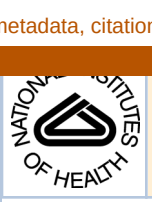

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Sugar-sweetened soda consumption, hyperuricemia, and kidney disease

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Abstract

The metabolism of high-fructose corn syrup used to sweeten soda drinks may lead to elevations in uric acid levels. Here we determined whether soda drinking is associated with hyperuricemia and, as a potential consequence, reduced kidney function. At baseline, 15,745 patients in the Atherosclerosis Risk in Communities Study completed a dietary questionnaire and had measurements of their serum creatinine and uric acid. After 3 and 9 years of follow-up, multivariate odds ratios from logistic regressions for binary outcome of hyperuricemia and chronic kidney disease (eGFR less than 60 ml/min per 1.73 m^2) were evaluated. Compared to participants who drank less, consumption of over one soda per day was associated with increased odds of prevalent hyperuricemia and chronic kidney disease. The odds ratio for chronic kidney disease significantly increased to 2.59 among participants who drank more than one soda per day and had a serum uric acid level over 9.0 mg/dl. In longitudinal analyses, however, drinking more than one soda per day was not associated with hyperuricemia or chronic kidney disease. Neither preexistent hyperuricemia nor development of hyperuricemia modified the lack of association between soda drinking and incident chronic kidney disease. Thus our study shows that high consumption of sugar-sweetened soda was associated with prevalent but not incident hyperuricemia and chronic kidney disease.

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DISCLOSURE

All the authors declared no competing interests.

Keywords

chronic kidney disease; epidemiology; fructose; soda; uric acid

Consumption of high-fructose corn syrup (HFCS) has increased nearly 2000% over the past three decades and has paralleled the epidemics of obesity, metabolic syndrome, and chronic kidney disease (CKD).[1] Estimates from the US Department of Agriculture report the average yearly intake of HFCS as an added sweetener to be as high as 62.4 pounds per person. Sweetened beverages such as regular soda account for over 70% of this intake.[2]

The metabolism of fructose, unique to that of other sugars, depletes hepatic adenosine triphosphate, increasing the degradation of nucleotides and promoting the synthesis of uric acid.[3] Data from the Third National Health and Nutrition Examination Survey suggested a link between regular, but not diet, soda consumption and the frequency of hyperuricemia,[4] concerning in the light of recent epidemio-logical studies in which elevated uric acid levels independently increased the risk for incident kidney disease and progression of established CKD.[5–8] In animals, fructose-associated hyperuricemia produces a metabolic syndrome associated with glomerular hypertension, renal hyper-trophy, and arteriolopathy of the renal vasculature, with resultant reductions in creatinine clearance and increases in proteinuria.[3,9–11]

The controversy over the potential dangers of HFCS has been playing out not only in the medical literature[12–17] but also in the mainstream media, including advertising campaigns funded by the corn-producing industry. Defenders of HFCS point out that this sweetener comprises, approximately, 40–55% fructose (the other components being glucose and polymers of glucose); therefore findings from animal and human studies that use 100% fructose formulations may not apply to HFCS.[18]

Two recent investigations have suggested that sugar-sweetened soda consumption is associated with albuminuria[19] and elevated serum creatinine,[20] yet both focused solely on prevalent disease and neither directly examined whether elevated uric acid levels were responsible for the effects of soda (and HFCS) on the kidney. We therefore investigated whether sugar-sweetened soda consumption is associated with hyperuricemia and kidney disease in both cross-sectional and longitudinal analyses of data from the Atherosclerosis Risk in Communities (ARIC) Study.

RESULTS

At the baseline ARIC visit, 15,745 participants provided information about their regular consumption of sugar-sweetened sodas. More than 80% of these participants reported drinking less than one soda per day, whereas approximately 5% drank more than one soda per day (Table 1). Participants in the highest exposure category were more likely to be male, African-American, and current smokers compared with participants who drank less than one soda per day. Participants who completed high school and college were less likely to drink soda on a daily basis. Although there was only a slight difference in mean body mass index among exposure groups, participants with higher soda consumption had significantly greater sodium, animal protein, and total calorie intake. Hypertensive status did not differ among exposure groups, although diabetic participants were most represented in the group with the least amount of sugar-sweetened soda consumption. In this generally healthy cohort, only 4% of diabetics drank more than one regular soda per day, whereas 16% of diabetics drank more than one diet soda per day. The three exposure groups had essentially equal serum

creatinine measurements, but uric acid levels were slightly higher in the groups with higher soda consumption.

Cross-sectional analyses

Thirty-seven percent (n = 5790) of participants at visit 1 met criteria for hyperuricemia; 24% (n = 3718) of participants had baseline uric acids above 7.0 mg/dl. In univariate and multivariate analyses, the odds of hyperuricemia significantly rose with increased daily consumption of sugar-sweetened soda (Table 2). Participants who drank less than one soda per day were the referent in this and all subsequent analyses. The multivariate odds ratio for hyperuricemia was 1.31 (1.12–1.53, P = 0.001) for participants who drank more than one soda per day.

Of the 15,642 participants with creatinine measurements at visit 1, 479 (3.1%) were identified as having prevalent CKD. The odds of having prevalent CKD were not related to the degree of soda consumption in univariate analysis, but parsimonious and multivariate analyses suggested increased odds of CKD with higher soda use (Table 2). The multivariate odds ratio for prevalent CKD was 1.46 (0.96–2.22, P = 0.07) for participants who drank more than one soda per day.

Logistic regression for the association of CKD and sugar-sweetened soda consumption, using fully adjusted models stratified by uric acid levels, suggested that the association between soda consumption and kidney function was directly related to uric acid levels (Table 3). The odds ratio for CKD among participants who drank more than one soda per day was 0.76 (0.23–2.45, P = 0.6) in those without hyperuricemia and 1.50 (0.95–2.37, P = 0.08) in those with hyperuricemia. The prevalence odds ratios for CKD increased with rising uric acid levels, from 0.28 (0.04–2.03, P = 0.2) in participants with uric acid <6.0 mg/dl to 2.59 (1.18–5.71, P = 0.02) in participants with uric acid levels ≥9.0 mg/dl.

Longitudinal analyses

Over 3 years of follow-up, 15,642 participants had uric acid levels checked at baseline and visit 2. Of the 9451 participants without hyperuricemia at visit 1, 3288 (34.8%) developed hyperuricemia by visit 2. Although univariate analysis suggested that sugar-sweetened soda intake increased the odds of hyperuricemia, both parsimonious and multivariate models revealed no significant association (Table 4). Participants who drank less than one soda per day were again the referent in all longitudinal analyses. The multivariate odds ratio for incident hyperuricemia was 1.17 (0.95–1.43, P = 0.1) among participants who drank more than one soda per day. Multivariate linear regression, with uric acid levels as continuous variables and comparing subjects who drank >1 soda per day to the same referent, showed no influence of increased soda consumption on the change in uric acid level from visit 1 to visit 2 (β coefficient 0.025, 95% CI 0.109 to 0.058).

Over 9 years of follow-up, 15,642 participants had serum creatinine levels checked at baseline, 14,292 had repeat levels at 3 years, and 11,559 had levels checked at 9 years. Of the 14,002 participants without prevalent CKD at visit 1, 1160 (8.3%) met our criteria for incident CKD by visit 2 or 4. Multivariate analysis found no association between sugar-sweetened soda consumption and odds of developing kidney disease (Table 4). The odds ratio for incident kidney disease was 0.82 (0.59–1.16, P = 0.3) among participants who drank >1 soda per day. Sensitivity analyses excluding diabetic participants, using a more conservative definition of incident CKD detailed above, and using change in serum creatinine as the outcome did not significantly change these estimates. Multivariate linear regression evaluating the continuous change in estimated glomerular filtration rate (eGFR) from visit 1 to visit 2 (β coefficient –0.442, 95% CI –1.690 to 0.805) and change in eGFR

from visit 1 to visit 4 (β coefficient –0.467, 95% CI –1.990 to 1.055) were likewise not significant for participants who consumed >1 soda per day.

As with the cross-sectional analyses, we stratified the multivariate logistic models for the association of incident CKD and soda consumption by uric acid levels (Table 5). Neither the presence of hyperuricemia at visit 1 nor the development of hyperuricemia between visits 1 and 2 increased the odds of developing CKD among high-soda consumers in this cohort. Likewise, no degree of change in uric acid levels between visits 1 and 2 seemed to modify the lack of association between soda consumption and incident CKD during the study period. Only participants with uric acid levels of 9.0 mg/dl or higher at visit 1 showed an increased odds of developing CKD if they drank more than one soda per day (OR 3.90, 95% CI 1.55–9.82) compared to participants with similar uric acid elevations who drank less than one soda per day.

Diet soda consumption

We repeated our analyses substituting diet soda intake as the exposure of interest and using the same three categories of exposure (that is, participants who drank <1 diet soda per day were the referent category). In multivariate models, consumption of >1 diet soda was not associated with prevalent hyperuricemia (OR 1.10, 95% CI 0.98–1.24), prevalent CKD (OR 1.29, 95% CI 0.95–1.74), incident hyperuricemia (OR 0.97, 95% CI 0.83–1.14), or incident CKD (OR 0.80, 95% CI 0.64–1.00) (Supplementary Table S1). Multivariate linear regression comparing subjects who drank >1 diet soda per day to those who drank <1 diet soda per day similarly showed no influence of increased diet soda consumption on the change in uric acid level from visit 1 to visit 2 (β coefficient 0.024, 95% CI –0.039 to 0.087), change in eGFR from visit 1 to visit (β coefficient –0.380, 95% CI –1.313 to 0.553), or change in eGFR from visit 1 to visit 4 (β coefficient –0.184, 95% CI –1.319 to 0.950). Finally, in stratified analysis, subjects with baseline uric acid levels ≥9.0 mg/dl who drank >1 diet soda per day did not have increased odds of either prevalent CKD (OR 0.71, 95% CI 0.28–1.83) or incident CKD (OR 0.44, 95% CI 0.12–1.52).

DISCUSSION

In this study, increased consumption of regular soft drinks was associated with prevalent hyperuricemia and CKD. Stratified analysis also suggested that the association between such sweetened beverages and kidney function was primarily among participants with elevated uric acid levels. However, in longitudinal analyses, these associations did not hold. These findings present new but conflicting evidence as to whether sugar-sweetened sodas, and potentially the HFCS used to sweeten them, are a dietary risk factor for development of hyperuricemia and CKD.

The results of this study complement a growing body of literature tying sugar-sweetened soda consumption to higher rates of chronic diseases such as obesity, hypertension, and diabetes.[21–23] Our findings are consistent with previously published reports in which high sugar-sweetened soda consumption was associated with prevalent hyperuricemia and renal injury.[4,19,20] Yet this study, to the best of our knowledge, is the first to examine whether sugar-sweetened soda consumption is associated with incident forms of these diseases. The results of these incidence analyses add an important note of caution to the literature on sugar-sweetened soda and HFCS. Although the cross-sectional analyses performed in this and other studies[4,19] support a hypothesis that increased HFCS-sweetened soda consumption leads to higher uric acid levels that in turn induce renal damage, the longitudinal analyses do not support this theory.

Indeed, the associations shown in our cross-sectional analyses must be viewed in context of the lack of association in our longitudinal analyses, which arguably would provide stronger evidence for a causative role if they were sufficiently powered and free of bias. Post hoc power analyses showed that we had >80% power to detect a 6.5% higher incidence of hyperuricemia and a 3% higher incidence of CKD in participants who drank >1 soda per day compared with participants who drank <1 soda per day. Therefore, if the proposed causal link between sugar-sweetened soda consumption, hyperuricemia, and CKD that is suggested by ours and others' cross-sectional analyses is real, we must explore the lack of association between soda consumption and incident disease in this cohort. We suggest four possible explanations.

First, the duration of sugar-sweetened soda exposure may be important. The mean follow-up in this cohort was approximately 9 years, and a longer exposure period may be needed to produce incident disease. This interpretation, admittedly, does not support a role for HFCS in the prevalence data, as the participants at visit 1 (1987–1989) would have likely had an even shorter exposure period to HFCS, which was only widely introduced in the early 1980s. Second, it is conceivable that enrollment in this study may have led to an improvement in general health behaviors that modified soda consumption over the course of the study period. Our sensitivity analysis of participants who reported high intake of soda at both visits 1 and 3, however, showed lower point estimates for the odds of developing new hyperuricemia or CKD. The third, and in our opinion most plausible, explanation is the role of survival bias in this type of analysis. Participants who had not yet developed hyperuricemia or CKD by the time of the initial ARIC visit, when mean age was 54.2 years, may have some unidentified protective factor making them less likely to develop either of these conditions in later years. If sugar-sweetened soda consumption truly elevated uric acid levels and/or reduced kidney function, it may be unlikely for this effect to first manifest after the age 50. Theoretically, a modern cohort of younger subjects with a longer duration of follow-up might yield different results from those presented here. Finally, as with all such observational studies, unmeasured confounding may have influenced the cross-sectional and/or longitudinal analyses.

This study has a number of limitations. Our exposure of interest is based on participants' dietary recall, and measurement error is inevitable. However, when compared to values from the typical American diet, values for daily sodium, protein, and caloric intake reported by these participants (Table 1) suggest underreporting across all exposure categories that should bias estimates toward the null if such misclassification is assumed to be nondifferential.[24] Conversely, as sodium intake has previously been shown to be higher in individuals with heavy regular soda consumption,[21] misclassification for this covariable may not be entirely random. Repeated-measures sensitivity analyses using dietary data from both visits 1 and 3 produced similar point estimates for our outcomes of interest, and multivariate models using a five-level category of exposure were consistent with our main models (Supplementary Table S2). We did not have detailed information on participants' medications and therefore were unable to adjust for use of drugs that could affect uric acid (for example, diuretics) or creatinine (for example, ACE inhibitors or ARBs) measurements. Similarly, we lacked data regarding heavy metal exposure that could also have affected uric acid and creatinine levels.

Like most epidemiologic studies of CKD, our definition of CKD is based on a limited number of isolated creatinine measurements that were not repeated within 3 months to confirm a chronic reduction in GFR.[25] Nevertheless, the 3% prevalence and 8% incidence rates of CKD in this cohort are quite low when compared to national data (approximately 7% prevalence of eGFR<60 ml/min per 1.73 m^2 among all US adults),[26] particularly given the age of ARIC participants. The probable underdiagnosis of CKD in this cohort, if anything, biased our results again toward the null. Furthermore, sensitivity analyses using a

more conservative definition of incident CKD and defining incident CKD by continuous changes in serum creatinine and eGFR produced similar results. Further, ancillary ARIC data on urinary albumin excretion from visit 4 found no association between increased soda consumption and either micro- or macro-albuminuria (Supplementary Table S3). The prevalence and incidence rates of hyperuricemia in this study were slightly higher than the national average (18% prevalence rate for all US adults),[4] but this is likely explained by the age of ARIC participants as our data concur with the prevalence of hyperuricemia published in a large middle-aged cohort in which the baseline prevalence approached 50%.[5]

Finally, our results strictly pertain to the intake of sugar-sweetened sodas in a generally healthy cohort; for these individuals, sugar-sweetened sodas were not associated with incident hyperuricemia and kidney disease. These findings do not justify unbridled consumption of sugar-sweetened sodas by individuals with and without CKD. Rather, our study is an important addition to the large and still-growing body of literature surrounding the potential health consequences of sugar-sweetened soda, which is based principally on observational studies such as this one.[12–15] Our 'negative' study results—subject to the same potential sources of error (bias, chance, confounding) as others' 'positive' study results — should be used to further inform, rather than end, the heated debate regarding this important public health issue. In addition, this study should not be interpreted as suggesting that uric acid does not have a role in the development of kidney injury and CKD, as shown in recent studies.[5–8] This study is similar to the recently published study by Forman *et al*. that found no association between fructose intake and the risk for incident hypertension over 14–20 years of follow-up[27] despite substantial evidence that elevated uric acid levels increase the risk for developing hypertension.[28–33] In fact, in both our cross-sectional and longitudinal studies, increased consumption of sugar-sweetened sodas in the presence of very elevated uric acid levels (≥9.0 mg/dl) did appear to influence development of kidney disease, although only 812 subjects had uric acid levels ≥9 mg/dl at the baseline visit, and only 64 (8%) drank more than one soda per day, so caution should be used when interpreting the results.

In this large biracial cohort, high consumption of sugar-sweetened sodas appeared to be associated with prevalent hyperuricemia and CKD. In stratified analysis, the association between soda and kidney function became more pronounced as uric acid levels increased. However, similar associations were not seen in longitudinal analyses of incident hyperuricemia and CKD. Therefore, our findings add to but in no way close the heated discussion over the potential dangers of sugar-sweetened soda.[12,13,15–17,33,34]

MATERIALS AND METHODS

Participants and study design

Data were obtained from the ARIC Study, a prospective biracial observational cohort assembled from four field centers in Jackson, Mississippi; Forsyth County, North Carolina; suburban Minneapolis, Minnesota; and Washington County, Maryland. A full description of ARIC is available elsewhere.[35] A total of 15,792 participants, men and women aged 45–64 years, were enrolled at the baseline visit (visit 1) between 1987 and 1989. Three follow-up visits occurred approximately every 3 years at community-based clinics. In addition to physical examinations and laboratory studies at each visit, surveys were also administered to each participant to obtain demographic data, medical history, and social habits. Included in these surveys were detailed food frequency questionnaires (FFQs) for dietary intake data. This study uses laboratory and questionnaire data from visits 1, 2, 3, and 4. The ARIC protocol was approved by the institutional review boards of all participating centers. Informed consent was obtained from all participants.

Outcomes

The outcomes of interest were prevalent and incident hyperuricemia and CKD. Serum uric acid (mg/dl) was evaluated at the first and second visits. We defined hyperuricemia using sex-specific cut points of >5.7 mg/dl in women and >7.0 mg/dl in men as suggested by the literature.[4,36–38] For sensitivity analyses, we used a gender-neutral definition of hyperuricemia as >7.0 mg/dl. We also divided participants into five categories of uric acid levels at visit 1 (<6.0, 6.0–6.9, 7.0–7.9, 8.0–8.9, and >9.0 mg/dl) and changes in uric acid levels between visits 1 and 2 (≤0.0, 0.1–1.0, 1.1–2.0, 2.1–3.0, and >3.0 mg/dl) for stratified analyses of our CKD outcomes.

Kidney function was evaluated at the first, second, and fourth visits by serum creatinine (mg/dl). We calculated eGFR using the Modification of Diet in Renal Disease formula.[39] ARIC creatinines were calibrated by subtracting 0.24 mg/dl at visits 1 and 2 and adding 0.18 mg/dl at visit 4, as published elsewhere.[5] Consistent with current guidelines on classifying CKD,[25] we defined prevalent CKD as a baseline eGFR <60 ml/min per 1.73 m^2. For analyses of incident CKD, we excluded all participants with eGFR <60 ml/min per 1.73 m^2 at visit 1, and, for the remaining participants, we defined incident CKD as eGFR <60 ml/min per 1.73 m^2 at visits 2 and 4, at visit 2 with missing data at visit 4, at visit 4 with missing data at visit 2, and at visit 4 alone. For sensitivity analyses, we used a conservative definition of incident CKD that included only those participants with complete data at visits 1, 2, and 4 whose eGFR dropped from ≥60 ml/min per 1.73 m^2 at visit 1 to <60 ml/min per 1.73 m^2 at visits 2 and 4, as well as a definition for incident kidney disease based on change in serum creatinine (>0.4 mg/dl or >150% increase).

Predictors

At ARIC visits 1 and 3, participants completed a 66-item semiquantitative FFQ developed and validated by Willett *et al*.[40] Sugar-sweetened soda consumption was determined from FFQs administered at visit 1, using data from the question on ‘regular soft drinks, such as Coke, Pepsi, 7Up, Ginger Ale.’ As mentioned in the introduction, the HFCS used to sweeten these soft drinks is typically ≤55% fructose, the other components being glucose and readily hydrolyzable polymers of glucose. Participants were allowed nine potential responses (in glasses): almost never, 1–3 per month, 1 per week, 2–4 per week, 5–6 per week, 1 per day, 2–3 per day, 4–6 per day, and >6 per day. We collapsed these responses into three levels: less than one soda per day, one soda per day, and more than one soda per day. We chose this categorization scheme to capture significant degrees of exposure with easily communicable levels of beverage intake. We used the same three-category exposure scheme to evaluate whether diet soda intake (assessed in a virtually identical question on the dietary survey) was associated with our outcomes of interest. In sensitivity analyses, we also used a five-level exposure category for soda consumption: almost never, no more than one soda per week, 2–6 sodas per week, one soda per day, and more than one soda per day. Finally, dietary data from visit 3 of the study were included in sensitivity analyses of the longitudinal studies using the highest exposure category from either visit 1 or 3 and the mean of data from both FFQs.

Other baseline characteristics included demographics, lifestyle and dietary characteristics, medical history, and physical examination findings. A composite variable for race and field center was used given that approximately 90% of the African-American participants were enrolled at the Jackson site. Tobacco and alcohol were dichotomized by current use. Diabetes was defined by medication use or fasting glucose level ≥126 mg/dl. Hypertension was defined by systolic pressure ≥140 mm Hg, diastolic pressure ≥90 mm Hg, or use of antihypertensive medication. Daily nutrient intakes were derived from the baseline FFQ responses using the Harvard nutrient database.

Statistical analyses

Prevalence odds ratios were obtained using univariate and multivariate logistic regression. Logistic regression was also used to assess the relationship between baseline soda consumption, incident hyperuricemia, and incident CKD because we could not determine specific time points at which an individual met our criteria for hyperuricemia or CKD. We used proportional hazards models for secondary analyses of both prevalent and incident outcomes (for prevalent outcomes, we set a constant time interval,[41] and for incident outcomes, we set the time interval to be the halfway point between visit 1 and the visit at which CKD or hyperuricemia were first identified). To isolate the potential effects of HFCS, we performed parallel analyses using diet soda, instead of regular soft drinks, as the main exposure. Because hyperuricemia was felt to be a causal intermediate in the association of sugar-sweetened soda consumption and CKD, we analyzed these outcomes separately and in stratified analyses.

Potential covariates for each outcome were based on directed acyclic graphs[42] and included age, sex, animal protein intake, sodium intake, caloric intake, caffeine intake, education, diabetic status, hypertensive status, body mass index, renal function, current tobacco and alcohol use, ARIC field center, and race. All covariates were treated as continuous variables when appropriate. We evaluated effect-measure modification by each covariate using likelihood ratio tests that compared models with and without interaction terms. A conservative *P*-value of 0.15 for such tests of interaction identified no important interactions; by choosing $P<0.15$ as the threshold, we reduced the risk of a type II error (that is, a false negative for the test of interaction). After univariate analysis, a parsimonious adjusted model was constructed using change-in-estimate testing for each covariate against a full model that included all directed acyclic graph-identified covariates. The parsimonious models included only those covariates that, when removed from the fully adjusted model, changed the exposure estimates by ≥10%. Finally, we performed analyses for full models that included all covariates, regardless of significance testing, that were identified as potential confounders by the directed acyclic graphs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline characteristics of study population, stratified by sugar-sweetened soda consumption

	<1 soda per day (*n*=12,981)	1 soda per day (*n*=1902)	>1 soda per day (*n*=862)
Age	54.4 (5.8)	53.6 (5.7)	52.0 (5.5)
Female	7373 (56.8%)	919 (48.3%)	398 (46.2%)
Race			
White	9882 (76.1%)	1004 (52.8%)	572 (66.4%)
Black	3056 (23.5%)	895 (47.1%)	288 (33.4%)
Other	43 (0.3%)	3 (0.2%)	2 (0.2%)
Years completed education			
≤11 years	2804 (21.6%)	667 (35.2%)	276 (32.1%)
12–16 years	5286 (40.8%)	738 (38.9%)	373 (43.3%)
≥17 years	4872 (37.6%)	492 (25.9%)	212 (24.6%)
Current smoking	3146 (24.3%)	638 (33.6%)	333 (38.7%)
Current alcohol use	7462 (57.6%)	861 (45.4%)	441 (51.3%)
Body mass index (kg/m^2)	27.6 (5.3)	28.1 (5.7)	27.9 (5.7)
Hypertension[a]	4479 (34.7%)	710 (37.5%)	294 (34.3%)
Diabetes[b]	1604 (12.5%)	187 (10.0%)	73 (8.5%)
Caloric intake (kcal/day)	1547.0 (581.0)	1748.2 (649.2)	2010.5 (744.8)
Sodium intake (mg/day)	1456.1 (589.8)	1537.2 (610.6)	1635.0 (673.4)
Animal protein intake (g/day)	53.3 (23.7)	54.4 (23.8)	55.9 (25.1)
Serum creatinine (mg/dl)	1.1 (0.4)	1.1 (0.5)	1.1 (0.2)
Estimated GFR (ml/min per 1.73 m^2)[c]	91.2 (20.6)	94.6 (24.0)	94.1 (21.3)
Serum uric acid (mg/dl)	6.0 (1.5)	6.2 (1.6)	6.3 (1.6)

Abbreviations: ARIC, atherosclerosis risk in communities; GFR, glomerular filtration rate.

Categorical data presented as *n* (%); continuous data presented as mean (s.d.).

[a] Hypertension defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or use of antihypertensive medication(s).

[b] Diabetes defined as previous diagnosis of diabetes, use of hypoglycemic medications, or fasting blood glucose ≥126mg/dl.

[c] Estimated glomerular filtration rate calculated from serum creatinine by the Modification ofDiet in Renal Disease (MDRD) formula with calibration for ARIC creatinine values: $eGFR=186 \times (\text{serum creatinine}-0.24)^{-1.154} \times (\text{age})^{-0203} \times 1.212$ (if black) × 0.742 (if female).

Table 2

Association of sugar-sweetened soda consumption with prevalent hyperuricemia and CKD

	< 1 soda per day Odds ratio (95% CI)	1 soda per day Odds ratio (95% CI)	> 1 soda per day Odds ratio (95% CI)
(a) Hyperuricemia, defined by sex-specific cut points (>5.7 mg/dl in women, >7.0 mg/dl in men)			
Univariate analysis	1.00 (referent)	1.17 (1.06–1.29)	1.20 (1.04–1.38)
Parsimonious model[a]	1.00 (referent)	1.17 (1.06–1.29)	1.20 (1.04–1.38)
Multivariate model[b]	1.00 (referent)	1.12 (1.01–1.25)	1.31 (1.12–1.53)
(b) Chronic kidney disease, defined by estimated GFR <60 ml/min per 1.73 m^2			
Univariate analysis	1.00 (referent)	0.88 (0.65–1.18)	1.02 (0.69–1.51)
Parsimonious model[c]	1.00 (referent)	1.03 (0.76–1.39)	1.22 (0.81–1.83)
Multivariate model[d]	1.00 (referent)	1.14 (0.84–1.55)	1.46 (0.96–2.22)

Abbreviation: GFR, glomerular filtration rate.

[a] Change in estimate testing for hyperuricemia suggested that univariate analysis was also the appropriate parsimonious model (i.e., no covariates, when removed from the fully adjusted model, changed the exposure estimates by >10%).

[b] Multivariate model for hyperuricemia adjusted for age, sex, animal protein intake, caffeine intake, hypertension, body mass index, renal function, current tobacco and alcohol use, ARIC field center, and race.

[c] Change in estimate testing for chronic kidney disease suggested a model adjusted only for diabetes, sodium intake, and the composite covariate of ARIC field center, and race.

[d] Multivariate model for chronic kidney disease adjusted for age, sex, body mass index, sodium intake, caloric intake, hypertension, diabetes, current tobacco and alcohol use, education, ARIC field center, and race.

Table 3

Adjusted odds ratios of prevalent CKD according to sugar-sweetened soda consumption, stratified by uric acid status

	< 1 soda per day Odds ratio (95% CI)[a]	1 soda per day Odds ratio (95% CI)[a]	> 1 soda per day Odds ratio (95% CI)[a]
Hyperuricemia, defined by sex-specific cut points [b]			
Absent	1.00 (referent)	1.46 (0.81–2.60)	0.76 (0.23–2.45)
Present	1.00 (referent)	1.00 (0.69–1.44)	1.50 (0.95–2.37)
Hyperuricemia, defined as serum uric acid >7.0 mg/dl			
Absent	1.00 (referent)	1.17 (0.70–1.79)	0.64 (0.26–1.58)
Present	1.00 (referent)	1.15 (0.75–1.74)	1.96 (1.18–3.25)
Uric acid levels (mg/dl)			
Uric acid <6.0	1.00 (referent)	1.17 (0.61–2.22)	0.28 (0.04–2.03)
6.0 ≤uric acid <7.0	1.00 (referent)	1.08 (0.52–2.24)	0.68 (0.21–2.25)
7.0 ≤uric acid <8.0	1.00 (referent)	0.93 (0.42–2.03)	1.31 (0.49–3.49)
8.0 ≤uric acid <9.0	1.00 (referent)	0.82 (0.37–1.81)	1.72 (0.63–4.67)
Uric acid ≥9.0	1.00 (referent)	1.59 (0.82–3.10)	2.59 (1.18–5.71)
Uric acid levels (mg/dl) [c]			
Uric acid <6.0	1.00 (referent)	1.17 (0.61–2.22)	0.28 (0.04–2.03)
6.0 ≤uric acid <7.0	2.34 (1.71–3.20)	2.09 (1.03–4.23)	1.62 (0.50–5.21)
7.0 ≤uric acid <8.0	3.21 (2.28–4.53)	3.18 (1.50–6.76)	4.41 (1.72–11.31)
8.0 ≤uric acid <9.0	7.60 (5.30–10.89)	6.63 (3.06–14.39)	11.00 (4.15–29.10)
Uric acid ≥9.0	12.05 (8.25–17.61)	20.03 (10.57–37.95)	31.32 (15.19–64.58)

[a] Adjusted for age, sex, body mass index, sodium intake, caloric intake, hypertension, diabetes, current tobacco and alcohol use, education, ARIC field center, and race.

[b] Hyperuricemia defined as serum uric acid >7.0 mg/dl in men and >5.7 mg/dl in women.

[c] Ancillary analyses using a common referent group of participants with uric acid levels <6.0 mg/dl and soda consumption <1 per day.

Table 4

Association of sugar-sweetened soda consumption with incident (a) hyperuricemia and (b) CKD

	<1 soda per day Odds ratio (95% CI)	1 soda per day Odds ratio (95% CI)	>1 soda per day Odds ratio (95% CI)
(a) Hyperuricemia, defined by sex-specific cut points (>5.7 mg/dl in women, >7.0 mg/dl in men)			
Univariate analysis	1.00 (referent)	1.23 (1.07–1.40)	1.23 (1.02–1.49)
Parsimonious model[a]	1.00 (referent)	1.09 (0.96–1.25)	1.17 (0.97–1.42)
Multivariate model[b]	1.00 (referent)	1.11 (0.97–1.28)	1.17 (0.95–1.43)
(b) Chronic kidney disease, defined by estimated GFR <60 ml/min per 1.73 m^2			
Univariate analysis	1.00 (referent)	0.70 (0.57–0.87)	0.60 (0.43–0.83)
Parsimonious model[c]	1.00 (referent)	0.77 (0.63–0.96)	0.69 (0.49–0.95)
Multivariate model[d]	1.00 (referent)	0.86 (0.69–1.06)	0.82 (0.59–1.16)

Abbreviation: GFR, glomerular filtration rate.

[a] Change in estimate testing for hyperuricemia suggested a model adjusted only for the composite covariate of ARIC field center and race.

[b] Multivariate model for hyperuricemia adjusted for age, sex, caffeine intake, animal protein intake, hypertension, body mass index, renal function, current tobacco and alcohol use, ARIC field center, and race.

[c] Change in estimate testing for chronic kidney disease suggested a model adjusted only for caloric intake and the composite covariate of ARIC field center and race.

[d] Multivariate model for chronic kidney disease adjusted for age, sex, body mass index, sodium intake, caloric intake, hypertension, diabetes, current tobacco and alcohol use, education, ARIC field center, and race.

Table 5

Adjusted odds ratios of incident kidney disease according to sugar-sweetened soda consumption, stratified by uric acid status

	<1 soda per day Odds ratio (95% CI)[a]	1 soda per day Odds ratio (95% CI)[a]	>1 soda per day Odds ratio (95% CI)[a]
Hyperuricemia[b] at visit 1			
Absent	1.00 (referent)	0.68 (0.49–0.96)	0.61 (0.35–1.06)
Present	1.00 (referent)	1.03 (0.77–1.38)	1.01 (0.65–1.56)
Development of hyperuricemia[b] between visits 1 and 2[c]			
Absent	1.00 (referent)	0.57 (0.35–0.94)	0.84 (0.45–1.57)
Present	1.00 (referent)	0.81 (0.50–1.31)	0.32 (0.10–1.03)
Change in uric acid levels between visits 1 and 2 (mg/dl)			
Δ Uric acid ≤0.0	1.00 (referent)	1.07 (0.72–1.59)	1.34 (0.75–2.39)
0.0 <Δ Uric acid ≤1.0	1.00 (referent)	0.74 (0.51–1.08)	0.83 (0.49–1.40)
1.0 <Δ Uric acid ≤2.0	1.00 (referent)	0.74 (0.45–1.21)	0.46 (0.18–1.15)
2.0 <Δ Uric acid ≤3.0	1.00 (referent)	0.81 (0.36–1.82)	0.31 (0.04–2.43)
Δ Uric acid >3.0	1.00 (referent)	1.35 (0.46–4.00)	2.47 (0.41–15.07)
Uric acid levels at visit 1 (mg/dl)			
Uric acid <6.0	1.00 (referent)	0.63 (0.43–0.92)	0.63 (0.35–1.14)
6.0 ≤Uric acid <7.0	1.00 (referent)	1.00 (0.65–1.53)	0.57 (0.26–1.25)
7.0 ≤Uric acid <8.0	1.00 (referent)	1.33 (0.83–2.12)	0.74 (0.33–1.68)
8.0 ≤Uric acid <9.0	1.00 (referent)	0.87 (0.44–1.69)	0.72 (0.25–2.12)
Uric acid ≥9.0	1.00 (referent)	0.57 (0.19–1.73)	3.90 (1.55–9.82)
Uric acid levels at visit 1 (mg/dl)[d]			
Uric acid <6.0	1.00 (referent)	0.63 (0.43–0.92)	0.63 (0.35–1.14)
6.0 ≤Uric acid <7.0	1.30 (1.09–1.55)	1.32 (0.88–1.98)	0.72 (0.33–1.55)
7.0 ≤Uric acid <8.0	1.62 (1.31–1.99)	2.00 (1.29–3.09)	1.25 (0.57–2.75)
8.0 ≤Uric acid <9.0	2.06 (1.58–2.68)	1.84 (0.98–3.44)	1.50 (0.53–4.27)
Uric acid ≥9.0	1.87 (1.34–2.62)	0.97 (0.34–2.73)	5.72 (2.64–12.36)

[a] Adjusted for age, sex, body mass index, sodium intake, caloric intake, hypertension, diabetes, current tobacco and alcohol use, education, ARIC field center, and race.

[b] Hyperuricemia defined as serum uric acid >7.0 mg/dl in men and >5.7 mg/dl in women.

[c] Analysis excludes participants with hyperuricemia at visit 1.

[d] Ancillary analyses using a common referent group of participants with uric acid levels <6.0 mg/dl and soda consumption <1 per day.