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Research paper

The relationship between depression and relative fat mass (RFM): A population-based study

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ABSTRACT

Background: Relative fat mass (RFM) is a novel indicator for measuring body fat. The relationship between RFM and depression was explored using National Health and Nutrition Examination Survey (NHANES) data from 2005 to 2018.

Methods: A general statistical description of the population included in the study was performed, and logistic analyses were used to explore the association between body mass index (BMI), waist circumference (WC), RFM and depression. Sensitivity analyses and restricted cubic spline (RCS) were also conducted to investigate the association between RFM and depression.

Results: A total of 28,836 participants were included in the study. In multivariate models, all obesity indices were associated with depression ($P < 0.001$). An increase of 1 SD in BMI, WC, and RFM was associated with a respective increased risk of depression of 2.3 %, 1.0 %, and 3.3 %. Excluding those taking antidepressants, the risk of depression was OR 1.88 (95 % CI: 1.26–2.79) for those with RFM in the highest quartile compared with those in the lowest quartile. After Inverse probability of weighting (IPW), the risk of depression in individuals with RFM in the highest quartile compared with individuals in the lowest quartile was 2.62 (95 % CI: 2.21–3.09). The RCS showed a possible nonlinear relationship between RFM and depression.

Conclusions: RFM is associated with depression, suggesting that attention to RFM may be helpful for depression research.

1. Introduction

Depressive disorder is a mental disorder characterised by persistent low mood, which may be accompanied by cognitive changes that affect the patient's ability to learn and work and, in severe cases, may lead to suicide (Ross et al., 2023; O'Connor et al., 2023). Depression ranks first in the global burden of mental illness and is a major public health problem (GBD 2019 Mental Disorders Collaborators, 2022). The etiology of depression is complex and may involve genetic, socio-environmental, and neurobiological aspects (Gal et al., 2023; Campbell et al., 2022; Malhi and Mann, 2018). Several studies have demonstrated a correlation between depression and obesity (He et al., 2023; Baldini et al., 2021; Silva et al., 2020).

Obesity is usually defined as excessive fat storage, and obesity has a major impact on physical health (Oliveros et al., 2014; Safaei et al., 2021). Body mass index (BMI) is a common measure of obesity. However, BMI is not sufficient to assess obesity because people with the same BMI can have different body shapes and fat distributions (Piché et al., 2018). In addition, BMI does not distinguish well between abdominal fat distribution. Waist circumference (WC) is a simple and reliable indicator of abdominal obesity (Ross et al., 2020). Researchers have developed a new indicator of obesity, relative fat mass (RFM), which includes WC and height to better assess fat mass (Woolcott and Bergman, 2018). When determining a person's proportion of total body fat, RFM is a more accurate measure than BMI (Woolcott and Bergman, 2018). RFM has been associated with a number of diseases including venous

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thromboembolism (Caiano et al., 2021), coronary heart disease (Efe et al., 2021), hypertension (Yu et al., 2020) and type 2 diabetes (Suthahar et al., 2023).

The relationship between depression and RFM is unclear. This study uses data from NHANES to explore the relationship between RFM and depression and to compare BMI, WC, and the strength of the association between RFM and depression.

2. Methods

2.1. Study design and participants

The National Health and Nutrition Examination Survey (NHANES) is a research programme that focuses on understanding the nutrition and health status of the population in the U.S. NHANES is primarily conducted by the National Center for Health Statistics (NCHS). We used NHANES data from 2005 to 2018 for our analyses. All participants were informed about the study and signed an informed consent form. Ethical content is available on the website (NHANES — NCHS Research Ethics Review Board Approval (cdc.gov)). Exclusion criteria were as follows: age <18 years, missing the Patient Health Questionnaire-9 (PHQ-9), RFM and covariates. Specific results are shown in the flowchart in Fig. 1.

2.2. Variables

2.2.1. Depression

In this study, depressive symptoms were assessed using the PHQ-9. PHQ-9 was used to assess mood over the past 2 weeks. Previous research has shown that if structured professional interviews are used as the criteria, a PHQ-9 score > 10 has a sensitivity of 88 % and a specificity of 88 % for major depressive disorder, representing clinically significant depression regardless of diagnostic status (Kroenke et al., 2001; Zhao et al., 2011).

2.2.2. Relative fat mass (RFM)

The RFM is calculated by WC, height and sex. RFM = 64 − (20 × height / waist circumference) + (12 × sex), sex = 1 for women and 0 for men (Woolcott and Bergman, 2018). Height and waist circumference were measured by a health professional in Mobile Examination Center (MEC). MEC had a special height measuring device on which the participants stood together, barefoot, with their backs to the board and their heads level, and then took the measurements. At the end of normal breathing, the line above the iliac crest in the mid-axillary line was the waist circumference, and measurements were accurate to within 0.1 cm (Ma et al., 2021).

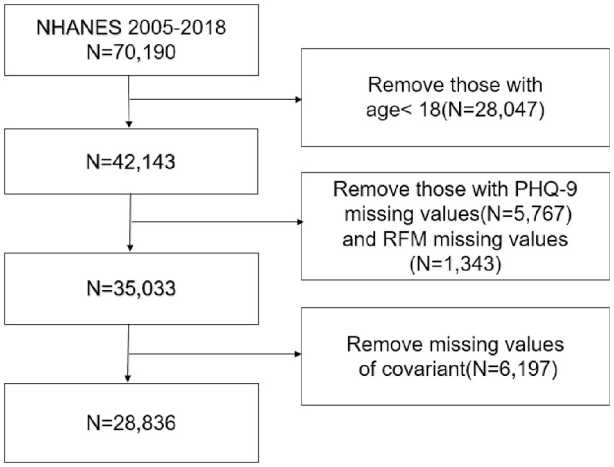

Fig. 1. Flow chart.

2.2.3. Covariates

The main covariates were demographic information, health habits, hypertension and diabetes. Demographic information was age, weight, height, poverty, race and marital status. Health habits were smoking and alcohol consumption. The race was categorised as White (non-Hispanic white), Mexican American, Black (non-Hispanic black), and other race. Education was categorised as: less than a high school education, high school graduate (including GED), some college or AA degree, college graduate or above. Marital status was categorised as: never married, married (including living with partner), divorced (including separated) and widowed. Smoking is categorised as: current (regular smoker, smoked >100 cigarettes), ever (ever smoked >100 cigarettes, currently not smoking), never (smoked <100 cigarettes in a lifetime). Alcohol consumption is categorised as: current (>12 drinks in the past year); ever (no alcohol in the past year, >12 drinks in the past); never (<12 drinks in a lifetime). There were three diagnostic criteria for hypertension: current use of antihypertensive medication, notification of diagnosed hypertension by a physician, and mean systolic blood pressure ≥ 140 mmHg or mean diastolic blood pressure ≥ 90 mmHg (Unger et al., 2020). There were six diagnostic criteria for diabetes mellitus (DM): reported diabetes mellitus, glycosylated haemoglobin ≥ 6.5 %, use of glucose-lowering medication and insulin, random blood glucose or 2-h OGTT blood glucose ≥11.1 mmol/l, and fasting blood glucose ≥7.0 mmol/l (American Diabetes Association, 2010).

2.3. Statistical analysis

To make the results more representative, we weighted the data from 2005 to 2018. Descriptive statistics were used to explore general characteristics of the depression and non-depression populations in the United States. Continuous variables were expressed as standard deviation (SD) ± and categorical variables were expressed as percentages.4 Logistic regression models were used to explore the association between BMI, WC, RFM and depression. In addition, we categorised RFM into quartiles (Q1: <−29.067, Q2: 29.067–34.771, Q3: 34.771–42.631, Q4: ≥42.631), with the lowest quartile as the reference category. The original models were not adjusted for any variables and model 1 was adjusted for age, sex and race. Model 2 adjusted for marital status, poverty and education based on model 1. Model 3 adjusted for smoking, alcohol consumption, hypertension and diabetes on top of model 2. Age was first transformed into a categorical variable with three age groups: 18–40 (excluding 40 years), 40–60 (excluding 60 years), and ≥60 years. We performed subgroup analyses and interactions for sex, age, race, smoking, alcohol consumption, diabetes, and hypertension. Sensitivity analyses were also performed. Logistic analyses were performed after excluding patients on antidepressants. We used Inverse probability of weighting (IPW) regression analysis on the unweighted raw data to deal with potential confounders (Chesnaye et al., 2022). Finally, restricted cubic spline (RCS) analysis was performed on RFM. All data were statistically analyzed using R4.3.2. Two-sided tests were used and differences were considered statistically significant when $p < 0.05$.

3. Results

3.1. Characteristics of the participant

A total of 28,836 subjects were included in the study, weighted to represent 178 million US adults. Differences in clinical characteristics between the depression and non-depression groups are shown in Table 1. Body weight (84.64 ± 0.67 vs. 82.92 ± 0.24), WC (102.34 ± 0.53 vs. 98.97 ± 0.22), RFM (38.09 ± 0.23 vs. 34.91 ± 0.09), and BMI (30.55 ± 0.22 vs. 28.88 ± 0.09) were higher in the depression group than in the non-depression group, and the differences were statistically significant ($p = 0.01$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$). Poverty, gender, height, race, education, marital status, smoking, alcohol consumption, hypertension and diabetes mellitus differed

Table 1
Weighted baseline characteristics of patients with or without depression.

Variable	Total	Without depression	With depression	*p*-Value
Age (years)	47.07 ± 0.25	47.14 ± 0.26	46.20 ± 0.42	0.05
Poverty	3.05 ± 0.03	3.13 ± 0.03	2.13 ± 0.06	<0.0001
RFM	35.15 ± 0.09	34.91 ± 0.09	38.09 ± 0.23	<0.0001
Weight (kg)	83.05 ± 0.24	82.92 ± 0.24	84.64 ± 0.67	0.01
Height (cm)	168.97 ± 0.10	169.17 ± 0.10	166.51 ± 0.26	<0.0001
WC (cm)	99.23 ± 0.21	98.97 ± 0.22	102.34 ± 0.53	<0.0001
BMI (m/kg^2)	29.01 ± 0.08	28.88 ± 0.09	30.55 ± 0.22	<0.0001
Sex (%)				<0.0001
Female	50.57	49.52	63.38	
Male	49.43	50.48	36.62	
Race (%)				<0.001
Black	10.58	10.39	12.95	
Mexican American	7.96	7.98	7.63	
Other race	12.06	11.89	14.13	
White	69.4	69.73	65.28	
Marital (%)				<0.0001
Divorced	12.90	12.07	23.10	
Married	64.04	65.32	48.31	
Never married	17.80	17.50	21.54	
Widowed	5.26	5.11	7.05	
Education (%)				<0.0001
College graduate or above	30.21	31.51	14.18	
High school graduate	23.12	22.78	27.19	
Less than high school	14.76	13.97	24.48	
Some college or AA degree	31.92	31.74	34.15	
Smoking (%)				<0.0001
Never	54.71	56.09	37.76	
Former	24.85	25.07	22.22	
Now	20.44	18.84	40.03	
Drinking (%)				<0.0001
Never	10.24	10.37	8.58	
Former	13.09	12.56	19.52	
Yes	76.67	77.06	71.9	
DM (%)				<0.0001
DM	13.63	13.11	19.98	
IFG	4.7	4.77	3.75	
IGT	3.48	3.44	3.9	
No	78.19	78.67	72.37	
Hypertension (%)				<0.0001
Yes	37.37	36.57	47.2	
No	62.63	63.43	52.8	

Abbreviations: RFM: relative fat mass; WC: waist circumference; BMI: body mass index; DM: diabetes mellitus.

between the depressed and non-depressed groups (all $p < 0.0001$).

3.2. Association of RFM with depression

The relationship between BMI, WC, RFM and depression is shown in Table 2. RFM was divided into four groups. After adjustment for sex, age, race, PIR, marital status, smoking, height, educational level, history of hypertension, diabetes mellitus and alcohol consumption, the ORs (95 % CI) for depression from the lowest to the highest RFM were 1. 00 (reference), 1.176 (0.965,1.434), 1.341 (1.041,1.729) and 1.987 (1.508,2.619), respectively. Between increasing levels of RFM and the risk of depression (p for trend <0.0001). In a multifactorial logistic regression analysis model, all obesity-related indices were significantly associated with depression ($p < 0.001$). The risk of depression increased by 2.3 % and 1 % for each 1 SD increase in BMI and WC, respectively. The risk of depression increased by 3.3 % for each 1 SD increase in RFM, respectively. The results are shown in Table 2, and the results of the RCS showed a "J" shaped relationship between RFM and depression (p for non-linear <0.0001). The results are presented in Fig. 2.

3.3. Subgroup analyses

The results of the subgroup analyses are shown in Table 3. Compared with the lowest RFM (Q1), the highest RFM (Q4) was found in males (6.00, OR; 95 % CI, 1.40,25.72), whites (2.00, OR; 95 % CI, 1.15,3.47), those without diabetes (2. 05, OR; 95 % CI, (1.35, 3.12)) or without hypertension (2.85, OR; 95 % CI, (1.65, 4.94)), drinking (1.83, OR; 95 %

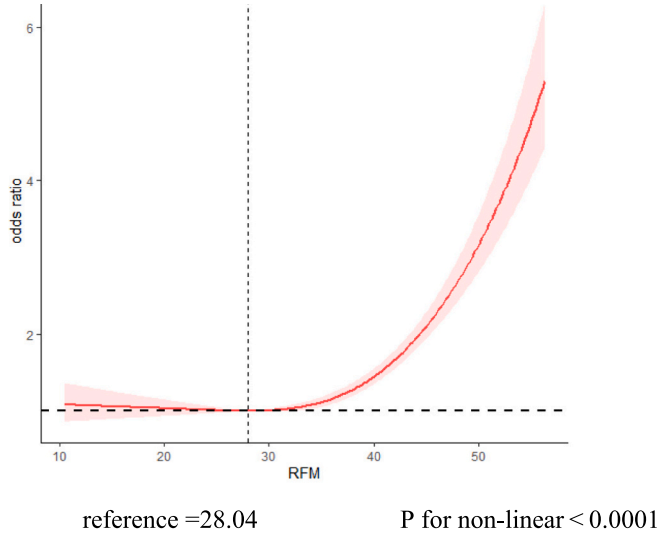

Fig. 2. Nonlinear relationship between the RFM and depression, results from the restricted cubic spline (RCS) analysis.

Table 2
Association between BMI, WC, RFM and depression.

	Crude model OR (95 % CI)	Model 1 OR (95 % CI)	Model 2 OR (95 % CI)	Model 3 OR (95 % CI)
BMI	1.033 (1.025,1.042)	1.032 (1.023,1.040)	1.032 (1.024,1.040)	1.023 (1.015,1.031)
WC	1.012 (1.008,1.016)	1.016 (1.012,1.019)	1.014 (1.011,1.018)	1.010 (1.006,1.014)
RFM	1.045 (1.038,1.053)	1.053 (1.040,1.065)	1.046 (1.034,1.058)	1.033 (1.021,1.044)
RFMQ				
Q1 (<−29.067)	Ref	Ref	Ref	Ref
Q2 (29.067–34.771)	1.131 (0.945,1.354)	1.208 (1.001,1.459)	1.293 (1.065,1.572)	1.176 (0.965,1.434)
Q3 (34.771–42.631)	1.460 (1.220,1.747)	1.562 (1.226,1.991)	1.577 (1.226,2.028)	1.341 (1.041,1.729)
Q4 (≥42.631)	2.615 (2.213,3.091)	2.880 (2.215,3.743)	2.590 (1.981,3.387)	1.987 (1.508,2.619)
p for trend	<0.0001	<0.0001	<0.0001	<0.0001

Abbreviations: WC: waist circumference; BMI: body mass index; RFM: relative fat mass. Model 1: adjusted for age, sex and race; Model 2: adjusted for age, sex, race, marital status, poverty, educational level; Model 3: further adjusted for drinking, smoking, hypertension, diabetes based on Model 2.

Table 3
Subgroup analyses stratified by sex, race, smoking, drinking, age, diabetes and hypertension.

RFM	Q1 (<−29.067)	Q2 (29.067–34.771)	*p*	Q3 (34.771–42.631)	*p*	Q4 (≥42.631)	*p*	*p* for trend	*p* for interaction
Race									0.01
Black	Ref	1.83(1.34,2.49)	<0.001	1.32(0.77,2.27)	0.31	1.62(0.78,3.37)	0.2	0.44	
White	Ref	1.08(0.78,1.49)	0.63	1.41(0.91,2.18)	0.12	2.00(1.15,3.47)	0.01	0.01	
Other race	Ref	0.92(0.59,1.44)	0.71	0.90(0.51,1.60)	0.73	1.64(0.73,3.71)	0.23	0.14	
Mexican American	Ref	1.46(0.89,2.39)	0.13	0.83(0.37,1.87)	0.65	1.08(0.41,2.88)	0.87	0.76	
Smoking									0.95
Never	Ref	1.20(0.85,1.70)	0.29	1.49(0.94,2.35)	0.09	2.53(1.46,4.38)	0.001	<0.001	
Former	Ref	1.25(0.81,1.92)	0.31	1.68(1.00,2.83)	0.05	2.60(1.30,5.22)	0.01	0.01	
Now	Ref	1.01(0.70,1.46)	0.97	0.91(0.56,1.48)	0.71	1.13(0.58,2.18)	0.72	0.67	
Drinking									0.89
Never	Ref	1.17(0.49,2.80)	0.72	1.32(0.42,4.08)	0.63	1.75(0.47,6.50)	0.4	0.31	
Former	Ref	1.24(0.79,1.94)	0.35	1.25(0.65,2.41)	0.5	1.95(0.87,4.39)	0.1	0.08	
Yes	Ref	1.12(0.85,1.47)	0.42	1.27(0.89,1.82)	0.19	1.83(1.17,2.86)	0.01	0.004	
DM									0.61
No	Ref	1.22(0.95,1.58)	0.12	1.38(0.98,1.96)	0.06	2.05(1.35,3.12)	0.001	<0.001	
Yes	Ref	1.03(0.64,1.64)	0.91	1.17(0.63,2.19)	0.61	1.92(0.93,4.00)	0.08	0.09	
Hypertension									0.24
Yes	Ref	0.86(0.63,1.19)	0.36	0.87(0.56,1.34)	0.51	1.17(0.68,2.00)	0.57	0.41	
No	Ref	1.45(1.07,1.97)	0.02	1.81(1.21,2.70)	0.004	2.85(1.65,4.94)	<0.001	<0.001	
Sex									0.68
Women	Ref	1.22(0.53,2.77)	0.64	1.19(0.53,2.67)	0.66	1.66(0.73,3.74)	0.22	0.01	
Men	Ref	1.22(0.95, 1.57)	0.12	1.81(1.16,2.84)	0.01	6.00(1.40,25.72)	0.02	0.01	
Age									0.75
18–40	Ref	1.34(0.96,1.87)	0.09	1.41(0.92,2.18)	0.12	2.26(1.30,3.91)	0.004	0.004	
40–60	Ref	1.01(0.67,1.54)	0.95	1.24(0.74,2.09)	0.4	1.92(0.97,3.79)	0.06	0.03	
≥60	Ref	0.91(0.55,1.49)	0.7	1.07(0.54,2.11)	0.85	1.38(0.61,3.14)	0.44	0.29	

Abbreviations: RFM: relative fat mass; DM: diabetes mellitus. Adjusted for age, sex, race, marital status, poverty, educational level, drinking, smoking, hypertension, diabetes except the stratification factor itself.

CI, 1.17, 2.86) and those aged 18–40 years (2.26, OR; 95 % CI,1.30, 3.91), never smoking, (2.53, OR; 95 % CI, 1.46,4.38), ever smoking (2.60, OR; 95 % CI, 1.30,5.22). However, black, other race, Mexican American, smoking, never drink, ever drink, hypertension, diabetes, female, 40–60, ≥60 had no positive association.

3.4. Sensitivity analyses

The results of sensitivity analysis are presented in Table 4. After excluding antidepressant individuals, the OR for the highest versus lowest quartile was 1.88 (95 % CI: 1.26–2.79). After IPW, the OR for the highest versus lowest quartile was 2.62 (95 % CI: 2.21–3.09). The test for trend was also positive for both (*p* for trend <0.01).

Table 4
Sensitivity analyses.

RFM	OR (95 % CI)	*p* for trend
Excluding participants take antidepressants		
Q1 (<−29.067)	Ref	
Q2 (29.067–34.771)	1.15(0.90,1.48)	
Q3 (34.771–42.631)	1.28(0.93,1.77)	
Q4 (≥42.631)	1.88(1.26,2.79)	<0.001
Inverse probability of weighting		
Q1 (<−29.067)	Ref	
Q2 (29.067–34.771)	1.13(0.95,1.35)	
Q3 (34.771–42.631)	1.46(1.22,1.75)	
Q4 (≥42.631)	2.62(2.21,3.09)	<0.001

Adjusted for age, sex, race, marital status, poverty, educational level, drinking, smoking, hypertension and diabetes.

4. Discussion

This cross-sectional study examined the association between RFM and depression. Our study found that people with high levels of RFM were prone to depression and that there may be a J-shaped relationship between RFM and depression. In addition, we performed sensitivity analyses and subgroup analyses to confirm the reliability of the results. To our knowledge, this is the first study to explore the relationship between RFM and depression in a representative US population.

Obesity and depression are two conditions that significantly affect the lives of individuals and the general public (Milaneschi et al., 2019). BMI and WC are common measures of obesity (Wiltink et al., 2013). Obesity increases the risk of depression in children and adolescents, according to a meta-analysis (Rao et al., 2020), and adolescent obesity may be associated with depression in late adulthood, according to a Finnish birth cohort study (Herva et al., 2006). A longitudinal cohort study in Taiwan showed a negative association between older adults and depression, which may be related to cultural differences, age and different measures of obesity (Chang and Yen, 2012). Obesity has also been shown to be associated with multiple episodes of depression (Nigatu et al., 2015).

In addition, there are some new indicators of obesity that have been linked to depression. A study by Cho et al. showed that visceral adiposity was associated with depression in women (Cho et al., 2019)). Pericardial adipose tissue volume was greater in depressed patients than in healthy controls (Kahl et al., 2014). RFM may also be a reliable indicator of the relationship between depression and obesity. Future clinical and longitudinal studies with larger samples are needed to investigate the relationship between RFM and depression.

BMI was first developed by a Belgian mathematician 200 years ago and is currently the most widely used tool for diagnosing obesity (Eknoyan, 2007). BMI cannot differentiate between lean and fat mass, visceral and subcutaneous fat (Humphreys, 2010). Because of these limitations, several studies have begun to explore WC or visceral adiposity as an alternative to BMI (Ross et al., 2020; Woolcott and Bergman, 2018). RFM is a novel obesity index developed by researchers in the United States that provides a more accurate estimate of the proportion of total body fat compared to BMI (Woolcott and Bergman, 2018). In large cohorts from the United States, Brazil and Korea, adiposity measured by dual-energy X-ray absorptiometry (DXA) correlated more strongly with RFM than with BMI (14,32,33). Our study found a stronger correlation between RFM (OR = 1.033) and depression than BMI (OR = 1.023) and WC (OR = 1.010).

It has been shown that improving lifestyle can prevent and reduce

depression (Zhao et al., 2020; Harvey et al., 2018). In the 2005 to 2018 cohort of the NHANES, we found that all obesity indicators were associated with depression. Among all age groups, RFM was most strongly associated with depression in the younger cohort (18–40 years). These findings are similar to those of the Chen study (Chen et al., 2009), in which young obese individuals were strongly associated with depression. In the younger population, depression may be influenced by BMI through emotional eating (Lazarevich et al., 2016). This study found a strong association between RFM and depression in the middle-aged male population. This may be related to the fact that the amount of fat is lower in men than in women, male RFM is more abnormal in lipid metabolism than in women, and abnormal lipid metabolism is associated with depression (Li et al., 2017; Kobo et al., 2019; Zhu et al., 2023).

Our study has a number of strengths: first, we used a large representative sample of the US population. Second, RFA is easier to measure than DXA and has no radiation intensity, making it easier to use in practice. Third, we performed IPW and excluded the effects of antidepressant medication and still found an association between RFM and depression. This study also has some drawbacks. It is a cross-sectional study and a causal relationship between RFM and depression cannot be inferred. Second, we used the PHQ-9 scale to diagnose depression and were unable to examine the effect of disease duration on RFM. The data used are representative of the US population and may not be representative of other countries.

5. Conclusion

RFM was positively associated with depression in the U.S. population. RFM was a conveniently measured indicator of obesity that can be used in clinical practice for depression. Prospective studies are needed to reveal the relationship between RFM and depression.

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CRediT authorship contribution statement

Xianlin Zhu: Writing – review & editing, Writing – original draft, Software, Formal analysis, Data curation. **Ya Yue:** Writing – original draft, Software, Resources. **Lin Li:** Writing – original draft. **Liying Zhu:** Writing – original draft. **Yuexi Cai:** Writing – original draft. **Yanping Shu:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors report no conflicts of interest in this work.

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