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# Dietary factors are associated with serum uric acid trajectory differentially by race among urban adults

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## Abstract

Serum uric acid (SUA), a causative agent for gout, is linked to dietary factors, perhaps differentially by race. Cross-sectional ($SUA_{base}$, i.e. baseline SUA) and longitudinal ($SUA_{rate}$; i.e. annual rate of change in SUA) associations of SUA with diet were evaluated across race and sex-race groups, in a large prospective cohort study of urban adults. Of 3,720 African-American (AA) and White urban adults participating in the Healthy Aging in Neighborhood of Diversity across the Life Span study, longitudinal data (2004–2013, k=1.7 repeats, follow-up, mean±SD:4.64±0.93y) on n=2,136 participants were used. The main outcome consisted of up to two repeated measures on SUA. Exposures included the dietary factors "added sugar", "alcoholic beverages", "red meat", "total fish", "legumes", "total dairy", "caffeine", "vitamin C" and a composite measure termed "dietary urate index". Mixed-effects linear regression models were conducted, stratifying by race and by race×sex. A positive association between legume intake and $SUA_{rate}$ was restricted to AA, while alcohol intake was positively associated with $SUA_{base}$ overall without racial differences. Added sugars were directly related to $SUA_{base}$ among White men ($P<0.05$ for race×sex interaction), while dairy intake was linked with slower $SUA_{rate}$ among AA women, unlike among White women. Nevertheless, dairy intake was associated with a lower $SUA_{base}$ among Whites. Finally, the dietary urate index was positively associated with both $SUA_{base}$ and $SUA_{rate}$, particularly among African-Americans. In sum, race and sex interactions with dietary intakes of

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**AUTHOR CONTRIBUTIONS**

M. A. B: wrote and revised the manuscript, planned analysis, performed data management and statistical analysis and had primary responsibility for the final content; M. T. F-K: wrote and revised the manuscript, participated in data acquisition, plan of analysis and literature review; J. A. C: wrote and revised the manuscript, participated in the plan of analysis and literature review; H. A. B.: wrote and revised the manuscript and participated in literature search and review; M. K. E: wrote and revised the manuscript, participated in data acquisition; A. B. Z: Wrote and revised the manuscript, participated in data acquisition and plan of analysis. All authors read and approved the final version of the manuscript.

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added sugars, dairy and legumes were detected in determining SUA. Similar studies are needed to replicate these findings.

**Keywords**

Serum uric acid; diet; racial differences; urban adults

## INTRODUCTION

Gout is a painful medical condition characterized by urate crystal deposition in various joints and affecting 6–8% of the elderly (80+y) and ~3.9% of the entire US population.[1] Hyperuricemia, or elevated serum uric acid (SUA) is the principal causative agent behind gout and independently predicts myocardial infarction and premature death. [2] Furthermore, uric acid (UA) is the final catabolic product of purine oxidation.[3] Two key physiological mechanisms determine hyperuricemia, namely increased liver production of urate from dietary and/or endogenous substrates that raise purine levels and reduced renal and/or gut excretion of UA.[4]

In recent genome-wide association studies various genetic loci influencing SUA were identified. Those with strongest influence include *ABCG2*, NPT4(*SLC17A3*), NPT1(*SLC17A1*), URAT1(*SLC22A12*), OAT4(*SLC22A11*), and GLUT9(*SLC2A9*).[1] Notably, genetic variations on these loci differ markedly between race and ethnic groups. Given that certain risk alleles in combination can affect either SUA at one point in time or the rate of change in SUA, as was shown recently in a study among AA,[5] race can be a strong cross-sectional and/or longitudinal predictor of SUA.

In addition to the strong genetic influence on SUA, dietary factors may act either independently or interactively with the individual's genetic risk for hyperuricemia. Overall dietary patterns such as the Mediterranean Diet Score [6; 7] or specific dietary components have been shown to have equally important effects.[1] In fact, recent research[3; 8; 9; 10; 11; 12; 13] suggests that red meat and seafood consumption is positively linked with gout and/or hyperuricemia,[3; 10] with similar adverse effects observed in the case of alcohol intake (e.g. beer and liquor)[3; 8; 10; 11; 14; 15] and fructose-containing foods including soft drinks[3; 10; 12; 13], as well as intake of legumes in animal studies.[16] Conversely, other dietary factors were linked to lower SUA such as dairy products, particularly low-fat milk and yogurt,[3; 10; 11; 15] caffeine [3; 10; 15] and vitamin C[3; 10; 15] intakes. While most of these studies were conducted in one racial/ethnic group, there is paucity of evidence of an interaction between race and diet in affecting SUA over time.

Using dietary and SUA data available among urban adults participating in the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS), [17] this study evaluated the relationship between the eight previously described dietary factors and SUA at baseline and change over-time, while examining race and sex-race interactions in those associations. We hypothesize that the relationship between various dietary factors and SUA over time varies appreciably according to race and race-sex groups.

# METHODS

## Database

HANDLS, a prospective cohort study, recruited at baseline a representative sample of African-American (AA) and White urban adults aged 30–64 years, residing in Baltimore city. The study design is described in detail previously. [17] In brief, data were collected at two phases during the baseline visit (2004–2009; visit 1), with Phase 1 examining socio-demographic information (age, sex, education, poverty status, etc.), physiological and psychological chronic exposure, and including the first 24-hr dietary recall. Phase 2 of the baseline visit consisted of in-depth examinations in a Mobile Research Vehicles (MRV) and included a second 24-hr dietary recall, psychometric, anthropometric, body composition and laboratory parameter measurements.[17] Initiated in 2009 and focusing on MRV in-depth examinations through 2013, visit 2 of HANDLS followed a similar protocol. Of all the data collected at the MRV during visit 2, only follow-up SUA was utilized in this study, using the same laboratory testing methods as in visit 1. Time elapsed between visits ranged between <1y and ~8y, with a mean of 4.64±0.93y.

Procedures followed the ethical standards of the institution and approval was obtained from The MedStar Institutional Review Board and written informed consent was obtained from all HANDLS participants.

## Study participants

Data were derived from baseline visit 1 (2004–2009) and the first follow-up examination (visit 2; 2009–2013), and were appended in long format to facilitate mixed-effects regression modeling analyses (N=number of persons, N′=Number of observations, k=Number of observations/person). Follow-up time (range:<1-~8y), had a mean±SD of 4.64±0.93y, with time=0 for the baseline visit and time=elapsed years to the nearest day for follow-up visit. HANDLS initially recruited $N_1$=3,720 participants (**Sample 1**), with total observations at both visits being $N_1'$=6,025. Among all HANDLS participants, complete baseline dietary data with 2 24 hr recalls was available for 2,177 participants (**Sample 2**). Of these, 39 had missing data on SUA at both visits and thus were excluded. The final sample (**Sample 3a**), consisted of 2,138 participants with complete data on dietary intakes at baseline and SUA data at either visit ($N'_{3a}$=3,661, k=1.7). **Sample 3a** differed from the unselected participants of **Sample 1**, by having a higher proportion of women (56.5% vs. 52.3%, p=0.010), with no notable differences by poverty status or age (Figure S1). This potential sample selectivity was adjusted for in the analysis using 2-stage Heckman selection approach (See statistical methods).

## Serum uric acid (SUA)

Using 1 ml of fasting blood serum, SUA concentration was measured with a standard spectrophotometry method at both visits of HANDLS (Quest Diagnostics, Chantilly, VA). Reference ranges for adults are 4.8–8.0 mg/dL for men and 2.5–7.0 mg/dL for women.

## Dietary assessment

All dietary factors considered in this study, were measured at the baseline visit. Both baseline 24-hour dietary recalls were measured using the US Department of Agriculture (USDA) Automated Multiple Pass Method, a computerized structured interview.[18] Using measurement aids such as measuring cups, spoons, ruler, and an illustrated Food Model Booklet, both recalls were administered in-person by trained interviewers, 4–10 days apart. Trained nutrition professionals utilized Survey Net, matching foods consumed with 8-digit codes from the Food and Nutrient Database for Dietary Studies version 3.0.[19]

My Pyramid Equivalents Database (MPED) for food groups (MPED 2: http://www.ars.usda.gov/SP2UserFiles/Place/80400530/pdf/mped/mped2_doc.pdf) were used to create food groups. Eight dietary factors were selected based on previous evidence of an association with variations in SUA: **(1)** added sugars (tsp/d or ~4.2 grams/d), **(2)** alcoholic beverages (drinks/d, with 1 drink defined as 12 fluid ounces of beer, 5 fluid ounces of wine, or 1½ fluid ounces of 80-proof distilled spirits; 1 grams~=0.03 fl oz), **(3)** ounce equivalents/d of red meats (1 oz=28.3 grams), **(4)** ounce equivalents/d of fish (sum of fish high and low in omega-3 fatty acids), and **(5)** cup equivalents/d of legumes, **(6)** cup equivalents/d of dairy products (milk, cheese and yogurt), **(7)** dietary vitamin C from foods in mg/d, and **(8)** caffeine from all sources (g/d); the later three were associated with reduced SUA. [3; 10] Each of these dietary factors were estimated as the mean from the two dietary assessments completed at phases 1 and 2 of visit 1, 4–10 days apart. Thus, dietary assessments at visit 2 were not utilized in this present study.

In addition, a dietary urate index was computed based on quintiles of each of the 8 components, 5 of which were then summed up to create the total score (Added sugar, alcohol, red meat, legumes and fish), while components 6 through 8 (Dairy, vitamin C and caffeine) were subtracted from the index given their putative inverse relationship with SUA. Thus, the total score could potentially range between −10 (lowest risk of hyperuricemia due to diet) and +22 (highest risk of hyperuricemia due to diet) (Supplemental Method 1).

## Supplemental vitamin C

In a secondary analysis, supplemental vitamin C intake was also considered among the main exposure variables, controlling for all other exposures and covariates. A dietary supplement questionnaire adapted from NHANES 2007–08 was used [20] Each visit 2 participant provided supplement bottles and reported information on Over-The-Counter (OTC) vitamin and mineral supplements, antacids, prescription supplements, and botanicals. Supplement users were further probed on dose strength, dose amount consumed and length of supplement use (converted to days) among others.

A database consisting of 4 files was integrated to generate daily intake of each nutrient consumed by a dietary supplement user. [See detailed description at the HANDLS study website: https://handls.nih.gov/]. Vitamin C supplemental intake was ascertained for the baseline visit (i.e. visit 1) if the daily amount (mg/d) was non-zero at visit 2 and the length of time for intake was greater or equal than the length of time (days) between the two visits, per participant. Thus, participants' supplemental use was categorized as either either 0: non-

vitamin C containing supplement user at baseline or follow-up, 1: vitamin-C containing supplement user at baseline and during follow-up, 2: vitamin-C containing supplement user during follow-up only.

## Covariates

Covariates considered as potential confounders in the analyses included age, sex, education [<High School (HS) (grades 1–8), HS (grades 9–12), >HS (13+)], poverty status (household incomes below or above 125% of the 2004 Federal poverty guidelines), smoking status (current smoker vs. not use of cigarettes), illicit drug use (current vs. not use of either marijuana, cocaine or opiates), body mass index (BMI)=(measured weight)/(squared measured height), in $kg/m^2$, and other key food group servings obtained from the MPED2, [21] namely total fruits, total vegetables (cup equivalents/d), total grains (ounce equivalents/day), other meats (ounce equivalents/d), and discretionary solid fats and oils (g/d). Race (AA vs. Whites) was the main effect modifier in these analyses.

## Statistical methods

Using Stata 15.0.,[22] weighted means and proportions were estimated and compared across race groups, using design-based F-test (svy:tab for categorial variables and svy:reg for continuous variables). Boxplots of baseline and follow-up SUA were also presented and compared by race, using a linear regression model that accounted for sampling weights.[23] $SUA_{base}$ and $SUA_{rate}$ empirical bayes estimators were obtained from a mixed-effects linear regression model with TIME as the only predictor. These two parameters are presented among characteristics stratified by race and by sex within each race group. Importantly, several sets of time-interval mixed-effects regression models were conducted with the outcome being SUA measured at either visits 1 or 2, while assuming missingness at random.[24] In fact, only individuals with SUA missing at both visits were excluded from the model (Supplemental Method 2).

In a first model set, 8 dietary components predicted baseline SUA ($SUA_{base}$) and annual rate of change in SUA ($SUA_{rate}$), overall and stratifying by race. Type I error in analyses examining dietary factors was corrected for multiple testing using Bonferroni correction, assuming an initial type I error rate of 0.05 for main effects and 0.10 for 2-way interaction terms and 0.20 for 3-way interaction terms, yielding a corrected error rates of 0.05/8=0.006, 0.10/8=0.013 and 0.20/8=0.025, respectively. [25; 26] The same model was carried out with main exposure being the composite measure dietary urate index and thus excluding all individual components but retaining all other food groups and covariates. No correction for multiple testing was done for this model (i.e. type I error was 0.05 for main effects, 0.10 for 2-way interaction terms and 0.20 for 3-way interaction terms). In a third model, the main exposure of interest was vitamin C-containing supplement use (baseline, follow-up vs. none). No correction for multiple testing was done for these latter models.

In a second model set, stratifying the analysis by sex, race-diet interactions were tested, whereby each of 8 dietary factors were separately interacted with race to test their interactive effects on $SUA_{base}$. Similarly, 3-way interactions between each dietary component, time and race were also examined in separate models. Predictive margins were estimated and plotted

across time, stratifying by exposure group, from selected mixed-effects regression models. This process was repeated for the dietary urate index and the vitamin C-containing supplement use, as above, without correction for multiple testing.

Moreover, selection bias caused by non-random participant self-selection into the final sample as compared to the target study population can occur. To reduce its impact, a 2-stage Heckman selection process was carried out whereby a probit model was used to compute an inverse mills ratio at the first stage (derived from the predicted probability of being selected, conditional on the covariates in the probit model, mainly baseline age, sex, race, poverty status and education). At the second stage, this inverse mills ratio was entered as a covariate into the final mixed-effects regression model, as was done in previous studies.[27; 28] A number of sensitivity analyses were also carried out, including additional covariates (e.g. total energy intake, use of diuretics) and excluding subjects with only one SUA measurement among others.

## RESULTS

Table 1 describes baseline characteristics of the study sample by race. While 57.9% of the sample consisted of AA, and 45.4% were men, mean age overall was estimated at 46.9y. Poverty status, current smoking and drug use were more prevalent among AA compared to Whites. Whites consumed greater amounts of legumes, dairy products, caffeine, and total grains, fruit, and vegetables, while the reverse was true for fish, and other meats. The dietary urate index differed markedly by race (P<0.001), with AAs consuming a significantly more hyperuricemic diet compared to Whites. Only a marginally significant association between vitamin C-containing supplement use and race was detected indicating a more prolonged use among Whites (Table 1). Predicted $SUA_{base}$ and $SUA_{rate}$ from a simple linear mixed-effects regression model with only TIME as the main parameter, suggested that $SUA_{rate}$ (overall mean: +0.037 mg/dL) on average was suggestive of an upward sloping trajectory overall and among AAs, particularly AA men. $SUA_{base}$ (overall mean: 5.45 mg/dL) did not differ by race or sex within each race group. Figure S2 presents the race-specific mean SUA at baseline and at follow-up by race. Using a linear regression model accounting for sampling weights, each SUA mean was compared by race. AA had higher SUA at baseline compared to Whites, with no significant difference detected at follow-up. (Figure S2)

Several key findings emerged from the mixed-effects regression models (Tables 2–3). After correction for multiple testing, overall, a positive overall association of legume intake with $SUA_{rate}$ was restricted to AA [$\gamma$=+0.10±0.03, p=0.005], while alcohol intake was positively associated with $SUA_{base}$ in the total population [$\gamma$=+0.118±0.018, p<0.001], without racial differences [Table 2, Model A]. Other notable findings include a positive association between added sugars and $SUA_{base}$ in Whites, which was significantly stronger in that group compared to AA (p=0.045 for race×[added sugar] interaction is separate model with main effect of race added). In contrast, total dairy product intake was associated with slower rate of increase in SUA among AA (p=0.043 for race×dairy×TIME interaction term) and a lower $SUA_{base}$ among Whites. Moreover, vitamin C and caffeine both trended towards an inverse association $SUA_{base}$ without passing correction for multiple testing and no difference by race. In **Model B** of Table 2, dietary urate index was positively associated with $SUA_{base}$ and

$SUA_{rate}$, a finding that was mostly detected among AAs. Differences in SUA trajectories across levels of the dietary urate index are illustrated in Figure 1. Specifically, and as expected, a higher dietary urate index was linked to a higher $SUA_{base}$, with each 5-unit increase being linked to ~2% higher $SUA_{base}$ and each unit with a ~10% increase in $SUA_{rate}$. Finally, an inverse association was detected between follow-up use of vitamin C-containing supplements and $SUA_{rate}$ among Whites and baseline use and $SUA_{base}$ among AAs.

In Table 3, among women, a synergistic interaction between race and red meat consumption in relation to $SUA_{base}$ ($\gamma_{039}$=+0.080±0.039, p=0.040) was detected, whereby red meat consumption was associated with higher $SUA_{base}$ only among AA women, as opposed to White women. Importantly, and after correcting for multiple testing, added sugars were associated with higher $SUA_{base}$ particularly among White men with a significantly weaker association among AA men ($\gamma_{01}$=+0.013±0.004, p=0.001; $\gamma_{019}$=−0.010±0.005, p=0.037). In contrast, an inverse association between baseline dairy consumption and $SUA_{rate}$ was observed among AA women, with a significantly stronger association than among White women ($\gamma_{16}$=+0.016±0.011, p=0.69; $\gamma_{169}$=−0.45±0.018, p=0.015). Furthermore, the positive association between alcohol consumption and $SUA_{base}$ was similar between men and women, with no racial differences within each sex group. Finally, the dietary urate index's positive association with $SUA_{base}$ was restricted to men without racial differentials within that sex group.

In a sensitivity analysis, the use of diuretics (~7% of the total population) was entered as a potential confounding factor in the association between dietary factors and $SUA_{base}$ and/or $SUA_{rate}$. Our main findings were not significantly altered with this additional adjustment. A sensitivity analysis was also conducted adjusting for total energy intake. Given the comprehensive adjustment for many food groups, this further adjustment did not alter our findings. Excluding participants with only 1 SUA measurement, another sensitivity analysis was conducted on the main mixed-effects regression models (N=1,525, N′=3,050). The results remained largely unaltered.

## DISCUSSION

To our knowledge, this is the first study to evaluate cross-sectional ($SUA_{base}$) and longitudinal ($SUA_{rate}$) associations between selected dietary factors and SUA in a sample of urban adults, while examining race-specific and sex-race specific associations and interactions. Previous studies examined the relationship between diet and SUA and failed to test race or race by sex differences. Large prospective cohort studies found an association between meat and seafood intakes, and gout risk and elevated SUA concentrations.[3; 9] However, no association was found for other purine-rich foods such as peas, lentils, beans, spinach, mushrooms and cauliflower,[3] highlighting the importance of certain aspects of purines in foods, including amount, bioavailability and types.[3] The positive association between legume consumption and $SUA_{rate}$ was restricted to AA. This finding is novel and worth exploring further in larger adult samples. However, the positive association between legume intake and SUA was found only in animal studies. [16] In fact, a 1 cup equivalent increase in legume intake was associated with +0.07 increase in annual rate of change in

SUA (predicted mean $SUA_{rate}$=+0.03), a significant effect on the SUA trajectory, particularly among AAs. Thus, reducing the annual rate of increase in the SUA by half among AAs can be achieved by reducing intake of legumes to close to 0 cups per day among those who consume ~ ½ cup/day.

Fructose intake can influence SUA directly through liver ATP utilization for phosphorylation and production of ADP. In fact, oral fructose administration among hyperuricemic patients further increased SUA.[3; 29] Using national data (The third National Health and Nutrition Examination Survey, n= 14,761 adults), a dose-response relationship was identified between soft drink consumption and SUA, with an effect ranging from +0.08 mg/dl higher SUA (for <0.5 servings vs. no intake), to 0.42 mg/dl higher SUA (for ≥4 servings/day vs. no intake), p-trend=0.003. Similar findings were observed for sugar-sweetened soft drinks' relationship with hyperuricemia,[12] and were replicated only in men in another analysis of a recent NHANES wave of data (2001–02).[13] Examining gene-diet interactions, at least one study found a non-additive interaction between SLC2A9 genotype and sugar-sweetened beverage consumption in determining the risk of gout.[30] This present study detected an association between added sugars and $SUA_{base}$ only among White subjects, possibly due to genetic differences that would make White subjects more susceptible to hyperuricemia with increased consumption of sugars as opposed to AA. However, this association suggested that a reduction of added sugars from 35tsp to 5 tsp/day would only potentially alter $SUA_{base}$ by about 2–3%, a small effect considering that the target effect is usually closer to 10%. Nonetheless, larger epidemiological studies of adult populations are needed to verify those findings, and the underlying gene-diet interaction should be studied among both Whites and AA.

A recent meta-analysis of 42,924 adults reported a linear dose-response relationship between alcohol consumption and the risk for gout. Taking no/little alcohol drinking as a common referent, light (≤1 drink/day), moderate (>1 to <3 drinks/day) and heavy drinking (≥3 drinks/day) had a risk ratio, RR (95% CI) of 1.16 (1.07–1.25), 1.58 (1.50–1.66) and 2.64 (2.26–3.09), respectively.[31] Studies also showed that this positive association between alcohol and SUA pertained mostly to beer and liquor/spirits.[8] Similar to fructose, alcohol increases UA liver production through ATP degradation, leading to accumulation of ADP and AMP. In addition, alcohol intake leads to dehydration and metabolic acidosis, resulting in a decreased urate excretion.[3] Findings from this present study, however, indicated a positive association between alcoholic beverage consumption and $SUA_{base}$, without race or race by sex interaction. Similar to what was shown for added sugars, the effect size detected indicated that going from 2 drinks/d to 1 drinks/d (mean=1.5, SD=0.5) would reduce $SUA_{base}$ by 2%, a relatively weak effect. Thus, a large effect is only noticeable among heavy drinkers going from 5 drinks or more/d to 0–1 drinks/d. The same $SUA_{base}$ effect size was observed for the dietary urate index, going from −5 to 0 or from 0 to +5.

Vitamin C may also be inversely related to SUA based on a cross-sectional study [32] and a meta-analysis of randomized controlled trials that administered a median dose of 500mg/day.[33] Biological mechanisms involved include a uricosuric effect of vitamin C at the URAT1 and a sodium-dependent anion co-transporter SLCA5A8/A12; enhanced higher fractional kidney clearance of UA; and a lower oxidative damage of body cells which

reduces SUA.[15] In this present study, among men, low vitamin C was shown to increase $SUA_{base}$, with no significant interaction by race. Similarly, supplemental vitamin C was shown to be inversely related to $SUA_{rate}$ among Whites and $SUA_{base}$ among AAs. However, randomized controlled trials among men are needed to confirm this observation.

Several studies reported an inverse association between dairy product consumption and SUA/gout, [11; 15] suggesting for the most part a protective effect of milk and low-fat yogurt against gout occurrence and hyperuricemia.[9] The evidence also points to a tendency of vegan diet lacking dairy products to be more hyperuricemic than a vegetarian or a fish-eating type of diet, especially among men.[34] Several underlying mechanisms were suggested, including the effects of orotic acid in milk which enhances renal urate excretion, the uricosuric effect of milk casein and lactalbumin, and a potential biological relationship between vitamin D on SUA.[15] The current study found that $SUA_{rate}$ was negatively related to dairy intake, especially among AA women (significant interaction by race among women), though stratum-specific findings did not pass correction for multiple testing. Although milk constitutes a substantial portion of dairy consumption among HANDLS participants, yogurt on the other hand contributes little to the total serving of dairy among this population.

Finally, although some components of the dietary urate index had a stronger influence on SUA than others, the index itself was associated with both baseline and rate of change in SUA though only among AAs. Among the dietary quality indices, (higher in fruit, vegetables, nuts, whole grains, and low-fat dairy and lower in red meats) which incorporates many of the components used to create the dietary urate index has been shown to be effective in lowering blood pressure [35], serum homocysteine [36] and SUA [37; 38] which is more substantial among individuals with hyperuricemia. [39] In our sample, it was shown to have a weak to moderate inverse correlation with the dietary urate index. Several studies have examined the potential effect of DASH diet on SUA and gout. In a prospective study involving 44,444 men from the Health Professionals Follow-Up cohort with Rai and colleagues evaluated the relationship between the dietary patterns (DASH vs. Western) on the incident gout risk over a follow-up time of 26 years. They found that the DASH diet was associated with reduced risk whereas the Western diet was associated with increased risk of incident gout.[40] Juraschek and colleagues report the results of two ancillary studies from a randomized, crossover, clinical trial comparing the DASH diet to a control diet. In the first study, the authors evaluated the effect of dietary pattern assignment among 103 adults with prehypertension or stage I hypertension on change in serum uric acid level according to randomly assigned level of sodium consumption (low, medium, high). The study suggested that DASH diet was associated with reduced uric acid level, especially among patients with high baseline uric acid level and that high sodium level was also beneficial in terms of reducing uric acid level.[39] In the second study (in press), the authors examined the effect of partial DASH replacement among African American subjects with controlled hypertension who were assigned to the DASH-Plus intervention (coach-directed dietary advice, assistance with DASH-related food purchase, home food delivery) or the control (DASH brochure and debit account to purchase foods) and were followed-up from baseline until 8 weeks post-treatment to measure change in serum uric acid. The authors obtained similar results to the first study, suggesting a beneficial effect of the DASH diet on serum uric acid levels.[41]

Among its strengths, our present study systematically evaluated SUA's race-specific association with selected dietary factors, as well as simultaneous effect modification by sex and race. Despite its strengths, some limitations include a statistical power-limiting small sample size (See Supplemental Method 3), which precluded further adjustment for incomplete potential confounders, such as lipid profiles, ferritin, C-reactive protein and depressive symptoms. In fact, further analyses suggested that the power to detect the effect that was detected in the present study's models was more adequate for the total population than for race-stratified models. Another limitation is the lack of adequately measured baseline covariates that could potentially act as confounders, including baseline physical activity. Residual confounding could be of significant concern due to the lack of this covariate. Finally, the use of the dietary urate index, though a novel addition, was not conducted or validated elsewhere. Nevertheless, this index was found to be weakly but inversely correlated with the Healthy Eating Index (HEI-2010, $r = -0.17$, $P<0.001$), which was used in numerous studies including HANDLS.[42; 43; 44; 45; 46] Similarly, the dietary urate index was also weakly and inversely related to the Dietary Approaches to Stop Hypertension (DASH) and Mean Adequacy Ratio (MAR) diet quality total scores. Specifically, the dietary urate index when examined as quintiles was linearly and inversely associated with the following HEI-2010 components: total vegetables, total fruits, whole fruits, whole grains, dairy and the Solid Fat, alcohol and added sugars (SOFAAS) component. Most of the remaining HEI-2010 components were positively related to the dietary urate index. In the case of DASH components, those that have a shown a linear inverse relationship with the dietary urate index included: cholesterol, fiber, magnesium, calcium and potassium. Other components, however, such as saturated fat, fat and sodium were directly and linearly associated with the dietary urate index (Table S1, supplemental methods 1). Similarly, a higher dietary urate index was specifically inversely related to the calcium, magnesium, vitamins B1, B2, C and D as well as the folate components of the MAR score.

In sum, race and sex interactions with dietary intakes were detected in determining SUA. Specifically, added sugar's positive association with $SUA_{base}$ was restricted to White men whereas the inverse association of dairy consumption on $SUA_{rate}$ was restricted to AA women. Similarly, $SUA_{rate}$ was positively linked to legume consumption only among AA. Nevertheless, the positive association between alcohol consumption and $SUA_{base}$ was largely similar across race and sex groups. Supplemental vitamin C may have putative protective effects among both Whites and AAs. Further studies of similar adult populations and incorporating larger samples of urban adults are needed to replicate these findings.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## ABBREVIATIONS

| | |
|---|---|
| **AA** | African-American |
| **Base** | baseline |
| **BMI** | Body Mass Index |
| **HANDLS** | Healthy Aging in Neighborhoods of Diversity Across the Life Span |
| **HS** | High School |
| **MPED** | Mypyramid Equivalents Database |
| **NHANES** | National Health and Nutrition Examination Surveys |
| **OSM** | Online Supplemental Material |
| **Rate** | Rate of change |
| **SEE** | Standard Error of the Estimate |
| **SUA** | Serum Uric Acid |
| **$SUA_{base}$** | baseline serum uric acid concentration |
| **$SUA_{rate}$** | annual rate of change in serum uric acid concentration |
| **US** | United States |
| **USDA** | United States Department of Agriculture |

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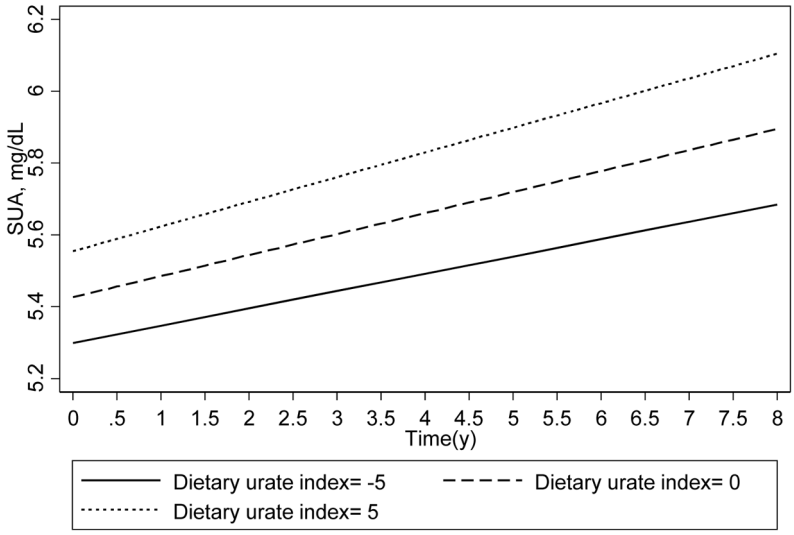


**Figure 1.**

Predictive margins of SUA by Time and the dietary urate index, from mixed-effects regression model, among urban adults participating in the HANDLS with complete data on SUA at either of 2 visits (N=2,138), 2004–2013[a]

[a]Predictive margins obtained from mixed-effects regression model with SUA as the outcome, random effects added to slope and intercept, and both slopes and intercept adjusted for multiple factors including age, sex, race, poverty status, marital status, education, smoking and drug use, several dietary factors, BMI, and an inverse mills ratio. The Figure simulates the trajectory of a population with comparable characteristics (covariates set at their observed values in the sample) when exposed alternatively to 3 values of the dietary urate index (−5, 0, 5)

## TABLE 1

Baseline study dietary factors and covariates by race among urban adults participating in the HANDLS study and with complete data on SUA at either of two visits (N=2,138), 2004–2013

| | ***Total* (N=2,138)** | ***By Race*** | | **p[a]** |
|---|---|---|---|---|
| | | **Whites (N=903)** | **African-Americans (N=1,238)** | |
| **Age**, *Mean±SEM* | 46.9±0.3 | 46.2±0.4 | 47.2±0.4 | 0.11 |
| **Sex,** % men | 45.4 | 45.8 | 45.1 | 0.84 |
| **Marital status, %** | | | | **<0.001** |
| Married | **33.5** | **43.7** | **27.8** | |
| Missing | **3.8** | **3.5** | **3.9** | |
| **Education, %** | | | | **<0.001** |
| <High School | **4.3** | **5.8** | **3.5** | |
| High School | **53.4** | **40.6** | **60.4** | |
| > High School | **42.2** | **53.6** | **36.0** | |
| Missing | **0.1** | **0.0** | **0.1** | |
| **Poverty Income Ratio<125%, %** | **19.4** | **11.4** | **23.9** | **<0.001** |
| **Current smoking status** | | | | **<0.001** |
| Yes, % | **43.0** | **34.6** | **47.6** | |
| Missing, % | **5.2** | **3.7** | **6.0** | |
| **Current illicit drug use** | | | | **<0.001** |
| Yes, % | **17.1** | **9.1** | **21.5** | |
| Missing, % | **7.6** | **10.4** | **6.0** | |
| **Body mass index**, *Mean±SEM* | 29.4±0.3 | 29.1±0.3 | 29.5±0.4 | 0.41 |
| **Key dietary intake factors**, *Mean±SEM* | | | | |
| Added sugars, tsp/d | 20.7±0.7 | 19.4±0.7 | 21.4±1.0 | 0.10 |
| Alcoholic beverages, drinks/d | 0.67±0.06 | 0.62±0.07 | 0.69±0.10 | 0.52 |
| Red meat, oz equiv/d | 1.70±0.09 | 1.76±0.11 | 1.66±0.12 | 0.56 |
| Fish, oz equiv/d | **0.97±0.08** | **0.67±0.07** | **1.13±0.11** | **0.001** |
| Legumes, cup equiv/d | **0.04±0.00** | **0.06±0.01** | **0.03±0.01** | **0.003** |
| Dairy products, cups equiv/d | **1.12±0.04** | **1.45±0.06** | **0.94±0.05** | **<0.001** |
| Vitamin C, mg/d | 79.2±2.9 | 74.8±4.0 | 81.6±3.9 | 0.22 |
| Caffeine, mg/d | **130±5** | **223±10** | **79±4** | **<0.001** |
| Dietary urate index | 2.89±0.14 | 1.84±0.19 | 3.48±0.19 | **<0.001** |
| Vitamin C-containing supplement | (N=1,521) | (N=605) | (N=916) | 0.051 |
| None | 64.6±2.2 | 62.1±2.7 | 65.8±3.0 | |
| Baseline and follow-up | 9.7±1.3 | 13.9±1.8 | 7.6±1.8 | |
| During follow-up only | 25.7±2.1 | 23.9±2.4 | 26.6±2.9 | |
| **Other dietary intake factors**, *Mean±SEM* | | | | |
| Total grains, oz equiv/d | **6.14±0.13** | **6.68±0.18** | **5.84±0.18** | **0.001** |
| Total fruits, cup equiv/d | 0.79±0.03 | 0.88±0.05 | 0.74±0.04 | 0.05 |
| Total vegetables, cup equiv/d | **1.43±0.05** | **1.57±0.06** | **1.35±0.07** | **0.013** |

| | ***Total* (N=2,138)** | ***By Race*** | | **p[a]** |
|---|---|---|---|---|
| | | **Whites (N=903)** | **African-Americans (N=1,238)** | |
| Other meats, oz equiv/d | **4.31±0.13** | **3.74±0.17** | **4.62±0.17** | **<0.001** |
| Discretionary oil, g/d | 17.8±0.8 | 17.7±0.7 | 17.8±1.1 | 0.90 |
| Discretionary solid fat, g/d | 46.6±1.2 | 48.1±1.8 | 45.7±1.5 | 0.31 |
| **SUA**[c], mg/dL | | | | |
| $SUA_{base}$ | 5.453±0.003 | 5.453±0.003 | 5.453±0.003 | 0.96 |
| Men | 5.448±0.004 | 5.448±0.006 | 5.448±0.005 | |
| Women | 5.457±0.004 | 5.456±0.003 | 5.458±0.006 | |
| $SUA_{rate}$ | **+0.037±0.041** | **−0.080±0.054** | **+0.102±0.056** | **0.019** |
| Men | **+0.485±0.056**[b] | **+0.472±0.073** [b] | **+0.492±0.077** [b] | |
| Women | **−0.334±0.053** | **−0.548±0.063** | **−0.218±0.074** | |

[a] P-value for trend was based on design-based *F*-test for trend in exposures by race.

[b] P<0.05 for null hypothesis of no difference by sex, design-based *F*-test.

[c] Empirical bayes predictions from a mixed-effects linear regression model with TIME as the only covariate, and random effects added to the intercept and TIME parameters.

[d] *Abbreviations*: HANDLS=Health Aging in Neighborhoods of Diversity Across the Life Span; SEM=Standard Error of the Mean; SUA=Serum Uric Acid.

**TABLE 2**

Mixed-effects regression models of SUA by individual dietary factors and by the dietary urate index, stratified by race among urban adults participating in the HANDLS with complete data on SUA at either of 2 visits (N=2,138), 2004–2013

| | **Total: Model 1**[a] | | **Whites: Model 2**[a] | | **African-Americans: Model 3**[a] | |
|---|---|---|---|---|---|---|
| | **γ±SEE** | **p-value** | **γ±SEE** | **p-value** | **γ±SEE** | **p-value** |
| **Serum Uric Acid** | **n=2,136**[c] | **n′=3,661**[c] | **n=903** | **n′=1,533** | **n=1,233** | **n′=2,128** |
| ***Model A: Individual dietary factors*** | | | | | | |
| Added Sugar ($\gamma_{01}$ for $\pi_{0i}$) | +0.004±0.002 | 0.09 | **+0.007±0.003** | **0.014**[b] | +0.002±0.003 | 0.52 |
| Added Sugar×Time ($\gamma_{11}$ for $\pi_{1i}$) | +0.000±0.001 | 0.64 | +0.001±0.001 | 0.39 | +0.000±0.001 | 0.93 |
| Alcohol ($\gamma_{02}$ for $\pi_{0i}$) | **+0.118±0.018** | **<0.001** | **+0.118±0.027** | **<0.001** | **+0.123±0.025** | **<0.001** |
| Alcohol×Time ($\gamma_{12}$ for $\pi_{1i}$) | −0.005±0.004 | 0.22 | +0.003±0.007 | 0.71 | −0.010±0.06 | 0.08 |
| Red Meat ($\gamma_{03}$ for $\pi_{0i}$) | +0.014±0.012 | 0.25 | −0.019±0.018 | 0.29 | **+0.032±0.016** | **0.048** |
| Red Meat×Time ($\gamma_{13}$ for $\pi_{1i}$) | +0.001±0.003 | 0.66 | +0.005±0.004 | 0.28 | −0.001±0.004 | 0.86 |
| Fish ($\gamma_{04}$ for $\pi_{0i}$) | −0.013±0.017 | 0.45 | −0.029±0.029 | 0.33 | −0.002±0.020 | 0.92 |
| Fish×Time ($\gamma_{14}$ for $\pi_{1i}$) | +0.002±0.004 | 0.61 | −0.001±0.007 | 0.84 | +0.002±0.004 | 0.64 |
| Legumes ($\gamma_{05}$ for $\pi_{0i}$) | −0.18±0.14 | 0.19 | −0.023±0.223 | 0.92 | −0.30±0.17 | 0.09 |
| Legumes×Time ($\gamma_{15}$ for $\pi_{1i}$) | **+0.07±0.03** | **0.016** | +0.016±0.058 | 0.78 | **+0.10±0.034** | **0.005** |
| Dairy ($\gamma_{06}$ for $\pi_{0i}$) | −0.05±0.03 | 0.07 | **−0.086±0.33** | **0.009** | −0.000±0.058 | 1.00 |
| Dairy×Time ($\gamma_{16}$ for $\pi_{1i}$) | −0.01±0.01 | 0.50 | +0.003±0.009 | 0.77 | −0.024±0.013 | 0.059[b] |
| Vitamin C ($\gamma_{07}$ for $\pi_{0i}$) | **−0.0013±0.0006** | **0.021** | −0.001±0.001 | 0.17 | **−0.002±0.001** | **0.047** |
| Vitamin C×Time ($\gamma_{17}$ for $\pi_{1i}$) | +0.0000±0.0001 | 0.79 | −0.000±0.000 | 0.95 | +0.000±0.000 | 0.47 |
| Caffeine ($\gamma_{08}$ for $\pi_{0i}$) | −0.0003±0.0002 | 0.09 | −0.0003±0.0002 | 0.09 | +0.000±0.000 | 0.99 |
| Caffeine×Time ($\gamma_{18}$ for $\pi_{1i}$) | −0.0001±0.0001 | 0.26 | −0.000±0.000 | 0.38 | −0.000±0.000 | 0.40 |
| ***Model B: Dietary urate index*** | | | | | | |
| Dietary urate index ($\gamma_0$ for $\pi_{1i}$) | **+0.021±0.008** | **0.005** | +0.021±0.011 | 0.060 | **+0.022±0.010** | **0.032** |
| Dietary urate index×Time ($\gamma_1$ for $\pi_{1i}$) | **+0.0038±0.0018** | **0.038** | +0.0030±0.0030 | 0.30 | **+0.0050±0.0023** | **0.031** |
| ***Model C: Vitamin C supplements*** | **n=1,524**[c] | **n′=2,956**[c] | **n=607** | **n′=1,195** | **n=917** | **n′=1,761** |
| Baseline ($\gamma_{01}$ for $\pi_{1i}$) | −0.24±0.12 | 0.05 | +0.06±0.16 | 0.71 | **−0.44±0.18** | **0.018** |
| Baseline×Time ($\gamma_{11}$ for $\pi_{1i}$) | −0.026±0.027 | 0.34 | −0.06±0.04 | 0.11 | −0.02±0.04 | 0.63 |

| Serum Uric Acid | Total: Model 1[a] γ±SEE n=2,136[c] | p-value n′=3,661[c] | Whites: Model 2[a] γ±SEE n=903 | p-value n′=1,533 | African-Americans: Model 3 [a] γ±SEE n=1,233 | p-value n′=2,128 |
|---|---|---|---|---|---|---|
| Follow-up ($\gamma_{02}$ for $\pi_{1i}$) | +0.10±0.08 | 0.25 | +0.16±0.12 | 0.21 | +0.03±0.11 | 0.78 |
| (Follow-up)×Time ($\gamma_{12}$ for $\pi_{1i}$) | −0.029±0.017 | 0.10 | **−0.05±0.03** | **0.048** | −0.01±0.02 | 0.71 |

[a]Mixed-effects regression model with SUA as the outcome, random effects added to slope and intercept, and both slopes and intercept adjusted for multiple factors including baseline age, sex, race, poverty status, marital status, education, smoking and drug use, several dietary factors, BMI, and an inverse mills ratio. The main exposures were each of the 8 dietary factors entered simultaneously and adjusted for all other dietary factors in addition to total grains, total fruits, total vegetables, other meats, discretionary solid fat and discretionary oils, and the inverse mills ratio. Baseline age was centered at 50y, and all dietary factors were centered at their weighted means (See Table 1, Total). **Model A** is a single multivariable-adjusted mixed-effects linear regression model that included all 8 individual dietary factors among others. **Model B** is a single multivariable-adjusted mixed-effects linear regression model that included only the dietary urate index and not the individual dietary factors. **Model C** includes all individual dietary factors (as in Model A), but adds vitamin C-containing supplement as a main exposure with its Time interaction term.

[b]p<0.05 for interaction with race to test effect modification by race for each of the 8 dietary factors (including the dietary urate index) on SUA at baseline ($SUA_{base}$) and SUA annual rate of change ($SUA_{rate}$).

[c]Values are regression coefficients γ ± standard error of the estimate (SEE). n=number of participants in the analysis; n′=total number of visits included in the analysis. Shaded values passed correction for multiple testing. Random effects are not shown for simplicity. See supplemental method 2 for description of $\pi_S$ and $\gamma_S$ in the mixed-effects regression models.

[d]*Abbreviations*: $Age_{base}$=Baseline age at visit 1, SEE=Standard Error of the Estimate; SUA=Serum Uric Acid; $SUA_{base}$=Baseline serum uric acid concentration; $SUA_{rate}$=Annual rate of change in serum uric acid concentration.

**TABLE 3**

Sex-specific interactions of race with dietary factors and the dietary urate index in their association with SUA among urban adults participating in the HANDLS with complete data on SUA at either of 2 visits (N=2,138), 2004–2013: mixed-effect regression models

| | **Men**[a,b] | | **Women**[a,b] | |
|---|---|---|---|---|
| | **γ±SEE** | **p-value** | **γ±SEE** | **p-value** |
| **Serum Uric Acid** | **n= 929** | **n′= 1,553** | **n= 1,207** | **n′= 2,108** |
| ***Add Sugar*** | | | | |
| **Model 1.A: Added Sugar vs. $SUA_{base}$** | | | | |
| Added Sugar ($\gamma_{01}$ for $\pi_{0i}$) | **+0.013±0.004** | **0.001** | −0.001±0.004 | 0.84 |
| Race ($\gamma_{09}$ for $\pi_{0i}$) | +0.14±0.11 | 0.18 | −0.103±0.100 | 0.30 |
| Added Sugar×Race ($\gamma_{019}$ for $\pi_{0i}$) | **−0.010±0.005** | **0.037** | −0.003±0.005 | 0.53 |
| **Model 1.B: Added Sugar vs. $SUA_{rate}$** | | | | |
| Added Sugar×Time ($\gamma_{11}$ for $\pi_{1i}$) | +0.0006±0.0010 | 0.54 | +0.0002±0.0010 | 0.79 |
| Race×Time ($\gamma_{19}$ for $\pi_{1i}$) | −0.016±0.028 | 0.57 | +0.005±0.023 | 0.84 |
| Added Sugar×Race×Time ($\gamma_{119}$ for $\pi_{1i}$) | −0.001±0.001 | 0.33 | +0.0006±0.0013 | 0.45 |
| ***Alcohol*** | | | | |
| **Model 2.A: Alcohol vs. $SUA_{base}$** | | | | |
| Alcohol ($\gamma_{02}$ for $\pi_{0i}$) | **+0.121±0.033** | **<0.001** | **+0.173±0.050** | **0.001** |
| Race ($\gamma_{09}$ for $\pi_{0i}$) | +0.133±0.109 | 0.23 | −0.097±0.101 | 0.34 |
| Alcohol×Race ($\gamma_{029}$ for $\pi_{0i}$) | −0.022±0.041 | 0.60 | −0.005±0.060 | 0.94 |
| **Model 2.B: Alcohol vs. $SUA_{rate}$** | | | | |
| Alcohol×Time ($\gamma_{12}$ for $\pi_{1i}$) | +0.009±0.010 | 0.34 | −0.017±0.012 | 0.14 |
| Race×Time ($\gamma_{19}$ for $\pi_{1i}$) | −0.016±0.028 | 0.56 | +0.005±0.023 | 0.82 |
| Alcohol×Race×Time ($\gamma_{129}$ for $\pi_{1i}$) | −0.019±0.012 | 0.10 | +0.006±0.015 | 0.66 |
| ***Red Meat*** | | | | |
| **Model 3.A: Red Meat vs. $SUA_{base}$** | | | | |
| Red Meat ($\gamma_{03}$ for $\pi_{0i}$) | +0.003±0.023 | 0.90 | +0.008±0.029 | 0.78 |
| Race ($\gamma_{09}$ for $\pi_{0i}$) | +0.124±0.110 | 0.26 | −0.071±0.100 | 0.48 |
| Red Meat×Race ($\gamma_{039}$ for $\pi_{0i}$) | +0.005±0.026 | 0.85 | **+0.080±0.039** | **0.040** |
| **Model 3.B: Red Meat vs. $SUA_{rate}$** | | | | |

| Serum Uric Acid | Men[a,b] γ±SEE n= 929 | p-value n′= 1,553 | Women[a,b] γ±SEE n= 1,207 | p-value n′= 2,108 |
|---|---|---|---|---|
| Red Meat×Time ($\gamma_{13}$ for $\pi_{1i}$) | +0.002±0.006 | 0.78 | +0.002±0.007 | 0.77 |
| Race×Time ($\gamma_{19}$ for $\pi_{1i}$) | −0.018±0.028 | 0.53 | +0.011±0.023 | 0.96 |
| Red Meat×Race×Time ($\gamma_{139}$ for $\pi_{1i}$) | −0.003±0.007 | 0.65 | −0.007±0.009 | 0.45 |
| ***Fish*** | | | | |
| **Model 4.A: Fish vs. $SUA_{base}$** | | | | |
| Fish ($\gamma_{04}$ for $\pi_{0i}$) | −0.046±0.040 | 0.25 | +0.004±0.045 | 0.94 |
| Race ($\gamma_{09}$ for $\pi_{0i}$) | +0.128±0.109 | 0.24 | −0.095±0.101 | 0.34 |
| Fish×Race ($\gamma_{049}$ for $\pi_{0i}$) | +0.003±0.050 | 0.95 | −0.001±0.051 | 0.99 |
| **Model 4.B: Fish vs. $SUA_{rate}$** | | | | |
| Fish×Time ($\gamma_{14}$ for $\pi_{1i}$) | −0.006±0.009 | 0.49 | +0.001±0.012 | 0.93 |
| Race×Time ($\gamma_{19}$ for $\pi_{1i}$) | −0.018±0.028 | 0.51 | +0.003±0.023 | 0.91 |
| Fish×Race×Time ($\gamma_{149}$ for $\pi_{1i}$) | +0.014±0.011 | 0.22 | −0.001±0.013 | 0.91 |
| ***Legumes*** | | | | |
| **Model 5.A: Legumes vs. $SUA_{base}$** | | | | |
| Legumes ($\gamma_{05}$ for $\pi_{0i}$) | +0.32±0.32 | 0.32 | −0.50±0.32 | 0.12 |
| Race ($\gamma_{09}$ for $\pi_{0i}$) | +0.166±0.112 | 0.14 | −0.104±0.100 | 0.30 |
| Legumes×Race ($\gamma_{059}$ for $\pi_{0i}$) | −0.66±0.46 | 0.16 | +0.23±0.36 | 0.53 |
| **Model 5.B: Legumes vs. $SUA_{rate}$** | | | | |
| Legumes×Time ($\gamma_{15}$ for $\pi_{1i}$) | −0.012±0.087 | 0.88 | −0.007±0.083 | 0.93 |
| Race×Time ($\gamma_{19}$ for $\pi_{1i}$) | −0.017±0.029 | 0.56 | −0.002±0.023 | 0.92 |
| Legumes×Race×Time ($\gamma_{159}$ for $\pi_{1i}$) | −0.049±0.118 | 0.88 | +0.144±0.089 | 0.11 |
| ***Dairy*** | | | | |
| **Model 6.A: Dairy vs. $SUA_{base}$** | | | | |
| Dairy ($\gamma_{06}$ for $\pi_{0i}$) | −0.014±0.043 | 0.74 | −0.078±0.048 | 0.66 |
| Race ($\gamma_{09}$ for $\pi_{0i}$) | +0.124±0.108 | 0.25 | −0.101±0.100 | 0.31 |
| Dairy×Race ($\gamma_{069}$ for $\pi_{0i}$) | −0.025±0.013 | 0.08 | −0.032±0.074 | 0.66 |
| **Model 6.B: Dairy vs. $SUA_{rate}$** | | | | |

| Serum Uric Acid | Men[a,b] γ±SEE n= 929 | p-value n′= 1,553 | Women[a,b] γ±SEE n= 1,207 | p-value n′= 2,108 |
|---|---|---|---|---|
| Dairy×Time ($\gamma_{16}$ for $\pi_{1i}$) | −0.021±0.017 | 0.22 | +0.016±0.011 | 0.69 |
| Race×Time ($\gamma_{19}$ for $\pi_{1i}$) | −0.019±0.028 | 0.49 | −0.006±0.023 | 0.79 |
| Dairy×Race×Time ($\gamma_{169}$ for $\pi_{1i}$) | −0.004±0.021 | 0.85 | **−0.045±0.018** | **0.015** |
| ***Vitamin C*** | | | | |
| **Model 7.A: Vitamin C vs. $SUA_{base}$** | | | | |
| Vitamin C ($\gamma_{07}$ for $\pi_{0i}$) | **−0.002±0.001** | **0.015** | +0.001±0.001 | 0.43 |
| Race ($\gamma_{09}$ for $\pi_{0i}$) | +0.127±0.109 | 0.24 | −0.122±0.100 | 0.22 |
| Vitamin C×Race ($\gamma_{079}$ for $\pi_{0i}$) | −0.000±0.001 | 0.94 | −0.002±0.001 | 0.11 |
| **Model 7.B: Vitamin C vs. $SUA_{rate}$** | | | | |
| Vitamin C×Time ($\gamma_{17}$ for $\pi_{1i}$) | +0.000±0.000 | 0.68 | −0.000±0.000 | 0.33 |
| Race×Time ($\gamma_{19}$ for $\pi_{1i}$) | −0.020±0.028 | 0.47 | +0.011±0.024 | 0.63 |
| Vitamin C×Race×Time ($\gamma_{179}$ for $\pi_{1i}$) | −0.000±0.000 | 0.95 | 0.000±0.000 | 0.12 |
| ***Caffeine*** | | | | |
| **Model 8.A: Caffeine vs. $SUA_{base}$** | | | | |
| Caffeine ($\gamma_{08}$ for $\pi_{0i}$) | **−0.0006±0.0003** | **0.031** | +0.000±0.000 | 0.96 |
| Race ($\gamma_{09}$ for $\pi_{0i}$) | +0.144±0.109 | 0.19 | −0.119±0.101 | 0.24 |
| Caffeine ×Race ($\gamma_{089}$ for $\pi_{0i}$) | +0.001±0.001 | 0.12 | −0.001±0.001 | 0.20 |
| **Model 8.B: Caffeine vs. $SUA_{rate}$** | | | | |
| Caffeine ×Time ($\gamma_{18}$ for $\pi_{1i}$) | −0.000±0.000 | 0.27 | +0.000±0.000 | 0.91 |
| Race×Time ($\gamma_{19}$ for $\pi_{1i}$) | −0.021±0.028 | 0.46 | +0.002±0.023 | 0.92 |
| Caffeine ×Race×Time ($\gamma_{189}$ for $\pi_{1i}$) | +0.000±0.000 | 0.96 | −0.000±0.000 | 0.60 |
| ***Dietary urate index*** | | | | |
| **Model 9.A: Dietary urate index vs. $SUA_{base}$** | | | | |
| Dietary urate index ($\gamma_{010}$ for $\pi_{0i}$) | **+0.044±0.017** | **0.011** | −0.003±0.014 | 0.84 |
| Race ($\gamma_{011}$ for $\pi_{0i}$) | +0.089±0.100 | 0.37 | −0.058±0.093 | 0.54 |
| Dietary urate index×Race ($\gamma_{012}$ for $\pi_{0i}$) | −0.017±0.021 | 0.42 | +0.024±0.018 | 0.19 |
| **Model 9.B: Dietary urate index vs. $SUA_{rate}$** | | | | |

| Serum Uric Acid | Men[a,b] γ±SEE n= 929 | p-value n′= 1,553 | Women[a,b] γ±SEE n= 1,207 | p-value n′= 2,108 |
|---|---|---|---|---|
| Dietary urate index ×Time ($\gamma_{110}$ for $\pi_{1i}$) | +0.004±0.005 | 0.41 | +0.001±0.004 | 0.89 |
| Race×Time ($\gamma_{111}$ for $\pi_{1i}$) | +0.001±0.025 | 0.98 | +0.002±0.021 | 0.91 |
| Dietary urate index ×Race×Time ($\gamma_{112}$ for $\pi_{1i}$) | −0.002±0.006 | 0.80 | +0.006±0.004 | 0.21 |
| ***Vitamin C Supplement*** | | | | |
| **Model 10.A: Vitamin C Supplement vs. $SUA_{base}$** | n=619 | n′=1,197 | n=905 | n′=1,759 |
| Baseline ($\gamma_{010}$ for $\pi_{0i}$) | −0.05±0.24 | 0.85 | −0.07±0.20 | 0.70 |
| Race ($\gamma_{011}$ for $\pi_{0i}$) | +0.18±0.15 | 0.24 | −0.06±0.13 | 0.65 |
| Baseline×Race ($\gamma_{012}$ for $\pi_{0i}$) | −0.35±0.36 | 0.34 | −0.49±0.28 | 0.08 |
| Follow-up ($\gamma_{020}$ for $\pi_{0i}$) | +0.23±0.21 | 0.26 | +0.04±0.15 | 0.81 |
| Follow-up×Race ($\gamma_{022}$ for $\pi_{0i}$) | −0.28±0.26 | 0.29 | +0.05±0.19 | 0.79 |
| **Model 10.B: Vitamin C Supplement vs. $SUA_{rate}$** | n=619 | n′=1,197 | n=905 | n′=1,759 |
| Baseline ×Time ($\gamma_{110}$ for $\pi_{1i}$) | +0.00±0.06 | 0.93 | −0.07±0.05 | 0.19 |
| Race×Time ($\gamma_{111}$ for $\pi_{1i}$) | −0.04±0.03 | 0.18 | −0.05±0.13 | 0.70 |
| Baseline×Race×Time ($\gamma_{112}$ for $\pi_{1i}$) | −0.10±0.09 | 0.24 | +0.09±0.07 | 0.17 |
| Follow-up×Time ($\gamma_{120}$ for $\pi_{1i}$) | +0.40±0.22 | 0.08 | −0.03±0.03 | 0.47 |
| Follow-up×Race×Time ($\gamma_{122}$ for $\pi_{1i}$) | +0.10±0.06 | 0.10 | +0.00±0.04 | 0.96 |

[a] Mixed-effects regression model with SUA as the outcome, random effects added to slope and intercept, and both slopes and intercept adjusted for multiple factors including baseline age, sex, race, poverty status, marital status, education, smoking and drug use, several dietary factors, BMI, and an inverse mills ratio. The main exposures were each of the 9 dietary factors entered simultaneously and adjusted for all other dietary factors in addition to total grains, total fruits, total vegetables, other meats, discretionary solid fat and discretionary oils, and the inverse mills ratio. Baseline age was centered at 50y, and all dietary factors were centered at their weighted means (See Table 1, Total). In addition, a 2-way interaction was added in **Models 1A–9A** to examine the interactive effect of race and dietary factors on baseline SUA ($SUA_{base}$). Similarly, a 3-way interaction between Time, Race and the dietary factor was added in **Models 1B–9B** to examine the interactive effect of diet and race on SUA's annual rate of change ($SUA_{rate}$). Note that for **models 9A** and **9B**, individual dietary factors were not included alongside the dietary urate index. **Models 10A–10B** are the equivalent of **Model C** in Table 2, with additional testing for interaction between vitamin C-containing supplements and race for baseline and rate of change in SUA.

[b] Values are regression coefficients γ ± standard error of the estimate (SEE). n=number of participants in the analysis; n′=total number of visits included in the analysis. Shaded values passed correction for multiple testing. Random effects are not shown for simplicity. See supplemental method 2 for description of $\pi_S$ and $\gamma_S$ in the mixed-effects regression models.

[c] *Abbreviations*: $Age_{base}$=Baseline age at visit 1, SEE=Standard Error of the Estimate; SUA=Serum Uric Acid; $SUA_{base}$=Baseline serum uric acid concentration; $SUA_{rate}$=Annual rate of change in serum uric acid concentration.