Original Article

Dietary antioxidant index and cardiometabolic risks in normal-weight individuals: Evidence from the National Health and Nutrition Examination Survey

Ting Xue MD, PhD[1†], Xiuying He MMed[2,3†], Yiyang Xu MD, PhD[4], Ji Fang BM[1], Min Lin BM[1], Lihua Cai MSN[1], Tian Zheng MMed[5], Li Li MD, PhD[1]

[1]Center of Health Management, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, Fuzhou University Affiliated Provincial Hospital, Fuzhou, China
[2]Department of Endocrinology, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, Fuzhou University Affiliated Provincial Hospital, Fuzhou, China
[3]Department of Endocrinology, Fuqing City Hospital Affiliated to Fujian Medical University, Fuzhou, China
[4]Department of Orthopaedics, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, Fuzhou University Affiliated Provincial Hospital, Fuzhou, China
[5]Department of Clinical Nutrition, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, Fuzhou University Affiliated Provincial Hospital, Fuzhou, China
[†]Both authors contributed equally to this manuscript

Background and Objectives: Caloric restriction is the most popular dietary intervention for preventing metabolic disorders. However, its benefits are limited in normal-weight individuals. This study aimed to examine the association between composite dietary antioxidant index (CDAI) and metabolically unhealthy normal weight (MUNW), as well as the relationship between CDAI and cardiometabolic mortality among normal-weight individuals, in order to provide personalized dietary recommendations. **Methods and Study Design:** This study consisted of two parts: (1) a cross-sectional analysis exploring the association between CADI and MUNW; and (2) a prospective cohort analysis assessing CDAI in relation to cardiometabolic mortality. Adult participants with normal weight from the National Health and Nutrition Examination Survey (2007-2018) were enrolled and classified into quartile groups based on CDAI for the analyses. **Results:** Among 4,590 participants included in this study, 472(7.82%) were diagnosed with MUNW. After full adjustment, the odds ratios (95% confidence intervals) for MUNW across the increasing CDAI levels were 0.80 (0.50-1.29), 0.85 (0.51-1.41), and 0.48 (0.26-0.87), respectively (*p* for trend = 0.026). This inverse association appeared to be attenuated among participants aged 20~59 years old (*p* for interaction = 0.035). During 32,113 person-years of follow-up, 82 cardiometabolic deaths occurred. After full adjustment, the hazard ratios (95% confidence intervals) for cardiometabolic mortality across the increasing CDAI levels were 0.78 (0.35-1.73), 0.51 (0.20-1.27), and 0.40 (0.19-0.87), respectively (*p* for trend = 0.014). **Conclusions:** CDAI was inversely associated with MUNW and cardiometabolic mortality in a normal-weight population in the United States. These findings warrant confirmation through interventional studies.

Key Words: antioxidant, metabolically unhealthy normal weight, nutrition, the National Health and Nutrition Examination Survey, cardiometabolic mortality

INTRODUCTION

Metabolically unhealthy normal weight (MUNW) phenotype refers to normal weight individuals diagnosed with metabolic syndrome (MetS) or exhibit components of MetS, including central obesity, impaired glucose metabolism, elevated blood pressure (BP), and dyslipidemia.[1, 2] MetS reflects metabolic dysfunction and represents a major risk factor for cardiometabolic diseases, with mortality being the most severe and clinically significant outcome.[3] The prevalence of MUNW varies widely (5-45%), depending on the population studied and the diagnostic criteria applied.[4] A recent study reported that in 2018, up to 17.2% of American adults met the criteria for MUNW phenotype.[5] The health hazards of MUNW have often

Corresponding Author: Dr Li Li, Center of Health Management, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, Fuzhou University Affiliated Provincial Hospital, No.134, Dongjie Street, Gulou District, Fuzhou, Fujian, China, 350001
Tel: +86 591 88219612; Email: lilifuzhou@fzu.edu.cn
Dr Tian Zheng, Department of Clinical Nutrition, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, Fuzhou University Affiliated Provincial Hospital, No.134, Dongjie Street, Gulou District, Fuzhou, Fujian, China, 350001
Tel: +86 591 87557768; Email: fjzhengtian@fjmu.edu.cn
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been overlooked due to the presence of a normal weight. However, recent studies found that compared to metabolically healthy normal weight (MHNW) or obese individuals, individuals with MUNW face a higher risk of adverse cardiometabolic outcomes, second only to those with metabolically unhealthy obesity.[6-9] These findings highlight the significant clinical burden posed by the MUNW phenotype, which presents challenges to healthcare systems. Therefore, targeted interventions in normal-weight populations deserve greater attention to improve cardiometabolic outcomes and reduce healthcare expenditures.

Healthy dietary behavior is a key aspect of personal behavior modification for managing metabolic disorders. Caloric restriction aimed at weight loss is the most widely used traditional dietary intervention for managing metabolic disorders.[10] However, the benefits of energy-restricted diets appeared to be limited in individuals with normal weight.[10] In order to provide personalized dietary guidance, more research is needed to identify metabolically beneficial dietary patterns specifically for the normal-weight population.

An antioxidant-rich diet is a potential candidate for metabolic health improvement, as recent studies have suggested an inverse association between antioxidant-rich diets and MetS in the general population.[11] However, it remains unclear whether an antioxidant-rich dietary pattern can effectively protect metabolism and improve cardiometabolic outcomes in normal weight individuals. Composite dietary antioxidant index (CDAI) is a summary score based on the dietary intake of vitamins A, C, and E; carotenoids; zinc; and selenium. It is a validated and reliable tool for evaluating the overall antioxidant properties of a diet.[12-15] Previous studies have reported a weak inverse association between CDAI and MetS, as well as its individual components, in the general population.[11, 12] In this study, we aimed to explore the association between CDAI and MUNW, as well as the relationship between CDAI and cardiometabolic mortality in normal-weight individuals, in order to provide further evidence to support personalized dietary guidance

METHODS

Study population

This was a nationwide study consisting of two parts. The first part was a cross-sectional analysis based on data from the National Health and Nutrition Examination Survey (NHANES), covering survey cycles from 2007 to 2018. NHANES is a nationally representative survey designed to assess the health and nutritional status of the non-institutionalized US population through a stratified, multistage probability sampling design. The second part involved a longitudinal analysis using mortality follow-up data derived from linkage to the National Death Index (NDI). The National Center for Health Statistics (NCHS) links NHANES data with NDI records to obtain mortality information for survey participants. The NDI is a comprehensive database that includes detailed records of all deaths occurring in the United States. These records are collected annually based on legally mandated death certificates and are subject to standardized coding, quality control, and integration by the NCHS. In this study, mortality follow-up was conducted from the date of the NHANES interview through December 31, 2019, allowing for the evaluation of long-term outcomes. All NHANES protocols were approved by the NCHS Ethics Review Board, and written informed consent was obtained from all participants. Detailed information about NHANES is available on the website of the U.S. Centers for Disease Control and Prevention (https://www.cdc.gov/nchs/nhanes/).

This study enrolled adult participants (aged ≥ 20 years) with normal weight, defined as a body mass index (BMI) between 18.5 and 25.0 kg/m^2, from the NHANES 2007-2018 cycles (n = 8,941). Participants were excluded based on the following criteria: 1) pregnancy (n = 93); 2) missing nutritional information required to assess CDAI (n = 779); 3) missing data necessary for the diagnosis of MUNW (n = 2,777); and 4) incomplete covariate data (n = 1,202). A total of 4,590 participants were included in the final analysis. The average follow-up duration was 7.0 ± 0.6 years. This study was approved by the Ethics Committee of Fujian Provincial Hospital (approval number: K2021-07-038). The research design flow is illustrated in Figure 1.

Assessment of MUNW

Metabolic phenotypes were defined according to the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III) criteria.[16] Participants meeting at least three of the following five criteria were classified as MUNW: 1) central obesity, defined as waist circumference ≥102 cm in men or ≥88 cm in women; 2) elevated BP, defined as BP ≥ 130/85 mmHg or current treatment for hypertension; 3) elevated fasting blood glucose (FBG), defined as FBG ≥ 100 mg/dL or current treatment for diabetes; 4) elevated triglycerides (TG), defined as TG ≥ 150 mg/dL or current treatment for hypertriglyceridemia; and 5) reduced high-density lipoprotein cholesterol (HDL-C), defined as HDL-C < 40 mg/dL in men or < 50 mg/dL in women. Participants who did not meet three or more of the above criteria were classified as MHNW.

Cardiometabolic mortality

According to previous studies, cardiometabolic diseases were defined as heart disease, cerebrovascular disease, and diabetes.[17] Cardiometabolic mortality was defined as death attributed to these conditions. The cause of death was determined using the underlying cause recorded in the NDI, which is coded according to the International Classification of Diseases, 10th Revision (ICD-10). Specifically, cardiac disease–related mortality was identified using ICD-10 codes I00–I09, I11, I13, and I20–I51; cerebrovascular disease–related mortality using codes I60–I69; and diabetes-related mortality using codes E10–E14.

Assessment of CDAI and energy

Each participant completed two 24-hour dietary recalls to assess dietary intake. The first diet recall was conducted in person, and the second was via telephone 3–10 days later. Daily dietary intake was calculated as the average of the two 24-hour dietary recalls. Nutrient and energy intake from all the foods were estimated using the Food and Nutrient Database for Dietary Studies developed by the United States Department of Agriculture. The dietary intake of each antioxidant was calculated as the sum of

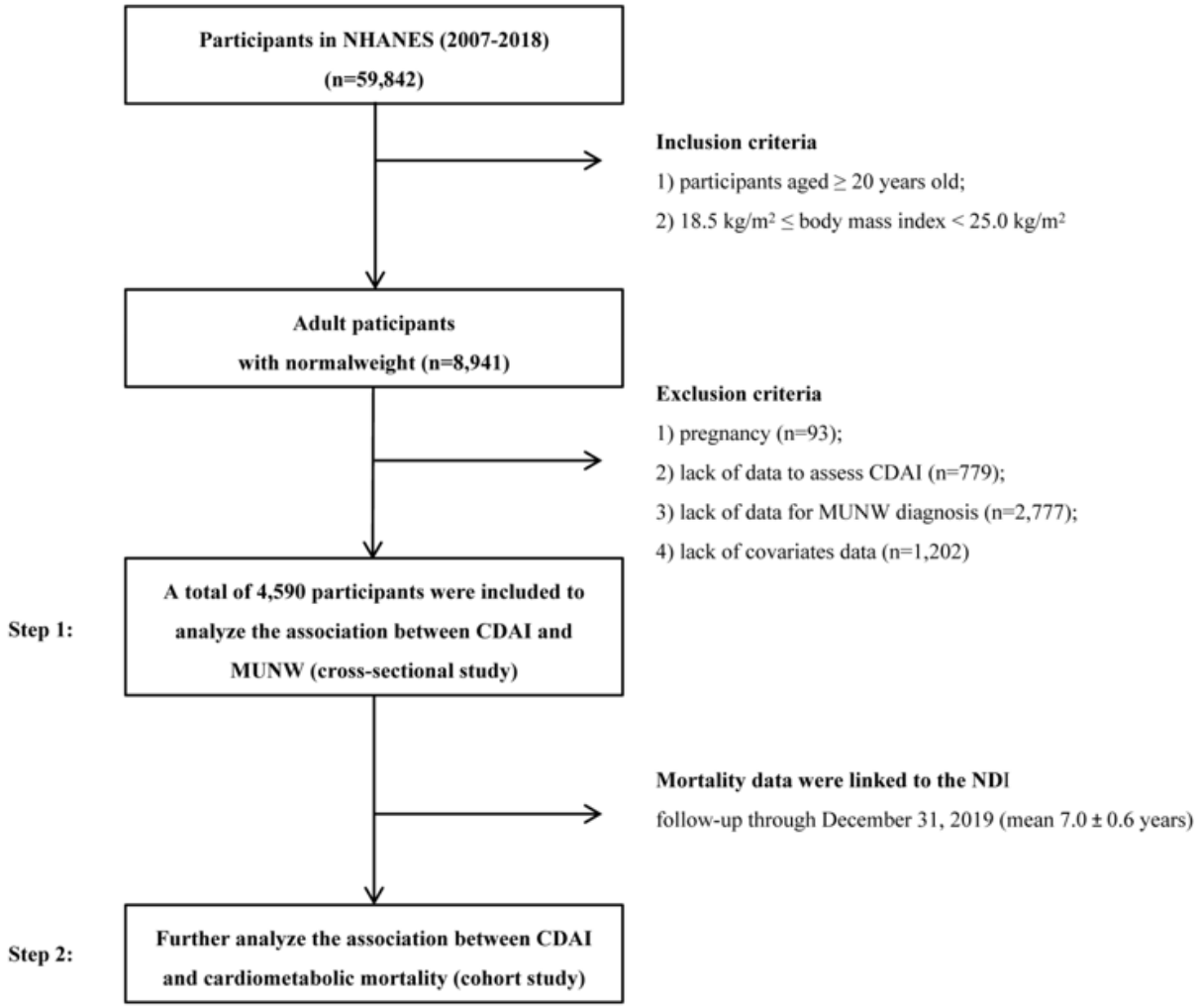

Figure 1. Flowchart of the study design

contributions from both food sources and dietary supplements. Six antioxidants (vitamins A, C, and E; carotenoids; zinc; and selenium) were standardized by subtracting the population mean and dividing by the standard deviation. The CADI was calculated as the sum of these standardized values.[14, 15] The formula for CDAI was as follows:

$$CDAI = \sum^{6}_{(n=1)} [(x\text{-mean})/SD]$$

where x represents the intake of each antioxidants, mean represents the population mean intake, and SD represents the standard deviation.

Assessment of covariates

Sociodemographic characteristics included age (years), sex (men/women), race (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, or other races), ratio of family income to poverty (PIR, %), marital status (married or cohabiting, never married, divorced or separated), and education, categorized as low (less than high school), medium (high school or equivalent), or high (college and above). Personal behaviors included smoking status (never, former, or current), drinking status (never, former, or current), physical activity (mild, moderate or vigorous), and energy intake (kcal/d). Moderate or vigorous physical activity was defined as engaging in more than 150 min per week of moderate physical activity, or 75 min per week of vigorous physical activity, or an equivalent combination.[18] Anthropometric data included only body mass index (BMI), calculated as weight in kilograms divided by height in meters squared.

Statistical methods

Considering the complex, stratified sampling design of NHANES, weighted samples were applied in accordance with CDC guidelines to enhance sample representativeness and minimize sampling error.[19] Continuous variables were presented as weighted means with standard errors, while categorical variables were expressed as weighted frequencies with estimated proportions. Weighted linear regression was used to assess the distribution of continuous variables, and the Rao-Scott chi-square test was employed to examine the distribution of categorical variables.

All participants were classified into one of four groups based on the interquartile range of the CDAI, with the first quartile serving as the reference group. The associations between CDAI and MUNW, as well as its components, were examined using logistic regression models. Model 1 was a minimally adjusted model, controlling only for the NHANES cycle. Model 2 was further adjusted for sociodemographic variables (age, sex, race, PIR, marital status, and education level) and anthropometric measurements (BMI). Model 3 additionally included personal behaviors such as smoking status, drinking status,

physical activity, and energy intake. To test for heterogeneity, stratified analyses were performed according to sex, age, PIR, education, BMI, smoking status, drinking status, physical activity, and energy intake. Sensitivity analyses were performed by re-running the models using an alternative definition of MUNW, defined as individuals with normal weight and at least two components of MetS.[4] In a separate sensitivity analysis, we re-ran the models after excluding participants with baseline comorbidities, including stoke (n = 121), liver or kidney diseases (n = 135), and cancer (n = 345).

The relationship between CDAI and cardiometabolic mortality in the normal-weight population was evaluated using Cox proportional hazards regression models. The proportional hazards assumption was tested by introducing an interaction term between follow-up time and CDAI, and no significant violation of the assumption was detected.[20] We applied the same three multivariate adjustment models and conducted stratified analyses. Sensitivity analyses were performed by re-running the Cox proportional hazards regression models after excluding participants with baseline stroke, liver or kidney diseases, and cancer. Additionally, we re-ran the Cox proportional hazards regression models excluding participants whose cardiometabolic mortality occurred within the first year of follow-up. Furthermore, we conducted a competing risk analysis to assess the association between CDAI and cardiometabolic mortality, treating non-cardiometabolic mortality as a competing event. This approach allows for a more accurate and clinically relevant estimation of cause-specific risk by accounting for the influence of competing outcomes, thereby minimizing potential bias and overestimation.

A two-tailed *p*-value less than 0.5 was considered statistically significant. All analyses were conducted using SAS (version 9.4; SAS Institute Inc). Forest plots illustrating the results of the stratified analyses were generated using R (version 4.3.1).

RESULTS

The baseline characteristics of the participants are summarized in Table 1. A total of 4,590 participants were included in the study. The weighted mean (standard error) age was 43.07 (0.36) years, and men accounted for 44.0% of the sample. The weighted prevalence of MUNW, central obesity, elevated BP, elevated FBG, elevated TG, and reduced HDL-C was 7.82%, 7.93%, 17.4%, 36.0%, 18.4%, and 8.97%, respectively. To assess potential temporal trends, we compared participant distributions across NHANES cycles, but found no significant differences (p = 0.09). Significant differences were observed between MHNW and MUNW participants in terms of race, marital status, level of education, smoking status, and drinking status (all p <0.001). In addition, participants with MUNW were older and had higher BMI values compared to those with MHNW (p <0.001). They also tended to engage in less moderate or vigorous physical activity and had lower energy intake, dietary vitamin E, carotenoid, and selenium intake, as well as lower CDAI scores (all p <0.001).

Three multivariable logistic regression models were constructed to examine the association between CDAI, MUNW, and its components (Table 2). A higher CDAI score was associated with a lower risk of MUNW. In Model 1, odds ratios (ORs) (95% confidence intervals [CIs]) across the increasing CDAI levels were 0.75 (0.50~1.12), 0.76 (0.49~1.18), and 0.45 (0.30~0.68), respectively (p for trend <0.001). After full adjustment for potential confounders, these inverse associations were slightly attenuated, with ORs (95% CIs) of 0.80 (0.50~1.29), 0.85 (0.51~1.41), and 0.48 (0.26~0.87), respectively (p for trend = 0.026). Similar results were observed in sensitivity analyses using alternative MUNW criteria (Supplementary Table 1). Additionally, sensitivity analyses excluding participants with history of stroke, liver or kidney diseases, and cancer showed consistent findings (Supplementary Table 2). According to Table 2, similar inverse associations were observed for central obesity, elevated BP, and elevated TG. In the full adjusted models, the ORs (95% CIs) for the highest CDAI categories were 0.45 (0.22~0.92; p for trend = 0.011) for central obesity; 0.65 (0.48~0.86; p for trend = 0.023) for elevated BP, and 0.44 (0.24~0.79; p for trend = 0.023) for elevated TG. In Model 1, the ORs (95% CIs) for reduced HDL-C across the increasing CDAI levels were 0.81 (0.57~1.17), 0.51 (0.34~0.75), and 0.46 (0.30~0.69), respectively (p for trend < 0.001). This inverse association was attenuated in the further adjusted model and disappeared in the fully adjusted model. No significant association was found between CDAI and elevated FBG levels in any model. Figure 2 presents the results of stratified analyses. Sex, race, education, marital status, PIR, drinking status, smoking status, and physical activity did not significantly modify the association between CDAI and MUNW (p for interaction >0.05). However, the inverse association between CDAI and MUNW appeared to be attenuated among participants aged 20~59 years (p for interaction = 0.035).

We further assessed the association between baseline CDAI and subsequent cardiometabolic mortality among normal-weight participants using Cox proportional hazards regression models (Table 3). During 32,113 person-years of follow-up, 82 cardiometabolic deaths were recorded. In Model 1, no significant association was observed between CDAI and cardiometabolic mortality (p for trend > 0.05). However, inverse associations emerged in both the partially adjusted (p for trend = 0.045) and fully adjusted (p for trend = 0.014) models. After full adjustment, participants in the highest CDAI category had a 60% lower risk of cardiometabolic mortality compared with those in the reference group (hazard risk [HR], 95%CI: 0.40 [0.19~0.87]). As shown in Figure 3, age, sex, race, education level, marital status, PIR, drinking status, smoking status, and physical activity did not significantly modify the association between CDAI and cardiometabolic mortality (all p for interaction >0.05). Sensitivity analyses yielded similar results when individuals with baseline comorbidities were excluded (Supplementary Table 3). When participants who experienced cardiometabolic death in the first year of follow-up were excluded, the association remained consistent (Supplementary Table 4). Similar results were also observed in competing risk analyses (Supplementary Table 5).

Table 1. Characteristics of the participants

Characteristic	Overall (n=4,590)	MHNW (n=4,118)	MUNW (n=472)	*p* value
Cycle, n (%)				0.090
2007-2008	790 (17.3)	687 (17.0)	103 (21.3)	
2009-2010	851 (16.0)	783 (16.4)	68 (11.0)	
2011-2012	815 (18.4)	744 (18.2)	71 (20.0)	
2013-2014	837 (17.5)	766 (17.9)	71 (13.2)	
2015-2016	671 (15.7)	598 (15.3)	73 (20.1)	
2017-2018	626 (15.2)	540 (15.3)	86 (14.5)	
Age, years	43.1 (0.36)	41.6 (0.37)	61.0 (1.05)	<0.001*
Sex, n (%)				0.173
Men	2,132 (44.0)	1,952 (44.4)	180 (38.8)	
Women	2,458 (56.1)	2,166 (55.6)	292 (61.2)	
Race, n (%)				0.008*
Mexican American	419 (5.54)	384 (5.70)	35 (3.67)	
Other Hispanic	394 (4.78)	352 (4.87)	42 (3.76)	
Non-Hispanic White	2,155 (70.1)	1,926 (70.1)	229 (69.3)	
Non-Hispanic Black	718 (7.75)	646 (7.90)	72 (5.94)	
Other races	904 (11.8)	810 (11.4)	94 (17.3)	
PIR, %	3.12 (0.03)	3.12 (0.04)	3.04 (0.12)	0.548
Marital status, n (%)				<0.001*
Married/cohabiting	2,617 (59.1)	2,357 (59.0)	260 (60.4)	
Never married	1,156 (26.6)	1,129 (28.2)	27 (6.85)	
Divorced/separated	817 (14.4)	632 (12.8)	185 (32.8)	
Education, n (%)				<0.001*
Low	790 (11.6)	651 (11.0)	139 (19.7)	
Medium	2,227 (48.1)	1,995 (47.3)	232 (57.0)	
High	1,573 (40.3)	1,472 (41.8)	101 (23.3)	
Smoking status, n (%)				0.002*
Never	2,716 (60.7)	2,498 (61.8)	218 (48.7)	
Former	845 (18.7)	728 (18.4)	117 (22.2)	
Current	1,029 (20.6)	892 (19.9)	137 (29.0)	
Drinking status, n (%)				<0.001*
Never	576 (9.91)	490 (9.31)	86 (17.0)	
Former	819 (14.0)	684 (13.3)	135 (22.0)	
Current	3,195 (76.1)	2,944 (77.4)	251 (61.0)	
Physical activity, n (%)				<0.001*
Mild	1,469 (25.9)	1,226 (24.4)	243 (42,7)	
Moderate or vigorous	3,121 (74.2)	2,892 (75.6)	229 (57.3)	
Energy intake, kcal/day	2,122 (19.0)	2,147 (20.2)	1,834 (50.9)	<0.001*
Dietary vitamin A intake, μg/day	680 (12.6)	683 (13.4)	641 (35.3)	0.264
Dietary vitamin C intake, mg/day	182 (6.57)	185 (7.00)	156 (15.7)	0.090
Dietary vitamin E intake, mg/day	10.5 (0.22)	10.7 (0.24)	8.04 (0.38)	<0.001*
Dietary carotenoids intake, μg/day	111,444 (303)	11,597 (321)	9,645 (844)	0.030*
Dietary zinc intake, mg/day	15.8 (0.25)	15.8 (0.26)	15.6 (0.69)	0.730
Dietary selenium intake, μg/day	130 (1.57)	131 (1.67)	118 (3.99)	0.005
CDAI	0.33 (0.09)	0.40 (0.10)	-0.45 (0.22)	<0.001*
BMI, kg/m^2	22.4 (0.04)	22.3 (0.04)	23.3 (0.08)	<0.001*
Central obesity, n (%)	363 (7.93)	144 (4.20)	219 (52.0)	<0.001*
Elevated BP, n (%)	1,090 (17.4)	685 (12.0)	405 (80.6)	<0.001*
Elevated FBG, n (%)	1,194 (35.9)	822 (29.3)	372 (89.2)	<0.001*
Elevated TG, n (%)	551 (18.4)	278 (11.9)	273 (73.5)	<0.001*
Reduced HDL-C, n (%)	509 (8.97)	240 (4.87)	269 (57.6)	<0.001*

MHNW, metabolically healthy normal weight; MUNW, metabolically unhealthy normal weight; PIR, ratio of family income to poverty; CDAI, composite dietary antioxidant index; BMI, body mass index; BP, blood pressure; FBG, fasting blood glucose; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol.

†Continuous variables are shown as weighted means (standard errors) and categorical variables are expressed as weighted frequencies (estimated proportions). Weighted linear regression was used to test the distribution of continuous variables. The Rao-Scott chi-square test was used to test the distributions of categorical variables.

*$p < 0.05$.

DISCUSSION

To the best of our knowledge, this is the first study to investigate the association between CDAI and MUNW, as well as the relationship between CDAI and cardiometabolic mortality among normal-weight individuals. We found that higher CDAI scores were significantly associated with lower odds of MUNW, central obesity, elevated BP, and elevated TG levels. In addition, a higher CDAI was linked to a reduced risk of cardiometabolic mortality. These findings highlight the potential role of dietary antioxidants in preventing metabolic abnormalities and

Table 2. ORs (95%CIs) for MUNW and its components across quartiles of the CDAI

	Quartile 1 (<-2.47)	Quartile 2 (-2.47~-0.73)	Quartile 3 (-0.73~1.55)	Quartile 4 (>1.55)	*p* for trend
MUNW					
Model 1†	1.00	0.75 (0.50~1.12)	0.76 (0.49~1.18)	0.45 (0.30~0.68)	<0.001*
Model 2‡	1.00	0.77 (0.48~1.25)	0.76 (0.45~1.29)	0.40 (0.24~0.68)	0.001*
Model 3§	1.00	0.80 (0.50~1.29)	0.85 (0.51~1.41)	0.48 (0.26~0.87)	0.026*
Central obesity					
Model 1†	1.00	1.12 (0.71~1.73)	0.90 (0.56~1.42)	0.56 (0.35~0.88)	<0.001*
Model 2‡	1.00	1.60 (0.91~2.81)	1.19 (0.63~2.23)	0.65 (0.35~1.22)	0.095
Model 3§	1.00	1.29 (0.71~2.33)	0.92 (0.46~1.83)	0.45 (0.22~0.92)	0.011*
Elevated BP					
Model 1†	1.00	0.71 (0.59~0.87)	0.77 (0.64~0.93)	0.68 (0.56~0.82)	0.001*
Model 2‡	1.00	0.80 (0.63~1.03)	0.85 (0.66~1.09)	0.66 (0.51~0.85)	0.008*
Model 3§	1.00	0.80 (0.63~1.04)	0.85 (0.65~1.11)	0.65 (0.48~0.86)	0.023*
Elevated FBG					
Model 1†	1.00	1.14 (0.83~1.56)	1.14 (0.82~1.60)	1.37 (0.99~1.89)	0.727
Model 2‡	1.00	1.04 (0.73~1.48)	1.03 (0.69~1.52)	0.99 (0.67~1.43)	0.912
Model 3§	1.00	1.08 (0.75~1.56)	1.05 (0.69~1.64)	1.07 (0.67~1.68)	0.860
Elevated TG					
Model 1†	1.00	0.59 (0.38~0.90)	0.61 (0.40~0.92)	0.59 (0.39~0.90)	0.030*
Model 2‡	1.00	0.47 (0.30~0.74)	0.51 (0.32~0.82)	0.39 (0.24~0.63)	0.001*
Model 3§	1.00	0.49 (0.31~0.78)	0.55 (0.33~0.92)	0.44 (0.24~0.79)	0.023*
Reduced HDL-C					
Model 1†	1.00	0.81 (0.57~1.17)	0.51 (0.34~0.75)	0.46 (0.30~0.69)	<0.001*
Model 2‡	1.00	0.90 (0.64~1.31)	0.58 (0.38~0.87)	0.52 (0.34~0.82)	0.001*
Model 3§	1.00	1.06 (0.71~1.57)	0.71 (0.48~1.08)	0.71 (0.43~1.17)	0.065

ORs, odds ratios; CIs, confidence intervals; MUNW, metabolically unhealthy normal weight; CDAI, composite dietary antioxidant index; BP, blood pressure; FBG, fasting blood glucose; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol.
†Model 1 adjusted for the National Health and Nutrition Examination Survey cycle.
‡Model 2 was further adjusted for age, sex, race, ratio of family income to poverty, marital status, education level, and BMI.
§Model 3 was further adjusted for smoking and drinking status, physical activity, and energy intake.
*$p < 0.05$

Table 3. HRs (95%CIs) for cardiometabolic mortality across quartiles of the CDAI

	Quartile 1 (<-2.47)	Quartile 2 (-2.47~-0.73)	Quartile 3 (-0.73~1.55)	Quartile 4 (>1.55)	p for trend
Case/N	28/1,148	19/1,147	18/1,147	17/1,148	
Person-years	7,942	8,115	7,867	8,187	
Model 1†	1.00	0.75 (0.37~1.59)	0.52 (0.24~1.10)	0.60 (0.27~1.32)	0.158
Model 2‡	1.00	0.81 (0.37~1.79)	0.52 (0.23~1.20)	0.47 (0.20~1.11)	0.045*
Model 3§	1.00	0.78 (0.35~1.73)	0.51 (0.20~1.27)	0.40 (0.19~0.87)	0.014*

HRs, hazard ratios; CIs, confidence intervals; CDAI, composite dietary antioxidant index.
†Model 1 adjusted for the National Health and Nutrition Examination Survey cycle.
‡Model 2 was further adjusted for age, sex, race, ratio of family income to poverty, marital status, education level, and BMI.
§Model 3 was further adjusted for smoking and drinking status, physical activity, and energy intake.
*$p < 0.05$..

reducing cardiometabolic mortality in normal-weight populations.

Insulin resistance, along with the underlying pathophysiological mechanisms that contribute to its development, rather than obesity, has been identified as initiating factors in the development of MetS.[10] Antioxidants may help ameliorate insulin resistance by enhancing insulin receptor sensitivity and improving pancreatic beta-cell function, which could partially explain the observed inverse association between CDAI and both MUNW and cardiometabolic mortality in normal body weight individuals.[14] Specifically, selenium acts as an essential co-factor for glutathione peroxidase and other selenoproteins, thereby lowering oxidative stress and modulating genes involved in glucose homeostasis.[21] Zinc up-regulates metallothionein, scavenges reactive oxygen species, and inhibits protein-tyrosine-phosphatase 1B, a negative regulator of insulin signalling, collectively improving insulin sensitivity.[22,23] Vitamins C, E and β-carotene work synergistically to reduce endothelial adhesion molecules and HOMA-IR in young adults.[24] The active metabolite of vitamin A, retinoic acid, enhances insulin signaling and alleviates insulin resistance by activating nuclear receptors RAR and PPARβ/δ.[25] A potential synergistic effect among these antioxidants may also contribute to the observed metabolic benefits. Interestingly, the inverse association between CDAI and MUNW appeared to be attenuated among younger participants, possibly due to the protective effects of relatively higher sex hormone levels against insulin resistance in this population.[26,27]

We observed an inverse association between CDAI and cardiometabolic mortality among our normal-weight

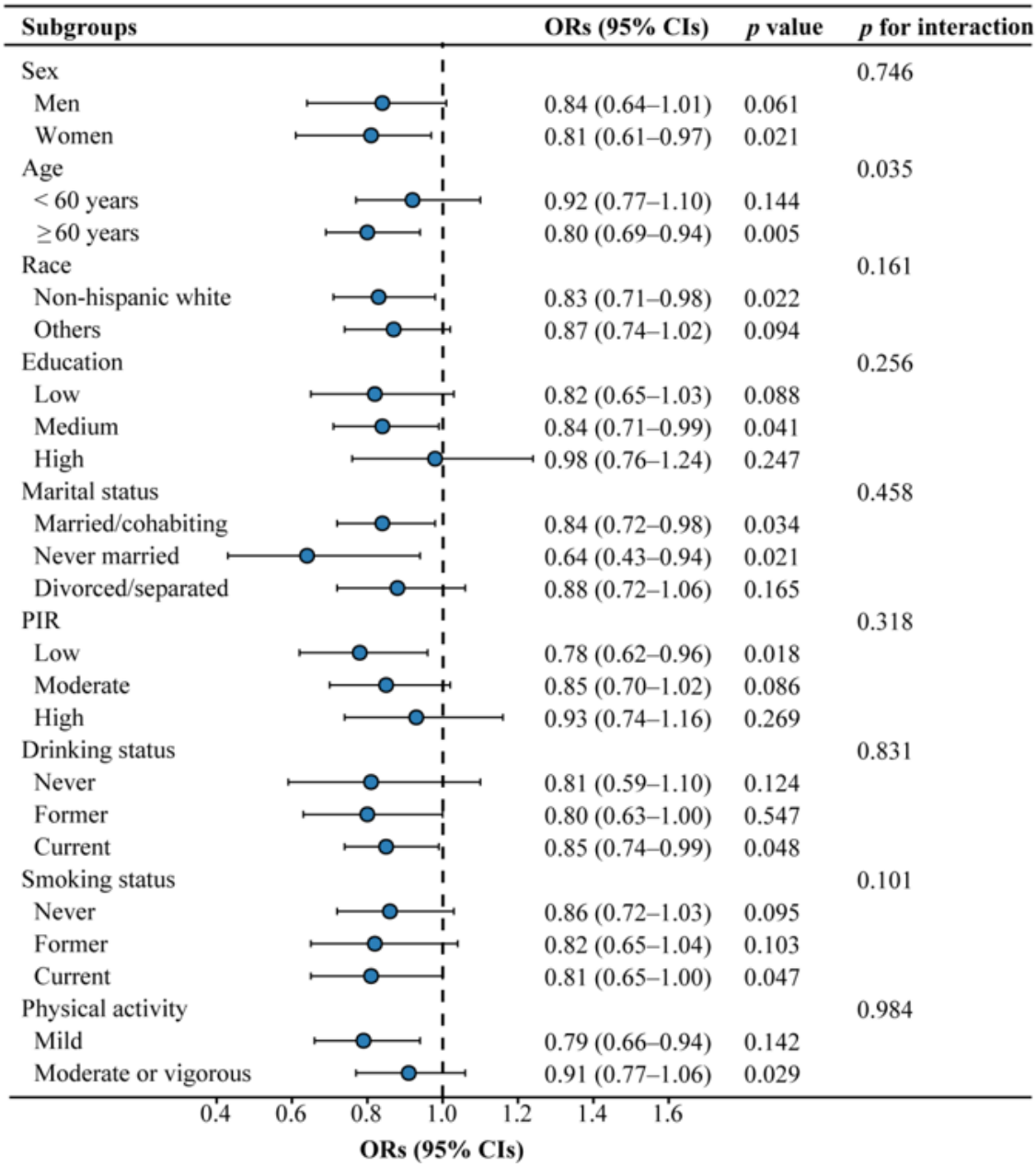

Figure 2. ORs (95% CIs) for MUNW across increasing CDAI quartiles, stratified by selected factors

individuals, with those in the highest CDAI category experiencing a 60% lower risk compared to those in the lowest category. This association appeared stronger than that reported in studies of the general population, where individuals in the highest CDAI category showed only a 19% risk reduction in cardiometabolic mortality risk.[11] Similarly, the inverse associations between CDAI and MetS, central obesity, and elevated TG, were more pronounced in our normal-weight population than in the general population, based on prior literature.[11] Notably, the negative association between CDAI and elevated BP was observed in our normal-weight population but has not been reported in previous studies conducted in the general population. In contrast, while a negative association between CDAI and reduced HDL-C has been reported in the general population, we did not observe this association in our normal-weight population. The mechanism underlying these differences between normal-weight and general populations remain unclear and warrant further investigation. We also found no significant association between CDAI and elevated FPG in our normal-weight participants, which is consistent with previous findings in the general population.[11,13] Further studies evaluating the association of CDAI with MUNW and cardiometabolic mortality in normal-weight participants are needed to confirm the robustness of our findings and to clarify the potential mechanisms through which an antioxidant-rich diet may influence metabolic health and cardiometabolic outcomes in this population.

This study has several notable strengths. First, we identified a potential protective of a dietary pattern characterized by a high CDAI on MUNW and cardiometabolic mortality among normal-weight individuals, who may derive less benefit from commonly recommended energy-restricted diets. Second, the present study was nationwide with a large sample size, providing sufficient statistical power, and we applied samples weighting to enhance representativeness. Third, as a study with an average

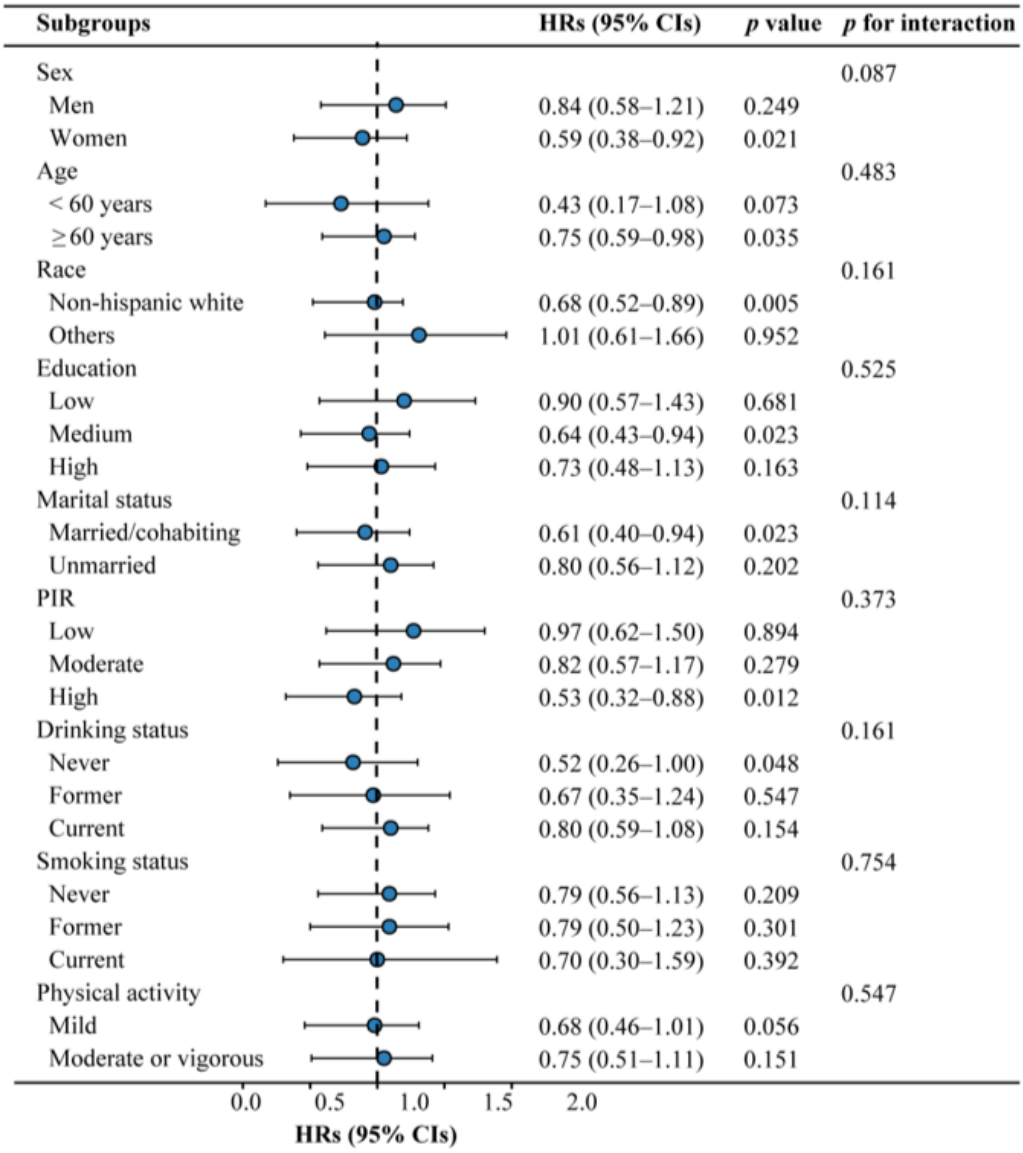

Figure 3. HRs (95% CIs) for cardiometabolic mortality across increasing CDAI quartiles, stratified by selected factors

follow-up of 7.0 ± 0.6 years in a real-world setting, it yielded adequate outcome events to reliably assess the relationship between CDAI and cardiometabolic mortality. Finally, detailed information on potential confounders was available, allowing us to adjust for theses factors and reduce residual confounding.

This study also has some limitations. First, our analysis was based on data from NHANES, a survey designed to assess the health and nutritional status of the U.S. population; Thus, the generalization of our findings to other demographic groups remains unclear. Second, dietary intake was self-report and subject to day-to-day variability, which may have introduced measurement errors affecting our estimates. However, such errors are typically random in large population samples and are unlikely to substantially bias our conclusions.

Conclusion

CDAI was significantly inversely associated with MUNW and cardiometabolic mortality among normal-weight adults in the United States. These associations warrant replication in interventional studies to confirm their causal nature and evaluate the potential of antioxidant-rich diets as a preventive strategy.

SUPPLEMENTARY MATERIALS

All supplementary materials are available upon request to the editorial office.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURES

The author(s) report no conflicts of interest in this work.

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Supplementary Tables

Supplementary Table 1. ORs (95%CIs) for MUNW across quartiles of the CDAI when MUNW was defined as individuals with normal weight have two components of MetS

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*p* for trend
Model 1†	1.00	0.75 (0.56~1.01)	0.77 (0.56~1.04)	0.69 (0.51~0.93)	0.032*
Model 2‡	1.00	0.68 (0.47~1.00)	0.75 (0.51~1.13)	0.54 (0.36~0.81)	0.007*
Model 3§	1.00	0.69 (0.46~1.03)	0.77 (0.50~1.19)	0.54 (0.33~0.88)	0.028*

ORs, odds ratios; CIs, confidence intervals; MUNW, metabolically unhealthy normal weight; CDAI, composite dietary antioxidant index; MetS, metabolic syndrome.
†Model 1 adjusted for the National Health and Nutrition Examination Survey cycle.
‡Model 2 further adjusted for age, gender, race, ratio of family income to poverty, marital status, level of education, and BMI.
§ Model 3 further adjusted for smoking status, drinking status, physical activity, and energy intake.
*$p < 0.05$

Supplementary Table 2. ORs (95%CIs) for MUNW across quartiles of the CDAI when participants with history of stroke, liver or kidney diseases, and cancer were further excluded

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*p* for trend
Model 1†	1.00	0.67 (0.43~1.03)	0.70 (0.43~1.12)	0.44 (0.28~0.68)	<0.001*
Model 2‡	1.00	0.75 (0.46~1.22)	0.73 (0.41~1.31)	0.40 (0.23~0.70)	0.002*
Model 3§	1.00	0.80 (0.48~1.34)	0.80 (0.45~1.41)	0.46 (0.23~0.91)	0.031*

ORs, odds ratios; CIs, confidence intervals; MUNW, metabolically unhealthy normal weight; CDAI, composite dietary antioxidant index.
†Model 1 adjusted for the National Health and Nutrition Examination Survey cycle.
‡Model 2 further adjusted for age, gender, race, ratio of family income to poverty, marital status, level of education, and BMI.
§ Model 3 further adjusted for smoking status, drinking status, physical activity, and energy intake.
*$p < 0.05$

Supplementary Table 3. HRs (95%CIs) for cardiometabolic mortality across quartiles of the CDAI when participants with history of stroke, liver or kidney diseases, and cancer were further excluded

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*p* for trend
Case/N	23/1,083	15/1,083	15/1,084	14/1,084	
Person-years	7,489	7,544	7,418	7,720	
Model 1†	1.00	0.61 (0.26~1.43)	0.46 (0.20~1.10)	0.54 (0.24~1.21)	0.139
Model 2‡	1.00	0.73 (0.32~1.67)	0.50 (0.20~1.28)	0.43 (0.20~1.28)	0.039*
Model 3§	1.00	0.69 (0.32~1.52)	0.45 (0.17~1.20)	0.35 (0.18~0.67)	0.001*

HRs, hazard ratios; CIs, confidence intervals; CDAI, composite dietary antioxidant index.
†Model 1 adjusted for the National Health and Nutrition Examination Survey cycle.
‡Model 2 was further adjusted for age, sex, race, ratio of family income to poverty, marital status, education level, and BMI.
§Model 3 was further adjusted for smoking and drinking status, physical activity, and energy intake.
*$p < 0.05$

Supplementary Table 4. HRs (95%CIs) for cardiometabolic mortality across quartiles of the CDAI excluding participants whose cardiometabolic mortality occurred in the first year of follow-up

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*p* for trend
Case/N	24/1,144	16/1,145	17/1,146	15/1,146	
Person-years	7,939	8,114	7,867	8,186	
Model 1†	1.00	0.75 (0.33~1.67)	0.56 (0.25~1.23)	0.53 (0.23~1.20)	0.105
Model 2‡	1.00	0.82 (0.35~1.93)	0.57 (0.23~1.39)	0.41 (0.16~1.09)	0.053
Model 3§	1.00	0.82 (0.35~1.89)	0.60 (0.23~1.55)	0.38 (0.16~0.92)	0.026*

HRs, hazard ratios; CIs, confidence intervals; CDAI, composite dietary antioxidant index.
†Model 1 adjusted for the National Health and Nutrition Examination Survey cycle.
‡Model 2 was further adjusted for age, sex, race, ratio of family income to poverty, marital status, education level, and BMI.
§Model 3 was further adjusted for smoking and drinking status, physical activity, and energy intake.
*Statistical significance was defined as $p < 0.05$

Supplementary Table 5. HRs (95%CIs) for cardiometabolic mortality across quartiles of the CDAI when non-cardiometabolic mortality regarded as a competing event

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*p* for trend
Case/N	28/1,148	19/1,147	18/1,147	17/1,148	
Person-years	7,942	8,115	7,867	8,187	
Model 1[†]	1.00	0.75 (0.36~1.59)	0.51 (0.24~1.10)	0.60 (0.27~1.32)	0.105
Model 2[‡]	1.00	0.81 (0.37~1.80)	0.53 (0.23~1.20)	0.47 (0.20~1.12)	0.053
Model 3[§]	1.00	0.77 (0.35~1.70)	0.49 (0.23~1.21)	0.42 (0.20~0.88)	0.026*

HRs, hazard ratios; CIs, confidence intervals; CDAI, composite dietary antioxidant index.
[†]Model 1 adjusted for the National Health and Nutrition Examination Survey cycle.
[‡]Model 2 was further adjusted for age, sex, race, ratio of family income to poverty, marital status, education level, and BMI.
[§]Model 3 was further adjusted for smoking and drinking status, physical activity, and energy intake.
*$p < 0.05$