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The mediating effects of depression in sedentary behavior and the metabolic syndrome with its components

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Abstract

Background Previous studies have shown a positive association between sedentary behavior (SB) and metabolic syndrome (MetS), but no studies have assessed the mediating effect of depressive symptoms in this process.

Methods Participants from the 2007–2018 National Health and Nutrition Examination Survey (NHANES) were included. Multiple logistic regression analyses and restricted cubic splines (RCSs) were adopted to assess the correlations among SB duration, depressed mood and MetS. A mediation effect model was constructed to analyze whether there was a mediating effect of depressed mood on the relationship between SB duration and MetS.

Results This study included 15,944 adults (7,268 patients with MetS in total). We identified high SB duration as an independent risk factor for MetS in a regression model adjusted for relevant confounders (odds ratio (OR) = 1.29, 95% CI [1.08, 1.53]). RCS analysis revealed a nonlinear relationship between SB duration and MetS. The mediation effect analysis revealed that depressive symptoms accounted for 6.70% of the mediation effect between SB duration and MetS. Depressive symptoms were also partially mediated in the analyses with MetS subcomponents.

Conclusion SB is closely associated with MetS, and this association is not only caused by SB itself but also partially mediated by depressive symptoms.

Keywords Metabolic syndrome, Sedentary behavior, Depressive symptoms, Mediation effect, NHANES

Introduction

Previous epidemiological studies have shown that a lack of physical activity increases the risk of many chronic noncommunicable diseases, including coronary heart disease (CHD) and type 2 diabetes [1]. The term "sedentary" can be defined as all behaviors involving sitting or lying down with low energy expenditure [2]. Research has revealed a strong correlation between sedentary behavior (SB) and cardiovascular health status [3]. In an analysis of the association between SB and metabolic syndrome (MetS), researchers reported that when the daily SB duration exceeds 8 h, the prevalence of MetS in patients is greater [4]. In addition, a recent meta-analysis revealed

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that SB is associated with an increased risk of all-cause mortality in patients with MetS, which includes abdominal obesity, hyperglycemia, hypertension, and dyslipidemia [5].

Depression is one of the most common mental illnesses in adults, severely limiting social functioning and reducing quality of life, and this disorder will likely be the leading cause of the global burden of disease in 2030 [6]. Depression has increased by 49.86% globally over the past 30 years [7]. Of great concern is the fact that sedentary people have a greatly increased risk of depression [8]. A meta-analysis revealed that people with a longer SB duration had a 1.28-fold greater risk of depression than did those who spent less time sitting in front of a screen [9].

MetS is defined as the presence of at least three metabolic disorders, including hypertension, hyperglycemia, abdominal obesity, and dyslipidemia [10]. Among American adults aged 18 and above, the prevalence of MetS has increased by more than 35% [11]. MetS is a response by the body to overnutrition, negative lifestyle, and the resulting obesity [12]. The prevalence of MetS is very high (43.6%) in patients with depression [13]. These findings seem to indicate that patients with depression are at a much greater risk of developing MetS. However, we still do not know whether there is a mediating effect of depressed mood between SB and MetS.

In this study, we aimed to clarify the mediating role of depressive mood in sedentary behavior and MetS by utilizing information from a sample of adults from the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2018.

Methods and materials

Study population

A total of 6 cycles of participants in the NHANES from 2007 to 2018 (total of 59,842) were included in this study. The NHANES is a nationally representative survey of the U.S. population conducted by the National Center for Health Statistics (NCHS). The NHANES study protocol was approved by the NCHS Research Ethics Review Board. Detailed data are available at https://www.cdc.gov/nchs/nhanes/. The exclusion criteria for this study are shown in Supplementary Figure S1. The final sample consisted of 15,944 participants.

Exposure factor, mediating variable and outcome variables

The exposure factor and mediating variable for this study were obtained from the participants' questionnaire. One of the questions about SB was asked in the following way: Excluding time spent sleeping, how much time do you usually spend sitting? (Including time spent sitting in an office, riding in a car or bus, reading, playing cards, watching TV, or using a computer.) With respect to depressive symptom screening, the investigators questioned the participants using the Patient Health Questionnaire-9 (PHQ-9). On the basis of a previous study [14], PHQ-9 scores ≥ 10 indicated depression. MetS was defined as the presence of three or more of the following metabolic disorders: hypertension, low high-density lipoprotein cholesterol (HDL-C) level, high triglyceride (TG) level, hyperglycemia, and abdominal obesity [15]. Each metabolic disease was defined as follows [16]: (1) hypertension: two consecutive measurements of systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg at rest; previous diagnosis of hypertension; or currently taking an antihypertensive medication; (2) low HDL-C level: males, HDL-C < 1 mmol/L; females, HDL-C < 1.3 mmol/L; or currently taking drugs for low HDL-C; (3) high TG level: TG ≥ 1.7 mmol/L or currently taking TG-lowering medications; (4) hyperglycemia: fasting plasma glucose (FPG) ≥ 100 mg/dL; glycosylated hemoglobin (HbA1c) ≥ 6%; or currently taking hypoglycemic drugs; and (5) abdominal obesity: males, waist circumference ≥ 102 cm; and females, waist circumference ≥ 88 cm. Patients were categorized into MetS and non-MetS groups on the basis of MetS status.

Covariates and definitions

Baseline population information, including age, sex, race, education level, marital status, smoking history, alcohol consumption history, caloric intake, ratio of family income to poverty (PIR), physical activity, and difficulty sleeping, was included in this study. Laboratory serologic markers included alanine aminotransferase (ALT) and alanine transaminase (AST) for liver function and serum creatinine (SCr) for renal function. Participants with self-reported angina, coronary heart disease, and heart attack were considered to have cardiovascular disease (CVD) [17]. Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [18].

Among the race classifications were Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other race. Education level was classified as follows: below high school, high school, and above high school. Marital status was defined as follows: participants who answered married or living with a partner were defined as "married/living with partner", those who answered widowed, divorced, or separated were defined as "widowed/divorced/separated", and those who answered never married were defined as "never". For smoking history [19], participants who had not smoked more than 100 cigarettes in their lifetime were defined as "Never", those who had smoked more than 100 cigarettes in their lifetime but were no longer current smokers were defined as "Smoking former", and those who

were current smokers were defined as "Smoking now". For alcohol consumption history [19], individuals who reported drinking at least 12 alcoholic beverages in a year were defined as an alcohol user. Calorie intake was defined as follows: an average daily intake of less than 2,000 calories for men and less than 1,600 calories for women was defined as a low-calorie diet; an average daily intake of more than 2,000 and less than 3,000 calories for men and more than 1,600 and less than 2,400 calories for women was defined as a moderate-calorie diet; and an average daily intake of more than 3,000 calories for men and more than 2,400 calories for women was defined as a high-calorie diet. PIR was classified as follows: low income, ≤ 1.3; middle income, between 1.3, 3.5; and high income, > 3.5. In accordance with the Physical Activity Guidelines for Americans [20], regarding physical activity, the number of days and minutes of exercise in a week were extracted, the total time was calculated, and 1 min of strenuous exercise was converted to 2 min of moderate exercise; >150 min of moderate physical activity per week constituted the active group and < 150 min constituted the inactive group.

Statistical analysis

We performed statistical analyses using NHANES complex sampling weights in accordance with the Centers for Disease Control and Prevention (CDC) guidelines [21]. Given the complex sampling nature of the NHANES database, we selected the "WTMEC2YR" weight data. Since we selected six cycles of the population from 2007 to 2018, we divided the "WTMEC2YR" weights by six to calculate the weighting variables used in this paper. The study population was divided into a MetS group (7268) and a non-MetS group (8676) on the basis of whether the included individuals had MetS. Categorical variables are expressed as the number of cases and weighted percentages and standard error (SE), which were compared between groups using the chi-square test. We used weighted mean and SE for continuous numerical variables and t tests for between-group comparisons. In addition, the percentage of each component of MetS and the comparison of SB duration and PHQ-9 score for each component were analyzed. The association between the PHQ-9 score and SB duration was analyzed using weighted generalized linear regression, with the PHQ-9 score as the outcome variable. The association between depression and SB duration was analyzed using weighted logistic regression with depression as the outcome variable. Directed acyclic graphs (DAGs) (Fig. 1) were constructed to analyze the confounders and mediating variables between the exposure factor and outcome variables. SB duration quartiles were used to divide the included members into four groups (Group Q1, Group Q2, Group Q3, and Group Q4), a weighted multivariate logistic regression model was constructed to analyze the correlation between ST and MetS, and a trend test was performed. To prevent multicollinearity, for continuous variables, multicollinearity tests were performed to exclude variables with a variance inflation factor (VIF) > 5. The selection scheme for potential confounders was as follows: (1) refer to previous relevant references [4, 22]; (2) for variables with a change in outcome estimates > 10% or a significance level, a P value < 0.1 was used in the univariate logistic regression analysis [23]. Therefore, the correlation between MetS and the PHQ-9 score was analyzed using the same adjustment strategy and included confounders (age, sex, race, education level, marital status, smoking history, alcohol consumption history, physical activity, caloric intake, PIR, trouble sleeping, CVD, CKD, ALT, and AST), with the Q1 group serving as the reference group. The correlations between MetS and the PHQ-9 score and depression were analyzed using the same adjustment strategy. The nonlinear correlations between ST, PHQ-9, and MetS were analyzed using restricted cubic spline (RCS) curves (the adjustment strategy was consistent with the regression model). In the process of constructing the RCS model, we choose four RCS knot numbers with knot locations of P5, P35, P65, and P95. For the selection of reference points, we referred to previous literature [4, 24]: 8 h of sedentary behavior and a PHQ-9 score of 10 were selected as reference points. Considering the effects of age, sex, and physical activity, we performed subgroup analyses with interaction tests. A mediated effects model was constructed with SB duration as the exposure factor, MetS as the outcome variable, and the PHQ-9 score as the mediating variable. In addition, we analyzed the mediating effect between SB duration and MetS when depression, a binary categorical variable, was used as a mediating variable. Statistical analysis was performed using R Studio (version R4.2.3) and EmpowerStats (version 4.1). A two-sided significance level less than 0.05 was considered statistically significant.

Results

Comparison of baseline information

This study included a total of 15,944 participants, including 7,268 MetS participants and 8,676 non-MetS participants. Among the participants, 57.10% had abdominal obesity, and 32.8% had hyperglycemia (Fig. 2.a). Among the MetS participants, 43.74% had three metabolic abnormalities, 37.27% had four metabolic abnormalities, and 18.99% had five metabolic abnormalities (Fig. 2.b). Compared with non-MetS patients, MetS patients were older and had a greater percentage of people with a high BMI, married people, poorer families, people with trouble sleeping, and people with CVD and CKD; individuals with a higher education, nonsmokers, heavy

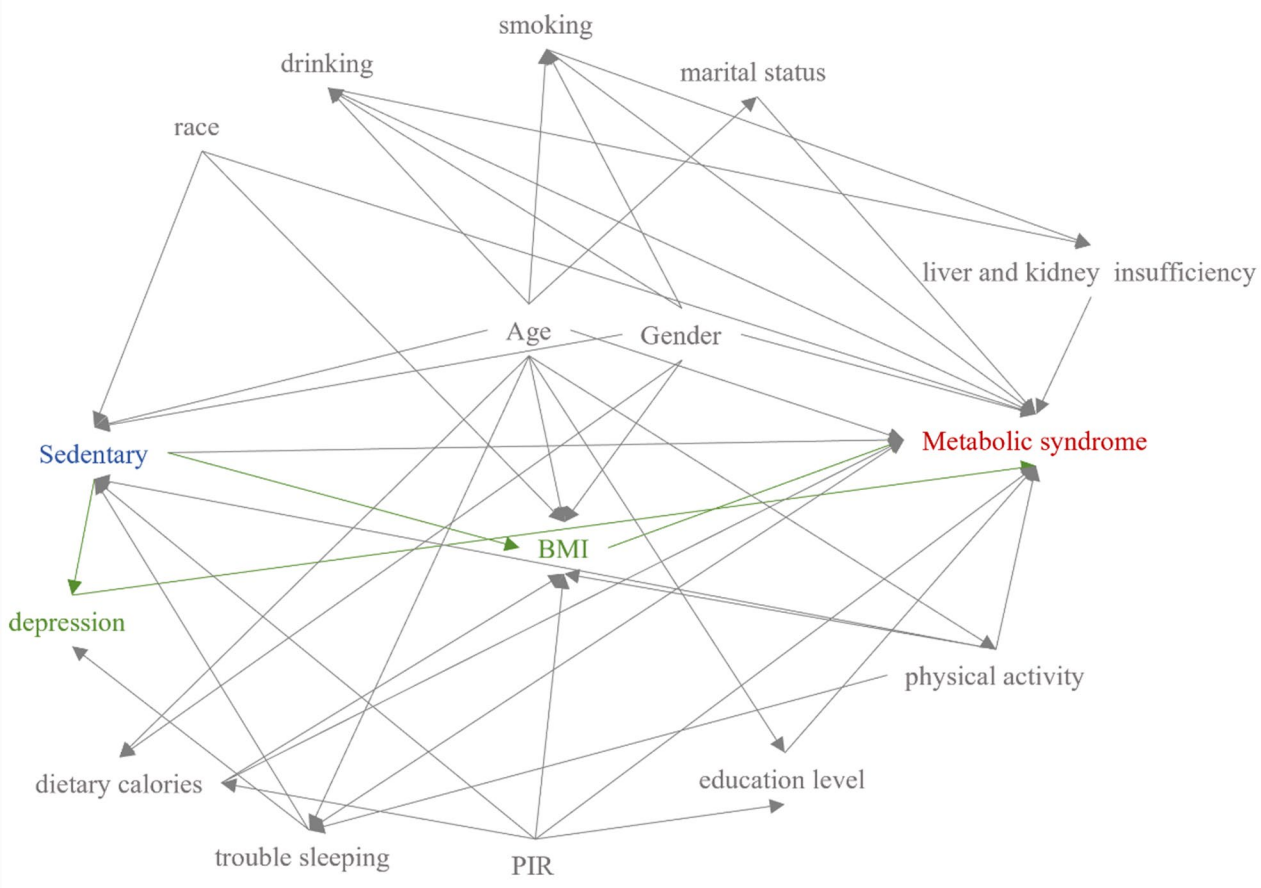

Fig. 1 Directed acyclic graph. Blue text: exposure factor, green text: mediating variable, red text: outcome variable. BMI: ratio of weight to height squared, PIR: ratio of family income to poverty

drinkers, and individuals who consumed high-calorie diets accounted for a lower percentage of the population and had a shorter duration of physical activity. Additionally, MetS patients had lower albumin levels, higher ALT, AST, Scr, and FPG levels, higher PHQ-9 scores, and a longer SB duration (Table 1).

The differences in SB duration and PHQ-9 score were compared among the MetS subcomponents. The SB duration was longer for individuals with low HDL-C levels and abdominal obesity than in individuals in the reference group; there was no statistically significant difference with regard to SB duration and other MetS subcomponents (Fig. 2.c). For each MetS subcomponent, the PHQ-9 score was significantly greater than that of the reference group (Fig. 2.d).

Correlations among SB duration, PHQ-9 score and MetS incidence and its subcomponents

Logistic regression models were constructed using the Q1 group of SB duration as the reference group. In the unadjusted model, SB duration was associated with MetS (Q2 vs. Q1: OR = 1.20 [1.06, 1.35]; Q3 vs. Q1: OR = 1.30 [1.14, 1.49]; Q4 vs. Q1: OR = 1.27 [1.09, 1.47]), and in the fully adjusted regression model, we found that Q4 group demonstrated 1.29 times the odds of having metabolic syndrome than the reference (Table 2). We found an increased risk of MetS in depressed patients (OR = 1.34 [1.13, 1.58]) when depression was included as an exposure factor in the regression model (Table 3).

Both SB duration (OR = 1.02 [1.00, 1.04]) and the PHQ-9 score (OR = 1.03 [1.02, 1.04]) were independent risk factors for MetS after incorporating SB duration and the PHQ-9 score as continuous numerical variables in a weighted regression model under full adjustment (Tables 2 and 3). Additionally, we analyzed the relationships among SB duration, PHQ-9 score, and MetS subcomponents. We found that SB duration was strongly associated with low HDL-C and abdominal obesity ($P < 0.05$) and that PHQ-9 score was strongly associated with all MetS subcomponents ($P < 0.05$) (Supplementary Table S1 and Supplementary Table S2).

We subsequently constructed an RCS model to investigated the nonlinear relationships among SB duration, PHQ-9 score and MetS and its subcomponents. The results revealed that SB duration was linearly correlated with hyperglycemia and high TG level and nonlinearly

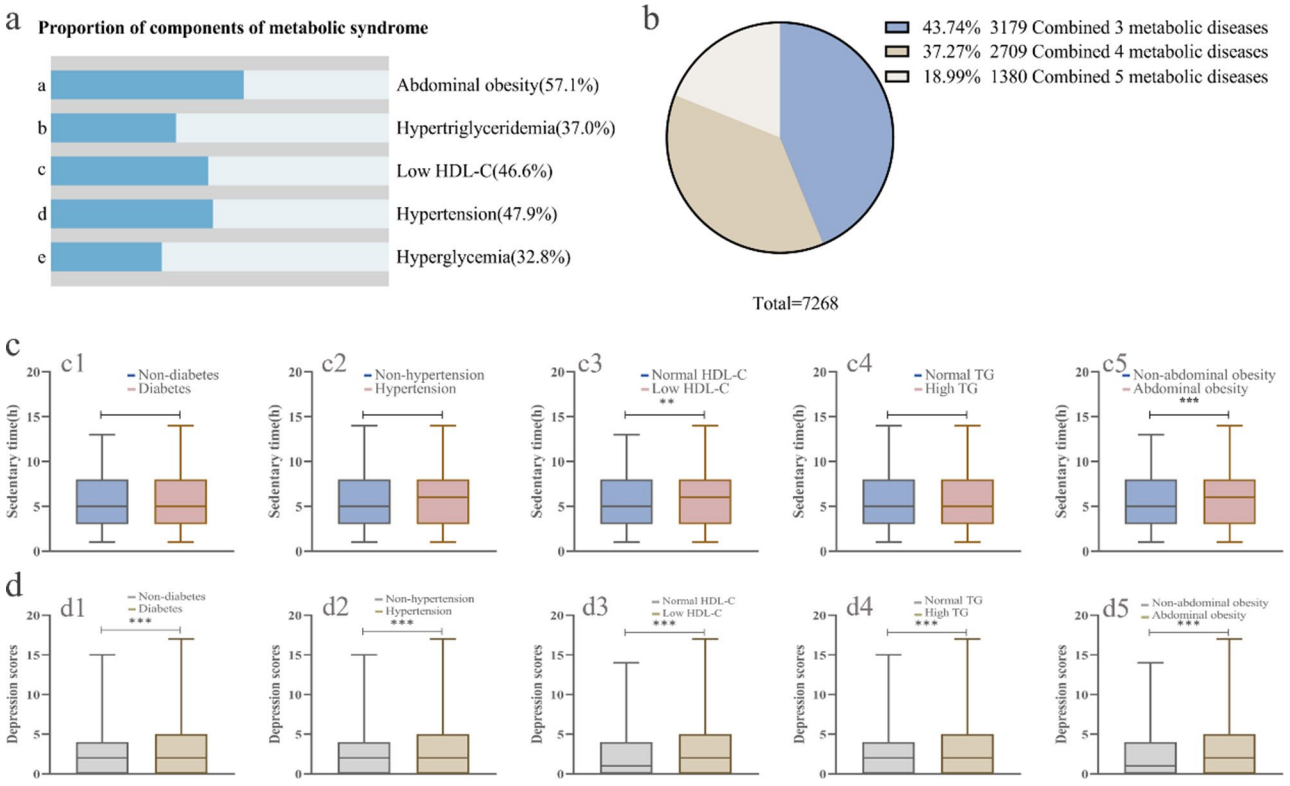

Fig. 2 Percentage of each component of metabolic syndrome and its relationship with sedentary behavior duration and Patient Health Questionnaire-9 score. Figure 2.**a**: Percentage of MetS components, Fig. 2.**b**: Percentage of MetS patients with different number of metabolic disorders combined, Fig. 2.**c**: Comparison of SB time of MetS subcomponents, Fig. 2.**d**: Comparison of PHQ-9 of MetS subcomponents. MetS: metabolic syndrome, SB: sedentary behavior, PHQ-9: Patient Health Questionnaire-9

correlated with MetS, hypertension, low HDL-C level, and abdominal obesity (Fig. 3). PHQ-9 score was linearly correlated with hyperglycemia, hypertension, and low HDL-C level and nonlinearly correlated with MetS, high TG level, and abdominal obesity (Fig. 4).

Subgroup analysis

We performed risk analyses of age, sex, and physical activity subgroups. We subsequently observed that SB duration was associated with MetS in all subgroups. As SB duration increased, the risk of developing MetS increased. Interestingly, we found that the OR for SB duration was greater in individuals younger than 60 years of age. Furthermore, we observed that for those who were physically active for less than 150 min a week, the risk of SB was higher, and an interaction test revealed that there was an interaction effect between SB duration and physical activity (Supplementary Figure S2). In the subgroup analysis of PHQ-9 score and MetS, we found that the PHQ-9 score was a risk factor for MetS in all subgroups except for males and individuals under 60 years of age, and an interaction test revealed that there was an interaction effect between the PHQ-9 score and physical activity (Supplementary Figure S3).

Analysis of mediation effects

A generalized linear regression model was constructed using the PHQ-9 score as the outcome variable, and the results indicated that for PHQ-9 score and SB duration, the linear regression coefficient β was 0.05 ($P<0.001$). A logistic regression model was constructed using depression as the outcome variable, and the OR was 1.04 ($P=0.004$). These results suggest that there is a correlation between depression and SB duration and that SB duration is an independent risk factor for depression (Supplementary Table S3).

We assessed the mediating role of depressed mood on the basis of the hypothesis that SB duration leads to MetS through depressed mood. We found a partial mediation effect of the PHQ-9 score between ST and MetS, hypertension, low HDL-C, high TG level, and abdominal obesity ($P<0.05$) (Supplementary Figure S4). Specifically, the PHQ-9 score mediated 6.7% of the effects between ST and MetS, with the PHQ-9 score having the highest mediating effects between ST and high TG (9.34%) and the lowest mediating effects between ST and abdominal obesity (3.47%) (Supplementary Table S4). In the mediation effect analysis with depression as the mediating variable, we found a partial mediation effect of depression

Table 1 Comparison of baseline data between metabolic syndrome and non- metabolic syndrome patients

Variable	Non-MetS (8676)	MetS (7268)	*P* value
Age (years)	41.29 (14.97)	52.97 (14.86)	< 0.001
Gender (%)			0.4379
Male	(4384) 49.60 (48.40, 50.80)	(3468) 48.76 (47.23, 50.28)	
Female	(4292) 50.40 (49.20, 51.60)	(3800) 51.24 (49.72, 52.77)	
BMI (kg/m^2)			< 0.001
< 25	(3814) 44.08 (42.40, 45.77)	(661) 8.27 (7.46, 9.16)	
≥ 25	(4862) 55.92 (54.23, 57.60)	(6607) 91.73 (90.84, 92.54)	
Race/Ethnicity (%)			0.001
Mexican American	(1240) 8.08 (6.64, 9.81)	(1222) 8.63 (6.86, 10.82)	
Other Hispanic	(875) 5.52 (4.52, 6.74)	(775) 4.98 (3.89, 6.35)	
Non-Hispanic White	(3789) 68.80 (65.56, 71.87)	(3184) 69.73 (66.16, 73.08)	
Non-Hispanic Black	(1752) 10.39 (8.94, 12.04)	(1513) 10.69 (9.06, 12.57)	
Other Race	(1020) 7.20 (6.36, 8.15)	(574) 5.97 (5.17, 6.88)	
Education (%)			< 0.001
Below high school	(1661) 13.01 (11.67, 14.49)	(1917) 17.65 (16.00, 19.44)	
High school	(1836) 19.78 (18.32, 21.33)	(1809) 25.46 (23.54, 27.49)	
Above high school	(5179) 67.21 (64.67, 69.65)	(3542) 56.88 (54.27, 59.46)	
Marital status (%)			< 0.001
Never married	(2240) 24.05 (22.09, 26.14)	(800) 10.84 (9.67, 12.14)	
Widowed/Divorced/Separated	(1316) 12.67 (11.73, 13.68)	(1932) 22.21 (20.70, 23.79)	
Married/Living with partner	(5120) 63.27 (61.27, 65.24)	(4536) 66.94 (64.95, 68.88)	
Smoking status (%)			< 0.001
Never	(5171) 59.91 (58.01, 61.78)	(3780) 51.44 (49.79, 53.09)	
Smoking former	(1648) 20.26 (18.79, 21.81)	(2077) 29.43 (27.73, 31.19)	
Smoking now	(1857) 19.84 (18.40, 21.35)	(1411) 19.13 (17.87, 20.45)	
Drinking status (%)			< 0.001
Rarely drinker	(1056) 9.71 (8.35, 11.26)	(1131) 12.10 (11.08, 13.20)	
Light drinker	(1002) 9.12 (8.37, 9.93)	(1108) 13.68 (12.40, 15.06)	
Excessive drinker	(6618) 81.17 (79.53, 82.71)	(5029) 74.22 (72.52, 75.84)	
Dietary calories (%)			0.001
Low-calorie diet	(3253) 34.58 (33.26, 35.93)	(3223) 38.26 (36.46, 40.09)	
Moderate-calorie diet	(3762) 45.81 (44.44, 47.18)	(2985) 44.31 (42.63, 46.01)	
High-calorie diet	(1661) 19.61 (18.46, 20.82)	(1060) 17.42 (15.97, 18.98)	
PIR(%)			< 0.001
≤ 1.3	(2614) 20.38 (18.58, 22.32)	(2479) 22.51 (20.54, 24.62)	
1.3–3.5	(3133) 34.14 (32.26, 36.07)	(2739) 36.67 (35.04, 38.34)	
> 3.5	(2929) 45.47 (42.72, 48.25)	(2050) 40.81 (38.16, 43.52)	
Physical exercise(%)			< 0.001
Inactive group	(2662) 27.10 (25.74, 28.50)	(3386) 42.75 (41.08, 44.44)	
Active group	(6014) 72.90 (71.50, 74.26)	(3882) 57.25 (55.56, 58.92)	
Trouble sleeping (%)			< 0.001
Yes	(1720) 21.81 (20.35, 23.35)	(2278) 33.26 (31.58, 34.98)	
No	(6956) 78.19 (76.65, 79.65)	(4990) 66.74 (65.02, 68.42)	
CVD (%)			< 0.001
Yes	(100) 0.93 (0.69, 1.25)	(466) 5.78 (5.08, 6.57)	
No	(8576) 99.07 (98.75, 99.31)	(6802) 94.22 (93.43, 94.92)	
CKD (%)			< 0.001
Yes	(2358) 25.97 (23.51, 28.60)	(2849) 35.73 (33.25, 38.29)	
No	(6318) 74.03 (71.40, 76.49)	(4419) 64.27 (61.71, 66.75)	
Depression(%)			< 0.001
Yes	(604) 6.02 (5.39, 6.71)	(792) 9.75 (8.87, 10.70)	
No	(8072) 93.98 (93.29, 94.61)	(6476) 90.25 (89.30, 91.13)	
Albumin(g/dL)	4.36 (0.312)	4.25(0.31)	< 0.001

Table 1 (continued)

Variable	Non-MetS (8676)	MetS (7268)	*P* value
ALT (U/L)	23.70 (16.34)	28.73(24.99)	< 0.001
AST (U/L)	24.82 (15.04)	27.21 (18.39)	< 0.001
SCr (mg/dL)	0.86 (0.23)	0.91 (0.41)	< 0.001
FPG (mg/dL)	89.48 (16.85)	112.26 (44.68)	< 0.001
TG (mg/dL)	110.08 (68.99)	216.03 (168.69)	< 0.001
TC (mg/dL)	192.13 (37.69)	199.07 (45.36)	< 0.001
HDL-C (mg/dL)	58.03 (16.00)	46.21 (14.28)	< 0.001
PHQ-9 score	2.69 (3.72)	3.42 (4.43)	< 0.001
SB duration (h)	6.21 (3.37)	6.41 (3.38)	0.015

All continuous numeric variables are expressed using weighted mean (SE) and categorical variables are quantified as numbers (weighted percentages)

BMI: ratio of weight to height squared, PIR: ratio of family income to poverty, CVD: cardiovascular disease, CKD: chronic kidney disease, ALT: alanine aminotransferase, AST: alanine transaminase, SCr: serum creatinine, FPG: fasting plasma glucose, TG: triglycerides, TC: total cholesterol, HDL-C: high density lipoprotein cholesterol, PHQ-9: Patient Health Questionnaire-9, SB: sedentary behavior

Table 2 Regression analysis between sedentary behavior duration and metabolic syndrome

Variable	Non-adjusted	Adjust I	Adjust II
SB duration (continuous variable)	1.02(1.00, 1.03) *	1.02(1.00, 1.04) *	1.03(1.01, 1.04) **
SB duration (quartile)			
Q1	ref	ref	ref
Q2	1.20(1.06, 1.35) **	1.08(0.95, 1.23)	1.16(1.01, 1.34) *
Q3	1.30(1.14, 1.49) ***	1.18(1.03, 1.36) *	1.32(1.15, 1.52) ***
Q4	1.27(1.09, 1.47) **	1.18(1.01, 1.38) *	1.29(1.08, 1.53) **
P for trend	0.011	0.039	0.008

P-value: *$P < 0.05$ **$P < 0.01$ ***$P < 0.001$. SB: sedentary behavior

Adjust I: Adjusted for age, sex. Adjust II: Adjusted for age, sex, race, education level, marital status, smoking history, alcohol history, caloric intake, physical activity, trouble sleeping, PIR, CVD, CKD, ALT, AST

Table 3 Regression analysis between depression, patient health Questionnaire-9 score and metabolic syndrome

Variable	Non-adjusted	Adjust I	Adjust II
Depression			
No	ref	ref	ref
Yes	1.69(1.47, 1.94) ***	1.88(1.61, 2.19) ***	1.34(1.13, 1.58) ***
PHQ-9	1.05(1.04, 1.05) ***	1.06(1.05, 1.07) ***	1.03(1.02, 1.04) ***

P-value: *$P < 0.05$ **$P < 0.01$ ***$P < 0.001$. PHQ-9: Patient Health Questionnaire-9

Adjust I: Adjusted for age, sex. Adjust II: Adjusted for age, sex, race, education level, marital status, smoking history, alcohol history, caloric intake, physical activity, trouble sleeping, PIR, CVD, CKD, ALT, AST

between ST and MetS, with a mediation effect percentage of 2.16% (Supplementary Table S5).

Discussion

In recent years, an increasing number of studies have shown that there is a relationship among SB, PHQ-9 score, and MetS and that prolonged SB and a higher PHQ-9 score may increase the risk of developing metabolic syndrome [5, 25–27]. However, there are no investigations of the intrinsic associations among SB, PHQ-9, and MetS. In the present study, we assessed the mediating role of the PHQ-9 score on the basis of the hypothesis that prolonged SB causes MetS by increasing the PHQ-9 score. The results revealed that both SB duration and PHQ-9 score are independent risk factors for MetS, and we observed consistent results in a regression model fully adjusted for relevant confounders. In the RCS-based analysis, we found a nonlinear relationship among SB duration, PHQ-9 score, and MetS. In the mediation effect analysis, we found a partially mediated effect of the PHQ-9 score between SB duration and MetS (mediation percentage of 6.7%).

MetS comprises a group of metabolic disorders, including hypertension, hyperglycemia, dyslipidemia, and abdominal obesity, which are risk factors that increase the probability of cardiovascular disease, stroke, and other diseases that are public health concerns [28]. In this study, we identified SB as a significant independent risk factor for low HDL-C and abdominal obesity by different analysis methods. Obesity is associated with mononuclear macrophage infiltration into adipose tissue, and the proinflammatory polarized state of these inflammatory cells leads to the release of numerous inflammatory cytokines and other factors that contribute to reduced insulin signaling [29]. These processes play a key role in the development of insulin resistance (IR) [30]. Recently, abdominal obesity was shown to be an independent risk factor for IR [31]. SB serves as a constant facilitator in this process.

SB, defined as prolonged sitting activity, is an important risk factor for adverse cardiovascular outcomes and other cardiometabolic diseases [32]. A lack of physical activity and long-term SB are major threats to public health; however, there are still many people with physical activity levels below recommended levels [33]. Research suggests that some of the variation in SB may be explained by genetic factors [34]. In a study that included 3,702 middle-aged and older adults, researchers used a data-driven clustering approach to accurately characterize differences

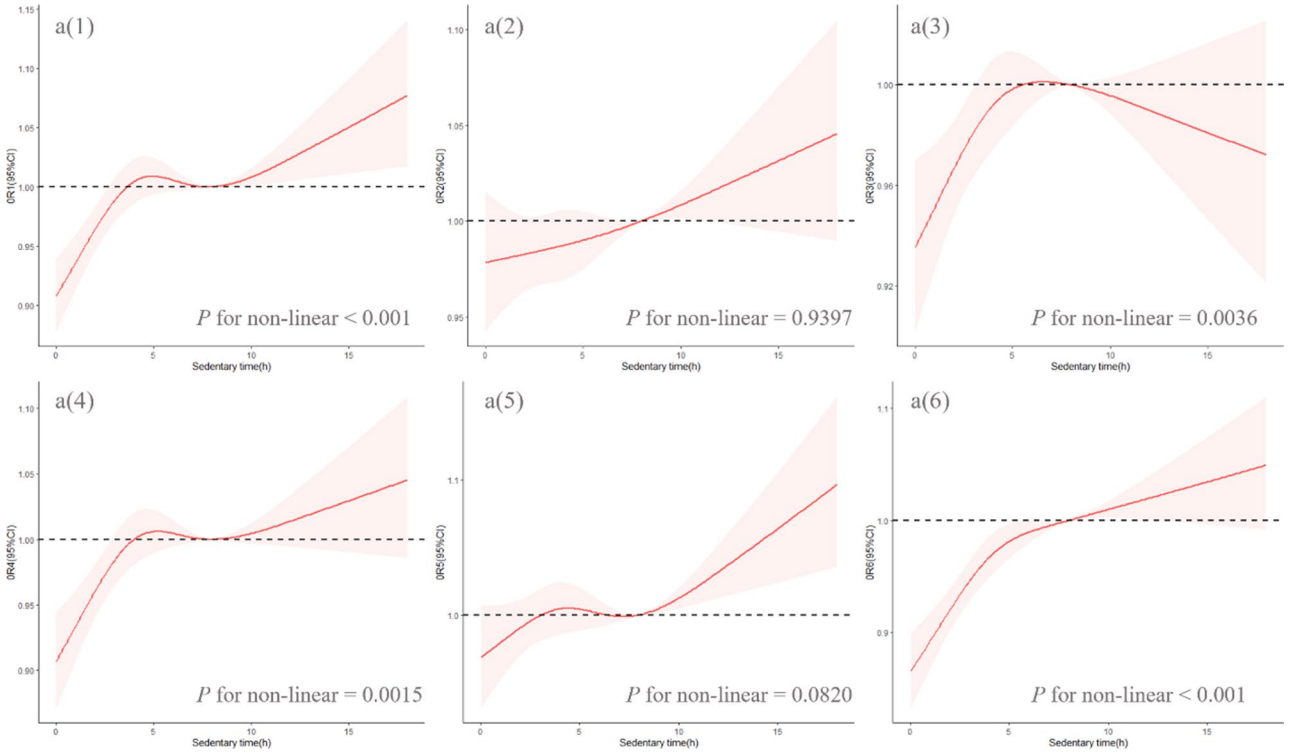

Fig. 3 Restricted cubic spline analysis between sedentary behavior duration and metabolic syndrome and its subcomponents. a (1): RCS model between SB time and MetS, a (2): RCS model between SB time and hyperglycemia, a (3): RCS model between SB time and hypertension, a (4): RCS model between SB time and low HDL-C, a (5): RCS model between SB time and high TG, a (6): RCS model between SB time and abdominal obesity. The solid red line is the fully adjusted hazard ratio, the shaded area indicates the 95% confidence interval, and the horizontal dashed line indicates an OR of 1. RCS: restricted cubic spline, SB: sedentary behavior, MetS: metabolic syndrome, HDL-C: high density lipoprotein cholesterol, TG: triglycerides, OR: odds ratio, CI: confidence interval

in sedentary time and physical activity intensity, and they discovered that engaging in more above-light physical activity and less SB duration was associated with better cardiometabolic health [35]. In the present study, we performed subgroup analyses using 150 min of moderate physical activity as the cutoff and found that the OR of SB was significantly lower in individuals with moderate physical activity longer than 150 min each week than in individuals with moderate physical activity shorter than 150 min each week. That finding is consistent with the results of previous studies. All of the above studies have shown that there is a strong association between SB and public health. In the present study, we observed an association between SB and MetS and its subcomponents, and notably, this association may be partially mediated by depressed mood.

A prolonged SB duration is associated with depressive symptoms. A cohort study of Korean adults suggested that maintaining an appropriate level of physical activity over the course of a year is beneficial for reducing depressive symptoms [36]. Consistent with the above studies, the present study revealed a significant positive correlation between SB duration and PHQ-9 score ($P<0.001$). Several mechanisms could explain the association between SB and the risk of depressive symptoms. First, prolonged SB reduces communication between individuals, leading to decreased socialization and a consequent increase in the likelihood of depression [37]. Second, a recent meta-analysis confirmed that depression is associated with smaller hippocampal volumes [38] and that prolonged moderate-intensity aerobic activity leads to an increase in hippocampal volume [39], whereas SB indirectly leads to a reduction in time spent engaging in physical activity [40]. On this basis, we believe that reducing SB duration alleviates depressive mood.

In a mediated effects model with MetS subcomponents as the outcome variable, we observed that the PHQ-9 score partially mediated the effect of hypertension, low HDL-C level, high TG level, and abdominal obesity. Depression and metabolic syndrome frequently coexist, forming a vicious cycle. Patients with metabolic syndrome are more prone to depressive symptoms due to poor physical health and diminished social functioning; furthermore, depression can exacerbate metabolic disturbances and promote the progression of metabolic syndrome through mechanisms such as the dysregulation of the neuroendocrine system and increased inflammatory responses. A cross-sectional study involving NHANES

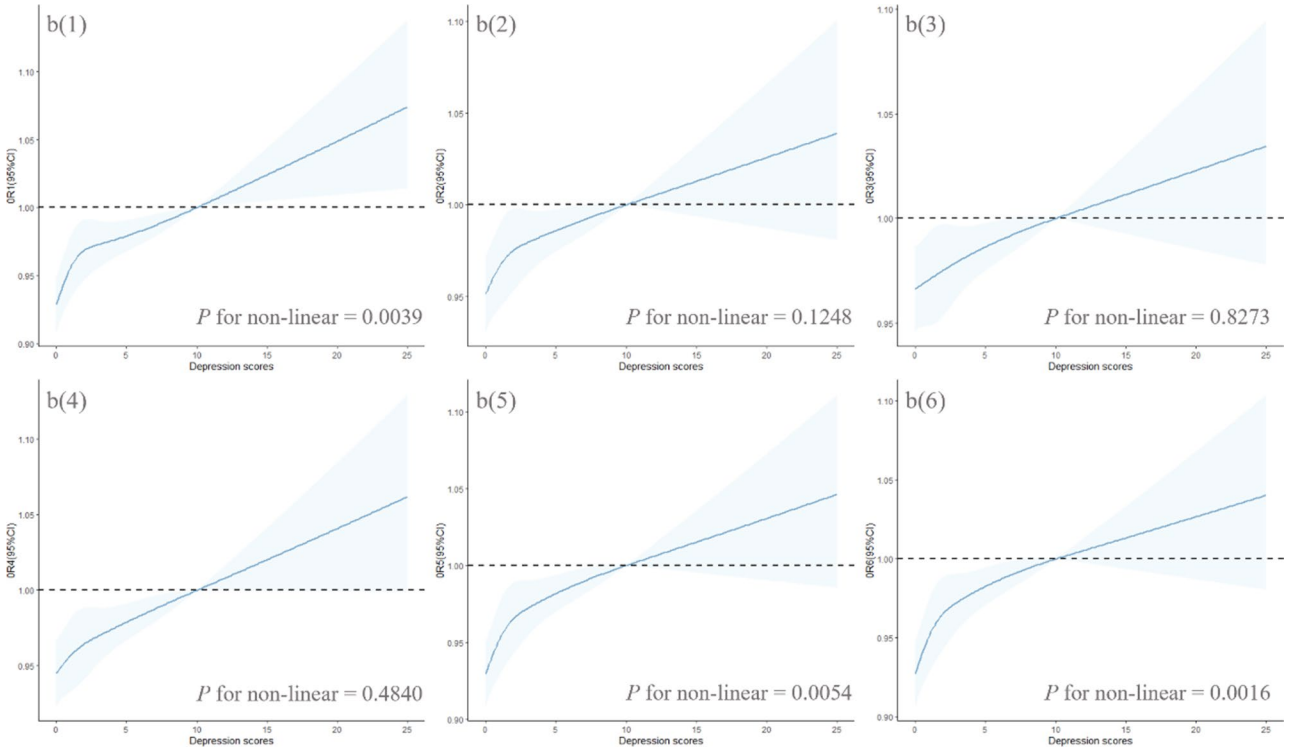

Fig. 4 Restricted cubic spline analysis between Patient Health Questionnaire-9 score and metabolic syndrome and its subcomponents. a (1): RCS model between PHQ-9 and MetS, a (2): RCS model between PHQ-9 and hyperglycemia, a (3): RCS model between PHQ-9 and hypertension, a (4): RCS model between PHQ-9 and low HDL-C, a (5): RCS model between PHQ-9 and high TG, and a (6): RCS model between PHQ-9 and abdominal obesity. The solid blue line is the fully adjusted hazard ratio, the shaded area indicates the 95% confidence interval, and the horizontal dashed line indicates an OR of 1. RCS: restricted cubic spline, PHQ-9: Patient Health Questionnaire-9, MetS: metabolic syndrome, HDL-C: high density lipoprotein cholesterol, TG: triglycerides, OR: odds ratio, CI: confidence interval

data revealed that the risk of IR increased with increasing depressive status [41]. In another cross-sectional study, researchers recruited 662 consecutive depressed patients and reported that depressed patients with suicidal behavior had higher levels of TC and LDL-C and lower levels of HDL-C [42]. Both depression and obesity can be caused by the hyperactivation of the hypothalamic–pituitary–adrenal (HPA) axis. Prolonged stress and sleep disorders can lead to the activation of the HPA axis, which can lead to excessive cortisol release and obesity [43]. Additionally, most obese patients exhibit chronically elevated cortisol concentrations [44]. It seems to be a vicious cyclical process.

On the basis of the aforementioned findings, SB is not only a significant risk factor for metabolic syndrome but also a potential risk factor for depression. Prolonged sedentariness diminishes social engagement, restricts physical activity, and disrupts neurotransmitter secretion in the brain, thereby increasing susceptibility to depressive symptoms. Additionally, depression further reduces motivation for physical exertion, perpetuates sedentary habits and reinforces a bidirectional vicious cycle. This reciprocal relationship amplifies both MetS and psychological distress through intertwined neurobiological, inflammatory, and behavioral mechanisms.

In conclusion, the results of our investigation suggest a significant association between prolonged SB duration and MetS, which can also be partially mediated by depressive mood. From the perspective of community health, encouraging the community to reduce sedentary time and increase physical activity can effectively reduce the risk of chronic diseases. Through these initiatives, physical fitness can improve, the incidence of chronic diseases may decrease, medical expenditures may decrease, and economic pressure on families may decrease, thus fundamentally reducing the economic and social burden on the public. We suggest that reducing sedentary time as well as enhancing the prevention and treatment of depression may reduce the incidence of MetS and its subcomponents.

Our study has several limitations. First, the depressed mood of the included members was evaluated by the PHQ-9 scale, which is a screening tool for depressive symptoms and is not the "gold standard" for the diagnosis of depression. Second, our study was based on a cross-sectional survey and thus was not able to determine the causal relationship between SB and MetS; the results

need to be validated by a large cohort study. In addition, although we adjusted for the main covariates, there may have been other confounders that were not detected or considered. NHANES is part of a health and nutrition survey, and for the variables we included, including the exposure factor, SB duration, and the mediator variable, PHQ-9, which were self-reported data from patients, there may have been a certain amount of measurement bias.

Conclusion

The present study revealed a positive correlation between SB and MetS on the basis of a cross-sectional survey of NHANES data. In addition, MetS may be partially dependent on depressed mood. The above findings emphasize the detrimental role of SB in the development of MetS and suggest the need to investigate the role of depressed mood in that association.

Abbreviations

SB	Sedentary behavior
MetS	Metabolic syndrome
NHANES	National Health and Nutrition Examination Survey
RCS	Restricted cubic spline
OR	Odds ratio
SE	Standard error
PHQ-9	Patient Health Questionnaire-9
DAGs	Directed acyclic graphs
HDL-C	High density lipoprotein cholesterol
TG	Triglycerides
FPG	Fasting plasma glucose
HbA1c	Glycosylated hemoglobin
PIR	Ratio of family income to poverty
ALT	Alanine aminotransferase
AST	Alanine transaminase
SCr	Serum creatinine
CKD	Chronic kidney disease
CVD	Cardiovascular disease
IR	Insulin resistance
HPA	Hypothalamic-pituitary-adrenal
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
ACME	Mediation effect
ADE	Direct effect
HPA	Hypothalamic-pituitary-adrenal

Supplementary Information

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Supplementary Material 1

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Author contributions

XW, WWY, LQW and CML designed the study. XW, SQL, ZPZ, JW, BH, NL and BMH performed the statistical analysis of the data and the graphing. XW, WWY, ZPZ, JW, BH and LQW wrote the first draft. CML, SQL, CL and JF reviewed and revised the paper. All authors read and approved the final draft.

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Data availability

This study analyzed datasets from the publicly available database NHANES from 2007 to 2018. These data can be found here: https://www.cdc.gov/nchs/nhanes/.

Declarations

Ethics approval and consent to participate

All study protocols of NHANES were approved by the Research Ethics Review Board of the NCHS. All participants provided written informed consent (https://www.cdc.gov/nchs/nhanes/index.htm).All the methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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