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Dietary oleic acid intake, olive oil consumption, and risk of cardiovascular and all-cause mortality

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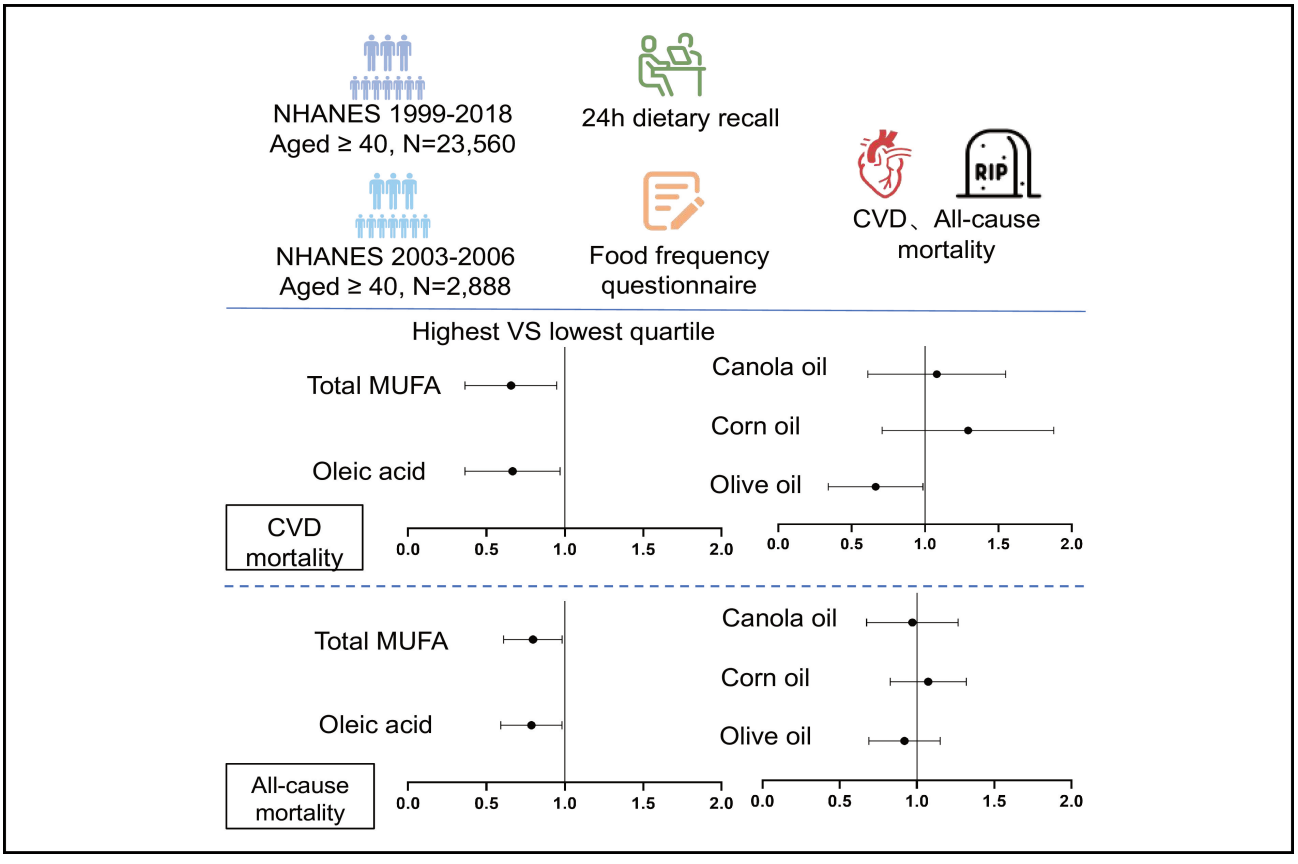
Graphical abstract



Study design chart and adjusted HRs (95% CIs) for the associations between the dietary intake of oleic acid and the consumption of other specific subtypes of MUFAs, olive oil, and other vegetable oils and CVD and all-cause mortality.

Public summary

- Higher dietary oleic acid intake and olive oil consumption are associated with a lower risk of CVD mortality, suggesting the importance of habitual intake of oleic acid and olive oil for improving cardiovascular health.
- For promoting cardiovascular health, our findings may provide some dietary recommedations.

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Abstract: *Objective*: Oleic acid, a subtype of monounsaturated fatty acid (MUFA), is present in abundance in certain edible oils, particularly olive oils. Epidemiological evidence concerning dietary oleic acid intake and the long-term risk of mortality is lacking. This study aimed to evaluate the associations of the dietary intake of oleic acid and other specific subtypes of MUFAs, olive oil, and other vegetable oils with cardiovascular disease (CVD) and all-cause mortality. *Methods*: This prospective cohort study included adults aged 40 years or older who participated in the included U.S. adults National Health and Nutrition Examination Survey (NHANES). Dietary MUFA intake was assessed via 24-h dietary recall interviews in NHANES 1999–2018, and the consumption of olive oil and other vegetable oils was assessed via a food frequency questionnaire in NHANES 2003–2006. Deaths and underlying causes of death were ascertained by linkage to the National Death Index through December 31, 2019. Weighted Cox proportional hazards regression models were used to estimate the hazard ratio (HR) and 95% CIs. *Results*: Dietary intake of total MUFAs and oleic acid was associated with a lower risk of CVD mortality, with HRs (95% CI) of 0.62 (0.39–0.99) and 0.61 (0.39–0.97), respectively. Total MUFA and oleic acid intake were inversely associated with all-cause mortality; the multivariable-adjusted HRs were 0.77 (95% CI: 0.60–0.99) and 0.78 (95% CI: 0.62–0.99), respectively. There was no significant association between palmitoleic acid intake and all-cause mortality. The habitual consumption of olive oil, but not the consumption of other vegetable oils, was inversely associated with the risk of cardiovascular mortality. In the joint association analysis, the HRs (95% CI) of cardiovascular mortality were 0.36 (0.19–0.69) for people who exclusively consumed olive oil, 0.59 (0.27–1.32) for people who consumed both olive oil and other vegetable oils, and 0.73 (0.46–1.14) for people who exclusively consumed other vegetable oils compared with people who never consumed vegetable oils. *Conclusions*: In a U.S. nationally representative prospective cohort, higher dietary oleic acid intake and olive oil consumption were associated with a lower risk of cardiovascular mortality.

Keywords: oleic acid; monounsaturated fatty acid; olive oil; cardiovascular mortality; all-cause mortality

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1 Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide, making it a major focus of medical and public health efforts[1]. Dietary modification is a key step in the management and prevention of CVD[2], in which dietary fats and oils, especially olive oil, have drawn particular attention. The prevailing dietary guidelines recommend limiting the consumption of saturated fatty acids and trans-fatty acids while increasing the intake of unsaturated fatty acids in place of saturated fatty acids, on the basis of a wealth of literature[3]. However, the evidence regarding the association between monounsaturated fatty acid (MUFA) intake and the risk of mortality is controversial, and the relationships between specific MUFA subtypes and the risk of death are unclear. Oleic acid, a subtype of MUFA, is present in abundance in certain edible oils, particularly olive oil. Epidemiological evidence concerning dietary oleic acid intake and the long-term risk of mortality is lacking. An increasing number of epidemiological studies have reported the beneficial effects of olive oil on cardiometabolic health; however, evidence on the long-term effects of olive oil consumption on cardiovascular mortality and all-cause mortality is still sparse[4–7].

In this prospective cohort study, we aimed to examine the associations of dietary intake of oleic acid and other specific subtypes of MUFA, olive oil, and vegetable oils with the risk of cardiovascular and all-cause mortality in a nationally representative population of the United States.

2 Materials and methods

2.1 Study population

The National Health and Nutrition Examination Survey

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(NHANES), conducted by the National Center for Health Statistics at the U.S. Centers for Disease Control and Prevention, is a nationally representative survey in the United States. Data, including demographics, socioeconomic status, diet, lifestyle, and medical conditions, were obtained from face-to-face interviews and physical examinations, and laboratory measurements were performed. The National Center for Health Statistics Ethics Review Board granted ethical approval for the NHANES study, and written informed consent was obtained from all participants. Since this study employs deidentified data, further ethical approval is not required. All analyses were conducted in strict adherence to the guidelines and regulations set forth by NHANES.

We included participants 40 years or older from NHANES 1999–2018 who were free of a history of CVD or cancer disease at baseline and had mortality follow-up information, including the underlying cause of death. After excluding people who had missing information about MUFA intake, we ultimately included 23,560 participants in this analysis. In addition, in a subcohort analysis regarding vegetable oil consumption and mortality risk, we included 2,888 participants from the NHANES 2003–2006 cycles because vegetable oil consumption was only evaluated in these cycles. Fig. 1 depicts the sample selection process.

2.2 Outcome ascertainment

To determine the mortality status of the participants, we used data from the NHANES public-use linked mortality file through December 31, 2019, which was linked by the National Center for Health Statistics (NCHS) to the National Death Index with probability matching algorithms[8]. Data concerning the underlying causes of death were used for case definition according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) for deaths that occurred[9]. According to the NCHS and ICD-10, CVD mortality was classified as death from either cerebrovascular disease or heart disease. The follow-up time for each person was calculated as the difference between the NHANES survey date and the last known date alive or censored from the NHANES mortality study.

2.3 Exposure measurement

The nutrient intakes in NHANES 1999–2018 were assessed via 24-h recall by a trained interviewer and were calculated via the automated multiple-pass method from the U.S. Department of Agriculture (USDA) Food and Nutrient Databases for Dietary Studies[10]. The NHANES dietary data included four individual monounsaturated fatty acids (palmitoleic acid, oleic acid, gadoleic acid, and erucic acid). The total MUFA intake was calculated as the sum of these individual MUFAs.

Information about olive oil and other vegetable oil consumption was collected through additional questionnaires administered in NHANES 2003–2006[11]. The participants were asked "How often did you eat foods with oils added or with oils used in cooking (do not include baked goods or salads)?", and a further detailed question was asked: "What kind of oils do you usually eat? (Mark all that apply)". According to the response, the type of vegetable oil was identified.

2.4 Covariate assessment

Information on age, sex, race/ethnicity, education, family income, smoking status, alcohol intake, and physical activity was collected during the interviews. Race/ethnicity was categorized as Hispanic (including Mexican and non-Mexican Hispanic), non-Hispanic White, non-Hispanic Black, or other. Education was classified as less than high school, high school, or more than high school. The ratio of family income to poverty was categorized as <1, 1 to 1.9, 2 to 3.9, or 4 or higher[12]. In accordance with the NCHS classifications, indi-

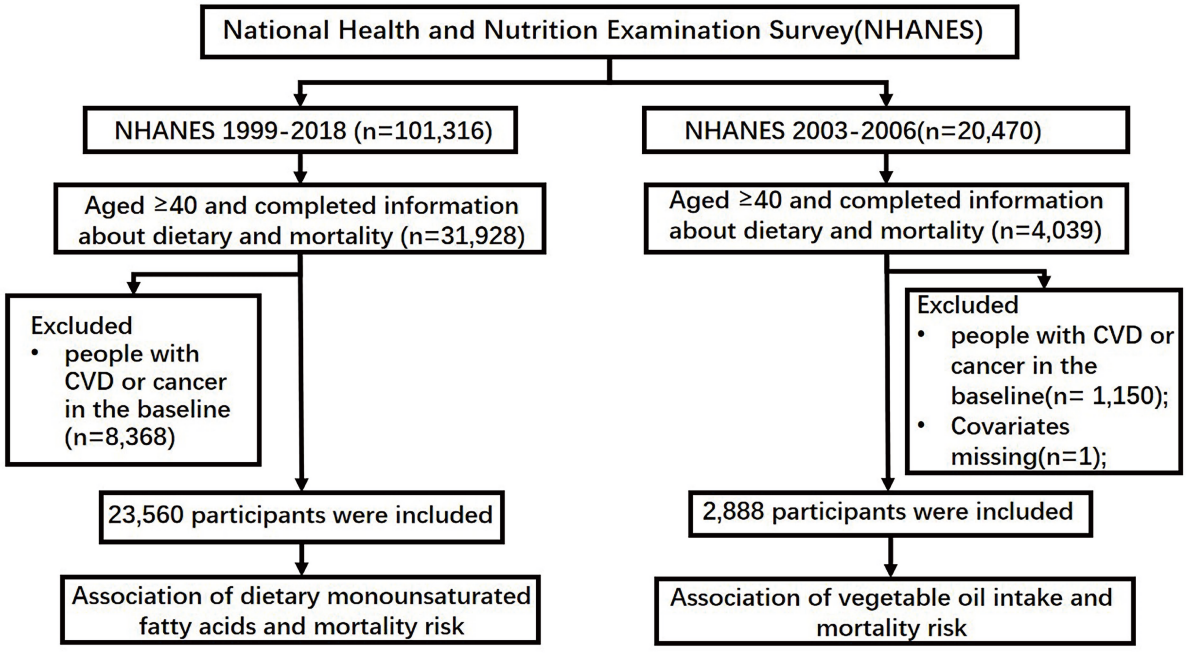

Fig. 1. Flow chart of participant selection.

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viduals who smoked fewer than 100 cigarettes in their lifetime were defined as never smokers; those who had smoked more than 100 cigarettes but did not smoke at the time of the survey were considered former smokers; and those who had smoked more than 100 cigarettes in their lifetime and smoked cigarettes at the time of the survey were considered current smokers. Alcohol intake was categorized as nondrinking (0 g/d), moderate drinking (0.1 to 28 g/d for males and 0.1 to 14 g/d for females), and heavy drinking (≥28 g/d for males and ≥ 14 g/d for females). Physical activity was divided into three groups in accordance with the guidelines: (i) low (<150 min per week), (ii) medium (150–300 min per week), and (iii) high (>300 min per week)[13]. The total energy intake was calculated via the U.S. Department of Agriculture automated multiple-pass method. HEI-2015 scores, ranging from 0 to 100, were calculated to represent overall diet quality, and higher scores indicate better diet quality[14]. Body weight and height were measured by trained technicians at the mobile examination center, and body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. The intake of saturated fat, polyunsaturated fat, protein, and carbohydrates was estimated via 24-h dietary recall.

2.5 Statistical analysis

All the statistical analyses incorporated sample weights, strata, and primary sampling units in the complex NHANES survey design to ensure that the calculated estimates were representative of the U.S. general population. Comparisons of characteristics were performed via linear regression for continuous variables. The Taylor series linearization method was used to calculate the variance and standard error, but for the variable "mean total energy intake", we used the balanced repeated replication (BRR) method to compute the variance and standard error and χ^2 tests for categorical variables. We used Cox proportional hazards regression models to estimate hazard ratios (HRs) and 95% confidence intervals (95% CIs) for the associations of dietary MUFA consumption and vegetable oil consumption with the risk of mortality. The covariates in the models included age, sex, race/ethnicity, education, family income level, smoking status, alcohol intake, physical activity, total energy intake, overall diet quality indicated by the HEI-2015, and BMI. We additionally adjusted for intakes of saturated fat, polyunsaturated fat, protein intake, carbohydrate intake, and mutual adjustment for the remaining MUFAs where appropriate (palmitoleic acid, oleic acid, gadoleic acid, and erucic acid) when dietary MUFA intake was modeled as the exposure of interest. For the models concerning the consumption of olive oil or other vegetable oils (corn oil, canola oil), we additionally adjusted for the consumption of nonvegetable dietary fats (margarine, butter, and mayonnaise) and mutually adjusted for the consumption of the remaining oils (olive oil, corn oil, and canola oil). E values were calculated to examine the robustness of the findings. All the statistical analyses were performed via survey procedures in SAS software version 9.4 (SAS Institute). All the statistical tests were two-sided, and *P* values less than 0.05 were considered statistically significant.

3 Results

This study included 23,560 participants aged 40 years or older. During 226,257 person-years of follow-up (median follow-up 9.3 years; maximum follow-up 20.8 years), 3,877 deaths occurred, including 1,135 deaths from cardiovascular disease. The baseline characteristics of the participants according to the quartiles of dietary MUFAs are shown in Table 1. Compared with participants with lower total MUFA intake, those with higher total MUFA intake were more likely to be non-Hispanic white and physically active, and had higher levels of education, more family income, and higher total energy intake.

Dietary total MUFA intake was significantly and inversely associated with the risk of CVD and all-cause mortality (Tables 2 and 3**).** After adjustment for age, sex, race/ethnicity, socioeconomic status, dietary and lifestyle factors, and BMI, there was a lower risk for cardiovascular mortality (HR: 0.62; 95% CI: 0.39–0.99) and all-cause mortality (HR: 0.77; 95% CI: 0.60–0.99) among individuals in the highest quartile of total MUFA intake than among those in the lowest quartile. The multivariable-adjusted HRs for all-cause mortality and CVD mortality compared with the lowest quartile of oleic acid intake were 0.78 (95% CI: 0.62–0.99) and 0.61 (95% CI: 0.39–0.97), respectively. There was no significant association between palmitoleic acid intake and CVD or all-cause mortality. Additionally, no significant associations between dietary gadoleic acid or erucic acid intake and mortality outcomes were found. The E value for the association between those in the highest quartile of oleic acid and CVD mortality was 2.66 with the lower confidence bound of 1.21; for all-cause mortality, the E value was 1.88 with the lower confidence bound of 1.11. In addition, sensitivity analyses after excluding participants who died within one year of follow-up yielded similar results for both CVD and all-cause mortality.

The habitual consumption of olive oil was associated with a lower risk of death from CVD (Table 4). After adjustment for age, sex, race/ethnicity, socioeconomic status, dietary and lifestyle factors, and BMI, there was a 39% lower risk of cardiovascular mortality (HR: 0.61; 95% CI: 0.37–1.01) among individuals who consumed olive oil than among those who never consumed olive oil. There was no significant association between corn oil or canola oil consumption and mortality. Compared with those of people who never consumed vegetable oil, the HRs (95% CI) of cardiovascular mortality were 0.36 (0.19–0.69) for people who exclusively consumed olive oil, 0.59 (0.27–1.32) for people who consumed both olive oil and other vegetable oils, and 0.73 (0.46–1.14) for people who exclusively consumed other vegetable oils, compared with people who never consumed vegetable oil (Table 5).

4 Discussion

In this prospective study of a nationally representative sample of U.S. adults, we observed that dietary oleic acid intake and total MUFA intake were significantly and inversely associated with CVD and all-cause mortality. There was no significant association of palmitoleic acid, gadoleic acid or

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Table 1. Characteristics of the participants according to dietary monounsaturated fatty acid intake.

	Total MUFA intake				*P* value[1]
	Q1	Q2	Q3	Q4	
Number of participants	5890	5890	5890	5890	
Age (year)	57.4 (0.2)	56.3 (0.2)	55.2 (0.2)	53.0 (0.2)	<0.001
Sex					
Male	28.9 (0.9)	35.7 (0.8)	48.5 (1.1)	67.6 (0.9)	<0.001
Female	71.1 (0.9)	64.3 (0.8)	51.5 (1.1)	32.4 (0.9)	
Race/ethnicity					
Hispanic	14.5 (1.0)	11.9 (0.8)	11.0 (0.8)	10.1 (0.8)	
Non-Hispanic White	63.3 (1.5)	71.2 (1.2)	72.5 (1.2)	75.0 (1.1)	<0.001
Non-Hispanic Black	12.9 (1.0)	10.4 (0.7)	10.3 (0.6)	10.2 (0.6)	
Other	9.4 (0.7)	6.5 (0.5)	6.2 (0.5)	4.6 (0.4)	
Education					
Less than high school	22.6 (0.9)	17.0 (0.7)	15.4 (0.7)	14.2 (0.7)	
High school	25.0 (0.9)	23.9 (1.0)	24.7 (0.9)	24.8 (1.0)	<0.001
More than high school	52.4 (1.2)	59.1 (1.2)	59.9 (1.1)	61.0 (1.2)	
Ratio of family income to poverty					
< 1	14.3 (0.7)	10.0 (0.5)	9.4 (0.6)	8.3 (0.5)	
1–1.9	20.6 (0.9)	17.0 (0.7)	17.0 (0.7)	13.9 (0.7)	<0.001
2–3.9	25.5 (1.0)	25.9 (1.0)	27.3 (1.0)	26.4 (1.0)	
≥ 4	39.6 (1.2)	47.2 (1.2)	46.2 (1.4)	51.5 (1.3)	
Smoking status[2]					
Never smoker	56.0 (1.1)	53.4 (1.1)	53.5 (0.9)	48.6 (1.1)	
Current smoker	18.6 (0.9)	18.4 (0.7)	18.4 (0.9)	19.8 (0.7)	<0.001
Ever smoker	25.3 (0.9)	28.2 (1.0)	28.2 (0.9)	31.6 (1.0)	
Alcohol drinking status[3]					
Nondrinker	64.5 (1.0)	61.9 (1.1)	60.0 (1.1)	56.6 (1.1)	
Moderate drinker	5.8 (0.4)	5.8 (0.5)	7.3 (0.4)	8.2 (0.6)	<0.001
Heavy drinker	12.1 (0.7)	14.1 (0.8)	17.0 (0.9)	18.2 (0.8)	
Missing	17.6 (0.8)	18.2 (0.8)	15.7 (0.7)	17.0 (0.8)	
Physical activity					
< 150 (min per week)	45.7 (1.0)	41.8 (1.0)	39.5 (1.1)	35.0 (1.0)	
150–299 (min per week)	13.4 (0.8)	13.3 (0.6)	11.9 (0.6)	11.9 (0.6)	<0.001
≥ 300 (min per week)	41.0 (1.0)	44.9 (1.0)	48.6 (1.1)	53.0 (0.9)	
Total energy intake (kcal/d)	1206.7 (9.1)	1701.3 (8.8)	2181.6 (13.8)	3090.9 (21.5)	0.006
HEI-2015[4] (min per week)	53.7 (0.3)	53.1 (0.3)	51.1 (0.3)	50.0 (0.3)	<0.001

The values are weighted means (SEs) for continuous variables or percentages (SEs) for categorical variables.

[1]*P* comparisons of covariates among different groups were performed via linear regression for continuous variables and the χ^2 test for categorical variables.

[2]Never smoker was defined as less than 100 cigarettes; ever smoker, more than 100 cigarettes but quit smoking; current smoker, more than 100 cigarettes and still smoking.

[3]A nondrinker was defined as alcohol consumption of 0 g/d. A moderate drinker was defined as having alcohol consumption of 0.1–28 g/d for males and 0.1–14 g/d for females. A heavy drinker was defined as alcohol consumption ≥28 g/d for males and ≥14 g/d for females.

[4]HEI-2015 = Healthy Eating Index-2015

erucic acid intake with CVD or all-cause mortality. We found that olive oil consumption, but not the consumption of other vegetable oils, was associated with a lower risk of CVD mortality.

To our knowledge, this study is the first prospective cohort study linking dietary oleic acid intake with the long-term risk

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Table 2. HRs (95% CIs) for CVD mortality according to quartiles of dietary MUFA intake.

	Quartiles of different dietary MUFA intake				*P* value for trend
	Q1	Q2	Q3	Q4	
Total MUFA					
Median intake (g/d)	11.13	20.12	29.72	46.65	
Deaths/person-years	370/55348	300/56726	274/56322	191/57860	
Model 1	1.00 (Ref.)	0.81 (0.64−1.01)	0.86 (0.69−1.07)	0.76 (0.56−1.02)	0.08
Model 2	1.00 (Ref.)	0.77 (0.59−1.01)	0.77 (0.55−1.09)	0.62 (0.38−1.00)	0.05
Model 3	1.00 (Ref.)	0.78 (0.60−1.01)	0.77 (0.55−1.07)	0.62 (0.39−0.99)	0.047
Palmitoleic acid					
Median intake (g/d)	0.36	0.74	1.19	2.07	
Deaths/person-years	330/52377	288/55578	275/57542	242/60759	
Model 1	1.00 (Ref.)	0.77 (0.62−0.96)	0.81 (0.64−1.01)	0.82 (0.62−1.07)	0.13
Model 2	1.00 (Ref.)	0.76 (0.60−0.96)	0.76 (0.53−0.98)	0.75 (0.53−1.06)	0.12
Model 3	1.00 (Ref.)	0.77 (0.61−0.97)	0.75 (0.58−0.97)	0.74 (0.52−1.04)	0.09
Oleic acid					
Median intake (g/d)	10.27	18.72	27.69	43.59	
Deaths/person-years	364/55481	304/56450	279/56403	188/57922	
Model 1	1.00 (Ref.)	0.88 (0.71−1.09)	0.90 (0.71−1.13)	0.75 (0.56−1.01)	0.08
Model 2	1.00 (Ref.)	0.86 (0.66−1.12)	0.82 (0.59−1.14)	0.62 (0.39−0.97)	0.05
Model 3	1.00 (Ref.)	0.86 (0.66−1.11)	0.81 (0.58−1.12)	0.61 (0.39−0.97)	0.043
Gadoleic acid					
Median intake (g/d)	0.06	0.14	0.25	0.47	
Deaths/person-years	430/64533	290/57896	238/54169	177/49659	
Model 1	1.00 (Ref.)	0.80 (0.65−1.00)	0.93 (0.75−1.15)	0.90 (0.69−1.17)	0.40
Model 2	1.00 (Ref.)	0.85 (0.66−1.07)	0.98 (0.75−1.28)	0.99 (0.68−1.45)	0.71
Model 3	1.00 (Ref.)	0.84 (0.66−1.08)	1.00 (0.76−1.30)	1.01 (0.69−1.48)	0.61
Erucic acid					
Median intake (g/d)	0.00	0.003	0.01	0.06	
Deaths/person-years	364/62237	220/52729	277/54003	274/57288	
Model 1	1.00 (Ref.)	0.87 (0.67−1.09)	0.93 (0.74−1.16)	0.93 (0.74−1.17)	0.65
Model 2	1.00 (Ref.)	0.93 (0.73−1.17)	0.96 (0.75−1.22)	1.00 (0.78−1.28)	0.69
Model 3	1.00 (Ref.)	0.94 (0.74−1.18)	0.97 (0.76−1.24)	1.01 (0.78−1.29)	0.71

The values are *n* or hazard ratios (95% confidence intervals).

Model 1: Adjusted for age, sex, and race/ethnicity.

Model 2: Adjusted for covariates in Model 1 plus education, family income, smoking status, alcohol intake, physical activity, HEI-2015, total energy intake, PUFA intake, SFA intake, protein intake, carbohydrate intake, and mutual adjustment for remaining MUFAs where appropriate (palmitoleic acid, oleic acid, gadoleic acid, and erucic acid).

Model 3: Adjusted for covariates in Model 2 plus body mass index (calculated as kg/m^2).

of mortality. While many previous studies have investigated the relationship between total dietary MUFA intake and all-cause mortality[15–20], little is known regarding the influence of specific subtypes of MUFAs on mortality in humans. Our findings show that oleic acid, the most crucial component of the MUFA group, was associated with cardiovascular and all-cause mortality, which is consistent with the findings for MUFAs. Currently, studies addressing the effects of palmitoleic acid on CVD remain inconclusive[21]. Research has shown that the addition of macadamia oil rich in palmitoleic

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Table 3. HRs (95% CIs) for all-cause mortality according to quartiles of dietary MUFA intake.

	Quartiles of different dietary MUFA intake				*P* value for trend
	Q1	Q2	Q3	Q4	
Total MUFA					
Median intake (g/d)	11.13	20.12	29.72	46.65	
Deaths/person-years	1214/55348	1010/56726	944/56322	709/57860	
Model 1	1.00 (Ref.)	0.86 (0.75−0.98)	0.85 (0.74−0.98)	0.74 (0.63−0.87)	<0.001
Model 2	1.00 (Ref.)	0.90 (0.77−1.04)	0.91 (0.75−1.10)	0.77 (0.60−1.00)	0.08
Model 3	1.00 (Ref.)	0.90 (0.77−1.04)	0.90 (0.74−1.09)	0.77 (0.60−0.99)	0.07
Palmitoleic acid					
Median intake (g/d)	0.36	0.74	1.19	2.07	
Deaths/person-years	1072/52377	1013/55578	945/57542	847/60759	
Model 1	1.00 (Ref.)	0.92 (0.82−1.03)	0.88 (0.77−1.00)	0.89 (0.76−1.04)	0.10
Model 2	1.00 (Ref.)	0.94 (0.82−1.09)	0.92 (0.79−1.07)	0.93 (0.74−1.16)	0.52
Model 3	1.00 (Ref.)	0.96 (0.83−1.10)	0.92 (0.79−1.07)	0.93 (0.75−1.16)	0.54
Oleic acid					
Median intake (g/d)	10.27	18.72	27.69	43.59	
Deaths/person-years	1209/55481	1010/56450	943/56403	715/57922	
Model 1	1.00 (Ref.)	0.88 (0.77−1.01)	0.86 (0.75−0.99)	0.74 (0.63−0.87)	<0.001
Model 2	1.00 (Ref.)	0.92 (0.79−1.06)	0.92 (0.76−1.11)	0.79 (0.63−1.00)	0.08
Model 3	1.00 (Ref.)	0.91 (0.79−1.06)	0.91 (0.76−1.10)	0.78 (0.62−0.99)	0.06
Gadoleic acid					
Median intake (g/d)	0.06	0.14	0.25	0.47	
Deaths/person-years	1431/64533	1043/57896	755/54169	648/49659	
Model 1	1.00 (Ref.)	0.95 (0.84−1.06)	0.82 (0.73−0.93)	0.83 (0.73−0.94)	<0.001
Model 2	1.00 (Ref.)	1.05 (0.92−1.20)	0.95 (0.83−1.09)	1.03 (0.87−1.24)	0.64
Model 3	1.00 (Ref.)	1.05 (0.92−1.19)	0.96 (0.84−1.09)	1.05 (0.89−1.25)	0.60
Erucic acid					
Median intake (g/d)	0.00	0.003	0.01	0.06	
Deaths/person-years	1181/62237	870/52729	913/54003	913/57288	
Model 1	1.00 (Ref.)	0.92 (0.82−1.04)	0.84 (0.75−0.94)	0.84 (0.74−0.95)	0.20
Model 2	1.00 (Ref.)	1.02 (0.90−1.15)	0.90 (0.80−1.02)	0.96 (0.84−1.09)	0.34
Model 3	1.00 (Ref.)	1.02 (0.90−1.15)	0.91 (0.80−1.02)	0.95 (0.84−1.09)	0.32

The values are *n* or hazard ratios (95% confidence intervals).

Model 1: Adjusted for age, sex, and race/ethnicity.

Model 2: Adjusted for covariates in Model 1 plus education, family income, smoking status, alcohol intake, physical activity, HEI-2015, total energy intake, PUFA intake, SFA intake, protein intake, carbohydrate intake, and mutual adjustment for remaining MUFAs where appropriate (palmitoleic acid, oleic acid, gadoleic acid, and erucic acid).

Model 3: Adjusted for covariates in Model 2 plus body mass index (calculated as kg/m^2).

acid to the diet leads to a reduction in total plasma cholesterol, LDL cholesterol, and body weight[22,23]. Additionally, HDL-C levels were observed to increase, whereas no significant changes were noted in triglyceride levels. In a study of cardiovascular health, high levels of palmitoleic acid-containing phospholipids in plasma were associated with increased HDL cholesterol and decreased LDL cholesterol but elevated triacylglycerol levels[24]. Although we did not find an association between the intake of gadoleic acid or erucic acid and CVD mortality, some previous studies have suggested that

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Table 4. Associations of the consumption of olive oil or other vegetable oils with cardiovascular and all-cause mortality.

	Vegetable oil consumption	
	No	Yes
Olive oil		
CVD mortality		
Deaths/person-years	143/19592	77/19473
Model 1	1.00 (Ref.)	0.48 (0.31−0.76)
Model 2	1.00 (Ref.)	0.61 (0.37−0.99)
Model 3	1.00 (Ref.)	0.61 (0.37−1.01)
All-cause mortality		
Deaths/person-years	394/19592	269/19473
Model 1	1.00 (Ref.)	0.73 (0.58−0.91)
Model 2	1.00 (Ref.)	0.89 (0.70−1.13)
Model 3	1.00 (Ref.)	0.90 (0.70−1.16)
Corn oil		
CVD mortality		
Deaths/person-years	142/26333	78/12732
Model 1	1.00 (Ref.)	1.44 (0.92−2.25)
Model 2	1.00 (Ref.)	1.22 (0.75−1.98)
Model 3	1.00 (Ref.)	1.17 (0.78−1.93)
All-cause mortality		
Deaths/person-years	437/26333	226/12732
Model 1	1.00 (Ref.)	1.19 (0.96−1.48)
Model 2	1.00 (Ref.)	1.08 (0.86−1.35)
Model 3	1.00 (Ref.)	1.05 (0.84−1.33)
Canola/rapeseed oil		
CVD mortality		
Deaths/person-years	155/24388	65/14677
Model 1	1.00 (Ref.)	0.86 (0.54−1.39)
Model 2	1.00 (Ref.)	1.02 (0.65−1.59)
Model 3	1.00 (Ref.)	1.01 (0.65−1.58)
All-cause mortality		
Deaths/person-years	450/24388	213/14677
Model 1	1.00 (Ref.)	0.82 (0.60−1.13)
Model 2	1.00 (Ref.)	0.93 (0.68−1.29)
Model 3	1.00 (Ref.)	0.94 (0.69−1.28)

The values are *n* or hazard ratios (95% confidence intervals).

Model 1: Adjusted for age, sex, and race/ethnicity.

Model 2: Adjusted for covariates in Model 1 plus education, family income, smoking status, alcohol intake, physical activity, HEI-2015, total energy intake, consumption of nonvegetable dietary fats (margarine, butter, and mayonnaise), and mutual adjustment for consumption of remaining oils (olive oil, corn oil, and canola oil).

Model 3: Adjusted for covariates in Model 2 plus body mass index (calculated as kg/m^2).

these two MUFAs may have a protective effect against CVD[25,26]. In a cohort study, gadoleic acid was positively associated with paraoxonase 1 (PON1) activity, and PON1 is a cardioprotective, HDL-associated glycoprotein enzyme with broad substrate specificity[25]. Previously, some oils contained elevated levels of erucic acid, rendering them nutritionally unsuitable for both humans and animals. The consumption of erucic acid has been associated with myocardial lipidosis, a condition in which the heart muscle experiences decreased contractility due to inadequate oxidation caused by the buildup of triacylglycerol in the heart[26].

This study also added new evidence to the limited number of available studies regarding the potentially protective effects of olive oil consumption on cardiovascular deaths. Consistent with our findings, previous studies conducted among the Mediterranean population[4,5,27] and non-Hispanic whites[7] reported that olive oil consumption was associated with lower CVD mortality. In the EPIC cohort conducted among Spanish individuals, there was a 44% reduction in CVD mortality in participants who had the highest quartile of olive oil consumption compared with those in the lowest quartile[4]. Findings from a secondary analysis of the PREDIMED study reported that higher baseline total olive oil consumption was associated with a 48% reduction in CVD mortality[5]. In the NIH-AARP Diet and Health Study, a 5% reduction in CVD mortality was found in participants in the highest tertile of olive oil consumption compared with the reference[27]. Findings from the Nurses' Health Study and the Health Professionals Follow-up Study also revealed that higher olive oil intake was associated with a lower risk of CVD mortality[7].

Several mechanisms may explain the long-term cardiovascular benefits of dietary oleic acid intake, MUFA intake, and olive oil consumption. First, inflammation is one of the most important triggers of chronic diseases such as cardiovascular disease, and oleic acid supplementation is associated with lower levels of inflammatory factors, such as C-reactive protein concentrations, and oleic acid intake is associated with some cardiovascular metabolic biomarkers, such as flow-mediated dilation (FMD)[28,29]. Second, evidence from clinical trials has shown that olive oil consumption can improve an array of cardiometabolic parameters, including lipid profiles, blood pressure, and glucose metabolism[30–33]. In addition to a high proportion of MUFAs, especially oleic acid, olive oil also contains minor components such as phenolic compounds, vitamin E, and lipid molecules. These ingredients endow olive oil with antioxidant and anti-inflammatory properties that have been demonstrated to have health benefits[34]. Third, emerging evidence suggests that olive oil may influence cardiovascular disease risk via modifications to the gut microbiota[35]. Olive oil modulates the gut microbiota by stimulating the growth of beneficial bacteria such as *Lactobacillus* and *Bifidobacterium* in humans.

There are several strengths in the present study. First, we used a large, multiracial/ethnic, nationally representative sample, which facilitates the generalizability of the findings to the general U.S. adult population. Second, the comprehensive data from the NHANES allow us to adjust for various confounders, including demographic, socioeconomic, dietary, and lifestyle factors. This study also has several limitations.

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Table 5. Associations of vegetable oil consumption with cardiovascular and all-cause mortality.

	Vegetable oil consumption			
	No vegetable oil	Olive oil exclusively	Olive oil and other vegetable oil	Other vegetable oil
CVD mortality				
Deaths/person-years	46/4276	25/7401	48/11427	101/15963
Model 1	1.00 (Ref.)	0.30 (0.17−0.51)	0.46 (0.23−0.91)	0.73 (0.49−1.09)
Model 2	1.00 (Ref.)	0.36 (0.19−0.69)	0.59 (0.27−1.31)	0.71 (0.46−1.11)
Model 3	1.00 (Ref.)	0.36 (0.19−0.69)	0.59 (0.27−1.32)	0.73 (0.46−1.14)
All-cause mortality				
Deaths/person-years	107/4276	101/7401	153/11427	302/15963
Model 1	1.00 (Ref.)	0.66 (0.49−0.89)	0.68 (0.47−0.97)	0.89 (0.65−1.21)
Model 2	1.00 (Ref.)	0.79 (0.55−1.14)	0.83 (0.57−1.21)	0.88 (0.65−1.20)
Model 3	1.00 (Ref.)	0.80 (0.55−1.17)	0.84 (0.58−1.23)	0.89 (0.65−1.22)

The values are *n* or hazard ratios (95% confidence intervals).

Model 1: Adjusted for age, sex, and race/ethnicity.

Model 2: Adjusted for covariates in Model 1 plus education, family income, smoking status, alcohol intake, physical activity, HEI-2015 score, total energy intake, and consumption of nonvegetable dietary fats (margarine, butter, and mayonnaise).

Model 3: Adjusted for covariates in Model 2 plus body mass index (calculated as kg/m^2).

First, although the 24-h dietary recalls and dietary questionnaires used in the NHANES have been previously validated, measurement errors from recall bias or reporting bias are still possible. Second, information about dietary intake was collected only at baseline. It is possible that participants have changed their dietary habits over time. Further investigations are warranted to determine the effects of changes in dietary oleic acid intake and olive oil consumption on the risk of CVD mortality. Finally, although we adjusted for many possible confounders, the possibility of residual confounding cannot be fully ruled out.

Our findings may have significant public health implications. Cardiovascular disease continues to be a major public health threat worldwide, and it is imperative and important to provide evidence-informed recommendations to dietary guidelines. The intake of oleic acid-rich edible oils, such as olive oil, may be incorporated into the routine diet to improve cardiovascular health and prevent cardiovascular diseases. Further investigation is needed for populations that traditionally have relatively low consumption of oleic acid-rich edible oils.

5 Conclusions

In this nationally representative prospective cohort of U.S. adults, higher dietary oleic acid intake and olive oil consumption were associated with a lower risk of cardiovascular mortality. Our findings support the inclusion of oleic acid-rich oils in dietary strategies for promoting cardiovascular health.

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Conflict of interest

The authors declare that they have no conflict of interest.

Biographies

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