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ORIGINAL RESEARCH

Association Between Sleep Duration and Stroke in Different Status of Metabolic Syndrome: A Cross-Sectional Study in Shanghai Adult Residents

Han Wu*, Yang Zheng*, Dan-Ni Liu, Xiao-Xia Liu, Qun-Di Yang, Qiu-Yun Su, Ying-Quan Wang, Yu-Zhuo Wang, Xue-Na La, Yan Shi*, Chen Fu*

Division of Noncommunicable Diseases and Injury, Shanghai Municipal Center for Disease Control and Prevention, Shanghai, People's Republic of China

*These authors contributed equally to this work

Correspondence: Yan Shi; Chen Fu, Tel +86-21-62758710, Email shiyan@scdc.sh.cn; fuchen@scdc.sh.cn

Purpose: This study aimed to investigate the relationship between sleep duration (SD) and stroke, and examine the effects of SD on stroke with or without metabolic syndrome (Mets) and its components among the adult residents in Shanghai, China.

Participants and Methods: A total of 20,245 participants (51.72% male, mean age 44.66 years) were included from Shanghai Chronic Disease and Risk Factors Surveillance (SCDRFS) in 2017. The weighted logistic regressions were performed to examine the associations between SD and stroke in different status of Mets and its components.

Results: The mean SD was 7.51±0.03 h/d. After adjusting for all the potential factors, SD<6 h/d (OR=1.73, 95% CI: 1.35–2.20) or ≥10 h/d (OR=1.66, 95% CI: 1.08–2.57) was significantly positively associated with stoke in the total participants; moreover, in the non-Mets group, only SD<6 h/d (OR=1.77, 95% CI: 1.19, 2.64) significantly increased the risk of stroke; while, in the Mets group, SD<6 h/d (OR=1.80, 95% CI:1.17–2.76) and ≥10 h/d (OR=1.97, 95% CI: 1.00–3.88) both had a positive significantly association with stoke. In addition, the effects of SD<6 h/d on stroke were more pronounced among those with high WC (OR=2.24, 95% CI: 1.40–3.58) and high TG (OR=2.60, 95% CI: 1.86–3.62), and the effects of SD≥10 h/d on stroke were more evident among those with high TG (OR=2.28, 95% CI: 1.02–5.08) and high FBG (OR=2.58, 95% CI: 1.30–5.10).

Conclusion: Both short and long SD were significantly positively associated with stroke in the total participants, and the associations were stronger in the Mets group; conversely, in the non-Mets group, only short SD was significantly positively associated with stroke, and no significant association was observed between long SD and stroke. Therefore, more precise sleep measures may be needed to prevent stroke according to the different status of Mets.

Keywords: sleep duration, metabolic syndrome, stroke, Shanghai

Introduction

Stroke is defined as a neurological deficit attributed to an acute focal injury of the central nervous system (CNS) by a vascular cause,[1] and is characterized by rapid onset, high mortality, and high recurrence rate. Currently, stroke has been a major public health concern due to its health, economic and social burden in China. Global Burden of Disease (GBD) 2019 reported that there were 3.94 million new stroke cases, 28.76 million current stroke cases, 2.19 million deaths and 45.95 million disability-adjusted life-years (DALYs) caused by stroke in China.[2] The growing evidence suggests that the occurrence and development of stroke are closely related with multifactorial origin rather than the traditional single risk factor, such as obesity, hypertension, diabetes mellitus, hyperlipidemia, smoking, alcohol drinking, and so on,[3–5] of which sleep is also an important factor that cannot be ignored and attracts ever-growing attention among researches or policy makers in recent years.

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Sleep, a basic physiological need of human, occupies nearly one-third of our life and plays a vital role on health maintenance. However, the sleep duration (SD) status is poor among Chinese, and thus may need to be improved.[6] In recent years, with the rapid development of internet technology and electronic devices, SD has decreased as time went by among Chinese; moreover, both insufficient SD and excessive SD coexist in those population. According to the data from China Health and Nutrition Survey (CHNS), the average SD of the subjects (mean age, 46.72 years) decreased from 8.24 h/d in 2004 to 7.81 h/d in 2015; and the participants with SD <6 h/d and ≥8 h/d accounted for 12.8% and 20.0%, respectively.[7]

The association between SD and stroke was analyzed in the previous studies, while the results remain inconsistent.[4,8–11] Some studies reported a J-shaped,[4,10,12,13] whereas other results showed a U-shaped[5,8,9] or null[11] relationship between SD and stroke. The inconsistency may be explained by the metabolic disorders, for instance obesity, hypertension, diabetes mellitus, hyperlipidemia, and metabolic syndrome (Mets).[4,14–17] Mets is characterized by a cluster of risk factors composed of raised blood pressure (BP), raised triglycerides (TG), lowered high-density lipoprotein cholesterol (HDL-C), raised fasting glucose (FBG), and central obesity for cardiovascular disease and type 2 diabetes mellitus,[18] which can reflect the overall metabolic levels of body. Some insights indicated that SD had a different association with stroke among those with or without Mets and its components, but the results were also inconsistent[4,17,19]; thus, the associations between SD and stoke with different status of Mets and its components remain to be elucidated. However, to date, the above related studies are scare, especially in Shanghai adult residents, which is a super city with highly developed economics and a fast-paced life in China.

Therefore, we aimed to study the association between SD and stroke in a cross-sectional study of 20,245 Shanghai residents aged 18 years and above. Furthermore, we further investigated the effects of SD on stroke in different status of Mets, as well as its components.

Methods

Data Source

The present study used data from the Shanghai Chronic Disease and Risk Factors Surveillance (SCDRFS) programme in 2017. According to the World Health Organization (WHO) STEPS Instrument[20] and China Chronic Disease and Risk Factors Surveillance (CCDRFS) programme design,[21] the SCDRFS was designed and organized by the Shanghai Municipal Center for Disease Control and Prevention (SCDC) to investigate the epidemic status and main risk factors of chronic non-communicable diseases (NCDs) in Shanghai ordinarily adult residents. So far, four filed surveys have been carried out in 2007, 2010, 2013, and 2017, respectively. For the SCDRFS-2017 in the present study, the adopted multistage stratified random sampling method is shown in Figure 1. The SCDRFS-2017 combined the questionnaire survey, physical examinations, and laboratory tests. The questionnaire survey incorporated the basic characteristics, and the NCDs' prevalent states and main risk factors by the face-to-face interview. Physical examinations included the measurements of the height, weight, waist circumference (WC), and BP. The laboratory tests measured FBG and blood lipid. Overall, 23,346 adults were invited, of whom 20,616 completed the survey with an average response rate of 88.31%. After excluding those participants with missing data, a total of 20,245 adults were included in the study's final analysis. All the data were collected by the trained investigators from community health service centers. All the participants signed the consent forms after they were informed of the purpose and demands of the survey. The survey protocol was approved by the ethics committee of the SCDC (No. 2016–10).

Definition of SD, Mets, and Stroke

The data of SD and stroke were collected by the participants' self-report. The SD was calculated according to the question: "How much do you sleep usually in a day?", and the SD was divided into five groups: <6, 6–7.9, 8–8.9, 9–9.9, ≥10 h/d. The stroke was defined by this question: "Have you ever been diagnosed with stroke by the doctors from the township health centers/community health service centers or above medical institutions?", the participants could answer "Yes" (the stroke group) or "No" (the non-stroke group). Mets was determined as the presence of at least three of the five components according to the modified criteria for Chinese people jointly proposed by the International Diabetes

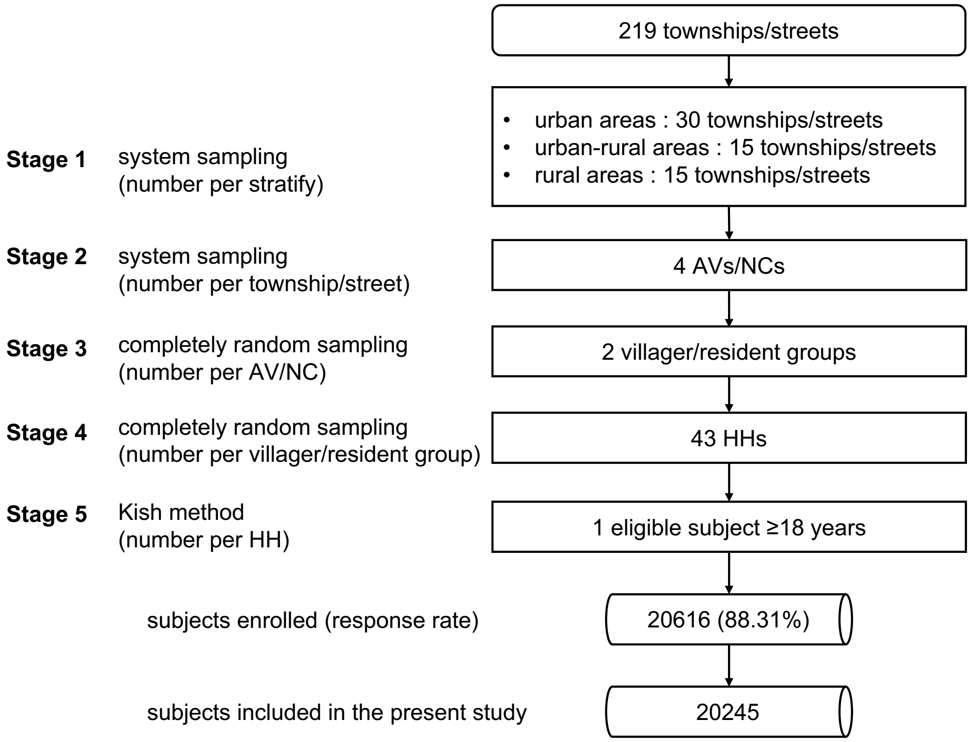

Figure 1 Sampling frame of the Shanghai Chronic Disease and Risk Factor Surveillance in 2017. Urban areas: the population with non-agricultural household registration accounted for >70% and the permanent urban agricultural migrant population accounted for ≤35%; urban–rural areas: the population with non-agricultural household registration accounted for >70% and the permanent urban agricultural migrant population accounted for >35%; rural areas: the population with non-agricultural household registration accounted for ≤70%.
Abbreviations: AV, administrative village; NC, neighborhood committees; HH, household.

Federation (IDF), National Heart, Lung, and Blood Institute (NHLBI), and the other institutions in 2009.[18] The criteria are as follows: (1) Elevated WC: males ≥85 cm; females ≥80 cm; (2) Elevated TG (drug treatment for elevated TG is an alternate indicator): ≥1.7 mmol/L; (3) Reduced HDL-C (drug treatment for reduced HDL-C is an alternate indicator): males <1.0mmol/L; females <1.3 mmol/L; (4) Elevated BP (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator): systolic ≥130 and/or diastolic ≥85 mmHg; (5) Elevated FBG (drug treatment of elevated glucose is an alternate indicator): ≥100 mg/dL.[18] The participants were categorized into the non-Mets group (<3) and Mets group (≥3) according to the number of the Mets components.

Covariates Assessment

For the present study, the covariates of interest included sociodemographic, behavioral, and health characteristics. The sociodemographic characteristics used in the present study were gender (male, female), age group (18–44, 45–59, 60–74, ≥75), education (primary school and lower, junior and senior middle, college middle school and higher), occupation (employment and unemployment), and marriage (living alone: never married, separated, divorced, and widowed; married), and urbanization (rural, urban–rural, urban).

Of the behavioral characteristics, smoking was categorized into current smoking and current non-smoking. Alcohol status ("Yes" or "No")/tea drinking ("Yes" or "No") were defined by asking whether the participants drank alcohol/tea in the past year. Physical activity was determined according to the Global Physical Activity Questionnaire (GPAQ) designed by the WHO.[22] Physical activity per week (MET-minute/week) was calculated based on the data of the types, intensity, frequency, and time of physical activity of the participants in the past 7 days. Participants were further divided into three activity intensity groups (low, medium, and high levels).[23] Four major dietary patterns were identified by using dietary data based on the Food Frequency Questionnaire (FFQ), which we labeled the "Fruit juice & pork pattern", "Tuber & high-protein pattern", "Dairy & egg & fruit pattern", and "Grain & vegetable pattern".

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The health characteristics included family history ("Yes" or "No"), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and body mass index (BMI). The professionals measured the participants' body height, weight, TC, and LDL-C by using the standardized methods. BMI was calculated as body weight (kg) divided by body height squared (m^2).

Statistical Analysis

The participants' general characteristics are expressed as weighted means (standard errors) for the continuous variables and numbers (weighted%) for the categorical variables. Considering the natural structure of the population, weight calculation was conducted in the present study. The final weigh value equals the product values of the multistage sampling, non-response, and post-stratification weights; and post-stratification weight was constructed based on the data of Shanghai permanent population in 2016. Rao-Scott Chi-square tests were performed to identify the significant differences in the general characteristics, the SD distributions, and the prevalence of the Mets or its components. The weighted logistic regressions were performed to examine the associations between SD and stroke in different status of Mets and its components. All the above analyses accounted for complex sampling design consisting of stratification, clustering, and sample weights. Restricted cubic splines (RCS) were adopted to examine the shape of the dose–response association and linearity between SD and stroke risk in the multivariable logistic regression models. We kept five knots (located at 5th, 25th, 50th, 75th, and 95th) and set the median SD (7 h/d) as the reference. SAS macro program %RCS_Reg for curve fitting was developed by Desquilbet and Mariotti.[24] All statistical tests were two-sided, and significantly difference was considered at $p<0.05$. Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results

Participant General Characteristics

General Characteristics of the Participant Stratified by Mets/Stroke

The participants (n=20,245, mean age 44.66 years) in the study included 8214 (51.72%) males and 12,031 (48.28%) females. The proportions of the total participants aged 18–44, 45–59, 60–74, and ≥75 years were 53.56%, 25.58%, 13.47%, and 7.40%, respectively. Of the total study population, 1098 (2.38%) participants had suffered a stroke. The characteristics of age, education, occupation, family history, BMI, and dietary pattern were significantly associated with stroke. Participants who were older or retired were more likely to report stroke than not reporting. People who had lower education levels, family history, higher BMI, and a weaker tendency to follow fruit juice and pork pattern were more likely to have a stroke (Table 1).

General characteristics of the study population stratified by Mets and stroke are shown in Table 2. There were 11,178 (65.06%) participants without Mets and 9067 (34.94%) participants with Mets in the study, respectively. Of the participants without Mets, 420 (1.45%) had stoke, while in those with Mets, 678 (4.09%) had stroke. For those without Mets, age, education, occupation, urbanization, SD, family history, and dietary pattern showed significant associations with stroke; and for those who had Mets, gender, age, education, occupation, physical activity level, family history, and BMI were significantly associated with stroke.

The Distribution of SD

Figure 2 depicts the distribution of SD among the study population. Of the total study population, the participants with SD<6, 6–7.9, 8–8.9, 9–9.9, and >10 h/d accounted for 4.96%, 41.83%, 40.40%, 6.97%, and 5.83%, respectively. Compared with the non-stroke group, those with stroke were more likely to sleep less or more. Similarly, for both non-Mets group and Mets group, the study population with stroke tended to have a shorter or longer SD.

The Prevalence of Mets and Its Components

The distribution of Mets and its components among the study population is illustrated in Figure 3. Of the total participants, the overall prevalence of Mets, high WC, high TG, low HDL-C, high BP, and high FBG were 34.94%, 53.99%, 35.31%, 33.70%, 45.73%, 23.66%, respectively. The stroke group presented a significantly higher prevalence of Mets (60.19% vs 34.33%), high WC (64.62% vs 53.73%), high TG (46.47% vs 35.04%), low HDL-C (43.82% vs 33.45%), high BP (85.29% vs 44.76%), and high FBG (47.52% vs 23.08%) than the non-stroke group. For both non-Mets group and Mets group, the prevalence of high

Table 1 General Characteristics of the Study Population Stratified by Stroke [n (Weighted %), Mean (SE)]

Characteristics	Total (n=20,245)	Non-Stroke (n=19,147)	Stroke (n=1098)	χ^2/t	*P*
Gender					
Male	8214 (51.72)	7773 (51.81)	441 (47.96)	2.00	0.1569
Female	12,031 (48.28)	11,374 (48.19)	657 (52.04)		
Age (years)					
18–44	2143 (53.56)	2137 (54.73)	6 (5.32)	677.47	<0.0001
45–59	5804 (25.58)	5684 (25.68)	120 (21.50)		
60–74	10,017 (13.47)	9376 (12.97)	641 (34.27)		
≥75	2281 (7.40)	1950 (6.63)	331 (38.91)		
Education					
Primary school and lower	5837 (11.81)	5357 (11.21)	480 (36.51)	229.91	<0.0001
Junior and senior middle school	11,915 (51.10)	11,377 (51.02)	538 (54.44)		
College middle school and higher	2493 (37.09)	2413 (37.77)	80 (9.05)		
Occupation					
Employment	8288 (65.70)	7923 (66.54)	365 (31.14)	196.75	<0.0001
Unemployment	11,957 (34.30)	11,224 (33.46)	733 (68.86)		
Marriage					
Living alone	2757 (24.76)	2511 (24.81)	246 (22.87)	0.40	0.5271
Married	17,488 (75.24)	16,636 (75.19)	852 (77.13)		
Urbanization					
Rural	5126 (13.95)	4813 (13.90)	313 (15.95)	4.86	0.0881
Urban–rural	5089 (25.95)	4837 (26.21)	252 (15.15)		
Urban	10,030 (60.10)	9497 (59.89)	533 (68.90)		
Current smoking	3282 (17.33)	3141 (17.42)	141 (13.53)	2.81	0.0939
Alcohol drinking	5387 (30.64)	5086 (30.60)	301 (31.89)	0.12	0.7258
Tea drinking	8045 (44.73)	7650 (44.84)	395 (40.11)	2.96	0.0854
SD (h/d)	7.51 (0.03)	7.52 (0.03)	7.26 (0.13)	−1.95	0.0562
Physical activity level					
Low	4397 (26.13)	4173 (26.23)	224 (21.92)	5.77	0.0559
Medium	7867 (41.31)	7415 (41.16)	452 (47.80)		
High	7981 (32.56)	7559 (32.62)	422 (30.27)		
Family history	3171 (14.16)	2867 (13.89)	304 (25.28)	60.61	<0.0001
TC (mmol/L)	4.82 (0.04)	4.82 (0.04)	4.86 (0.08)	0.69	0.4949
LDL-C (mmol/L)	2.98 (0.03)	2.98 (0.03)	2.95 (0.06)	−0.53	0.5974
BMI (kg/m^2)	23.93 (0.10)	23.92 (0.10)	24.34 (0.17)	2.17	0.0343
Dietary pattern					
Fruit juice and pork pattern	3699 (28.43)	3506 (28.65)	193 (19.36)	10.67	0.0137
Tuber & high-protein pattern	4515 (24.07)	4286 (23.97)	229 (28.21)		
Dairy & egg and fruit pattern	5566 (26.50)	5240 (26.44)	326 (29.03)		
Grain & vegetable pattern	6465 (21.00)	6115 (20.94)	350 (23.41)		

Abbreviations: SD, sleep duration; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; BMI, body mass index.

BP and high FBG were significantly diverse among those categorized by stroke; whereas, there were only significant differences in the prevalence of low HDL-C among those classified by stroke in the non-Mets group.

The Association of SD with Stroke in Mets

The association of SD with stroke in the study population is shown in Figure 4. Multivariate analyses, which controlled for all the potential factors indicated that SD<6 h/d (OR=1.73, 95% CI: 1.35–2.20) or ≥10 h/d (OR=1.66, 95% CI: 1.08–2.57), were significantly positively associated with stoke in the total study population compared to SD=6–7.9; moreover, in the non-Mets group, SD<6 h/d (OR=1.77, 95% CI:1.19–2.64) significantly increased the risk of stroke, while this

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Table 2 General Characteristics of the Study Population Stratified by Mets and Stroke [n (Weighted %), Mean (SE)]

Characteristics	Non-Mets (n=11,178)				Mets (n=9067)			
	Non-Stroke (n=10,758)	Stroke (n=420)	χ^2/t	*P*	Non-Stroke (n=8389)	Stroke (n=678)	χ^2/t	*P*
Gender								
Male	4534 (50.61)	192 (53.01)	0.21	0.6507	3239 (54.10)	249 (44.62)	5.57	0.0183
Female	6224 (49.39)	228 (46.99)			5150 (45.90)	429 (55.38)		
Age (years)								
18–44	1549 (61.35)	4 (8.90)	228.14	<0.0001	588 (42.06)	2 (2.96)	152.18	<0.0001
45–59	3338 (23.08)	47 (20.50)			2346 (30.64)	73 (22.16)		
60–74	4884 (10.45)	219 (30.39)			4492 (17.77)	422 (36.83)		
≥75	987 (5.11)	150 (40.21)			963 (9.53)	181 (38.05)		
Education								
Primary school and lower	2793 (9.38)	173 (34.83)	80.34	<0.0001	2564 (14.70)	307 (37.62)	76.88	<0.0001
Junior and senior middle school	6416 (48.61)	216 (55.85)			4961 (55.64)	322 (53.51)		
College middle school and higher	1549 (42.01)	31 (9.33)			864 (29.67)	49 (8.87)		
Occupation								
Employment	4798 (68.93)	144 (33.76)	42.17	<0.0001	3125 (61.99)	221 (29.42)	45.70	<0.0001
Unemployment	5960 (31.07)	276 (66.24)			5264 (38.01)	457 (70.59)		
Marriage								
Living alone	1421 (27.75)	104 (28.09)	0.01	0.9406	1090 (19.18)	142 (19.42)	0.00	0.9473
Married	9337 (72.25)	316 (71.91)			7299 (80.82)	536 (80.58)		
Urbanization								
Rural	2782 (14.13)	120 (16.85)	7.55	0.0229	2031 (13.46)	193 (15.35)	1.52	0.4670
Urban–rural	2729 (27.70)	87 (10.77)			2108 (23.37)	165 (18.04)		
Urban	5247 (58.17)	213 (72.37)			4250 (63.17)	320 (66.61)		
Current smoking	1832 (16.32)	58 (13.54)	0.82	0.3662	1309 (19.53)	83 (13.51)	3.69	0.0548
Alcohol drinking	2931 (31.12)	119 (27.26)	0.67	0.4139	2155 (29.62)	182 (34.95)	1.65	0.1986
Tea drinking	4307 (45.04)	159 (41.83)	0.47	0.4945	3343 (44.47)	236 (38.97)	2.14	0.1437
SD (h/d)	7.57 (0.03)	7.15 (0.18)	−2.33	0.0232	7.43 (0.04)	7.34 (0.14)	−0.61	0.5471
Physical activity level								
Low	2309 (25.51)	87 (20.12)	2.17	0.3383	1864 (27.60)	137 (23.12)	6.33	0.0421
Medium	4143 (42.05)	162 (47.46)			3272 (39.45)	290 (48.03)		
High	4306 (32.44)	171 (32.42)			3253 (32.95)	251 (28.85)		
Family history	1508 (13.44)	107 (26.62)	25.60	<0.0001	1359 (14.76)	197 (24.40)	21.29	<0.0001
TC (mmol/L)	4.73 (0.06)	4.86 (0.12)	1.10	0.2747	4.97 (0.03)	4.87 (0.09)	−1.24	0.2215
LDL-C (mmol/L)	2.95 (0.04)	2.98 (0.09)	0.27	0.7869	3.04 (0.03)	2.94 (0.07)	−1.52	0.1339
BMI (kg/m^2)	22.80 (0.09)	22.83 (0.33)	0.08	0.9357	26.06 (0.18)	25.34 (0.19)	−3.04	0.0036
Dietary pattern								
Fruit juice and pork pattern	2021 (30.50)	64 (18.27)	7.82	0.0499	1485 (25.12)	129 (20.08)	5.02	0.1702
Tuber & high-protein pattern	2406 (23.47)	93 (28.34)			1880 (24.93)	136 (28.12)		
Dairy & egg and fruit pattern	2950 (26.45)	123 (26.41)			2290 (26.42)	203 (30.76)		
Grain & vegetable pattern	3381 (19.58)	140 (26.99)			2734 (23.53)	210 (21.04)		

Abbreviations: SD, sleep duration; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; BMI, body mass index; Mets, metabolic syndrome.

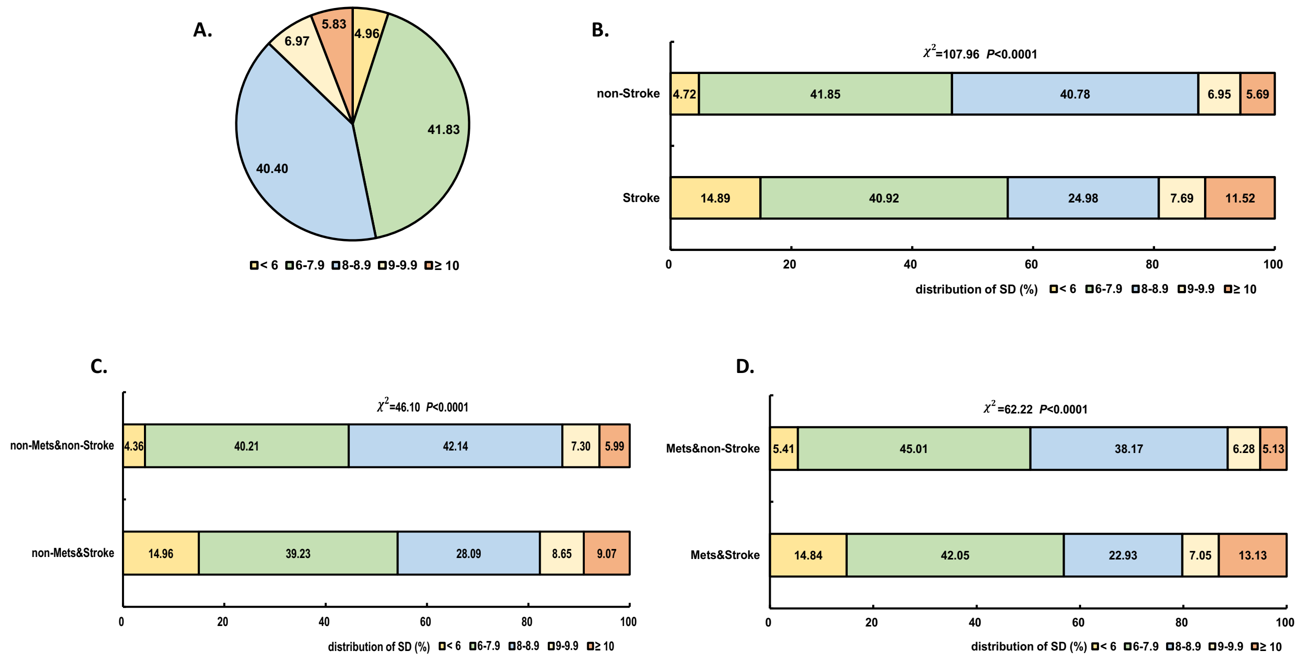

Figure 2 The distribution of SD among the study population; (**A**) for the total participants, (**B**) for the participants stratified by stroke, (**C**) for the non-Mets group stratified by stroke, (**D**) for the Mets group stratified by stroke.
Abbreviations: SD, sleep duration; Mets, metabolic syndrome.

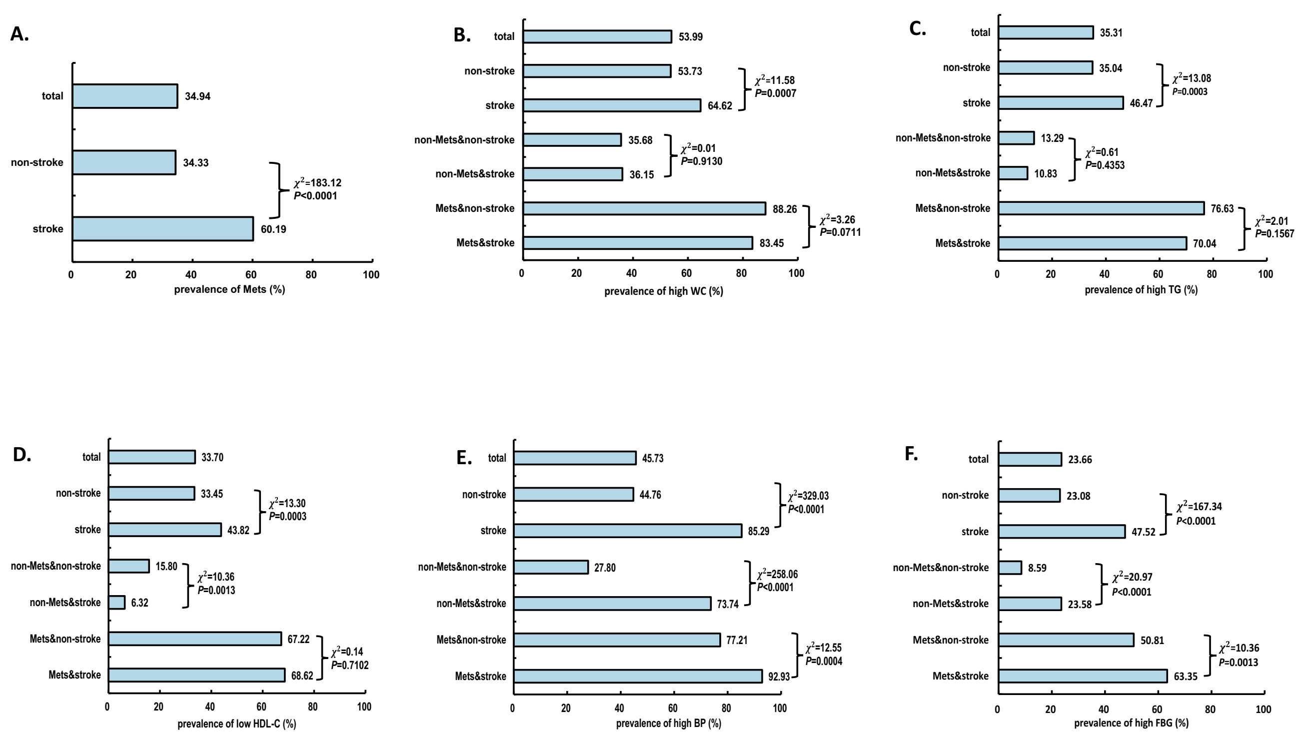

Figure 3 The distribution of Mets and its components among the study population. (**A**) Mets, (**B**) high WC, (**C**) high TG, (**D**) low HDL-C, (**E**) high BP, and (**F**) high FBG.
Abbreviations: WC, waist circumference; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; BP, blood pressure; FBG, fasting blood glucose; Mets, metabolic syndrome.

relationship was not observed between SD≥10 h/d and stroke; besides, in the Mets group, SD<6 h/d (OR=1.80, 95% CI:1.17–2.76) or ≥10 h/d (OR=1.97, 95% CI:1.00–3.88) both had a positive significantly association with stoke.

RCS analysis showed significant association of SD with stroke in the total population, the non-Mets group, and the Mets group (*P*-overall association <0.0001, *P*-nonlinearity association <0.0001). Among the above three groups, the

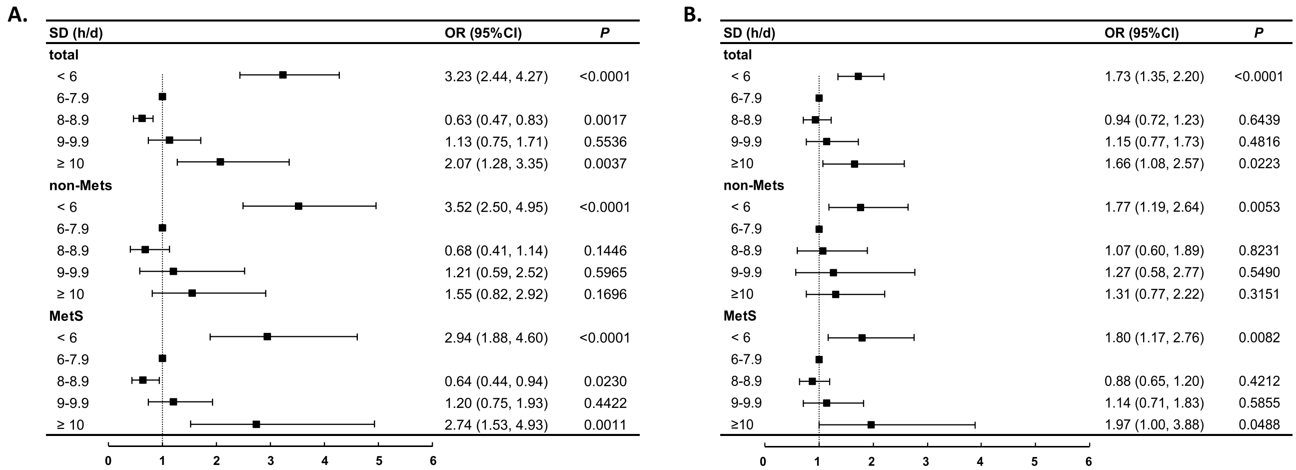

Figure 4 Association of SD with stroke in the study population. (**A**) crude model. (**B**) adjusted with gender, age, education, occupation, marriage, urbanization, smoking, alcohol drinking, tea drinking, physical activity level, family history, TC, LDL-C, BMI, dietary pattern.

Abbreviations: SD, sleep duration; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; BMI, body mass index; Mets, metabolic syndrome; OR, odds ratio; CI, confidence interval.

dose–response relationship between SD and stroke followed a U shape, indicating that when SD was relatively low, there was a significantly negative association between SD and stroke; in addition, when SD exceeded 7 h/d, the risk of stroke increased significantly (Figure 5).

The Association of SD with Stroke in Mets Components

Table 3 shows the associations of SD with stroke in the study population in Mets components. After adjustment for covariates, there were significantly positive correlations of SD <6 h/d with stroke in the groups of high WC (OR=2.24, 95% CI: 1.40–3.58), high TG (OR=2.60, 95% CI: 1.86–3.62), low HDL-C (OR=1.98, 95% CI: 1.23–3.19), high BP

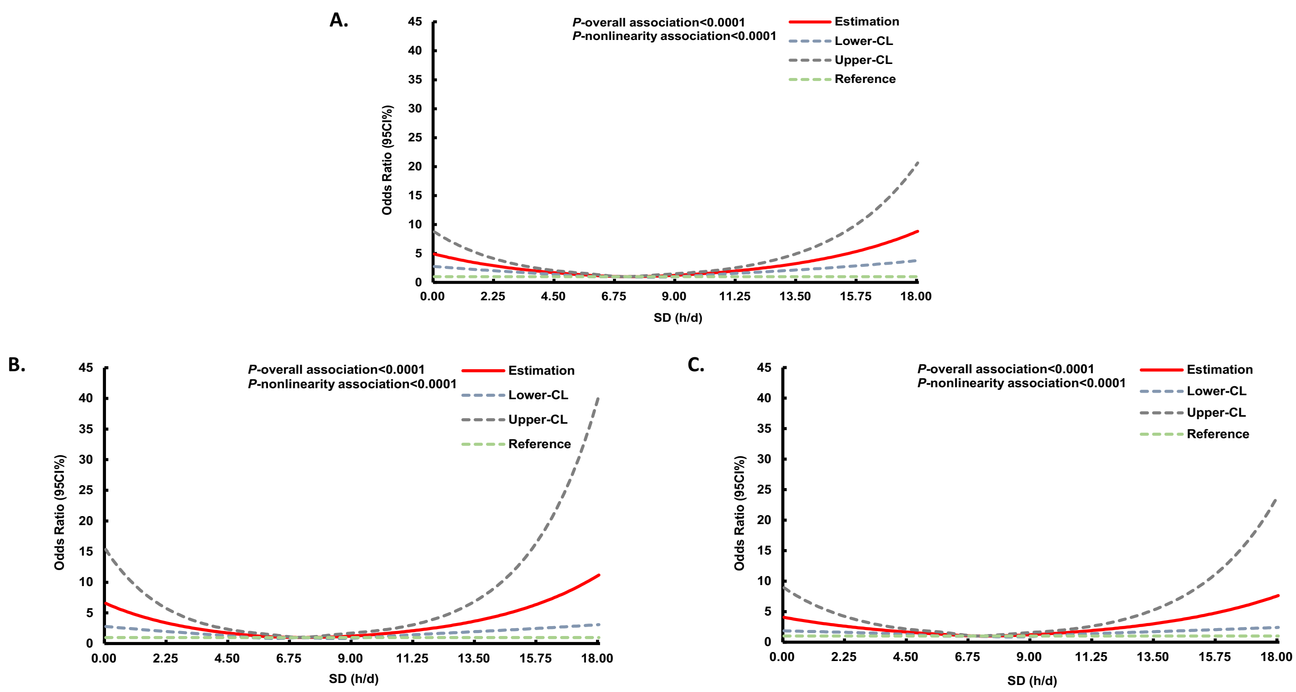

Figure 5 Multivariable-adjusted ORs and 95CI% for risk of stroke according to SD with 5 knot restricted cubic spline (the reference SD=7 h/d). (**A**) the total study population, (**B**) the non-Mets group, (**C**) the Mets group; Models were adjusted with gender, age, education, occupation, marriage, urbanization, smoking, alcohol drinking, tea drinking, physical activity level, family history, TC, LDL-C, BMI, dietary pattern.

Abbreviations: SD, sleep duration; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; BMI, body mass index; Mets, metabolic syndrome; OR, odds ratio; CI, confidence interval.

Table 3 Association of SD with Stroke in the Study Population in Mets Components

SD (h/d)	Model 1		Model 2	
	OR (95% CI)	*P*	OR (95% CI)	*P*
High WC				
<6	3.87 (2.41, 6.20)	<0.0001	2.24 (1.40, 3.58)	0.0011
6–7.9	Reference	Reference	Reference	Reference
8–8.9	0.66 (0.46, 0.95)	0.0269	0.97 (0.67, 1.42)	0.8863
9–9.9	1.38 (0.78, 2.45)	0.2694	1.48 (0.85, 2.59)	0.1655
≥10	2.81 (1.70, 4.64)	0.0001	1.96 (1.09, 3.52)	0.0250
High TG				
<6	4.08 (2.71, 6.16)	<0.0001	2.60 (1.86, 3.62)	<0.0001
6–7.9	Reference	Reference	Reference	Reference
8–8.9	0.72 (0.48, 1.08)	0.1081	0.96 (0.68, 1.34)	0.7895
9–9.9	1.24 (0.62, 2.49)	0.5339	1.16 (0.59, 2.29)	0.6671
≥10	2.95 (1.44, 6.08)	0.0040	2.28 (1.02, 5.08)	0.0444
Low HDL-C				
<6	3.41 (2.11, 5.52)	<0.0001	1.98 (1.23, 3.19)	0.0054
6–7.9	Reference	Reference	Reference	Reference
8–8.9	0.56 (0.40, 0.80)	0.0015	0.81 (0.58, 1.13)	0.2075
9–9.9	0.96 (0.51, 1.83)	0.9061	0.93 (0.54, 1.61)	0.7990
≥10	1.47 (0.78, 2.78)	0.2261	1.04 (0.59, 1.81)	0.8999
High BP				
<6	2.51 (1.74, 3.63)	<0.0001	1.60 (1.12, 2.30)	0.0114
6–7.9	Reference	Reference	Reference	Reference
8–8.9	0.72 (0.50, 1.05)	0.0859	0.96 (0.68, 1.34)	0.7958
9–9.9	1.38 (0.85, 2.24)	0.1874	1.25 (0.77, 2.03)	0.3674
≥10	2.68 (1.79, 4.01)	<0.0001	1.95 (1.20, 3.17)	0.0081
High FBG				
<6	2.56 (1.68, 3.90)	<0.0001	1.60 (1.10, 2.32)	0.0138
6–7.9	Reference	Reference	Reference	Reference
8–8.9	0.66 (0.43, 1.02)	0.0581	0.79 (0.52, 1.20)	0.2531
9–9.9	1.46 (0.80, 2.66)	0.2110	1.32 (0.70, 2.47)	0.3831
≥10	3.08 (1.71, 5.55)	0.0003	2.58 (1.30, 5.10)	0.0074

Notes: model 1, crude model; model 2, adjusted with gender, age, education, occupation, marriage, urbanization, smoking, alcohol drinking, tea drinking, physical activity level, family history, TC, LDL-C, BMI, dietary pattern.

Abbreviations: SD, sleep duration; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; BMI, body mass index; WC, waist circumference; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; BP, blood pressure; FBG, fasting blood glucose; OR, odds ratio; CI, confidence interval.

(OR=1.60, 95% CI: 1.12–2.30), and high FBG (OR=1.60, 95% CI: 1.10, 2.32); meanwhile, SD ≥10 h/d significantly increased the risk of stroke of participants with high WC (OR=1.96, 95% CI: 1.09–3.52), high TG (OR=2.28, 95% CI: 1.02–5.08), high BP (OR=1.95, 95% CI: 1.20–3.17), and high FBG (OR=2.58, 95% CI: 1.30–5.10).

Discussion

In this study, we found that SD had a significant association with stroke, and the effects were different among Mets and its components. In the non-Mets group, only short SD (<6 h/d) was significantly positively linked to stroke; while, in the Mets group, both short SD (<6 h/d) and long SD (≥10 h/d) significantly increased stroke risks. The metabolic level of the participants may play an important role in the relationship between SD and stroke. Furthermore, a U shape of the association between SD and stroke was observed in those with or without Mets. In addition, the effects of SD on stroke were different in

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Mets components, which were more pronounced in those with high WC and high TG for short SD (<6 h/d), more evident in those with high TG and high FBG for long SD (≥10 h/d).

The associations between SD and stroke in the participants with or without Mets were inconclusive. The present study result was partially consistent with the previous studies.[4,17,19] For example, one retrospective study of 8968 Chinese participants had reported that long SD (>9 h/d) significantly increased the risk of stroke in individuals with Mets, while no significant association was observed between short SD (<6 h/d) and stroke; furthermore, SD had no significant association with stroke in the study population without Mets.[17] In addition, the present study showed a U-shaped association between SD and stroke, which indicated that individuals with short or long SD had a significant higher stroke risk. The result was also partially consistent with the previous studies. Some studies also reported a U-shaped relationship between SD and stroke,[5,8,9] while other studies reported a J-shaped association.[4,10,12,13] Our finding suggests that choosing optimal SD can contribute to decreasing the possibility of having stroke. The discrepancy in results may be partially explained by the differences of study samples, SD classifications, Mets assessments and so on.

The present study suggested associations between SD and stroke from a cross-section study, which only indicated correlativity rather than causality between exposure and outcome. In the present study, short SD (<6 h/d) was significantly positively associated with stroke regardless of the status of Mets, while long SD (≥10 h/d) only showed a significantly positively correlation with stroke in the Mets group; and these conclusions did not totally support the results from some Mendelian randomization (MR) analyses,[25–28] which leverage genetic variants as instrument variables to provide unconfounded estimates and causal inferences between exposure and outcome.[28] For instance, a previous study found suggestive evidence that per doubling of genetic liability for short SD (≤6 h/d) was associated with a modest increase in risk of large artery stroke (LAS) and little evidence for causal effects of long SD (≥9 h/d) on any ischemic stroke subtype was observed.[26] Additionally, another recent MR study in UK Biobank showed no evidence on the adverse causal effects of having a genetically predicted short SD (≤6 h/d) or long SD (≥9 h/d) on ischemic stroke.[28] However, the aforementioned MR studies mostly focused on European ancestry, and scarcely paid attention on Chinese residents; therefore, more experimental studies or MR studies are needed in future to identify the causal effects of SD on stroke in Chinese.

The underlying biologic mechanisms between SD and stroke are not well understood, which might be partially explained as follows: firstly, inflammation may be one possible potential biological pathway, as one previous study showed that sleep deprivation could cause endothelial dysfunction, increased markers of vascular/systemic oxidative stress, and inflammation;[29] also, other related studies demonstrated that long SD was also significantly associated with increased biomarkers of inflammatory such as C-reactive protein (CRP) and interleukin-10 (IL-10).[30,31] Secondly, the unreasonable SD could lead to metabolic level changes,[32,33] which may be accounted for the development of stroke. Several studies showed that short SD might increase plasma cortisol levels by overactivation of the sympathetic activity and the hypothalamic-pituitary-adrenal (HPA) axis,[17,34,35] which could increase blood pressure, potentially result in hypertension. In addition, the previous research showed that short SD was significantly with reduced leptin and elevated ghrelin that may lead to increased appetite,[36] increased caloric intake,[37,38] overeating unhealthy foods,[39] and reduced physical activity due to fatigue,[40] which possibly result in obesity. Short SD was also associated with higher levels of endocannabinoids[41] and reduced insulin sensitivity[42,43] that suggesting ß-cell dysfunction and thus, diabetes. Besides, short SD was also significantly associated with dyslipidemia,[44,45] which because short SD could increase consumption of high saturated fat foods by reducing leptin and elevating ghrelin and increase lipolysis by elevated catecholamine secretion due to the overactivation of the sympathetic activity.[36,45,46] However, the mechanism of long SD on stroke has been less investigated. Some studies showed that long SD was often accompanied by less physical activity and more sedentary activity,[47] which are significantly related with stroke;[48] in addition, depression caused by long SD may result in stroke.[49,50] Future studies are required to explore the potential mechanism of long SD on stroke. These above factors had been confirmed by many studies that they could promote the occurrence and development of stroke.[51–54] Our study also verified the related results that the magnitude of the association between SD and stroke was significantly higher in the participants with Mets compared to those without Mets.

The present study had several strengths. First of all, the present study explored the relationship between SD and stroke among the participants with Mets or its components, which provided new evidence for this issue considered rarely in the previous studies. Moreover, as a result of scientific sampling methods, the participants from SCDRFS-2017 is the representative of the Shanghai residents; in addition, quality control schemes/networks and trained teams of professional investigators could make our dataset true and reliable. Finally, a wide range of factors that may act as confounders or modifiers were taken into account in investigating the relationship between SD and stroke.

However, some limitations also should be acknowledged. Firstly, due to the cross-sectional nature of the present study, the causal relationship between SD and stroke cannot be clarified, thus further epidemiological studies are needed to provide conclusive evidences. Secondly, SD was determined by the self-report questionnaire of individuals rather than polysomnography, which is a golden standard for objective assessment of sleep quantity. Although self-report may lead to perceptual bias, it is still a convenient and most frequently used method to assess SD in a large population.[4,55,56] Thirdly, we collected information on total SD per day instead of distinguishing between SD at night and midday napping, which could limit further investigation into the joint and separate effects of SD on stroke. Finally, stroke subtypes consisting of ischemic stroke and hemorrhagic stroke had different pathophysiological characteristics,[57] while many missing values of stroke subtypes included in our data render us unable to explore whether SD had a different relationship with stroke subtypes.

Conclusion

Our study revealed that SD had a significant association with stroke, and the effects were different among Mets and its components. In the non-Mets group, only short SD (<6 h/d) had a significant relationship with stroke; while in the Mets group, both short SD (<6 h/d) and long SD (≥10 h/d) were significantly associated with stroke. Moreover, the effects of short SD (<6 h/d) and long SD (≥10 h/d) on stroke were more evident in those with high TG among the components of Mets. Our findings highlight that optimal SD plays an important role in stroke prevention and promote that more precise interventions may be needed to prevent stroke among the population with different metabolic levels.

Abbreviations

CNS, central nervous system; GBD, Global Burden of Disease; DALYs, disability-adjusted life-years; SD, sleep duration; CHNS, China Health and Nutrition Survey; Mets, metabolic syndrome; BP, blood pressure; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; FBG, fasting glucose; SCDRFS, Shanghai Chronic Disease and Risk Factors Surveillance; WHO, World Health Organization; CCDRFS, China Chronic Disease and Risk Factors Surveillance; SCDC, Shanghai Municipal Center for Disease Control and Prevention; NCDs, chronic non-communicable diseases; WC, waist circumference; IDF, International Diabetes Federation; NHLBI, National Heart, Lung, and Blood Institute; GPAQ, Global Physical Activity Questionnaire; FFQ, Food Frequency Questionnaire; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; BMI, body mass index; CRP, C-reactive protein; IL-10, interleukin-10; HPA, hypothalamic-pituitary-adrenal.

Data Sharing Statement

The data used in this study are available on request from the corresponding authors. The data are not publicly available due to availability restrictions reported in the informed consent signed by all participants.

Ethics Approval and Informed Consent

All participants signed the consent forms after they were informed of the purpose and demands of the survey. The Ethics Committee of Shanghai Municipal Center for Disease Control and Prevention approved the study protocol (No.2016-10).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; have agreed on the journal to which the article has been submitted; reviewed and agreed on all versions of the article before submission, during revision, the final version accepted for publication, and any significant changes introduced at the proofing stage; and agree to take responsibility and be accountable for the contents of the article.

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Disclosure

The authors declare no conflicts of interest in this work.

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