Coffee consumption and risk of incident gout in women: the Nurses' Health Study[1–3]

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ABSTRACT

Background: Coffee is one of the most widely consumed beverages in the world and may affect the risk of gout via various mechanisms, but prospective data on the relation between coffee intake and the risk of incident gout are limited.

Design: Over a 26-y period, we prospectively examined the relation between coffee intake and risk of incident gout in 89,433 female participants in the Nurses' Health Study. We assessed the consumption of coffee, decaffeinated coffee, tea, and total caffeine in participants every 2–4 y through validated questionnaires. We used a supplementary questionnaire to ascertain whether participants met the survey criteria of the American College of Rheumatology for gout.

Results: During the 26 y of follow-up, we documented 896 confirmed incident cases of gout. There was an inverse association between higher coffee intake and the risk of gout. The multivariate relative risks (RRs) for incident gout according to coffee-consumption categories [ie, 0, 1–237, 238–947, and ≥948 mL coffee/d (237 mL = one 8-ounce cup)] were 1.00, 0.97, 0.78 (95% CI: 0.64, 0.95), and 0.43 (95% CI: 0.30, 0.61; *P* for trend < 0.0001), respectively. For decaffeinated coffee, the multivariate RRs according to consumption categories (0, 1–237, and ≥237 mL decaffeinated coffee/d) were 1.00, 1.02, and 0.77 (95% CI: 0.63, 0.95; *P* for trend = 0.02), respectively. There was an inverse association between total caffeine from all sources and the risk of gout; the multivariate RR of the highest quintile compared with the lowest quintile was 0.52 (95% CI: 0.41, 0.68; *P* for trend <0.0001).

Conclusion: These prospective data suggest that long-term coffee consumption is associated with a lower risk of incident gout in women. *Am J Clin Nutr* 2010;92:922–7.

INTRODUCTION

Gout, a common and excruciatingly painful inflammatory arthritis, has historically been considered a male disease, and most gout research has focused on men (1–6). However, growing evidence suggests a substantial disease burden of gout in elderly women (≤5% of women >70 y old), whose representation in the general population has grown with increased longevity (7, 8). Identifying the risk factors for gout that are modifiable is an important first step in the prevention and management of this common and painful condition (3, 4, 9).

Coffee is one of the most widely consumed beverages in the world. For example, >50% of Americans drink coffee, and the average per capita intake is ≈2 cups/d (10, 11). Coffee consumption may reduce the risk of gout via various mechanisms including reducing serum uric acid concentrations (12, 13) and influencing insulin resistance (11, 14–20). Caffeine (1,3,7-trimethyl-xanthine) is a methyl-xanthine and may be a competitive inhibitor of xanthine oxidase as observed in rats (13). This potential property of caffeine may exert a protective effect against gout that is similar to the effect of allopurinol. Higher long-term coffee intake is associated with lower insulin concentrations (19) and increased insulin sensitivity (21). Because there is a strong positive relation between serum insulin resistance and hyperuricemia (22–26), and insulin reduces the renal excretion of urate (24, 27, 28), decreased insulin resistance and insulin concentrations from coffee consumption may lead to a lower risk of hyperuricemia and gout (5). Indeed, cross-sectional studies in Japanese men (12) and US adults (29) showed a significant inverse association between coffee consumption and serum uric acid concentrations. Furthermore, a recent, large, prospective study in men showed that coffee consumption was associated with a substantially lower risk of incident gout (ie, ≥40% risk reduction association with coffee consumption ≥4 cups/d (5). To date, no study has investigated the relation in women. Because of the significant role of female hormones on serum uric acid concentrations and the substantial gender difference in the incidence of gout and, perhaps, in uric acid metabolism (30), extrapolation of data on the risk factors for gout from men to women should be done with caution.

To investigate these issues specifically in women, we prospectively evaluated the relation between intakes of coffee, decaffeinated coffee, tea, and total caffeine and the incidence of gout in a cohort of 89,433 women with no history of gout in the Nurses' Health Study.

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[2] Supported by grants AR056042, AR47785, and P01CA087969 from the National Institutes of Health.

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Received March 22, 2010. Accepted for publication July 12, 2010.

First published online August 25, 2010; doi: 10.3945/ajcn.2010.29565.

SUBJECTS AND METHODS

Study population

The Nurses' Health Study was established in 1976 when 121,700 female registered nurses (age range: 30–55 y) who were living in 11 large states completed a mailed questionnaire in which they provided detailed information about their medical history, lifestyles, and other risk factors. The information is updated every 2 y to identify newly diagnosed diseases, and the follow-up rate exceeds 90%. In 1980, a food-frequency questionnaire was added. For our analyses, we excluded women who had a previous diagnosis of gout at baseline or participants who did not complete >10 items on the 1980 dietary questionnaire, which left 89,433 eligible women who were followed from 1980 to 2006.

Assessment of coffee and dietary intake

To assess dietary intake including coffee intake, we used a validated food-frequency questionnaire that inquired about the average consumption of foods and beverages during the previous year (3, 4, 9, 31, 32). The dietary questionnaires were completed in 1980, 1984, 1986, 1990, 1994, 1998, and 2002. On all questionnaires, participants were asked how often, on average, during the previous year they had consumed coffee and tea. Decaffeinated coffee was first assessed in 1984. We assessed the total intake of caffeine by summing the caffeine content for a specific amount of each food during the previous year (1 cup for coffee or tea, one 12-oz bottle or can for carbonated beverages, and 1 oz for chocolate) multiplied by a weight proportional to the frequency of its consumption. The participants could choose from 9 frequency responses (ie, never, 1–3 servings/mo, 1, 2–4, and 5–6 servings/wk, and 1, 2–3, 4–5, and ≥6 servings/d). With the use of the food-composition sources of the US Department of Agriculture, we estimated that the caffeine content was 137 mg/cup of coffee, 47 mg/cup of tea, 46 mg/bottle or can of cola beverage, and 7 mg/serving of chocolate candy. Food and nutrient intakes that were assessed by this dietary questionnaire were previously validated against two 1-wk diet records in this cohort (31, 33). Specifically, high correlations were recorded for coffee and other caffeinated beverage intake (coffee: $r = 0.78$; tea: $r = 0.93$; and cola: $r = 0.84$) (34). Other relevant dietary data (ie, intakes of meats, seafood, dairy foods, alcohol, and vitamin C) were also validated (34).

Assessment of nondietary factors

At baseline, and every 2 y thereafter, the participants provided information on weight, regular use of medications (including diuretics), and medical conditions (including hypertension) (9). These data were shown to be reliable in validation studies, and many studies have shown the ability to predict the risk of relevant future diseases (35–37). Body mass index (BMI) was calculated by dividing the updated weight in kilograms by the square of the baseline height in meters.

Ascertainment of incident cases of gout

We ascertained incident cases of gout by the survey gout criteria of the American College of Rheumatology as previously described (3, 4, 9). Briefly, in 1982, 1984, 1986, 1988, 2002, and thereafter, biennial questionnaires were used to ask participants whether they had received a physician diagnosis of gout and, if so, the date of the first occurrence. We mailed a supplementary questionnaire to those participants with a self-reported incident gout diagnosed in 1980 and onward to confirm the report and to ascertain the survey gout criteria of the American College of Rheumatology (3, 4, 9, 38). The primary endpoint in this study was an incident case of gout that met ≥6 of the 11 gout criteria (3, 4, 9, 38). To confirm the validity of the survey gout criteria in our cohort, we reviewed the relevant medical records from a sample of 56 of the women who reported having gout. The concordance rate of confirming the report of gout between the gout survey criteria and the medical record review was 91%.

Statistical analyses

We computed the person time of follow-up for each participant from the return date of the 1980 questionnaire to the date of the diagnosis of gout, death from any cause, or the end of the study period (June 2006), whichever came first. Women who died or reported having gout on previous questionnaires were excluded from subsequent follow-up.

To represent long-term coffee- and caffeine-intake patterns of individual subjects, we used cumulative average intakes on the basis of the information from the 1980, 1984, 1986, 1990, 1994, 1998, and 2002 dietary questionnaires (3, 4, 9, 39, 40). For example, the incidence of gout from 1980 through 1984 was related to the coffee intake reported on the 1980 questionnaire, and the incidence of gout from 1984 through 1986 was related to the average intake reported on the 1980 and 1984 questionnaires. Secondary analyses that used only information from baseline questionnaires (1980) yielded similar results.

We used Cox proportional hazards modeling (with the PROC PHREG procedure in SAS software, version 9.1; SAS Institute Inc, Cary, NC) to estimate the relative risk (RR) for incident gout in all multivariate analyses. For these analyses, coffee consumption was categorized into 4 groups as follows: never, <1, 1–3, and ≥4 cups/d (11). Caffeine intake was categorized into quintiles (11, 19). Multivariate models were adjusted for age (continuous), total energy intake (7 groups), alcohol (7 categories), sugar-sweetened soft drinks (5 categories), BMI (7 categories), menopause (yes or no), postmenopausal hormone use (never, past, and current use), use of diuretics (thiazide or furosemide) (yes or no), history of hypertension (yes or no), daily average intakes of meats, seafood, dairy foods, and total vitamin C (quintiles), and chocolate intake (yes or no) (3, 4, 9). Linear trends in gout risk across categories of coffee or caffeine intake were assessed in Cox proportional hazards models by using the median values of intake for each category to minimize the influence of outliers. An examination of log-log survival curves for each of the variables in our model showed that assumptions of proportional hazards were met. We conducted analyses stratified by BMI (in kg/m^2) categories (<25, 25–29.9, and ≥30), by alcohol consumption (yes or no), use of diuretics (yes or no), and low-fat dairy intake [≤ 0.57 servings/d (median value) compared with > 0.57 servings/d] to assess possible effect modification. We tested the significance of the interaction with a likelihood ratio test by comparing a model with the main effects of each intake and the stratifying variable and the

interaction terms with a reduced model with only the main effects. For all RRs, we calculated 95% CIs. All *P* values are 2 sided.

RESULTS

During 26 y of follow-up, we documented 896 newly diagnosed cases that met the criteria of the American College of Rheumatology for gout. The characteristics of the cohort according to coffee-consumption categories at baseline are shown in **Table 1**. With increased coffee consumption, the frequency of a history of hypertension, postmenopausal hormone use, and consumption of low-fat dairy food, sugar-sweetened soft drinks, and tea tended to decrease, but consumption of alcohol and meat tended to increase (Table 1).

Increased coffee intake was inversely associated with the risk of gout (**Table 2**). The multivariate RRs for incident gout according to coffee-consumption categories [ie, 0, <237, 238–947, and ≥948 mL coffee/d (237 mL = an 8-oz cup)] were 1.00, 0.97, 0.78 (95% CI: 0.64, 0.95), and 0.43 (95% CI: 0.30, 0.61; *P* for trend <0.0001), respectively. These RRs did not change materially after additional adjustment for smoking (multivariate RR for ≥948 mL coffee/d: 0.42; 95% CI: 0.29, 0.60). When we restricted our analyses to women who did not use diuretics (number of gout cases = 485), the multivariate RRs were 1.00, 0.94, 0.70 (95% CI: 0.54, 0.91), and 0.35 (95% CI: 0.22, 0.56; *P* for trend <0.0001).

There was a modest inverse association between decaffeinated-coffee consumption and the incidence of gout (Table 2). The multivariate RRs according to decaffeinated coffee–consumption categories (ie, 0, <237, and ≥237 mL decaffeinated coffee/d) were 1.00, 1.02 (95% CI: 0.85, 1.22), and 0.77 (95% CI: 0.63, 0.95; *P* for trend = 0.02), respectively. Tea consumption was not associated with the risk of gout (*P* for trend = 0.66) (Table 2). The multivariate RR associated with chocolate intake of any amount was 0.89 (95% CI: 0.74, 1.06) compared with the multivariate RR associated with no chocolate intake.

There was a significantly inverse association between total caffeine intake and the risk of gout (**Table 3**). The multivariate RR of gout in women in the highest quintile of caffeine intake, compared with the multivariate RR of gout in women in the lowest quintile of caffeine intake, was 0.52 (95% CI: 0.41, 0.68; *P* for trend <0.001). To evaluate the effect of noncoffee sources of caffeine, we examined the association between caffeine intake and the risk of gout in noncoffee users and observed a null result (multivariate RR for comparison of extreme categories, RR = 0.67; 95% CI: 0.16, 2.79). Furthermore, when we additionally adjusted for caffeine intake in the multivariate model in Table 2, the inverse association with coffee intake did not change materially (multivariate RR for ≥4 cups/d: 0.49; 95% CI: 0.29, 0.82), which suggested that noncaffeine components of coffee also contributed to the observed inverse association.

We conducted stratified analyses to evaluate whether the association between coffee consumption and gout varied according to BMI, alcohol consumption, diuretic use, and low-fat dairy intake. Relative risks from these stratified analyses consistently suggested inverse associations similar to those from the main analyses, and there was no significant interaction between these variables and coffee intake (**Table 4**).

DISCUSSION

In this large prospective study in women, the risk of incident gout decreased with increased coffee intake. The risk of gout was 22% lower with a coffee intake of 1–3 cups/d and 57% lower with a coffee intake of ≥4 cups/d compared with the risk of gout in individuals with no coffee consumption. We also showed

TABLE 1
Baseline characteristics according to coffee consumption (1980)[1]

	Coffee consumption				
Variable	0 mL/d (0 cups/d)	1–237 mL/d (1 cup/d)	238–947 mL/d (1–3 cups/d)	≥948 mL/d (≥4 cups/d)	All participants
Participants (*n*)	20,673	7505	39,048	22,207	89,433
Age (y)	46 ± 7[2]	46 ± 7	47 ± 7	46 ± 7	46 ± 7
BMI (kg/m^2)	24.7 ± 4.8	24.5 ± 4.6	24.2 ± 4.3	24.1 ± 4.1	24.3 ± 4.4
Diuretic use (%)	11	11	10	8	10
History of hypertension (%)	19	18	16	12	16
Menopause (%)	33	32	33	33	33
Postmenopausal hormone use (%)	22	22	21	18	20
Alcohol (g/d)	4.5 ± 9.1	5.5 ± 9.7	7.1 ± 10.7	7.2 ± 11.2	6.4 ± 10.5
Total meat (servings/d)	1.1 ± 0.7	1.2 ± 0.7	1.2 ± 0.7	1.3 ± 0.7	1.2 ± 0.7
Seafood (servings/d)	0.2 ± 0.2	0.2 ± 0.2	0.2 ± 0.2	0.2 ± 0.2	0.2 ± 0.2
Low-fat dairy foods (servings/d)	1.0 ± 1.1	0.9 ± 1.0	0.9 ± 1.0	0.8 ± 1.0	0.9 ± 1.0
High-fat dairy foods (servings/d)	1.4 ± 1.4	1.4 ± 1.3	1.4 ± 1.3	1.5 ± 1.4	1.4 ± 1.4
Sugar-sweetened soft drinks (servings/d)	0.4 ± 0.8	0.3 ± 0.6	0.3 ± 0.7	0.2 ± 0.7	0.3 ± 0.6
Chocolate (servings/d)	0.2 ± 0.4	0.2 ± 0.3	0.2 ± 0.3	0.2 ± 0.3	0.2 ± 0.3
Total caffeine intake (mg/d)	117 ± 116	150 ± 104	368 ± 115	794 ± 111	398 ± 275
Tea (mL/d)	355 ± 437	273 ± 382	218 ± 300	164 ± 300	246 ± 355
Tea (cups/d)	1.3 ± 1.6	1.0 ± 1.4	0.8 ± 1.1	0.6 ± 1.1	0.9 ± 1.3

[1] Data, except for age, were directly standardized to the age distribution of each study sample. Statistical tests for the association between coffee consumption and covariates were all significant, $P < 0.05$.

[2] Mean ± SD (all such values).

TABLE 2
Relative risk (RR) of incident gout according to coffee, tea, and decaffeinated-coffee consumption[1]

Coffee and tea consumption	No. of cases	Person-years	Age-adjusted RR (95% CI)	Multivariate RR (95% CI)[2]
Coffee				
0 mL/d (0 cups/d)	143	327,035	1.0	1.0
1–237 mL/d (1 cup/d)	241	410,171	0.98 (0.80, 1.21)	0.97 (0.78, 1.20)
238–947 mL/d (1–3 cups/d)	470	1,111,684	0.78 (0.65, 0.95)	0.78 (0.64, 0.95)
≥948 mL/d (≥4 cups/d)	42	283,257	0.37 (0.26, 0.52)	0.43 (0.30, 0.61)
P value for trend	—	—	<0.0001	<0.0001
Tea				
0 mL/d (0 cups/d)	126	384,687	1.0	1.0
1–237 mL/d (1 cup/d)	552	1,153,959	1.08 (0.89, 1.32)	1.05 (0.86, 1.28)
238–947 mL/d (1–3 cups/d)	196	543,579	0.99 (0.79, 1.24)	0.92 (0.74, 1.16)
≥948 mL/d (≥4 cups/d)	22	49,922	1.62 (1.03, 2.55)	1.55 (0.98, 2.47)
P value for trend	—	—	0.92	0.66
Decaffeinated coffee[3]				
0 mL/d (0 cups/d)	227	517,738	1.0	1.0
1–237 mL/d (1 cup/d)	375	644,208	0.99 (0.84, 1.17)	1.02 (0.85, 1.22)
>237 mL/d (>1 cup/d)	176	428,171	0.77 (0.64, 0.94)	0.77 (0.63, 0.95)
P value for trend	—	—	0.01	0.02

[1] Because of missing data, the number of gout cases did not add up to the total.
[2] Adjusted for age, total energy intake, BMI, menopause, use of hormonal replacement, diuretic use, history of hypertension, and intakes of alcohol, sugar-sweetened soft drinks, total meats, seafood, chocolate, dairy foods, total vitamin C, and beverages presented in the table. RRs were computed by using a Cox proportional hazards model.
[3] Analyses used 1984 as the baseline year.

a modest inverse association with decaffeinated-coffee consumption of ≥1 cup/d. These associations were independent of other risk factors for gout such as adiposity, age, alcohol consumption, diuretic use, hypertension, menopause, and intakes of dairy, meat, seafood, and sugar-sweetened soft drinks. To our knowledge, the current study provides the first prospective data about the inverse association between coffee intake and the risk of gout specifically in women.

Caffeine (1,3,7-trimethyl-xanthine) is metabolized by demethylation, and the major human pathway results in paraxanthine (1,7-dimethylxanthine), which leads to the principal urinary metabolites l-methylxanthine and 1-methyluric acid and an acetylated uracil derivative. Methyl-xanthines, such as caffeine, theophylline, and theobromine, were all shown to competitively inhibit xanthine oxidase in vitro and in in vivo studies in rats (13). Caffeine, the predominant methylxanthine of coffee, may reduce the risk of gout via xanthine oxidase inhibition in humans as observed in the current study. Similarly, theobromine, the predominant methylxanthine of chocolate, may explain its observed protective trend with chocolate intake.

However, the modest inverse association with decaffeinated coffee suggests that components of coffee other than caffeine may also contribute to the observed inverse association between coffee and gout. This inference was consistent with the null association with tea intake, which is another source of caffeine, although we cannot rule out the possibility that tea may also contain certain offending factors that counteract the potential protective effect of caffeine. Nonetheless, these results are closely in line with Japanese cross-sectional study (12) and the Third National Health and Nutrition Examination Survey study (29) that showed coffee consumption, but not tea consumption, was inversely associated with serum uric acid concentrations. Furthermore, these results agree with the data from this cohort about the relation between these beverages and serum insulin concentration (19), which is a strong correlate of serum uric acid concentrations (24, 27, 28). Both caffeinated and decaffeinated

TABLE 3
Relative risk (RR) of incident gout according to caffeine intake

Caffeine intake (quintiles)	No. of cases	Person-years	Age-adjusted RR (95% CI)	Multivariate RR (95% CI)[1]
≤131 mg/d	226	425,396	1.0	1.0
132–238 mg/d	207	426,508	0.89 (0.74, 1.08)	0.84 (0.70, 1.02)
239–358 mg/d	220	425,553	0.95 (0.79, 1.14)	0.91 (0.75, 1.10)
359–497 mg/d	158	427,028	0.79 (0.64, 0.97)	0.77 (0.62, 0.94)
≥498 mg/d	85	427,663	0.49 (0.38, 0.63)	0.52 (0.41, 0.68)
P value for trend	—	—	<0.001	<0.001

[1] Adjusted for age, total energy intake, BMI, menopause, use of hormonal replacement, diuretic use, history of hypertension, and intakes of alcohol, total meats, seafood, total vitamin C, and dairy foods. Values were computed by using a Cox proportional hazards model.

TABLE 4
Multivariate relative risk (RR) of gout according to total dairy food consumption stratified by BMI, alcohol consumption, diuretic use, and low-fat dairy intake

	Multivariate RR (95% CI)[1]					
Variable	0 mL/d (0 cups/d)	1–237 mL/d (<1 cup/d)	238–947 mL/d (1–3 cups/d)	≥948 mL/d (≥4 cups/d)	*P* for trend	*P* for interaction
BMI						0.09
<25 kg/m^2	1.0	1.70 (1.03, 2.79)	0.90 (0.56, 1.45)	0.35 (0.16, 0.81)	<0.0001	
25–29.9 kg/m2	1.0	0.97 (0.66, 1.45)	0.84 (0.58, 1.20)	0.58 (0.32, 1.05)	0.05	
≥30 kg/m^2	1.0	0.81 (0.59, 1.10)	0.73 (0.55, 0.97)	0.37 (0.22, 0.64)	0.001	
Alcohol consumption						0.20
No	1.0	1.20 (0.87, 1.67)	1.13 (0.83, 1.53)	0.47 (0.24, 0.90)	0.19	
Yes	1.0	0.88 (0.63, 1.22)	0.67 (0.50, 0.90)	0.36 (0.22, 0.58)	<0.0001	
Diuretic use						0.41
No	1.0	0.94 (0.70, 1.25)	0.70 (0.54, 0.91)	0.35 (0.22, 0.56)	<0.0001	
Yes	1.0	1.01 (0.73, 1.40)	0.88 (0.65, 1.19)	0.55 (0.32, 0.93)	0.03	
Low-fat dairy intake						0.14
<1.5 servings/d	1.0	1.03 (0.74, 1.43)	0.68 (0.50, 0.92)	0.49 (0.31, 0.79)	<0.0001	
≥1.5 servings/d	1.0	0.95 (0.72, 1.27)	0.87 (0.66, 1.13)	0.35 (0.20, 0.61)	0.003	

[1] Adjusted for age, total energy intake, BMI, menopause, use of hormonal replacement, diuretic use, history of hypertension, and intake of alcohol, total meats, seafood, total vitamin C, and dairy foods. RRs were computed from Cox proportional hazards models.

coffee were shown to be inversely associated with C-peptide concentrations (a marker of endogenous insulin concentrations), but tea intake was not (19). Because insulin reduces the renal excretion of urate (24, 27, 28), decreased insulin concentrations associated with long-term coffee consumption may lower the risk of gout (5).

Coffee contains many noncaffeine components that may contribute to the inverse association. For example, coffee contains substantial amounts of potassium, magnesium, and antioxidants including the phenol chlorogenic acid, which is a strong antioxidant (11). These factors may have beneficial effects on the development of gout though synergistic or independent actions on insulin resistance (11). Previous studies suggested that plasma glucose concentrations are reduced by chlorogenic acid (41), which may combine with other antioxidants in coffee to decrease oxidative stress (19). Antioxidants may improve insulin sensitivity (42, 43) and decrease insulin concentrations in rats (44). Chlorogenic acid also acts as a competitive inhibitor of glucose absorption in the intestine (45). Indeed, decaffeinated coffee seemed to delay intestinal absorption of glucose and increase glucagon-like peptide 1 (GLP-1) concentrations in an intervention study in humans (46). GLP-1 is well known for its beneficial effects on glucose-induced insulin secretion and insulin action (47). Tea also contains many different types of antioxidants; however, the antioxidant capacity per serving and total contributions are substantially higher in coffee than in tea (19, 48–50). It has also been suggested that noncaffeine xanthines contained in coffee may inhibit xanthine oxidase and, thus, contribute to lower serum uric acid concentrations (12).

There were several strengths and potential limitations of our study. Our study had a large number of cases of confirmed female gout, and dietary data, which included coffee-intake information, were prospectively collected and validated. A potential biased recall of diet was avoided in this study because the intake data were collected before the diagnosis of gout. Because coffee consumption was self-reported by questionnaire, some misclassification of exposure is inevitable. However, self-reported coffee consumption has been extensively validated in subsamples of this cohort (34), and any remaining misclassification would have likely biased the results toward the null. The use of repeated dietary assessments in the analyses accounted for changes in coffee consumption over time and decreased the measurement error. The validity of gout ascertainment in this cohort and our companion male cohort (3, 4, 9) has been documented by the high degree of concordance with medical record reviews.

The restriction to registered nurses in our cohort is both a strength and a limitation. The cohort of well-educated women minimized the potential for confounding associated with socioeconomic status, and we were able to obtain high quality data with minimal loss to follow-up. Although the absolute rates of gout and distribution of coffee intake may not be representative of a random sample of US women, the biological effects of coffee intake on gout should be similar. Our findings are most directly generalizable to middle-age and elderly women with no history of gout.

In conclusion, our findings provide prospective evidence that long-term coffee consumption is associated with a lower risk of incident gout in women.

The authors' responsibilities were as follows—HKC and GC: study design, acquisition of data, analysis and interpretation of data, manuscript preparation; and HKC: statistical analyses. Neither author had a conflict of interest.

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