DASH Diet and Risk of Subsequent Kidney Disease

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ABSTRACT

Background: There are established guidelines for recommended dietary intake for hypertension treatment and cardiovascular disease prevention. Evidence is lacking for effective dietary patterns for kidney disease prevention.

Study Design: Prospective cohort study

Setting & Participants: ARIC study participants with baseline estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m^2 (N=14,882)

Predictor: The Dietary Approaches to Stop Hypertension (DASH) diet score was calculated based on self-reported dietary intake of red and processed meat, sweetened beverages, sodium, fruits, vegetables, whole grains, nuts and legumes, and low-fat dairy products, averaged over two visits.

Outcomes: Cases were ascertained based on development of eGFR <60 mL/min/1.73 m^2 accompanied by ≥25% eGFR decline from baseline, an ICD-9/10 code for a kidney disease-related hospitalization or death, or end-stage renal disease from baseline through 2012.

Results: A total of 3,720 participants developed kidney disease during a median follow-up of 23 years. Participants with a DASH diet score in the lowest tertile were 16% more likely to develop kidney disease than those with the highest score tertile (HR: 1.16, 95% CI: 1.07, 1.26; p-value for trend <0.001), after adjusting for socio-demographics, smoking status, physical activity, total caloric intake, baseline eGFR, overweight/obese status, diabetes status, hypertension status, systolic blood pressure, and anti-hypertensive medication use. Of the individual components of the DASH diet score, high intake of red and processed meat was adversely associated with kidney disease and high intake of nuts, legumes, and low-fat dairy products was associated with reduced risk of kidney disease.

Limitations: Potential measurement error due to self-reported dietary intake and lack of data on albuminuria

Conclusions: Consuming a DASH-style diet was associated with lower risk for kidney disease, independent of demographic characteristics, established kidney risk factors, and baseline kidney function. Healthful dietary patterns, such as the DASH diet, may be beneficial for kidney disease prevention.

Key words: chronic kidney disease; diet; dietary protein; health promotion; incidence

INTRODUCTION

The Dietary Approaches to Stop Hypertension (DASH) diet, a dietary pattern that is high in fruits, vegetables, and low-fat dairy products, substantially lowers blood pressure.[1] The addition of sodium reduction to the DASH diet further lowers blood pressure and reduces the risk of hypertension, type 2 diabetes, cardiovascular disease, stroke, and mortality.[1-6] The DASH diet has been recommended by multiple clinical guidelines for health promotion and disease prevention.[7-11]

While treatment of traditional cardiovascular risk factors such as hypertension and diabetes is the primary approach to prevent kidney disease, evidence for dietary approaches to prevent kidney disease are lacking. Current clinical guidelines focus primarily on dietary restriction of protein and sodium to prevent kidney disease progression, but the evidence supporting this suggestion is weak (graded as level 2B).[12] A comprehensive approach, such as that prescribed in the DASH diet, may be more meaningful given that nutrients likely have additive or synergistic effects.[13] Further, dietary patterns rather than nutrient restriction may be easier to implement given the success of the DASH diet for the prevention and treatment of other chronic conditions.[14]

Previous research has demonstrated a significant association between the DASH diet and kidney function decline in older Caucasian women.[15,16] The objective of this study was to assess the longitudinal relationship between consuming a DASH-style diet with sodium reduction and subsequent risk of kidney disease in a more diverse general population sample, including African-American and Caucasian men and women. Elucidating this relationship could inform the use of dietary modification as a preventative strategy for kidney disease.

METHODS

Study Population & Design

We conducted a prospective analysis of the Atherosclerosis Risk in Communities (ARIC) study.[17] The ARIC study is a community-based observational study of 15,792 middle-aged (45-64 years), predominantly African-American and Caucasian, men and women. Study participants were enrolled in 1987-1989 from four U.S. communities: Forsyth County, North Carolina; Jackson, Mississippi; suburbs of Minneapolis, Minnesota; and Washington County, Maryland. Follow-up study visits occurred in 1990-1992 (study visit 2), 1993-1995 (study visit 3), 1996-1998 (study visit 4), and 2011-2013 (study visit 5). The Institutional Review Board at each site approved the study protocol and study participants provided informed consent at each study visit (IRB #H.34.99.07.02.A1). After excluding participants with missing dietary intake data (n=18), implausibly low caloric intake (<600 kcal for men; <500 kcal for women; n=149), and implausibly high caloric intake (>4,200 kcal for men; >3,600 kcal for women; n=152), those with baseline estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 or end-stage renal disease identified by linkage to the U.S. Renal Data System registry (n=356), those who were neither African-American nor Caucasian (n=48), and those with missing covariates (n=187), our analytic sample size was 14,882 (**Figure S1**).[18]

Measurement of Dietary Intake

Usual dietary intake was assessed at study visit 1 (baseline, 1987-1989) and visit 3 (1993-1995) using a semi-quantitative 66-item food frequency questionnaire, modified from the Willett questionnaire.[19-21] The questionnaire was administered in person by a trained interviewer with visual representations of portions (glasses and measuring cups of different sizes). Participants reported how often, on average, they consumed each food item of a particular portion size in the preceding year. Nutrient intake was calculated by multiplying self-reported frequency of consumption and portion size by the nutritional content of each food item from USDA data sources. The reliability of these diet data was previously assessed in a randomly selected subset of participants from all four sites who repeated the food frequency questionnaire at a follow-up visit (study visit 2, 1990-1992; n=419).[19] For the analysis, we incorporated the two measurements of dietary intake (baseline and visit 3) by using the cumulative average diet, which improves estimation of usual dietary intake relative to a single measurement.[22] That is, for those who developed kidney disease or were censored between baseline and visit 3, the baseline dietary intake data are used. Otherwise, for those who developed kidney disease or were censored after visit 3, the mean of the values from baseline and visit 3 is used.

Definition of the DASH Diet Score

We assessed the degree to which study participants followed a DASH-style diet with reduced sodium using two previously developed indices.[4,16,23,24] Study participants were not advised to follow a DASH diet, nor had the DASH diet results been published by the time of dietary assessment, and study participants did not receive dietary counseling. The primary analysis used a score based primarily on food items: low intake of 1) red and processed meat, 2) sweetened beverages, and 3) sodium; and high intake of 4) fruits, 5) vegetables, 6) whole grains, 7) nuts and legumes, and 8) low-fat dairy (**Table S1**).[4] Each component was scored from 1 to 5 based on ranked distribution in quintiles, which is ideally suited to this analysis since the food frequency questionnaire is designed to rank individuals on dietary intake rather than quantify absolute nutrient intake levels.

In sensitivity analyses, we used an alternative score based on nine nutrients: low intake of 1) saturated fat, 2) total fat, 3) cholesterol, and 4) sodium; and high intake of 5) protein, 6) fiber,

7) magnesium, 8) calcium, and 9) potassium (**Table S2**).[16,23,24] For the purposes of our study, the food item-based score and the nutrient-based score were both analyzed as tertiles. A higher score signifies that a participant's dietary pattern more closely resembles a DASH-style diet. Mean levels of DASH diet scores and individual components of the DASH diet scores for the overall study population and by case status are presented in **Table S3**.

Ascertainment of Kidney Disease

Blood levels of creatinine were measured using the modified kinetic Jaffe method, standardized to the National Institute of Standards and Technology standard, and calibrated to account for laboratory drift.[25,26] Kidney function was assessed using the 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation for eGFR based on creatinine.[27] Measurement of urine albumin to creatinine ratio was not available in this study and thus was not included in the composite outcome variable.

Kidney disease cases were ascertained by meeting at least one of the following criteria: 1) estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 accompanied by ≥25% eGFR decline at any follow-up study visit relative to baseline; 2) kidney disease-related hospitalization or death based on International Classification of Disease (ICD)-9/10 codes identified through active surveillance and linkage to the National Death Index; or 3) treated end-stage renal disease (dialysis or transplant) identified by linkage to the U.S. Renal Data System registry between baseline (study visit 1, 1987-1989) and December 31, 2012. This outcome was designed to mitigate potential selection bias by disease status and allow for more complete outcome ascertainment during periods of time between study visits. As a sensitivity analysis, cases of kidney disease were identified using visit-based measures exclusively, i.e. eGFR <60 mL/min/1.73 m^2 at a subsequent study visit accompanied by ≥25% eGFR decline relative to baseline.

Measurement of Covariates

At the baseline study visit, demographic characteristics (age, sex, race), socioeconomic status (education level), health behaviors (physical activity, smoking), and health history (diagnosed disease, medication use) were ascertained using a structured questionnaire administered by trained interviewers. Body mass index was calculated as weight in kilograms divided by height in meters squared using measurements taken while participants were wearing light clothing without shoes. Three seated measurements of blood pressure were taken by a certified technician using a random-zero sphygmomanometer after resting for five minutes. The average of the second and third blood pressure readings was used in the analysis. Fasting blood specimens were collected from participants during the baseline study visit. Blood levels of glucose were measured by the modified hexokinase/glucose-6-phosphate dehydrogenase method.

Overweight or obese status was defined as BMI ≥25 kg/m^2. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or current anti-hypertensive medication use in the preceding two weeks. Diabetes was defined as fasting blood glucose ≥126 mg/dL, non-fasting blood glucose ≥200 mg/dL, self-reported history of diagnosed diabetes, or current diabetes medication use in the preceding two weeks.

Statistical Analysis

Descriptive statistics (means, proportions) were used to characterize the study population with respect to baseline demographic and clinical factors according to tertile of DASH diet score. Cox proportional hazards regression was used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association between DASH diet score and kidney disease, incorporating time to event. The minimally adjusted regression model (model 1) included demographic characteristics (age, sex, race-center), socioeconomic status (education level), health behaviors (physical activity, smoking), and total caloric intake (the standard method for energy adjustment).[22,28,29] In model 2, we additionally adjusted for baseline kidney function (eGFR modeled as two linear spline terms with one knot at 90 mL/min/1.73 m^2). In model 3, we additionally adjusted for co-morbidities relevant to dietary behavior and kidney disease risk [overweight/obese status, diabetes status, hypertension status, systolic blood pressure, use of angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs)]. Effect modification by demographic factors (sex, race), socioeconomic status (education level), and clinical characteristics (overweight/obese status, diabetes status, hypertension status) was assessed by conducting stratified analyses and tests of interaction. In a sensitivity analysis, we performed the same analyses using the alternative, nutrient-based DASH diet score. In addition, we investigated the relationship between the individual components of each score and risk of kidney disease, modeling all factors together in the fully adjusted model (model 3). Due to the expected underestimation of dietary sodium intake from the food frequency questionnaire, as a sensitivity analysis, we modified both DASH diet indices to exclude sodium. Tests for linear trend were conducted using quantiles as ordinal variables (tertiles for the total scores, quintiles for components of the primary DASH diet score in accordance with the classification of the individual components in this score). Stata version 14 was used for all analyses (StataCorp LP, College Station, Texas).

RESULTS

Baseline Characteristics

Baseline characteristics of study participants included in this analysis of the ARIC study were similar to the total ARIC study population (**Table S4**). The subset of excluded study participants (n=910, 5.8% of the total ARIC study population) was more likely to be African-American and overweight or obese, to have diabetes and hypertension, and less likely to have a high school education. By definition, excluded participants had worse kidney function at baseline.

Study participants with a DASH diet score in the lowest tertile were younger, more likely to be male and African-American, and less likely to have completed high school than participants (**Table 1**). They also had lower levels of physical activity, were more likely to smoke, and had a higher prevalence of overweight/obesity status. Higher DASH diet score was also associated with lower systolic blood pressure and higher prevalence of diabetes. Baseline eGFR was statistically but not clinically different across tertiles of the DASH diet score.

DASH Diet Score and Subsequent Kidney Disease

There were 3,720 cases of kidney disease during a median follow-up of 23 years. After adjusting for age, sex, race-center, education level, smoking status, physical activity, and total caloric intake, baseline eGFR, overweight/obese status, diabetes, hypertension, systolic blood pressure, and use of ACE inhibitors or ARBs, participants with a DASH diet score in the lowest tertile were 1.16-times more likely to develop kidney disease than those with the highest tertile of the DASH score (Model 3 HR for tertile 3 vs. 1: 1.16, 95% CI: 1.07, 1.26; p-value for trend across tertiles <0.001; **Table 2**).

The association between DASH diet score and risk of kidney disease was likewise evident using the secondary DASH diet index that incorporates nutrients rather than food items (Model 3 HR for tertile 3 vs. 1: 1.11, 95% CI: 1.02, 1.22; p for trend=0.007; **Table S5**). Similar patterns were observed using indices modified to exclude dietary intake of sodium from the score (**Table S6**). In a sensitivity analysis using eGFR exclusively for the outcome definition, there were 2,030 cases of kidney disease (55% out of a total of 3,720 cases) and effect estimates were stronger than those for the primary method for ascertaining cases of kidney disease (Model 3 HR for tertile 3 vs. 1: 1.22, 95% CI: 1.08, 1.36; p for trend=0.001; **Table S7**).

In stratified analysis, the association between DASH diet and kidney disease was similar by sex, race, and education level (**Figure 1**). The relationship between DASH diet and kidney disease appeared to be stronger among those without diabetes and without hypertension, but the test for interaction was not statistically significant. DASH diet score was more strongly associated with kidney disease among those who were not overweight/obese.

Components of the DASH Diet Score and Subsequent Kidney Disease

Of the individual components of the DASH diet score, higher intake of red and processed meat was significantly associated with higher risk of kidney disease, and higher intake of nuts and legumes as well as low-fat dairy products was associated with a lower risk of kidney disease (**Table 3**). For the secondary DASH diet score, higher intake of magnesium and calcium was statistically significantly associated with a reduced risk of kidney disease, and higher dietary protein intake was associated with a higher risk of kidney disease (**Table S8**).

DISCUSSION

Our study of 14,882 middle-aged African-American and Caucasian men and women suggests that following a low-sodium DASH-style diet is associated with lower risk of kidney disease. Specifically, individuals with the lowest DASH diet score were 16% more likely to develop kidney disease than those with the highest DASH diet score. Higher intake of red and processed meat was associated with elevated risk of kidney disease, whereas consumption of other sources of protein including nuts, legumes, and low-fat dairy products, was associated with lower risk of kidney disease.

The present study is the first to report a prospective association between a DASH-style dietary pattern and subsequent kidney disease in a diverse study population. A cross-sectional analysis of an 869-person subset of the Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS) study showed that those in the lowest vs. highest tertile of the DASH diet score had a three-fold higher odds of reduced eGFR (<60 mL/min/1.73 m^2) after adjusting for age, sex, race, education, health care access, diabetes, hypertension, smoking, and caloric intake among participants who were living in poverty (42% of the study population; OR: 3.15, 95% CI: 1.51, 6.56), but there was no association among participants not living in poverty.[16] In a prospective analysis of 3,121 older Caucasian women in the Nurses' Health Study, the highest vs. lowest quartile of the DASH diet score was associated with lower risk of eGFR decline ≥30% after adjusting for age, hypertension, body mass index, physical activity, caloric intake, smoking, diabetes, diabetes duration, cardiovascular disease, and use of ACE inhibitors or ARBs (OR: 0.55, 95% CI: 0.38, 0.80), with no variation by diabetes status.[15] Our study extends this research by reporting associations in the general population setting for a large (N=14,882) and broadly generalizable study population. We observed similar effect estimates for men and women, Caucasians and African-Americans, and according to education level as a proxy for socioeconomic status.

An interesting aspect of our study is that the DASH diet was more strongly associated with risk of kidney disease among individuals who were not overweight or obese at baseline. It is plausible that those who were overweight or obese at baseline were previously advised to modify their diet due to their weight. As such, characterizing their dietary pattern at baseline may overestimate the quality of their diet over the lifetime. Another possibility is that risk estimates were attenuated among those who were overweight or obese due to reporting bias of dietary intake.[30] Among study participants without diabetes and those without hypertension, the DASH diet-kidney disease association appeared to be stronger, although the interaction was not statistically significant. Further research is necessary to replicate these findings among individuals with co-morbidities.

There are several possible mechanisms by which the DASH diet may impact risk of kidney disease. It may reduce blood pressure, as was the original intention of the diet. It also has a lower dietary acid load (-25.5 mEq/day) than a typical diet (50-75 mEq/day).[31,32] We have previously demonstrated that higher dietary acid load was associated with incident kidney disease in the ARIC study.[33] The association between dietary acid load and kidney disease, which has also been reported by other investigators, may be due to activation of the renin-angiotensin system or increase in endothelin-1 levels.[34-45] Alternatively, as has been reported with other dietary patterns, not following a DASH-style diet may stimulate an inflammatory response and endothelial dysfunction, which is a shared pathophysiologic mechanism for the development of both cardiovascular and kidney disease.[46-50]

Individual components of the DASH diet score may also drive the association with risk of kidney disease. In the present study, after adjusting for age, sex, race-center, education, smoking, physical activity, caloric intake, baseline eGFR, overweight/obese status, diabetes, hypertension, systolic blood pressure, and use of ACE inhibitors or ARBs, higher intake of red and processed meat was associated with higher risk of kidney disease; and higher intake of nuts, legumes, and low-fat dairy was associated with lower risk of kidney disease. The significant associations from the secondary DASH diet score (protein, magnesium, calcium) were consistent with the main analysis: red and processed meat is a source of protein, nuts and legumes are rich sources of magnesium, and dairy products are a rich source of calcium.[51] Increased dietary intake of protein is recommended for cardio-protection, whereas it is potentially harmful to the kidney.[52] However, plant protein may protect against kidney disease through increases in serum bicarbonate and decreases in fibroblast growth factor-23.[53] Lower serum levels of magnesium are associated with higher production of inflammatory and pro-atherogenic cytokines in endothelial cells, a pathway that could contribute to kidney function decline.[54,55] Milk protein contains peptides (casokinins and lactokinins) that have vasoactive properties, such as inhibiting the angiotensin converting enzyme and reducing blood pressure, an established kidney disease risk factor.[56,57] Taken together, our results suggest that protein from meat confers higher risk of adverse kidney outcomes whereas vegetable and dairy sources of protein confer kidney protective effects. Future research and recommendations on dietary intake and kidney disease risk should differentiate between sources of protein.

There are certain strengths and limitations of our study. As with any observational study design, residual confounding may be present. However, participants were extensively characterized with respect to demographic, socioeconomic, clinical, and behavioral factors at ARIC study visits, allowing adjustment for many important confounders. The ascertainment of cases using a composite of criteria (eGFR, hospitalizations, deaths, U.S. Renal Data System registry) is clinically relevant, appropriate for research studies, and allows for the detection of a large number of cases.[58] In a validation study, compared to medical chart review, this outcome demonstrated high specificity (96%) and low sensitivity (36%).[58] Several ARIC study publications have used this composite outcome.[59-61] In a sensitivity analysis of kidney disease based only on eGFR, the association between DASH diet and kidney disease was slightly stronger than that with the composite outcome. The lack of data on albuminuria, which is strongly associated with kidney function decline, is a limitation. eGFR may have been affected by non-GFR determinants of serum creatinine level including protein intake and muscle mass.[62]

The strengths and limitations of dietary assessment deserve mention. Assessment of dietary intake by self-report is prone to reporting bias and other sources of measurement error.[63] We reduced measurement error and reporting bias specifically by using data from questionnaires administered by trained interviewers following a standard protocol, using visual aids to represent portion sizes, and incorporating repeated measurements of dietary intake.[22] In addition, administration of the food frequency questionnaire was repeated in a subset of 419 ARIC study participants to quantify reproducibility of dietary assessment.[19] The 66-item food frequency questionnaire allows for ranking of dietary intake of the food items assessed. Absolute amounts of consumed food items and nutrients (especially sodium) were likely to be underestimated due to the limited number of items on the questionnaire and lack of information on food brands and snack foods.[64] However, in a sensitivity analysis excluding sodium from the DASH diet score, the effect estimates were essentially unchanged. Further, our finding that high intake of red and processed meat was associated with higher risk of kidney disease may in part be due to the fact that meat is a leading source of sodium according to the National Health and Nutrition Examination Survey (specifically, cold cuts/cured meat, pasta with meat sauce, and mixed meat dishes).[65] Nonetheless, results of analyses that present individual food and nutrient relationships should be interpreted cautiously.

The evidence on dietary patterns such as the DASH diet should be evaluated for potential inclusion in clinical recommendations for kidney disease prevention. Our results provide support for promotion of a DASH-style diet in an even broader segment of the U.S. population for reduced risk of kidney disease in addition to blood pressure reduction and cardiovascular disease prevention.

In conclusion, consumption of a DASH-style diet was associated with lower risk of kidney disease, independent of demographic characteristics, caloric intake, socioeconomic status, lifestyle factors, comorbid conditions, anti-hypertensive medication use, and baseline kidney function in this general population sample of African-American and Caucasian men and women. The DASH diet, designed for blood pressure reduction and now widely recommended for reducing the risk of cardiovascular disease and other chronic diseases, may also protect against kidney disease.

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FIGURE LEGENDS

Figure 1. Risk[a] of Kidney Disease for Low (Tertile 1) vs. High (Tertile 3) DASH Diet Score According to Demographic, Socioeconomic, and Clinical Characteristics

[a] Hazard ratios for kidney disease are presented for the low (tertile 1) vs. high (tertile 3) DASH diet score, adjusted for age, sex, race-center, education level, smoking status, physical activity, total caloric intake, baseline eGFR (linear spline terms with one knot at 90 mL/min/1.73 m^2), overweight/obese status, diabetes, hypertension, systolic blood pressure, use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers

Table 1. Baseline Demographics, Clinical Characteristics, and Dietary Factors According to Tertile of DASH Diet Score

	Tertile of DASH Diet Score			
	Tertile 1 (8-22): Low Score	Tertile 2 (23-26): Moderate Score	Tertile 3 (27-40): High Score	P-value[a]
Age, years	53.5 (5.7)	54.1 (5.7)	54.9 (5.7)	<0.001
Female, % (n)	43.7 (2,517)	55.8 (2,383)	68.3 (3,306)	<0.001
African-American, % (n)	35.5 (2,044)	22.4 (958)	17.9 (867)	<0.001
Diabetes, % (n)	9.2 (530)	12.4 (528)	13.0 (629)	<0.001
Hypertension, % (n)	35.9 (2,070)	33.5 (1,430)	32.7 (1,586)	0.002
SBP, mmHg	122.3 (19.1)	120.9 (18.2)	119.6 (18.3)	<0.001
ACEI or ARB use, % (n)	2.9 (165)	3.7 (159)	3.4 (164)	0.05
Current smoker, % (n)	35.7 (2,059)	23.3 (997)	17.2 (832)	<0.001
At least HS graduate, % (n)	67.7 (3,903)	80.4 (3,435)	84.3 (4,081)	<0.001
Physical activity index	2.27 (0.74)	2.44 (0.79)	2.63 (0.82)	<0.001
Serum creatinine, mg/dL	0.75 (0.18)	0.72 (0.18)	0.68 (0.17)	<0.001
eGFR, mL/min/1.73 m^2	104.4 (15.1)	102.5 (14.2)	102.4 (13.4)	<0.001
BMI ≥25 kg/m^2, % (n)	67.7 (3,903)	69.5 (2,969)	62.8 (3,042)	<0.001
Caloric intake, kcal/day	1,687 (582)	1,588 (565)	1,570 (489)	<0.001
Caloric intake, kcal/kg	21.9 (8.8)	20.8 (8.1)	21.4 (7.5)	<0.001
Protein intake, g/day	69.1 (27.1)	71.0 (28.2)	74.1 (27.5)	<0.001
Protein intake, g/kg	0.89 (0.39)	0.93 (0.39)	1.01 (0.40)	<0.001

Red and processed meat, servings/day	1.4 (0.8)	1.0 (0.7)	0.7 (0.6)	<0.001

[a] Mean (standard deviation) and p-value from linear regression for continuous variables; proportion (frequency) and p-value from χ^2 test for categorical variables.

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; eGFR, estimated glomerular filtration rate; HS, high school; SBP, systolic blood pressure

Conversion factor for creatinine in mg/dL to μmol/L, x88.4.

Table 2. Risk of Kidney Disease by Tertile of the DASH Diet Score

Model	Effect Estimate	Tertile of DASH Diet Score: Tertile 1 (8-22): Low Score	Tertile 2 (23-26): Moderate Score	Tertile 3 (27-40): High Score	P-value for trend
Unadjusted	IR (95% CI)	13.3 (12.7, 14.0)	12.8 (12.1, 13.6)	11.8 (11.1, 12.5)	0.002
	IRD (95% CI)	-1.6 (-0.6, -2.5)	-1.0 (-0.0, -2.1)	1 [Reference]	
Model 1	HR (95% CI)	1.11 (1.03, 1.21)	1.10 (1.02, 1.20)	1 [Reference]	0.01
Model 2	HR (95% CI)	1.10 (1.01, 1.20)	1.09 (1.00, 1.18)	1 [Reference]	0.03
Model 3	HR (95% CI)	1.16 (1.07, 1.27)	1.09 (1.00, 1.18)	1 [Reference]	<0.001

Model 1: Adjusted for age, sex, race-center, education level, smoking status, physical activity, total caloric intake

Model 2: Model 1 + baseline eGFR (linear spline terms with one knot at 90 mL/min/1.73 m^2)

Model 3: Model 2 + overweight/obese status, diabetes, hypertension, systolic blood pressure, use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers

CI, confidence interval; HR, hazard ratio; IR, incidence rate per 1,000 person-years; IRD, incidence rate difference per 1,000 person-years

Table 3. Dietary Intake of the Individual Components of the DASH Diet Score and Risk of Kidney Disease

Individual Component of the DASH Diet Score		Quintile 1: Low Intake	Quintile 2	Quintile 3: Moderate Intake	Quintile 4	Quintile 5: High Intake	P-value for trend
Sodium	Range, mg/day	251-1,021	1,022-1,287	1,288-1,553	1,554-1,906	1,907-5,030	--
	Model 1	1 [Reference]	0.98 (0.88, 1.09)	0.94 (0.83, 1.07)	0.97 (0.84, 1.12)	0.97 (0.81, 1.17)	0.5
	Model 2	1 [Reference]	0.97 (0.86, 1.08)	0.92 (0.81, 1.04)	0.94 (0.81, 1.08)	0.92 (0.77, 1.11)	0.2
	Model 3	1 [Reference]	0.95 (0.86, 1.07)	0.93 (0.82, 1.06)	0.92 (0.80, 1.06)	0.91 (0.75, 1.09)	0.2
Red and processed meat	Range, servings/day	0.0-0.4	0.5-0.7	0.8-1.1	1.2-1.5	1.6-13.7	--
	Model 1	1 [Reference]	1.13 (1.01, 1.25)	1.19 (1.06, 1.32)	1.26 (1.12, 1.42)	1.49 (1.31, 1.70)	<0.001
	Model 2	1 [Reference]	1.12 (1.00, 1.24)	1.17 (1.05, 1.31)	1.23 (1.09, 1.38)	1.47 (1.29, 1.68)	<0.001
	Model 3	1 [Reference]	1.04 (0.93, 1.16)	1.04 (0.93, 1.16)	1.06 (0.94, 1.19)	1.22 (1.07, 1.40)	0.02
Sweetened beverages	Range, glasses/day	0.0-0.0	0.0-0.1	0.2-0.4	0.5-0.9	1.0-10.0	--
	Model 1	1 [Reference]	0.83 (0.75, 0.92)	0.85 (0.76, 0.94)	0.84 (0.75, 0.93)	0.86 (0.77, 0.97)	0.01
	Model 2	1 [Reference]	0.82 (0.74, 0.91)	0.85 (0.77, 0.94)	0.86 (0.77, 0.95)	0.86 (0.76, 0.97)	0.02
	Model 3	1 [Reference]	0.91 (0.82, 1.01)	0.94 (0.85, 1.04)	0.93 (0.84, 1.04)	0.94 (0.83, 1.06)	0.3
Fruits	Range, servings/day	0.0-0.9	1.0-1.5	1.6-2.2	2.3-3.0	3.1-23.6	--

	Model 1	1 [Reference]	1.03 (0.92, 1.14)	1.03 (0.93, 1.15)	1.09 (0.97, 1.22)	1.22 (1.08, 1.37)	0.002
	Model 2	1 [Reference]	1.02 (0.92, 1.14)	1.04 (0.93, 1.16)	1.08 (0.97, 1.21)	1.24 (1.10, 1.40)	0.001
	Model 3	1 [Reference]	0.99 (0.90, 1.11)	0.97 (0.87, 1.08)	0.99 (0.88, 1.10)	1.06 (0.94, 1.20)	0.5
Vegetables	Range, servings/day	0.0-0.5	0.6-0.9	1.0-1.2	1.3-1.7	1.8-18.1	--
	Model 1	1 [Reference]	1.05 (0.95, 1.17)	0.97 (0.87, 1.08)	1.04 (0.93, 1.16)	0.99 (0.88, 1.12)	0.8
	Model 2	1 [Reference]	1.05 (0.94, 1.16)	0.97 (0.87, 1.08)	1.05 (0.94, 1.18)	1.01 (0.89, 1.13)	0.9
	Model 3	1 [Reference]	1.02 (0.92, 1.13)	0.95 (0.85, 1.06)	0.99 (0.89, 1.11)	0.94 (0.83, 1.06)	0.2
Nuts and legumes	Range, servings/day	0.0-0.4	0.5-0.6	0.7-0.9	1.0-1.3	1.4-10.6	--
	Model 1	1 [Reference]	0.91 (0.82, 1.01)	0.93 (0.83, 1.03)	0.87 (0.78, 0.98)	0.89 (0.79, 1.01)	0.03
	Model 2	1 [Reference]	0.93 (0.84, 1.03)	0.93 (0.83, 1.03)	0.87 (0.78, 0.97)	0.89 (0.79, 1.01)	0.02
	Model 3	1 [Reference]	0.96 (0.87, 1.07)	0.94 (0.85, 1.05)	0.89 (0.79, 0.99)	0.91 (0.81, 1.03)	0.04
Whole grains	Range, servings/day	0.0-0.2	0.3-0.5	0.6-0.9	1.0-1.5	1.6-8.6	--
	Model 1	1 [Reference]	0.97 (0.88, 1.07)	0.95 (0.85, 1.05)	1.03 (0.93, 1.14)	0.89 (0.80, 1.00)	0.2
	Model 2	1 [Reference]	0.98 (0.89, 1.08)	0.96 (0.86, 1.07)	1.05 (0.94, 1.16)	0.93 (0.83, 1.04)	0.5
	Model 3	1 [Reference]	0.94 (0.85, 1.04)	0.94 (0.85, 1.05)	1.01 (0.91, 1.12)	0.91 (0.81, 1.02)	0.3
Low-fat dairy	Range, servings/day	0.0-0.1	0.2-0.4	0.5-0.8	0.9-1.3	1.4-10.8	--

Model 1	1 [Reference]	0.92 (0.83, 1.02)	0.85 (0.76, 0.94)	0.84 (0.75, 0.94)	0.86 (0.77, 0.97)	0.001
Model 2	1 [Reference]	0.90 (0.81, 0.99)	0.81 (0.73, 0.90)	0.81 (0.73, 0.91)	0.82 (0.73, 0.92)	<0.001
Model 3	1 [Reference]	0.93 (0.84, 1.03)	0.83 (0.75, 0.92)	0.85 (0.76, 0.94)	0.84 (0.75, 0.95)	<0.001

Model 1: Adjusted for age, sex, race-center, education level, smoking status, physical activity, total caloric intake, and all other factors in the DASH diet score (all eight individual components of the DASH diet score were included in the same model, i.e., 1. sodium, 2. red and processed meat, 3. sweetened beverages, 4. fruits, 5. vegetables, 6. nuts and legumes, 7. whole grains, 8. low-fat dairy products)

Model 2: Model 1 + baseline eGFR (linear spline terms with one knot at 90 mL/min/1.73 m^2)

Model 3: Model 2 + overweight/obese status, diabetes, hypertension, systolic blood pressure, use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers

CI, confidence interval; HR, hazard ratio

SUPPLEMENTARY MATERIAL

Table S8. Risk of Kidney Disease Associated with the Individual Components of the Alternative DASH Diet Score Based on Nutrients

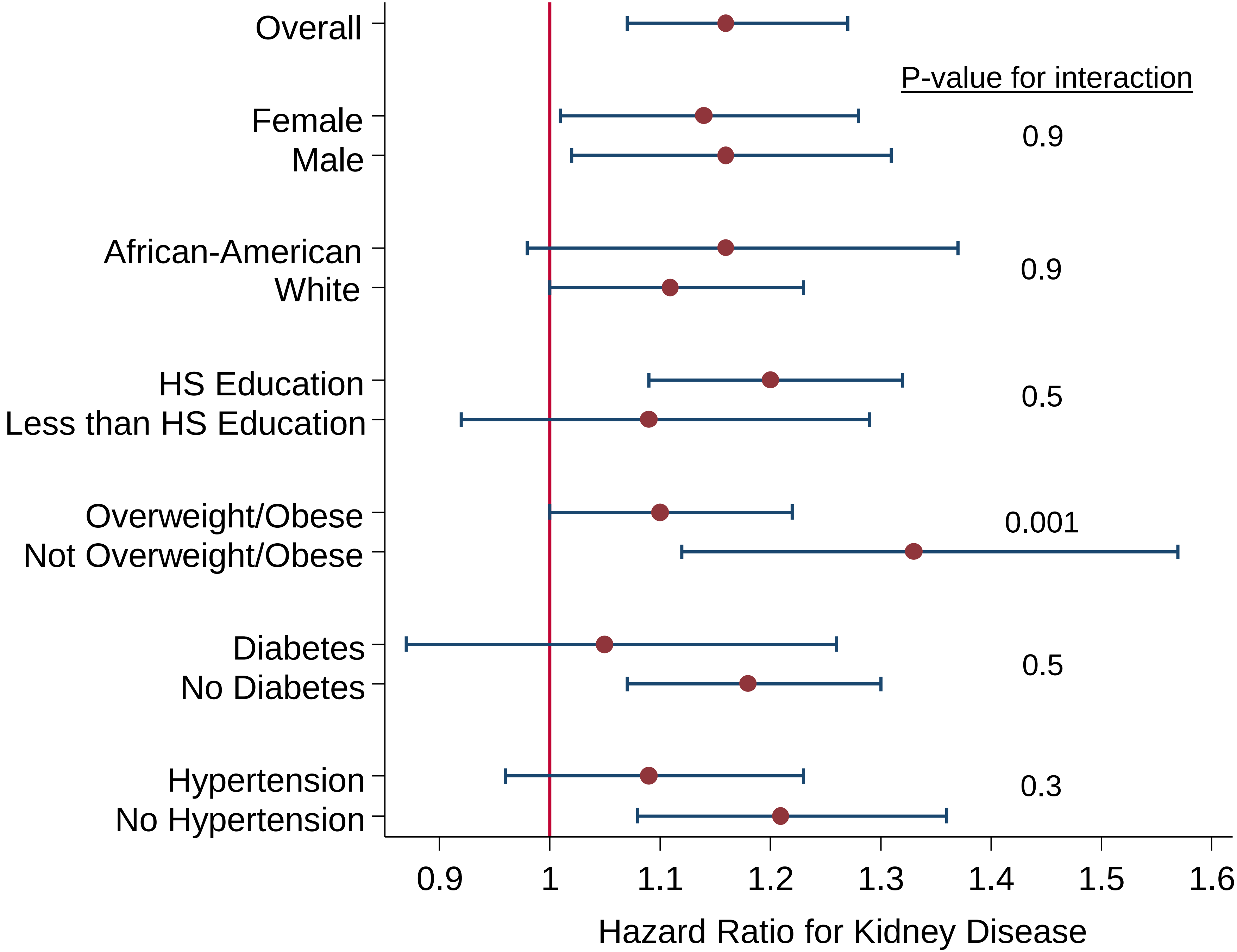
Overall
P-value for interaction
Female
Male
0.9
African-American
White
0.9
HS Education
Less than HS Education
0.5
Overweight/Obese
Not Overweight/Obese
0.001
Diabetes
No Diabetes
0.5
Hypertension
No Hypertension
0.3
0.9
1
1.1
1.2
1.3
1.4
1.5
1.6
Hazard Ratio for Kidney Disease

Figure S1

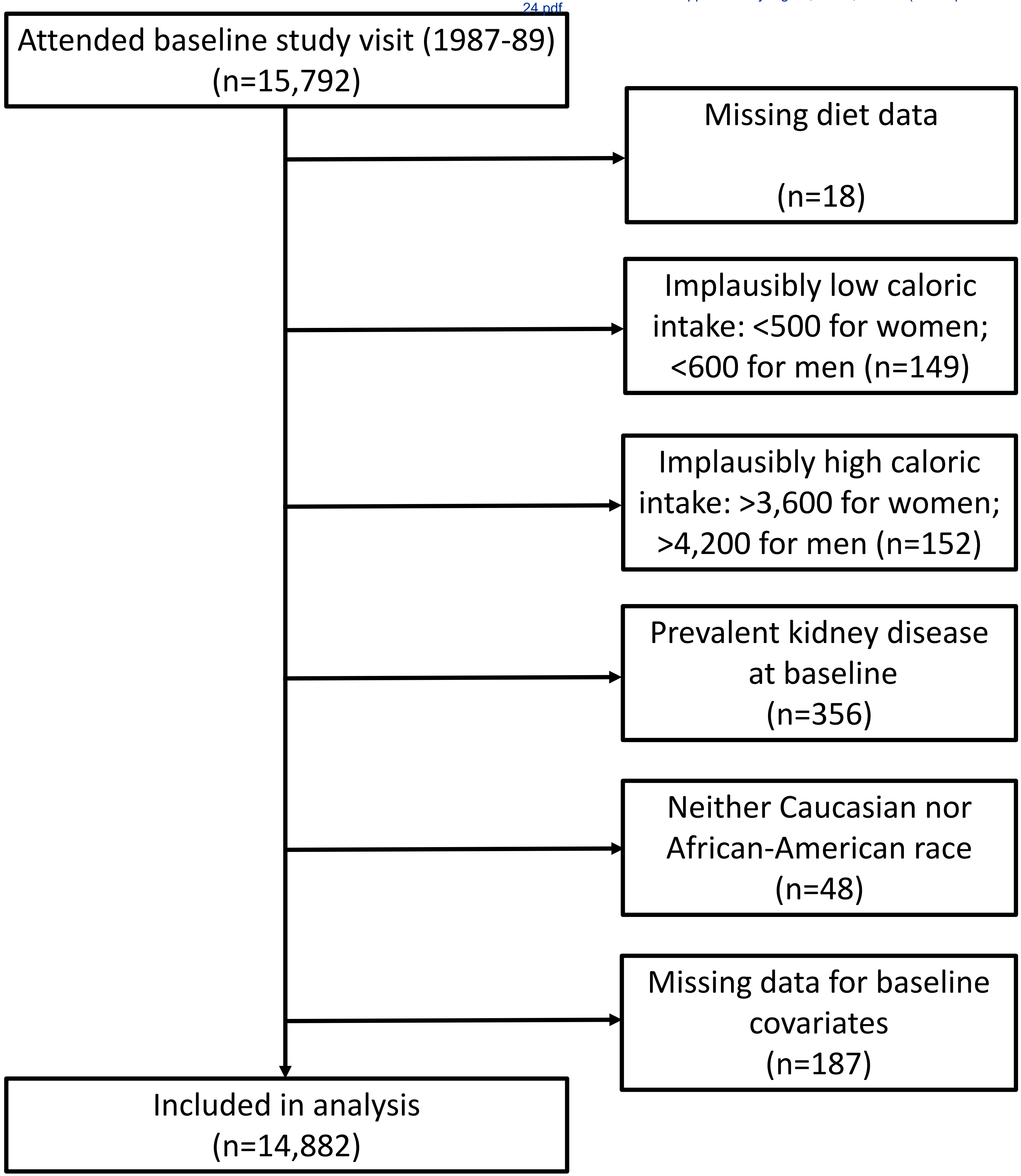
Attended baseline study visit (1987-89)
(n=15,792)
Missing diet data
(n=18)
Implausibly low caloric intake: <500 for women; <600 for men (n=149)
Implausibly high caloric intake: >3,600 for women; >4,200 for men (n=152)
Prevalent kidney disease at baseline
(n=356)
Neither Caucasian nor African-American race
(n=48)
Missing data for baseline covariates
(n=187)
Included in analysis
(n=14,882)

Table S1. Classification of the Components of the DASH Diet Score Based Primarily on Food Items

Food/Nutrient	**Description of Food/Nutrient from the ARIC Study**	**Scoring Criteria**[a]
Sodium	Sodium content of foods in food frequency questionnaire	Quintile 1: 5 points Quintile 2: 4 points Quintile 3: 3 points Quintile 4: 2 points Quintile 5: 1 point
Red and processed meat	Hamburgers; hot dogs; processed meats (sausage, salami, bologna, etc.); bacon; beef, pork, or lamb	
Sweetened beverages	Regular soft drinks (Coke, Pepsi, 7-Up, ginger ale); fruit-flavored punch or non-carbonated beverages (lemonade, Kool-Aid, Hawaiian Punch)	
Fruits	Fresh apples or pears; oranges; orange or grapefruit juice; peaches, apricots, or plums; bananas; other fruits	Quintile 1: 1 point Quintile 2: 2 points Quintile 3: 3 points Quintile 4: 4 points Quintile 5: 5 points
Vegetables	Broccoli; cabbage, cauliflower, brussels sprouts; carrots; corn; spinach, collards, or other greens; dark yellow, winter, squash (acorn, butternut); sweet potatoes; tomatoes	
Nuts and legumes	Nuts; peanut butter; beans (string beans, green beans); peas or lima beans; beans or lentils	
Whole grains	Cooked cereals (oatmeal, grits, cream of wheat); dark or whole grain bread	
Low-fat dairy	Skim or low-fat milk, yogurt, cottage cheese or ricotta cheese	

[a] Participants received higher scores for lower intake of: 1) sodium, 2) red and processed meats, and 3) sweetened beverages. Participants received higher scores for higher intake of: 4) fruits, 5) vegetables, 6) nuts and legumes, 7) whole grains, and 8) low-fat dairy.

Table S2. Classification[a] of the Components of the DASH Diet Score Based on Nutrients

Nutrient[b]	Target Level (1 point)	Intermediate Level (0.5 points)	Neither Target nor Intermediate Level (0 points)
Saturated fat (%kcal)	≤6	>6-11	>11
Total fat (%kcal)	≤27	>27-32	>32
Cholesterol (mg/1,000 kcal)	≤71.4	>71.4-107.1	>107.1
Sodium (mg/1,000 kcal)	≤1,143	>1,143-1,286	>1,286
Protein (%kcal)	≥18	16.5-<18	<16.5
Fiber (g/1,000 kcal)	≥14.8	9.5-<14.8	<9.5
Magnesium (mg/1,000 kcal)	≥238	158-<238	<158
Calcium (mg/1,000 kcal)	≥590	402-<590	<402
Potassium (mg/1,000 kcal)	≥2,238	1,534-<2,238	<1,534

[a] Nutrients were indexed to total caloric intake and then classified as target level (1 point), intermediate level (0.5 points), or neither target nor intermediate level (0 points) based on pre-determined thresholds.

[b] Reliability coefficients[1]: saturated fat: 0.43-0.63; total fat: 0.48-0.62; cholesterol: 0.41-0.61; protein: 0.45-0.64; fiber: 0.41-0.63; calcium: 0.26-0.69; potassium: 0.42-0.66

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Table S3. Description[a] of Dietary Intake for the Overall Study Population and According to Case Status

	Overall Study Population	Kidney Disease	No Kidney Disease
DASH diet score	24.0 (5.0)	23.8 (5.1)	24.0 (5.0)
Alternative DASH diet score	3.4 (1.5)	3.4 (1.4)	3.5 (1.5)
Sodium, mg/day	1,486 (547)	1,496 (559)	1,483 (544)
Red and processed meat, servings/day	1.1 (0.7)	1.1 (0.8)	1.1 (0.7)
Sweetened beverages, glasses/day	0.5 (0.8)	0.6 (0.8)	0.5 (0.8)
Fruits, servings/day	2.1 (1.5)	2.1 (1.4)	2.1 (1.5)
Vegetables, servings/day	1.3 (0.9)	1.3 (0.9)	1.3 (0.9)
Nuts and legumes, servings/day	0.9 (0.7)	0.9 (0.7)	0.9 (0.7)
Whole grains, servings/day	1.0 (0.9)	0.9 (0.9)	1.0 (0.9)
Low-fat dairy products, servings/day	0.9 (0.9)	0.8 (0.9)	0.9 (1.0)
Saturated fat, g/day	22.0 (10.7)	22.2 (11.0)	21.9 (10.6)
Total fat, g/day	59.9 (27.0)	60.6 (27.6)	59.7 (26.8)
Cholesterol, mg/day	249 (119)	253 (117)	248 (119)
Fiber, g/day	17.3 (7.4)	17.3 (7.4)	17.3 (7.4)
Magnesium, mg/day	254 (86)	250 (85)	255 (87)
Calcium, mg/day	659 (338)	648 (329)	662 (340)
Potassium, mg/day	2,648 (888)	2,629 (887)	2,654 (889)
Protein, g/day	71.3 (28)	71.6 (27.9)	71.2 (27.5)

[a] Mean (standard deviation)

Table S4. Baseline Demographic and Clinical Characteristics for Included Study Participants, Excluded Study Participants, and the Total ARIC Study Population[a]

	Included Study Participants	Excluded Study Participants	Total ARIC Study Population
N (%)	14,882 (94.2%)	910 (5.8%)	15,792 (100%)
Age, years	54.1 (5.7)	54.8 (6.0)	54.2 (5.8)
Female, % (n)	55.1 (8,206)	55.4 (504)	55.2 (8,710)
African-American, % (n)	26.0 (3,869)	43.6 (397)	27.0 (4,266)
Diabetes, % (n)	11.4 (1,687)	23.3 (183)	12.0 (1,870)
Hypertension, % (n)	34.2 (5,086)	50.4 (418)	35.0 (5,504)
SBP, mmHg	121.0 (18.6)	126.6 (23.3)	121.4 (19.0)
Current smoker, % (n)	26.1 (3,888)	27.1 (244)	26.2 (4,132)
At least HS graduate, % (n)	76.7 (11,419)	65.6 (579)	76.1 (11,998)
Physical activity index	2.44 (0.79)	2.30 (0.77)	2.43 (0.79)
Serum creatinine, mg/dL	0.72 (0.18)	1.16 (1.69)	0.74 (0.42)
eGFR, mL/min/1.73 m^2	103.2 (14.3)	88.0 (30.3)	102.5 (15.8)
BMI ≥25 kg/m^2, % (n)	66.6 (9,914)	72.3 (640)	66.9 (10,554)
Caloric intake, kcal/day	1620 (551)	1553 (611)	1618 (553)

[a] Mean (standard deviation) for continuous variables; proportion (frequency) for categorical variables

ARIC, Atherosclerosis Risk in Communities; BMI, body mass index; eGFR, estimated glomerular filtration rate; HS, high school; SBP, systolic blood pressure

Conversion factor for creatinine in mg/dL to μmol/L, x88.4.

Table S5. Risk of Kidney Disease by Tertile of the Alternative DASH Diet Score Based on Nutrients

	Tertile of the Alternative DASH Diet Score (Nutrients)			P-value for trend
	Tertile 1 (0-2.5): Low Score	Tertile 2 (3-4): Moderate Score	Tertile 3 (4.5-9): High Score	
Model 1	1.06 (0.97, 1.15)	0.96 (0.89, 1.05)	1 [Reference]	0.16
Model 2	1.04 (0.95, 1.14)	0.93 (0.86, 1.01)	1 [Reference]	0.26
Model 3	1.11 (1.02, 1.22)	0.94 (0.87, 1.03)	1 [Reference]	0.007

Model 1: Adjusted for age, sex, race-center, education level, smoking status, physical activity, total caloric intake

Model 2: Model 1 + baseline eGFR (linear spline terms with one knot at 90 mL/min/1.73 m^2)

Model 3: Model 2 + overweight/obese status, diabetes, hypertension, systolic blood pressure, use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers

Table S6. Risk of Kidney Disease by Tertile of the DASH Diet Scores Modified to Exclude Sodium

	Tertile of Modified DASH Diet Score (Food Items)			P-value for trend
	Tertile 1 (7-19): Low Score	Tertile 2 (20-23): Moderate Score	Tertile 3 (24-35): High Score	
Model 1	1.10 (1.01, 1.20)	1.09 (1.00, 1.18)	1 [Reference]	0.02
Model 2	1.09 (1.00, 1.18)	1.06 (0.98, 1.16)	1 [Reference]	0.047
Model 3	1.16 (1.07, 1.26)	1.09 (1.00, 1.19)	1 [Reference]	0.001
	Tertile of Modified DASH Diet Score (Nutrients)			**P-value for trend**
	Tertile 1 (0-1.5): Low Score	Tertile 2 (2-3): Moderate Score	Tertile 3 (3.5-7.5): High Score	
Model 1	1.04 (0.96, 1.14)	0.96 (0.88, 1.04)	1 [Reference]	0.30
Model 2	1.03 (0.95, 1.12)	0.93 (0.86, 1.01)	1 [Reference]	0.40
Model 3	1.11 (1.02, 1.21)	0.95 (0.87, 1.03)	1 [Reference]	0.01

Model 1: Adjusted for age, sex, race-center, education level, smoking status, physical activity, total caloric intake

Model 2: Model 1 + baseline eGFR (linear spline terms with one knot at 90 mL/min/1.73 m^2)

Model 3: Model 2 + overweight/obese status, diabetes, hypertension, systolic blood pressure, use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers

Table S7. Risk of Kidney Disease (Ascertained Based on Estimated Glomerular Filtration Rate) by Tertile of the DASH Diet Score

	Tertile of DASH Diet Score			P-value for trend
	Tertile 1 (8-22): Low Score	Tertile 2 (23-26): Moderate Score	Tertile 3 (27-40): High Score	
Model 1	1.23 (1.09, 1.37)	1.17 (1.04, 1.31)	1 [Reference]	<0.001
Model 2	1.19 (1.06, 1.34)	1.16 (1.03, 1.29)	1 [Reference]	0.003
Model 3	1.22 (1.08, 1.36)	1.12 (1.00, 1.25)	1 [Reference]	0.001

Model 1: Adjusted for age, sex, race-center, education level, smoking status, physical activity, total caloric intake

Model 2: Model 1 + baseline eGFR (linear spline terms with one knot at 90 mL/min/1.73 m^2)

Model 3: Model 2 + overweight/obese status, diabetes, hypertension, systolic blood pressure, use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers

Table S8. Risk of Kidney Disease Associated with the Individual Components of the Alternative DASH Diet Score Based on Nutrients

Nutrient	Model	Tertile 1: Low Intake	Tertile 2: Moderate Intake	Tertile 3: High Intake	P-value for trend
Saturated fat	1	1 [Reference]	1.17 (1.05, 1.31)	1.17 (1.01, 1.35)	0.09
	2	1 [Reference]	1.16 (1.04, 1.29)	1.13 (0.98, 1.31)	0.2
	3	1 [Reference]	1.19 (1.06, 1.33)	1.17 (1.01, 1.35)	0.1
Total fat	1	1 [Reference]	0.84 (0.75, 0.94)	0.95 (0.82, 1.09)	0.6
	2	1 [Reference]	0.83 (0.74, 0.92)	0.92 (0.80, 1.06)	0.3
	3	1 [Reference]	0.85 (0.76, 0.95)	0.97 (0.84, 1.11)	0.8
Cholesterol	1	1 [Reference]	0.98 (0.90, 1.07)	0.96 (0.87, 1.06)	0.4
	2	1 [Reference]	1.03 (0.94, 1.12)	1.04 (0.94, 1.15)	0.5
	3	1 [Reference]	1.00 (0.92, 1.09)	0.96 (0.87, 1.06)	0.4
Sodium	1	1 [Reference]	1.01 (0.93, 1.10)	1.03 (0.94, 1.12)	0.6
	2	1 [Reference]	1.02 (0.94, 1.11)	1.02 (0.94, 1.12)	0.7
	3	1 [Reference]	1.02 (0.94, 1.11)	1.01 (0.92, 1.10)	0.9
Protein	1	1 [Reference]	1.16 (1.06, 1.27)	1.29 (1.16, 1.42)	<0.001
	2	1 [Reference]	1.12 (1.03, 1.22)	1.24 (1.12, 1.37)	<0.001
	3	1 [Reference]	1.09 (1.00, 1.19)	1.12 (1.01, 1.24)	0.03
Fiber	1	1 [Reference]	0.95 (0.87, 1.03)	1.08 (0.97, 1.20)	0.4
	2	1 [Reference]	0.92 (0.85, 1.00)	1.06 (0.95, 1.17)	0.6
	3	1 [Reference]	0.91 (0.83, 0.99)	1.00 (0.90, 1.11)	0.6
Magnesium	1	1 [Reference]	0.87 (0.79, 0.96)	0.76 (0.67, 0.86)	<0.001

	2	1 [Reference]	0.91 (0.82, 1.00)	0.81 (0.71, 0.92)	0.003
	3	1 [Reference]	0.90 (0.82, 0.99)	0.85 (0.75, 0.97)	0.03
Calcium	1	1 [Reference]	0.87 (0.80, 0.94)	0.82 (0.75, 0.91)	<0.001
	2	1 [Reference]	0.86 (0.79, 0.93)	0.82 (0.74, 0.90)	<0.001
	3	1 [Reference]	0.88 (0.81, 0.96)	0.85 (0.77, 0.94)	0.001
Potassium	1	1 [Reference]	1.00 (0.91, 1.11)	1.13 (0.99, 1.29)	0.08
	2	1 [Reference]	0.97 (0.88, 1.08)	1.08 (0.94, 1.23)	0.3
	3	1 [Reference]	0.95 (0.86, 1.05)	1.05 (0.92, 1.20)	0.5

Model 1: Adjusted for age, sex, race-center, education level, smoking status, physical activity, total caloric intake, and all other factors in the DASH diet score (all nine individual components of the alternative DASH diet score based on nutrients were included in the same model, i.e., 1. saturated fat, 2. total fat, 3. cholesterol, 4. sodium, 5. protein, 6. fiber, 7. magnesium, 8. calcium, 9. potassium)

Model 2: Model 1 + baseline eGFR (linear spline terms with one knot at 90 mL/min/1.73 m^2)

Model 3: Model 2 + overweight/obese status, diabetes, hypertension, systolic blood pressure, use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers