≥18 years. Weight coefficients accommodated the sampling scheme for unequal probabilities of sample selection, as well as the post-stratification weights, which harmonized the standard population of the 2009 Nanjing Sixth National Population Census by two genders and 12 age groups (5-year intervals) [36].

Considering the previous research showed a U/J-type association between sleep duration and cardiovascular disease and the inconsistent relationship between sleep duration and abnormal serum lipids [27,37], we used a penalized cubic regression spline [38]. The nonlinear relationship between sleep duration and dyslipidemia, high TC, high TG, low HDL-C and high LDL-C was assessed through generalized additive model (GAM). GAM is a non-parametric extension of the traditional generalized linear model, which can effectively deal with the complex nonlinear relationship between the predictors and the evaluation results. The basic residual plots were checked to assure good compliance with model assumptions [39]. The range of sleep duration in our study was from 3 to 12 h, so we set the number of knots as 10. When the disease prevalence rate is large (>10%), if the odds ratio (OR) is still used to describe the strength of the association, the association between exposure and disease will be overestimated [40,41]. Thompson et al. [42] suggested that the prevalence ratio (PR) should be used to describe the strength of the relationship between exposure and disease in cross-sectional studies. The maximum likelihood estimate (MLE) of PR can be obtained by fitting a log-binomial model [43,44]. Therefore, considering that dyslipidemia is a common outcome, we defined the family function in the GAM as negative binomial.

In the GAM, dyslipidemia, high TC, high TG, low HDL-C, and high LDL-C were treated as outcome variables and their adjusted associations with sleep duration were modeled as a smooth function. In our study, the predictive factors included sex, age, area, education, marital status, low intake of vegetables and fruits, high intake of red meat, sedentary time, regular exercise, current smoker, current drinker. We used the forward stepwise selection algorithm to select the appropriate predictors into the final GAM model.

The reported effective degree of freedom (EDF) values in GAM indicates the degree of smooth curvature. EDF = 1 is a sign of linear correlation between predictors and outcome. EDF >1 is the sign of a more complex relationship between sleep duration and abnormal serum lipids. In the multivariate GAM model, the estimated smooth functions with 95% confidence bands were plotted.

Statistical analyses were conducted by the Package "leaps","mgcv" in R software 3.6.3 or SPSS software (version 20; IBM, Armonk, NY, USA). All *P*-values were two-tailed with a significant level of <0.05.

2.7. Ethical approval

The study was approved by the academic ethics committee of Nanjing Municipal Center for Disease Control and Prevention approval (number: PJ2017-B001-01). Written informed consent was obtained from each enrolled participant.

3. Results

3.1. Baseline characteristics according to dyslipidemia

Among the 60,283 subjects, the mean [standard deviation (SD)] of sleep duration was 7.2(1.1) h. The average durations of sleep duration for men and women were 7.2 (1.0) h and 7.2 (1.1) h, respectively.

Table 1
Baseline characteristics of participants according to dyslipidemia.

Variable	Male			Female			Total		
	No	Yes	*P*	No	Yes	*P*	No	Yes	*P*
N (%)	20,663 (67.7)	9185 (32.3)		22,527 (72.7)	7908 (27.3)		43,190 (70.2)	17,093 (29.8)	
age(years), mean ± SD	44.9 ± 17.5	50.4 ± 16.0	<0.001	44.3 ± 16.8	54.4 ± 16.7	0.007	44.5 ± 17.1	52.3 ± 16.4	<0.001
WC (cm), mean ± SD	84.0 ± 8.9	87.6 ± 9.1	0.001	77.5 ± 8.6	81.1 ± 9.1	<0.001	80.6 ± 9.3	84.6 ± 9.6	<0.001
Sedentary behavior (h), mean ± SD	5.0 ± 3.0	4.9 ± 3.1	<0.001	4.7 ± 3.1	4.3 ± 2.8	<0.001	4.8 ± 3.0	4.7 ± 3.0	0.092
Sleep duration (h), mean ± SD	7.3 ± 1.0	7.1 ± 1.1	<0.001	7.3 ± 1.0	7.1 ± 1.2	<0.001	7.3 ± 1.0	7.1 ± 1.1	<0.001
BMI (kg/m^2), mean ± SD	23.8 ± 3.0	25.3 ± 3.1	<0.001	22.8 ± 3.2	24.3 ± 3.4	<0.001	23.3 ± 3.2	24.8 ± 3.3	<0.001
SBP (mmHg), mean ± SD	125.3 ± 17.7	129.4 ± 17.7	<0.001	120.7 ± 19.0	127.2 ± 22.5	<0.001	122.9 ± 18.5	128.4 ± 20.1	<0.001
DBP (mmHg), mean ± SD	78.3 ± 14.8	80.8 ± 11.4	<0.001	75.6 ± 15.1	77.9 ± 12.3	0.019	76.9 ± 15.0	79.4 ± 11.9	<0.001
FPG (mmol/L), mean ± SD	5.2 ± 1.4	5.8 ± 1.8	<0.001	5.1 ± 1.3	5.6 ± 1.8	<0.001	5.2 ± 1.3	5.7 ± 1.8	<0.001
TC (mmol/L), mean ± SD	4.4 ± 0.8	4.9 ± 1.4	<0.001	4.4 ± 0.8	5.2 ± 1.5	<0.001	4.4 ± 0.8	5.1 ± 1.5	<0.001
TG (mmol/L), mean ± SD	1.2 ± 0.4	2.4 ± 2.0	<0.001	1.2 ± 0.4	2.1 ± 1.5	<0.001	1.2 ± 0.4	2.2 ± 1.8	<0.001
HDL-C (mmol/L), mean ± SD	1.5 ± 0.5	1.2 ± 0.5	<0.001	1.5 ± 0.5	1.4 ± 0.6	<0.001	1.5 ± 0.5	1.3 ± 1.7	<0.001
LDL-C (mmol/L), mean ± SD	2.5 ± 0.7	2.9 ± 1.1	<0.001	2.5 ± 0.7	3.1 ± 1.1	<0.001	2.5 ± 0.7	3.0 ± 1.1	<0.001
Area, n (%)			<0.001			<0.001			<0.001
Urban	13,202 (64.0)	6119 (67.0)		14,159 (63.9)	5334 (68.3)		27,361 (64.0)	11,453 (67.6)	
Rural	7461 (36.0)	3066 (33.0)		8368 (36.1)	2574 (31.7)		15,829 (36.0)	5640 (32.4)	
Education, n (%)			<0.001			<0.001			<0.001
Primary school and lower	1197 (7.2)	591 (7.4)		2418 (13.3)	1252 (19.1)		3615 (10.4)	1843 (12.8)	
Junior or Senior high school	8777 (45.8)	4657 (52.6)		9347 (43.4)	4239 (53.1)		18,124 (44.5)	8896 (52.8)	
College and higher	10,689 (47.0)	3937 (40.0)		10,762 (43.3)	2417 (27.8)		21,451 (45.0)	6354 (34.3)	
Marital status, n (%)			<0.001			<0.001			<0.001
Single	4974 (18.8)	1069 (9.0)		3894 (14.7)	619 (6.8)		8868 (16.6)	1688 (8.0)	
Married or living with a partner	15,228 (78.3)	7811 (87.3)		17,772 (79.9)	6725 (83.7)		33,000 (79.1)	14,536 (85.6)	
Separated, divorced, or widowed	461 (2.9)	305 (3.7)		861 (5.4)	564 (9.5)		1322 (4.2)	869 (6.4)	
Current smoker, n (%)	7088 (35.1)	4008 (43.2)	<0.001	222 (1.1)	112 (1.5)	0.002	7310 (17.3)	4120 (23.8)	<0.001
Current drinker, n (%)	9305 (45.0)	4927 (53.1)	<0.001	2559 (11.0)	861 (10.4)	0.253	11,864 (27.2)	5788 (33.3)	<0.001
Low intake of vegetables and fruits, n (%)	10,884 (52.2)	4419 (47.9)	<0.001	11,413 (50.8)	3811 (48.1)	<0.001	22,297 (51.4)	8230 (48.0)	<0.001
High intake of red meat, n (%)	12,987 (61.8)	5681 (60.6)	0.099	12,065 (52.8)	3991 (49.7)	<0.001	25,052 (57.1)	9672 (55.5)	0.001
Regular exercise, n (%)	10,115 (47.8)	4542 (49.0)	0.427	9092 (40.1)	3282 (41.0)	0.075	19,207 (43.8)	7824 (45.3)	0.004
Diabetes, n (%)	1384 (8.1)	1700 (20.0)	<0.001	1244 (6.6)	1335 (18.6)	<0.001	2628 (7.3)	3035 (19.3)	<0.001
Hypertension, n (%)	4587 (26.0)	3992 (46.9)	<0.001	3933 (20.5)	3174 (44.1)	<0.001	8520 (23.1)	7166 (45.6)	<0.001

WC, waist circumference; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; SD, standard deviation.

Baseline characteristics according to dyslipidemia were shown in Table 1. The weighted prevalence of dyslipidemia in the general population was 29.8% (male: 32.3% and female: 27.3%). The weighted prevalence of high TC, high TG, high LDL-C, and low HDL-C in male was 5.6%, 13.3%, 4.9% and 10.8%, respectively (Supplemental Table 1). The weighted prevalence of high TC, high TG, high LDL-C, and low HDL-C in female was 7.7%, 9.2%, 5.5% and 6.0%, respectively (Supplemental Table 2).

As shown in Table 1, men and women with dyslipidemia were significantly different from those with normal serum lipids in terms of age, area, education, marital status, low intake of vegetables and fruits, current smoker, diabetes, hypertension, sleep duration, sedentary behavior, WC, BMI, SBP, DBP, FPG, TC, TG, HDL-C, and LDL-C (All $P < 0.05$).

3.2. Prevalence of abnormal serum lipids level according to sleep duration

Among men, the prevalence of dyslipidemia, high TC, high TG, and high LDL-C were significantly different in four sleep duration groups (All $P < 0.001$), while the prevalence of low HDL-C was not($P = 0.117$). The prevalence of dyslipidemia, high TC, and high TG were highest in the <7 h sleep duration group, and the prevalence of high LDL-C was highest in the ≥9 h sleep duration group. Table 2.

Likewise, among women, the prevalence of dyslipidemia, high TC, high TG, and high LDL-C differed significantly across sleep duration groups (All $P < 0.001$), while the prevalence of low HDL-C did not($P = 0.461$). The prevalence of dyslipidemia, high TC, high TG, and high LDL-C were highest in the <7 h sleep duration group Table 2.

3.3. Associations between sleep duration and abnormal serum lipids

Table 3 presented the output of the multivariable generalized additive model using the forward stepwise selection for dyslipidemia. It included the smoothing estimate for sleep duration in male and female in association with dyslipidemia adjusted for age, low intake of vegetables and fruits, marital status, and current smoker. Fig. 1 showed that evaluation of interaction of sex and sleep duration by using multivariable GAM revealed a U-shaped correlation between sleep duration and dyslipidemia in male (EDF = 4.60, $P < 0.001$) and female (EDF = 4.69, $P < 0.001$).

Tables 4–7 presented the output of the multivariable generalized additive model using the forward stepwise selection for high TC, high TG, low HDL-C, and high LDL-C, respectively. Table 4 included the smoothing estimate for sleep duration in male and female in association with high TC adjusted for age, marital status. Table 5 included the smoothing estimate for sleep duration in male and female in association with high TG adjusted for age, low intake of vegetables and fruits, and marital status. Table 6 included the smoothing estimate for sleep duration in male and female in association with low HDL-C adjusted for marital status, high intake of red meat. Table 7 included the smoothing estimate for sleep duration in male and female in association with high LDL-C adjusted for age, marital status, low intake of vegetables and fruits.

Fig. 2 showed that evaluation of interaction of sex and sleep duration by using multivariable GAM revealed a U-shaped correlation between sleep duration and high TC in male (EDF = 3.38, $P < 0.001$) and female (EDF = 3.33, $P < 0.001$). Fig. 3 showed that evaluation of interaction of sex and sleep duration by using

Table 2
Prevalence of abnormal serum lipid levels according to sleep duration [n (%)].

Sleep duration	<7 h	7-<8 h	8-<9 h	≥9 h	*P* Value
Serum lipid					
Male					
High TC	418 (6.8)	543 (5.2)	505 (5.2)	93 (5.7)	<0.001
High TG	935 (14.9)	1390 (12.9)	1265 (12.7)	217 (12.1)	<0.001
Low HDL-C	1094 (17.2)	1801 (16.4)	1647 (15.8)	291 (16.4)	0.117
High LDL-C	354 (5.7)	478 (4.5)	441 (4.5)	94 (6.0)	<0.001
Dyslipidemia	2345 (37.9)	3359 (31.5)	2935 (29.6)	546 (31.8)	<0.001
Female					
High TC	684 (10.3)	728 (7.1)	688 (6.6)	147 (7.9)	<0.001
High TG	723 (11.0)	927 (8.9)	836 (8.0)	200 (10.0)	<0.001
Low HDL-C	663 (9.8)	1046 (9.7)	1013 (9.8)	193 (9.1)	0.461
High LDL-C	495 (7.3)	516 (5.1)	476 (4.7)	103 (5.5)	<0.001
Dyslipidemia	2291 (35.1)	2696 (26.0)	2406 (23.5)	515 (25.7)	<0.001

TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.

Table 3
Adjusted associations of dyslipidemia and independent variables measured by generalized additive model using forward stepwise selection method.

	Outcome: Dyslipidemia	
	B	*P*
Age	0.01	<0.001
Marital status		
Single	Reference Group	
Married or living with a partner	0.58	<0.001
Separated, divorced, or widowed	0.76	<0.001
Low intake of vegetables and fruits		
No	Reference Group	
Yes	−0.08	<0.001
Current smoker		
No	Reference Group	
Yes	0.09	<0.001
Sleep duration*Sex		
male	Smooth Curve, EDF = 4.60	<0.001
female	Smooth Curve, EDF = 4.69	<0.001

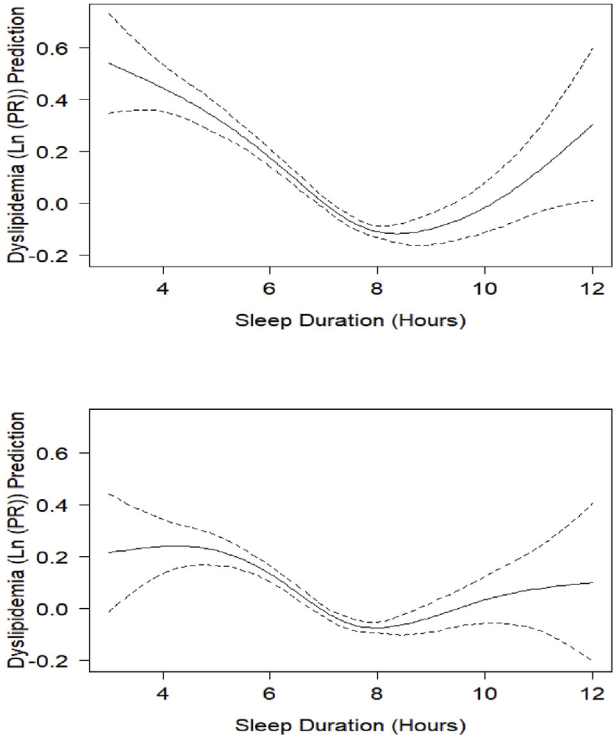

Fig. 1. Interaction of sleep duration and sex in adjusted GAM. EDF = 4.60 in male model (upper plot), EDF = 4.69 in female model (lower plot), All $P < 0.001$.

Table 4
Adjusted associations of High TC and independent variables measured by generalized additive model using forward stepwise selection method.

	Outcome: High TC	
	B	*P*
Age	0.01	<0.001
Marital status		
Single	Reference Group	
Married or living with a partner	1.27	<0.001
Separated, divorced, or widowed	1.46	<0.001
Sleep duration*Sex		
male	Smooth Curve, EDF = 3.38	<0.001
female	Smooth Curve, EDF = 3.33	<0.001

Table 5
Adjusted associations of High TG and independent variables measured by generalized additive model using forward stepwise selection method.

	Outcome: High TG	
	B	*P*
Age	0.01	<0.001
Marital status		
Single	Reference Group	
Married or living with a partner	0.67	<0.001
Separated, divorced, or widowed	0.68	<0.001
Low intake of vegetables and fruits		
No	Reference Group	
Yes	−0.11	<0.001
Sleep duration*Sex		
male	Smooth Curve, EDF = 3.84	<0.001
female	Smooth Curve, EDF = 1.82	0.028

Table 6
Adjusted associations of Low HDL-C and independent variables measured by generalized additive model using forward stepwise selection method.

	Outcome: Low HDL-C	
	B	*P*
Marital status		
Single	Reference Group	
Married or living with a partner	0.01	0.718
Separated, divorced, or widowed	0.16	0.030
High intake of red meat		
No	Reference Group	
Yes	0.08	0.006
Sleep duration*Sex		
male	Smooth Curve, EDF = 1.04	0.002
female	Smooth Curve, EDF = 3.18	0.080

Table 7
Adjusted associations of High LDL-C and independent variables measured by generalized additive model using forward stepwise selection method.

	Outcome: High LDL-C	
	B	*P*
Age	0.01	<0.001
Marital status		
Single	Reference Group	
Married or living with a partner	1.06	<0.001
Separated, divorced, or widowed	1.26	<0.001
Low intake of vegetables and fruits		
No	Reference Group	
Yes	−0.25	<0.001
Sleep duration*Sex		
male	Smooth Curve, EDF = 3.67	<0.001
female	Smooth Curve, EDF = 3.21	<0.001

multivariable GAM revealed two different smoothing shapes between sleep duration and high TG; U-shaped in male (EDF = 3.84, $P < 0.001$) and semi-linear in female (EDF = 1.82, $P = 0.028$). Fig. 4 showed that evaluation of interaction of sex and sleep duration by using multivariable GAM revealed a linear correlation between sleep duration and low HDL-C in male (EDF = 1.04, $P = 0.002$), but no significant correlation in female (EDF = 3.18, $P = 0.080$). Fig. 5 showed that evaluation of interaction of sex and sleep duration by using multivariable GAM revealed a U-shaped correlation between sleep duration and high LDL-C in male (EDF = 3.67, $P < 0.001$) and female (EDF = 3.21, $P < 0.001$). In addition, we analyzed the non-linear relationship between sleep duration and serum abnormal lipids in the total population, the results showed that there was a U-shaped correlation between sleep duration and dyslipidemia, high TC, high TG, and high LDL-C, while an inverted U-shaped correlation between sleep duration and low HDL-C (Supplemental Figs. 1,2,3,4,5).

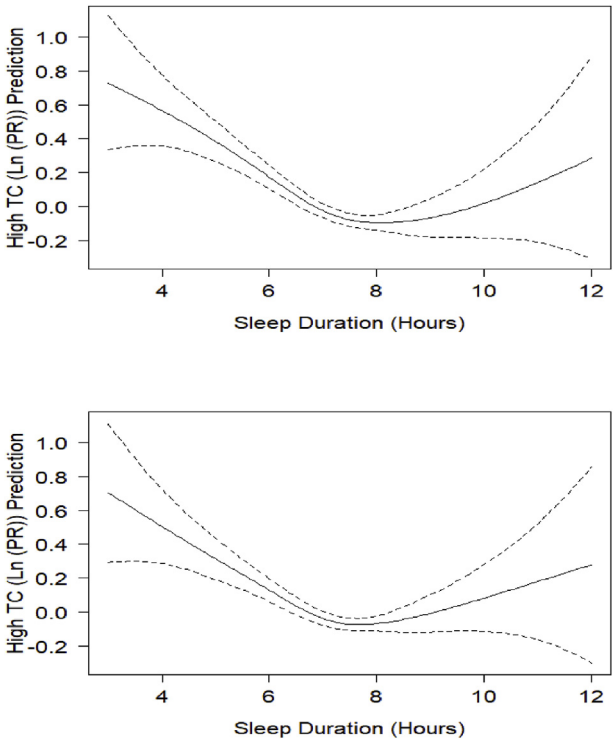

Fig. 2. Interaction of sleep duration and sex in adjusted GAM. EDF = 3.38 in male model (upper plot), EDF = 3.33 in female model (lower plot), All $P < 0.001$.

4. Discussion

This study assessed the cross-sectional association between sleep duration and dyslipidemia, high TC, high TG, low HDL-C, and high LDL-C in men and women through GAM. In dyslipidemia and high TC, and high LDL-C model, EDF was greater than three in both man and women, indicating a nonlinear correlation between sleep duration and dyslipidemia and high TC, and high LDL-C in men and women. In high TG model, EDF was greater than three in man and was closed to two in female, indicating a nonlinear association between sleep duration and high TG in men and women. Short sleep duration showed similar associations with high TG in men and women, while the association of long sleep duration was different; sharply increased PR of high TG in men and no change or slightly decreased PR of high TG in women. In low HDL-C model, the evaluation of interaction of sex and sleep duration revealed a linear correlation between sleep duration and high HDL-C in men but no significant correlation in women.

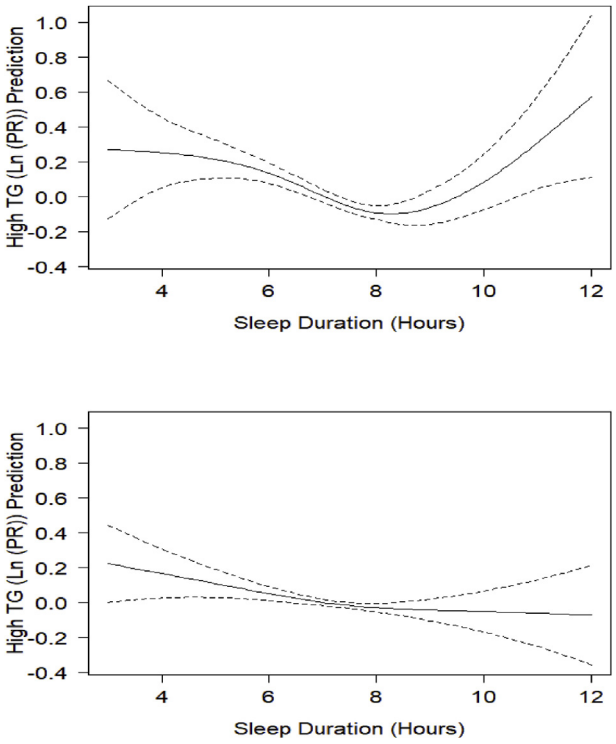

Fig. 3. Interaction of sleep duration and sex in adjusted GAM. EDF = 3.84 in male model (upper plot), $P < 0.001$; EDF = 1.82 in female model (lower plot), P value = 0.028.

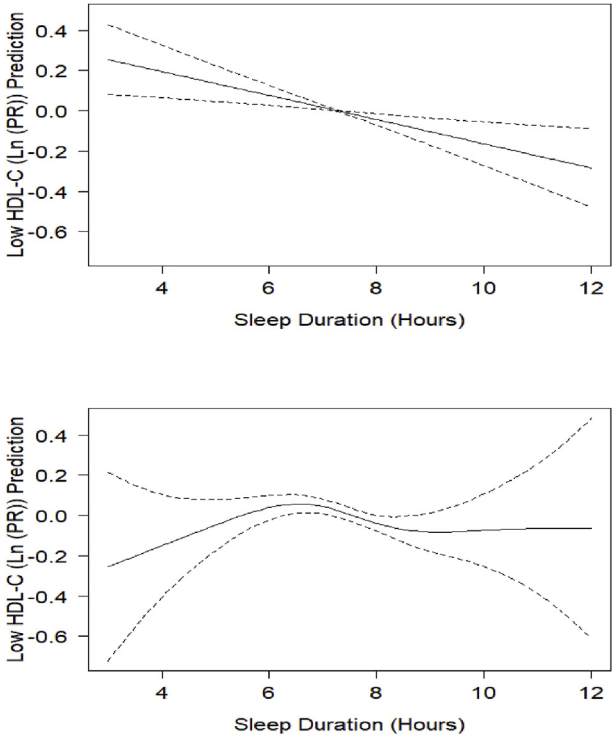

Fig. 4. Interaction of sleep duration and sex in adjusted GAM. EDF = 1.04 in male model (upper plot), P value = 0.002; EDF = 3.18 in female model (lower plot), P value = 0.080.

A few studies have focused on the association of sleep duration with abnormal serum lipids in men and women. Yiqiang Zhan et al., using data from the 2009 China Health and Nutrition Survey, reported that compared with sleep duration of 8 h, less than 6 h and more than 10 h of sleep were associated with dyslipidemia, high TC, high TG, and high LDL-C levels in women but not in men [45]. Yoshitaka Kaneita et al., demonstrated that shorter and longer sleep duration was associated with higher TG and lower HDL-C in women, but not in men from the Japan Health and Nutrition Survey [46]. A cohort study with 6 years of follow-up showed that short sleep duration was associated with increased risk of future low HDL cholesterol and high TG in men [23]. Although all of the above studies included sleep duration as a categorical variable in multivariate logistic regression models to analyze the association between sleep duration and abnormal serum lipids, which may have lost the information of sleep duration as a continuous variable, their results still indicated the inconsistent association between sleep duration and abnormal serum lipids in men and women.

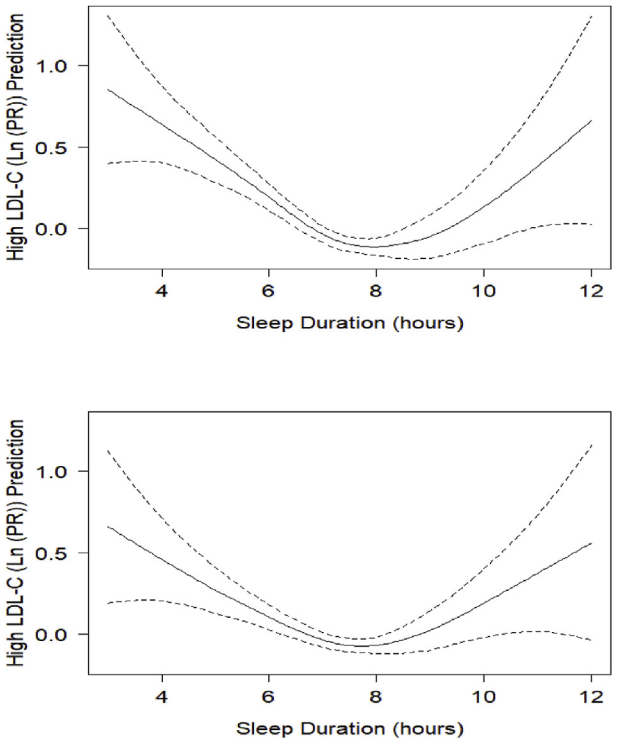

Fig. 5. Interaction of sleep duration and sex in adjusted GAM. EDF = 3.67 in male model (upper plot), EDF = 3.21 in female model (lower plot), All $P < 0.001$.

In this study, we used multivariable generalized additive model with forward stepwise selection method to analyze the nonlinear relationship between sleep duration and abnormal serum lipids. Application of the generalized additive model to examine the nonlinear association of sleep duration and abnormal serum lipids improved risk adjustment compared with logistic regression [26]. When there is a non-linear relationship between sleep duration and abnormal serum lipids, using dummy variables on the category to adjust the risk may lead to residual confounding [47]. Our results showed that the relationship between sleep duration and abnormal serum lipids differs between men and women. Both short and long sleep duration were associated with dyslipidemia, high TC, high LDL-C in men and women. Both short and long sleep duration was associated with high TG in men, while short sleep duration was associated with high TG in women. Short and long sleep duration were associated with low HDL-C in men, but not in women. Smiley A et al., using multivariable generalized additive model, conclude that short sleep duration was associated with low HDL-C and high

TG, but the evaluation of interaction of sex and sleep duration showed no statistically significant association between sleep duration and HDL-C in men and women [27]. Differences in the age distribution and ethnicity of the study subjects maybe could explain the differences between their study and our study.

There are some mechanisms may explain the difference in the association between sleep duration and abnormal serum lipids in men and women. Firstly, St-Onge MP et al., reported that sleep duration affected total ghrelin levels in men but not in women, and affected glucagon-like peptide 1(GLP-1) levels in women, but not in men. Their results indicated that there are different mechanisms of sleep duration that affect the regulation of food intake between men and women [48].

Secondly, the major sex hormones, testosterone in men and estrogen and progesterone in women, have different mechanisms for regulating sleep duration and sleep quality [49]. Studies on sleep restriction in animals and humans have shown that sleep disturbances induce changes in the gonadal endocrine axis, leading to lower circulating levels of testosterone. In addition, female reproductive milestones such as menarche, pregnancy, breast-feeding and menopause have profound implications for endogenous steroid exposure [50,51]. Thirdly, a review [52] indicated that advanced glycosylation end products (AGEs) are lipoproteins that are glycosylated due to exposure to sugars seen in degenerative diseases such as atherosclerosis and diabetes. They are significantly increased in chronic sleep deprivation. AGEs can induce endothelial damage through apoptosis of endothelial cells. Gastrin has a protective effect on this process. However, after sleep deprivation, males and females respond differently to gastrin and AGEs.

Sleep is a very critical factor in maintaining health, and sufficient sleep is not only an important standard of health, but also an important way for the human body to adjust itself, restore function and energy, and resist disease risks [53]. Our research showed that excessive and insufficient sleep duration were associated with abnormal serum lipids in men and women. According to the Healthy China Initiative (2019−2030), the suitable sleep duration for adults 18 years of age and above is 7−8 h, while the sleep duration compliance rate for men was 37.2% and that for women was 35.5% in eastern China. With the rapid development of the economy, modern people face the problems of fast-paced life and high social pressure, which easily lead to anxiety, depression and other emotional disorders, thus causing insomnia, poor sleep quality [54]. Improving the quality of sleep and achieving sufficient sleep time is very important for the maintenance of personal health. Currently, in addition to medication, complementary and alternative medicine are being used worldwide to treat insomnia and poor sleep quality [55,56]. Applying pressure to specific points on the body is a traditional treatment method called acupressure. Traditional Chinese medicine (TCM) acupressure is one of the most empirically studied forms of acupressure and is closely related to acupuncture in Chinese medicine. However, practitioners of TCM acupressure use fingers, knuckles, or blunt instruments instead of needles. It has received more attention because of its safe complementary and alternative effects that can significantly relieve the symptoms of certain diseases. Therefore, in the near future, TCM acupressure may be a successful treatment for patients with sleep disorders [57]. In the future, we can increase publicity on the relationship between sleep and health through media, radio and other channels, and improve the status of sleep duration compliance rate in eastern China.

There are some advantages of this study. Firstly, this population-based cross-sectional epidemiologic study was conducted in a large representative sample of eastern Chinese adults aged 18 and over. Secondly, in order to ensure the authenticity and reliability of the data, the Nanjing Centers for Disease Control and Prevention has formulated a strict quality control plan, which is implemented before, during and after the investigation. Moreover, we used a multivariable generalized additive model to analyze the relationship between sleep duration and abnormal serum lipids in men and women. Based on the above, we provide objective and accurate information about the association between sleep duration and abnormal serum lipids.

However, there are some limitations of this study that need to be considered. Firstly, this study is a cross-sectional study, which cannot infer a causal relationship between sleep duration and abnormal serum lipids. Secondly, some participants may have changed their lifestyles after knowing their lipid levels, which may lead to Ney-man bias. This bias may overestimate or underestimate the association between influencing factors and disease. Thirdly, the quality of sleep is also associated with abnormal serum lipids [58,59]. Sleep quality was not investigated in this study, so we could not analyze the effect of sleep quality on serum lipids. In the future, we will design a cohort study taking into account sleep quality to further validate the association between sleep duration and abnormal serum lipids.

5. Conclusion

Both short and long sleep duration were associated with dyslipidemia, high TC, high LDL-C in men and women. Both short and long sleep duration was associated with high TG in men, while short sleep duration was associated with high TG in women. Short and long sleep duration were associated with low HDL-C in men, but not in women.

Funding

Study funded by Nanjing Municipal Medical Science and Technique Development Foundation, China (YKK17199, ZKX18049).

Data statement

The raw data of the study is currently not available to publicly share because further research is underway. However, the corresponding author will consider sharing data on reasonable request.

Credit author statement

JLD and YJC contributed to the conception or design of the work;
NZ, YJC, WWW, XH contributed to the data collection;
JLD drafted the manuscript;
YJC, NZ, WWW, XH, YQS critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Acknowledgements

The authors thank all the participants, staffs, and investigators for the Chronic Disease and Risk Factor Surveillance in Nanjing.

Conflict of interest

None declared.
The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2022.04.004.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2022.04.004.

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