International Journal for Vitamin and Nutrition Research

*Int. J. Vitam. Nutr. Res.* **2025**; 95(4): 37256
https://doi.org/10.31083/IJVNR37256

*Original Communication*

# The Generalized Association Between Niacin Intake and Cardiovascular Events in US Adults Living With Chronic Kidney Disease

Dong Zhang[1], Hui Wu[2,3,4,*], Shengyu Gong[5], Gang Zhou[2,3,4], YanFang Liu[2,3,4], Yi Li[2,3,4], Xiaoting Yang[2,3,4]

[1]Interventional Diagnosis and Treatment Center, Yichang Central People's Hospital, 443000 Yichang, Hubei, China
[2]Institute of Cardiovascular Disease, China Three Gorges University, 443005 Yichang, Hubei, China
[3]Department of Cardiology, Yichang Central People's Hospital, 443000 Yichang, Hubei, China
[4]Central Laboratory, The First College of Clinical Medical Science, China Three Gorges University, 443005 Yichang, Hubei, China
[5]Pharmaceutical Department, Yichang Central People's Hospital, 443000 Yichang, Hubei, China
*Correspondence: wuhui@ctgu.edu.cn (Hui Wu)
Academic Editor: Torsten Bohn
Submitted: 17 January 2025 Revised: 14 May 2025 Accepted: 20 May 2025 Published: 31 July 2025

**Abstract**

**Background**: The effects of dietary niacin on the risk of cardiovascular disease (CVD) and mortality in patients with chronic kidney disease (CKD) remain unclear. **Methods**: CKD patients with estimated glomerular filtration rates (eGFRs) 20–59 mL/min/1.73 $m^2$ or urinary albumin/creatinine ratio ≥30 mg/g were identified in the National Health and Nutrition Examination Survey (NHANES) data from 2003 to 2018. Age, gender, race, education level, marital status, body mass index, blood pressure, and smoking and drinking history were considered as confounders. **Results**: The present study encompassed 3815 CKD patients eligible for inclusion based on the study criteria. Participants with a niacin intake of >27.7 mg/d (quartile 4) had a lower prevalent CVD risk than those with an intake of ≤14.67 mg (quartile 1) (odds ratio (OR), 0.710, 95% CI: 0.560–0.900; *p* for trend = 0.004). In the follow-up with a median of 7.0 years, 323 from CVD. After adjustment, a higher niacin intake (>27.7 mg) reduced CVD mortality compared to a lower intake (≤14.67 mg) (hazard ratio (HR), 0.610, 95% CI: 0.480–0.770; *p* for trend <0.001). Adding dietary niacin to clinical variables increased the C-index from 0.746 to 0.749 for CVD prevalence and from 0.659 to 0.682 for mortality. The net reclassification improvement increased by 9.0% and 13.1% for CVD and mortality, respectively, and the integrated discrimination improvement increased by 0.3% and 1%, respectively. **Conclusions**: Higher dietary niacin intake may reduce CVD and its mortality in individuals with CKD.

**Keywords:** niacin; cardiovascular disease; chronic kidney disease

## 1. Background

Chronic kidney disease (CKD) and cardiovascular disease (CVD) exhibit a robust bidirectional association, underpinned by shared pathophysiological mechanisms. These conditions represent a global public health challenge, with epidemiological studies consistently demonstrating a substantially higher incidence of cardiovascular events in CKD populations compared to the general cohort [1]. Research indicates that a substantial percentage of CKD patients suffer from cardiovascular illness, and CVD mortality accounts for a significant proportion in advanced CKD patients [2]. Emerging evidence highlights that CKD-specific pathophysiological processes—such as uremia-induced vascular calcification, chronic systemic inflammation, and myocardial fibrosis—substantially amplify cardiovascular morbidity in this population [3]. Therefore, mitigating CVD and its mortality associated with CKD is of paramount importance. CKD exists on a pathological continuum with CVD, a leading cause of death in CKD patients [4]. Progressive renal impairment in CKD drives multisystem dysregulation, including metabolic acidosis, chronic inflammatory states, and oxidative stress, which collectively potentiate cardiovascular pathogenesis [5,6]. Although the CKD-CVD pathophysiological nexus is well-characterized, investigative efforts have predominantly focused on modulating conventional cardiovascular risk profiles. Contemporary investigations prioritize elucidating CVD risk determinants in CKD cohorts, whereas cardioprotective mechanisms and resilience factors in this population remain underexplored.

Niacin, a water-soluble B-complex vitamin, plays a critical role in maintaining physiological homeostasis and systemic metabolic equilibrium. Its biochemical significance stems from its role as the primary biosynthetic precursor to nicotinamide adenine dinucleotide ($NAD^+$) and nicotinamide adenine dinucleotide phosphate ($NADP^+$), coenzymes integral to redox reactions and cellular energetics [7]. Energy metabolism, cell signaling, DNA repair, and antioxidant defense are the main functions of NAD and NADP, two vital coenzymes in cells that participate in over 400 metabolic activities [8]. Niacin exists in the body as

nicotinamide, contributing to the formation of coenzyme I and coenzyme II, and participating in the synthesis of substances and regulation of energy metabolism reactions in the body. Niacin further contributes to the glucose tolerance factor (GTF), a metalloprotein essential for insulin receptor sensitization and glycemic regulation. Pharmacologically, niacin demonstrates pleiotropic effects, including attenuation of atherogenic dyslipidemia (reduced low-density lipoprotein (LDL)-cholesterol and triglycerides) and endothelial-dependent vasodilation via prostaglandin modulation [9]. Epidemiological studies associate dietary niacin with reduced CVD incidence in the general population [10], however, its cardioprotective efficacy remains inadequately characterized in CKD cohorts [11,12]. Preclinical evidence suggests niacin ameliorates CKD-associated cardiovascular risks by modulating mineral metabolism (reducing hyperphosphatemia and hypercalcemia), suppressing pro-inflammatory cytokines, and improving endothelial dysfunction [13–15]. A non-linear, J-shaped association exists between dietary niacin intake and hypertension incidence, with nadir risk observed at a daily intake of 14.3–16.7 mg [16]. Currently, no globally standardized guidelines exist for optimal daily niacin intake thresholds tailored to distinct clinical populations. Furthermore, the pharmacokinetics and dose-response relationship of niacin in CKD patients remain unexplored, limiting evidence-based recommendations. This study establishes a novel tripartite association between CKD, CVD, and niacin bioavailability, interrogating the dose-dependent effects of elevated niacin intake on cardiovascular and its mortality in renal-impaired populations. Elucidating this underexplored nexus, our findings provide mechanistic insights into nutrient-mediated cardiorenal protection, informing precision dietary strategies for high-risk CKD cohorts. Integrating niacin optimization into multimodal CKD management may represent a scalable, cost-effective adjuvant therapy to attenuate cardiovascular burden and mortality in this vulnerable demographic. This therapeutic paradigm could potentially mitigate the incidence and severity of CVD in CKD populations, bridging a critical gap in preventive nephrology.

The multifactorial interplay between niacin bioavailability, CKD, and CVD has emerged as a focal point in translational nephrology and cardiometabolic research. To date, a paucity of evidence exists to delineate the tripartite mechanistic and epidemiological relationships linking niacin status, CKD progression, and CVD pathogenesis. Employing a hybrid cross-sectional and longitudinal design, this study interrogates the temporal and dose-response relationships between dietary niacin exposure and both incident CVD and its mortality within a nationally representative cohort of U.S. adults with CKD. This investigation is poised to provide substantial insights to the current body of medical literature.

## 2. Methods

### *2.1 Study Design and Population*

The National Health and Nutrition Examination Survey, also known as NHANES, is a survey that is conducted by the National Center for Health Statistics, which is part of the Centers for Disease Control and Prevention. It examines the state of health among the general population in the United States of America. It offers an abundance of information regarding demographics, socioeconomics, health behaviors, and conditions. Data from participants is collected via standardized questionnaires administered by trained interviewers, covering a spectrum of health-related topics. Mobile examination centers offer lab tests and physical exams by medical professionals. The research follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) requirements for rigorous reporting. The study exemplifies a commitment to ethical research standards, as evidenced by the evaluation and approval from the relevant Institutional Review Board and the informed consent acquired from each participant in NHANES (https://www.cdc.gov/nchs/nhanes/irba98.htm).

We examined data from NHANES, covering 8 cycles from 2003–2004 to 2017–2018, focusing on American adults aged 18 years and older. 55,719 participants in our cohort research had their estimated glomerular filtration rate (eGFR) as well as the albumin or creatinine levels in the urine were examined. After excluding individuals due to pregnancy (n = 45), age under 18 years (n = 2310), albumin-to-creatinine ratio (ACR) $\leq$30 mg/g, incomplete data of mortality (n = 2) and absence of dietary niacin intake (n = 1050), a final sample of 3815 CKD patients was utilized for this study (Fig. 1).

### *2.2 Assessment of Daily Dietary Niacin Intake*

The NHANES' What We Eat in America research uses the Automated Multiple-Pass Method to efficiently and accurately collect nutritional intake data for large nationwide surveys. In two 24-hour dietary recall interviews, subjects report their 24-hour food intake. While the first recall is done in the Mobile Examination Center, the second is done by phone three to ten days later. The reported foods' nutritional value is calculated using the US Department of Agriculture (USDA)'s Food and Nutritional Database for Dietary Studies (https://www.usda.gov/). The mean of the two dietary recalls or a single recall value was used to estimate daily niacin intake in this investigation. 542 (14.2%) of 3815 participants recalled a meal.

### *2.3 Definition of CKD*

CKD was diagnosed when ACR exceeded 30 mg/g or when eGFR fell below 60 mL/min/1.73 $m^2$ [17].

### *2.4 Outcomes*

The results of this study included the rates of CVD and death from CVD. CVD diagnoses were validated via in-

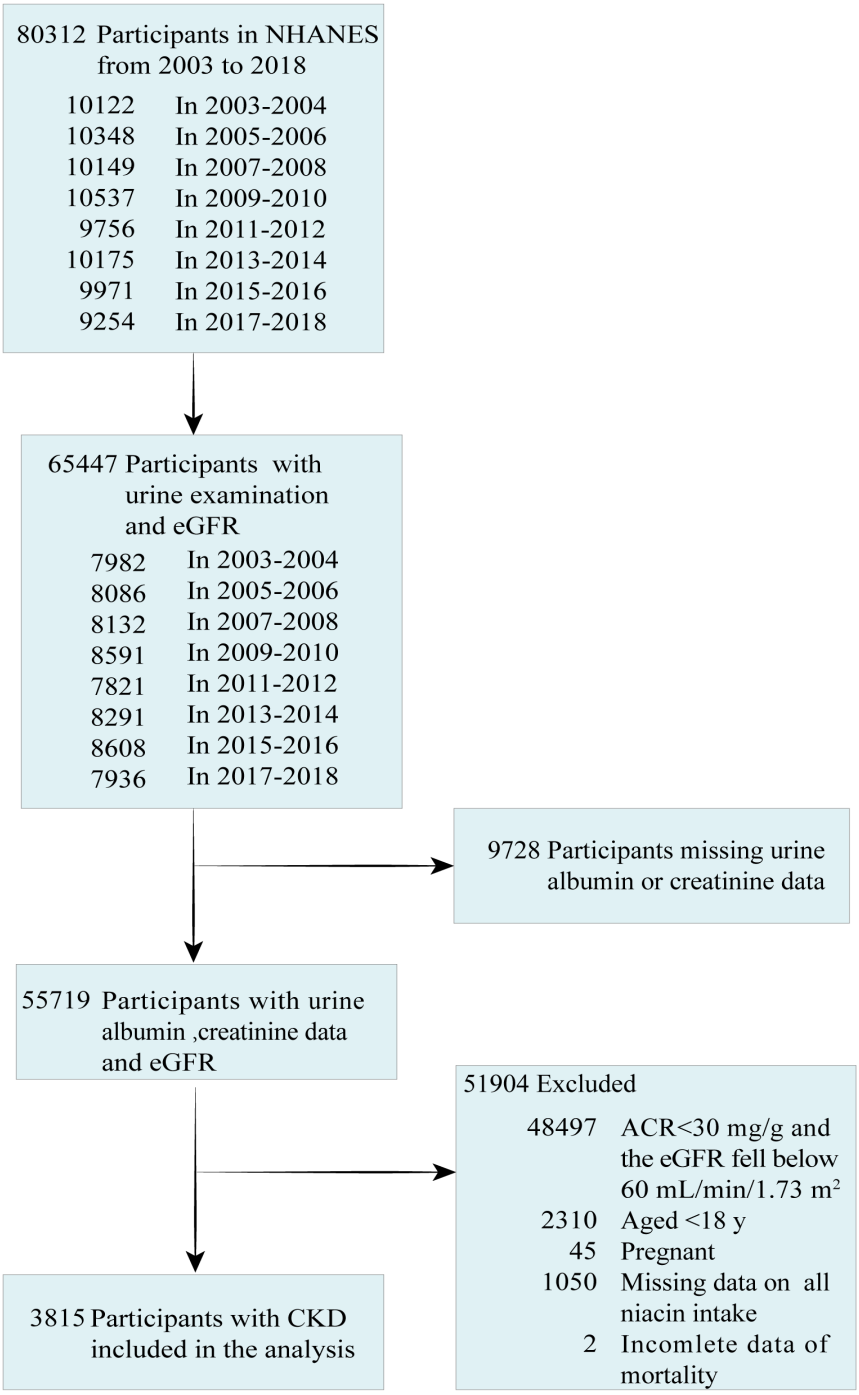


**Fig. 1. National Health and Nutrition Examination Survey (NHANES) 2003–2018 study population selection flowchart.** eGFR, estimated glomerular filtration rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.

dividual interviews, during which participants were asked: "Do you know whether you've ever had a heart attack, coronary heart disease, angina, congestive heart failure, or stroke? How did your doctor tell you this?" Participants who responded "Yes" were classified as CVD patients. Data on mortality and follow-up status were connected to the National Death Index over the period of time ending December 31, 2019. The codes from the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) were utilized in order to determine the major cause of death (https://www.who.int). CVD mortality refers to deaths caused by heart disease, classified under codes I00–I09, I11, I13, I20–I51, or I60–I69.

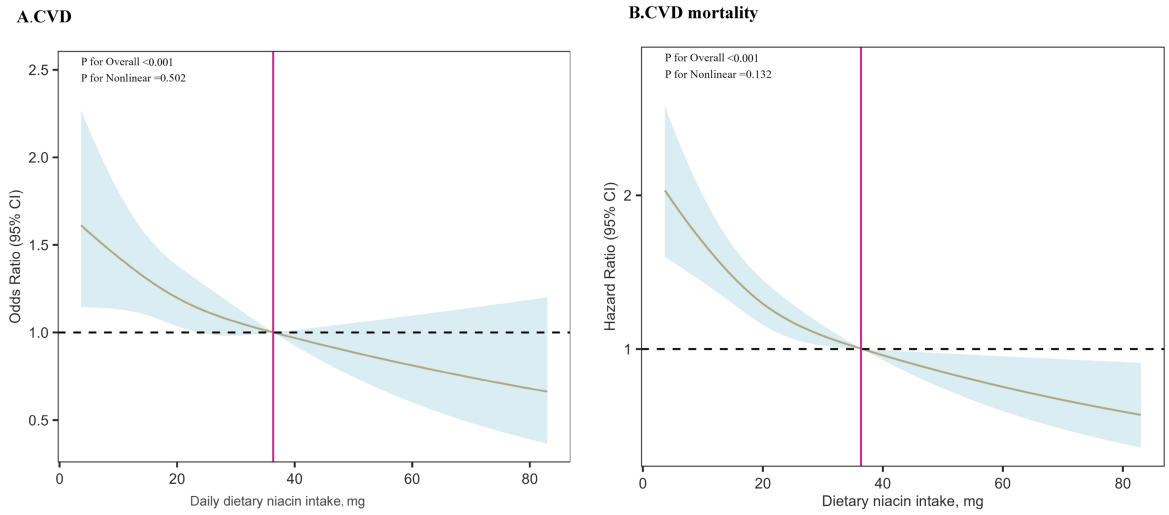


**Fig. 2. Restricted cubic splines (RCS) for independent associations of dietary niacin intake exposure with CVD and CVD mortality.** (A) Association of dietary niacin intake with CVD among individuals with CKD. (B) Association of dietary niacin intake with CVD mortality among individuals with CKD. Odd ratios or hazard ratios were adjusted for age, sex, BMI, race and ethnicity, education level, smoking status, marital status, alcohol consumption, and hypertension. Shaded areas represent 95% CIs. CVD, cardiovascular disease; BMI, body mass index. Study Population in NHANES from 2003 to 2018.

### *2.5 Assessment of Covariates*

Participants were categorized into two age groups: those under 60 years and those aged 60 years and above. The self-reported race and ethnicity data from NHANES were classified into categories including Mexican American, non-Hispanic Black, non-Hispanic White, and other categories, which included other Hispanic, other non-Hispanic, and non-Hispanic multiple races. Education levels were classified into three categories: below high school, high school, and some college or higher. Smoking habits were categorized based on lifetime cigarette intake: never smokers ($<$100 cigarettes), current smokers ($\geq$100 cigarettes), and former smokers ($\geq$100 cigarettes who have quit). Body mass index (BMI, kg/m$^2$) was classified into three categories: less than 25.0, 25.0 to 29.9, and greater than 29.9. Alcohol intake was evaluated via self-reporting, dividing participants into strong drinkers (four or more drinks per day) and low to moderate drinkers (less than four drinks per day). The individuals themselves claimed a history of hypertension diagnosed by a physician. In statistical analysis, we typically select variables with a $p$-value below 0.05, as this indicates a significant association with the study outcome. However, BMI and hypertension are special cases. They are confounding factors linked to both niacin and CVD. These confounding factors can influence study results and obscure the accurate analysis of the relationship between exposure and outcome variables. Therefore, we need to include these confounding factors as control variables in the analysis model. This allows for a correct analysis of the relationship between exposure and outcome variables. We conducted comprehensive collinearity diagnostics for all covariates. The resultant variance inflation factor (VIF) values, all below 5, point to weak correlations among covariates. This means collinearity is within acceptable limits and won't greatly affect the study's reliability (**Supplementary Table 1**).

### *2.6 Statistical Analysis*

We included the study's sampling strategy, data clustering, and subsample weights into the analysis. Kolmogorov Smirnov analysis was conducted on the intake of dietary niacin, and the results showed that it did not follow a normal distribution. Unweighted frequencies and medians with interquartile ranges (IQRs) are used for all data. To compare the differences between groups, $\chi^2$ test were utilized for categorical variables.

We determined OR and 95% CI for the connection between dietary niacin intake and CVD risks by use weighted logistic regression. In order to determine the risk of CVD mortality associated with dietary niacin intake, for the purpose of calculating the hazard ratio (HR) and the 95% CI, we made use of weighted Cox proportional hazards regression models. The use of Schoenfeld residuals allowed us to verify that the proportional hazards assumption was correct. In order to calculate the survival time, we utilized either the date of death or the day that the follow-up period came to an end (December 31, 2019), whichever came first, or the date of the NHANES interview. We started with an unadjusted model, then we added age, sex, and body mass index adjustments to Model 2, and finally, we used Model 2 to further adjust for racial/ethnic background, education, smoking status, marital status, alcohol intake, hypertension, and alcohol intake in Model 3.

**Table 1. Baseline Characteristics of Participants with CKD in NHANES 2003 to 2018.**

| Characteristic | | Patients, No. (%) | | | | *p* value |
|---|---|---|---|---|---|---|
| | | Q1, <14.67 mg/d[a] | Q2, 14.67–20.1 mg/d[a] | Q3, 20.2–27.7 mg/d[a] | Q4, >27.7 mg/d[a] | |
| Patients, No. | 3815 | 954 | 953 | 954 | 954 | |
| Age, y | | | | | | |
| <60 | 1762 (46.2) | 333 (35.0) | 399 (41.9) | 467 (49.0) | 563 (59.0) | <0.001 |
| ≥60 | 2053 (53.8) | 621 (65.1) | 554 (58.1) | 487 (51.1) | 391 (41.0) | |
| Sex | | | | | | |
| Male | 1825 (47.8) | 312 (32.7) | 388 (40.7) | 484 (50.7) | 641 (67.2) | <0.001 |
| Female | 1990 (52.2) | 642 (67.3) | 565 (59.3) | 470 (49.3) | 313 (32.8) | |
| Race and ethnicity | | | | | | |
| Mexican American | 643 (16.9) | 159 (16.7) | 155 (16.3) | 173 (18.1) | 156 (16.4) | 0.011 |
| Other Hispanic | 360 (9.4) | 99 (10.4) | 93 (9.8) | 94 (9.8) | 74 (7.8) | |
| Non-Hispanic White | 1525 (40.0) | 334 (35.0) | 419 (44.0) | 369 (38.7) | 403 (42.2) | |
| Non-Hispanic Black | 969 (25.4) | 275 (28.8) | 217 (22.8) | 237 (24.8) | 240 (25.2) | |
| Other race[b] | 318 (8.3) | 87 (9.1) | 69 (7.2) | 81 (8.5) | 81 (8.5) | |
| Educational level | | | | | | |
| <High school | 1272 (33.3) | 426 (44.7) | 313 (32.8) | 291 (30.5) | 242 (25.4) | <0.001 |
| High school | 860 (22.5) | 201 (21.1) | 214 (22.5) | 226 (23.7) | 219 (23.0) | |
| Some college or above | 1683 (44.2) | 327 (34.3) | 426 (44.7) | 437 (45.8) | 493 (51.7) | |
| Marital status | | | | | | |
| Married | 2530 (66.3) | 636 (66.7) | 654 (68.6) | 638 (66.9) | 602 (63.1) | <0.001 |
| Divorced | 461 (12.1) | 130 (13.6) | 120 (12.6) | 116 (12.2) | 95 (10.0) | |
| Unmarried | 824 (21.6) | 188 (19.7) | 179 (18.8) | 200 (21.0) | 257 (27.0) | |
| BMI (kg/m$^2$) | | | | | | |
| <25 | 1008 (26.4) | 238 (25.0) | 268 (28.1) | 241 (25.3) | 261 (27.4) | 0.314 |
| 25–29.9 | 1057 (27.7) | 285 (29.9) | 266 (27.9) | 256 (26.8) | 250 (26.2) | |
| >29.9 | 1750 (45.9) | 431 (45.2) | 419 (44.0) | 457 (47.9) | 443 (46.4) | |
| Alcoholic over 4 drinks/day | | | | | | |
| Yes | 311 (8.2) | 60 (6.3) | 66 (6.9) | 78 (8.2) | 107 (11.2) | <0.001 |
| No | 3504 (91.8) | 894 (93.7) | 887 (93.1) | 876 (91.8) | 847 (88.8) | |
| Smoking status | | | | | | |
| Current | 646 (17.0) | 147 (15.4) | 152 (16.0) | 150 (15.7) | 197 (20.7) | <0.001 |
| Former | 104 (2.7) | 15 (1.6) | 23 (2.4) | 24 (2.5) | 42 (4.4) | |
| Never | 3065 (80.3) | 792 (83.0) | 778 (81.6) | 780 (81.8) | 715 (75.0) | |
| Hypertension | | | | | | |
| Yes | 2193 (57.5) | 580 (60.8) | 526 (55.9) | 542 (56.8) | 545 (57.1) | 0.088 |
| No | 1622 (42.5) | 374 (39.2) | 427 (44.8) | 412 (43.2) | 409 (42.9) | |

[a] Daily dietary niacin intake. [b] Including Multi-Racial.

In order to investigate the non-linear association between dietary niacin intake and CVD as well as death from CVD, a restricted cubic spline (RCS) was applied. Four knots were chosen to represent the tenth, fiftieth, and ninetieth percentiles of the distribution. To determine whether or not there was non-linearity, the likelihood ratio test was utilized.

We conducted a further stratification based on baseline characteristics to assess how niacin affects CVD and death across subgroups. We also evaluated the interaction between niacin intake and baseline characteristics using the product term (niacin intake × baseline characteristics).

Two models were developed to evaluate the predictive capability of niacin in cardiovascular outcomes: one model included only conventional clinical variables, while the other integrated niacin with the clinical variables. Additionally, to evaluate the predictive power of adding dietary niacin to clinical data, we calculated the C-index, integrated discrimination improvement (IDI), and net reclassification improvement (NRI). The effects of dietary niacin on baseline features in CKD patients were examined using a stratified approach.

A series of sensitivity analyses was conducted to validate the robustness of the findings. (1) Participants who died within the first 24 months were excluded from the Cox model analysis, and those with a BMI greater than 29.9 were excluded from the logistic follow-up model to mitigate reverse causality; (2) We excluded individuals with only a

**Table 2. NHANES 2003–2018 CKD participants' CVD ORs & CVD mortality HRs.**

| Model | Odd ratio (95% CI)/Hazard ratio (95% CI) | | | | *p* value for trend |
|---|---|---|---|---|---|
| | Q1, <14.670 mg/d[a] | Q2, 14.670–20.100 mg/d[a] | Q3, 20.200–27.700 mg/d[a] | Q4, >27.700 mg/d[a] | |
| CVD | 282 of 911 | 235 of 920 | 211 of 921 | 192 of 909 | NA |
| Model 1[b] | 1.000 [Reference] | 0.770 (0.620–0.940) | 0.660 (0.540–0.820) | 0.600 (0.480–0.740) | <0.001 |
| Model 2[c] | 1.000 [Reference] | 0.790 (0.630–0.980) | 0.730 (0.580–0.920) | 0.780 (0.610–0.990) | 0.003 |
| Model 3[d] | 1.000 [Reference] | 0.800 (0.640–1.000) | 0.740 (0.590–0.930) | 0.710 (0.560–0.900) | 0.004 |
| CVD mortality | 107 of 954 | 95 of 953 | 63 of 954 | 58 of 954 | NA |
| Model 1[b] | 1.000 [Reference] | 0.810 (0.660–1.000) | 0.660 (0.531–0.815) | 0.490 (0.396–0.613) | <0.001 |
| Model 2[c] | 1.000 [Reference] | 0.850 (0.700–1.040) | 0.740 (0.600–0.910) | 0.620 (0.500–0.780) | <0.001 |
| Model 3[d] | 1.000 [Reference] | 0.830 (0.670–1.010) | 0.740 (0.600–0.920) | 0.610 (0.480–0.770) | <0.001 |

OR, odd ratio; HR, hazard ratio; NA, not available.

[a] Daily dietary niacin intake.

[b] Crude model.

[c] Adjusted for age, sex, and BMI.

[d] Further adjusted race and ethnicity, education level, smoking status, marital status, alcohol consumption, and hypertension.

**Table 3. C-index, NRI, IDI comparison across models predicting CVD & CVD mortality in participants.**

| Model | C-index | Continuous NRI (95% CI) | IDI (95% CI) |
|---|---|---|---|
| Logistic regression model | | | |
| Model 1: Traditional predictors | 0.7460 | | |
| Model 2: Traditional predictors + niacin | 0.7490 | 0.0900 (0.0150, 0.1600) | 0.0030 (0.0008, 0.0046) |
| Cox proportional hazards model | | | |
| Model 1: Traditional predictors | 0.6590 | | |
| Model 2: Traditional predictors + niacin | 0.6820 | 0.1310 (0.0830, 0.1680) | 0.0100 (0.0050, 0.0150) |

C-index, Concordance index; NRI, the net reclassification index; IDI, the continuous integrated discrimination improvement.

single dietary recall; (3) We reanalyzed the data, excluding CKD patients who died within the first 24 months and had incomplete dietary recall data; (4) In order to do further studies, we altered the number of knots in the RCS model. Specifically, we used four knots at the twenty-fifth, fifty, seventy-five and ninety-five percentiles, and we used five knots at the fifth, twenty-seventh, fifty, seventy-five, and ninety-five percentiles. The approaches that were utilized allowed for a comprehensive investigation of the nonlinear relationship that exists between the intake of dietary niacin and the outcomes of cardiovascular health, which in turn supported the findings of the study.

All of the statistical tests were carried out using a two-sided approach, and the threshold for significance was established at $p < 0.05$. R program (version 4.2.3, R Foundation for Statistical Computing, Vienna, Austria), was utilized throughout each and every type of statistical analysis.

## 3. Results

### *3.1 Patient Characteristics*

A total of 3815 patients with CKD were included in the study that investigated the relationship between niacin and CVD mortality. Of these patients, 323 had passed away due to causes connected to CVD. Following the exclusion of 154 persons due to the absence of CVD information from individual interviews, a total of 3661 participants were reviewed for the purpose of determining the connection between niacin and the occurrence of CVD. Among these participants, 920 were experiencing CVD. The participants' average age was 57.5 years (SD 18.8), with 2053 individuals aged 60 or older (53.8%) and 1825 males (47.8%). We divided the baseline features of 3815 patients with CKD into quartiles depending on the amount of dietary niacin they intaked: quartile 1 (niacin intake <14.67 mg/d, n = 954); quartile 2 (14.67–20.1 mg/d, n = 953); quartile 3 (20.2–27.7 mg/d, n = 954); and quartile 4 (>27.7 mg/d, n = 954), as presented in Table 1.

### *3.2 Dietary Niacin Intake and the Prevalence of CVD*

In Model 3, after adjusting for a range of covariates, OR and 95% CI for CVD were calculated for ascending levels of dietary niacin intake. The values were 1.00 for the quartile 1 (reference), 0.80 (0.64–1.00) for quartile 2, 0.74 (0.59–0.93) for quartile 3, and 0.71 (0.56–0.90) for quartile 4. This analysis revealed a statistically significant decline across the niacin intake categories ($p$ trend = 0.004), as presented in Table 2. Moreover, as can be seen in Fig. 2A, the RCS found that there is inverse association between the amount of dietary niacin consumed and the risk of developing CVD ($p$ for Nonlinear = 0.502).

**Table 4. NHANES 2003–2018 CKD participants' baseline dietary niacin intake & CVD associations.**

| Characteristic | Odd ratio (95% CI) | | | | *p* value for interaction |
|---|---|---|---|---|---|
| | Q1, <14.67 mg/d[a] | Q2, 14.67–20.1 mg/d[a] | Q3, 20.2–27.7 mg/d[a] | Q4, >27.7 mg/d[a] | |
| Patients, No. | 911/3661 | 920/3661 | 921/3661 | 909/3661 | |
| Age, y | | | | | |
| <60 | 1.00 [Reference] | 0.56 (0.33–0.94) | 0.89 (0.56–1.40) | 0.71 (0.45–1.13) | 0.11 |
| ≥60 | 1.00 [Reference] | 0.92 (0.73–1.16) | 0.76 (0.59–0.97) | 0.89 (0.68–1.15) | |
| Sex | | | | | |
| Male | 1.00 [Reference] | 0.79 (0.58–1.08) | 0.61 (0.45–0.83) | 0.47 (0.35–0.63) | 0.54 |
| Female | 1.00 [Reference] | 0.66 (0.50–0.88) | 0.56 (0.41–0.76) | 0.55 (0.38–0.78) | |
| Race and ethnicity | | | | | |
| Mexican American | 1.00 [Reference] | 0.86 (0.49–1.49) | 0.61 (0.34–1.08) | 0.45 (0.23–0.83) | |
| Other Hispanic | 1.00 [Reference] | 0.78 (0.39–1.53) | 0.60 (0.29–1.20) | 0.52 (0.23–1.12) | |
| Non-Hispanic White | 1.00 [Reference] | 0.94 (0.69–1.28) | 0.77 (0.56–1.06) | 0.71 (0.52–0.98) | 0.50 |
| Non-Hispanic Black | 1.00 [Reference] | 0.45 (0.30–0.69) | 0.62 (0.42–0.92) | 0.50 (0.33–0.75) | |
| Other race | 1.00 [Reference] | 0.57 (0.24–1.31) | 0.41 (0.17–0.96) | 0.47 (0.20–1.07) | |
| Educational level | | | | | |
| <High school | 1.00 [Reference] | 0.82 (0.60–1.12) | 0.68 (0.48–0.94) | 0.72 (0.50–1.02) | |
| High school | 1.00 [Reference] | 0.78 (0.51–1.18) | 0.77 (0.51–1.17) | 0.61 (0.39–0.93) | 0.95 |
| Some college or above | 1.00 [Reference] | 0.76 (0.54–1.09) | 0.63 (0.44–0.90) | 0.57 (0.40–0.82) | |
| Marital status | | | | | |
| Married | 1.00 [Reference] | 0.83 (0.65–1.05) | 0.67 (0.53–0.86) | 0.55 (0.43–0.71) | |
| Divorced | 1.00 [Reference] | 0.52 (0.29–0.93) | 0.83 (0.48–1.44) | 0.88 (0.49–1.55) | 0.08 |
| Unmarried | 1.00 [Reference] | 0.67 (0.36–1.23) | 0.49 (0.26–0.91) | 0.75 (0.44–1.30) | |
| BMI (kg/m$^2$) | | | | | |
| <25 | 1.00 [Reference] | 0.55 (0.36–0.85) | 0.56 (0.35–0.87) | 0.59 (0.38–0.91) | |
| 25–29.9 | 1.00 [Reference] | 0.88 (0.61–1.28) | 0.63 (0.42–0.93) | 0.59 (0.39–0.88) | 0.62 |
| >29.9 | 1.00 [Reference] | 0.83 (0.61–1.11) | 0.73 (0.55–0.98) | 0.61 (0.45–0.82) | |
| Alcoholic over 4 drinks/day | | | | | |
| Yes | 1.00 [Reference] | 0.86 (0.42–1.76) | 0.84 (0.42–1.69) | 0.53 (0.27–1.04) | 0.72 |
| No | 1.00 [Reference] | 0.75 (0.61–0.93) | 0.64 (0.51–0.79) | 0.59 (0.47–0.74) | |
| Smoking status | | | | | |
| Current | 1.00 [Reference] | 0.60 (0.36–0.99) | 0.49 (0.29–0.82) | 0.54 (0.33–0.87) | |
| Former | 1.00 [Reference] | 0.56 (0.12–2.44) | 0.18 (0.02–1.00) | 0.47 (0.13–1.85) | 0.56 |
| Never | 1.00 [Reference] | 0.81 (0.65–1.02) | 0.72 (0.58–0.91) | 0.61 (0.48–0.78) | |
| Hypertension | | | | | |
| Yes | 1.00 [Reference] | 0.82 (0.63–1.06) | 0.79 (0.61–1.02) | 0.58 (0.44–0.75) | 0.10 |
| No | 1.00 [Reference] | 0.72 (0.51–0.99) | 0.50 (0.35–0.72) | 0.64 (0.45–0.90) | |

[a] Adjusted for age, sex, BMI, race and ethnicity, education level, smoking status, marital status, alcohol consumption, and hypertension.

### *3.3 Niacin Intake and Mortality Rates Related to CVD*

Model 3 showed the HR and 95% CI for CVD mortality across the different amounts of dietary niacin intake after the entire set of modifications. Specifically, the values were 1.00 for the quartile 1 (reference), 0.83 (0.67–1.01) for quartile 2, 0.74 (0.60–0.92) for quartile 3, and 0.61 (0.48–0.77) for quartile 4. This analysis showed a statistically significant decline across the niacin intake categories ($p$ trend $< 0.001$), as detailed in Table 2. Additionally, Fig. 2B illustrates that the RCS identified a substantial linear correlation between CVD mortality and dietary niacin intake ($p$ for Nonlinear = 0.132).

### *3.4 Predictive Ability of Dietary Niacin Intake for CVD*

In Table 3, Logistic regression model, which solely incorporated traditional clinical variables (Model 1), attained a C-index of 0.746. In addition, incorporating dietary niacin intake into Model 1 resulted in a modest improvement in prediction accuracy, with the C-index increasing to 0.749 (Model 2). Additionally, the computed NRI and IDI were 0.09 (95% CI: 0.015–0.16) and 0.003 (95% CI: 0.0008–0.0046), respectively, when compared to Model 1.

### *3.5 CVD Mortality Prediction and Dietary Niacin Intake*

Similarly, when utilizing the Cox proportional hazards model with only traditional clinical variables (Model 1), the C-index was 0.659. Moreover, after adding dietary niacin intake based on Model 1 (Model 2), led to a slight enhance-

**Table 5. NHANES 2003–2018 CKD participants' baseline dietary niacin intake & CVD mortality associations.**

| Characteristic | Hazard ratio (95% CI) | | | | *p* value for interaction |
|---|---|---|---|---|---|
| | Q1, <14.67 mg/d[a] | Q2, 14.67–20.1 mg/d[a] | Q3, 20.2–27.7 mg/d[a] | Q4, >27.7 mg/d[a] | |
| Patients, No. | 954/3815 | 953/3815 | 954/3815 | 954/3815 | |
| Age, y | | | | | |
| <60 | 1.00 [Reference] | 0.83 (0.47–1.46) | 0.49 (0.38–1.54) | 0.75 (0.46–1.23) | 0.69 |
| ≥60 | 1.00 [Reference] | 0.89 (0.72–1.10) | 0.78 (0.63–0.96) | 0.68 (0.53–0.87) | |
| Sex | | | | | |
| Male | 1.00 [Reference] | 1.09 (0.80–1.48) | 0.77 (0.56–1.06) | 0.48 (0.35–0.65) | 0.69 |
| Female | 1.00 [Reference] | 0.67 (0.51–0.88) | 0.49 (0.36–0.67) | 0.41 (0.28–0.58) | |
| Race and ethnicity | | | | | |
| Mexican American | 1.00 [Reference] | 0.71 (0.43–1.20) | 0.41 (0.22–0.74) | 0.41 (0.21–0.78) | |
| Other Hispanic | 1.00 [Reference] | 0.71 (0.32–1.56) | 0.60 (0.26–1.37) | 0.52 (0.21–1.27) | |
| Non-Hispanic White | 1.00 [Reference] | 0.77 (0.59–1.00) | 0.63 (0.48–0.84) | 0.44 (0.33–0.58) | 0.67 |
| Non-Hispanic Black | 1.00 [Reference] | 0.55 (0.38–0.79) | 0.62 (0.43–0.88) | 0.49 (0.34–0.72) | |
| Other race[b] | 1.00 [Reference] | 1.21 (0.52–2.85) | 0.91 (0.35–2.36) | 1.05 (0.44–2.50) | |
| Educational level | | | | | |
| <High school | 1.00 [Reference] | 0.96 (0.73–1.27) | 0.77 (0.57–1.04) | 0.48 (0.34–0.69) | |
| High school | 1.00 [Reference] | 0.57 (0.38–0.86) | 0.61 (0.41–0.90) | 0.52 (0.35–0.77) | 0.91 |
| Some college or above | 1.00 [Reference] | 0.98 (0.68–1.42) | 0.72 (0.48–1.07) | 0.56 (0.39–0.82) | |
| Marital status | | | | | |
| Married | 1.00 [Reference] | 0.77 (0.61–0.97) | 0.61 (0.48–0.77) | 0.47 (0.37–0.61) | |
| Divorced | 1.00 [Reference] | 0.72 (0.42–1.25) | 0.75 (0.40–1.44) | 0.67 (0.36–1.23) | 0.47 |
| Unmarried | 1.00 [Reference] | 1.23 (0.61–2.47) | 1.03 (0.49–2.15) | 0.63 (0.33–1.19) | |
| BMI (kg/m$^2$) | | | | | |
| <25 | 1.00 [Reference] | 0.73 (0.51–1.04) | 0.52 (0.35–0.76) | 0.36 (0.24–0.55) | |
| 25–29.9 | 1.00 [Reference] | 0.71 (0.50–1.02) | 0.50 (0.34–0.74) | 0.39 (0.26–0.58) | 0.15 |
| >29.9 | 1.00 [Reference] | 0.97 (0.70–1.33) | 0.90 (0.65–1.25) | 0.69 (0.50–0.96) | |
| Alcoholic over 4 drinks/day | | | | | |
| Yes | 1.00 [Reference] | 0.94 (0.41–2.16) | 0.55 (0.25–1.22) | 0.58 (0.26–1.29) | 0.56 |
| No | 1.00 [Reference] | 0.80 (0.65–0.99) | 0.66 (0.53–0.83) | 0.48 (0.38–0.60) | |
| Smoking status | | | | | |
| Current | 1.00 [Reference] | 0.93 (0.58–1.48) | 0.65 (0.39–1.09) | 0.49 (0.30–0.80) | |
| Former | 1.00 [Reference] | 0.52 (0.15–1.84) | 1.82 (0.539–2.16) | 0.82 (0.23–2.90) | 0.53 |
| Never | 1.00 [Reference] | 0.80 (0.64–1.00) | 0.63 (0.506–0.80) | 0.48 (0.37–0.61) | |
| Hypertension | | | | | |
| Yes | 1.00 [Reference] | 0.84 (0.65–1.08) | 0.74 (0.57–0.95) | 0.52 (0.39–0.68) | 0.39 |
| No | 1.00 [Reference] | 0.83 (0.59–1.16) | 0.55 (0.38–0.81) | 0.47 (0.33–0.68) | |

[a] Adjusted for age, sex, BMI, race and ethnicity, education level, smoking status, marital status, alcohol consumption, and hypertension. [b] People of other ethnic groups.

ment of the C-index to 0.682. In comparison to Model 1, the NRI and IDI that were estimated were 0.131 (95% CI: 0.083–0.168) and 0.01 (95% CI: 0.005–0.015), respectively, as shown in Table 3.

### *3.6 Niacin Intake and CVD and Death by Baseline Parameters*

The prevalence of CVD among individuals with CKD was similar for those with higher dietary niacin intake (≥14.67 mg/d) and those with lower intake (<14.67 mg/d), regardless of baseline characteristics (Table 4). There was no significant interaction found between the concentration of dietary niacin intake and the baseline features of CVD in patients with CKD. Moreover, both high and low dietary niacin intake exhibited similar effects on CVD mortality in CKD patients across subgroups defined by baseline characteristics (Table 5). The *p* for interaction examined the confounder effect on association between niacin and CVD. For most case, the higher niacin quartile exhibited a lower risk of CVD.

### *3.7 Sensitivity Analyses*

The original findings of an inverse relationship between dietary niacin intake and CVD prevalence in CKD patients were maintained after removing individuals who died within two years of follow-up (**Supplementary Table 2**). The exclusion of subjects with a single dietary recall did not notably influence the relationship between niacin intake and CVD (**Supplementary Table 2**). After removing people who died during the first two years

of the study and those who only provided a single food recall, the results still showed strength (**Supplementary Table 2**). The findings from the RCS, utilizing different quantities of knots—namely, four knots at the twenty-fifth, fifty, seventy-five and ninety-five percentiles, and we used five knots at the fifth, twenty-seventh, fifty, seventy-five, and ninety-five percentiles—were consistent with the results derived from the model that incorporated 3 knots (**Supplementary Fig. 1A,B**). Following the same pattern, the negative connection between dietary niacin intake and CVD mortality was observed after eliminating patients who had gone away during the first two years of the study's follow-up (**Supplementary Table 3**). Even when patients who reported only a single food recall were excluded from the study, the link between niacin intake and CVD mortality remained unchanged (**Supplementary Table 3**). Participants with CKD who had gone away within two years of the follow-up and had just one dietary recall were removed from the study. The results were consistent with those obtained from the repeated analysis (**Supplementary Table 3**). The findings from RCS, incorporating different knot quantities—four knots at the twenty-fifth, fifty, seventy-five and ninety-five percentiles, and we used five knots at the fifth, twenty-seventh, fifty, seventy-five, and ninety-five percentiles—were consistent with the results from the model that employed 3 knots (**Supplementary Fig. 2A,B**). In this study, $P_{40}$ was set as the reference standard for all participants to analyze the association between niacin concentration and CVD and its mortality. The results show that CVD and its mortality decrease significantly with higher niacin concentration (**Supplementary Fig. 3**).

## 4. Discussion

This study systematically investigates the dose-dependent relationships between dietary niacin intake and both incident CVD its mortality in CKD populations. This water-soluble vitamin is crucial for health, demonstrating considerable benefits for those with CKD [18,19]. CKD-driven cardiovascular pathogenesis is mechanistically underpinned by chronic low-grade inflammation, atherogenic dyslipidemia, and redox imbalance, which collectively accelerate vascular remodeling and myocardial injury [20]. Emerging treatment strategies, notably the use of niacin, offer potential cardiovascular protection for CKD patients. Previous investigations have examined binary associations between niacin, CKD, or CVD in isolation. In contrast, our integrative analytical framework elucidates the tri-directional interplay among niacin bioavailability, renal dysfunction, and cardiovascular outcomes, employing systems biology principles. Despite evidence supporting niacin's cardioprotective properties in general populations, CKD cohorts remain disproportionately burdened by residual cardiovascular risk, underscoring unmet therapeutic needs. Our study innovatively reveals niacin's protective role against CVD in CKD patients. These results bridge a critical knowledge gap while providing actionable insights for precision nutrition strategies in cardio-renal syndrome management. Specifically, our findings suggest that CKD patients can reduce their CVD risk and related mortality by precisely controlling their dietary niacin intake, thus improving prognosis and informing treatment strategies. In patients with CKD, our study found that there is a significant inverse connection between the amount of dietary niacin consumed and CVD, as well as mortality from CVD. The association persisted as statistically following rigorous adjustment for covariates spanning demographic, biochemical, and comorbidity profiles. The fact that we were able to corroborate these findings led to an increase in our degree of confidence. This was accomplished by doing stratified and sensitivity analyses. Furthermore, a prediction model was constructed in order to evaluate the association between the amount of dietary niacin available and the risk of CVD and mortality. It is interesting that multiple subgroup analyses consistently indicated the benefits of increased dietary niacin intake, highlighting its broad applicability and usefulness across diverse groups.

CKD promotes atherosclerosis via chronic inflammation, heightened reactive oxygen species (ROS), and disruptions in lipid and electrolyte metabolism, resulting in nitric oxide (NO) deficiency, mitochondrial and DNA damage, and uremic toxin accumulation [21]. The CKD milieu is characterized by a pro-inflammatory phenotype marked by elevated circulating levels of CRP, interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-$\alpha$), which transcriptionally activate profibrotic pathways driving myocardial hypertrophy and extracellular matrix deposition. IL-6 emerges as a central mediator, potentiating both CKD progression (via tubular epithelial mesenchymal transition) and atherosclerotic plaque vulnerability through matrix metalloproteinase-9 induction [22]. Additional international multicenter studies have demonstrated that elevated IL-6 levels are predictive of risk for all-cause mortality, stroke, and myocardial infarction [23]. A meta-analysis by the CKD Prognosis Consortium (CKD-PC) also confirmed this, after adjusting for potential confounders like diabetes and blood pressure, a lower eGFR and a higher ACR were independently associated with increased CVD mortality [24]. CKD-associated dyslipidemia manifests as a distinct atherogenic profile: elevated triglyceride-rich remnant lipoproteins, small dense LDL particles, and dysfunctional high density lipoprotein (HDL) depleted of apolipoprotein A-I, creating a perfect condition for accelerated atherogenesis [25–27]. Uremic toxins, such as asymmetric dimethylarginine, impair the vascular protective function of HDL, while hyperphosphatemia facilitates the development of vascular smooth muscle cells into osteoblast-like cells, leading to heart hypertrophy, fibrosis, arterial wall thickening, capillary rarefaction, and microvascular illness [28–30]. This pathophysiological continuum between renal impairment and cardiovascular dis-

ease constitutes a multidimensional network where inflammatory, metabolic, and hemodynamic perturbations reciprocally amplify end-organ damage through positive feedback loops.

A growing body of evidence has delineated the pathophysiological nexus between CKD and CVD, mediated by dysregulated inflammatory cascades, atherogenic dyslipidemia, and systemic oxidative stress [31–33]. Emerging therapeutic modalities within nephrology research have identified niacin as a promising pharmacological agent for attenuating cardiovascular morbidity in CKD cohorts through pleiotropic mechanisms. In a randomized, double-blind, placebo-controlled experiment conducted by Rakesh Malhotra and associates, patients with CKD were administered niacin (1500 or 2000 mg/day) or a placebo. Participants receiving niacin demonstrated an annual reduction of 0.08 mg/dL in plasma phosphate levels compared to the placebo group, correlating with a lower risk of CVD development [34]. Niacin can decrease plasma triglycerides and LDL cholesterol, increase HDL cholesterol, and improve insulin sensitivity, which helps stabilize blood glucose. This positively affects phosphate metabolism, thereby optimizing lipid metabolism and indirectly influencing phosphate metabolism [35]. Furthermore, Roberto S. Kalil and his team [36] discovered that in a clinical trial, the addition of extended-release niacin to the control group resulted in a significant reduction in triglycerides and an increase in high-density lipoprotein cholesterol over a three-year follow-up among CKD participants, despite the comparable incidence of CVD events between groups. Another foundational study found that in a rat model of CKD with renal ablation, subjects treated with niacin showed significant improvement in hypertension, leading to a reduction in cardiovascular events [37]. A pharmacokinetic study revealed that Nispan® (an extended-release niacin formulation) effectively treated hypertriglyceridemia with low high-density lipoprotein levels, a significant factor in CVD, indirectly reducing the prevalence of CVD [38]. Our investigation revealed that CKD patients with a dietary niacin intake below 14.67 mg/d demonstrated a markedly reduced risk of CVD compared to those with an intake of 14.67 mg/d or more, with results consistent across many models. The ultimate outcome for CKD patients often involves death due to comorbidities, with CVD mortality being a leading cause. A randomized controlled trial analyzing 278 CKD patients revealed that a higher proportion of these patients died from cardiovascular causes, with elevated phosphate levels noted in this group [39]. Notably, another study discovered that niacin may decrease serum phosphate levels in patients with CKD [40]. Chronic inflammation, often present in CKD patients, is a significant contributor to CVD mortality [41]. Recent literature has reported that in 15 randomized controlled trials, niacin significantly reduced inflammation levels, thereby suppressing the body's inflammatory response [42]. Niacin exerts anti-inflammatory effects in macrophages by activating its receptor HM74A. Specifically, it limits the activation of *NF-$\kappa$B p65* and *I$\kappa$B$\alpha$*, thereby reducing inflammatory cytokine production. Moreover, HM74A activation stimulates *PPAR$\gamma$*, an anti-inflammatory nuclear protein. When PPAR$\gamma$ is activated in macrophages, it boosts *ABCA1/ABCG1* expression, promoting cholesterol efflux and reducing foam cell formation, thus alleviating atherosclerotic lesions [43]. Research indicates that niacin can reduce vascular calcification by activating the GPR109A receptor. This activation inhibits inflammatory cytokine production and release, lessens vascular wall inflammation, and ultimately reduces vascular calcification [44]. Interestingly, some studies have found that niacin can enhance endothelial function, reduce local and systemic inflammation, and promote vascular health. This protective effect helps maintain normal vascular function and prevent vascular disease [45]. According to the combined data, one of the main causes of death for CKD patients is CVD. However, various studies have demonstrated that niacin may decrease CVD mortality through several mechanisms. In our research, we found that during a median survival period of 7 years (ranging from 4.7 to 10.4 years), CKD patients with a dietary niacin intake of $\geq$14.67 mg/d exhibited significantly lower CVD mortality compared to those with an intake of $<$14.67 mg/d. Discrepancies in findings across studies may result from statistical biases related to sample size. Variables linked to both research characteristics and disease outcomes may not be totally constant among studies, potentially influencing or masking the true relationship. Variability in study results could be due to the sample size leading to statistical variations. It is also possible that characteristics related to both research factors and disease outcomes are not completely aligned in each study, which could affect or obscure the actual relationship.

CVD is a leading cause of death globally, it is essential for patients to be able to estimate its incidence and mortality risk with accuracy [46]. Some past studies have examined niacin intake's link to CVD risk in the general population. For instance, research has shown an inverse correlation between dietary niacin intake and CVD risk [47]. Another study found that higher niacin intake was associated with lower all-cause mortality in non-alcoholic fatty liver disease patients, but not necessarily with lower CVD mortality [48]. However, these studies didn't focus on CKD patients, suggesting niacin's effects may vary across different disease contexts. CKD patients, characterized by complex metabolic disturbances and an inflammatory state, have a different CVD pathogenesis than those already diagnosed with CVD [49]. In CKD patients, maintaining appropriate niacin levels is crucial for lipid metabolism, inflammation reduction, and vascular health. Studies investigating the potential association between niacin intake and CVD risk have only just begun. Using the C-index, NRI, and IDI, in this study, which is the first of its type, the predictive potential of dietary niacin intake on the risk of CVD

and death associated to cardiac disease is investigated. Our findings indicate that the inclusion of niacin intake in traditional clinic models can enhance the C-index, reflecting improved discriminatory power of the model. Moreover, the NRI of 0.089 (95% CI: 0.015–0.164) and the IDI of 0.003 (95% CI: 0.001–0.005) suggest that dietary niacin intake significantly improves the reclassification of CVD risk. Additional evidence that dietary niacin intake plays a substantial role in predicting the risk of mortality from CVD is provided by an NRI of 0.131 (95% CI: 0.083–0.168) and an IDI of 0.01 (95% CI: 0.005–0.015) values. Enhancement of the C-index, in the Logistic regression model, the C-index rose from 0.746 (with only traditional clinical variables) to 0.847 (with niacin intake included), indicating a marked improvement in the model's discriminatory power. In the Cox proportional hazards model, it increased from 0.6592 to 0.6817. Although the rise was modest, it still held some predictive value in survival analysis. Improvement in NRI and IDI, the positive values of NRI and IDI show that the model's ability to reclassify patient risk became better with the inclusion of niacin intake, allowing for more precise identification of high and low risk patients. From a clinical perspective, these improvements suggest: Better risk stratification, incorporating niacin intake into models helps doctors more accurately identify CVD high risk patients, enabling more targeted prevention and treatment. Personalized prevention, for CKD patients, ensuring adequate niacin intake could be a simple, cost effective way to reduce CVD risk. Complementing existing tools, despite limited enhancement, adding niacin intake to current clinical prediction models can improve CVD risk prediction. This indicates that dietary niacin intake is a significant predictor of CVD risk. After combining these findings, we draw the conclusion that dietary niacin intake is a reliable indicator that improves the precision of estimating mortality and CVD risk. The optimal level of the C-index indicates a high discriminative ability of the model, while the results for NRI and IDI demonstrate that dietary niacin intake can markedly improve the reclassification and predictive accuracy of disease risk. These discoveries emphasize the importance of dietary niacin intake in the assessment of CVD risk and offer new perspectives for future research and clinical practice.

Individuals with CKD often grapple with dyslipidemia, a factor that elevates the risk of CVD [50]. Research indicated that niacin can reduce triglyceride levels in the blood, potentially offering a positive impact on decreasing the risk of cardiovascular events [51]. Additionally, individuals with CKD often endure a persistent state of inflammation, which is strongly linked to the advancement of CVD [52]. Niacin possesses significant anti-inflammatory properties, able to reduce inflammatory markers such C-reactive protein (CRP) levels, thereby contributing to a reduction of cardiovascular risk [53,54]. As kidney function declines, CKD patients may encounter an accumulation of metabolic waste and oxidative stress markers, exacerbating the damage to the cardiovascular system [55–57]. The antioxidant effects of niacin help mitigate this damage, further reducing the risk of cardiovascular events [58]. Hyperphosphatemia, prevalent in CKD patients, can be mitigated by niacin's ability to inhibit intestinal phosphate absorption, aiding in the control of serum phosphorus levels and minimizing the likelihood of cardiovascular incidents [59–61]. Endothelial dysfunction, a frequent complication in CKD patients, is associated with a heightened risk of CVD [62]. Niacin improves endothelium-dependent vasorelaxation and increases the production of NO, which is essential for maintaining vascular health and preventing CVD. This is achieved by enhancing the activity of endothelial nitric oxide synthase (eNOS) [63]. In summary, niacin positively influences the cardiovascular health of CKD patients through multiple mechanisms, including the improvement of dyslipidemia, anti-inflammatory effects, antioxidant actions, control of serum phosphorus levels, and enhancement of endothelial function. These effects highlight the importance of niacin in the management of CKD patients and offer new perspectives for future research and therapeutic approaches. CKD patients often necessitate dietary restrictions and potentially dialysis, which may lead to insufficient levels of niacin within the body [64]. Our research indicates that niacin intake for CKD patients should exceed 27.7 mg per day, a level that can be achieved through the consumption of niacin-rich foods. Furthermore, if optimal niacin levels are not achieved, niacin supplements can be taken as needed. The present investigation presents both strengths and limitations. The strengths are noteworthy: this is the most comprehensive examination to date of the relationship between dietary niacin intake levels and CVD and its mortality among CKD patients, considering a wide range of potential confounding factors. Significant findings were obtained from predictive studies of the association between dietary niacin intake levels and CVD and related mortality in CKD. The results may be more broadly applied since they are based on a statistically valid sample of persons living in the United States who have CKD. However, several limitations should be considered. There is missing data for some variables, such as BMI, which may impact the results when adjusting the model. The research was conducted in an observational fashion, which means we are unable to establish a causal association between the two variables. The National Death Index has a moderate level of accuracy in classifying CVD mortality, while being a trustworthy indicator of vital condition. We categorized dietary niacin intake by study population quartiles, which may make our results not comparable to other research using different cut points. Furthermore, some potential confounding factors may not have been adequately considered, leading to the existence of residual and unidentified confounders that cannot be completely excluded. Additionally, we recognize the limitations of NHANES dietary recall data, including re-

call bias and measurement error, as this self-reported data depends on participants' memory, which can be inaccurate. Therefore, we've addressed these issues by rigorously cleaning the data and removing unreliable entries. Meanwhile, the diagnosis of CVD, relying on self-reported physician diagnoses, has certain limitations. Yet, in line with most research, this is currently the best method. Lastly, our observational study of CKD patients reveals a potential inverse association between high dietary niacin intake and CVD risk, yet causality cannot be confirmed. A strength is the use of large-scale population data to identify correlations. However, residual confounding may influence results despite controlling for known variables. This is currently the best method. This limitation stems from database constraints, common in studies based on NHANES. In future research, we will incorporate our own clinical data.

## 5. Conclusions

According to the findings of this cohort study of people in the United States who have CKD, a higher intake of dietary niacin may be associated with a lower risk of CVD and subsequent mortality. Furthermore, it is clinically noteworthy that dietary niacin intake levels in CKD patients can be used to predict CVD and related mortality. The dose-response connection between dietary niacin and CVD and death in CKD patients needs further study. This will determine ideal intake. Based on the results of our study, it is currently recommended that CKD patients should have a dietary niacin intake of more than 27.7 mg of per day.

In summary, the strengths of this investigation are noteworthy. This investigation is the most comprehensive examination to date of the relationship between dietary niacin intake levels and CVD and its mortality among CKD, considering a wide range of potential confounding factors. Furthermore, significant findings were obtained from predictive studies of the association between dietary niacin intake levels and CVD and related mortality in CKD. The results may be more broadly applied since they are based on a statistically valid sample of persons living in the United States who have CKD.

## Availability of Data and Materials

All data used in the study were accessible to HW. At the following website: https://wwwn.cdc.gov/nchs/nhanes/Default.aspx, visitors can freely access the information that was gathered from the National Health and Nutrition Examination Survey.

## Author Contributions

HW was solely responsible for ensuring that the data was accurate and complete. Concept and design by DZ. SYG, GZ, YFL, YL and XTY contributed to the acquisition, analysis, or interpretation of data. Manuscript drafted by DZ. Thorough evaluation of the manuscript for significant intellectual contributions: All authors. Statistical analysis conducted by DZ. Funding acquired: HW. All authors performed a comprehensive assessment of the manuscript's significant intellectual contributions, approved the final manuscript and have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

The NCHS Research Ethics Review Board reviewed and approved the NHANES protocols. Therefore, no ethical approval was required for this study and all participants signed the informed consent.


## Acknowledgment

This study utilized the US National Health and Nutrition Examination Survey. We express our gratitude to the participants and the data administrators.

## Funding

This research received funding from the National Natural Science Foundation of China (Grant No. 81600234).


## Conflict of Interest

The authors declare no conflict of interest.

## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/IJVNR37256.

## References


[1] Carré JE, Affourtit C. Mitochondrial Activity and Skeletal Muscle Insulin Resistance in Kidney Disease. International Journal of Molecular Sciences. 2019; 20: 2751. https://doi.org/10.3390/ijms20112751.

[2] Matsushita K, Ballew SH, Wang AYM, Kalyesubula R, Schaeffner E, Agarwal R. Epidemiology and risk of cardiovascular disease in populations with chronic kidney disease. Nature Reviews. Nephrology. 2022; 18: 696–707. https://doi.org/10.1038/s41581-022-00616-6.

[3] Speer T, Dimmeler S, Schunk SJ, Fliser D, Ridker PM. Targeting innate immunity-driven inflammation in CKD and cardiovascular disease. Nature Reviews. Nephrology. 2022; 18: 762–778. https://doi.org/10.1038/s41581-022-00621-9.

[4] Jiang L, Xu L, Sun W, Bian K, Wang Y. Association between the coexistence of chronic kidney disease and sarcopenia with cardiovascular disease and mortality. Aging Clinical and Experimental Research. 2025; 37: 92. https://doi.org/10.1007/s40520-025-03003-w.

[5] Li G, Liu B, Yang H, Zhang D, Wang S, Zhang Z, *et al*. Omega-3 polyunsaturated fatty acids alleviate renal fibrosis in chronic kidney disease by reducing macrophage activation and infiltration through the JAG1-NOTCH1/2 pathway. International Immunopharmacology. 2025; 152: 114454. https://doi.org/10.1016/j.intimp.2025.114454.

[6] Rodelo-Haad C, Rodríguez-Ortiz ME, Garcia-Sáez R, Rivas-Domínguez A, Jurado-Montoya D, Martín-Malo A, *et al*. The true cost of phosphate control in chronic kidney disease. Clinical Kidney Journal. 2025; 18: i46–i60. https://doi.org/10.1093/ckj/sfae434.

[7] Freese R, Lysne V. Niacin - a scoping review for Nordic Nutrition Recommendations 2023. Food & Nutrition Research. 2023; 67. https://doi.org/10.29219/fnr.v67.10299.
[8] Chen L, Xing X, Zhang P, Chen L, Pei H. Homeostatic regulation of NAD (H) and NADP (H) in cells. Genes & Diseases. 2024; 11: 101146. https://doi.org/10.1016/j.gendis.2023.101146.
[9] Wuerch E, Urgoiti GR, Yong VW. The Promise of Niacin in Neurology. Neurotherapeutics: the Journal of the American Society for Experimental NeuroTherapeutics. 2023; 20: 1037–1054. https://doi.org/10.1007/s13311-023-01376-2.
[10] Ren W, Li Y, Lu C, Liu S, Shao Y, Shi X. Comprehensive assessment on the association of dietary vitamins with all-cause and cardiovascular mortality among individuals with prediabetes: evidence from NHANES 1999-2018. Food & Function. 2024; 15: 10037–10050. https://doi.org/10.1039/d4fo02893g.
[11] Xie Z, Peng S, Ou G, Zhou X, Zhang G, Jiang H, *et al*. U-shape association between dietary niacin intake and chronic kidney disease among US elderly: a nationwide cross-sectional study. Frontiers in Endocrinology (Lausanne). 2024; 15: 1438373. https://doi.org/10.3389/fendo.2024.1438373.
[12] Isakova T, Ix JH, Sprague SM, Raphael KL, Fried L, Gassman JJ, *et al*. Rationale and Approaches to Phosphate and Fibroblast Growth Factor 23 Reduction in CKD. Journal of the American Society of Nephrology: JASN. 2015; 26: 2328–2339. https://doi.org/10.1681/ASN.2015020117.
[13] Malhotra R, Katz R, Hoofnagle A, Bostom A, Rifkin DE, Mcbride R, *et al*. The Effect of Extended Release Niacin on Markers of Mineral Metabolism in CKD. Clinical Journal of the American Society of Nephrology: CJASN. 2018; 13: 36–44. https://doi.org/10.2215/CJN.05440517.
[14] Mansouri F, Jafari F, Ranjbar S, Souni F, Jahromi SE, Shateri Z, *et al*. Dietary inflammatory index could increase the risk of sarcopenia in patients with chronic kidney disease. Scientific Reports. 2024; 14: 15284. https://doi.org/10.1038/s41598-024-65340-6.
[15] Tannous C, Booz GW, Altara R, Muhieddine DH, Mericskay M, Refaat MM, *et al*. Nicotinamide adenine dinucleotide: Biosynthesis, consumption and therapeutic role in cardiac diseases. Acta Physiologica (Oxford, England). 2021; 231: e13551. https://doi.org/10.1111/apha.13551.
[16] Zhang Z, Liu M, Zhou C, He P, Zhang Y, Li H, *et al*. Evaluation of Dietary Niacin and New-Onset Hypertension Among Chinese Adults. JAMA Network Open. 2021; 4: e2031669. https://doi.org/10.1001/jamanetworkopen.2020.31669.
[17] Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International. 2024; 105: S117–S314. https://doi.org/10.1016/j.kint.2023.10.018.
[18] Chu X, Raju RP. Regulation of $NAD^+$ metabolism in aging and disease. Metabolism: Clinical and Experimental. 2022; 126: 154923. https://doi.org/10.1016/j.metabol.2021.154923.
[19] Kędzierska-Kapuza K, Szczuko U, Stolińska H, Bakaloudi DR, Wierzba W, Szczuko M. Demand for Water-Soluble Vitamins in a Group of Patients with CKD versus Interventions and Supplementation-A Systematic Review. Nutrients. 2023; 15: 860. https://doi.org/10.3390/nu15040860.
[20] Ogata H, Sugawara H, Yamamoto M, Ito H. Phosphate and Coronary Artery Disease in Patients with Chronic Kidney Disease. Journal of Atherosclerosis and Thrombosis. 2024; 31: 1–14. https://doi.org/10.5551/jat.RV22012.
[21] Fularski P, Krzemińska J, Lewandowska N, Młynarska E, Saar M, Wronka M, *et al*. Statins in Chronic Kidney Disease-Effects on Atherosclerosis and Cellular Senescence. Cells. 2023; 12: 1679. https://doi.org/10.3390/cells12131679.
[22] Keller CR, Odden MC, Fried LF, Newman AB, Angleman S, Green CA, *et al*. Kidney function and markers of inflammation in elderly persons without chronic kidney disease: the health, aging, and body composition study. Kidney International. 2007; 71: 239–244. https://doi.org/10.1038/sj.ki.5002042.
[23] Batra G, Ghukasyan Lakic T, Lindbäck J, Held C, White HD, Stewart RAH, *et al*. Interleukin 6 and Cardiovascular Outcomes in Patients With Chronic Kidney Disease and Chronic Coronary Syndrome. JAMA Cardiology. 2021; 6: 1440–1445. https://doi.org/10.1001/jamacardio.2021.3079.
[24] Haris M, Raveendra K, Travlos CK, Lewington A, Wu J, Shuweidhi F, *et al*. Prediction of incident chronic kidney disease in community-based electronic health records: a systematic review and meta-analysis. Clinical Kidney Journal. 2024; 17: sfae098. https://doi.org/10.1093/ckj/sfae098.
[25] Chen Y, Li S, Yang K, Wu B, Xie D, Peng C, *et al*. Triglyceride-glucose index and prognosis in individuals afflicted with heart failure and chronic kidney disease. ESC Heart Failure. 2024; 11: 3120–3132. https://doi.org/10.1002/ehf2.14898.
[26] Geng T, Xu W, Gao H, Zhang J, Zou J, Wang K, *et al*. Relationship Between Control of Cardiovascular Risk Factors and Chronic Kidney Disease Progression, Cardiovascular Disease Events, and Mortality in Chinese Adults. Journal of the American College of Cardiology. 2024; 84: 1313–1324. https://doi.org/10.1016/j.jacc.2024.06.041.
[27] Cashmore BA, Cooper TE, Evangelidis NM, Green SC, Lopez-Vargas P, Tunnicliffe DJ. Education programmes for people with chronic kidney disease and diabetes. The Cochrane Database of Systematic Reviews. 2024; 8: CD007374. https://doi.org/10.1002/14651858.CD007374.pub3.
[28] Xie H, Yang N, Lu L, Sun X, Li J, Wang X, *et al*. Uremic Toxin Receptor AhR Facilitates Renal Senescence and Fibrosis via Suppressing Mitochondrial Biogenesis. Advanced Science (Weinheim, Baden-Wurttemberg, Germany). 2024; 11: e2402066. https://doi.org/10.1002/advs.202402066.
[29] Dong QQ, Tu YC, Gao P, Liao QQ, Zhou P, Zhang H, *et al*. SGK3 promotes vascular calcification via Pit-1 in chronic kidney disease. Theranostics. 2024; 14: 861–878. https://doi.org/10.7150/thno.87317.
[30] Zhou C, Shi Z, Ouyang N, Ruan X. Hyperphosphatemia and Cardiovascular Disease. Frontiers in Cell and Developmental Biology. 2021; 9: 644363. https://doi.org/10.3389/fcell.2021.644363.
[31] Donate-Correa J, Ferri CM, Mora-Fernández C, Pérez-Delgado N, González-Luis A, Navarro-González JF. Pentoxifylline ameliorates subclinical atherosclerosis progression in patients with type 2 diabetes and chronic kidney disease: a randomized pilot trial. Cardiovascular Diabetology. 2024; 23: 314. https://doi.org/10.1186/s12933-024-02393-x.
[32] Tian L, Jaeger BC, Scialla JJ, Budoff MJ, Mehta RC, Jaar BG, *et al*. Progression of Coronary Artery Calcification and Risk of Clinical Events in CKD: The Chronic Renal Insufficiency Cohort Study. American Journal of Kidney Diseases: the Official Journal of the National Kidney Foundation. 2025; 85: 67–77.e1. https://doi.org/10.1053/j.ajkd.2024.06.018.
[33] Rossing P, Hansen TW, Kümler T. Cardiovascular and non-renal complications of chronic kidney disease: Managing risk. Diabetes, Obesity & Metabolism. 2024; 26: 13–21. https://doi.org/10.1111/dom.15747.
[34] Taketani Y, Masuda M, Yamanaka-Okumura H, Tatsumi S, Segawa H, Miyamoto K, *et al*. Niacin and Chronic Kidney Disease. Journal of Nutritional Science and Vitaminology. 2015; 61 Suppl: S173–175. https://doi.org/10.3177/jnsv.61.s173.
[35] Ferrell M, Wang Z, Anderson JT, Li XS, Witkowski M, DiDonato JA, *et al*. A terminal metabolite of niacin promotes vascular inflammation and contributes to cardiovascular disease risk. Nature Medicine. 2024; 30: 424–434. https://doi.org/10.1038/

s41591-023-02793-8.
[36] Kalil RS, Wang JH, de Boer IH, Mathew RO, Ix JH, Asif A, *et al*. Effect of extended-release niacin on cardiovascular events and kidney function in chronic kidney disease: a post hoc analysis of the AIM-HIGH trial. Kidney International. 2015; 87: 1250–1257. https://doi.org/10.1038/ki.2014.383.
[37] Cho KH, Kim HJ, Rodriguez-Iturbe B, Vaziri ND. Niacin ameliorates oxidative stress, inflammation, proteinuria, and hypertension in rats with chronic renal failure. American Journal of Physiology. Renal Physiology. 2009; 297: F106–F113. https://doi.org/10.1152/ajprenal.00126.2009.
[38] Kjeldsen EW, Thomassen JQ, Frikke-Schmidt R. HDL cholesterol concentrations and risk of atherosclerotic cardiovascular disease - Insights from randomized clinical trials and human genetics. Biochimica et Biophysica Acta. Molecular and Cell Biology of Lipids. 2022; 1867: 159063. https://doi.org/10.1016/j.bbalip.2021.159063.
[39] Lioufas NM, Pedagogos E, Hawley CM, Pascoe EM, Elder GJ, Badve SV, *et al*. Aortic Calcification and Arterial Stiffness Burden in a Chronic Kidney Disease Cohort with High Cardiovascular Risk: Baseline Characteristics of the Impact of Phosphate Reduction On Vascular End-Points in Chronic Kidney Disease Trial. American Journal of Nephrology. 2020; 51: 201–215. https://doi.org/10.1159/000505717.
[40] Ginsberg C, IX jh. Nicotinamide and phosphate homeostasis in chronic kidney disease. Current Opinion in Nephrology and Hypertension. 2016; 4: 285–291. https://doi.org/10.1097/mnh.0000000000000236.
[41] Yong K, Mori T, Chew G, Beilin LJ, Puddey I, Watts GF, *et al*. The Effects of OMEGA-3 Fatty Acid Supplementation Upon Interleukin-12 and Interleukin-18 in Chronic Kidney Disease Patients. Journal of Renal Nutrition: the Official Journal of the Council on Renal Nutrition of the National Kidney Foundation. 2019; 29: 377–385. https://doi.org/10.1053/j.jrn.2019.01.001.
[42] Rad EY, Saboori S, Tammam J, Thondre PS, Coe S. The effect of niacin on inflammatory markers and adipokines: a systematic review and meta-analysis of interventional studies. European Journal of Nutrition. 2024; 63: 2011–2024. https://doi.org/10.1007/s00394-024-03425-8.
[43] Hong W, Chen X, Xiao J, Chen G, Yang J, Zhang P, *et al*. Dehydrocostus lactone attenuates atherogenesis by promoting cholesterol efflux and inhibiting inflammation via TLR2/PPAR-γ/NF-κB signaling pathway. Molecular Medicine. 2025; 31: 243. https://doi.org/10.1186/s10020-025-01265-8.
[44] Kothawade PB, Thomas AB, Chitlange SS. Novel Niacin Receptor Agonists: A Promising Strategy for the Treatment of Dyslipidemia. Mini Reviews in Medicinal Chemistry. 2021; 21: 2481–2496. https://doi.org/10.2174/1389557521666210125144921.
[45] Curran CS, Kopp JB. The complexity of nicotinamide adenine dinucleotide (NAD), hypoxic, and aryl hydrocarbon receptor cell signaling in chronic kidney disease. Journal of Translational Medicine. 2023; 21: 706. https://doi.org/10.1186/s12967-023-04584-8.
[46] Markina YV, Kirichenko TV, Tolstik TV, Bogatyreva AI, Zotova US, Cherednichenko VR, *et al*. Target and Cell Therapy for Atherosclerosis and CVD. International Journal of Molecular Sciences. 2023; 24: 10308. https://doi.org/10.3390/ijms241210308.
[47] Yang R, Zhu M, Fan S, Zhang J. Niacin intake and mortality (total and cardiovascular disease) in patients with cardiovascular disease: Insights from NHANES 2003-2018. Nutrition Journal. 2024; 23: 123. https://doi.org/10.1186/s12937-024-01027-y.
[48] Pan J, Zhou Y, Pang N, Yang L. Dietary Niacin Intake and Mortality Among Individuals With Nonalcoholic Fatty Liver Disease. JAMA Network Open. 2024; 7: e2354277. https://doi.org/10.1001/jamanetworkopen.2023.54277.
[49] Li X, Lindholm B. Cardiovascular Risk Prediction in Chronic Kidney Disease. American Journal of Nephrology. 2022; 53: 730–739. https://doi.org/10.1159/000528560.
[50] Kochan Z, Szupryczynska N, Malgorzewicz S, Karbowska J. Dietary Lipids and Dyslipidemia in Chronic Kidney Disease. Nutrients. 2021; 13: 3138. https://doi.org/10.3390/nu13093138.
[51] Kosmas CE, Bousvarou MD, Papakonstantinou EJ, Tsamoulis D, Koulopoulos A, Echavarria Uceta R, *et al*. Novel Pharmacological Therapies for the Management of Hyperlipoproteinemia (a). International Journal of Molecular Sciences. 2023; 24: 13622. https://doi.org/10.3390/ijms241713622.
[52] Kadatane SP, Satariano M, Massey M, Mongan K, Raina R. The Role of Inflammation in CKD. Cells. 2023; 12: 1581. https://doi.org/10.3390/cells12121581.
[53] Wu HHL, McDonnell T, Chinnadurai R. Physiological Associations between Vitamin B Deficiency and Diabetic Kidney Disease. Biomedicines. 2023; 11: 1153. https://doi.org/10.3390/biomedicines11041153.
[54] Zivkovic S, Maric G, Cvetinovic N, Lepojevic-Stefanovic D, Bozic Cvijan B. Anti-Inflammatory Effects of Lipid-Lowering Drugs and Supplements-A Narrative Review. Nutrients. 2023; 15: 1517. https://doi.org/10.3390/nu15061517.
[55] Fularski P, Czarnik W, Frankenstein H, Gąsior M, Młynarska E, Rysz J, *et al*. Unveiling Selected Influences on Chronic Kidney Disease Development and Progression. Cells. 2024; 13: 751. https://doi.org/10.3390/cells13090751.
[56] Graterol Torres F, Molina M, Soler-Majoral J, Romero-González G, Rodríguez Chitiva N, Troya-Saborido M, *et al*. Evolving Concepts on Inflammatory Biomarkers and Malnutrition in Chronic Kidney Disease. Nutrients. 2022; 14: 4297. https://doi.org/10.3390/nu14204297.
[57] Kong ASY, Lai KS, Hee CW, Loh JY, Lim SHE, Sathiya M. Oxidative Stress Parameters as Biomarkers of Cardiovascular Disease towards the Development and Progression. Antioxidants (Basel, Switzerland). 2022; 11: 1175. https://doi.org/10.3390/antiox11061175.
[58] Manolis AA, Manolis TA, Melita H, Manolis AS. Role of Vitamins in Cardiovascular Health: Know Your Facts-Part 2. Current Vascular Pharmacology. 2023; 21: 399–423. https://doi.org/10.2174/1570161121666230911115725.
[59] Chen TK, Knicely DH, Grams ME. Chronic Kidney Disease Diagnosis and Management: A Review. JAMA. 2019; 322: 1294–1304. https://doi.org/10.1001/jama.2019.14745.
[60] Yamada S, Nakano T. Role of Chronic Kidney Disease (CKD)-Mineral and Bone Disorder (MBD) in the Pathogenesis of Cardiovascular Disease in CKD. Journal of Atherosclerosis and Thrombosis. 2023; 30: 835–850. https://doi.org/10.5551/jat.RV22006.
[61] Doshi SM, Wish JB. Past, Present, and Future of Phosphate Management. Kidney International Reports. 2022; 7: 688–698. https://doi.org/10.1016/j.ekir.2022.01.1055.
[62] Sarakpi T, Mesic A, Speer T. Leukocyte-endothelial interaction in CKD. Clinical Kidney Journal. 2023; 16: 1845–1860. https://doi.org/10.1093/ckj/sfad135.
[63] Huang PH, Lin CP, Wang CH, Chiang CH, Tsai HY, Chen JS, *et al*. Niacin improves ischemia-induced neovascularization in diabetic mice by enhancement of endothelial progenitor cell functions independent of changes in plasma lipids. Angiogenesis. 2012; 15: 377–389. https://doi.org/10.1007/s10456-012-9267-z.
[64] Moldovan D, Rusu CC, Potra AR, Tirinescu D, Ticala M, Maslyennikov Y, *et al*. Nutritional Intervention and Musculoskeletal Health in Chronic Kidney Disease. Nutrients. 2025; 17: 896. https://doi.org/10.3390/nu17050896.