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The relationship between VAI, LAP, and depression and the mediation role of sleep duration–evidence from NHANES 2005–2020

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Abstract

Background The relationship between obesity and mental health has attracted attention. However, large sample studies on the relationship between visceral fat obesity and depression are lacking. This study aimed to explore the relationship between visceral fat obesity and depression by using visceral adiposity index (VAI) and lipid accumulation product (LAP). Additionally, it sought to explore the potential mediating role of sleep duration in these associations.

Methods The data used in the current cross-sectional investigation are from the National Health and Nutrition Examination Survey (NHANES) spanning from 2005 to 2020, including 19,659 participants. Depression was measured using the nine-item Patient Health Questionnaire. Weighted multivariable regression analysis was used to evaluate the correlation of VAI and LAP with depression. The potential non-linear relationship was determined using smooth curve fitting and threshold effect analysis. Additionally, mediation analysis was performed to investigate the potential mediating role of sleep duration. The stability of the relationship was assessed through sensitivity analysis.

Results VAI and LAP were closely related to depression. In the fully adjusted model, VAI and LAP in the highest quartile increased the association of depression by 52% (OR = 1.52, 95% CI 1.20–1.92, $P < 0.001$) and 51% (OR = 1.51, 95% CI 1.19–1.91, $P < 0.001$), respectively, compared with the lowest quartile. Specific saturation effects for VAI, LAP, and depression were identified by smoothed curve fitting, with inflection points of 3.81 and 98.55, respectively. Additionally, mediation analysis revealed that 5.1% and 2.8% of the associations between VAI and LAP with depression were mediated through sleep duration. The results of the sensitivity analysis showed interactions between hypertension and cardiovascular disease in the associations of VAI, and depression ($P < 0.05$).

Conclusion VAI and LAP are associated with depression in US adults. The associations between VAI and LAP with depression are non-linear, which may be mediated through sleep duration. The study highlights the potential of VAI and LAP as valuable tools for the prevention and management of depression.

Keywords NHANES, Visceral adiposity index, Lipid accumulation product, Depression, Sleep duration

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Introduction

Depression is a prevalent mental health disorder within a wide community, and it ranks as one of the top three contributors to the global disability-adjusted life-years [1, 2]. In the report on the prevalence of mental disorders among children and adolescents, the prevalence of depressive disorders reached 1.84%, accounting for 46.29 million participants [3]. Depression is a risk factor for cognitive impairment, cardiovascular diseases, and suicidal behavior [4–6]. Depression-related suicides are a major cause of death among individuals with mental disorders [7]. Despite the high prevalence and remarkable influence of depressive symptoms, they are often overlooked, underdiagnosed, and undertreated [8]. Identifying risk factors for depression is crucial for the monitoring and treatment of affected patients [9, 10].

Obesity is widely acknowledged as a risk factor for developing depression [11]. Traditional studies have used body mass index (BMI) as the standard measure of obesity, but in recent years, the effectiveness of BMI in predicting depression has been debated [12, 13]. The primary limitation of BMI is that it focuses on overall body weight without distinguishing fat distribution and tissue composition [14, 15]. With increasing attention to central obesity, weight-adjusted-waist index (WWI) has gained attention as a new measure of obesity [16]. WWI is recognized for its ability to reflect individual fat, muscle, and bone characteristics [17, 18]. WWI showed a closer association with depression than BMI [9, 10]. However, previous studies on WWI and depression have yielded inconsistent results. Shen Yun et al. [19] found that the association between WWI and depression became significant only after WWI reached a certain threshold (OR = 1.024, 95% CI: 1.001–1.049, $P = 0.045$). Conversely, other researchers have not observed this threshold effect. The relationship between WWI and depression remains consistent even after adjusting for various subgroups [9, 10]. These inconsistent findings raise questions about the precise relationship between WWI and depression. Additionally, WWI has limitations, including its focus on central obesity related to abdominal fat and an inability to distinguish between visceral fat, which restricts further exploration of the biochemical factors related to obesity and depression [16, 20]. Therefore, comprehensive metabolic indicators of visceral fat are needed to elucidate this relationship. Visceral Adiposity Index (VAI) and Lipid Accumulation Product (LAP), which combine individual fat distribution and blood biochemical characteristics, are promising new tools for exploring the potential of fat metabolism in the context of depression [21].

As novel indices for assessing adult visceral fat distribution and functional impairment, VAI and LAP have been widely utilized in research [22, 23]. Compared with gold-standard imaging techniques for evaluating visceral fat obesity, such as magnetic resonance imaging and computed tomography, VAI and LAP offer an economical, efficient, and non-invasive approach [24]. VAI is calculated based on waist circumference and BMI, combined with biochemical parameters, including triglycerides (TGs) and high-density lipoprotein (HDL). VAI considers the differences in adipose tissue distribution, particularly the accumulation of visceral fat [22]. It focuses on evaluating the distribution and functional impairment of visceral fat, effectively identifying metabolic disorders associated with visceral fat obesity, such as cardiovascular diseases, diabetes, and other complications [22, 25]. The LAP index is derived from WC and TG, aiming to assess and display the excessive accumulation of lipids in the abdomen and emphasizing overall lipid metabolism. Compared with traditional indices like BMI and waist-to-height ratio, LAP demonstrates superior predictive capabilities in metabolic syndrome [26]. LAP also serves as a widely utilized predictor for metabolic disorders, including adult-onset diabetes mellitus, blood rheological abnormality, osteoarthritis (OA), and hyperuricemia [27–31]. Combining the advantages of both has become a popular trend in assessing visceral fat obesity. VAI and LAP demonstrate excellent predictive performance in examining insulin resistance, cardiovascular diseases, the metabolically obese normal weight (MONW) phenotype, obstructive sleep apnea, and other disorders related to visceral fat metabolism dysfunction [21, 24, 25, 32, 33].

The relationship between lipid metabolism and mental health may involve multivariable potential mechanisms[34–36]. Disruptions in lipid metabolism may negatively impact mental health through pathways such as inducing neuroinflammation, oxidative stress, and affecting neurotransmitter function [37–39]. The close association between lipid metabolism and the synthesis of steroid hormones, as well as vascular health, may also play a significant role in the development of mental health issues [40]. However, this relationship may be bidirectional [41]. Lifestyle changes in individuals with depression and their biological mechanisms (such as inflammatory responses and hypothalamic-pituitary-adrenal (HPA) axis dysregulation) may further lead to lipid metabolic abnormalities [42–44]. Some prospective studies have suggested that there may be a complex causal network between lipid metabolism and mental health, and further exploration of the underlying mechanisms and directionality is needed[45, 46].

Sleep is essential for physical, mental, and emotional well-being, yet sleep disturbances are increasingly common, with both insufficient and excessive sleep linked to obesity, metabolic disorders, and depression [24, 47–49].

Studies suggest a bidirectional relationship between sleep and depression, involving HPA axis dysregulation, neurotransmitter imbalances, and chronic inflammation[50]. Sleep disturbances also contribute to visceral obesity through metabolic dysregulation, altered circadian rhythms, and hormonal changes[51, 52]. Emerging evidence indicates that sleep duration may mediate the relationship between visceral obesity and depression via mechanical and biochemical pathways, yet few studies have examined these interactions comprehensively[45, 53, 54]. This study addresses these gaps by investigating the modifying and mediating effects of sleep duration on the association between VAI, LAP, and depression in a nationally representative cohort, highlighting non-linear dynamics often overlooked in previous research.

Existing research has demonstrated that visceral fat is significantly associated with an increased odds of depression prevalence using different fat indicators[55]. However, most existing studies lack a non-linear analysis, often treating the relationship between visceral fat and depression as linear without examining potential threshold or saturation effects. Additionally, limited attention has been given to mediating factors, such as sleep which could provide a deeper understanding of the mechanisms underlying the association between visceral fat obesity and depression. Therefore, this study aims to utilize data from the National Health and Nutrition Examination Survey (NHANES) to examine the associations between VAI, LAP and depression, and to assess the mediating effect of sleep duration, thereby filling a gap in the current literature. This report adheres to the STROBE statement for cross-sectional studies, ensuring a comprehensive and transparent presentation of the study design, implementation, analysis, and interpretation[56].

Subjects and methods

Data and sample sources

The data originated from NHANES conducted by Centers for Disease Control and Prevention (CDC). Detailed information regarding data collection is available on website. The cross-sectional research data spans seven periods from NHANES 2005 to 2020. Participants were included if they had complete data for PHQ-9 and measurements necessary for calculating VAI and LAP. VAI was calculated using waist circumference (WC), body mass index (BMI), and triglycerides (TG), while LAP was calculated using WC and TG levels. The NHANES Ethics Review Board supervised and supported the research program.

Among 92,065 participants in the NHANES 2005–2020, individuals were excluded if they were (1) minors under the age of 20; (2) participants with missing VAI or LAP measurement data, or those with VAI exceeding 40 or LAP exceeding 700; (3) participants with incomplete PHQ-9 questionnaire data, or those with a full PHQ-9 score indicating severe depression; (4) pregnant women; and (5) participants with missing covariates. Ultimately, A total of 19,659 participants participated in the final analysis (Fig. 1).

Assessment of variables

Depression

The "Mental Health—Depression Screener" module in the "Questionnaire Data" section of the NHANES database was the source of the depression-related data for this study. These data are typically collected at the Mobile Examination Center (MEC) through Computer Assisted Personal Interview (CAPI) system. Depression was assessed with PHQ-9, which was used to assess mental health over the past 2 weeks. The questionnaire has a total of nine questions with answers in different levels, ranging from "not at all" to "nearly every day" [57]. To ensure the independence of "sleep duration" as a mediator in this study, the sleep disturbance items in the PHQ-9 were removed to avoid interference from the relationship between sleep disturbances and sleep duration[58]. This approach ensures the independent assessment of the relationship between sleep duration, VAI, LAP, and depression. Meanwhile, sleep disturbance will be analyzed as an independent subgroup. The total score of PHQ-9 is calculated by summing the responses to the remaining eight items (possible range: 0—24). According to the MHP reinterview (criterion standard), when the PHQ-9 total score ≥ 9, the sensitivity for depression is 95%, and the specificity is 84% [57]. Therefore, participants' PHQ-9 scores in this study were divided into two groups: < 9 (no depression) and ≥ 9 (depression) [59].

VAI

VAI, a gender-specific measure, assesses visceral fat accumulation through anthropometric data (height, weight, and WC) and blood biochemical parameters (TGs and HDL-cholesterol). Anthropometric data are captured electronically by health technicians from the measuring instruments, avoiding potential data entry errors. The formula for VAI is shown in Fig. 2. The VAI formula consists of WC in centimeters, BMI in kilograms per square meter, TGs in millimoles per liter, and HDL in millimoles per liter [22].

LAP

LAP is an indicator of obesity that combines WC and TG, reflecting the total body fat, especially the accumulation of fat around the waist [23, 60]. The formula for LAP is shown in Fig. 2. The LAP formula consists of WC in centimeters and TG in millimoles per liter [24].

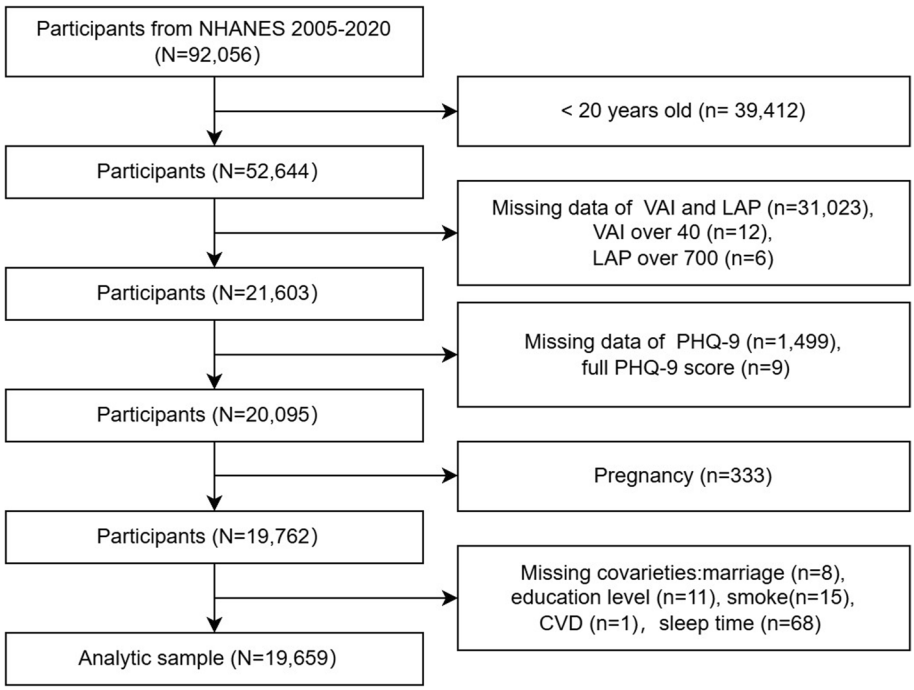

Fig. 1 Flowchart of sample selection from NHANES 2005–2020

$$LAP_{male} = (WC - 65) \times TG$$

$$LAP_{female} = (WC - 58) \times TG$$

$$VAI_{male} = \frac{WC}{39.68 + (1.88 \times BMI)} \times (TG/1.03) \times (1.31/HDL_c)$$

$$VAI_{female} = \frac{WC}{36.58 + (1.89 \times BMI)} \times (TG/0.81) \times (1.52/HDL_c)$$

Fig. 2 Formulas for VAI and LAP according to gender

Sleep duration and sleep disturbance

Participants self-reported their typical sleep duration on workdays or weekdays[61]. Sleep duration was measured using the following questions: "How many hours did you sleep?" (for the 2005—2016 period) and "How many hours do you usually sleep on workdays or weekdays?" (for the 2017—2020 period).

Sleep disturbance was assessed based on a question from the sleep disturbance questionnaire in PHQ-9: "In the past two weeks, how often have you been bothered by the following: difficulty falling asleep or staying asleep, or sleeping too much?" If participants answered "more than half of the days" or "nearly every day," they were considered to have a sleep disturbance. If they answered

"several days" or "not at all," they were considered to have no sleep disturbance. Participants who answered "refuse" or "don't know" were coded as missing and excluded from the analysis [62].

Covariables

Various demographic and health-related factors were considered as confounders, including age, gender, race, marital status, family-PIR, education level, BMI, smoking, excessive alcohol, hypertension, diabetes[63], and Cardiovascular Disease (CVD). Blood samples collected at the MEC laboratory were analyzed at the Johns Hopkins University Lipoprotein Analysis Laboratory. Quality control processes for NHANES data, including data collection and laboratory analysis, are detailed on the NHANES website. The selection of covariates was based on a theoretical basis, considering the complex relationship between obesity and depression involving demographic factors [24, 64], behavioral factors, and health-related factors[65–67]. Additionally, the selection of covariates was supported by existing literature on key variables recognized as potentially influencing this relationship [24, 62–65, 65–68].

Statistical analysis

The sample was analyzed following the NHANES weighting analysis guidelines. Continuous variables were described using mean ± SD and compared across percentile populations by using weighted linear regression models. Categorical variables were described in weighted percentages, and differences between groups were evaluated using weighted chi-square tests. Weighted chi-square tests and weighted t-tests were employed to assess baseline differences between categorical and continuous variables. VAI and LAP scores were treated as continuous variables or transformed into quartiles. For VAI, the quartiles were as follows: Quartile 1 (Q1): 0.09 to 0.83; Quartile 2 (Q2): 0.83 to 1.37; Quartile 3 (Q3): 1.38 to 2.33; Quartile 4 (Q4): ≥ 2.33; For Log LAP, the quartiles were as follows: Quartile 1 (Q1): −0.46 to 1.36; Quartile 2 (Q2): 1.36 to 1.62; Quartile 3 (Q3): 1.62 to 1.86; Quartile 4 (Q4): ≥ 1.86.

In the multivariable and sensitivity analyses, the missing data for covariates were addressed as follows: Missing data on excessive alcohol status (31.12%) were treated as a separate category and filled using multiple imputation methods; missing data on Family ratio of income to poverty (PIR) (9.3%) were imputed using mean values. In terms of data presentation, when VAI and LAP were included as continuous variables in the multivariable regression model, we applied a log10 transformation to these variables where appropriate, ensuring that the results are more interpretable and statistically robust. To assess the potential multicollinearity among covariates, the variance inflation factor (VIF) was examined[69]. A VIF value greater than 10 was considered indicative of serious multicollinearity, and the results indicate that no severe multicollinearity was detected. The results of the multicollinearity assessment are presented in the Supplementary Material (Supplement 3).

The association among VAI, LAP scores, and depression was investigated using weighted multivariable regression models. Three different models were designed for the study: model I without covariate adjustment, model 2 adjusted for demographic variables, and model 3 adjusted for additional covariates based on model 2. Generalized additive models (GAMs) were used to assess nonlinear relationships, and threshold effect analysis was applied to examine relationships on either side of inflection points. Mediation analysis was conducted to assess the mediated effect of sleep duration on the association between VAI and LAP and depression using the product of coefficients method [65]. This method evaluated the ratio of the indirect effect to the total effects of VAI and LAP on depression. The mediation effect was determined by calculating the percentage of the total effect attributable to the mediator. Subgroup stratification was performed to examine differences in the associations of VAI and Log LAP with depression across various factors. Interaction tests were employed to examine the consistency of associations between the subgroups. Analyses were conducted using R software and Empower Stats, and statistical significance was set at $P < 0.05$.

Results

Baseline characteristics of participants

A total of 19,659 participants were enrolled in the research, comprising 1,458 participants diagnosed with depression and 18,201 participants without depression diagnosis. The average age of the participants with depression was 47.40 ± 15.45 years, and the average age of those without depression was 48.00 ± 16.89 years. The male-to-female ratio was almost equal, with 49.87% males and 50.13% females. The individuals with depression were more likely to be less than 60 years old, female, non-Hispanic white, or higher educational level (> high school). Further details regarding characteristics of other study populations can be found in Table 1.

Association between VAI and depression

Three multivariable regression model were performed to explore the connection between depression and VAI (Table 2). When VAI was treated as a continuous variable, significant positive associations were found in the unadjusted model 1 (OR = 1.07, 95% CI: 1.05–1.09, $P < 0.001$) and model 2 (OR = 1.08, 95% CI: 1.05–1.10, $P < 0.001$).

Table 1 Weighted characteristics of the study population by depression

Characteristics	Total (*N*=19,659)	Depression		*P*-value
		Yes (*N*=1,458)	No(*N*=18,201)	
Age, (year)	47.97±16.80	47.40±15.45	48.00±16.89	0.227
Age, (%)				0.020
≤60	72.66	1,012 (75.55)	11,851 (72.47)	
＞60	27.34	446 (24.45)	6,350 (27.53)	
Gender, (%)				<0.001
Male	49.87	529 (36.67)	9,317 (50.73)	
Female	50.13	929 (63.33)	8,884 (49.27)	
Race, (%)				<0.001
Mexican American	8.41	215 (8.11)	2,710 (8.43)	
Other Hispanic	5.70	215 (8.98)	1,771 (5.48)	
Non-Hispanic White	68.30	560 (62.53)	7,607 (68.68)	
Non-Hispanic Black	10.17	342 (13.73)	3,886 (9.93)	
Other races	7.42	126 (6.65)	2,227 (7.47)	
Marital status, (%)				<0.001
Married/living with partner	64.22	643 (48.30)	11,192 (65.27)	
Widowed/divorced/ separated	23.17	638 (37.45)	4,953 (22.23)	
Never married	12.61	117 (14.25)	2,056 (12.50)	
Education level, (%)				<0.001
< High school	15.13	491 (25.52)	3,978 (14.45)	
High school	23.58	362 (26.18)	4,208 (23.41)	
> High school	61.29	605 (48.31)	10,015 (62.15)	
Smoking, (%)				<0.001
Yes	45.96	635 (61.27)	10,116 (44.96)	
No	54.04	823 (38.73)	8,085 (55.04)	
Excessive alcohol, (%)				<0.001
Yes	9.84	191 (13.50)	1,744 (9.60)	
No	59.04	768 (55.62)	10,839 (65.37)	
NA	31.12	499 (30.88)	5,618 (25.03)	
Diabetes, (%)				<0.001
Yes	13.79	374 (19.39)	14,837 (13.42)	
No	86.21	1,084 (80.61)	3,364 (86.58)	
Hypertension, (%)				<0.001
Yes	37.88	778 (49.49)	7,675 (37.12)	
No	62.12	680 (50.51)	10,526 (62.88)	
CVD, (%)				<0.001
Yes	8.06	250 (13.62)	1,717 (7.69)	
No	91.94	1,208 (86.38)	16,484 (92.31)	
Sleep disturbance, (%)				<0.001
Yes	14.75	964 (67.57)	2,115 (11.28)	
No	85.25	494 (32.43)	16,086 (88.72)	
Family PIR	3.06±1.63	2.14±1.56	3.12±1.61	<0.001
BMI, (kg/m2)	29.09+6.84	30.73±7.93	28.98±6.75	<0.001
WC, (cm)	99.52±16.59	102.70±17.74	99.31±16.49	<0.001
TG, (mmol/l)	1.39±1.03	1.54±1.06	1.38±1.03	<0.001
HDL-C, (mmol/l)	1.40±0.42	1.36±0.41	1.41±0.42	<0.001
LDL-C, (mmol/l)	2.93±0.91	2.96±0.96	2.93±0.91	<0.001
Sleep time, (hour)	7.15±1.43	6.81±1.96	7.17±1.39	<0.001
VAI	1.95±2.05	2.33±2.28	1.92±2.03	<0.001

Table 1 (continued)

Characteristics	Total (*N*=19,659)	Depression		*P*-value
		Yes (*N*=1,458)	No(*N*=18,201)	
LAP	56.58±53.14	68.81±62.13	55.77±52.39	<0.001
Log LAP	1.60±0.38	1.69±0.39	1.59±0.38	<0.001

Values are presented as weighted means (standard deviation) or number of participants (weighted percentages), unless otherwise specified. For continuous variables, the mean ± SD and *P*-value were calculated using a weighted linear regression model. For categorical variables, percentages and *P*-values were calculated using a weighted chi-square test. Among the 19,659 subjects, the missing value of the covariate of excessive drinking was 6,117 (31.12%), and the missing value of the family PIR was 1,839 (9.3%)

Abbreviation: *NA* Not Applicable, *CVD* Cardiovascular disease, *PIR* The ratio of income to poverty, *BMI* Body mass index, *WC* Waist circumference, *TG* Triglyceride, *HDL-C* High-density lipoprotein cholesterol, *LDL-C* Low-density lipoprotein cholesterol, *VAI* Visceral adiposity index, *LAP* Lipid accumulation product

Table 2 Weighted multivariate logistic regression of VAI and Log LAP in depression

Depression	Crude model (Model 1) OR (95% CI) *P*-value	Partly adjusted model (Model 2)	Fully adjusted model (Model 3)
VAI			
Continuous	1.07 (1.05, 1.09) <0.001	1.08 (1.05, 1.10) <0.001	1.04 (1.00, 1.07) 0.034
Categories			
Q1 (0.09 to 0.83)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Q2 (0.83 to 1.37)	1.15 (0.97, 1.36) 0.097	1.14 (0.96, 1.35) 0.133	1.08 (0.86, 1.37) 0.505
Q3 (1.38 to 2.33)	1.28 (1.09, 1.51) 0.003	1.29 (1.09, 1.52) 0.003	1.08 (0.85, 1.38) 0.527
Q4 (≥2.33)	2.00 (1.72, 2.33) <0.001	2.07 (1.77, 2.42) <0.001	1.52 (1.20, 1.92) <0.001
P for trend	<0.001	<0.001	<0.001
Log LAP			
Continuous	1.98 (1.71, 2.30) <0.001	2.14 (1.84, 2.50) <0.001	1.48 (1.18, 1.86) <0.001
Categories			
Q1 (-0.46 to 1.36)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Q2 (1.36 to 1.62)	0.99 (0.83, 1.17) 0.862	1.01 (0.85, 1.20) 0.902	0.96 (0.75, 1.23) 0.746
Q3 (1.62 to 1.86)	1.33 (1.13, 1.56) <0.001	1.38 (1.17, 1.62) <0.001	1.23 (0.97, 1.56) 0.087
Q4 (≥1.86)	1.96 (1.69, 2.28) <0.001	2.10 (1.80, 2.45) <0.001	1.51 (1.19, 1.91) <0.001
P for trend	<0.001	<0.001	<0.001

Model 1: no covariates were adjusted. Model 2: age, gender, and race were adjusted. Model 3: age, gender, race, educational level, Marital status, family-PIR, smoking, excessive alcohol, diabetes, hypertension, Cardiovascular disease (CVD), sleep disturbance. VAI and Log LAP scores were continuous variables, grouped according to quartiles (Quartile 1(Q1): lowest 25%, Quartile 4(Q2): highest 25%)

A significant association was found (OR = 1.04, 95% CI: 1.00–1.07, $P = 0.034$) after adjusting for all covariates in model 3. When VAI was categorized into quartiles, the positive correlations between VAI and odds of depression prevalence remained stable. In model 3, the participants in Quartile 4 (Q4) exhibited a 52% increased correlation of depression (OR = 1.52, 95% CI: 1.20–1.92, $P < 0.001$) compared with those in Quartile 1 (Q1) (Table 2).

Association between Log LAP and depression

Three multivariable regression models were developed to investigate the relationship between LAP and depression. When LAP was a continuous variable, the results were significant for the relationship in each model: model 1 (OR = 1.98, 95% CI: 1.71–2.30, $P < 0.001$); model 2 (OR = 2.14, 95% CI: 1.84–2.50, $P < 0.001$); model 3 (OR = 1.48, 95% CI: 1.18–1.86, $P < 0.001$). The stable positive association between Log LAP and depression was maintained when Log LAP was categorized by quartiles. In model 3, the participants in Quartile 4(Q4) had a 51% increased odds of depression prevalence (OR = 1.51, 95% CI: 1.19–1.91, $P < 0.001$) compared with those in the lowest quartile (Q1) (Table 2).

Non-linear association between VAI and LAP with depression

Smoothed curve fitting was performed on the basis of model 3 to visualize the association among LAP, VAI, and depression (Figs. 3 and 4). The results showed a non-linear relationship among these variables. Threshold effect analyses were performed (Table 3), and an inflection point of 3.82 was found for the VAI score (log-likelihood ratio < 0.001). When the VAI score was below 3.82, the odds of depression prevalence increased by 15.6%

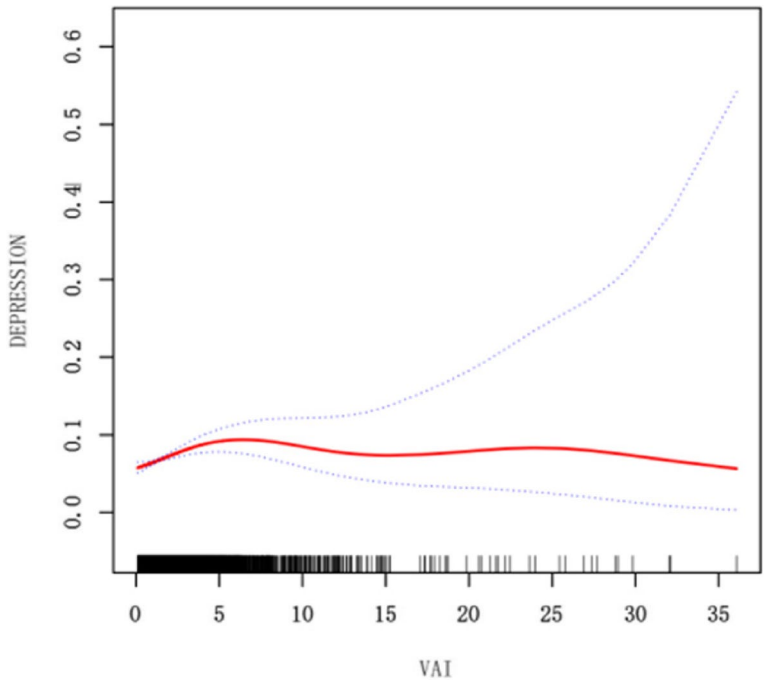

Fig. 3 Weighted non-linear relationship between VAI and depression by the generalized additive model

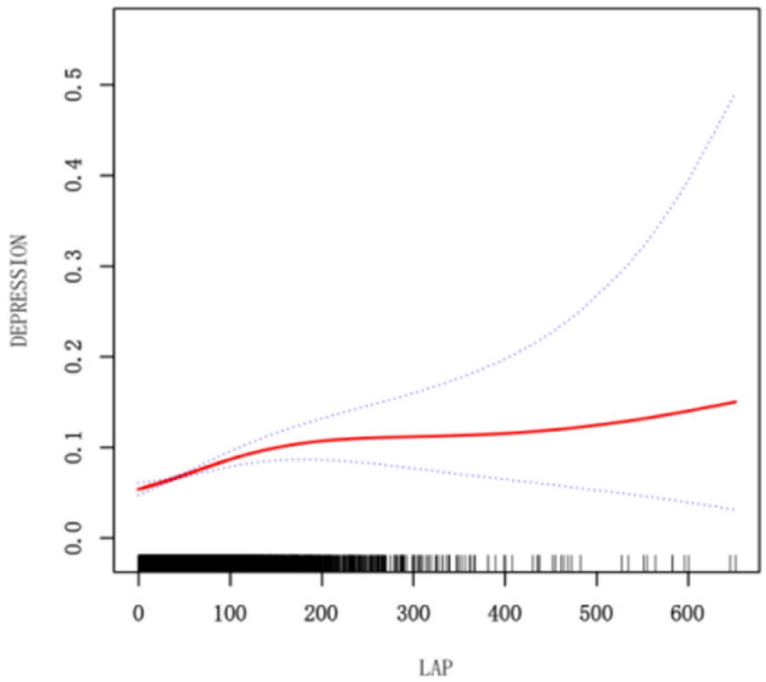

Fig. 4 Weighted non-linear relationship between LAP and depression by generalized additive model

for each unit increase. However, when the VAI score exceeded 3.82, the odds of depression prevalence no longer changed significantly with increasing VAI score. For the LAP score, similar results showed an inflection point of 98.55 (log-likelihood ratio = 0.028), suggesting

Table 3 Weighted threshold effect analysis of VAI or LAP on depression by two-piecewise linear regression model

Outcome	VAI OR (95% CI) *P*-value	LAP OR (95% CI) *P*-value
Fitting by the two-piecewise linear model		
Inflection point (K)	3.82	98.55
< K-segment effect	1.156(1.067,1.253) <0.001	1.005 (1.003, 1.008) <0.001
> K-segment effect	0.983 (0.930, 1.038) 0.527	1.001 (0.991, 1.000) 0.589
Log-likelihood ratio	<0.001	0.028

Age, gender, race, educational level, Marital status, family-PIR, smoking, excessive alcohol, diabetes, hypertension, Cardiovascular disease (CVD), sleep disturbance were adjusted

that the effect of LAP on the odds of depression prevalence varies above and below different thresholds.

Mediation effects of sleep duration on VAI/LAP and depression

The figures (Table 4, Figs. 5 and 6) displayed the mediation analysis of sleep duration on the association between VAI, LAP, and depression. The results showed significant indirect effects of VAI and LAP on depression through sleep duration, $P=0.004$ and $P<0.001$, respectively. Specifically, sleep duration was found to mediate 5.1% of the association between VAI and depression, and 2.8% of the association between LAP and depression[65].

Association between depression and VAI or Log LAP in sensitivity analysis

Weighted sensitivity analysis (Figs. 7 and 8) included major categorical covariates such as age, sex, race, diabetes, hypertension, cardiovascular disease (CVD), and sleep disturbance. No significant statistical differences were observed in the interaction results for VAI (All P for interaction >0.05). However, significant interaction

Table 4 Weighted mediation analysis for the association of VAI and LAP with depression

Independent variable	Mediator	Total effect	Indirect effect	Direct effect	Proportion of mediation (%) *P*-value
		Coefficient (95% CI) *P*-value			
VAI	Sleep duration	0.0036 (0.0012, 0.0060) 0.004	0.0002 (0.0001, 0.0003) 0.004	0.0035 (0.0010, 0.0058) 0.004	5.1 0.008
LAP		0.0092 (0.0059, 0.0123) <0.001	0.0003 (0.0001, 0.0005) <0.001	0.0090 (0.0056, 0.0120) <0.001	2.8 <0.001

The mediation analysis was adjusted for age, gender, race, educational level, Marital status, family-PIR, smoking, excessive alcohol, diabetes, hypertension, Cardiovascular disease (CVD)

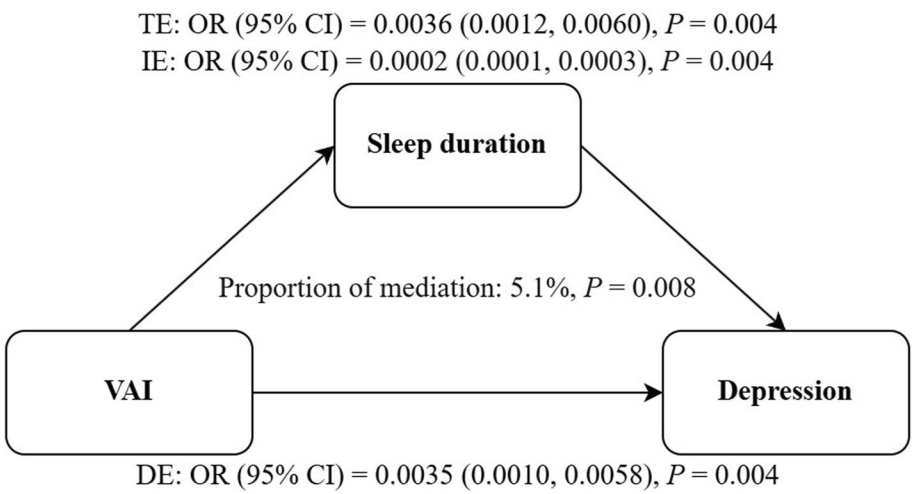

Fig. 5 Mediation effect of Sleep duration on the association of VAI and depression

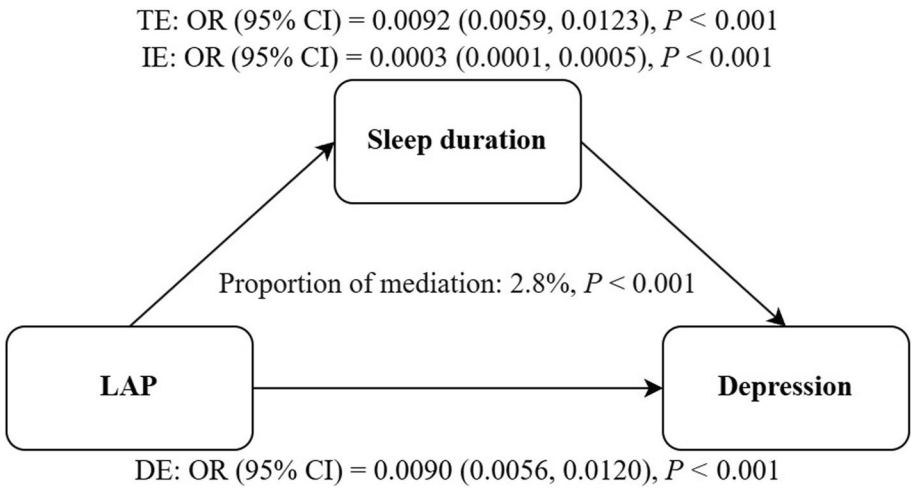

Fig. 6 Mediation effect of Sleep duration on the association of LAP and depression

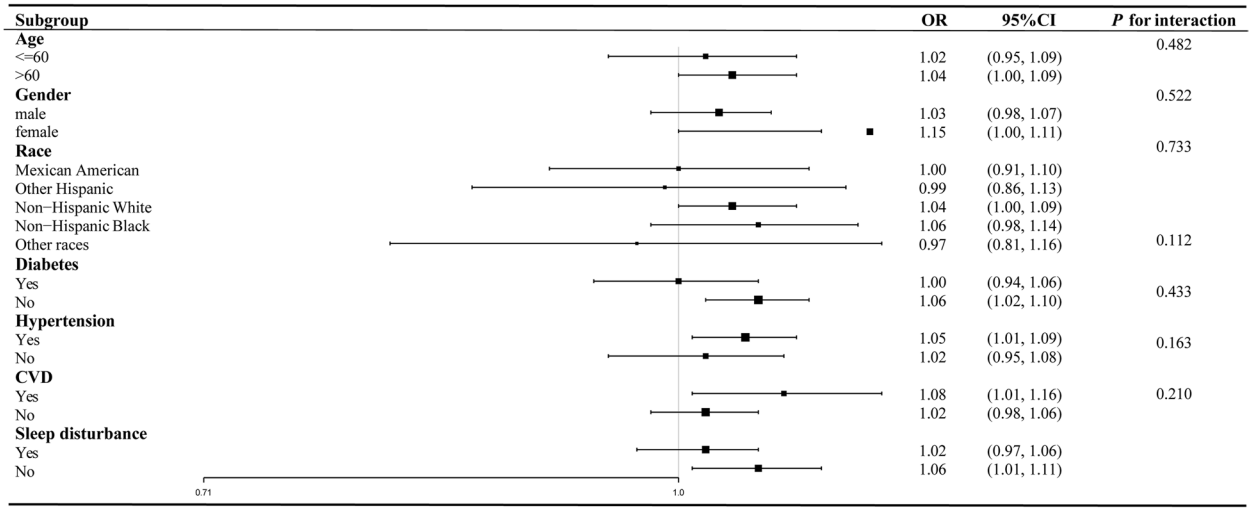

Fig. 7 Weighted sensitivity analysis of the association between VAI and depression

statistical differences were found in the results for Log LAP, with hypertension (*P* for interaction = 0.022) and CVD (*P* for interaction = 0.003).

Additionally, although no interaction was observed for sleep disturbance (*P* for interaction = 0.210), a significant positive association between VAI and depression was found in the non-sleep disturbance group (OR = 1.06, 95% CI: 1.01—1.11, *P* = 0.010), while this association was not significant in the sleep disturbance group (OR = 1.02, 95% CI: 0.97—1.06, *P* = 0.480). Similar results were observed for Log LAP: in the non-sleep disturbance group (OR = 1.95, 95% CI: 1.36—2.79, *P* < 0.001) and the sleep disturbance group (OR = 1.25, 95% CI: 0.93—1.67, *P* = 0.134), with the *P* for interaction being 0.553.

Discussion

This cross-sectional study involving a representative sample of 19,659 American adults identified a significant positive correlation among VAI, LAP, and depression. The analysis revealed that as the VAI and LAP levels increased, the association with depression increased even after adjusting for all covariates. The study observed a non-linear relationship among these variables, indicating a complex pattern. Specifically, within certain thresholds (VAI reaching 3.82 and LAP reaching 98.55), a significant increase can be observed in depression with increasing VAI and LAP. However, beyond these thresholds, this association was no longer significant. Sleep duration mediated 2.8% and 5.1% of the relationship between VAI,

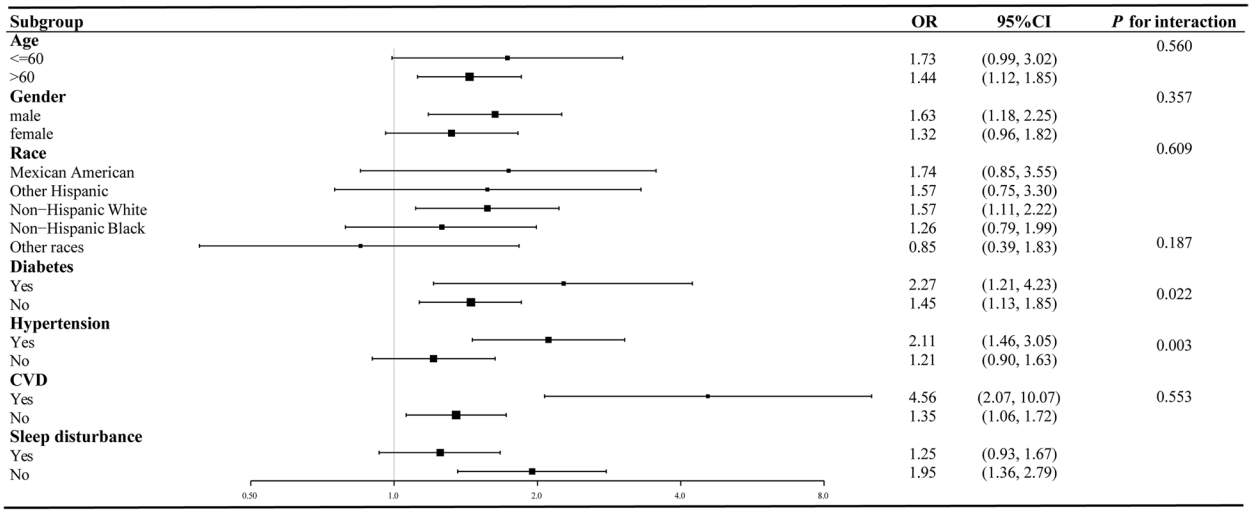

Fig. 8 Weighted sensitivity analysis of the association between Log LAP and depression

LAP, and depression, respectively, and interaction tests confirmed the robustness of these findings. Additionally, significant differences were observed in subgroups based on the presence or absence of hypertension and CVD.

This study contributes to the existing body of cross-sectional research on the association between visceral fat obesity and depression in a large cohort. Previous research has established a correlation between central obesity and depression [67, 12, 70]. For instance, studies on WWI and BMI have demonstrated positive associations between central obesity metrics and depression [71–73]. However, these studies have primarily relied on central obesity indicators that do not fully capture the metabolic and visceral fat-specific components of obesity. To address this limitation, this study incorporates VAI and LAP, which reflect visceral fat distribution and related metabolic abnormalities, offering a more precise assessment of the relationship between visceral obesity and depression[24, 32, 33]. By utilizing these two novel indicators, this study bridges a critical gap in understanding the association between visceral fat obesity and depression within a large-scale cohort.

VAI and LAP, have been widely studied as indicators of visceral fat metabolism in clinical settings, demonstrating strong predictive capabilities [60, 74]. The measurement of these two indicators features of body fat distribution and biochemical markers, allowing for a more comprehensive assessment of visceral fat accumulation and lipid metabolic abnormalities in individuals [30, 74]. Compared with individual visceral fat indicators, VAI and LAP offer significant advantages in predicting multivariable symptoms, such as cardiovascular metabolic risks, hyperuricemia, and diabetic retinopathy, with a notably strong correlation [32, 33, 75]. The present study found significant positive correlations among VAI, LAP, and depressive symptoms. This finding aligns with the results of Wang Ying et al. In middle-aged and older adults over 45 years, the ROC curve analysis indicated that LAP is an effective predictor of depressive symptoms [55]. Notably, the results showed that VAI failed to predict this association. This discrepancy may be attributed to ethnic differences and variations in the assessment scales for depressive symptoms. Similar positive correlations between VAI and depression were found by Lei et al. in their analysis of American adults [73]. Overall, the findings showed that both visceral fat obesity indicators are associated with depression, and some studies have confirmed this result. The comprehensive consideration of both indicators in the clinical management of depression could be beneficial for a comprehensive assessment of patients' conditions.

The relationship between depression and abdominal obesity is complex, with its underlying mechanisms yet to be fully elucidated. Possible explanatory mechanisms primarily involve immune stress and metabolic dysregulation [76, 77]. First, inflammatory processes originating from visceral adipose tissue may increase the odds of depression prevalence [77, 78]. Excess adipocytes secrete free fatty acids (FFAs) and inflammatory cytokines, such as CRP, TNF-α, and IL-6, leading to systemic inflammation and oxidative stress [78]. This inflammatory state activates microglia in the central nervous system, affecting serotonin synthesis and neuronal apoptosis, thus increasing the correlation of depression [79]. Simultaneously, neuroinflammation affects hypothalamic insulin signaling pathways that are related to depression [80].

Specifically, neuroinflammation further leads to insulin resistance, disrupting insulin's ability to inhibit gluconeogenesis and regulate adipocyte metabolism, thus causing metabolic dysregulation and increasing the association of depression [81, 82]. Second, abnormalities in HPA axis in individuals with abdominal obesity contribute to depression [40, 83]. High levels of cortisol attach to receptors in visceral fat, triggering lipoprotein lipase and preventing lipid mobilization, and this phenomenon leads to the retention of triglycerides within visceral fat, thereby increasing visceral fat accumulation [76, 84, 85]. The interaction of these mechanisms complicates the relationship between depression and obesity.

This study is the first to reveal the saturation effect between VAI, LAP, and depression. When visceral fat obesity reached a certain threshold, the association with depression was no longer significant. This phenomenon requires further explanation. One possible reason is that individuals excessive visceral fat often exhibit generalized obesity and abdominal obesity, thereby complicating this relationship [86]. Similar to obesity, depression is influenced by multivariable factors, and it can exhibit varying degrees of severity and irregularity [87–89]. Additionally, the negative effects of pro-inflammatory cytokines secreted by visceral fat can be counteracted by the protective effect of subcutaneous fat mass [90, 91]. The "obesity paradox" may provide strong evidence for the findings of the present study [92]. "Obesity paradox" refers to the protective effects of higher fat levels, initially observed in obese patients with Heart Failure with Reduced Ejection Fraction (HFrEF) who had better clinical outcomes [93]. Depression is related to "obesity paradox," with studies showing that underweight individuals have higher levels of depression than those with obesity [94, 95]. A possible explanation is that excessive obesity can increase antioxidant defense, store protective energy, exhibit a protective profile of fatty factors, and interact with endotoxin–lipoprotein, providing a survival advantage [90, 96–98]. Understanding these non-linear dynamics is crucial for developing effective interventions. Although previous studies have identified an association between VAI, LAP, and depression, most of these studies have used linear models and failed to uncover the non-linear relationships between variables [99, 73]. In contrast, this study employed smooth curve fitting and threshold effect analysis to reveal the non-linear relationship between VAI, LAP, and depression, a relationship that had not been explored in previous research. Additionally, to enhance the reliability of the results and accommodate the stratified design of NHANES data, this study applied weighted analysis methods and incorporated more relevant covariates and a longer time span, thereby improving statistical power and stability.

Sleep duration plays a mediating role in the relationship between VAI, LAP, and depression, providing a new perspective for understanding the complex relationship between visceral obesity and depression. First, visceral obesity may influence sleep duration through multivariable mechanisms [51]. The increase in pro-inflammatory cytokines and adipokines in individuals with visceral obesity can interfere with the nocturnal peak of melatonin and the diurnal rhythm of cortisol, disrupting the normal sleep cycle [51, 52, 100]. At the same time, the accumulation of abdominal fat increases intra-abdominal pressure, which may compress the diaphragm and subsequently increase the risk of obstructive sleep apnea (OSA) [24, 49]. The repeated apneas and hypoxemia associated with OSA can disrupt sleep continuity and reduce sleep quality [49]. On the other hand, both insufficient and excessive sleep are closely associated with depression. A meta-analysis of prospective studies found that adults with short and long sleep durations had a relative odds of depression prevalence 1.31 and 1.42 times higher, respectively, compared to adults with normal sleep duration [101]. There is a neurobiological overlap between depression and sleep disturbance, where insufficient or excessive sleep may alter hormone levels, particularly an abnormal increase in cortisol, through the hypothalamic-pituitary-adrenal axis, thus activating the "obesity-inflammation-depression" interaction mechanism [102, 103]. Mediation analysis in this study further quantified this effect: the mediating effect of sleep duration between VAI and depression was estimated to be 5.1% ($P=0.004$), while the mediating effect between LAP and depression was 2.8% ($P<0.001$). Subgroup analysis of sleep disturbance supported the results of the mediation analysis. For individuals without sleep disturbance, the association between VAI, LAP, and depression was more direct and significant; whereas, in individuals with sleep disturbance, sleep duration as a mediator modified the relationship between VAI, LAP, and depression.

The Sensitivity analysis revealed significant differences in the association between VAI, LAP, and depression in individuals with cardiovascular disease (CVD) or hypertension compared to those without CVD or hypertension. This finding is consistent with previous studies [42, 104]. Cardiovascular disease is closely associated with inflammatory processes, with pro-inflammatory cytokines such as IL-6 and TNF-α remaining active in the body [42, 105]. The increased inflammatory factors associated with visceral fat obesity can activate endothelial cells, promoting the formation of atherosclerosis [66]. Endothelial dysfunction, by affecting the release of bioactive substances from endothelial cells, can further disrupt neurotransmitter metabolism, including inducing insulin resistance and hypothalamic-pituitary-adrenal (HPA)

axis abnormalities, which may ultimately increase the risk of depressive symptoms [66, 106]. In contrast, individuals without cardiovascular disease typically exhibit lower overall inflammation levels [104, 107]. In the presence of visceral fat obesity, the body may compensate by increasing the secretion of anti-inflammatory factors, such as adiponectin, to maintain physiological balance [108].

In summary, this study comprehensively examined the non-linear relationships between visceral adiposity indicators, LAP and VAI, and depression, uncovering the significant mediating role of sleep duration in this association. These findings offer valuable insights for the clinical management of visceral fat obesity and its related mental health challenges, enabling healthcare providers to better address visceral fat levels to mitigate the odds of depression prevalence. From a community health perspective, the results emphasize the importance of monitoring and managing visceral adiposity indicators like VAI and LAP due to their strong connection with residents' overall health, including mental well-being. Community-based interventions focused on promoting healthy weight management can play a pivotal role in reducing the prevalence of mental health disorders, easing the burden on healthcare systems, and enhancing the overall quality of life [109]. By providing evidence-based guidance, this study supports policymakers in optimizing resources and implementing effective public health strategies, ultimately fostering sustainable improvements in community health.

Advantages and limitations

This study has several advantages. First, the study utilized cross-sectional data from NHANES to explore the potential association between VAI, LAP, and depression, and further examined the impact of sleep duration on this relationship, demonstrating a high degree of innovation. Second, VAI and LAP combine anthropometric measurements with laboratory biochemical data as tools for assessing visceral biomarkers, which are more efficient, simpler, and cost-effective than the expensive, complex, and radiation-intensive abdominal CT and MRI scans. Therefore, this approach is more suitable for routine clinical practice and large-scale screening. Third, the saturation effects and mediating role observed between visceral fat indicators and depression provide valuable guidance for clinical practice. When developing intervention strategies for individuals with visceral obesity, considering sleep quality can help improve patients' overall health more comprehensively.

Some of the limitations in this study are inherent. First, the evaluation of depression depended on self-reported questionnaires, which could be influenced by recall or reporting biases, potentially affecting the data's accuracy. Second, individuals with severe obesity and/or depression are often institutionalized for medical care, which may result in their disproportionate exclusion from the study. Third, the study design is cross-sectional, which means causality cannot be inferred. Cross-sectional studies collect data at a single point in time, so associations between variables can be observed without determining the direction of causality. Although the study found a significant association among VAI, LAP, and depression, whether changes in VAI and LAP lead to depression or whether depression affects these indicators due to simultaneous data collection cannot be determined. Future research should use longitudinal designs to track individuals over time and explore the causal relationship among VAI, LAP, and depression to obtain more robust evidence, thus better assessing the application value of these indicators in the prevention and intervention of depression.

Conclusion

This study found the connections of VAI and LAP with depression. VAI and LAP may be useful in assessing depression association. In addition, sleep duration is a mediator connecting VAI and LAP with depression. Incorporating these two easily accessible indicators of visceral fat obesity in community health needs assessments may provide more targeted interventions for depressive symptoms and improve patient outcomes. Although the results of this study provide some thresholds as reference indicators, further large-scale follow-up studies are needed to refine their application and validate the findings.

Abbreviations

VAI	Visceral adiposity index
LAP	Lipid accumulation product
NHANES	National Health and Nutrition Examination Survey
WWI	Weight-adjusted-waist index
CDC	Centers for Disease Control and Prevention
MEC	Mobile Examination Center
CAPI	Computer Assisted Personal Interview
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
BMI	Body mass index
WC	Waist measurement
PIR	The ratio of family income to poverty
TG	Triglyceride
HDL-C	High Density Lipoprotein cholesterol
LDL-C	Low-Density Lipoprotein Cholesterol
FFA	Free fatty acids; CRP: C-reactive protein
TNF-α	Tumor necrosis factor-alpha
IL-6	And interleukin-6
HPA	Hypothalamic–pituitary–adrenal axis
HFrEF	Heart failure with reduced ejection fraction
VIF	Variance inflation factor

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

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Authors' contributions
HYQ, ZD, and YZF wrote the first draft. HYQ, YZF, and WCN analyzed the results and provided graphs. ZD and QXCH provided the methodology and assisted with data organization. QXCH provided insights and suggestions during conceptualization, supervised, reviewed, and edited the manuscript. HYQ, WCN, and QXCH revised the manuscript. All authors reviewed the manuscript.

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Data availability
The datasets generated and/or analyzed during the current study are available in the NHANES database, [https://www.cdc.gov/nchs/nhanes/irba98.htm].

Declarations

Ethics approval and consent to participate
This study complies with the ethical principles set forth in the Declaration of Helsinki. The data used in this study were obtained from the National Health and Nutrition Examination Survey (NHANES), which is a publicly available and de-identified dataset. The data collection process of NHANES adheres to the Declaration of Helsinki, including obtaining informed consent from all participants and ensuring the confidentiality of their information. As this study involves secondary analysis of the NHANES data, no additional ethical approval or consent was required. This study was approved by the Ethics Review Board (ERB) of the National Center for Health Statistics (NCHS).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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