

Coffee Consumption and Incident Kidney Disease: Results From the Atherosclerosis Risk in Communities (ARIC) Study

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Background: Moderate coffee consumption has been suggested to be associated with lower risk for chronic conditions such as diabetes, a major precursor to chronic kidney disease (CKD). However, the association between coffee and CKD has not been fully established.

Study Design: Prospective cohort study.

Setting & Participants: 14,209 participants aged 45 to 64 years from the Atherosclerosis Risk in Communities (ARIC) Study.

Predictors: Coffee consumption (cups per day) was assessed at visits 1 (1987-1989) and 3 (1993-1995) using food frequency questionnaires.

Outcomes: Incident CKD defined as estimated glomerular filtration rate < 60 mL/min/1.73 m² accompanied by ≥25% estimated glomerular filtration rate decline, CKD-related hospitalization or death, or end-stage renal disease.

Results: There were 3,845 cases of incident CKD over a median of 24 years of follow-up. Men, whites,

current smokers, and participants without comorbid conditions were more likely to consume higher amounts of coffee per day. After adjustment for demographic, clinical, and dietary factors, higher categories of coffee consumption were associated with lower risk for incident CKD compared with those who never consumed coffee (HR for <1 cup per day, 0.90 [95% CI, 0.82-0.99]; 1-2 cups per day, 0.87 [95% CI, 0.77-0.97]; 2-3 cups per day, 0.84 [95% CI, 0.75-0.94]). In continuous analysis, for each additional cup of coffee consumed per day, risk for incident CKD was lower by 3% (HR, 0.97; 95% CI, 0.95-0.99; *P* < 0.001).

Limitations: Self-reported coffee consumption and observational design.

Conclusions: Participants who drank higher amounts of coffee had lower risk for incident CKD after adjusting for covariates. Coffee consumers may not be at adverse risk for kidney disease.

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Coffee is one of the most frequently consumed beverages in the United States, with ~75% of the US population 20 years and older reported to be coffee drinkers.¹ According to the 2015 to 2020 Dietary Guidelines for Americans, moderate coffee consumption (3-5 cups per day or 400 mg/d of caffeine) is not associated with long-term health risks such as cancer or cardiovascular disease and therefore can be incorporated into healthy eating styles.² Coffee consumption has been shown to be protective against multiple chronic conditions such as diabetes,^{3,4} coronary heart disease,⁵ cancer,^{6,7} and all-cause mortality.⁸⁻¹¹

Sparse literature exists as to whether coffee consumption is associated with chronic kidney disease (CKD), a disease with growing prevalence and costs.¹² A recent meta-analysis identified 4 cohort studies that found no significant association between coffee and CKD, but the pooled results suggested a potential inverse association among women.¹³ These 4 prior studies were conducted in Italy, Japan, and Korea. Few prior studies have examined a longitudinal association between coffee and CKD in the United States.

Our study seeks to examine the risk for incident CKD across different levels of coffee consumption in the United States, using data from the community-based Atherosclerosis Risk in Communities (ARIC) Study.

Methods

Study Population

The ARIC Study is a community-based cohort of 15,792 middle-aged (45-64 years) predominantly black and white men and women.¹⁴ Study participants were recruited and enrolled in 1987 to 1989 from 4 US communities: Forsyth County, NC; Jackson, MS; suburbs of Minneapolis, MN; and Washington County, MD. Participants attended follow-up visits in 1990 to 1992 (visit 2), 1993 to 1995 (visit 3), 1996 to 1998 (visit 4), and 2011 to 2013 (visit 5). An ethics committee at each site approved the study protocol, and study participants provided informed consent.

Due to small numbers, we excluded participants who were not black or white (*n* = 48), blacks from Washington County, MD (*n* = 33), and blacks from Minneapolis, MN (*n* = 22). We additionally excluded those who had prevalent CKD (estimated glomerular filtration rate [eGFR] < 60 mL/min/1.73 m²) or missing serum creatinine values (*n* = 353), were not fasting or were missing glucose measurement (*n* = 527), or were missing body mass index values (*n* = 10). We further excluded those who were missing data needed to calculate a DASH (Dietary Approaches to Stop Hypertension) diet score (*n* = 435), missing coffee consumption data (*n* = 28), missing

alcohol status ($n = 34$), or had implausible levels of total energy intake (<500 or $>3,500$ kcal/d for women; <700 or $>4,500$ kcal/d for men; $n = 93$). A total of 14,209 ARIC Study participants were included in our analysis.

Assessment of Coffee Consumption

Coffee consumption was assessed using a 66-item semi-quantitative food frequency questionnaire (FFQ), which was administered in person by a trained interviewer at visits 1 (1987-1989) and 3 (1993-1995). Participants were asked to report how frequently they consumed an 8-ounce cup of regular (nondecaffeinated) coffee on average during the past year. Frequency options included almost never, 1 to 3 cups per month, 1 cup per week, 2 to 4 cups per week, 5 to 6 cups per week, 1 cup per day, 2 to 3 cups per day, 4 to 6 cups per day, and more than 6 cups per day. From visit 1 to visit 3, a total of 44% of participants did not change their response in the FFQ about coffee consumption and 25% changed their response by 1 category. These categorical responses were converted into cups per week as a continuous variable (eg, for category 2-4 cups per week: 3 cups per week). We used a cumulative approach to incorporate data from both visits 1 and 3.¹⁵ For participants who remained event free at visit 3, we used the mean coffee consumption of visits 1 and 3 for a more precise estimate. For participants who developed incident CKD between visits 1 and 3 or did not have visit 3 coffee data, we used their coffee consumption from visit 1 to capture the amount of coffee they drank before their CKD event. After taking into account cumulative consumption from visits 1 and 3 coffee intake, the continuous variable was converted into cups per week and recategorized into 5 new groups: never, fewer than 1 cup per day, 1 or more to fewer than 2 cups per day, 2 or more to fewer than 3 cups per day, and 3 or more cups per day. Participants who responded “almost never” for both FFQs were categorized into the group labeled “never.”

Outcome Assessment

Incident CKD was defined as at least 1 of the following criteria: (1) eGFR < 60 mL/min/1.73 m² accompanied by $\geq 25\%$ eGFR decline at any subsequent study visit relative to baseline, (2) *International Classification of Diseases, Ninth/Tenth Revision* (ICD-9/10) code for a hospitalization related to CKD stage ≥ 3 , (3) ICD-9/10 code for a death related to CKD stage ≥ 3 identified through linkage to the National Death Index, or (4) end-stage renal disease (ESRD) identified by linkage to the US Renal Data System (USRDS) registry.¹⁶ For ICD-9/10 codes, any diagnosis (primary, secondary, etc) was included. eGFR was calculated using the 2009 CKD-EPI (CKD Epidemiology Collaboration) equation using serum creatinine measured using the modified kinetic Jaffé method.¹⁷⁻¹⁹ Competing events for this outcome included death due to malignant neoplasms in the lung, chronic obstructive pulmonary disease, acute myocardial infarction, and atherosclerotic heart disease.

As a sensitivity analysis for this composite definition of incident CKD, we defined incident CKD using visit-based measures only (eGFR < 60 mL/min/1.73 m² and $\geq 30\%$ eGFR decline). Competing events were the same as for the composite definition of incident CKD.

We also assessed the development of advanced kidney disease using a secondary outcome of ESRD. Cases were identified using the USRDS registry, representing cases of kidney transplantation and dialysis. Kidney failure was used as a sensitivity analysis for the ESRD definition,²⁰ defined as: (1) ESRD; (2) ICD-9 Clinical Modification (ICD-9-CM) and ICD-10-CM codes from hospitalizations and deaths that represented kidney failure, transplantation, and dialysis; and (3) a study visit eGFR < 15 mL/min/1.73 m².¹⁹ Any mention of the ICD-9/10 codes anywhere on the forms was included.

Assessment of Covariates

In our analysis, we adjusted for demographic, study design, lifestyle, and clinical factors that might influence coffee consumption and kidney outcomes. Information for age, sex, race, study center, education level, smoking status, physical activity, and alcohol status were assessed at baseline using an interviewer-administered questionnaire.¹⁴ Race and study center were combined into one variable given the nonuniform distribution of racial groups across study centers. Physical activity index score was calculated based on intensity and time dedicated to sport and nonsport exercise during leisure time. Possible values for this score ranged from 1 (lowest physical activity) to 5 (highest physical activity).¹⁴ Alcohol status was categorized into never, former, current (moderate), and current (heavy). Moderate alcohol drinkers consisted of women who drank fewer than 1 drink per day and men who drank fewer than 2 drinks per day. Heavy alcohol drinkers consisted of women who drank 1 or more drinks per day and men who drank 2 or more drinks per day. To capture diet quality, we used a DASH diet score based on low intake of red and processed meat, sweetened beverages, and sodium and high intake of fruits, vegetables, whole grains, nuts and legumes, and low-fat dairy.²¹ Each component was scored from 1 to 5 based on ranked distribution in quintiles.

Clinical factors included systolic and diastolic blood pressures, fasting glucose concentration, eGFR, diabetes, hypertension, and use of antihypertensive medication. Diabetes was defined at baseline as fasting blood glucose concentration ≥ 126 mg/dL, nonfasting glucose concentration ≥ 200 mg/dL, self-reported history of physician-diagnosed diabetes, or use of diabetes medication in the preceding 2 weeks. Hypertension was defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or use of antihypertensive medication in the past 2 weeks.

Cumulative energy intake was determined by calculating the mean energy intake of visits 1 and 3 for participants

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who developed the outcome after visit 3 and for those who did not develop the outcome but had information for both visits. We used only visit 1 energy intake for participants who had an incident CKD event between visits 1 and 3 or were missing visit 3 data.

Statistical Analysis

We reported demographic risk factors and clinical risk factors according to different categories of coffee consumption. We estimated hazard ratios (HRs) and associated 95% confidence intervals (CIs) for incident CKD and secondary outcomes with different categories of coffee intake using cause-specific hazards models.²² Time to event accumulated from visit 1 (1987-1989) until the end of follow-up (December 31, 2013). We evaluated 3 models: model 1 included age, sex, race-center, education, and total energy intake; model 2 additionally included physical activity, smoking, alcohol status, and DASH diet score; and model 3 included all variables in model 2 plus systolic blood pressure, diabetes status, antihypertensive medication use, and baseline eGFR. We calculated P values for trend across categories using the median value of each category of coffee consumption.

We also collapsed the coffee consumption categories to perform an analysis comparing participants who reported never drinking coffee with participants who reported drinking any coffee. To express the risk for CKD per additional cup of coffee, we analyzed coffee consumption using a continuous variable (cups per day).

We tested interaction terms between potential effect modifiers (sex, smoking, diabetes, race, physical activity, and DASH diet) and coffee consumption on incident CKD using the likelihood ratio test. We assessed the proportionality assumption in cause-specific models on the basis of Schoenfeld residuals.

All P values were 2 tailed, and statistical significance was set a priori at $P < 0.05$. All analyses were performed using Stata software (version 14.0; StataCorp).

Results

Baseline Characteristics of Participants

Of 14,209 participants included in our study, 19% of the population almost never drank coffee, 21% drank fewer than 1 cup per day, 25% drank 1 or more to fewer than 2 cups per day, 15% drank 2 or more to fewer than 3 cups per day, and 19% drank 3 or more cups per day. Men, whites, and current smokers were more likely to consume higher amounts of coffee (Table 1). About 36% of never drinkers were black compared to 7% of the group of 3 or more cups per day. Participants with lower body mass index, lower blood pressure, and without diabetes or hypertension also consumed more coffee. Among participants who drank at least 3 cups of coffee per day, baseline eGFR was slightly lower by ~ 3 mL/min/1.73 m²

compared with participants who never drank coffee. Serum magnesium concentrations slightly increased across coffee consumption categories.

Association Between Coffee Consumption and CKD

A total of 3,845 (27%) participants developed CKD during a median follow-up of 24 years. Higher coffee consumption was associated with lower risk for incident CKD, and findings were relatively consistent across the 3 models (Table 2). Compared with never drinkers, each category of coffee consumption was associated with 10% to 16% lower risk for CKD (<1 cup per day: 10% lower risk [HR, 0.90; 95% CI, 0.82-0.99]; 1-<2 cups per day: 10% lower risk [HR, 0.90; 95% CI, 0.82-0.99]; 2-<3 cups per day: 13% lower risk [HR: 0.87, 95% CI: 0.77-0.97]; and ≥ 3 cups per day: 16% lower risk [HR, 0.84; 95% CI, 0.75-0.94]; P for trend < 0.001). Each additional cup of coffee consumed per day was associated with 3% lower risk for incident CKD (HR, 0.97; 95% CI, 0.95-0.99). Compared with participants who never consumed coffee, participants who consumed any amount of coffee had 11% lower risk for CKD (HR, 0.89; 95% CI, 0.82-0.96; P for trend < 0.001).

Results for the visit-based definition for CKD (eGFR < 60 mL/min/1.73 m² and $\geq 30\%$ eGFR decline) were generally consistent with the main results (Table 2). In the fully adjusted model, consuming 3 or more cups of coffee per day was significantly associated with lower risk for incident CKD (HR for ≥ 3 cups per day vs never, 0.83; 95% CI, 0.72-0.97). However, the association between coffee consumption and incident CKD was not statistically significant for the other coffee consumption categories (<1, ≥ 1 -<2, and ≥ 2 -<3 cups per day) compared with nondrinkers. Each additional cup of coffee consumed per day was associated with 4% lower risk for incident CKD using the visit-based definition (HR, 0.96; 95% CI, 0.93-0.98, $P < 0.001$).

Association Between Coffee Consumption and Advanced Kidney Disease

There were 281 (2%) cases of ESRD during a median follow-up of 25 years. Coffee consumption was nominally protective of risk for ESRD in model 3 for all categories of coffee consumption, but this was not statistically significant (Table 3; model 3 P for trend = 0.5). In model 3, coffee consumption was associated with lower risk for kidney failure (HR for <1 cup per day vs never, 0.71 [95% CI, 0.58-0.88] and HR for 1-<2 cups per day vs never, 0.79 [95% CI, 0.65-0.97]). However, there was no significant linear trend across coffee consumption categories for the kidney failure outcome ($P = 0.6$).

Subgroup Analyses

We did not observe effect modification for the association between coffee consumption and incident CKD by sex

Table 1. Baseline Characteristics According to Daily Coffee Consumption

Baseline Characteristics	Coffee Consumption Level ^a					P ^b
	Never (n = 2,758)	<1 Cup/d (n = 3,024)	≥1-<2 Cups/d (n = 3,578)	≥2-<3 Cups/d (n = 2,102)	≥3 Cups/d (n = 2,747)	
Age, y	53.9 ± 6	54.3 ± 6	54.6 ± 6	54.1 ± 6	53.5 ± 6	0.1
Female	63.6%	56.9%	56.2%	50.9%	49.1%	<0.001
Race						<0.001
White	63.6%	69.5%	70.4%	84.0%	92.9%	
Black	36.4%	30.5%	29.7%	16.0%	7.1%	
Education level						<0.001
<High school	24.9%	22.1%	26.3%	21.0%	18.2%	
High school or equivalent	40.2%	40.6%	39.9%	41.7%	44.7%	
≥College	34.9%	37.3%	33.9%	37.4%	37.2%	
Center						<0.001
Forsyth County, NC	22.1%	25.9%	28.0%	29.9%	23.9%	
Jackson, MS	31.8%	26.3%	27.4%	14.4%	6.2%	
Minneapolis, MN	19.7%	23.9%	19.4%	27.7%	43.0%	
Washington County, MD	26.4%	23.9%	25.2%	28.1%	27.0%	
Smoking status						<0.001
Never smoker	55.3%	50.9%	42.1%	35.3%	23.4%	
Former smoker	26.0%	30.9%	34.7%	35.8%	34.8%	
Current smoker	18.7%	18.2%	23.2%	28.9%	41.8%	
Physical activity index score ^c (1-5)	2.4 ± 0.8	2.4 ± 0.8	2.4 ± 0.8	2.5 ± 0.8	2.5 ± 0.8	0.3
BMI, kg/m ²	28.2 ± 6	28.0 ± 5	27.8 ± 5	27.1 ± 5	26.7 ± 5	<0.001
Systolic BP, mm Hg	123.4 ± 20	121.5 ± 18	122.3 ± 19	119.4 ± 18	116.8 ± 17	<0.001
Diastolic BP, mm Hg	75.0 ± 12	74.4 ± 11	74.0 ± 11	72.7 ± 11	71.3 ± 11	<0.001
Diabetes	13.4%	11.4%	11.0%	8.9%	6.1%	<0.001
Hypertension	40.2%	37.3%	36.6%	30.2%	21.7%	<0.001
Antihypertensive medication	34.8%	33.3%	32.3%	26.7%	18.8%	<0.001
ACE inhibitors	3.6%	2.8%	3.1%	2.8%	2.1%	0.01
Fasting glucose, mg/dL	109.6 ± 40	106.8 ± 32	107.6 ± 35	105.7 ± 33	102.9 ± 26	<0.001
Baseline eGFR, mL/min/1.73 m ²	104.5 ± 16	103.5 ± 15	103.3 ± 15	101.8 ± 13	101.9 ± 12	<0.001
Baseline serum creatinine, mg/dL	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.2	0.9
Serum magnesium, mEq/L	1.61 ± 0.2	1.62 ± 0.2	1.63 ± 0.2	1.64 ± 0.2	1.66 ± 0.1	<0.001
Serum potassium, mmol/L	4.35 ± 0.5	4.37 ± 0.5	4.39 ± 0.5	4.47 ± 0.5	4.56 ± 0.5	0.1
Coffee consumption, ^a 8-oz cups/d	0	0.4 ± 0.3	1.2 ± 0.3	2.2 ± 0.2	4.9 ± 1.3	<0.001
Tea consumption, 8-oz cups/d	0.5 ± 1.1	0.5 ± 1	0.6 ± 0.9	0.6 ± 1	0.5 ± 1	<0.001
Soft drink consumption, 8-oz cups/d	0.4 ± 0.9	0.4 ± 0.4	0.4 ± 0.6	0.4 ± 0.6	0.3 ± 0.7	<0.001
Alcohol intake status ^d						<0.001
Never	37.3%	29.1%	25.4%	17.0%	12.3%	
Former	19.7%	17.4%	18.6%	18.0%	18.2%	
Current (heavy)	6.1%	8.0%	10.0%	11.9%	14.2%	
Current (moderate)	37.0%	45.6%	46.0%	53.1%	55.4%	
Total energy intake, ^a kcal/d	1,463 ± 530	1,448 ± 494	1,488 ± 507	1,508 ± 526	1,559 ± 533	<0.001
DASH diet score (0-40)	24.3 ± 5	24.4 ± 5	23.8 ± 5	23.7 ± 5	23.7 ± 5	0.001

Note: Values for categorical variables are given as number (percentage); for continuous variables, as mean ± standard deviation.

Abbreviations: ACE, angiotensin-converting enzyme; BMI, body mass index; BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension; eGFR, estimated glomerular filtration rate.

^aDietary factors (coffee and total energy) were estimated using cumulative average intake. The average of visits 1 and 3 dietary data for those who did not develop kidney disease and were not censored before visit 3. For those who developed kidney disease or were censored before visit 3, dietary data from visit 1 were used.

^bCategorical variables were analyzed using χ^2 test. Continuous variables were analyzed using analysis of variance test.

^cPhysical activity index score was calculated based on intensity and time of sport and exercise during leisure time; 1 is lowest and 5 is highest.

^dModerate alcohol consumption was defined as fewer than 1 drink per day for women and fewer than 2 drinks per day for men. Heavy alcohol consumption was defined as 1 or more drink per day for women and 2 or more drinks per day for men.

Table 2. Risk for Kidney Disease by Category of Daily Coffee Consumption

	Coffee Consumption Level ^a					P for Trend
	Never (n = 2,758)	<1 Cup/d (n = 3,024)	1-<2 Cups/d (n = 3,578)	2-<3 Cups/d (n = 2,102)	≥3 Cups/d (n = 2,747)	
CKD (composite definition) ^b						
No. of events	786	868	1,015	528	648	
Incidence rate per 1,000 person-y	14.5	13.9	13.9	12.5	11.5	
Model 1	1.00 (reference)	0.89 (0.81-0.98)	0.88 (0.80-0.97)	0.84 (0.75-0.94)	0.80 (0.72-0.89)	<0.001
Model 2	1.00 (reference)	0.89 (0.81-0.98)	0.86 (0.78-0.95)	0.82 (0.73-0.91)	0.74 (0.66-0.83)	<0.001
Model 3	1.00 (reference)	0.90 (0.82-0.99)	0.90 (0.82-0.99)	0.87 (0.77-0.97)	0.84 (0.75-0.94)	<0.001
CKD (visit-based definition) ^c						
No. of events	412	509	548	283	351	
Incidence rate per 1,000 person-y	11.7	11.8	11.3	10.3	9.1	
Model 1	1.00 (reference)	1.01 (0.89-1.15)	0.95 (0.84-1.08)	0.89 (0.76-1.03)	0.79 (0.69-0.92)	<0.001
Model 2	1.00 (reference)	1.01 (0.89-1.15)	0.93 (0.82-1.06)	0.88 (0.75-1.03)	0.77 (0.66-0.89)	<0.001
Model 3	1.00 (reference)	1.03 (0.90-1.17)	0.94 (0.83-1.08)	0.95 (0.81-1.11)	0.83 (0.72-0.97)	<0.001

Note: Unless otherwise indicated, values given as hazard ratio (95% confidence interval). Model 1: adjusted for age, sex, race-center, education, total energy intake; model 2: model 1 + physical activity, smoking, alcohol status; DASH diet score; and model 3: model 2 + diabetes status, body mass index, systolic blood pressure, antihypertensive medication use, and baseline eGFR.

Abbreviations: ARIC, Atherosclerosis Risk in Communities; CKD, chronic kidney disease; DASH, Dietary Approaches to Stop Hypertension; eGFR, estimated glomerular filtration rate; ICD-9/10, International Classification of Diseases, Ninth/Tenth Revision; USRDS, US Renal Data System.

^aAverage of visits 1 and 3 coffee intake calculated for participants with no CKD events or with CKD event after visit 3; visit 1 coffee intake used for participants with CKD event between visits 1 and 3.

^bDefined as eGFR < 60 mL/min/1.73 m² accompanied by ≥25% eGFR decline, ICD-9/10 code related to CKD stage 3+ through ARIC surveillance or National Death Index, or end-stage renal disease identified by USRDS registry.

^cDefined as eGFR < 60 mL/min/1.73 m² accompanied by ≥30% eGFR decline relative to baseline.

($P = 0.4$), smoking ($P = 0.4$), diabetes ($P = 0.7$), race ($P = 0.4$), physical activity ($P = 0.8$), or DASH diet ($P = 0.2$; Fig 1).

Discussion

Our analysis of 14,209 middle-aged adults in the United States suggests that increased coffee consumption is associated with lower risk for CKD in the ARIC Study. Men, whites, current smokers, and individuals without hypertension or diabetes were more likely to consume higher amounts of coffee per day. Inverse associations were observed for advanced kidney disease (ESRD and kidney failure), but these estimates were generally not statistically significant, which may be due to the relatively small number of events and correspondingly low power. Overall, higher amounts of coffee consumption were associated with lower risk for kidney disease and may be beneficial for reducing the long-term risk for kidney disease. Furthermore, our results suggest that participants who drank any amount of coffee had 11% reduced risk for incident CKD compared with those who never drank coffee. The association suggested a dose-response relationship, with the most robust associations among those consuming at least 3 cups of coffee per day. Results were consistent by sex, smoking status, diabetes status, and race. The association between coffee and CKD among whites was similar to the main analysis; however, there was no clear association among blacks. The lack of association may be attributed to low

power and low frequency of coffee consumption among blacks.

Several cross-sectional studies have suggested a significant protective association between coffee consumption and eGFR.²³⁻²⁶ A cross-sectional study involving Korean women found that 2 or more cups of coffee per day was associated with lower odds of decreased kidney function (eGFR < 60 mL/min/1.73 m²) compared with those who drank fewer than 1 cup per day (odds ratio, 0.59; 95% CI, 0.37-0.95).²³ They found that the protective association was more robust among women who had diabetes compared with those who did not have diabetes. The Doetinchem Cohort Study found that individuals who drank more than 6 cups of coffee per day had better kidney function compared with those who drank fewer than 1 cup per day (by 1.33 [95% CI, 0.24-2.43] mL/min/1.73 m²; P -trend = 0.02).²⁵ In contrast, in our study, eGFR was lower by ~3 mL/min/1.73 m² in the highest versus lowest coffee consumption category. However, this difference is minimal and not clinically significant. Furthermore, cross-sectional analyses do not capture the temporal association between coffee and incident kidney disease.

Few longitudinal studies have been performed on the association between coffee and kidney outcomes. The existing studies have reported mixed results.^{9,10,13} In a prospective analysis of 185,855 nonwhite US adults in the Multiethnic Cohort, consumption of at least 1 cup of coffee per day was found to be associated with lower risk for kidney disease compared to never drinking coffee (HR

Table 3. Risk for Advanced Kidney Disease Outcomes by Category of Daily Coffee Consumption

	Coffee Consumption Level ^a					P for Trend
	Never (n = 2,758)	<1 Cup/d (n = 3,024)	1-<2 Cups/d (n = 3,578)	2-<3 Cups/d (n = 2,102)	≥3 Cups/d (n = 2,747)	
ESRD^b						
No. of events	70	63	72	38	38	
Incidence rate per 1,000 person-y	1.2	0.9	0.9	0.8	0.6	
Model 1	1.00 (reference)	0.80 (0.57-1.12)	0.79 (0.57-1.10)	0.73 (0.48-1.10)	0.69 (0.46-1.04)	0.1
Model 2	1.00 (reference)	0.81 (0.58-1.14)	0.76 (0.55-1.06)	0.69 (0.45-1.05)	0.59 (0.39-0.90)	0.03
Model 3	1.00 (reference)	0.83 (0.59-1.16)	0.84 (0.60-1.17)	0.76 (0.50-1.16)	0.83 (0.54-1.28)	0.5
Kidney failure^c						
No. of events	187	159	201	117	120	
Incidence rate per 1,000 person-y	3.3	2.4	2.6	2.7	2.1	
Model 1	1.00 (reference)	0.69 (0.56-0.85)	0.75 (0.61-0.91)	0.82 (0.64-1.04)	0.73 (0.58-0.93)	0.2
Model 2	1.00 (reference)	0.69 (0.56-0.86)	0.72 (0.59-0.88)	0.76 (0.60-0.97)	0.62 (0.48-0.78)	<0.001
Model 3	1.00 (reference)	0.71 (0.58-0.88)	0.79 (0.65-0.97)	0.85 (0.67-1.08)	0.82 (0.64-1.05)	0.6

Note: Unless otherwise indicated, values given as hazard ratio (95% confidence interval). Model 1: adjusted for age, sex, race-center, education, total energy intake; model 2: model 1 + physical activity, smoking, alcohol status, DASH diet score; model 3: model 2 + diabetes status, body mass index, systolic blood pressure, antihypertensive medication use, and baseline eGFR.

Abbreviations: CKD, chronic kidney disease; DASH, Dietary Approaches to Stop Hypertension; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; ICD-9/10, International Classification of Diseases, Ninth/Tenth Revision; USRDS, US Renal Data System.

^aAverage of visits 1 and 3 coffee intake calculated for participants with no ESRD or kidney failure events or with ESRD or kidney failure event after visit 3; visit 1 coffee intake used for participants with CKD event between visits 1 and 3.

^bDefined as cases of kidney transplantation and dialysis, identified using the USRDS registry.

^cDefined by USRDS data, ICD-9/10 codes, or eGFR < 15 mL/min/1.73 m² during a study visit.

for 1 cup per day, 0.60 [95% CI, 0.46-0.78]; HR for 2-3 cups per day, 0.59 [95% CI, 0.45-0.79]; and HR for ≥4 cups per day, 0.42 [95% CI, 0.26-0.67]).¹⁰ Our results contradict a recent meta-analysis that found no association between coffee and CKD.¹³ Among 14,898 individuals

from 4 observational studies (2 from Japan, 1 from Korea, and 1 from Italy), there was no statistically significant difference in CKD risk among those consuming more than 1 cup of coffee per day compared with those who never consumed coffee (relative risk, 0.71; 95% CI, 0.47-1.08). When the analysis was stratified by sex, the authors observed a stronger protective relationship among women; however, it was also not significant. When we stratified our analysis by sex, there appeared to be a stronger protective association between coffee and CKD among women compared with men. However, there was no evidence of effect modification. Results of the meta-analysis may be due to an inability to distinguish between meaningful differences in coffee consumption categories (dichotomized as never or >1 cup per day in the meta-analysis vs ranging from never to ≥3 cups per day in the present study). Furthermore, a large (N = 90,317) prospective analysis of the US Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial found no significant association between coffee and mortality due to kidney disease.⁹ Consumption of 4 or more cups per day compared with never drinkers was inversely associated and coffee consumption for categories fewer than 1 cup per day, 1 cup per day, and 2 to 3 cups per day were directly associated with kidney disease mortality. This null finding could be due in part to limited statistical power because there were very few deaths due to kidney disease in their study (n = 108).

The biological mechanism by which coffee may influence kidney disease risk is unclear and the chemical makeup of coffee is highly complex. However, there are several speculations regarding how the components in

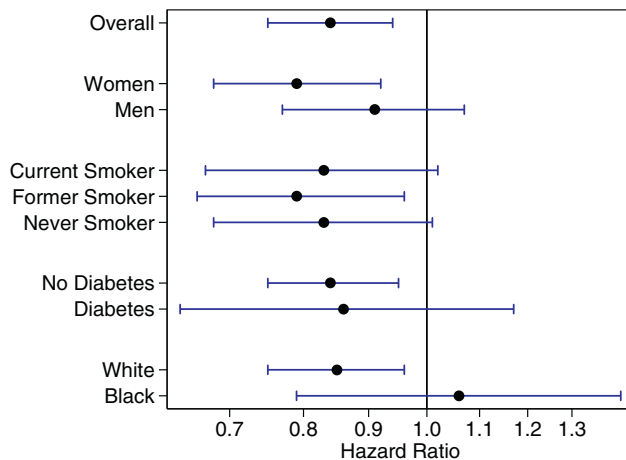


Figure 1. Adjusted risk for incident kidney disease for highest versus lowest category of coffee consumption (≥3 cups of coffee per day vs never) according to population subgroups. Hazard ratios (on logarithmic scale) for kidney disease are presented for 3 or more cups of coffee per day versus never, adjusted for age, sex, race-center, education, total energy intake, physical activity, smoking, alcohol status, DASH (Dietary Approaches to Stop Hypertension) diet score, diabetes status, body mass index, systolic blood pressure, antihypertensive medication use, and baseline estimated glomerular filtration rate.

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coffee may affect kidney disease. One hypothesis is that the antidiabetic effect of coffee may improve glycemia and lower the risk for diabetic nephropathy.^{2,3} Several studies have found coffee to be inversely associated with diabetes.^{3,4} One explanation for this association is the chlorogenic acid and other natural constituents of coffee beans that inhibit glucose absorption, reducing oxidative stress and liver glucose output.^{8,23,27-29} In our study, there were fewer individuals with diabetes in higher coffee consumption groups, confirming the previously found inverse associations between coffee and diabetes. However, we found no effect modification by diabetes on coffee and CKD ($P = 0.7$). Another explanation for coffee being protective of kidney disease is that the components within coffee (caffeic acid, hydroxyhydroquinone, quinides, niacin, trionelline, magnesium, and chlorogenic acid) may protect the glomerular endothelium from oxidative stress and reduce insulin resistance and systematic inflammation.^{13,30} Coffee consumption has been found to have an inverse association with hyperuricemia, which may be an explanation for slower progression to CKD.^{31,32} Caffeine has been suggested to increase eGFR and renal blood flow, so it is possible that caffeine enhances uric acid excretion; however, there is not enough evidence to confirm this hypothesis.³²

Our study has several strengths. We used a large community-based population. We also used average coffee consumption at visits 1 and 3 when applicable. Furthermore, we had well-measured outcomes for incident CKD and more advanced kidney disease (ESRD) and performed sensitivity analyses for both outcomes.

Limitations included self-reported coffee consumption, which is likely associated with some degree of misclassification. However, our exposure was categorized into specific categories so we could capture a wide range of coffee intake. Reverse causality is a potential concern for observational studies. However, we excluded participants with prevalent CKD at baseline, conducting a prospective analysis with baseline coffee consumption and subsequent kidney disease. Another limitation is the small sample size for the analysis of advanced kidney outcomes, which reduced the statistical power for detecting a significant association between coffee and ESRD. We did not have data for albuminuria or proteinuria at visit 1, which would have been useful in assessing kidney damage. Another limitation is that we do not know whether participants who consumed less coffee drank a higher amount of other types of fluids (tea or soft drinks) or if participants who drank higher amounts of coffee were replacing their consumption of other fluids with coffee. Our dietary assessment (FFQ) measured frequency and quantity of coffee consumed but did not ask specifically about type of coffee beans, how it was prepared, or how much sweetener and milk were added to coffee. Preparation of coffee should be investigated in future studies because different brewing methods for different types of beans have been found to influence the chemical

composition of coffee.³³⁻³⁵ For example, brewing time and water pressure influence the extraction of antioxidants and chlorogenic acid.³⁴ Furthermore, unfiltered coffee has been suggested to have adverse effects on lipids, whereas filtered coffee does not significantly change low-density lipoprotein cholesterol or triglyceride concentrations.³⁵

In this prospective study of 14,209 middle-aged blacks and whites in the United States, we found that coffee consumers had reduced risk for incident CKD, which was consistent in population subgroups (by sex, race, smoking, and diabetes). Our results provide further support for the 2015 to 2020 Dietary Guidelines for Americans, which state that 3 to 5 cups of coffee per day can be incorporated into a healthy lifestyle.² Future research should evaluate whether coffee preparation methods and sugar and milk added to coffee influence the renal protection association of coffee observed in the present study.

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