

Association of Unhealthy Plant-Based Diet with All-Cause Mortality in Chronic Kidney Disease Without Cardiovascular Diseases: A NHANES-Based Study

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Purpose: A plant-based diet (PBD) has been demonstrated to reduce the risk of chronic kidney disease (CKD) and cardiovascular diseases (CVD). This study aimed to examine the associations of PBD indices with all-cause and CVD mortality in a cohort of community-dwelling adults with predominantly early-stage CKD and no comorbid CVD.

Methods: Adult CKD patients, defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m² and/or urinary albumin-to-creatinine ratio (uACR) >30 mg/g, without known CVD, were included from the 1999–2018 National Health and Nutrition Examination Survey. The primary exposures were scores from the healthy PBD index (hPDI), unhealthy PBD index (uPDI), and total PDI. The Cox proportional hazards model was used for survival analysis.

Results: A total of 4098 participants (mean age 55.50 years, mean eGFR 80.62 mL/min/1.73m²) were included. During a median follow-up time of 102 months, 1191 (19.52%) participants died, of which 397 were from CVD mortality. Neither the total PDI nor the hPDI was associated with all-cause or CVD mortality. The hazard ratios and 95% confidence intervals for the association between uPDI and all-cause or CVD mortality were 1.02 (1.01–1.04) and 1.01 (0.98–1.04), respectively. Restricted cubic spline analysis indicated a linearly positive relationship between uPDI and all-cause mortality. Subgroup analysis revealed that the associations between uPDI and all-cause mortality were stronger in women and non-diabetic individuals compared to men and diabetic individuals.

Conclusion: Adherence to unhealthy PBD is associated with increased all-cause mortality in US CKD individuals without CVD, especially women and non-diabetic individuals.

Keywords: cardiovascular disease, chronic kidney disease, mortality, NHANES, plant-based diet

Introduction

The increasing prevalence of chronic kidney disease (CKD) represents a major public health issue that incurs a substantial burden on the family and society. Despite dramatic improvements have been made in the treatment and management of CKD, it is still associated with a high morbidity and mortality rate. In addition to pharmacological treatments, lifestyle modifications, including dietary management, have been demonstrated to serve as a critical component in retarding CKD progression and reducing of mortality.¹ Current guidelines generally recommend 0.60–0.80 grams of protein per kilogram of body weight per day for individuals with advanced CKD (stage 3 or higher) who are at high risk of malnutrition due to low appetite, chronic micro-inflammatory state, and acidemia-induced muscle breakdown.² Therefore, dietary management that provides essential and adequate nutrient intakes while minimizing kidney burden is of critical importance.

The plant-based diet (PBD), characterized by a preponderance of plant-based foods with a comparatively lower proportion of animal-sourced foods, is gaining popularity due to its purported health effects and environmental

sustainability.³ Observational studies have linked adherence to a healthful PBD pattern with a reduced prevalence of hypertension, diabetes, and cardiovascular disease (CVD).^{4–6} Although traditional viewpoint holds that animal proteins possess a higher biological value and thus superior to plant proteins,⁷ an increasing number of studies have indicated that a PBD is cross-sectionally associated with kidney function and may decrease the risk of diabetic nephropathy in patients with type 2 diabetes.^{8,9} Furthermore, a PBD represents the sole source of fiber capable of modulating gut microbiota and decreasing uremic toxins. Another notable advantage of PBD is its superior protein to phosphorus ratio compared to animal-based diets.¹⁰ To the best of our knowledge, the majority of previous studies have focused on the health effects of individual nutrients or nutrient quantities, with relatively less attention devoted to the assessment of diet quality.

We are aware that two earlier studies have already investigated the impact of PBD patterns on the mortality risk in patients with CKD.^{11,12} However, both studies included a predominantly advanced CKD cohort. It is currently unknown whether a PBD pattern also exerts a significant influence on the mortality risk of early stages of CKD, in which studies of nutritional management are relatively insufficient. To bridge this gap in the literature, our study examined the association between PBD indices and all-cause or cardiovascular mortality in a cohort of community-dwelling adults with predominantly early stages of CKD without comorbid CVD.

Methods

Data Source and Participant Selection

Publicly available data from the US 1999–2018 National Health and Nutrition Examination Survey (NHANES), an ongoing biennial cross-sectional survey, were used to conduct this mortality follow-up study. Ethical approval was obtained from the NCHS Research Ethics Review Board, and all participants provided informed consent. Based on the item 1 and 2 of Article 32 of the Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects dated February 18, 2023, China, our study is exempted from ethical approval from our institution. Detailed descriptions of data acquisition can be found elsewhere.¹³

Adult participants with CKD, defined as an estimated glomerular filtration rate (eGFR) calculated from 2009 serum creatinine-based equation¹⁴ <60 mL/min/1.73m² or a urinary albumin-to-creatinine ratio (uACR) >30 mg/g, were potentially eligible for inclusion. We further excluded participants for the following reasons: age < 20 years, pregnancy at the time of interview, with a history of malignancy or CVD (including self-reported stroke, heart attack, coronary heart disease, congestive heart failure, and angina pectoris), dialysis at the time of interview, missing data of PDI or follow-up, and those with missing covariates. As illustrated in [Figure 1](#), a total of 4098 CKD subjects with complete data were included in the final analysis.

Assessment of PBD Indices

The dietary intake data were derived from the first-round (1999–2002 cycles) or the average of the first-round and second-round (2003–2018 cycles) 24-hour dietary recall, as appropriate. Details of the construction of PBD indices have been delineated previously.¹⁵ First, a total of 17 food groups were categorized into the healthy PBD (whole grains, fruits, vegetables, nuts, legumes, vegetable oils, and coffee), unhealthy PBD (fruit juices, refined grains, potatoes, sugar-sweetened beverages, sweets and desserts) and animal-based foods (animal fats, dairy products, eggs, fish or seafood, meat, and miscellaneous animal-based foods), primarily based on our current knowledge of the relationships between specific foods and certain chronic diseases. Consequently, the healthy PBD index (hPDI) and the unhealthy PBD index (uPDI) were generated by dividing each food intake into cohort-specific quintiles and assigning a score of 1 to 5. For the calculation of hPDI, positive scores were assigned to higher quintiles of healthy PBD (ie, the highest and lowest quintiles were assigned a score of 5 and 1, respectively), and higher quintiles of unhealthy and animal-based foods (ie, the highest and lowest quintiles were assigned a score of 1 and 5, respectively) received inverse scores. A similar approach was employed during the calculation of uPDI, wherein positive scores were assigned to unhealthy PBD and inverse scores were allocated to healthy and animal-based foods. To semiquantitatively assess the relative intake of plant-based foods and animal-based foods, a total PDI was scored by assigning positive scores to healthy and unhealthy PBD and negative scores to animal-based foods.

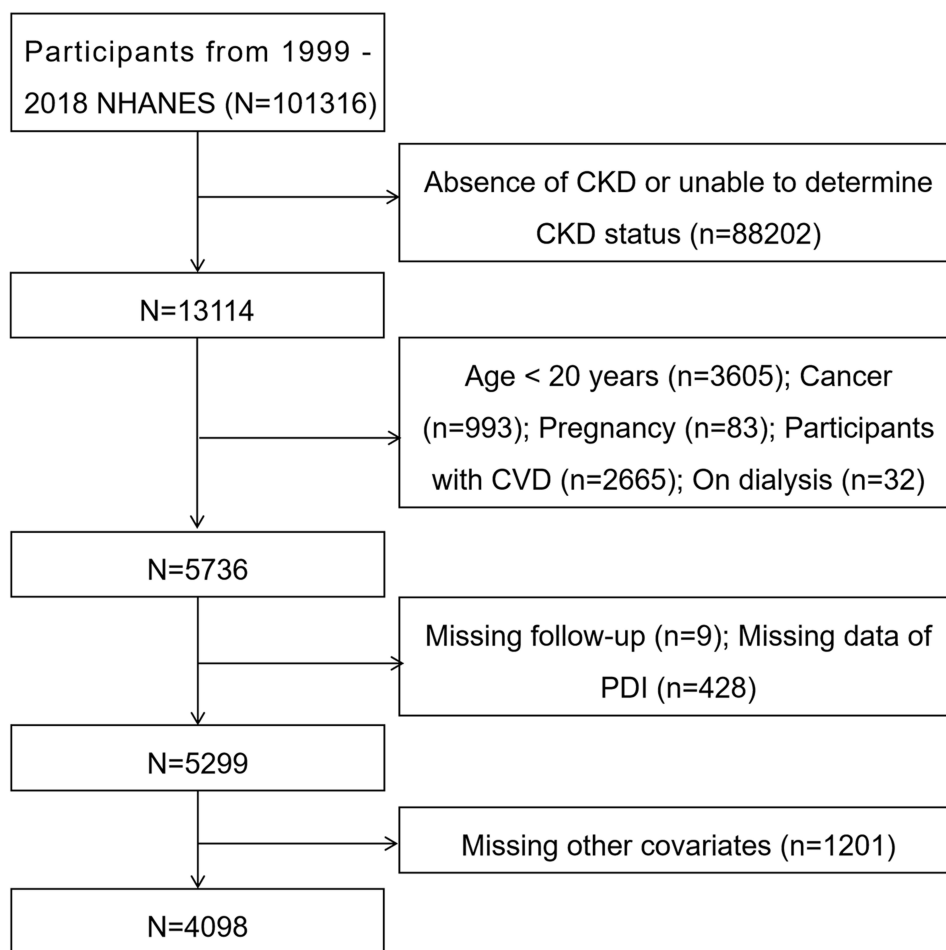


Figure 1 The participant flow diagram.

Abbreviations: CKD, chronic kidney disease; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; PDI, plant-based diet index.

Outcome Ascertainment

Information regarding survival status was derived from the National Center for Health Statistics Public-Use Linked Mortality Files by linking to the National Death Index with a probabilistic matching algorithm. Follow-up time was censored at the recorded date of participant death, or at December 31, 2019 for those without a recorded death. The International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) codes were employed to determine the leading cause of death. In this context, CVD mortality was defined by the ICD-10 codes I00–I09, I11, I13, I20–I51, or I60–I69.¹⁶

Covariates

We incorporated a range of participant-level characteristics into the analysis, including demographics, socioeconomic status, clinical features, relevant laboratory results, and medication use. Specifically, we retrieved participants' age (continuous), sex (men vs women), race (non-Hispanic white vs other), marital status (single vs non-single), poverty-income ratio (continuous), education level (less than high school vs high school vs higher than high school), body mass index (continuous, calculated as body weight in kilograms divided by height in meters squared), physical activity (none vs moderate vs vigorous), smoking (yes vs no), drinking (yes vs no), and total energy intake (continuous). The comorbidity variables included diabetes and hypertension. Laboratory tests included glycated hemoglobin, total cholesterol and triglycerides. Medication use assessed incorporated statins, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers. The poverty-income ratio was calculated as annual household incomes divided by the

family's assigned poverty threshold. Smoking and drinking were defined as having smoked >100 cigarettes and consumed >12 drinks throughout their lifetime, respectively.

Statistical Analysis

Statistical analysis was performed in accordance with the analytic guideline that advocates appropriate weighting to obtain nationally representative estimates. Comparisons were made among total PDI tertiles (T1, lowest tertile; T2, medium tertile; T3, highest tertile) via the one-way analysis of variance or chi-squared test, as appropriate. The Kaplan–Meier survival curves were plotted to estimate the cumulative survival rate, which was then compared among different groups with the Log rank test. Following the assessment of the proportional hazard assumption using the Schoenfeld residual method, we examined the associations between total PDI, hPDI or uPDI with all-cause or CVD mortality using the Cox proportional hazards regression models, with results reported as hazard ratios (HRs) and 95% confidence intervals (95% CI). Potential non-linear associations between PDI indices and all-cause or CVD mortality were identified using the restricted cubic spline curves. In addition to the crude analysis without adjustments, two additional models adjusting for confounding factors were also generated. Model 1 was adjusted for participant's age, sex, race, marital status, education level, and poverty-income ratio. Model 2 was further adjusted for body mass index, physical activity, smoking, drinking, hypertension, diabetes, glycated hemoglobin, total cholesterol, triglycerides, total energy intake, use of statins and angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, and eGFR and uACR. Subgroup analyses were also conducted stratified by participant's age, sex, diabetes status, eGFR, and uACR. We conducted two sensitivity analyses: 1) in the first sensitivity analysis, participants who had deceased within 24 months of the follow-up were excluded to mitigate the risk of reverse causation; 2) in the second sensitivity analysis, we further adjusted for serum uric acid levels, dietary oxidative balance score,¹⁷ and dietary phosphorus to protein ratio.¹⁸ The statistical analyses were conducted using the R software (version 4.2.3), and a two-tailed P value < 0.05 was considered statistically significant.

Results

Baseline Participant Characteristics

Table 1 presents the characteristics of the 4098 participants (mean age 55.50 years, 40.38% men) and comparisons of participants stratified by total PDI tertiles. The mean eGFR and uACR for the entire cohort were 80.62 mL/min/1.73m² and 153.12 mg/g, respectively. In comparison to the lowest total PDI tertile, those within the highest total PDI tertile were significantly older, more likely to be women, with higher educational attainment, more likely to be physically inactive, with a lower smoking prevalence, and a lower triglyceride level.

Table 1 Comparison of Baseline Characteristics in Individuals with Chronic Kidney Disease Stratified by the Tertile of the Total Plant-Based Diet Index

	Total (n = 4098)	T1 (n = 1413)	T2 (n = 1419)	T3 (n = 1266)	P
Total PDI	52.48 ± 0.13	45.93 ± 0.11	52.08 ± 0.06	57.74 ± 0.11	< 0.001
hPDI	51.41 ± 0.15	47.81 ± 0.25	50.93 ± 0.21	54.56 ± 0.25	< 0.001
uPDI	48.03 ± 0.15	48.04 ± 0.21	47.71 ± 0.26	48.34 ± 0.30	0.29
Age, years	55.50 ± 0.41	52.80 ± 0.59	55.63 ± 0.69	57.36 ± 0.62	< 0.001
Sex (n, %)					0.003
Male	1808 (40.38)	686 (47.38)	620 (39.06)	502(36.46)	
Female	2290 (59.62)	727 (52.62)	799 (60.94)	764 (63.54)	

(Continued)

Table 1 (Continued).

	Total (n = 4098)	T1 (n = 1413)	T2 (n = 1419)	T3 (n = 1266)	P
Race/ethnicity (n, %)					0.07
Non-Hispanic White	1831 (67.64)	619 (64.03)	643 (68.05)	569 (69.94)	
Other	2267 (32.36)	794 (35.97)	776 (31.95)	697 (30.06)	
Marital status (n, %)					0.36
Non-single	2286 (61.06)	774 (58.57)	776 (61.75)	736 (62.24)	
Single	1812 (38.94)	639 (41.43)	643 (38.25)	530 (37.76)	
Education level (n, %)					0.02
< High school	663 (7.93)	262 (8.27)	213 (8.38)	188 (7.24)	
High school	1670 (38.64)	622 (41.91)	593 (39.53)	455 (35.33)	
> High school	1765 (53.43)	529 (49.82)	613 (52.09)	623 (57.44)	
Poverty-income ratio	2.82 ± 0.05	2.67 ± 0.07	2.79 ± 0.07	2.97 ± 0.08	0.01
Body mass index, kg/m²	30.18 ± 0.18	30.51 ± 0.31	30.34 ± 0.33	29.78 ± 0.25	0.11
Physical activity (n, %)					0.005
None	2406 (54.76)	770 (48.58)	862 (58.27)	774 (55.92)	
Moderate	970 (25.00)	370 (27.92)	302 (21.51)	298 (26.24)	
Vigorous	722 (20.24)	273 (23.50)	255 (20.22)	194 (17.84)	
Smoking (n, %)	1939 (46.61)	734 (53.36)	670 (46.71)	535 (41.49)	< 0.001
Drinking (n, %)	2449 (66.91)	843 (65.00)	840 (66.64)	766 (68.60)	0.44
Hypertension (n, %)	2669 (59.78)	911 (58.18)	930 (60.98)	828 (59.79)	0.57
Diabetes (n, %)	1399 (29.05)	483 (30.42)	483 (29.25)	433 (27.84)	0.60
Statin use (n, %)	938 (22.69)	272 (21.80)	348 (23.35)	318 (22.69)	0.79
ACEI/ARB use (n, %)	80 (2.06)	26 (1.65)	24 (2.19)	30 (2.25)	0.74
HbA1C, %	6.06 ± 0.03	6.10 ± 0.06	6.07 ± 0.05	6.03 ± 0.05	0.66
Triglyceride, mmol/L	1.96 ± 0.04	2.12 ± 0.08	1.94 ± 0.06	1.87 ± 0.05	0.02
TC, mmol/L	5.20 ± 0.03	5.24 ± 0.05	5.17 ± 0.05	5.20 ± 0.05	0.53
Total energy intake, kcal/day	1940.11 ± 18.08	2041.02 ± 32.31	1949.44 ± 30.84	1855.97 ± 28.29	< 0.001
eGFR, mL/min/1.73m²	80.62 ± 0.65	84.10 ± 1.01	80.41 ± 0.98	78.24 ± 1.05	< 0.001
uACR, mg/g	153.12 ± 9.73	174.69 ± 21.62	153.52 ± 16.46	136.68 ± 13.62	0.34

Note: P value were derived from the comparisons among the three groups.

Abbreviations: ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; eGFR, estimated glomerular filtration rate; hPDI, healthy plant-based diet index; PDI, plant-based diet index; TC, total cholesterol; uACR, urinary albumin-to-creatinine ratio; uPDI, unhealthy plant-based diet index.

Kaplan–Meier Survival Analysis

During a median follow-up period of 102 (interquartile range 58–154) months, 1191 (19.52%) participants deceased, of which 397 were determined to be died of CVD causes. Specifically, the mortality rates were 23.40%, 20.31%, and

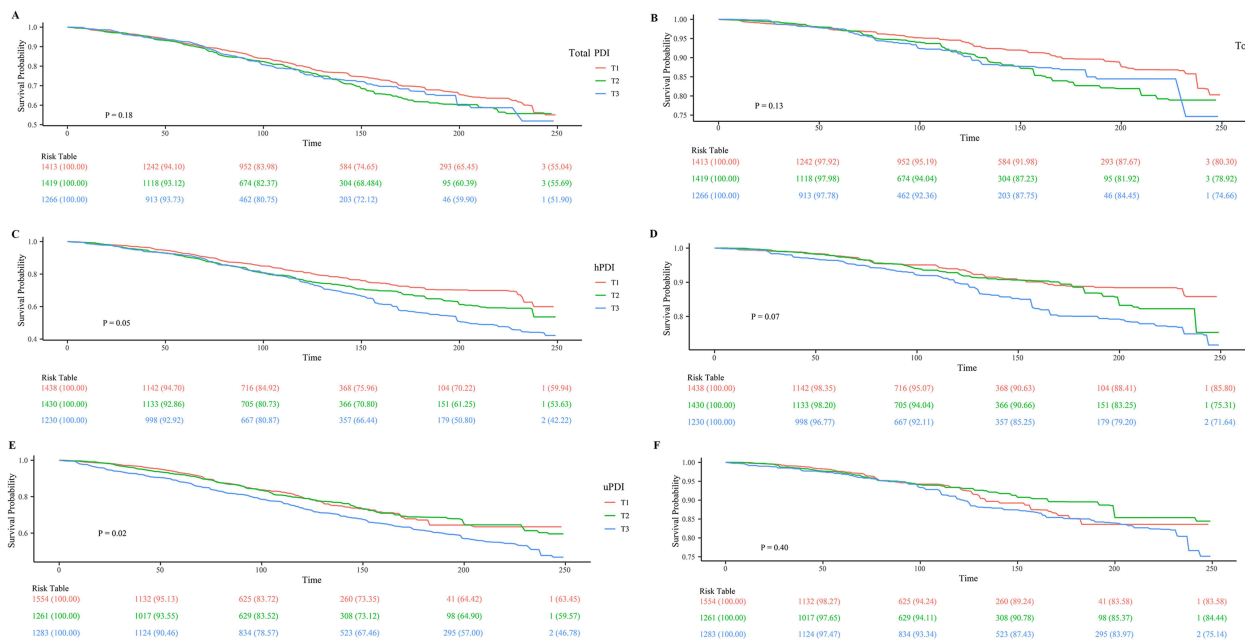


Figure 2 Kaplan–Meier survival curves for the associations between total plant-based dietary index (PDI, **A** and **B**), healthy PDI (hPDI, **C** and **D**), unhealthy PDI (uPDI, **E** and **F**) and all-cause mortality or cardiovascular mortality in US adults with chronic kidney disease.

15.85% for the total PDI T1, T2 and T3 groups, respectively. Of these, 161 (6.92%), 135 (7.16%) and 101 (5.78%) were attributed to CVD mortality. Kaplan–Meier survival curves (Figure 2) based on the total PDI, hPDI and uPDI tertiles showed significant differences in all-cause mortality rate among the three uPDI subgroups. All-cause mortality in the T1, T2 and T3 groups stratified by total PDI and hPDI, and CVD mortality stratified by total PDI, hPDI and uPDI tertiles were not statistically significant.

Associations Between Total PDI, hPDI, uPDI and All-Cause or CVD Mortality

As shown in Tables 2 and 3, total PDI and hPDI, as either continuous or categorical variables, were not associated with all-cause or CVD mortality. In the fully adjusted Model 2, an one-unit increase in uPDI was associated with a 2% increased risk of all-cause mortality. Similarly, the HRs and 95% CIs for the uPDI T2 and T3 groups were 0.98

Table 2 Associations Between Total PDI, hPDI, uPDI and All-Cause Mortality in US Adults with Chronic Kidney Disease

	Crude Analysis		Model 1		Model 2	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Total PDI (continuous)	0.99 (0.98–1.01)	0.24	1.00 (0.98–1.01)	0.66	1.00 (0.99–1.01)	0.93
Total PDI tertile						
T1	1 (Reference)	/	1 (Reference)	/	1 (Reference)	/
T2	0.95 (0.79–1.15)	0.60	0.98 (0.81–1.20)	0.87	1.01 (0.83–1.22)	0.95
T3	0.88 (0.72–1.07)	0.19	0.93 (0.77–1.14)	0.50	0.97 (0.80–1.17)	0.73
P for trend	0.18		0.50		0.73	
hPDI (continuous)	0.99 (0.98–1.01)	0.29	0.99 (0.98–1.01)	0.28	0.99 (0.98–1.01)	0.18

(Continued)

Table 2 (Continued).

	Crude Analysis		Model 1		Model 2	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
hPDI tertile						
T1	1 (Reference)	/	1 (Reference)	/	1 (Reference)	/
T2	0.91 (0.75–1.11)	0.37	0.91 (0.75–1.10)	0.32	0.93 (0.76–1.14)	0.50
T3	0.94 (0.74–1.18)	0.57	0.94 (0.74–1.19)	0.59	0.91 (0.71–1.17)	0.47
P for trend	0.57		0.59		0.48	
uPDI (continuous)	1.03 (1.01–1.04)	<0.001	1.02 (1.01–1.04)	0.005	1.02 (1.01–1.04)	0.002
uPDI tertile						
T1	1 (Reference)	/	1 (Reference)	/	1 (Reference)	/
T2	1.00 (0.81–1.23)	0.98	0.97 (0.79–1.20)	0.79	0.98 (0.79–1.20)	0.81
T3	1.57 (1.25–1.98)	<0.001	1.44 (1.13–1.83)	0.003	1.45 (1.15–1.83)	0.002
P for trend	<0.001		0.007		0.003	

Notes: Model 1 was adjusted for participant's age, sex, race, marital status, poverty-income ratio, and education level. Model 2 was adjusted for covariates in Model 2, plus body mass index, physical activity, smoking, drinking, comorbidity of diabetes, hypertension, glycosylated hemoglobin, total cholesterol, triglycerides, and use of statins and angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, total energy intake, estimated glomerular filtration rate and urinary albumin-to-creatinine ratio.

Abbreviations: CI, confidence interval; HR, hazard ratio.

Table 3 Associations Between Total PDI, hPDI, uPDI and Cardiovascular Mortality in US Adults with Chronic Kidney Disease

	Crude Analysis		Model 1		Model 2	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Total PDI (continuous)	1.01 (0.98–1.04)	0.76	1.01 (0.98–1.04)	0.49	1.01 (0.98–1.04)	0.43
Total PDI tertile						
T1	1 (Reference)	/	1 (Reference)	/	1 (Reference)	/
T2	1.13 (0.79–1.60)	0.51	1.17 (0.82–1.68)	0.39	1.22 (0.86–1.73)	0.27
T3	1.11 (0.70–1.78)	0.65	1.20 (0.75–1.92)	0.44	1.23 (0.78–1.95)	0.37
P for trend	0.65		0.44		0.37	
hPDI (continuous)	1.00 (0.98–1.02)	0.96	1.00 (0.98–1.02)	0.91	1.00 (0.98–1.02)	0.91
hPDI tertile						
T1	1 (Reference)	/	1 (Reference)	/	1 (Reference)	/
T2	0.77 (0.54–1.09)	0.14	0.77 (0.55–1.08)	0.13	0.80 (0.56–1.15)	0.23
T3	1.05 (0.73–1.51)	0.80	1.08 (0.74–1.57)	0.70	1.06 (0.72–1.57)	0.77
P for trend	0.796		0.71		0.76	

(Continued)

Table 3 (Continued).

	Crude Analysis		Model 1		Model 2	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
uPDI (continuous)	1.02 (1.00–1.05)	0.11	1.02 (0.99–1.05)	0.30	1.01 (0.98–1.04)	0.43
uPDI tertile						
T1	1 (Reference)	/	1 (Reference)	/	1 (Reference)	/
T2	0.85 (0.60–1.21)	0.36	0.82 (0.57–1.17)	0.27	0.81 (0.57–1.16)	0.25
T3	1.37 (0.86–2.19)	0.18	1.23 (0.75–2.01)	0.41	1.19 (0.72–1.97)	0.50
P for trend	0.27		0.52		0.59	

Notes: Model 1 was adjusted for participant's age, sex, race, marital status, poverty-income ratio, and education level. Model 2 was adjusted for covariates in Model 1, plus body mass index, physical activity, smoking, drinking, comorbidity of diabetes, hypertension, glycosylated hemoglobin, total cholesterol, triglycerides, and use of statins and angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, total energy intake, estimated glomerular filtration rate and urinary albumin-to-creatinine ratio.

Abbreviations: CI, confidence interval; HR, hazard ratio.

(0.79–1.20) and 1.45 (1.15–1.83), respectively (P for trend = 0.003), with the T1 group serving as the reference group. Correspondingly, the restricted cubic spline curves (Figure 3) also indicated a positive and linear relationship between uPDI and all-cause mortality.

Subgroup Analysis

Subgroup analysis (Figure 4) showed that the associations between uPDI and all-cause mortality were more pronounced in women and non-diabetics than in men and diabetics. The relationship between uPDI and all-cause mortality remained consistent across the spectrum of participant's age, eGFR, and uACR.

Sensitivity Analysis

Both sensitivity analysis (Supplementary Tables 1–3) demonstrated that a higher uPDI was associated with increased all-cause mortality.

Discussion

This study demonstrated, for the first time, that a higher intake of unhealthy PBD is related to an increased risk of all-cause mortality, but not incident cardiovascular mortality, in a nationally representative sample of US community-dwelling adults with predominantly early-stage CKD, especially in women and in those without diabetes. The hPDI and total PDI did not appear to have a significant relation to mortality risk in this population. In addition, the sensitivity analysis indicated that the study results were robust and are unlikely to be affected by reverse causation. Taken together, these data indicated that intakes of unhealthy PBD seemed to outweigh adherence to healthy PBD in influencing mortality risk in US adults with early stage CKD.

The PBD has been previously shown to confer a range of potential health benefits, including weight management, blood pressure and glucose regulation, and a reduced risk of CVD.¹⁹ Furthermore, earlier studies have also linked PBD with decreased risk of specific chronic conditions, including metabolic syndrome, liver cirrhosis, and colorectal cancer.^{20–22} A recent meta-analysis of 14 studies further demonstrated that the pooled relative risks for all-cause, CVD, and cancer mortality were 0.85, 0.85 and 0.91, respectively, for a higher hPDI, and 1.18, 1.19 and 1.10, respectively, for a higher uPDI,²³ underscoring the effects of PBD in mortality reduction. However, it should be noted that not all PBD are conducive to optimal health, and it is practically difficult to maintain a vegan diet for the majority of the US population. To overcome this limitation, Satija et al conceptualized a hierarchical dietary model consisting of total

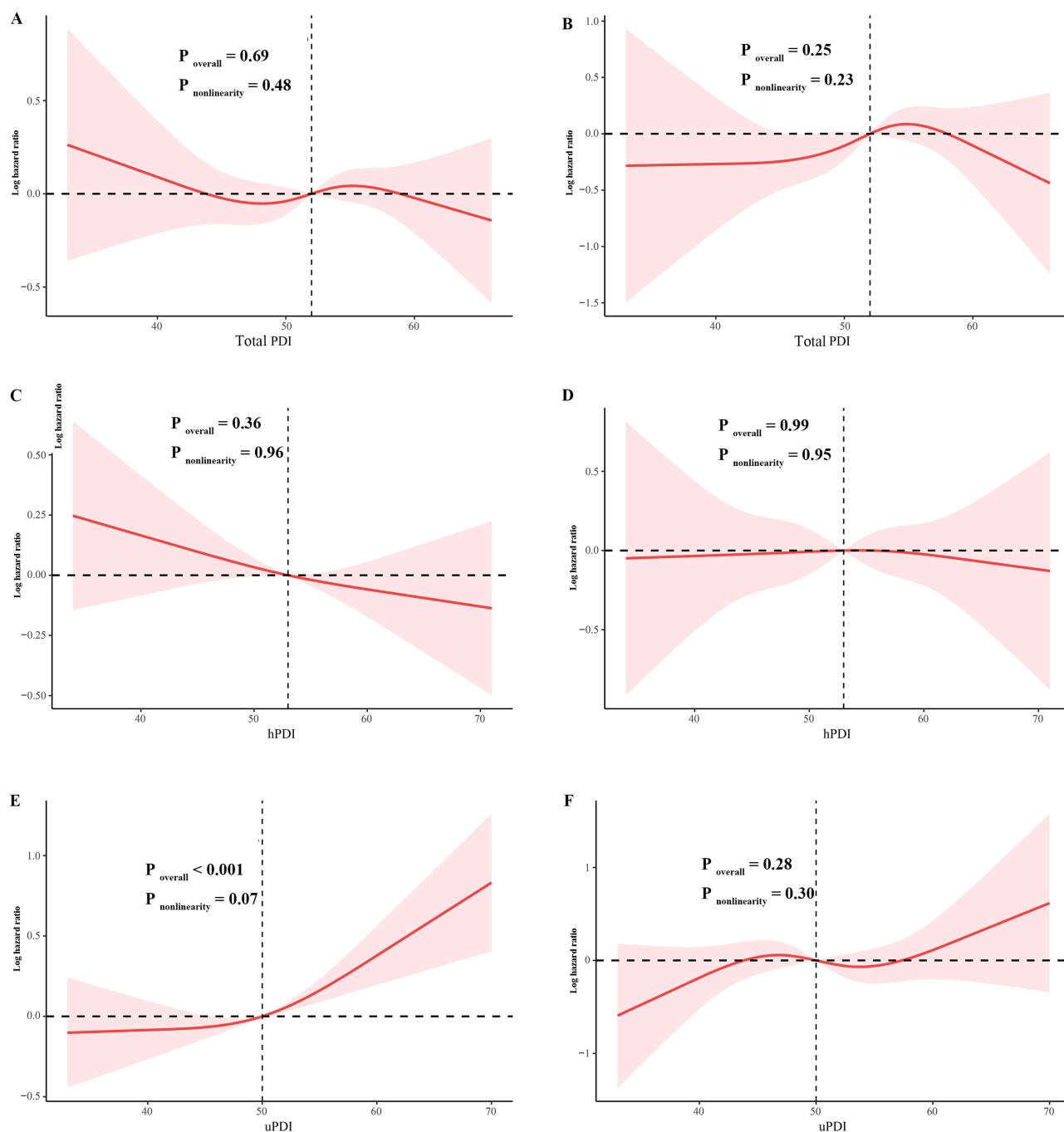


Figure 3 Restricted cubic spline curves for the associations between total plant-based dietary index (PDI, **A** and **B**), healthy PDI (hPDI, **C** and **D**), unhealthy PDI (uPDI, **E** and **F**) and all-cause mortality or cardiovascular mortality in US adults with chronic kidney disease.

PDI, hPDI, and uPDI, which enabled the understanding of how gradually increasing plant foods, while decreasing animal foods, affects health.²⁴

The applicability of findings from studies of PBD in the general population to CKD patients has not yet been established, as CKD patients often exhibit unique dietary patterns and nutrient needs. Cross-sectional studies, such as the Tehran Lipid and Glucose Study and the Multiethnic Study of Atherosclerosis, have all reported a decreased incidence of CKD with a PBD.^{25,26} Mechanistically, the beneficial effects of a plant-rich diet on kidney health may be related to its effect on inhibiting micro-inflammation, promoting intestinal mobility, modulating gut microbiota, reducing uremic toxin production, and providing nutrients of vitamins, minerals, fibers and phytochemicals.²⁷

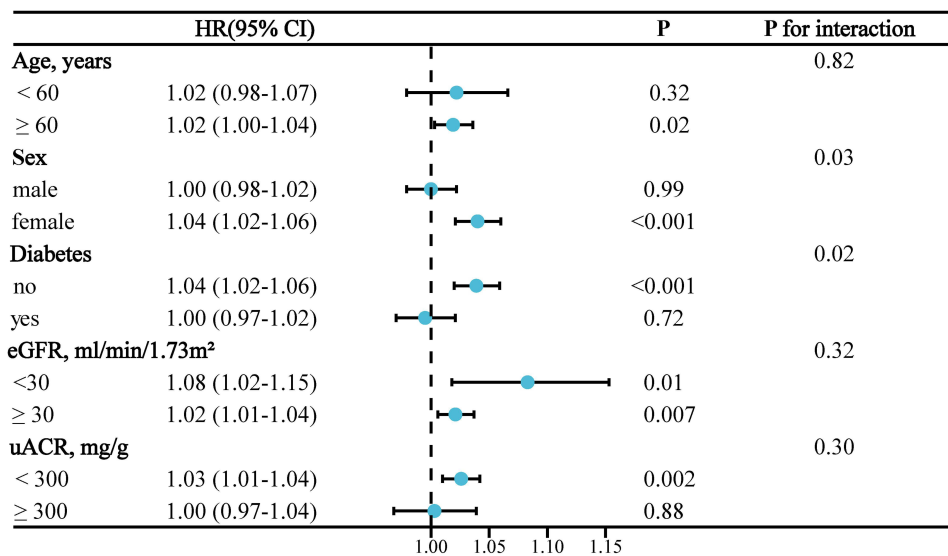


Figure 4 Subgroup analyses of the association between unhealthy plant-based dietary index and all-cause mortality in US adults with chronic kidney disease. **Abbreviations:** CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; uACR, urinary albumin-to-creatinine ratio.

To the best of our knowledge, the results of our study differ from those of several previous studies on the associations of PBD indices with mortality risk specifically in CKD patients.^{11,12} In a report of 2539 CKD participants from the Chronic Renal Insufficiency Cohort Study, Amir et al found that the highest tertile of total PDI and hPDI exhibited a 26% and 21% reduced risk of all-cause mortality.¹² Analogous findings have also been observed in an analysis of 4807 CKD patients from the UK Biobank.¹¹ It is noteworthy that both studies exclusively focused on all-cause mortality, without investigating CVD mortality. This study bridged this knowledge gap by demonstrating that total PDI, hPDI, and uPDI were all unrelated to CVD mortality. While the current study, along with the two aforementioned studies, has all observed a deleterious effect of uPDI on mortality risk in CKD patients, this study diverges from others in its finding of no associations between total PDI, hPDI, and mortality risk. The potential explanation for this discrepancy may be attributed to variations in participant characteristics, such as the severity of CKD. Specifically, the mean eGFR of the included patients in this study is 80.62 mL/min/1.73m², which is significantly higher than that reported by Amir et al (43.4 mL/min/1.73m²) and by Thompson et al (59.5 mL/min/1.73m²).^{11,12} More importantly, this study excluded participants with known diagnoses of CVD, whereas the other two studies did not. Consequently, the subjects in our study may represent a highly selected population with a more favorable cardiometabolic profile. This finding underscored that the consumption of unhealthy PBDs may exert a more substantial influence on the mortality risk in early-stage CKD without CVD than the adherence to a healthy PBD.

Our study showed that an unhealthy PBD has the potential to markedly elevate all-cause mortality risk, even among individuals with only mild CKD. An unhealthy PBD is typically high in refined and ultra-processed foods and less in healthy plants and animal-sourced foods. Its association with all-cause mortality in CKD patients may be attributable to its low micronutrient content, high caloric content, hyperorexia associated with high fat intake, and unfavorable effects of added sugars.²⁸

Subgroup analysis indicated that the association between uPDI and all-cause mortality in CKD patients were sex-specific that was only observed in women and non-diabetics. Similarly, Wang et al reported a stronger reverse relationship between hPDI and the aging process in females.²⁹ The potential explanation for these observed discrepancies include the differential influence of estrogen, which has been demonstrated to enhance fat transportation in women and promote serum triglyceride levels.³⁰ The consumption of sugar-sweetened beverages, a component of the uPDI, has been demonstrated to increase the risk of metabolic syndrome in women, but not in men,³¹ possibly due to the fact that triglycerides and lipoproteins in women appear to be more sensitive to changes in dietary carbohydrates or fats than in men.³² The attenuated effect of uPDI on all-cause mortality in individuals with diabetes may reflect post-diagnosis dietary improvements, as patients often adopt healthier eating habits after being diagnosed. Nevertheless, these findings underscore the importance of avoiding unhealthy plant-based diets, particularly in those without diabetes, to mitigate mortality risk.

Notable strengths of this study include large sample size and national representation, thus facilitating external generalization of study results to US CKD patients with similar characteristics. We contend that our analysis has broadened previous research by incorporating predominantly those with only mild renal impairment. Moreover, we have also adjusted for dietary oxidative balance score, dietary phosphorus intake, and uric acid, as previous studies have demonstrated that these factors could also influence outcomes in CKD.^{33,34} There are, however, several limitations inherent in this study that should be pointed out. First, the dietary information was collected through self-report, which may introduce recall bias. Second, dietary patterns were collected using the 24-hour recall method, which may not always be a precise reflection of habitual dietary patterns or potential dietary changes over time. Third, PBD indices negative scored all animal-based foods, whereas animal-sourced proteins are generally preferred over plant-sourced proteins for protein bioavailability and malnutrition prevention.³⁵ Finally, the observational nature of the study may be susceptible to residual confounding that may deviate results.

In conclusion, this population-based study showed that higher adherence to an unhealthy PBD is associated with an augmented risk of all-cause mortality in US adults with predominantly early stages of CKD, particularly in women and non-diabetics. Our results underscore the critical importance of avoiding unhealthy PBD in the management of early stages of CKD. In the future, further interventional studies are warranted to ascertain whether reducing unhealthy PBD may indeed improve outcomes in patients with early stages of CKD.

Data Sharing Statement

The dataset used for the current analysis are publicly available from the National Health and Nutrition Examination Survey at <https://www.cdc.gov/nchs/nhanes/>.

Ethical Approval and Consent to Participate

The NHANES has been approved by the NCHS Research Ethics Review Board. Informed consent was obtained from all participants.

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Disclosure

All the authors have declared no competing interests.

References

- Hu EA, Coresh J, Anderson CAM, et al. Adherence to healthy dietary patterns and risk of CKD progression and all-cause mortality: findings from the CRIC (Chronic Renal Insufficiency Cohort) Study. *Am J Kidney Dis.* 2021;77(2):235–244. doi:10.1053/j.ajkd.2020.04.019
- Ikizler TA, Burrowes JD, Byham-Gray LD, et al. KDOQI clinical practice guideline for nutrition in CKD: 2020 update. *Am J Kidney Dis.* 2020;76(3 Suppl 1):S1–S107. doi:10.1053/j.ajkd.2020.05.006
- Muscus AA, Wang DD, Janiszewski M, et al. Health and environmental impacts of plant-rich dietary patterns: a US prospective cohort study. *Lancet Planet Health.* 2022;6(11):e892–e900. doi:10.1016/S2542-5196(22)00243-1
- Tomé-Carneiro J, Visioli F. Plant-based diets reduce blood pressure: a systematic review of recent evidence. *Curr Hypertens Rep.* 2023;25(7):127–150. doi:10.1007/s11906-023-01243-7
- Sullivan VK, Kim H, Caulfield LE, Steffen LM, Selvin E, Rebholz CM. Plant-Based Dietary Patterns and Incident Diabetes in the Atherosclerosis Risk in Communities (ARIC) Study. *Diabetes Care.* 2024;47(5):803–809. doi:10.2337/dc23-2013
- Kim H, Caulfield LE, Garcia-Larsen V, Steffen LM, Coresh J, Rebholz CM. Plant-based diets are associated with a lower risk of incident cardiovascular disease, cardiovascular disease mortality, and all-cause mortality in a general population of middle-aged adults. *J Am Heart Assoc.* 2019;8(16):e012865. doi:10.1161/JAHA.119.012865
- Perraud E, Wang J, Salomé M, Huneau JF, Lapidus N, Mariotti F. Plant and animal protein intakes largely explain the nutritional quality and health value of diets higher in plants: a path analysis in french adults. *Front Nutr.* 2022;9:924526. doi:10.3389/fnut.2022.924526
- Moloudpour B, Jam SA, Darbandi M, et al. Association between plant-based diet and kidney function in adults. *J Ren Nutr.* 2024;34(2):125–132. doi:10.1053/j.jrn.2023.09.002
- Zarantonello D, Brunori G. The role of plant-based diets in preventing and mitigating chronic kidney disease: more light than shadows. *J Clin Med.* 2023;12(19):6137. doi:10.3390/jcm12196137
- Carrero JJ, González-Ortiz A, Avesani CM, et al. Plant-based diets to manage the risks and complications of chronic kidney disease. *Nat Rev Nephrol.* 2020;16(9):525–542. doi:10.1038/s41581-020-0297-2

11. Thompson AS, Gaggi M, Bondonno NP, et al. Adherence to a healthful plant-based diet and risk of mortality among individuals with chronic kidney disease: a prospective cohort study. *Clin Nutr.* 2024;43(10):2448–2457. doi:10.1016/j.clnu.2024.09.021
12. Amir S, Kim H, Hu EA, et al. Adherence to plant-based diets and risk of CKD progression and all-cause mortality: findings from the Chronic Renal Insufficiency Cohort (CRIC) Study. *Am J Kidney Dis.* 2024;83(5):624–635. doi:10.1053/j.ajkd.2023.09.020
13. Ahluwalia N, Dwyer J, Terry A, Moshfegh A, Johnson C. Update on NHANES dietary data: focus on collection, release, analytical considerations, and uses to inform public policy. *Adv Nutr.* 2016;7(1):121–134. doi:10.3945/an.115.009258
14. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med.* 2009;150(9):604–612. doi:10.7326/0003-4819-150-9-200905050-00006
15. Bigman G, Rusu ME, Kleckner AS, et al. Plant-based diets and their associations with physical performance in the Baltimore longitudinal study of aging. *Nutrients.* 2024;16(23):4249. doi:10.3390/nu16234249
16. Kong X, Wang W. Association between Life's Essential 8 and all-cause or cardiovascular-specific mortality in patients with rheumatoid arthritis. *Clin Exp Rheumatol.* 2024;42(7):1459–1466. doi:10.55563/clinexprheumatol/ppsp71
17. Lan Y, Tang H, Lin Z, Huang C, Chen L. Association of oxidative balance score with all-cause mortality among individuals with chronic kidney disease: a cohort study. *J Health Popul Nutr.* 2024;43(1):160. doi:10.1186/s41043-024-00657-6
18. Murtaugh MA, Filipowicz R, Baird BC, Wei G, Greene T, Beddhu S. Dietary phosphorus intake and mortality in moderate chronic kidney disease: NHANES III. *Nephrol Dial Transplant.* 2012;27(3):990–996. doi:10.1093/ndt/gfr367
19. Kim H, Rebholz CM. Plant-based diets for kidney disease prevention and treatment. *Curr Opin Nephrol Hypertens.* 2024;33(6):593–602. doi:10.1097/MNH.0000000000001015
20. Wiśniewska K, Okreglicka KM, Nitsch-Osusch A, Oczkowski M. Plant-based diets and metabolic syndrome components: the questions that still need to be answered—a narrative review. *Nutrients.* 2024;16(1):165. doi:10.3390/nu16010165
21. Tabar MS, Fotros D, Hekmatdoost A, et al. The association between plant-based diet indices and risk of mortality in patients with cirrhosis: a cohort study. *BMC Gastroenterol.* 2024;24(1):395. doi:10.1186/s12876-024-03475-6
22. Yarmand S, Rashidkhan B, Alimohammadi A, et al. A healthful plant-based diet can reduce the risk of developing colorectal cancer: case-control study. *J Health Popul Nutr.* 2024;43(1):111. doi:10.1186/s41043-024-00605-4
23. Tan J, Zhang S, Jiang Y, Li J, Yang C. Plant-based diet and risk of all-cause mortality: a systematic review and meta-analysis. *Front Nutr.* 2024;11:1481363. doi:10.3389/fnut.2024.1481363
24. Satija A, Bhupathiraju SN, Rimm EB, et al. Plant-based dietary patterns and incidence of type 2 diabetes in US men and women: results from three prospective cohort studies. *PLoS Med.* 2016;13(6):e1002039. doi:10.1371/journal.pmed.1002039
25. Thompson AS, Tresserra-Rimbau A, Jennings A, et al. Adherence to a Healthful Plant-Based Diet and Risk of Chronic Kidney Disease Among Individuals with Diabetes. *J Am Nutr Assoc.* 2025;44(3):212–222. doi:10.1080/27697061.2024.2415917
26. Kim H, Caulfield LE, Garcia-Larsen V, et al. Plant-based diets and incident CKD and kidney function. *Clin J Am Soc Nephrol.* 2019;14(5):682–691. doi:10.2215/CJN.12391018
27. Storz MA. What makes a plant-based diet? A review of current concepts and proposal for a standardized plant-based dietary intervention checklist. *Eur J Clin Nutr.* 2022;76(6):789–800. doi:10.1038/s41430-021-01023-z
28. Zhuang P, Wang F, Yao J, et al. Unhealthy plant-based diet is associated with a higher cardiovascular disease risk in patients with prediabetes and diabetes: a large-scale population-based study. *BMC Med.* 2024;22(1):485. doi:10.1186/s12916-024-03683-7
29. Wang J, Yang C, Dong X, et al. Healthful plant-based diets are negatively associated with the rate of biological aging: a national study based on US adults. *Nutr Res.* 2024;132:112–124. doi:10.1016/j.nutres.2024.10.005
30. Weng J, Mao Y, Xie Q, Sun K, Kong X. Gender differences in the association between healthy eating index-2015 and hypertension in the US population: evidence from NHANES 1999–2018. *BMC Public Health.* 2024;24(1):330. doi:10.1186/s12889-023-17625-0
31. Kuo CT, Chen DR, Chan CC, Yeh YP, Chen HH. Sex differences in the association between sugar-sweetened beverages consumption and metabolic risks among the working-age population in Taiwan. *Public Health Nutr.* 2023;26(3):653–660. doi:10.1017/S1368980022001549
32. Sanchez BN, Volek JS, Kraemer WJ, Saenz C, Maresh CM. Sex differences in energy metabolism: a female-oriented discussion. *Sports Med.* 2024;54(8):2033–2057. doi:10.1007/s40279-024-02063-8
33. Yin Y, Zhao C, Niu Y, Qi J, Zhang Y, Lu B. Associations between oxidative balance score and chronic kidney disease events in US adults: a population-based study. *Sci Rep.* 2024;14(1):13743. doi:10.1038/s41598-024-64147-9
34. Chang AR, Lazo M, Appel LJ, Gutiérrez OM, Grams ME. High dietary phosphorus intake is associated with all-cause mortality: results from NHANES III. *Am J Clin Nutr.* 2014;99(2):320–327. doi:10.3945/ajcn.113.073148
35. Meroño T, Zamora-Ros R, Hidalgo-Liberona N, et al. Animal protein intake is inversely associated with mortality in older adults: the INCHIANTI Study. *J Gerontol A Biol Sci Med Sci.* 2022;77(9):1866–1872. doi:10.1093/gerona/glab334