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Visceral adiposity index, premature mortality, and life expectancy in US adults

Mei Xue[1,2], Xiaoqian Zhang[1,2], Kening Chen[3,4], Fangjieyi Zheng[5], Bochun Wang[6], Qiushi Lin[7], Zhixin Zhang[3*], Xiaoqun Dong[7*] and Wenquan Niu[5*]

Abstract

Importance Visceral adiposity index (VAI) vividly reflects body fat distribution through comprehensively integrating body mass index, sex, waist circumference, triglycerides, and high-density lipoprotein cholesterol. While VAI is an established predictor of various clinical outcomes, its relationship with premature mortality and life expectancy remains unclear.

Objective To explore the association between VAI and premature mortality or life expectancy in a nationally representative cohort of US adults.

Methods This study included adults who participated in the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2018, linked to the National Death Index through December 31, 2019. Data were analyzed from August to October, 2024. VAI was categorized into quartiles from the lowest Q1 to the highest Q4. Primary endpoints were premature mortality (death before 80 years of age) and life expectancy.

Results A total of 43,672 participants (women: 22,164; men: 21,508) aged > 20 years were included. Over a median follow-up of 9.2 years (IQR: 4.9–13.8), 3,187 premature deaths were documented. Higher VAI quartiles were significantly associated with increased multi-adjusted premature mortality risk compared to Q1 (Q3 vs. Q1: hazard ratio [HR], 95% confidence interval [CI]: 1.30, 1.05 to 1.61; Q4 vs. Q1: 1.68, 1.34 to 2.11). This association was particularly pronounced in women (Q3 vs. Q1: 1.53, 1.01 to 2.30; Q4 vs. Q1: 2.36, 1.52 to 3.68), with significant linear trends ($P < 0.001$). Estimated life expectancy at age 40 years was 41.45 (95% CI: 41.24 to 41.66), 41.32 (41.11 to 41.53), 40.55 (40.35 to 40.75), and 39.26 (39.08 to 39.45) years in Q1, Q2, Q3, and Q4 of VAI, respectively. By sex, estimated life expectancy at age 40 in Q4 was reduced by 3.33 years in women and 1.24 years in men, compared to Q1. By race and ethnicity, it was shortened by 3.90 years in Black participants and 1.68 years in White participants in Q4 group, compared to Q1.

Conclusions In this nationwide cohort study, higher VAI was significantly associated with an increased risk of premature mortality and reduced life expectancy at age 40 among US adults. These associations we heterogeneous by sex, race and ethnicity, more pronounced in women and Black participants.

Keywords Visceral adiposity index, Premature mortality, Life expectancy

*Correspondence:
Zhixin Zhang
zhangzhixin032@163.com
Xiaoqun Dong
dongxi19@msu.edu
Wenquan Niu
niuwenquan_shcn@163.com
Full list of author information is available at the end of the article

Introduction

Obesity is a major contributor to premature mortality and reduced life expectancy worldwide. In 2019, an estimated 5 million premature deaths were attributed to obesity (body mass index [BMI] ≥ 30 kg/m^2) [1]. Traditionally, obesity is defined and classified by BMI; however, BMI cannot distinguish body fat from muscle mass [2–4]. Because fat distribution varies significantly among individuals with the same BMI [5], it is essential to identify alternative indices that can more accurately assess body fat distribution.

Visceral adiposity index (VAI) [6] has gained attention as a more comprehensive metric, integrating BMI, sex, waist circumference, triglycerides, and high-density lipoprotein (HDL) cholesterol. Lipid metabolism plays a critical role in visceral fat accumulation, as excessive triglycerides and reduced HDL cholesterol are hallmarks of dysfunctional adipose tissue [7]. These lipid abnormalities are closely linked to insulin resistance, systemic inflammation, and cardiovascular risk, making them key indicators of visceral adiposity [8]. In theory, VAI is designed to capture sex-specific distribution and functionality of body fat, providing a more precise assessment of visceral fat. Currently, VAI has been established as a strong predictor of various clinical endpoints, including cardiometabolic disorders [9], diabetic kidney disease [10], cancer [11], and all-cause or specific-cause mortality [12–14]. However, no study has investigated the relationship of VAI with premature mortality and life expectancy, largely due to the lack of lipid biomarkers in large cohorts and the extended follow-up required to record sufficient mortality events. To address this gap, we aimed to explore potential association of VAI with premature mortality or life expectancy in a nationally representative cohort of US adults.

Methods

Study participants

Participants were recruited from the US National Health and Nutrition Examination Survey (NHANES) [15]. Since 1999, NHANES has selected a series of nationally representative samples of the noninstitutionalized US civilian population in 2-year cycles by taking a complex, stratified, multistage cluster sampling strategy. The NHANES was approved by the ethics review board of the National Center for Health Statistics. All participants provided signed consents to perform health-related statistical research linked to the National Death Index.

This study included 10-cycle NHANES data between 1999–2000 and 2017–2018 collected through interviews, physical examinations, and laboratory measurements [16]. Initially, 101,316 participants from the NHANES 1999–2018 were included. After excluding 47,208 participants aged under ≤ 20 years, 1,301 being pregnant or breastfeeding at the time of examination, 9,002 having missing necessary information for VAI calculation, and 133 having incomplete survival data, totally 43,672 participants were included in the final analysis (Fig. 1).

VAI definition

VAI is an indicator for assessing visceral fat distribution and functionality. It simultaneously takes 6 indexes into consideration—sex, weight, height, waist circumference (WC, cm), triglycerides (TG, mmol/L), and HDL cholesterol (mmol/L). VAI is calculated according to the following sex-specific equations developed by Amato et al. [6]:

$$\text{For men}: \text{VAI} = \frac{\text{WC}}{39.68+(1.88*\text{BMI})} * \frac{\text{TG}}{1.03} * \frac{1.31}{\text{HDL}}$$
$$\text{For women}: \text{VAI} = \frac{\text{WC}}{36.58+(1.89*\text{BMI})} * \frac{\text{TG}}{0.81} * \frac{1.52}{\text{HDL}}$$

Here, BMI is calculated as weight (kg) divided by the square of height (m).

Survival outcomes

Two endpoints were assessed in this study: premature mortality and life expectancy. Mortality data were ascertained via linking NHANES to the National Death Index through December 31, 2019 [17]. Premature mortality was defined as deaths occurring before 80 years of age [18]. Follow-up time was computed from the date of recruitment until the date of deaths occurring before 80 years of age or December 31, 2019, whichever occurred first. Censoring was recorded for participants who surpassed 80 years of age irrespective of experience deaths before December 31, 2019 and who aged less than 80 years and did not experience deaths before December 31, 2019. Life expectancy from age of 20 to 100 years was estimated by VAI quartiles.

Additionally, cause-specific premature mortality was explored. The major specific causes of deaths were coded according to the International Statistical Classification of Diseases and Related Health Problems, 10 th version (ICD- 10), including cardiovascular disease (CVD) (I00-I99), cancer (C00-C97), and others.

Assessment of covariates and mediators

Covariates included age, sex, race/ethnicity, poverty income ratio (PIR), health insurance, cigarette smoking, alcohol drinking, and family history (CVD or diabetes). Race/ethnicity was self-reported based on questions with fixed category responses, including Hispanic American, non-Hispanic Black, non-Hispanic White, and other (American Indian or Alaska Native, Native Hawaiian or Pacific Islander, and non-Hispanic Asian). PIR was coded into low (≤ 1.0), intermediate (> 1.0 and ≤ 3.0), and high

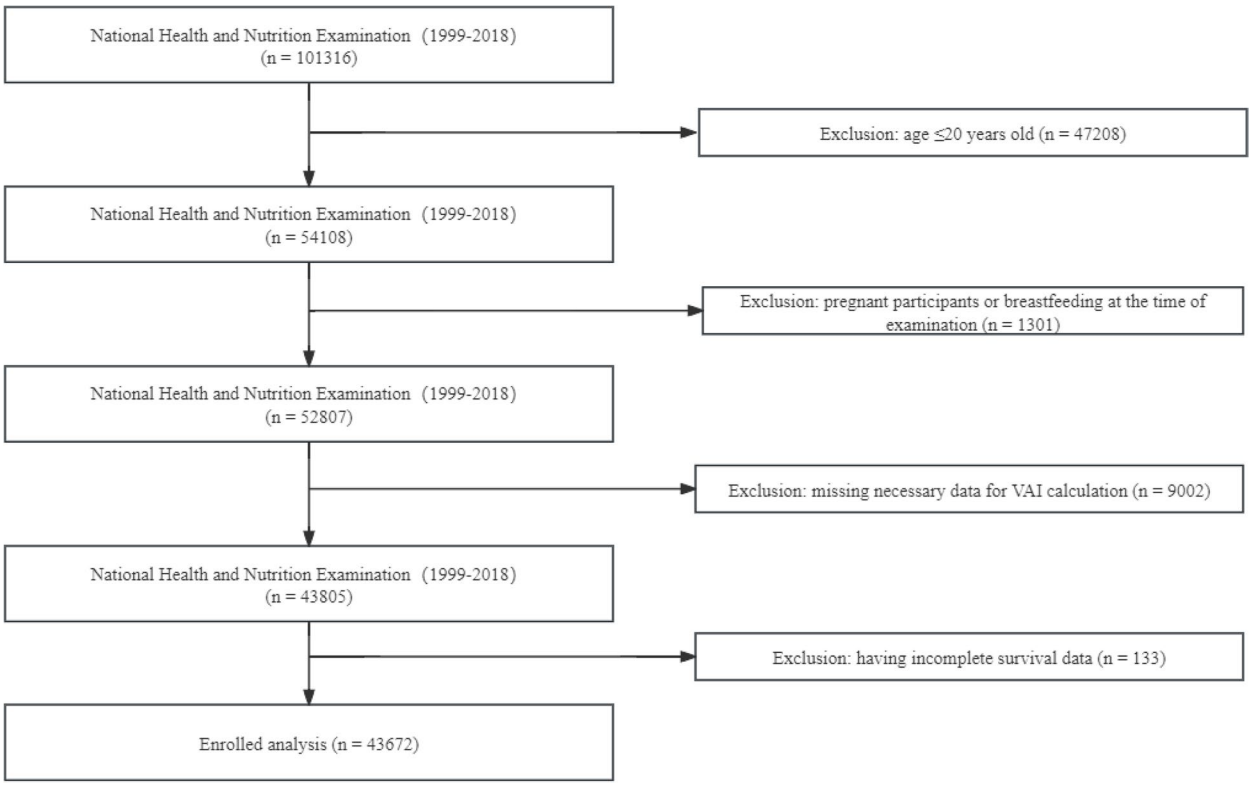

Fig. 1 Flowchart of Participant Selection from the US NHANES (1999–2018)

(> 3.0); health insurance coded into private insurance, government-sponsored insurance, and uninsured. Cigarette smoking was grouped into three categories: no, former, and current smoking; alcohol consumption grouped into four categories: no, light (up to 3 drinks per week), moderate (for women, 3–7 drinks per week; for men, 3–14 drinks per week), and heavy drinking (for women, > 7 drinks per week; for men, > 14 drinks per week). Family history of CVD or diabetes were collected during in-home interviews.

The association of VAI with mortality might be mediated by chronic diseases (such as diabetes, hypertension, CVD, and cancer) [9–11]. It is not appropriate to adjust for these chronic conditions. In this study, chronic diseases were considered in sensitivity analyses. Hypertension was defined as the presence of any of the following criteria: a self-reported history of hypertension, systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or the use of antihypertensive medications. Diabetes was defined as self-reported history of diabetes, fasting blood glucose ≥ 7.0 mmol/L, oral glucose tolerance test ≥ 11.1 mmol/L, glycated hemoglobin A1c (HbA1c) ≥ 6.5%, the use of antidiabetic medications, or injecting insulin to control blood glucose. CVD was coded based on a self-reported history of coronary heart disease, congestive heart failure, angina, or myocardial infarction. Cancer was identified through a self-reported history of any type of cancer or malignant neoplasm.

Statistical analysis

All statistical estimates are nationally representative. Sampling weights, primary sampling units, and strata were considered in all analyses to adapt to complex NHANES designs and address oversampling in subgroups. Restricted cubic spline (RCS) curve with 4 knots was depicted to illustrate the association between VAI and premature mortality and to test the likelihood of nonlinearity. Because of nonsignificant nonlinearity (Fig. 2), to facilitate data interpretation, VAI was coded into quartiles (Q1 to Q4) in all study participants. The first quartile (Q1) was assigned as the reference group. Before regressing VAI quantiles on premature mortality, proportional hazards assumption of Cox models was examined using both Schoenfeld test and Kaplan–Meier curve. If this assumption was violated, the assumption of Weibull models was tested, that is, $ln(-ln(S(t)))$ is linear with $\ln(t)$ (here, $S(t)$ is survival function, t is survival time, and ln is natural logarithm). The association between a VAI quantile and premature mortality was examined, with follow-up time defined as the time metric

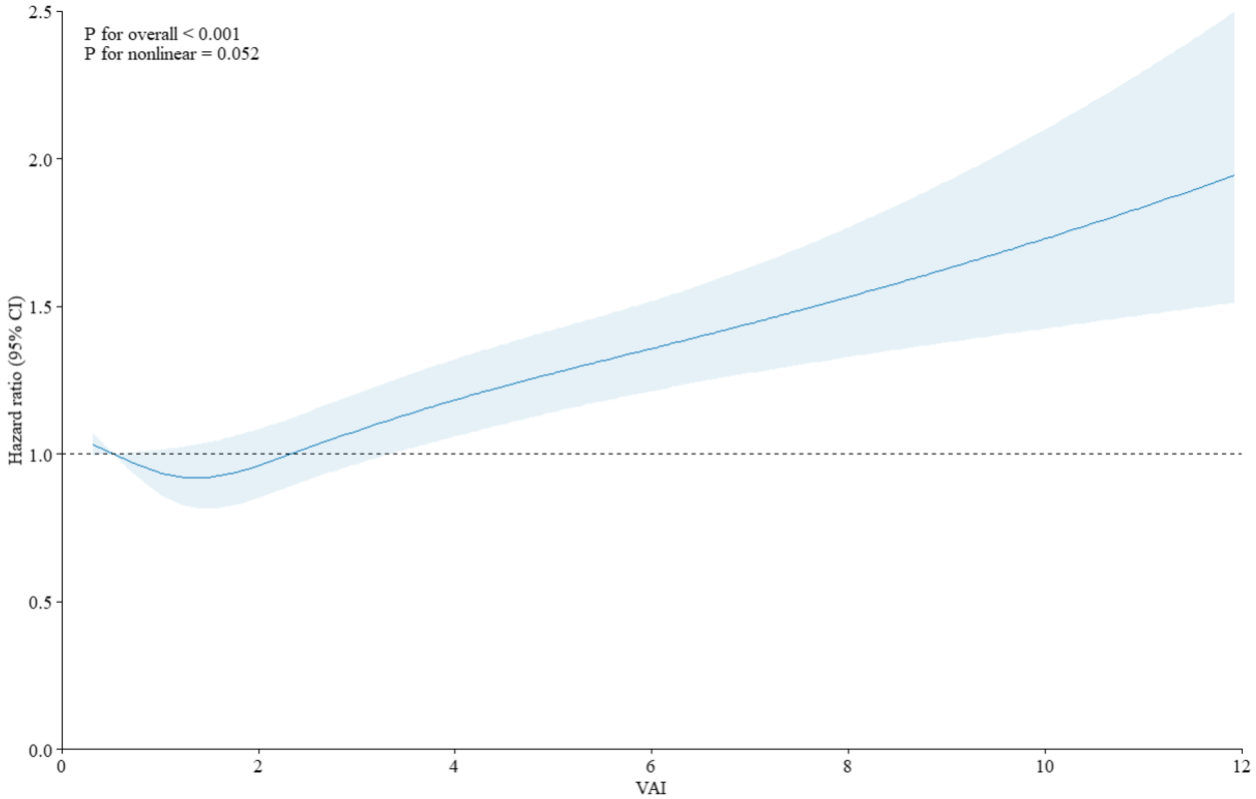

Fig. 2 Restricted Cubic Spline Analysis for VAI: Visual Inspection

before and after adjusting for pre-specified covariates in a graded manner. Risk estimates were quantified using hazard ratio (HR) and 95% confidence interval (CI). First, no adjustment was made; next, age, sex, and race/ethnicity were adjusted; then, PIR, insurance status, cigarette smoking, alcohol drinking, and family history (CVD or diabetes) were additionally adjusted. In addition, the Fine-Gray method was used to estimate the competing risk for the association between VAI and cause-specific premature mortality. Further subgroup analyses by sex and race and ethnicity were conducted. The interaction of VAI with sex or race/ethnicity was assessed by adding interaction terms to the Weibull models.

Several sensitivity analyses were performed to test the robustness of the results. First, premature mortality was redefined as deaths occurring before age of 75 years in association with VAI. Second, covariates with missing values were imputed by multiple-imputation method. Third, survey cycles were additionally adjusted in multivariable analyses. Fourth, VAI was categorized into deciles. Fifth, premature mortality risk (death prior to age 80) was analyzed across BMI quartiles and deciles, and the goodness-of-fit of models for VAI and BMI was compared.

Life expectancy was estimated using life table based on three key components: (i) age-specific population all-cause mortality rates derived from the National Vital Statistics System of National Center for Health Statistics (NCHS, https://www.cdc.gov/nchs/products/nvsr.htm, in 2019, from 20 to 100 years); (ii) age-specific (in 15-year intervals) prevalence of all VAI quartiles from the NHANES dataset; (iii) multi-adjusted HRs for premature mortality across VAI quartiles (relative to Q1 VAI) derived from the NHANES dataset. Because NHANES respondents aged 8+ 0 years and over at the time of screening are top-coded at age of 80 years, mortality rates over 80 years were not available and thus estimated using the Poisson regression model after adjusting for covariates aforementioned. This model included both linear and quadratic terms for the midpoints of single-year age groups minus 19.5 years, as presented in Fig. 3. The 95% CIs of life expectancy estimates were computed as previously described by the South East Public Health Observatory (SEPHO) [19]. Furthermore, the Arriaga's decomposition [20, 21] was employed to assess mortality inequalities in premature mortality (deaths from CVD, cancer, or other causes) between participants with the highest and lowest VAI quartiles. In subgroup analyses,

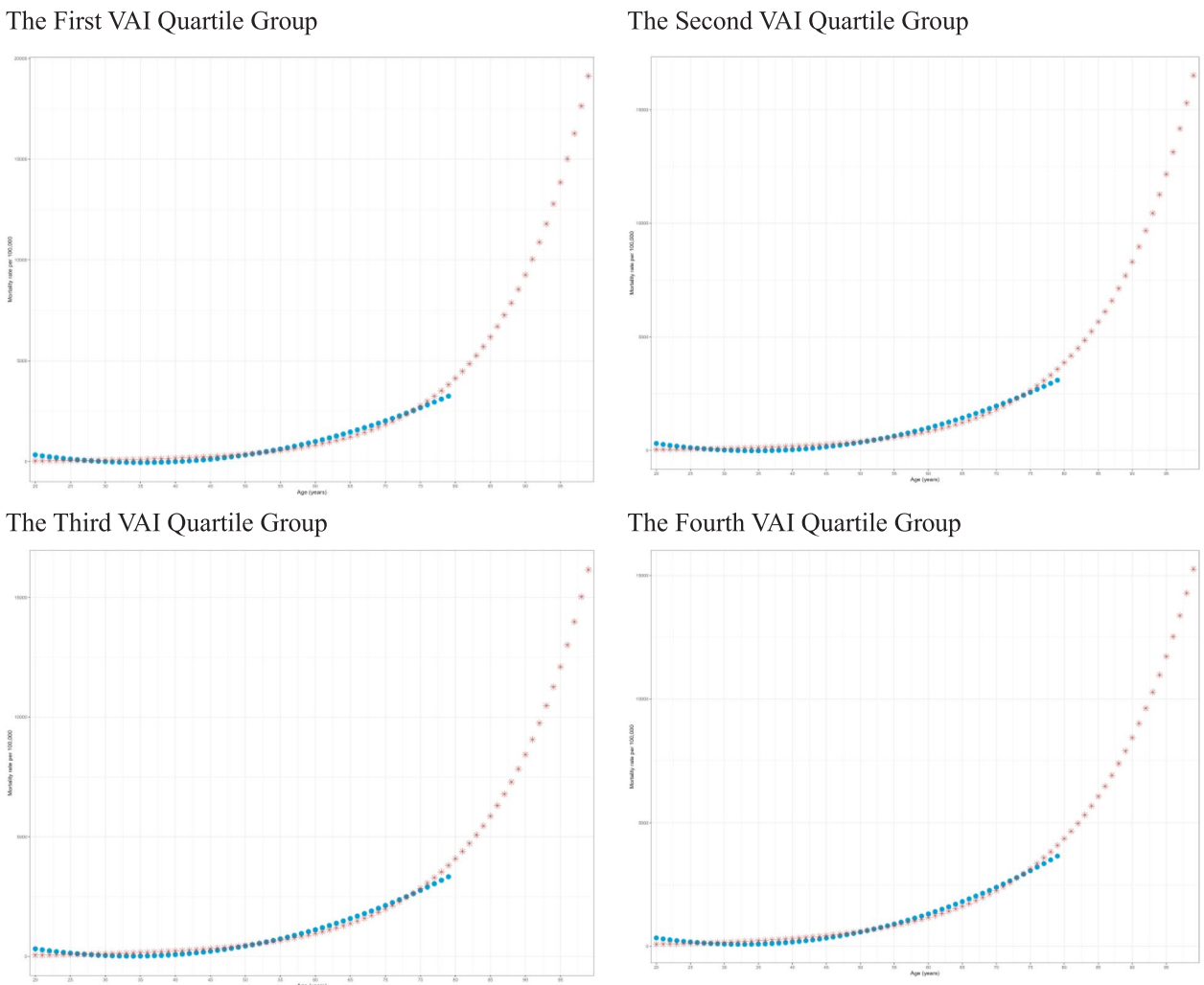

Fig. 3 Model Incorporating Linear and Quadratic Terms for Midpoints of Single-year Age Groups Minus 19.5 Years

Q1 and Q2 were combined as a single group in women due to the limited sample sizes.

All analyses were performed using STATA software (version 16.0, Stata Corp, College Station, TX, USA) and R coding platform (version 4.3.3). A two-tailed *P* value <0.05 was considered statistically significant. Data were analyzed between October 1 and December 30, 2024.

Results

Baseline characteristics

This study included 43,672 participants (women: 22,164; men: 21,508) aged >20 years from 10-cycle NHANES data. Weighted characteristics of participants across VAI quartiles by sex are presented in Table 1. The percentage (mean age ± SE) of women in Q1 (≤ 1.00), Q2 (1.00 to 1.70), Q3 (1.70 to 2.94), and Q4 (> 2.94) VAI was 29.70% (44.38 [0.36]), 27.77% (47.52 [0.41]), 23.95% (51.32 [0.38]), and 18.58% (52.32 [0.42]), respectively; for men, the corresponding percentage was 31.11% (44.69 [0.43]), 26.47% (47.10 [0.38]), 24.05% (47.48 [0.44]), and 18.37% (47.92 [0.43]), respectively. Generally, participants with higher VAI quartiles tended to be older or of Hispanic American or White origins, have lower levels of household income and education, have less access to health insurance, have more unfavorable lifestyles (smoking and drinking alcohol), and be more likely to have CVD, diabetes, hypertension, cancer, and family history (CVD or diabetes) in both sexes.

VAI and premature mortality

Over a median follow-up of 9.2 (interquartile range: 4.9–13.8) years, 3,187 deaths were documented. The Schoenfeld test and Kaplan–Meier curve revealed violation of proportional hazards assumption of Cox models (Fig. 4). Given the linear relation between ln(-ln(S(t))) and ln(t)

Table 1 Characteristics of Study Participants from the US NHANES 1999–2018 at Baseline According to VAI Quartiles[a]

Characteristic	VAI quartiles, weighted No. (%), millions			
	Q1 (≤ 1.00)	Q2 (1.00 to ≤ 1.70)	Q3 (1.70 to ≤ 2.94)	Q4 (> 2.94)
Women				
Participants	30.19 (29.70)	28.23 (27.77)	24.35 (23.95)	18.89 (18.58)
Age,[b] mean (SE), y	44.38 (0.36)	47.52 (0.41)	51.32 (0.38)	52.32 (0.42)
Race and ethnicity[c]				
Hispanic American	1.52 (5.03)	2.09 (7.40)	2.20 (9.03)	1.69 (8.96)
Non-Hispanic Black	5.03 (16.65)	3.48 (12.34)	2.24 (9.18)	0.99 (5.22)
Non-Hispanic White	19.88 (65.85)	19.30 (68.36)	16.63 (68.27)	13.92 (73.66)
Other	3.76 (12.47)	3.36 (11.90)	3.29 (13.52)	2.30 (12.16)
Marital status				
Married	18.85 (62.96)	17.36 (62.01)	15.09 (62.58)	11.46 (61.38)
Separated	5.62 (18.78)	6.83 (24.39)	6.05 (25.10)	5.46 (29.24)
Single	5.47 (18.26)	3.81 (13.60)	2.97 (12.31)	1.75 (9.38)
Education[b]				
Less than high school graduate	3.16 (10.46)	4.29 (15.20)	4.78 (19.67)	4.70 (24.91)
High school grad/GED	5.26 (17.43)	7.02 (24.86)	6.27 (25.77)	5.33 (28.22)
College or above	21.77 (72.11)	16.91 (59.94)	13.27 (54.56)	8.85 (46.87)
PIR[b]				
≤ 1.0	3.17 (11.24)	3.90 (14.74)	3.62 (15.95)	3.25 (18.54)
1.0 to ≤ 3.0	9.07 (32.15)	9.40 (35.58)	9.17 (40.38)	7.51 (42.77)
> 3.0	15.97 (56.61)	13.13 (49.68)	9.92 (43.67)	6.79 (38.69)
Health insurance coverage				
Private	21.64 (73.93)	18.17 (67.07)	15.00 (64.95)	10.81 (61.30)
Public health	3.69 (12.61)	4.62 (17.05)	4.17 (18.04)	3.51 (19.90)
No	3.94 (13.45)	4.31 (15.89)	3.93 (17.01)	3.31 (18.80)
Cigarette smoking				
No	20.15 (66.76)	17.17 (60.84)	14.30 (58.75)	9.14 (48.50)
Former	6.08 (20.15)	5.96 (21.14)	5.20 (21.37)	4.71 (25.00)
Current	3.95 (13.09)	5.09 (18.02)	4.84 (19.88)	4.99 (26.50)
Alcohol drinking				
No	3.05 (13.93)	3.73 (18.58)	3.55 (21.44)	3.75 (28.51)
Light	13.79 (62.98)	11.97 (59.61)	10.29 (62.13)	7.81 (59.42)
Moderate	2.79 (12.75)	2.52 (12.57)	1.45 (8.73)	0.83 (6.30)
Heavy	2.26 (10.34)	1.85 (9.23)	1.28 (7.70)	0.76 (5.77)
Chronic diseases				
Cardiovascular disease	0.93 (3.08)	1.35 (4.80)	1.69 (7.00)	1.66 (8.80)
Diabetes	1.41 (4.66)	2.71 (9.60)	3.94 (16.16)	5.22 (27.61)
Hypertension	9.32 (31.49)	12.04 (43.58)	13.01 (54.86)	11.97 (64.26)
Cancer	2.72 (9.00)	2.55 (9.04)	2.76 (11.35)	2.77 (14.64)
Family history of cardiovascular disease				
No	26.55 (89.51)	24.03 (86.97)	20.22 (84.93)	14.95 (81.14)
Yes	3.11 (10.49)	3.60 (13.03)	3.59 (15.07)	3.47 (18.86)
Family history of diabetes				
No	18.11 (61.04)	15.46 (55.74)	12.35 (51.59)	8.52 (45.85)
Yes	11.56 (38.96)	12.27 (44.26)	11.59 (48.41)	10.07 (54.15)
Men				
Participants	29.86 (31.11)	25.40 (26.47)	23.08 (24.05)	17.63 (18.37)
Age,[b] mean (SE), y	44.69 (0.43)	47.10 (0.38)	47.48 (0.44)	47.92 (0.43)

Table 1 (continued)

Characteristic	VAI quartiles, weighted No. (%), millions			
	Q1 (≤ 1.00)	Q2 (1.00 to ≤ 1.70)	Q3 (1.70 to ≤ 2.94)	Q4 (> 2.94)
Race and ethnicity[c]				
Hispanic American	2.28 (7.62)	2.29 (9.01)	2.30 (9.97)	1.68 (9.53)
Non-Hispanic Black	4.56 (15.26)	2.55 (10.03)	1.40 (6.04)	0.86 (4.85)
Non-Hispanic White	19.58 (65.59)	17.41 (68.56)	16.38 (70.96)	12.94 (73.38)
Other	3.44 (11.52)	3.15 (12.40)	3.00 (13.02)	2.16 (12.25)
Marital status				
Married	19.52 (65.98)	17.74 (70.77)	16.43 (71.97)	12.71 (72.91)
Separated	3.33 (11.25)	3.09 (12.31)	2.86 (12.54)	2.27 (13.01)
Never married	6.74 (22.77)	4.24 (16.92)	3.53 (15.49)	2.45 (14.07)
Education[b]				
Less than high school graduate	4.76 (15.95)	4.56 (17.98)	4.43 (19.21)	3.29 (18.64)
High school grad/GED	7.38 (24.74)	6.16 (24.25)	5.55 (24.04)	4.63 (26.27)
College or above	17.69 (59.31)	14.66 (57.76)	13.09 (56.75)	9.71 (55.09)
PIR[b]				
≤ 1.0	3.13 (11.29)	2.62 (10.92)	2.71 (12.45)	1.92 (11.68)
1.0 to ≤ 3.0	9.57 (34.51)	8.59 (35.84)	8.34 (38.28)	5.80 (35.18)
> 3.0	15.04 (54.20)	12.77 (53.24)	10.74 (49.28)	8.76 (53.14)
Health insurance coverage				
Private	19.44 (67.23)	16.43 (67.21)	14.50 (64.98)	11.19 (67.26)
Public health	3.42 (11.83)	3.24 (13.25)	3.02 (13.54)	2.19 (13.14)
No	6.06 (20.95)	4.77 (19.53)	4.79 (21.48)	3.26 (19.60)
Cigarette smoking				
No	15.03 (50.39)	11.52 (45.36)	10.15 (43.98)	7.29 (41.35)
Former	7.98 (26.77)	7.92 (31.21)	7.22 (31.28)	5.87 (33.28)
Current	6.81 (22.84)	5.95 (23.43)	5.71 (24.74)	4.47 (25.37)
Alcohol drinking				
No	3.21 (13.58)	3.53 (17.56)	3.39 (18.20)	2.78 (19.51)
Light	10.06 (42.62)	8.71 (43.36)	8.55 (45.89)	6.50 (45.58)
Moderate	7.62 (32.29)	5.88 (29.28)	4.91 (26.36)	3.44 (24.12)
Heavy	2.72 (11.51)	1.97 (9.80)	1.78 (9.56)	1.54 (10.79)
Chronic diseases				
Cardiovascular disease	1.73 (5.79)	1.97 (7.75)	2.22 (9.67)	2.02 (11.48)
Diabetes	2.52 (8.44)	2.87 (11.29)	3.80 (16.48)	4.08 (23.14)
Hypertension	12.69 (43.01)	13.15 (52.62)	12.97 (56.72)	11.11 (64.11)
Cancer	2.33 (7.79)	1.90 (7.48)	1.93 (8.36)	1.45 (8.21)
Family history of cardiovascular disease				
No	26.20 (89.82)	22.00 (88.48)	19.70 (87.46)	15.10 (88.09)
Yes	2.97 (10.18)	2.86 (11.52)	2.82 (12.54)	2.04 (11.91)
Family history of diabetes				
No	19.35 (66.47)	15.12 (60.80)	12.76 (56.37)	8.67 (50.54)
Yes	9.76 (33.53)	9.75 (39.20)	9.88 (43.63)	8.49 (49.46)

Abbreviations: *NHANES* National Health and Nutrition Examination Survey, *VAI* Visceral adiposity index, *GED* General equivalent diploma, *PIR* Poverty income ratio

[a] Nationally representative estimates of the non-pregnant US population aged 25 years or more by applying survey weights

[b] Age, sex, education, and PIR were based on self-reports. Income was converted to ratio of family income to poverty according to the Department of Health and Human Services' poverty thresholds

[c] Race and ethnicity were based on self-reports in closed categories

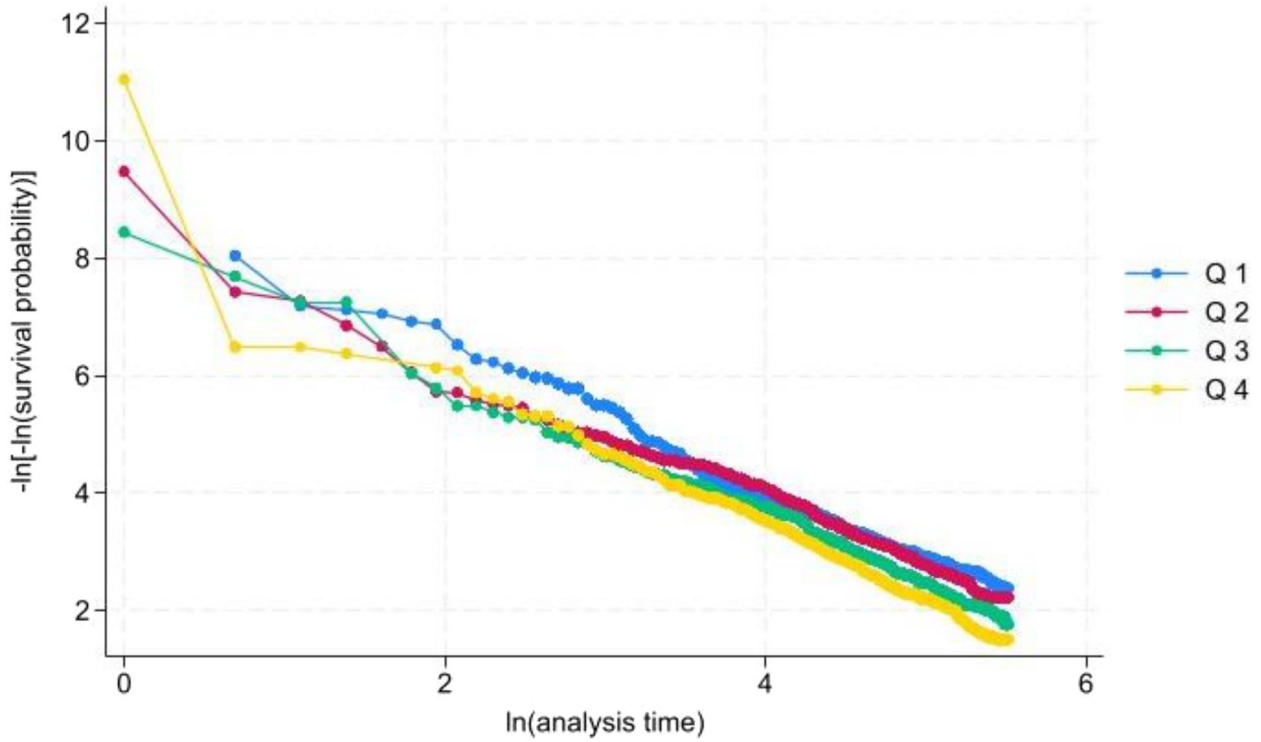

Fig. 4 Cox Assumption Assessment for VAI Quartiles: Visual Inspection

(Fig. 5), Weibull regression models were used to correlate VAI with premature mortality.

Table 2 summarized the risk estimates of premature mortality across VAI quartiles. Multi-adjusted hazard ratios (HRs) were statistically significant when comparing both Q3 and Q4 with Q1 of VAI overall (Q3 vs. Q1: HR, 95% CI: 1.30, 1.05 to 1.61; Q4 vs. Q1: 1.68, 1.34 to 2.11). This association was particularly pronounced in women (Q3 vs. Q1: 1.53, 1.01 to 2.30; Q4 vs. Q1: 2.36, 1.52 to 3.68), with obvious linear trends ($P < 0.001$). And multi-adjusted HRs were statistically significant when comparing Q4 with Q1 of VAI in men (1.36, 1.03 to 1.79), in Black participants (2.37, 1.47 to 3.84) and in White participants (1.50, 1.16 to 1.96), with obvious linear trends ($P < 0.05$). Interestingly, significant interaction existed between women and men, as well as between Blacks and Whites or Hispanic Americans ($P < 0.001$ for interaction).

In sensitivity analyses, no material changes were noted after redefining premature mortality as deaths occurring before age of 75 years (Table 3), after filling missing data using the multiple imputation method (Table 4), and after adjusting survey cycles (Table 5). Analysis of VAI deciles revealed more nuanced patterns, particularly in the highest deciles (eTable2). In contrast, no clear trend was observed between BMI and premature mortality risk (eTable 3 and eTable 4), and in some cases, higher BMI was associated with a lower risk of premature mortality, especially at very high levels. Regarding model performance, both AIC and BIC consistently indicated that VAI provided a superior fit compared to BMI, regardless of quartile or decile grouping (eTable 5 and eTable 6).

VAI and cause-specific premature mortality

Risk for cause-specific premature mortality across VAI quartiles was explored by considering completing risk (Table 6). Overall, Q4 was associated with a significantly increased risk of CVD-specific (multi-adjusted HR, 95% CI: 2.20, 1.36 to 3.54), cancer-specific (1.78, 1.17 to 2.71), and other causes related (1.43, 1.04 to 1.97) premature mortality compared with Q1.

By sex, multi-adjusted HRs were significant for Q4 with Q1 VAI in terms of CVD-specific (multi-adjusted HR, 95% CI: 2.79, 1.10 to 7.07 for women; 1.95, 1.11 to 3.41 for men). By race/ethnicity, VAI was significantly associated with CVD-specific premature mortality for Q4 with Q1 VAI (multi-adjusted HR, 95% CI: 4.42, 2.26 to 8.66 in Black participants; 1.96, 1.06 to 3.64 in White participants). In White participants, multi-adjusted HRs were significant for Q4 with Q1 VAI in terms of cancer-specific (1.73, 1.05 to 2.84).

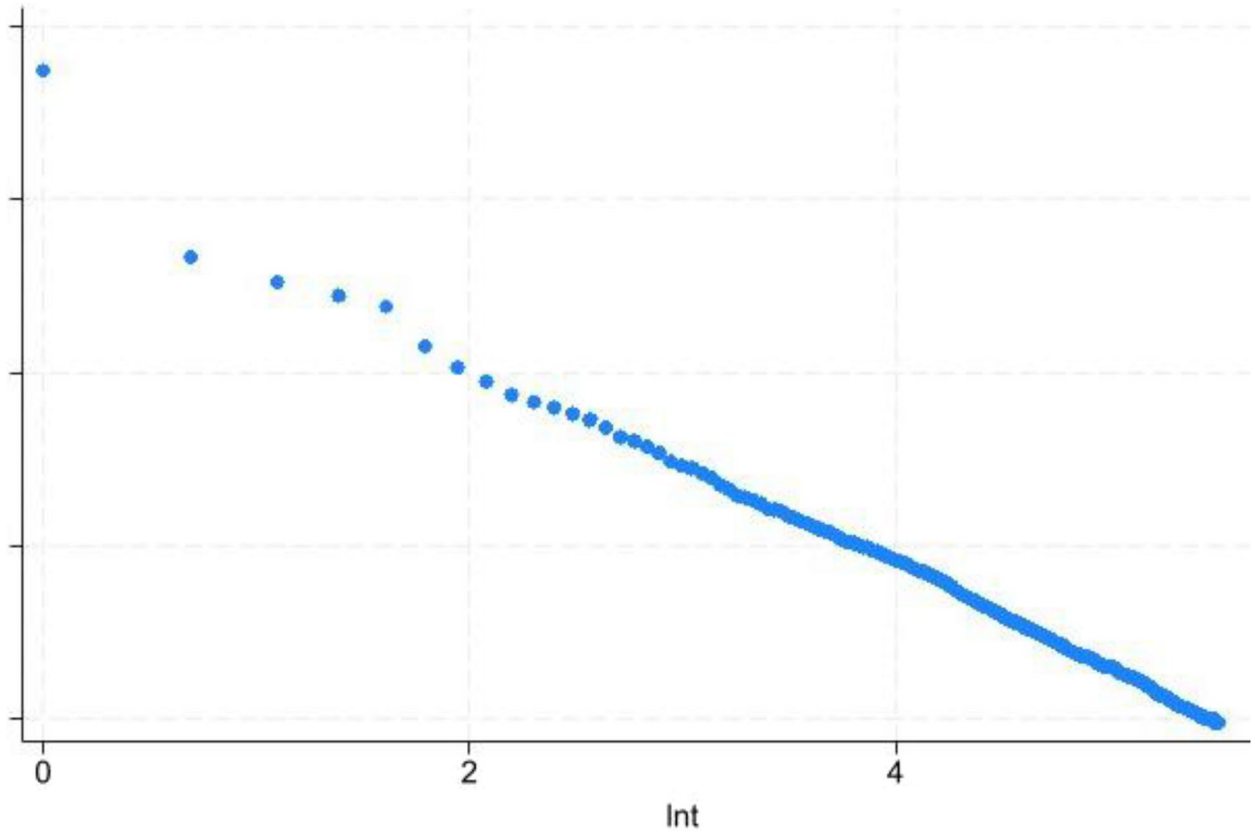

Fig. 5 Weibull Assumption Assessment for VAI Quartiles: Visual Inspection

VAI and life expectancy

As shown in Fig. 6A, estimated life expectancy at age of 40 years was 41.45 (95% CI: 41.24 to 41.66), 41.32 (41.11 to 41.53), 40.55 (40.35 to 40.75), and 39.26 (39.08 to 39.45) years in Q1, Q2, Q3, and Q4 VAI, respectively. Equivalently, participants in Q4 VAI had on average 2.19 fewer years in life expectancy at age 40 than those in Q1, with 19.10% of lost life expectancy attributable to CVD, 24.35% to cancer, and 56.55% to other causes related death.

By sex, estimated life expectancy at age 40 in women was shortened by 3.33 years (95% CI: 3.29 to 3.37) in Q4, with 13.12% of lost life expectancy at age 40 attributable to CVD, 30.79% to cancer, and 56.09% to other causes related death (Fig. 6B). For men, estimated life expectancy at age 40 was shortened by 1.24 years (1.23 to 1.25) in Q4, with 25.08% of lost life expectancy at age 40 attributable to CVD, 24.39% to cancer, and 50.53% to other causes related death (Fig. 6C).

By race/ethnicity, average life expectancy at age 40 in White participants was 1.68 years shorter (95% CI, 1.65 to 1.71) for Q4 compared with Q1, with 8.83% of lost life expectancy at age 40 attributable to CVD, 50.94% to cancer, and 40.23% to other causes related death (Fig. 7A). For Black participants, average life expectancy at age 40 in Q4 VAI was shortened by 3.90 years (95% CI: 3.85 to 3.94), compared with Q1, and 28.68% of life expectancy lost in Q4 (versus Q1) was attributable to CVD, 27.18% to cancer, and 44.14% to other causes related death (Fig. 7B).

Discussion

In this nationally representative cohort of 43,672 US adults, we explored potential association of VAI with premature mortality and life expectancy. Notably, higher VAI was significantly and independently associated with an enhanced risk of premature death, especially in women and Black participants. Furthermore, participants in Q4 (versus Q1) VAI could shorten life expectancy at age 40 by 3.33 years in women and 1.24 years in men. In Black participants, the greatest loss in life expectancy (3.90 years) was seen in Q4. To our knowledge, this is the first study to investigate the association of VAI with premature mortality and life expectancy, providing critical insights into the differential impacts of visceral fat accumulation across demographic groups.

Visceral adipose tissue differs from subcutaneous fat, and its highly metabolically active nature makes it a central driver of systemic metabolic disorders. From a

Table 2 HR (95% CI) for Premature Mortality (Death Prior to 80 Years) According to VAI Quartiles in Adults from the US NHANES 1999 - 2018[a]

Group and model	HR (95% CI) by VAI quartiles				
	Q1 (≤ 1.00)	Q2 (1.00 to ≤ 1.70)	Q3 (1.70 to ≤ 2.94)	Q4 (> 2.94)	P for trend
All					
None adjusted	1 [Ref]	1.16 (0.95, 1.41)	**1.58 (1.30, 1.93)*****	**2.16 (1.78, 2.63)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.08 (0.88, 1.31)	**1.40 (1.15, 1.70)*****	**1.96 (1.61, 2.39)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	1.02 (0.81, 1.28)	**1.30 (1.05, 1.61)***	**1.68 (1.34, 2.11)*****	< 0.001
Women					
None adjusted	1 [Ref]	1.38 (0.97, 1.96)	**2.08 (1.49, 2.91)*****	**3.51 (2.45, 5.03)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.28 (0.89, 1.83)	**1.72 (1.21, 2.43)*****	**2.89 (1.98, 4.22)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	1.23 (0.82, 1.84)	**1.53 (1.01, 2.30)***	**2.36 (1.52, 3.68)*****	< 0.001
Men					
None adjusted	1 [Ref]	1.08 (0.85, 1.38)	**1.37 (1.06, 1.77)***	**1.60 (1.24, 2.06)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.00 (0.79, 1.26)	**1.29 (1.00, 1.65)***	**1.57 (1.22, 2.03)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	0.94 (0.71, 1.22)	**1.22 (0.93, 1.60)**	**1.36 (1.03, 1.79)***	0.007
Non-Hispanic Black individuals					
None adjusted	1 [Ref]	**1.50 (1.08, 2.08)***	**1.92 (1.46, 2.54)*****	**2.69 (1.75, 4.11)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.37 (0.99, 1.89)	**1.70 (1.28, 2.24)*****	**2.52 (1.65, 3.84)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	1.33 (0.89, 2.01)	1.40 (0.99, 2.00)	**2.37 (1.47, 3.84)*****	0.001
Non-Hispanic White individuals					
None adjusted	1 [Ref]	1.06 (0.84, 1.35)	**1.51 (1.18, 1.94)***	**2.06 (1.63, 2.61)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.96 (0.76, 1.22)	1.27 (1.00, 1.62)	**1.78 (1.41, 2.25)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	0.88 (0.66, 1.17)	1.18 (0.92, 1.53)	**1.50 (1.16, 1.96)****	< 0.001
Hispanic American					
None adjusted	1 [Ref]	1.06 (0.65, 1.73)	**1.56 (1.01, 2.42)***	**1.69 (1.04, 2.74)***	0.005
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.88 (0.53, 1.46)	1.16 (0.72, 1.86)	1.20 (0.72, 1.99)	0.24
Multivariate adjusted[b]	1 [Ref]	0.91 (0.49, 1.68)	1.19 (0.66, 2.14)	1.06 (0.55, 2.06)	0.59

Abbreviations: *VAI* Visceral adiposity index, *NHANES* National Health and Nutrition Examination Survey, *HR* Hazard ratio, *95% CI* 95% confidence interval, *Ref* Reference group

[a] Nationally representative estimates of the non-pregnant US population aged > 20 years by applying survey weights

[b] Multivariate adjustment for age, sex, race and ethnicity, poverty income ratio, insurance status, cigarette smoking, alcohol drinking, and family history (cardiovascular disease or diabetes). Women compared with men: $P < 0.001$ for interaction. Black individuals compared with White individuals: $P < 0.001$ for interaction. Black individuals compared with Hispanic Americans individuals: $P < 0.001$ for interaction

$^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$

molecular mechanism perspective, visceral adipose tissue impacts health through three primary pathways. First, visceral fat cells exhibit stronger lipolytic activity, continuously releasing free fatty acids into the portal vein circulation, leading to ectopic fat deposition in the liver. This lipid overflow triggers hepatic insulin resistance by inhibiting tyrosine phosphorylation of insulin receptor substrate- 1, thereby disrupting glucose homeostasis [22]. Second, inflammatory Cytokine Storm: VAT is characterized by significant macrophage infiltration, which secretes pro-inflammatory cytokines such as TNF-α and IL- 6, while suppressing the synthesis of adiponectin. This chronic low-grade inflammatory state promotes the formation of atherosclerotic plaques through the NF-KB signaling pathway and induces β-cell dysfunction [23]. Third, excessive accumulation of visceral fat leads to abnormal secretion of leptin, resulting in hypothalamic leptin resistance. This further exacerbates appetite dysregulation [24].

The observed heterogeneous association of VAI with premature mortality between sexes is not surprising, given that VAI is a sex-specific indicator of visceral fat content. Women generally have thinner muscle mass and thicker fat layers compared to men [25–27], which may contribute to the sex-specific differences in the impact of visceral fat on health outcomes. Our study found that the association between VAI and premature mortality was more evident in women than in men, potentially due to the higher mortality risk associated with cardiovascular diseases (CVD) in women [28, 29]. As a result, women

Table 3 HR (95% CI) for Premature Mortality (Death Prior to 75 Years) According to VAI Quartiles in Adults from the US NHANES 1999 - 2018[a]

Group and model	HR (95% CI) by VAI quartiles				
	Q1 (≤ 1.00)	Q2 (1.00 to ≤ 1.70)	Q3 (1.70 to ≤ 2.94)	Q4 (> 2.94)	P for trend
All					
None adjusted	1 [Ref]	1.12 (0.87, 1.44)	**1.53 (1.21, 1.92)*****	**2.15 (1.72, 2.69)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.09 (0.84, 1.41)	**1.43 (1.14, 1.80)****	**2.06 (1.64, 2.59)*****	< 0.001
Multivariate adjusted[a]	1 [Ref]	1.05 (0.79, 1.40)	**1.36 (1.05, 1.77)***	**1.81 (1.37, 2.38)*****	< 0.001
Women					
None adjusted	1 [Ref]	1.34 (0.86, 2.07)	**2.12 (1.40, 3.20)*****	**3.62 (2.32, 5.66)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.32 (0.84, 2.06)	**1.97 (1.29, 3.01)****	**3.42 (2.13, 5.48)*****	< 0.001
Multivariate adjusted[a]	1 [Ref]	1.38 (0.82, 2.33)	**1.83 (1.09, 3.08)***	**3.01 (1.68, 5.41)****	< 0.001
Men					
None adjusted	1 [Ref]	1.06 (0.79, 1.42)	1.30 (0.98, 1.72)	**1.60 (1.21, 2.13)****	0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.01 (0.76, 1.34)	1.26 (0.95, 1.67)	**1.60 (1.20, 2.12)****	0.001
Multivariate adjusted[a]	1 [Ref]	0.94 (0.66, 1.32)	1.22 (0.89, 1.68)	**1.38 (1.01, 1.88)***	0.02
Non-Hispanic Black individuals					
None adjusted	1 [Ref]	**1.63 (1.12, 2.38)***	**2.19 (1.59, 3.01)*****	**3.09 (1.89, 5.03)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	**1.53 (1.06, 2.23)***	**2.01 (1.46, 2.77)*****	**2.92 (1.80, 4.75)*****	< 0.001
Multivariate adjusted[a]	1 [Ref]	1.48 (0.92, 2.39)	**1.74 (1.71, 2.60)****	**2.74 (1.60, 4.68)**	< 0.001
Non-Hispanic White individuals					
None adjusted	1 [Ref]	0.99 (0.73, 1.34)	**1.38 (1.03, 1.84)***	**1.96 (1.49, 2.57)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.93 (0.69, 1.27)	1.22 (0.92, 1.62)	**1.77 (1.35, 2.31)*****	< 0.001
Multivariate adjusted[a]	1 [Ref]	0.87 (0.61, 1.26)	1.18 (0.86, 1.62)	**1.54 (1.11, 2.13)****	0.002
Hispanic Americans					
None adjusted	1 [Ref]	1.09 (0.60, 1.97)	**1.69 (1.03, 2.76)***	**1.87 (1.08, 3.23)***	0.003
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.96 (0.52, 1.76)	1.34 (0.79, 2.26)	1.43 (0.80, 2.53)	0.08
Multivariate adjusted[a]	1 [Ref]	0.97 (0.49, 1.95)	1.27 (0.66, 2.44)	1.19 (0.59, 2.41)	0.41

Abbreviations: *VAI* Visceral adiposity index, *NHANES* National Health and Nutrition Examination Survey, *HR* Hazard ratio, *95% CI* 95% confidence interval, *Ref* Reference group

[a] Nationally representative estimates of the non-pregnant US population aged > 20 years by applying survey weights

[b] Multivariate adjustment for age, sex, race and ethnicity, poverty income ratio, insurance status, cigarette smoking, alcohol drinking, and family history (cardiovascular disease or diabetes). Women compared with men: $P < 0.001$ for interaction. Black individuals compared with White individuals: $P < 0.001$ for interaction. Black individuals compared with Hispanic Americans individuals: $P < 0.001$ for interaction

$^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$

in Q4 VAI were estimated to have, on average, 2.09 years shorter life expectancy at age 40 compared to men in the same quartile. Biologically, this observation is plausible. With aging, women typically experience a redistribution of body fat, particularly a shift from subcutaneous to visceral fat, which is closely related to hormonal changes in postmenopausal women. The significant increase in visceral fat in postmenopausal women is closely tied to the sharp decline in estradiol levels. Estrogen receptor α (ERα) inhibits fat breakdown by activating the AMPK pathway, while estrogen deficiency upregulates lipoprotein lipase activity in fat cells, promoting triglyceride storage [29, 30]. Additionally, the high expression of aromatase in visceral fat may exacerbate adipose tissue dysfunction through the local conversion of androgens to estrogens [31]. These hormonal and metabolic changes contribute to a variety of abnormalities, including reduced fatty acid oxidation, chronic inflammation, insulin resistance, and metabolic dysfunction [29–32]. Although the molecular mechanisms underlying the predisposition of high-VAI women to premature mortality are not fully understood, our findings underscore the need for special attention to adults, particularly women, in the highest VAI quartile to prevent premature death and extend lifespan.

Another significant finding of this study is the race- and ethnicity-specific association of VAI with premature mortality and life expectancy. Specifically, Black participants in Q4 VAI had an approximately 2.37 times higher risk of premature mortality compared to those

Table 4 HR (95% CI) for Premature Mortality (Death Prior to 80 Years) According to VAI Quartiles after Multiple Imputation for Covariates in Adults from the US NHANES 1999 - 2018[a]

Group and model	HR (95% CI) by VAI quartiles				
	Q1 (≤ 1.00)	Q2 (1.00 to ≤ 1.70)	Q3 (1.70 to ≤ 2.94)	Q4 (> 2.94)	P for trend
All					
None adjusted	1 [Ref]	1.08 (0.93, 1.25)	**1.39 (1.22, 1.57)*****	**1.87 (1.63, 2.14)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.99 (0.86, 1.15)	**1.20 (1.06, 1.35)****	**1.62 (1.41, 1.86)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	0.93 (0.80, 1.08)	1.07 (0.95, 1.21)	**1.35 (1.18, 1.55)*****	< 0.001
Women					
None adjusted	1 [Ref]	**1.45 (1.14, 1.85)****	**1.89 (1.51, 2.37)*****	**2.88 (2.31, 3.61)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	**1.30 (1.09, 1.68)***	**1.50 (1.18, 1.90)****	**2.30 (1.79, 2.88)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	1.12 (0.86, 1.44)	1.20 (0.94, 1.53)	**1.65 (1.29, 2.12)*****	< 0.001
Men					
None adjusted	1 [Ref]	0.94 (0.78, 1.12)	1.15 (0.97, 1.37)	**1.42 (1.19, 1.68)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.86 (0.72, 1.03)	1.07 (0.91, 1.27)	**1.35 (1.13, 1.61)****	< 0.001
Multivariate adjusted[b]	1 [Ref]	0.84 (0.70, 1.01)	1.02 (0.87, 1.20)	1.22 (1.03, 1.44)	0.003
Non-Hispanic Black individuals					
None adjusted	1 [Ref]	1.22 (0.94, 1.57)	**1.58 (1.25, 2.00)*****	**2.16 (1.63, 2.86)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.08 (0.84, 1.38)	**1.28 (1.02, 1.61)***	**1.67 (1.27, 2.20)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	1.07 (0.83, 1.37)	1.20 (0.95, 1.51)	**1.44 (1.09, 1.91)***	0.006
Non-Hispanic White individuals					
None adjusted	1 [Ref]	0.95 (0.79, 1.15)	**1.33 (1.13, 1.56)****	**1.86 (1.57, 2.21)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.87 (0.72, 1.05)	1.12 (0.95, 1.31)	**1.56 (1.31, 1.85)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	**0.80 (0.65, 0.96)***	0.96 (0.83, 1.11)	**1.24 (1.04, 1.47)***	< 0.001
Hispanic Americans					
None adjusted	1 [Ref]	1.20 (0.75, 1.91)	1.34 (0.89, 2.01)	**1.65 (1.14, 2.40)****	0.004
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.95 (0.58, 1.55)	0.92 (0.60, 1.42)	1.06 (0.74, 1.50)	0.57
Multivariate adjusted[b]	1 [Ref]	0.92 (0.58, 1.48)	0.88 (0.58, 1.34)	0.99 (0.71, 1.37)	0.48

Abbreviations: *VAI* Visceral adiposity index, *NHANES* National Health and Nutrition Examination Survey, *HR* Hazard ratio, *95% CI* 95% confidence interval, *Ref* Reference group

[a] Nationally representative estimates of the non-pregnant US population aged > 20 years by applying survey weights

[b] Multivariate adjustment for age, sex, race and ethnicity, poverty income ratio, insurance status, cigarette smoking, alcohol drinking, and family history (cardiovascular disease or diabetes). Women compared with men: $P < 0.001$ for interaction. Black individuals compared with White individuals: $P < 0.001$ for interaction. Black individuals compared with Hispanic Americans individuals: $P < 0.001$ for interaction

$^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$

in Q1, whereas the differences were less pronounced for White and Hispanic Americans participants. In terms of life expectancy, Q4 VAI was associated with a 3.90-year reduction in Black participants. Black adults are disproportionately affected by obesity [33, 34], which is likely due to persistent disparities in obesity care and health outcomes. Systemic racism has been cited as a root cause of these disparities, as it can restrict access to healthcare, nutritious foods, health insurance, and safe spaces for physical activity [34, 35]. Additionally, unconscious bias among healthcare providers can negatively influence the quality of care and social connections with obese patients, further exacerbating health inequities [36, 37]. However, it is important to note that the lower proportion of Black participants recruited in the NHANES may limit the power to accurately quantify the association between VAI and premature mortality in this group. Furthermore, the high pathogenicity of visceral adiposity in black populations may be related to differences in adipocyte dynamics. Studies have shown that subcutaneous adipocytes in people of African descent are less able to differentiate and have a lower lipid storage threshold, resulting in more lipid spillover to visceral and ectopic sites [38]. Future studies with larger and more diverse samples are needed to confirm these findings and explore the underlying mechanisms.

Notably, in this study, more than half of life expectancy loss associated with the highest versus lowest VAI quartile was attributable to deaths from other causes. Several factors may explain this phenomenon.

Table 5 HR (95% CI) for Premature Mortality (Death Prior to 80 Years) According to VAI Quartiles (Further Adjusted for Survey Cycles) in Adults from the US NHANES 1999 - 2018[a]

Group and model	HR (95% CI) by VAI quartiles				
	Q1 (≤ 1.00)	Q2 (1.00 to ≤ 1.70)	Q3 (1.70 to ≤ 2.94)	Q4 (> 2.94)	P for trend
All					
None adjusted	1 [Ref]	1.16 (0.95, 1.41)	**1.58 (1.30, 1.93)*****	**2.16 (1.78, 2.63)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.08 (0.88, 1.31)	**1.40 (1.15, 1.70)*****	**1.96 (1.61, 2.39)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	1.02 (0.81, 1.28)	**1.30 (1.05, 1.61)***	**1.67 (1.33, 2.10)*****	< 0.001
Women					
None adjusted	1 [Ref]	1.38 (0.97, 1.96)	**2.08 (1.49, 2.91)*****	**3.51 (2.45, 5.03)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.28 (0.89, 1.83)	**1.72 (1.21, 2.43)****	**2.89 (1.98, 4.22)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	1.23 (0.82, 1.84)	**1.54 (1.02, 2.33)***	**2.35 (1.50, 3.66)****	< 0.001
Men					
None adjusted	1 [Ref]	1.08 (0.85, 1.38)	**1.37 (1.06, 1.77)***	**1.60 (1.24, 2.06)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.00 (0.79, 1.26)	**1.29 (1.00, 1.65)***	**1.57 (1.22, 2.03)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	0.93 (0.71, 1.22)	1.21 (0.92, 1.58)	**1.35 (1.04, 1.78)***	0.01
Non-Hispanic Black individuals					
None adjusted	1 [Ref]	**1.50 (1.08, 2.08)***	**1.92 (1.46, 2.54)*****	**2.69 (1.75, 4.11)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.37 (0.99, 1.89)	**1.70 (1.28, 2.24)*****	**2.52 (1.65, 3.84)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	1.34 (0.90, 2.01)	**1.43 (1.00, 2.03)***	**2.40 (1.48, 3.89)*****	0.001
Non-Hispanic White individuals					
None adjusted	1 [Ref]	1.06 (0.84, 1.35)	**1.51 (1.18, 1.94)****	**2.06 (1.63, 2.61)*****	< 0.001
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.96 (0.76, 1.22)	1.27 (1.00, 1.62)	**1.78 (1.41, 2.25)*****	< 0.001
Multivariate adjusted[b]	1 [Ref]	0.88 (0.66, 1.17)	1.18 (0.92, 1.53)	**1.50 (1.15, 1.95)****	0.001
Hispanic Americans					
None adjusted	1 [Ref]	1.06 (0.65, 1.73)	**1.56 (1.01, 2.42)***	**1.69 (1.04, 2.74)***	0.005
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.88 (0.53, 1.46)	1.16 (0.72, 1.86)	1.20 (0.72, 1.99)	0.24
Multivariate adjusted[b]	1 [Ref]	0.92 (0.49, 1.72)	1.18 (0.65, 2.16)	1.03 (0.52, 2.06)	0.69

Abbreviations: *VAI* Visceral adiposity index, *NHANES* National Health and Nutrition Examination Survey, *HR* Hazard ratio, *95% CI* 95% confidence interval, *Ref* Reference group

[a] Nationally representative estimates of the non-pregnant US population aged > 20 years by applying survey weights

[b] Multivariate adjustment for age, sex, race and ethnicity, poverty income ratio, insurance status, cigarette smoking, alcohol drinking, family history (cardiovascular disease or diabetes), and cycles. Women compared with men: $P < 0.001$ for interaction. Black individuals compared with White individuals: $P < 0.001$ for interaction. Black individuals compared with Hispanic Americans individuals: $P < 0.001$ for interaction

$^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$

First, while VAI serves as an indicator of visceral fat by considering circumference, weight, body height, TG, and HDLC, it does not fully capture risks associated with metabolic and inflammatory disorders. The "other causes" category primarily includes chronic lower respiratory diseases, diabetes mellitus, Alzheimer's disease, nephritis, and cerebrovascular diseases. All these conditions are closely linked to metabolic dysfunction and chronic inflammation. For instance, systemic inflammation plays a well-established role in diabetes mellitus and chronic respiratory disorders [39–41], and emerging evidence suggests a mechanistic link of Alzheimer's disease with metabolic dysregulation [42–44]. Second, the combined impact of CVD and cancer on life expectancy loss was substantial, accounting for 43.45% of total loss in this study—19.10% from CVD and 24.35% from cancer. This effect was particularly pronounced in certain subgroups, especially men and Black participants.

Our findings have important implications for public health and clinical practice. The strong association between high VAI and increased risk of premature mortality, particularly in women and Black adults, highlights the need for targeted interventions to reduce visceral fat accumulation in these populations. Public health strategies should focus on improving access to healthcare, promoting healthy lifestyles, and addressing social determinants of health that contribute to obesity and metabolic dysfunction. Clinically, healthcare providers should consider VAI as a valuable tool for assessing visceral fat

Table 6 HR (95% CI) for Cause-Specific Premature Mortality Using the Fine-Gray Method According to VAI Quartiles in Adults from the US NHANES 1999 - 2018[a]

Specific causes of death	HR (95% CI) by VAI quartiles			
	Q1 (≤ 1.00)	Q2 (1.00 to ≤ 1.70)	Q3 (1.70 to ≤ 2.94)	Q4 (> 2.94)
All				
Cardiovascular mortality				
Cases, No./total No	350/10,918	413/10,918	462/10,918	462/10,918
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.28 (0.84, 1.95)	**1.85 (1.21, 2.83)****	**2.34 (1.53, 3.56)*****
Multivariable adjusted[b]	1 [Ref]	1.38 (0.87, 2.20)	**1.76 (1.09, 2.84)***	**2.20 (1.36, 3.54)****
Cancer mortality				
Cases, No./total No	339/10,918	372/10,918	405/10,918	387/10,918
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.09 (0.77, 1.56)	1.38 (0.97, 1.97)	**2.04 (1.44, 2.89)*****
Multivariable adjusted[b]	1 [Ref]	0.97 (0.64, 1.48)	1.35 (0.90, 2.04)	**1.78 (1.17, 2.71)****
Mortality from other causes				
Cases, No./total No	707/10,918	807/10,918	901/10,918	946/10,918
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.00 (0.75, 1.32)	1.23 (0.93, 1.62)	**1.72 (1.30, 2.27)*****
Multivariable adjusted[b]	1 [Ref]	0.94 (0.68, 1.29)	1.11 (0.82, 1.52)	**1.43 (1.04, 1.97)***
Women				
Cardiovascular mortality				
Cases, No./total No	110/5281	164/5710	208/5668	215/5505
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.39 (0.58, 3.31)	2.21 (0.95, 5.17)	**3.52 (1.49, 8.32)***
Multivariable adjusted[b]	1 [Ref]	1.36 (0.51, 3.63)	1.77 (0.69, 4.56)	**2.79 (1.10, 7.07)***
Cancer mortality				
Cases, No./total No	94/5281	143/5710	180/5668	171/5505
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.24 (0.65, 2.36)	1.33 (0.69, 2.57)	**2.73 (1.47, 5.08)****
Multivariable adjusted[b]	1 [Ref]	0.89 (0.41, 1.91)	0.98 (0.45, 2.13)	1.88 (0.89, 3.98)
Mortality from other causes				
Cases, No./total No	262/5281	362/5710	464/5668	480/5505
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.25 (0.78, 1.99)	**1.77 (1.10, 2.84)***	**2.65 (1.66, 4.22)*****
Multivariable adjusted[b]	1 [Ref]	1.42 (0.83, 2.44)	**1.85 (1.07, 3.17)***	**2.48 (1.40, 4.38)****
Men				
Cardiovascular mortality				
Cases, No./total No	240/5637	249/5208	254/5250	247/5413
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.24 (0.77, 2.00)	**1.71 (1.04, 2.81)***	**1.94 (1.18, 3.18)****
Multivariable adjusted[b]	1 [Ref]	1.38 (0.82, 2.33)	**1.73 (1.00, 3.01)***	**1.95 (1.11, 3.41)***
Cancer mortality				
Cases, No./total No	245/5637	229/5208	225/5250	216/5413
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.03 (0.68, 1.57)	1.48 (0.98, 2.25)	**1.74 (1.12, 2.71)***
Multivariable adjusted[b]	1 [Ref]	1.02 (0.62, 1.66)	**1.63 (1.02, 2.62)***	1.64 (0.96, 2.80)
Mortality from other causes				
Cases, No./total No	445/5637	445/5208	437/5250	466/5413
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.90 (0.63, 1.27)	1.00 (0.71, 1.42)	1.30 (0.91, 1.88)
Multivariable adjusted[b]	1 [Ref]	0.77 (0.51, 1.15)	0.86 (0.58, 1.27)	1.03 (0.68, 1.55)
Non-Hispanic Black individuals				
Cardiovascular mortality				
Cases, No./total No	111/3276	81/2474	81/1785	59/1163
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.33 (0.73, 2.45)	**1.92 (1.03, 3.55)***	**4.08 (2.24, 7.46)*****
Multivariable adjusted[b]	1 [Ref]	1.49 (0.76, 2.94)	1.76 (0.86, 3.62)	**4.42 (2.26, 8.66)*****
Cancer mortality				
Cases, No./total No	103/3276	90/2474	64/1785	45/1163
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.45 (0.84, 2.51)	1.81 (0.96, 3.44)	1.19 (0.51, 2.77)

Table 6 (continued)

Specific causes of death	HR (95% CI) by VAI quartiles			
	Q1 (≤ 1.00)	Q2 (1.00 to ≤ 1.70)	Q3 (1.70 to ≤ 2.94)	Q4 (> 2.94)
Multivariable adjusted[b]	1 [Ref]	1.21 (0.63, 2.29)	1.75 (0.84, 3.68)	1.03 (0.39, 2.73)
Mortality from other causes				
Cases, No./total No	179/3276	149/2474	143/1785	101/1163
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.33 (0.87, 2.04)	1.47 (0.90, 2.40)	**2.30 (1.35, 3.93)****
Multivariable adjusted[b]	1 [Ref]	1.31 (0.80, 2.14)	1.11 (0.61, 2.00)	**1.97 (1.04, 3.72)***
Non-Hispanic White individuals				
Cardiovascular mortality				
Cases, No./total No	190/4599	271/4835	281/4974	312/5193
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.20 (0.68, 2.10)	1.69 (0.96, 2.97)	**2.03 (1.17, 3.52)***
Multivariable adjusted[b]	1 [Ref]	1.29 (0.69, 2.40)	1.62 (0.86, 3.04)	**1.96 (1.06, 3.64)***
Cancer mortality				
Cases, No./total No	182/4599	207/4835	240/4974	244/5193
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.95 (0.60, 1.49)	1.15 (0.74, 1.79)	**2.00 (1.32, 3.02)****
Multivariable adjusted[b]	1 [Ref]	0.84 (0.50, 1.43)	1.13 (0.68, 1.87)	**1.73 (1.05, 2.84)***
Mortality from other causes				
Cases, No./total No	433/4599	491/4835	550/4974	578/5193
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.91 (0.63, 1.30)	1.19 (0.84, 1.67)	**1.53 (1.10, 2.13)***
Multivariable adjusted[b]	1 [Ref]	0.81 (0.54, 1.22)	1.08 (0.74, 1.59)	1.24 (0.85, 1.81)
Hispanic Americans				
Cardiovascular mortality				
Cases, No./total No	32/1294	37/1757	69/2217	60/2442
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.47 (0.49, 4.41)	1.57 (0.58, 4.30)	2.07 (0.68, 6.27)
Multivariable adjusted[b]	1 [Ref]	1.70 (0.44, 6.51)	1.55 (0.44, 5.48)	2.05 (0.49, 8.58)
Cancer mortality				
Cases, No./total No	35/1294	49/1757	64/2217	59/2442
Age, sex, and race/ethnicity adjusted	1 [Ref]	1.08 (0.47, 2.46)	1.58 (0.72, 3.44)	0.81 (0.32, 2.06)
Multivariable adjusted[b]	1 [Ref]	1.03 (0.40, 2.62)	1.54 (0.63, 3.75)	0.66 (0.21, 2.04)
Mortality from other causes				
Cases, No./total No	61/1294	104/1757	129/2217	177/2442
Age, sex, and race/ethnicity adjusted	1 [Ref]	0.59 (0.27, 1.31)	0.80 (0.40, 1.60)	1.12 (0.55, 2.26)
Multivariable adjusted[b]	1 [Ref]	0.58 (0.22, 1.53)	0.84 (0.38, 1.88)	0.96 (0.43, 2.14)

VAI was coded into quartiles (Q1 to Q4)

Abbreviations: *VAI* Visceral adiposity index, *NHANES* National Health and Nutrition Examination Survey, *HR* hazard ratios, *95% CI* 95% confidence interval, *Ref* Reference group

[a] Nationally representative estimates of the non-pregnant US population aged > 20 years by applying survey weights

[b] Multivariate adjustment for age, sex, race and ethnicity, poverty income ratio, insurance status, cigarette smoking, alcohol drinking, and family history (cardiovascular disease or diabetes)

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

and identifying individuals at higher risk of premature mortality, particularly in high-risk groups.

Strengths and limitations

Strengths of this study include comprehensive analyses of a nationally representative cohort with a long period of follow-up, consideration of a wide panel of potential covariates and mediators, and consistency of sensitivity indicating the robustness of the results. However, limitations should be noticed. First, all anthropometric and lipid-related data integral to calculate VAI were collected merely at the time of examination, and it is of great interest to explore dynamic changes of VAI in association with premature mortality. Second, the possibility of unknown or unmeasured residual confounding factors cannot be entirely excluded even though a wide range of potential covariates were considered. However, if an unknown or unmeasured covariate can explain our

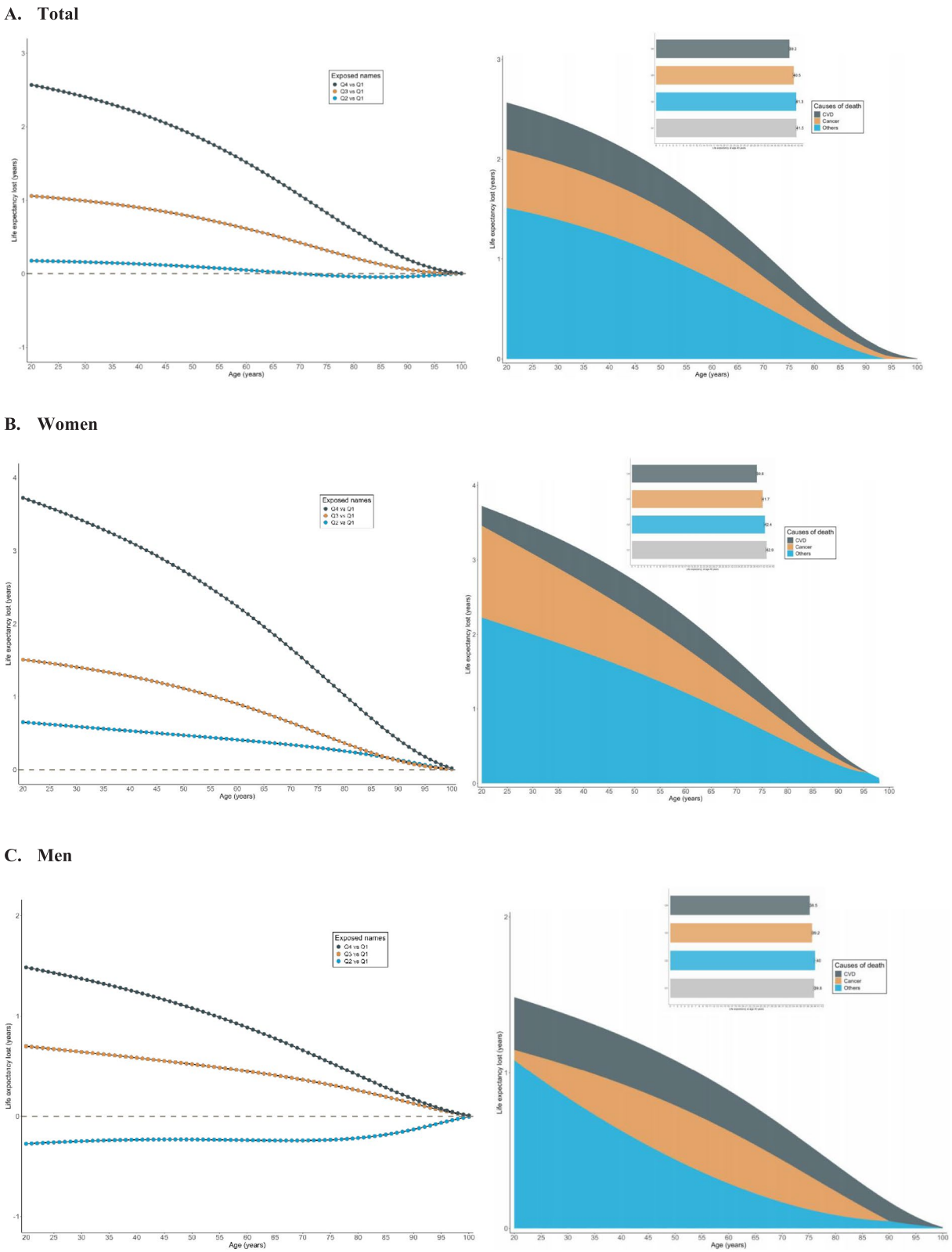

Fig. 6 Estimated Life Expectancy Loss by VAI Quartiles and Causes of Death in US Adults (NHANES 1999–2018): Stratified by Sex

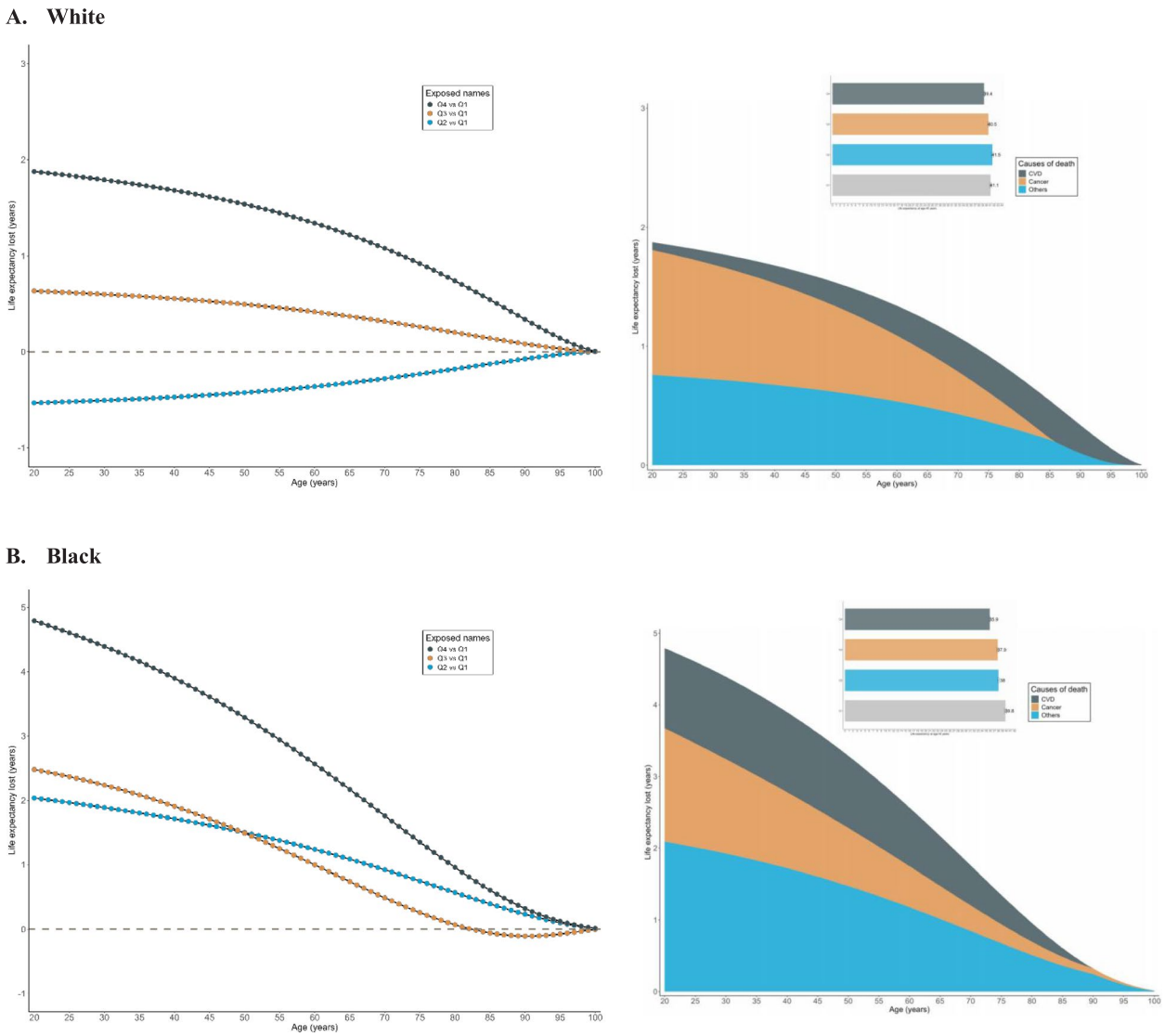

Fig. 7 Estimated Life Expectancy Loss by VAI Quartiles and Causes of Death in US Adults (NHANES 1999–2018): Stratified by Race and Ethnicity

findings, it must differ significantly across VAI quartiles and exhibit strong association with premature mortality risk. To our knowledge, no covariate fulfils these criteria.

Conclusions

In this nationwide cohort study, our findings indicated that higher VAI was significantly and independently associated with higher risk of premature mortality and shorter life expectancy at age 40 in US adults. This association was heterogeneous by sex and race/ethnicity, particularly in women and Black participants. These findings support VAI as a straightforward and comprehensive screening tool for assessing susceptibility to premature mortality and identifying high-risk adults. Moving forward, monitoring VAI could be integrated into public health strategies to reduce disease burden and increase longevity.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-025-02560-3.

Supplementary Material 1.

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Authors' contributions
Drs W. Niu and X. Dong had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Z. Zhang, W. Niu, X. Dong. Acquisition of data: W. Niu. Analysis and interpretation of data: M. Xue, X. Zhang, K. Chen, F. Zheng, B. Wang, Q. Lin. Drafting of the manuscript: M. Xue. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: M. Xue, X. Zhang, W. Niu. Study supervision: Z. Zhang, W. Niu, X. Dong.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The NHANES was approved by the ethics review board of the National Center for Health Statistics. Written informed consent was obtained from the parents.

Consent for publication
Not applicable.

Competing Interests
The authors declare no competing interests.

Author details
[1]Graduate School, Beijing University of Chinese Medicine, Beijing, China. [2]Department of Pediatrics, China-Japan Friendship Hospital, Beijing, China. [3]Institute of Clinical Medical Sciences, China-Japan Friendship Hospital, No.2 Yinghua East St., Chaoyang District, Beijing 100020, China. [4]Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China. [5]Center for Evidence-Based Medicine, Capital Institute of Pediatrics, Beijing 100020, China. [6]Northeast Forestry University, Harbin City, Heilongjiang Province, China. [7]Department of Radiology, College of Human Medicine, Precision Health Program, Michigan State University, 766 Service Road, East Lansing, MI 48824, USA.

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References

1. Dattani S. How do researchers estimate the death toll caused by each risk factor, whether it's smoking, obesity, or air pollution? 2023 Available from: https://ourworldindata.org/how-do-researchers-estimate-the-death-toll-caused-by-each-risk-factor-whether-its-smoking-obesity-or-air-pollution.
2. Li Y, Pan A, Wang DD, Liu X, Dhana K, Franco OH, et al. Impact of healthy lifestyle factors on life expectancies in the US population. Circulation. 2018;138(4):345–55.
3. Elmaleh-Sachs A, Schwartz JL, Bramante CT, Nicklas JM, Gudzune KA, Jay M. Obesity management in adults: a review. JAMA. 2023;330(20):2000–15.
4. Prillaman M. Why BMI is flawed - and how to redefine obesity. Nature. 2023;622(7982):232–3.
5. Jensen B, Moritoyo T, Kaufer-Horwitz M, Peine S, Norman K, Maisch MJ, et al. Ethnic differences in fat and muscle mass and their implication for interpretation of bioelectrical impedance vector analysis. Appl Physiol Nutr Metab. 2019;44(6):619–26.
6. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, et al. Visceral adiposity index: a reliable indicator of visceral fat function associated with cardiometabolic risk. Diabetes Care. 2010;33(4):920–2.
7. Chait A, den Hartigh LJ. Adipose tissue distribution, inflammation and its metabolic consequences, including diabetes and cardiovascular disease. Front Cardiovasc Med. 2020;7:22.
8. Yan S, Chai K, Yang J, Wang H. Association of visceral adiposity index and lipid accumulation product with frailty in U.S. adults: a cross-sectional study from NHANES. Lipids Health Dis. 2024;23(1):417.
9. Liu J, Liu W, Wang L, Wang N, Wu L, Liu X, et al. Association of visceral adiposity index and handgrip strength with cardiometabolic multimorbidity among middle-aged and older adults: findings from Charls 2011–2020. Nutrients. 2024;16(14):2277.
10. Li C, Wang G, Zhang J, Jiang W, Wei S, Wang W, et al. Association between visceral adiposity index and incidence of diabetic kidney disease in adults with diabetes in the United States. Sci Rep. 2024;14(1):17957.
11. Parra-Soto S, Boonpor J, Lynskey N, Araya C, Ho F, Pell JP, et al. Association between visceral adiposity index and cancer risk in the UK Biobank cohort. Cancer. 2025;131(1):e35576.
12. Fakhrolmobasheri M, Abhari AP, Heidarpour M, Paymannejad S, Pourmahdi-Boroujeni M, Saffari AS, et al. Lipid accumulation product and visceral adiposity index for incidence of cardiovascular diseases and mortality; results from 13 years follow-up in Isfahan cohort study. Obes Sci Pract. 2024;10(1):e713.
13. Liu W, Weng S, Chen Y, Cao C, Peng D. Age-adjusted visceral adiposity index (VAI) is superior to VAI for predicting mortality among US adults: an analysis of the NHANES 2011–2014. Aging Clin Exp Res. 2024;36(1):24.
14. Luo Y, Zhan X, Liu Y, Chen L, Zhu L, Cai W. Predicted visceral adiposity index in relation to risk of coronary heart disease and all-cause mortality: insights from NHANES. Front Endocrinol (Lausanne). 2023;14:1296398.
15. National Center for Health Statistics. NHANES questionnaires, datasets, and related documentation. Available from: https://wwwn.cdc.gov/nchs/nhanes/Default.aspx.
16. Centers for Disease Control and Prevention. The National Health and Nutrition Examination Survey. Available from: https://www.cdc.gov/nchs/nhanes.htm.
17. Centers for Disease Control and Prevention. NCHS data linked to mortality files. Available from: https://www.cdc.gov/nchs/?CDC_AAref_Val=https://www.cdc.gov/nchs/data_access/data_linkage/mortality.htm.
18. Johnson NB, Hayes LD, Brown K, Hoo EC, Ethier KA. CDC National Health Report: leading causes of morbidity and mortality and associated behavioral risk and protective factors–United States, 2005–2013. MMWR Suppl. 2014;63(4):3–27.
19. Silcocks PB, Jenner DA, Reza R. Life expectancy as a summary of mortality in a population: statistical considerations and suitability for use by health authorities. J Epidemiol Community Health. 2001;55(1):38–43.
20. Arriaga EE. Measuring and explaining the change in life expectancies. Demography. 1984;21(1):83–96.
21. Auger N, Feuillet P, Martel S, Lo E, Barry AD, Harper S. Mortality inequality in populations with equal life expectancy: Arriaga's decomposition method in SAS, Stata, and Excel. Ann Epidemiol. 2014;24(8):575–80 80.e1.
22. Saponaro C, Gaggini M, Carli F, Gastaldelli A. The subtle balance between lipolysis and lipogenesis: a critical point in metabolic homeostasis. Nutrients. 2015;7(11):9453–74.
23. Hotamisligil GS. Inflammation, metaflammation and immunometabolic disorders. Nature. 2017;542(7640):177–85.
24. Tchernof A, Després JP. Pathophysiology of human visceral obesity: an update. Physiol Rev. 2013;93(1):359–404.
25. de Ritter R, de Jong M, Vos RC, van der Kallen CJH, Sep SJS, Woodward M, et al. Sex differences in the risk of vascular disease associated with diabetes. Biol Sex Differ. 2020;11(1):1.
26. Karastergiou K, Smith SR, Greenberg AS, Fried SK. Sex differences in human adipose tissues - the biology of pear shape. Biol Sex Differ. 2012;3(1):13.
27. Schorr M, Dichtel LE, Gerweck AV, Valera RD, Torriani M, Miller KK, et al. Sex differences in body composition and association with cardiometabolic risk. Biol Sex Differ. 2018;9(1):28.
28. Dehghan A, Vasan SK, Fielding BA, Karpe F. A prospective study of the relationships between change in body composition and cardiovascular risk factors across the menopause. Menopause. 2021;28(4):400–6.
29. Neeland IJ, Ross R, Després JP, Matsuzawa Y, Yamashita S, Shai I, et al. Visceral and ectopic fat, atherosclerosis, and cardiometabolic disease: a position statement. Lancet Diabetes Endocrinol. 2019;7(9):715–25.
30 Rydén M, Gao H, Arner P. Influence of aging and menstrual status on subcutaneous fat cell lipolysis. J Clin Endocrinol Metab. 2020;105(4)::dgz245.
31. Morselli E, Frank AP, Palmer BF, Rodriguez-Navas C, Criollo A, Clegg DJ. A sexually dimorphic hypothalamic response to chronic high-fat diet consumption. Int J Obes (Lond). 2016;40(2):206–9.

32. Kalyani RR, Corriere M, Ferrucci L. Age-related and disease-related muscle loss: the effect of diabetes, obesity, and other diseases. Lancet Diabetes Endocrinol. 2014;2(10):819–29.
33. Himmelstein MS, Puhl RM, Quinn DM. Intersectionality: an understudied framework for addressing weight stigma. Am J Prev Med. 2017;53(4):421–31.
34. Kronenfeld LW, Reba-Harrelson L, Von Holle A, Reyes ML, Bulik CM. Ethnic and racial differences in body size perception and satisfaction. Body Image. 2010;7(2):131–6.
35. Bailey ZD, Krieger N, Agénor M, Graves J, Linos N, Bassett MT. Structural racism and health inequities in the USA: evidence and interventions. Lancet (London, England). 2017;389(10077):1453–63.
36. Ryan DH, Kahan S. Guideline recommendations for obesity management. Med Clin North Am. 2018;102(1):49–63.
37. Wharton S, Lau DCW, Vallis M, Sharma AM, Biertho L, Campbell-Scherer D, et al. Obesity in adults: a clinical practice guideline. CMAJ. 2020;192(31):E875–91.
38. Claussnitzer M, Dankel SN, Kim KH, Quon G, Meuleman W, Haugen C, et al. FTO obesity variant circuitry and adipocyte browning in humans. N Engl J Med. 2015;373(10):895–907.
39. Jia S, Chen Q, Huang W, Wang P, Zeng Y. Relationship between systemic immune response index (SIRI) and COPD: a cross-sectional study based on NHANES 2007–2012. Sci Rep. 2025;15(1):7887.
40. Schedel M, Heimel V, Taube C. Type 2 inflammation, a common denominator in chronic airway disease? Curr Opin Pulm Med. 2025;31(3):302–9.
41. Suhaimi SQA, Azemi AK, Mokhtar SS, Mat Zin AA, Rasool AHG. Impact of time-restricted feeding on glycemic indices, vascular oxidative stress, and inflammation in an obese prediabetes rat model induced by a high-fat diet and sugar drink. Nutrition. 2025;133:112692.
42. Lonkar N, Latz E, McManus RM. Neuroinflammation and immunometabolism in neurodegenerative diseases. Curr Opin Neurol. 2025;38(2):163–71.
43 Singh MK, Shin Y, Ju S, Han S, Kim SS, Kang I. Comprehensive overview of Alzheimer's disease: etiological insights and degradation strategies. Int J Mol Sci. 2024;25(13):6901.
44. Yoo ID, Park MW, Cha HW, Yoon S, Boonpraman N, Yi SS, et al. Elevated CLOCK and BMAL1 contribute to the impairment of aerobic glycolysis from astrocytes in alzheimer's disease. Int J Mol Sci. 2020;21(21):7862.

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