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Niacin intake and mortality (total and cardiovascular disease) in patients with cardiovascular disease: Insights from NHANES 2003–2018

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Abstract

Background Cardiovascular disease (CVD) poses a significant challenge to global public health. Dietary intervention therapy offers high cost-effectiveness for treating CVD. Currently, there is limited research on the dietary niacin intake and survival of CVD patients. This study aims to examine the association of dietary niacin intake with long-term survival in people with CVD.

Methods A nationally representative sample of 4,377 diabetes subjects was drawn from the NHANES (National Health and Nutrition Examination Survey) data collected between 2003 and 2018. Dietary niacin intake in this study represents either the average of the two recalls or the value from one recall (if only one recall was available for a participant). Weighted Cox proportional hazards regression models were used to calculate hazard ratios (HRs) and 95% CIs to examine the associations between dietary niacin intake and the risk of all-cause and CVD mortality.

Results After adjustment for multiple covariates, HRs and 95% CIs in model 3 indicated that participants in the highest quartile (Quartile 4) of dietary niacin intake were at lower risk for all-cause mortality (HR = 0.74, 95% CI: 0.60–0.90, *P* for trend = 0.010) and CVD mortality (HR = 0.67, 95% CI:0.51–0.89, *P* for trend = 0.020).

Conclusion Higher dietary niacin intake may be associated with a reduced risk of all-cause and cardiovascular disease mortality among CVD patients. Additionally, significant interactions were found between dietary niacin intake and BMI as well as vitamin B12 subgroups.

Keywords Cardiovascular disease (CVD), National health and nutrition examination survey (NHANES), Niacin

Introduction

Cardiovascular disease (CVD), encompassing various pathological conditions affecting the heart and blood vessels, is the leading cause of mortality globally [1]. According to statistics from the World Health Organization, CVD is estimated to claim the lives of 17.9 million people annually, accounting for 31% of the total global deaths, posing significant challenges to global public health (WHO, May 17, 2017). Therefore, reducing the burden of disease and the risk of CVD-related deaths is paramount. Recently, emerging dietary interventions have gradually gained attention as a highly cost-effective approach,

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demonstrating significant effects on therapeutic intervention for CVD [2, 3].

Niacin, also known as vitamin B3, is one of the essential 13 vitamins in the human body. It converts to nicotinamide within the body and serves as a component of coenzyme I and coenzyme II, playing crucial roles in lipid metabolism, tissue respiration, and anaerobic breakdown of carbohydrates, among other processes [4, 5]. Despite research suggesting positive effects of niacin on the general population, its role in individuals with CVD has been controversial. Some studies propose benefits [6, 7], while others argue for no effect [8, 9] or even potential harm [10].

Although animal studies have shown that niacin and chromium complexes can prevent morphological and biochemical degeneration of the thoracic aorta, elevate levels of steroidogenic acute regulatory protein (StAR), and potentially modulate cardiovascular diseases [11], there is still a lack of prospective research assessing the association between niacin intake levels from food and the risk of mortality in CVD patients. To address this gap, our study utilized a nationally representative sample of adult Americans to investigate the relationship between dietary niacin intake and the risk of all-cause and CVD mortality among CVD patients.

Methods

Study population

The National Health and Nutrition Examination Survey (NHANES) is a complex, multi-stage, stratified sampling health survey conducted in the United States. Data sources include structured interviews, telephone follow-ups, health screenings at mobile examination centers, and laboratory sample analysis. Prior to data collection, approval was obtained from the National Center for Health Statistics Institutional Review Board, and participants provided written informed consent upon enrollment. This study utilized data from adults aged 20 and older who participated in eight cycles of the NHANES survey (from 2003–2004 to 2017–2018) [12].

To ascertain whether participants have CVD, they are asked the following question: "Has a doctor or other health professional ever told you that you had coronary heart disease, congestive heart failure, heart attack, stroke or angina?" If a participant answers "yes" to this question at least once, they are considered to have CVD [13]. Among 80,312 participants, 5,205 had CVD disease. After excluding participants under 20 years old, pregnant women, and those with missing data on dietary niacin intake, follow-up time ('permth_int'), Body mass index (BMI, kg/m2)., marital status, and education level, a final sample of 4,377 individuals was included in this study.

Measurement of dietary niacin intake

The dietary interview component, known as "What We Eat in America" (WWEIA), is conducted in collaboration between the United States Department of Agriculture (USDA) and the Department of Health and Human Services (DHHS). Data on dietary niacin intake are collected through two 24-h dietary recall interviews. The first recall is conducted in-person at mobile examination centers, followed by a second recall via telephone 3 to 10 days later. These recalls are facilitated using the Computer-Assisted Dietary Interview System managed by NHANES interviewers. The USDA's Food and Nutrient Database for Dietary Studies (FNDDS) was utilized to calculate the nutrients and food components in all food items [14]. Dietary intake in this study represents either the average of the two recalls or the value from one recall (if only one recall was available for a participant). Among the 4,377 participants, 456 (10.4%) had data from only one dietary recall.

Ascertainment of main outcome

The outcome variables were mortality status including mortality of all-cause and CVD, which were determined by National Death Index (NDI) by 31 December 2019. The NDI is a highly reliable and widely used resource for death identification. The ICD-10 was used to determine disease-specific death [15]. Death due to CVD was defined as ICD-10 codes 100–109, 111, 113, 120–151 or 160–169. The total number of deaths was 1659, with 790 deaths attributed to CVD.

Covariates

The following covariates, which were all baseline measurements, were included in this study: age(years), sex(men/women), race (non- Hispanic white or other), marital status (married/unmarried/divorced), education(less than high school/high school or equivalent/college/above), annual poverty-income ratio of household income to the poverty line), energy intake (kcal), smoking status (current/previous/none), drinking status (current/previous/none), regular exercise (yes/no), BMI, hyperlipidemia (defined as the presence of one or more of the following serum measures: total cholesterol > 200 mg/dL, triglycerides > 200 mg/dL, high density lipoproteins < 40 mg/dL in males and < 50 mg/dL in females, low density lipoproteins > 130 mg/dL or current use of cholesterol lowering medications [16]), hypertension (defined as having a systolic blood pressure greater than or equal to 140 mmHg or diastolic blood pressure greater than or equal to 90 mmHg, or currently taking medication to lower high blood pressure) [17], chronic kidney disease (CKD) (defined as glomerular filtration

rate (eGFR) < 60 ml/min/1.73m2 and/or urinary albumin/creatinine ratio (ACR) > 30 mg/g) [18], and diabetes mellitus (DM) (defined by a self-reported diagnosis, medication for hyperglycemia, glycosylated hemoglobin (HbA1c) > 6.5%, or fasting blood glucose > 7.0 mmol/L, or random blood glucose/two-hour OGTT blood glucose > 11.1 mmol/L [19]). Meanwhile, we performed multicollinearity diagnostics for these covariates and found that multicollinearity was weak (all GVIF values were < 0.05) (Supplementary Table 1).

Statistical analysis

Given the complex sampling design of NHANES, all analyses in this study incorporate sample weights (wtmec2yr), strata, and primary sampling units. Baseline characteristics of sociodemographic information, lifestyle behaviours and disease status, were presented as mean ± SD (standard deviation) or numerical (percentage). General linear models and chi-square tests were used to compare the difference. Weighted Cox proportional hazards regression models were used to calculate hazard ratios (HRs) and 95% confidence intervals (Cis) to examine the associations between dietary niacin intake and the risk of all-cause mortality and CVD mortality. The survival time of participants is calculated from the NHANES interview date to the date of death or the end of follow-up (December 31, 2019), whichever occurs first. We adjusted for a series of confounding factors, including age, sex, race, marital status, smoking status, drinking status, regularly exercise, BMI, poverty income ratio, energy intake, DM, hyperlipidemia, hypertension and CKD. Additionally, we created continuous variables by taking the median of dietary niacin intake for each category and examined linear trends. We employed restricted cubic spline (RCS) analysis with four nodes (at the 25th, 50th, 75th and 95th percentiles) to investigate the non-linear relationship between dietary niacin intake and both all-cause mortality and CVD mortality.

Subgroup and sensitivity analysis

Further subgroup analysis will be conducted based on age (< 65 or ≥ 65), sex (male or female), race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, or Other), smoking status (never, former, or current), alcohol consumption (never, former, or current), regular exercise (no or yes), BMI (< 25, 25–29.9, or ≥ 30), CKD (no or yes), and DM (no or yes) to observe their interaction with dietary niacin. We also conducted a series of sensitivity analyses: (1) To minimize potential bias from reverse causality, participants with follow-up times less than two years were excluded ($n = 3811$). (2) Participants with only one dietary recall were excluded ($n = 3921$). (3) Repeat analyses were performed by excluding CVD participants who died within two years of follow-up and had only one dietary recall ($n = 3431$). (4)Sensitivity analyses were conducted by altering the number of nodes in the restricted cubic spline, using three nodes (at the 25th, 50th, and 75th percentiles) and five nodes (at the 20th, 40th, 50th, 60th and 80th percentiles), to further explore the relationship.

All statistical analyses were conducted by R 4.3.1, and p-values < 0.05 were considered statistically significant.

Results

Baseline characteristics of studying population

During 30,055 person-years of follow-up, a total of 1659 death cases were recorded, with 790 deaths attributed to CVD. Baseline characteristics of 4377 CVD participants were summarized in Table 1 according to quartiles of dietary niacin intake (1094 participants in quartile 1 [≤ 13.12 mg/d], 1095 participants in quartile 2 [13.12–19.17 mg/d], 1094 participants in quartile 3 [19.17–26.80 mg/d], and 1094 participants in quartile 4 [≥ 26.80 mg/d]). Participants in the highest quartile (Quartile 4) of the dietary niacin intake, compared to those in the lowest quartile, were more likely to be younger males, non-Hispanic white, smokers, and engaging in regular physical activity, with higher energy intake, and lower prevalence of DM and CKD. Similarities were observed among the four groups in terms of BMI, hypertension, and hyperlipidemia percentages (Table 1).

Dietary niacin intake and all-cause and CVD mortality

Table 2 shows the association between dietary niacin intake and all-cause and CVD mortality. After adjustment for multiple covariates, HRs and 95% CIs in model 3 indicated that participants in the higher quartile of dietary niacin intake were at lower risk for all-cause mortality (Q2: HR = 0.86, 95% CI: 0.74–0.99, Q3: HR = 0.90, 95% CI: 0.77–1.05, Q4: HR = 0.74, 95% CI: 0.60–0.90) and CVD mortality (Q2: HR = 0.81, 95% CI: 0.64–1.02, Q3: HR = 1.00, 95% CI: 0.82–1.22, Q4: HR = 0.67, 95% CI:0.51–0.89). The dose–response relationship between dietary niacin intake and all-cause mortality and CVD mortality is depicted in Fig. 1 (All-cause mortality: p for non-linearity = 0.052, CVD mortality: p for non-linearity = 0.529). This result suggests a potential non-linear relationship between dietary niacin intake and the risk of all-cause mortality, while no non-linear relationship was observed with the risk of CVD mortality.

Stratified and sensitivity analyses

We found a significant interaction between dietary niacin intake and BMI, with a significant overall risk for all-cause mortality (P for interaction = 0.003). In the subgroup with BMI < 25, participants in the fourth quartile had an HR

Table 1 Baseline characteristics of participants stratified by quartiles of dietary niacin intake

Characteristics	Dietary niacin intake (mg)					*P*-value
	Total	Q1, ≤ 13.12 mg/d	Q2, 13.12–19.17 mg/d	Q3, 19.17–26.80 mg/d	Q4, ≥ 26.80 mg/d	
	N = 4,377	*n* = 1,094	*n* = 1,095	*n* = 1,094	*n* = 1,094	
Age, years	66.46 ± 12.91	67.02 ± 13.00	67.46 ± 12.79	67.10 ± 12.17	64.27 ± 13.42	< 0.001
Sex, %						< 0.001
men	2,483 (57%)	411 (38%)	557 (51%)	687 (63%)	828 (76%)	
women	1,894 (43%)	683 (62%)	538 (49%)	407 (37%)	266 (24%)	
Non-Hispanic white, %	2,438 (56%)	550 (50%)	600 (55%)	654 (60%)	634 (58%)	< 0.001
Married, %	2,239 (51%)	494 (45%)	546 (50%)	595 (54%)	604 (55%)	< 0.001
College graduate or above, %	624 (14%)	99 (9.0%)	150 (14%)	181 (17%)	194 (18%)	< 0.001
Smoking status, %						< 0.001
no	1,686 (39%)	484 (44%)	447 (41%)	398 (36%)	357 (33%)	
previous	1,781 (41%)	390 (36%)	439 (40%)	473 (43%)	479 (44%)	
current	910 (21%)	220 (20%)	209 (19%)	223 (20%)	258 (24%)	
Drinking status, %						< 0.001
no	988 (23%)	324 (30%)	261 (24%)	228 (21%)	175 (16%)	
previous	1,290 (29%)	353 (32%)	341 (31%)	297 (27%)	299 (27%)	
current	2,099 (48%)	417 (38%)	493 (45%)	569 (52%)	620 (57%)	
Exercised regularly, %						0.005
no	3,652 (83%)	927 (85%)	922 (84%)	928 (85%)	875 (80%)	
yes	725 (17%)	167 (15%)	173 (16%)	166 (15%)	219 (20%)	
BMI, kg/m^2						0.500
< 25	960 (22%)	237 (22%)	226 (21%)	249 (23%)	248 (23%)	
25–29.9	1,451 (33%)	352 (32%)	362 (33%)	356 (33%)	381 (35%)	
≥ 30	1,966 (45%)	505 (46%)	507 (46%)	489 (45%)	465 (43%)	
Poverty income ratio	2.20 ± 1.46	1.91 ± 1.35	2.13 ± 1.42	2.31 ± 1.49	2.44 ± 1.54	< 0.001
energy (kcal), %	1,828.47 ± 874.83	1,142.71 ± 466.23	1,614.04 ± 524.07	1,915.01 ± 581.57	2,642.31 ± 1,022.96	< 0.001
DM, %	1,796 (41%)	471 (43%)	483 (44%)	457 (42%)	385 (35%)	< 0.001
Hyperlipidemia, %	3,762 (86%)	943 (86%)	921 (84%)	964 (88%)	934 (85%)	0.053
Hypertension, %	3,441 (79%)	890 (81%)	855 (78%)	853 (78%)	843 (77%)	0.075
CKD, %	1,951 (45%)	509 (47%)	511 (47%)	501 (46%)	430 (39%)	0.001
Follow-up period, months	82.40 ± 51.26	81.37 ± 52.79	83.68 ± 51.03	79.94 ± 50.49	84.61 ± 50.65	0.079

Continuous variables are presented as mean ± Standard deviation. Categorical variables are presented as numbers (%, percentage). *BMI* Body mass index, *DM* Diabetes mellitus and *CKD* Chronic kidney disease

of 0.53 (95% CI: 0.33–0.86) for all-cause mortality compared to the reference group. In the subgroup with BMI between 25–29.9, participants in the fourth quartile had an HR of 0.77 (95% CI: 0.56–1.06) for all-cause mortality compared to the reference group. In the subgroup with BMI ≥ 30, participants in the fourth quartile had an HR of 0.85 (95% CI: 0.60–1.20) for all-cause mortality compared to the reference group (Table 3). However, we did not find significant interactions between dietary niacin intake and other stratified variables for all-cause mortality risk. There was an interaction between dietary niacin intake and CVD mortality in BMI subgroups, but it did not confer a significant risk of CVD mortality (Table 3). Additionally, we observed a significant interaction between dietary niacin intake and vitamin B12 levels for all-cause mortality risk (P for interaction = 0.036). In the subgroup with vitamin B12 levels ≤ 3.4mcg, participants in the fourth quartile had an HR of 0.93 (95% CI: 0.62–1.40) for all-cause mortality compared to the reference group. In the subgroup with vitamin B12 levels > 3.4mcg, participants in the fourth quartile had an HR of 0.52 (95% CI: 0.38–0.70) for all-cause mortality compared to the reference group. However, we did not observe significant interactions between dietary niacin intake and other B-complex vitamins (Supplementary Table 2).

Table 2 HRs and 95% CI for all-cause and CVD mortality among participants with CVD in NHANES 2003 to 2018

Model	Hazard ratio (95% CI)				*P* for trend
	Quartile 1, ≤ 13.12 mg/d[a]	Quartile 2, 13.12–19.17 mg/d[a]	Quartile 3, 19.17–26.80 mg/d[a]	Quartile 4, ≥ 26.80 mg/d[a]	
All-cause mortality					
Case/N	445 of 1094	448 of 1095	410 of 1094	356 of 1094	
model 1[b]	Reference	0.91(0.77–1.08)	0.90(0.75–1.08)	0.67(0.57–0.79)	< 0.001
model 2[c]	Reference	0.85(0.73–0.98)	0.87(0.73–1.03)	0.73(0.62–0.87)	0.002
model 3[d]	Reference	0.86 (0.74–0.99)	0.90 (0.77–1.05)	0.74 (0.60–0.90)	0.010
CVD mortality					
Case/N	213 of 1094	207 of 1095	210 of 1094	160 of 1094	
model 1[b]	Reference	0.86(0.67–1.11)	0.97(0.80–1.18)	0.60(0.47–0.76)	< 0.001
model 2[c]	Reference	0.80(0.64–1.01)	0.95(0.79–1.15)	0.67(0.52–0.86)	0.006
model 3[d]	Reference	0.81 (0.64–1.02)	1.00 (0.82–1.22)	0.67 (0.51–0.89)	0.020

[a] Daily dietary niacin intake

[b] Crude model

[c] Adjusted for age and sex. d Further adjusted for race, marital status, education level, smoking status, drinking status, exercised regularly, BMI, family income to poverty ratio, energy intake, CKD, DM, hypertension and hyperlipidemia. BMI, body mass index, CKD, chronic kidney disease, DM, diabetes mellitus

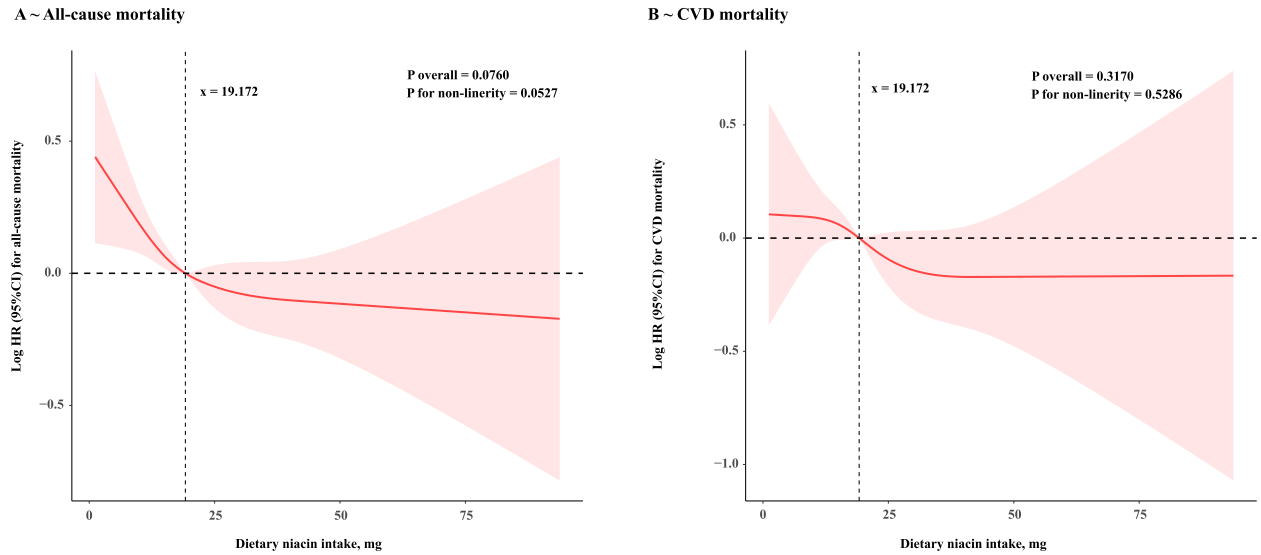

Fig. 1 RCS analysis between niacin and all-cause mortality and CVD mortality

In sensitivity analyses, whether excluding participants who died within 2 years of follow-up, excluding participants with only one dietary recall, or excluding participants who died within 2 years of follow-up and had only one dietary recall, all revealed a negative correlation between dietary niacin intake and both all-cause and CVD mortality (Supplementary Table 3–5). This further demonstrates the stability of the results. Results from RCS with 3 nodes and 5 nodes were consistent with those from RCS with 4 nodes.

Discussion

To the best of our knowledge, we conducted the first large-scale prospective cohort study investigating the relationship between dietary niacin intake and all-cause as well as cardiovascular disease (CVD) mortality among CVD patients. We found that, after adjusting for numerous confounding factors, individuals with higher dietary niacin intake had reduced risks of both all-cause and CVD mortality. Additionally, subgroup

Table 3 Associations of dietary niacin intake with all-cause and CVD mortality in various subgroups among participants with CVD in NHANES 2003-2018[a]

Subgroup	All-cause mortality						CVD mortality					
	Hazard ratio (95% CI)				P for trend	p for interaction	Hazard ratio (95% CI)				*P* for trend	p for interaction
	Quartile 1	Quartile 2	Quartile 3	Quartile 4			Quartile 1	Quartile 2	Quartile 3	Quartile 4		
Age, year						0.963						0.768
< 65	Reference	0.80(0.49–1.30)	0.85(0.45–1.59)	0.72(0.36–1.43)	0.417		Reference	0.83(0.44–1.55)	0.80(0.37–1.71)	0.78(0.32–1.91)	0.643	
≥ 65	Reference	0.86(0.74–1.01)	0.89(0.74–1.06)	0.73(0.58–0.91)	0.013		Reference	0.81(0.62–1.06)	0.99(0.78–1.26)	0.63(0.45–0.87)	0.013	
Sex						0.239						0.873
Male	Reference	0.80(0.61–1.04)	0.77(0.58–1.02)	0.69(0.50–0.95)	0.046		Reference	0.77(0.52–1.14)	0.97(0.67–1.41)	0.65(0.40–1.06)	0.099	
Female	Reference	0.99(0.80–1.23)	1.20(0.90–1.62)	0.81(0.61–1.07)	0.388		Reference	1.00(0.71–1.40)	1.08(0.71–1.62)	0.87(0.55–1.37)	0.671	
Race						0.651						0.814
Mexican American	Reference	1.15(0.62–2.13)	0.95(0.48–1.88)	0.94(0.43–2.05)	0.759		Reference	1.34(0.63–2.85)	1.54(0.70–3.40)	0.72(0.20–2.56)	0.808	
Other Hispanic	Reference	0.84(0.32-2.21)	1.24(0.39-3.94)	1.41(0.46-4.30)	0.382		Reference	1.34(0.34-5.23)	1.60(0.25-10.05)	1.14(0.25-5.30)	0.942	
Non-Hispanic White	Reference	0.89(0.74–1.07)	0.88(0.71–1.08)	0.75(0.59–0.95)	0.029		Reference	0.84(0.65–1.10)	0.97(0.76–1.25)	0.68(0.48–0.96)	0.046	
Non-Hispanic Black	Reference	1.04(0.69–1.56)	1.02(0.64–1.62)	0.90(0.52–1.56)	0.746		Reference	0.97(0.51–1.82)	0.80(0.47–1.36)	0.89(0.40–2.01)	0.692	
Other race	Reference	0.41(0.13-1.28)	0.80(0.24-2.72)	0.34(0.08-1.42)	0.226		Reference	0.43(0.07-2.54)	0.39(0.10-1.51)	0.47(0.07-3.13)	0.413	
Smoking status						0.297						0.401
never	Reference	1.03(0.79-1.34)	1.24(0.89-1.72)	1.02(0.73-1.43)	0.781		Reference	1.04(0.68–1.57)	1.30(0.85–1.98)	0.86(0.56–1.34)	0.618	
former	Reference	0.74(0.56–0.98)	0.67(0.51–0.88)	0.49(0.36–0.65)			Reference	0.61(0.42–0.91)	0.70(0.45–1.11)	0.44(0.25–0.77)	0.014	
current	Reference	0.95(0.59–1.53)	1.04(0.61–1.78)	1.31(0.65–2.65)	0.406		Reference	1.11(0.57–2.16)	1.31(0.65–2.65)	1.42(0.49–4.07)	0.493	
Drinking status						0.782						0.533
never	Reference	0.79(0.55–1.14)	0.81(0.54–1.20)	0.67(0.41–1.11)	0.134		Reference	1.10(0.65–1.85)	0.96(0.54–1.70)	1.03(0.50–2.14)	0.959	
former	Reference	1.06(0.82–1.36)	1.16(0.88–1.52)	0.88(0.62–1.24)	0.505		Reference	0.91(0.63–1.31)	1.26(0.89–1.80)	0.69(0.43–1.12)	0.238	
current	Reference	0.76(0.55–1.05)	0.77(0.54–1.11)	0.69(0.47–1.01)	0.107		Reference	0.69(0.45–1.05)	0.80(0.51–1.23)	0.61(0.38–0.99)	0.103	

Table 3 (continued)

Subgroup	All-cause mortality						CVD mortality					
	Hazard ratio (95% CI)				P for trend	p for interaction	Hazard ratio (95% CI)				*P* for trend	p for interaction
	Quartile 1	Quartile 2	Quartile 3	Quartile 4			Quartile 1	Quartile 2	Quartile 3	Quartile 4		
Regular exercise						0.496						0.146
no	Reference	0.88(0.75–1.04)	0.95(0.79–1.14)	0.77(0.60–0.97)	0.067		Reference	0.85(0.66–1.08)	1.09(0.88–1.35)	0.70(0.53–0.94)	0.076	
yes	Reference	0.95(0.61–1.46)	0.63(0.36–1.11)	0.77(0.43–1.39)	0.296		Reference	1.15(0.54-2.43)	0.68(0.33-1.41)	0.99(0.46-2.10)	0.836	
BMI						0.003						0.027
< 25	Reference	0.91(0.64–1.30)	0.79(0.53–1.16)	0.53(0.33–0.86)	0.004		Reference	1.01(0.61–1.67)	0.67(0.41–1.11)	0.59(0.28–1.23)	0.085	
25–29.9	Reference	0.70(0.53–0.92)	0.71(0.53–0.95)	0.77(0.56–1.06)	0.348		Reference	0.71(0.47–1.08)	0.75(0.48–1.19)	0.63(0.39–1.01)	0.138	
≥ 30	Reference	0.95(0.72–1.26)	1.13(0.83–1.53)	0.85(0.60–1.20)	0.440		Reference	0.79(0.56-1.12)	1.34(0.91-1.96)	0.73(0.48-1.13)	0.399	
DM						0.661						0.974
no	Reference	0.85(0.66–1.10)	0.85(0.66–1.10)	0.70(0.53–0.92)	0.011		Reference	0.78(0.56–1.09)	0.92(0.68–1.24)	0.64(0.44–0.94)	0.038	
yes	Reference	0.89(0.68–1.16)	0.91(0.69–1.19)	0.77(0.55–1.08)	0.170		Reference	0.87(0.59–1.28)	0.99(0.68–1.46)	0.73(0.46–1.15)	0.268	
CKD						0.621						0.596
no	Reference	0.89(0.66–1.21)	0.80(0.58–1.12)	0.71(0.52–0.98)	0.047		Reference	0.96(0.62–1.50)	0.78(0.52–1.17)	0.64(0.40–1.04)	0.054	
yes	Reference	0.93(0.78–1.12)	0.98(0.81–1.20)	0.85(0.64–1.12)	0.291		Reference	0.85(0.62–1.17)	1.10(0.79–1.54)	0.77(0.50–1.20)	0.401	

Abbreviations BMI Body mass index, *CKD* Chronic kidney disease, *DM* Diabetes mellitus

Data are weighted HRs and 95% CI,

Results were adjusted for age and sex, race, marital status, education level, smoking status, drinking status, exercised regularly, BMI, family income to poverty ratio, energy intake, CKD, DM, hypertension and hyperlipidemia

and sensitivity analyses were performed to confirm the stability of our results.

Niacin undergoes absorption, conversion into niacinamide, and serves as a coenzyme to participate in various metabolic activities within the body [20]. It remains a supplementary therapeutic method for cardiovascular diseases. Literature indicates that lipoprotein(a) [Lp(a)] is an independent risk factor for cardiovascular diseases. Elevated levels of Lp(a) in the body contribute to the formation of atherosclerosis, thereby increasing the risk of cardiovascular events such as heart disease and stroke [21, 22]. Niacin directly and non-competitively inhibits hepatic diacylglycerol acyltransferase 2, reducing hepatic triglyceride synthesis and subsequent VLDL/LDL secretion. It also inhibits the expression of hepatic surface β-chain ATP synthase, suppressing the removal of HDL-associated apolipoprotein AI, leading to an increase in HDL particles containing apolipoprotein AI [23]. This aids in elevating HDL levels, promoting reverse cholesterol transport, and accelerating the clearance of low-density lipoprotein (LDL) [24]. Niacinamide may also modulate the immune response by enhancing the activity of natural killer (NK) cells [25], as well as improving endothelial function, increasing vasodilation, and enhancing myocardial function, thereby reducing the risk of cardiovascular diseases [26]. In this study, we observed the benefits of niacin intake in patients with cardiovascular diseases. Meanwhile, epidemiological studies have found that higher dietary niacin intake can reduce all-cause mortality risk by 32% and CVD mortality risk by 37% in patients with metabolic syndrome [27], as well as reduce all-cause mortality risk by 30% in patients with non-alcoholic fatty liver disease [9]. In addition, dietary niacin intake is significantly inversely associated with cognitive and psychiatric disorders, as well as stroke [28–30]. These studies are consistent with our findings. Although some studies have found that dietary niacin intake does not reduce the risk of cardiovascular disease [9], the primary reason may lie in the fact that these studies focused on populations with non-alcoholic fatty liver disease (NAFLD). NAFLD patients often exhibit metabolic abnormalities (such as insulin resistance and dyslipidemia) and chronic inflammation, both of which contribute to an increased risk of cardiovascular disease [31]. Even with increased dietary niacin intake, these negative effects may be difficult to offset. Other studies have suggested that niacin fails to exert beneficial effects on cardiovascular disease incidence or mortality, possibly due to its combination with statin therapy [8, 10]. After adjusting for numerous confounding factors, higher dietary niacin intake was associated with a 26% reduction in all-cause mortality risk and a 33% reduction in cardiovascular disease mortality risk (26.80 mg/d vs 13.12 mg/d), consistent with the conclusions of the aforementioned studies. However, we did not observe an association between dietary niacin intake and reduced all-cause mortality risk in participants within the third quartile. Moreover, the RCS curve showed a P-value for non-linearity of 0.052, suggesting the possibility of a non-linear relationship between the two, despite an overall trend toward risk reduction.

Meanwhile, we have noted that several recently published articles relevant to our research focus on the relationship between niacin and cardiovascular risk, all of which utilize NHANES cohort data. However, these studies differ from ours in several significant ways. Although some articles have also found that increased niacin intake can reduce all-cause and cardiovascular disease mortality risk, their study populations primarily consist of individuals with prediabetes and those with metabolic syndrome [27, 32], which is fundamentally different from our research. Additionally, while some studies have explored the relationship between dietary niacin intake and disease incidence [33, 34], their outcome measures are diabetes, and their study populations are general populations rather than specific disease groups. Moreover, there are notable methodological differences; they employed binary logistic regression analysis, whereas we utilized Cox regression analysis that accounts for follow-up time. Additionally, there are slight differences in the study periods, with some studies analyzing data from NHANES 2005–2016 [33], while we focus on NHANES cohort data from 2003–2018.

In our study, we observed that when comparing the subgroup with BMI < 25 and the highest intake of niacin to the lowest intake (reference) group, the HR for all-cause mortality was 0.53 (95% CI: 0.33–0.86). When comparing the subgroup with BMI 25–29.9 and the highest intake of niacin to the reference group, the HR for all-cause mortality at the fourth quartile of dietary niacin intake was 0.77 (95% CI: 0.56–1.06). When comparing the subgroup with BMI ≥ 30, the HR for all-cause mortality at the fourth quartile of dietary niacin intake was 0.85 (95% CI: 0.60–1.20) (P for interaction = 0.003). It has been reported that obesity can elevate oxidative stress levels in the body [35], while niacin is a common antioxidant [36]. In an animal study, niacin administered at a dose of 50 mg/ml/kg body weight for 4 weeks on both normal and high-fat diets enhanced physical activity, exhibited anxiolytic effects, reduced oxidative stress, and increased antioxidant enzymes [36]. A population intervention study involving 25 subjects also found niacin to significantly reduce oxidative stress [37]. Therefore, we speculate that, with the same level of niacin intake, individuals with a high BMI may not be able to fully benefit from the positive effects of niacin due to their elevated

oxidative stress levels compared to individuals with a lower BMI. Considering the role of niacin in CVD subjects and the role of BMI in cardiovascular diseases, along with our subgroup analysis results, we believe that higher dietary niacin intake may be more strongly associated with lower all-cause mortality risk in CVD subjects with BMI < 25.

Another interesting finding in our study is that in the subgroup with vitamin B12 levels > 3.4 mcg, the HR for all-cause mortality at the fourth quartile of dietary niacin intake compared to the reference group was 0.52 (95% CI: 0.38–0.70). This result suggests that CVD patients with vitamin B12 intake higher than 3.4 mcg may derive more benefits from niacin. Studies have indicated that niacin plays an important role in the metabolism of fatty acids and amino acids [38, 39], while vitamin B12 also plays a crucial role in both of these metabolic pathways [40], as well as participating in coenzyme synthesis. At higher levels of vitamin B12 intake, the synergistic effects of niacin and vitamin B12 may enhance the protective effects of niacin. Therefore, CVD patients may derive greater benefits from dietary niacin intake when combined with vitamin B12 supplementation.

This study has several strengths. Firstly, it is the first investigation of the impact of dietary niacin intake on health outcomes in a nationally representative sample of cardiovascular disease patients in the United States, thereby enhancing the generalizability of our findings to a broader population of cardiovascular disease patients in the United States. Secondly, both subgroup and sensitivity analyses demonstrate the stability of our results. However, we also acknowledge certain limitations in our study. Firstly, dietary recall data typically consists of at least three recalls, while the NHANES database provides only two dietary assessments. Additionally, due to variations in daily food intake, these recalls are susceptible to measurement error. Secondly, while the National Death Index is reliable for determining mortality status, it does not provide more precise classification of cardiovascular diseases. Additionally, despite our efforts to control for numerous confounding factors, it is still possible that some variables we did not consider or unidentified variables may exist.

Clinical implications

The recommended daily intake (RDA) of niacin is 16 mg for adult males and 14 mg for adult females. Adequate intake of niacin not only helps regulate cholesterol levels but also improves overall cardiovascular health. Notably, our study found that the combination of vitamin B12 and niacin has unexpected benefits for CVD. Given the importance of nutritional therapy in the treatment of CVD, healthcare professionals specializing in cardiovascular care should pay appropriate attention to these findings to optimize patient treatment strategies.

Conclusion

This prospective cohort study among adults with cardiovascular disease (CVD) in the United States indicates that higher dietary niacin intake may be associated with a reduced risk of all-cause and cardiovascular disease mortality among CVD patients. Additionally, significant interactions were found between dietary niacin intake and BMI as well as vitamin B12 subgroups. Further molecular and cellular experiments are needed to explore the underlying mechanisms of dietary niacin intake in CVD patients.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12937-024-01027-y.

Supplementary Material 1.
Supplementary Material 2.
Supplementary Material 3.
Supplementary Material 4.
Supplementary Material 5.
Supplementary Material 6.
Supplementary Material 7.

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Authors' contributions

Y.R. conceived the study design. R.Y. did the statistical analysis. S.F. re-analyzed the results. M.Z. wrote the manuscript. All authors provided critical revisions of the draft and approved the submitted draft. J.Z. is the guarantor of this work and is responsible for the integrity of the data and the accuracy of the data analysis.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

NHANES adheres to the ethical principles of the Declaration of Helsinki. During the design and implementation of NHANES studies, ethical standards are ensured, including informed consent and participant privacy protection. NHANES has been approved by the Ethics Review Board (ERB) of the National Center for Health Statistics (Supplementary file 1).

Competing interest

The authors declare no competing interests.

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