Coffee Consumption and Risk of Type 2 Diabetes Mellitus

An 11-Year Prospective Study of 28,812 Postmenopausal Women

Mark A. Pereira, PhD; Emily D. Parker, MPH; Aaron R. Folsom, MD

Background: Coffee intake may be associated with reduced risk of type 2 diabetes mellitus because of minerals, phytochemicals, and antioxidants in coffee, but the role of caffeine is unclear. Our objective was to examine the association between total, caffeinated, and decaffeinated coffee intake, as assessed by food frequency questionnaire at baseline, and risk of incident type 2 diabetes mellitus.

Methods: This prospective analysis of the Iowa Women's Health Study (1986-1997) included 28,812 postmenopausal women free of diabetes and cardiovascular disease in the general community. The main outcome measure was incident type 2 diabetes mellitus as determined by mailed questionnaire.

Results: Coffee intake was categorized as 0, less than 1, 1 to 3, 4 to 5, and 6 or more cups per day. During 11 years of follow-up, there were 1,418 incident cases of diabetes. Relative risks (RRs) were adjusted for a variety of demographic, adiposity, and lifestyle measures. Compared with women who reported 0 cups of coffee per day, women who consumed 6 or more cups per day had a 22% lower risk (RR=0.78; 95% confidence interval [CI], 0.61-1.01) of diabetes (.06). This association appeared to be largely explained by decaffeinated coffee (RR=0.67; 95% CI, 0.42-1.08; .006) rather than regular coffee (RR=0.79; 95% CI, 0.59-1.05; .90). Intakes of magnesium and phytate did not explain these associations. Intakes of caffeine from all sources was not associated with risk of diabetes.

Conclusion: Coffee intake, especially decaffeinated, was inversely associated with risk of type 2 diabetes mellitus in this cohort of postmenopausal women.

Arch Intern Med. 2006;166:1311-1316

Several large prospective studies have reported an inverse association between coffee consumption and risk of type 2 diabetes mellitus. A recent systematic review on this topic concluded that this association between coffee intake and risk of type 2 diabetes mellitus is consistent across age, obesity, and study location (United States and Europe). The associations were relatively strong, followed a dose-response relation (higher coffee intake, lower diabetes incidence), and appeared to be independent of potentially confounding dietary and lifestyle factors. Purported mechanisms that may explain this association, if causal, include effects on insulin sensitivity and/or insulin secretion from a variety of minerals, antioxidants, and phytochemical compounds found in coffee. However, it remains unclear whether the caffeine itself may increase or decrease the risk of type 2 diabetes mellitus and therefore whether effects may differ between regular and decaffeinated coffee.

The purpose of the present study was to examine the association between coffee drinking habits and risk of type 2 diabetes mellitus in a large prospective study of postmenopausal women from the state of Iowa. Our study afforded the opportunity to determine if the findings from the previous studies would also be found in a relatively homogeneous cohort of older women with relatively high intakes of both regular coffee and decaffeinated coffee.

Methods

Research Design

The Iowa Women's Health Study is a prospective cohort study of postmenopausal women residing in the state of Iowa. In January 1986, a random sample of 99,826 women aged 55 to 69 years with a valid Iowa driver’s license were mailed a 16-page questionnaire and invited to participate in the study. The original study sample consisted of 41,836 women who returned the baseline questionnaire. Compared with nonrespondents, respondents had a lower...
mean body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters) (0.4 lower), were 3 months older, and were more likely to live in rural and less affluent counties compared with nonrespondents.13

Women were excluded from our analysis if they reported implausibly high (>5000 kcal) or low (<600 kcal) energy intakes, left 30 or more items blank on the food frequency questionnaire, or had diabetes, cardiovascular disease, or cancer (other than nonmelanoma skin cancer) at baseline, or were unsure whether they had diabetes. Women were considered to have diabetes at baseline if they responded yes to 1 of the following questions: (1) have you ever been told by a doctor that you have sugar diabetes? and (2) have you ever taken insulin or pills for sugar diabetes (or to lower blood glucose)? After these exclusions, 28812 women were included in the present analyses.

Diabetes incidence was determined by self-report using the following question asked on 4 follow-up mailed surveys in 1987, 1989, 1992, and 1997: “Since baseline (or most recent follow-up), were you diagnosed for the first time by a doctor as having sugar diabetes?” Response rates for the 4 follow-up surveys were 91%, 89%, 86%, and 79%, respectively. A validation study of self-reported diabetes was conducted on 83 cohort participants in 1988 after the first follow-up survey. Subjects tended to overreport having diabetes; of 44 women who reported having diabetes at baseline, 28 (64%) were confirmed as having diabetes by their physician. All 41 women who reported not having diabetes at baseline were confirmed noncases.14

The baseline questionnaire included questions on known or suspected risk factors for diabetes, such as age, BMI, waist-hip ratio (WHR), physical activity, alcohol consumption, and smoking history. Weight and height were self-reported, and WHR was calculated as the mean of 2 measurements taken by the participant’s spouse or friend using a paper tape measure that was included with the questionnaire.15 The women reported their frequency of moderate (eg, golf and long walks) and vigorous (eg, swimming and aerobics) physical activity, and these were combined into a simple 3-level index of total physical activity (low, moderate, and high).16 Pack-years of smoking was calculated from the intensity and duration of cigarette smoking. Alcohol consumption was assessed by the food frequency questionnaire, which queried the participants’ typical intakes of wine, beer, and spirits. The women also provided information on their marital status, educational attainment, residence, and use of hormone therapy.

A 127-item food frequency questionnaire was used to assess past-year typical food intake.17 Women were asked “Please fill in your average use during the past year, of each specified food.” For “decaffeinated coffee” and “coffee,” the standard serving size was assigned on the questionnaire as “1 cup,” and the intake frequency options ranged from “never or less than once per month” up to “6 or more cups per day.” The validity of the food frequency questionnaire was evaluated by comparing nutrient values with those from the average of 5 24-hour dietary recall surveys in 44 study participants.18 Reliability was evaluated by readministering the questionnaire 3 to 6 months later. The validity correlations for caffeine were $r=0.95$ (only alcohol was higher) and $r=0.82$ (only riboflavin was higher), respectively.

**STATISTICAL ANALYSIS**

The SAS version 9.1 package was used for all statistical analyses (SAS Institute Inc, Cary, NC). Person-time-at-risk was calculated from baseline to the date of the last completed follow-up survey for women who did not report a diagnosis of diabetes. For women who reported a diabetes diagnosis, person-time was calculated as the sum of the known disease-free period and half of the period during which the diagnosis was made. Relative risks (RRs) per category of coffee intake were estimated by Cox proportional hazards regression models (PROC PHREG; SAS Institute Inc) with simultaneous adjustment for many demographic, lifestyle, and dietary variables. Coffee categories were based on round and logical daily intake cut points that would also provide an ample number of participants and cases per category. Linear trend tests for the RRs across increase coffee intake categories were computed by reparameterization of the categorical coffee variables as if they were continuous. Three models were constructed, with only the final model including some components of coffee that may be on the causal pathway between coffee intake and risk of type 2 diabetes mellitus. Model 1 included baseline age (continuous), education (high school graduate vs not), and baseline hypertension (yes vs no). Model 2 included those variables in model 1, plus alcohol (0, <4 g/d, and ≥4 g/d), smoking status (smoker vs not), cigarette pack-years (quartiles), BMI (continuous), WHR (continuous), physical activity (high, moderate, and low), energy intake (kilocalories per day, continuous), and intake of total fat (grams per day, continuous), fatty acids and cholesterol level (Keys score, continuous), cereal fiber (grams per day, quintiles), tea (servings per day, quartiles), and sugar-sweetened beverages (servings per day, quintiles). Finally, model 3 included those variables in model 2, plus dietary intake of magnesium (milligrams per day, quintiles) and phytate (milligrams per day, quintiles).

**Table 1** includes the levels of coffee intake in this cohort, as well as intakes of other beverages and of caffeine. Nearly half the cohort ($n=14,224$; mean intake, 2.3 cups per day) reported consuming 1 to 3 cups of coffee per day, with fewer reporting no coffee consumption ($n=2928$) and 2875 reporting 6 or more cups per day ($mean=6.5$ cups per day). Regular coffee was more common than decaffeinated coffee, especially at high levels of coffee intake. Coffee and tea were found to be inversely correlated, whereas there appeared to be only a weak inverse association between soda (primarily sugar-sweetened carbonated beverages) intake and coffee intake. As expected, we observed a strong direct association between coffee intake and caffeine intake. Regular coffee drinkers tended to report less skim milk in their diets compared with coffee abstainers. Median intakes of whole milk and cream were 0 within each coffee category. Linear regression revealed statistically significant ($P<.05$) associations between coffee intake and all variables except soda and whole milk.

The baseline characteristics of the cohort by level of coffee consumption are given in **Table 2**. Generally, higher coffee intake was associated with lower BMI and WHRs, with higher consumption of alcohol and cigarettes, and with lower prevalence of vigorous activity and hypertension. Coffee intake was positively correlated with energy intake and all types of fat and inversely correlated with dietary fiber intake. Coffee intake was inversely associated with intake of fruit and low-fat dairy and positively associated with high-fat dairy. Finally, coffee intake was positively associated with intakes of magnesium and phytate. These associations were not materially different, without exception, when analyzed separately for caffeinated coffee and for decaffeinated coffee.
Relative risks for incident type 2 diabetes mellitus by category of coffee consumption are given in Table 3 for 3 different regression models. In model 1, adjusted for age, education, and baseline hypertension status, we observed a linear dose-response inverse association between coffee intake and diabetes risk (P<0.001). Women who reported drinking 6 or more cups per day had a 34% reduction in risk of diabetes (RR=0.66; 95% confidence interval [CI], 0.52-0.84) compared with those reporting no coffee intake. This association was attenuated by further adjustment in model 2 for a variety of other anthropometric, lifestyle, and dietary factors (RR=0.78; 95% CI, 0.61-1.01; P for linear trend, .06). The inverse associations between coffee intake and diabetes risk were stronger for decaffeinated coffee than for regular (caffeinated) coffee. Indeed, in model 2 there no longer appeared to be an association between caffeinated coffee and diabetes risk, whereas the association between decaffeinated coffee and diabetes risk was only marginally attenuated by anthropometric and lifestyle factors. In addition, the association between total coffee intake and diabetes risk was completely explained by adjustment for intake of decaffeinated coffee (data not shown). Further adjustment for intake of magnesium and phytate in model...
3 did not materially alter the relative risks. Caffeine intake, highly correlated with regular caffeinated coffee intake ($r=0.94$), was not associated with diabetes risk in this study (RR for quintile 5 vs quintile 1, 1.03; 95% CI, 0.86-1.04; $P$ for linear trend, .66).

When we excluded women who reported diabetes in the first 2 years of follow-up, the results were not materially altered. Including regular coffee and decaffeinated coffee in the same model also did not materially change the RR estimates, nor did adjustment for intake of milk and cream. In the full model 3, we observed a possible reduction in risk for women in the highest category of tea intake ($\geq 4$ servings per day: RR = 0.64; 95% CI, 0.40-0.95) relative to the lowest (0 servings per day), whereas intermediate levels of tea intake appeared to confer no protection (quartile 2 [$\geq 1$ serving per day], RR = 1.00 [95% CI, 0.83-1.20]; quartile 3 [1-3 servings per day], RR = 1.01 [95% CI, 0.84-1.21]).

### Table 3. Relative Risks of Incident Type 2 Diabetes Mellitus According to Total Coffee, Regular Coffee, and Decaffeinated Coffee Consumption in 28 812 Women in the Iowa Women’s Health Study, 1986-1997*

| Variable | No. of Cases | Model 1† | | Model 2‡ | | Model 3§ |
|----------|--------------|----------|----------|----------|----------|
|          |              | RR (95% CI) | P Value | RR (95% CI) | P Value | RR (95% CI) | P Value |
| Total coffee, cups per day | | | | | | | |
| 0        | 177          | 1.00      | <.001    | 1.00      | .06      | 1.00      | .07      |
| <1       | 166          | 0.84 (0.68-1.04) | .002    | 0.96 (0.77-1.19) | .001    | 0.95 (0.77-1.18) | .002    |
| 1-3      | 732          | 0.84 (0.71-0.99) | .001    | 1.01 (0.85-1.19) | .001    | 1.01 (0.85-1.19) | .001    |
| 4-5      | 239          | 0.74 (0.61-0.90) | .001    | 0.84 (0.69-1.03) | .001    | 0.85 (0.69-1.04) | .001    |
| $\geq 6$ | 104          | 0.66 (0.52-0.84) | .001    | 0.78 (0.61-1.01) | .001    | 0.79 (0.61-1.02) | .001    |
| Regular coffee, cups per day | | | | | | | |
| 0        | 177          | 1.00      | .03      | 1.00      | .90      | 1.00      | .53      |
| <1       | 524          | 0.79 (0.67-0.94) | .001    | 0.90 (0.76-1.17) | .001    | 0.92 (0.76-1.11) | .001    |
| 1-3      | 488          | 0.83 (0.70-0.99) | .001    | 1.02 (0.85-1.22) | .001    | 0.88 (0.70-1.12) | .001    |
| 4-5      | 161          | 0.80 (0.64-0.99) | .001    | 1.00 (0.80-1.25) | .001    | 0.89 (0.64-1.23) | .001    |
| $\geq 6$ | 68           | 0.67 (0.50-0.88) | .001    | 0.79 (0.59-1.05) | .001    | 1.00 (0.84-1.19) | .001    |
| Decaffeinated coffee, cups per day | | | | | | | |
| 0        | 177          | 1.00      | .001     | 1.00      | .006     | 1.00      | .002     |
| <1       | 765          | 0.82 (0.69-0.96) | .001    | 0.98 (0.82-1.16) | .001    | 0.98 (0.83-1.16) | .001    |
| 1-3      | 389          | 0.82 (0.69-0.99) | .001    | 1.00 (0.83-1.20) | .001    | 1.01 (0.84-1.21) | .001    |
| 4-5      | 67           | 0.61 (0.46-0.81) | .001    | 0.59 (0.44-0.80) | .001    | 0.59 (0.44-0.80) | .001    |
| $\geq 6$ | 20           | 0.58 (0.36-0.92) | .001    | 0.67 (0.42-1.08) | .001    | 0.68 (0.43-1.09) | .001    |

Abbreviations: CI, confidence interval; RR, relative risk.
†Model 1 adjusted for age (continuous), education (high school graduate vs not), and baseline hypertension (yes vs no).
‡Model 2 adjusted for model 1 variables, plus alcohol (0, <4 g/d, and $\geq 4$ g/d), smoking status (smoker vs not), cigarette pack-years (quartiles), body mass index (continuous), waist-hip ratio (continuous), physical activity (high, moderate, and low), energy intake (kilocalories per day, continuous), total fat (grams per day, continuous), Keys score (continuous), cereal fiber (grams per day, quintiles), tea consumption (servings per day, quartiles), and soda consumption (servings per day, quintiles).
§Model 3 adjusted for model 2 variables, plus magnesium (milligrams per day, quintiles) and phytate (milligrams per day, quintiles).

Among postmenopausal women living in the state of Iowa and followed over 11 years from 1986 to 1997, we observed a dose-response inverse association between intake of coffee, particularly decaffeinated coffee, and the risk of type 2 diabetes mellitus. When we computed separate models for regular coffee and for decaffeinated coffee, the inverse associations were considerably stronger for decaffeinated coffee than for regular (caffeinated) coffee. Indeed, in contrast to the findings of other observational studies,3 caffeine intake did not appear to be associated with diabetes risk in our study. While the association between caffeinated coffee and diabetes risk was confounded by adiposity and lifestyle factors, the association between decaffeinated coffee and diabetes risk was only moderately attenuated after these adjustments. That is, the association between decaffeinated coffee and diabetes appeared to be independent of many other potentially confounding anthropometric, lifestyle, and dietary factors, such as physical activity, BMI, and cereal fiber. This association did not appear to be explained by adjustment for 2 coffee components, magnesium and phytate, that were in our database.

At least 10 prior prospective cohort studies from the Netherlands,2,19 Finland,1,20,21 Sweden,4 and the United States5,3,22 have examined the association between coffee consumption habits and risk of type 2 diabetes mellitus. Seven of these studies reported inverse associations between coffee intake and risk of type 2 diabetes mellitus;1,5,19,21 although 2 of these were small underpowered studies.4,19 Tuomilehto and colleagues1 examined this question in a cohort study from Finland, a population with the highest coffee consumption in the world. More than 14 629 men and women were studied for an average follow-up period of 12 years, beginning in 1982. A strong inverse association between coffee intake and risk of type 2 diabetes mellitus was observed, independent of many other lifestyle and dietary factors, and with no apparent threshold for the risk reduction with very high intakes. That is, men and women who reported coffee...
consumption as high as more than 10 cups per day had the lowest RRs for type 2 diabetes mellitus (0.45 [95% CI, 0.25-0.81] for men and 0.21 [95% CI, 0.06-0.69] for women). The study did not, however, examine intake of decaffeinated coffee, presumably because the consumption of decaffeinated coffee was very low in the Finnish population. The results of the Finnish Twin Cohort Study also observed an inverse, albeit weaker, association between coffee intake and diabetes incidence, while one older Finnish study on this topic reported no association between coffee intake and diabetes risk.

Magnesium, for which coffee is a good source, could explain some of the inverse association between coffee intake and risk of type 2 diabetes mellitus through known beneficial effects on carbohydrate metabolism. However, when we entered magnesium into the final model, there was no attenuation of the RRs as one would have expected through causal mediation. Caffeine could not explain our findings because the association was essentially limited to decaffeinated coffee, and caffeine intake was not associated with diabetes risk. Our findings of a weak association between caffeinated coffee and diabetes and no association between caffeine intake and diabetes risk is at odds with the inverse associations reported by the US Nurses Health Study and Health Professionals Follow-up study. Perhaps high caffeine intake carries more detrimental effects in older adults than in middle aged adults, or perhaps the association between caffeine and diabetes in the present study was confounded by some unmeasured or poorly measured factor. Indeed, the literature is mixed on whether caffeine consumption, particularly decaffeinated coffee, could reduce the risk of diabetes. Certainly, the coffee bean is known to be a rich source of many minerals and phytochemicals, including polyphenols such as chlorogenic acid and phytic acid that may improve postprandial carbohydrate metabolism, inhibition of glucose-6-phosphatase activity, and inhibit gut incretin hormones. These mechanisms would be expected to attenuate blood glucose concentrations and possibly reduce the risk or delay the onset of type 2 diabetes mellitus. Furthermore, coffee may have powerful antioxidant properties that could potentially protect the pancreatic beta cell from oxidative stress or promote insulin sensitivity in the peripheral tissues, thereby delaying or preventing the onset of type 2 diabetes mellitus.

Based on data available on the antioxidant content of foods (as assessed by the ferric-reducing ability of plasma assay) and on food consumption data, a study of the Norwegian diet found coffee to contribute more antioxidants than any other dietary component. Unfortunately, typical nutritional data sources such as ours do not include the vast, although poorly understood, phytochemicals and other components of plant-based foods and beverages. Therefore, with the exception of phytate, which was not associated with diabetes risk in our study, we were unable to assess the possibility that these naturally occurring chemicals might explain the link between coffee intake and diabetes risk.

Our study has several limitations. Most notably, our findings are based on observational self-reported data. Both the exposure (diet) and the outcome were based on self-report, leaving possibilities for biases relative to studies with objective measures and studies using experimental designs. We cannot rule out residual confounding as an explanation for our findings. However, it should be noted that measurement error resulting in nondifferential misclassification would tend to bias results toward the null hypothesis. As such, it is possible that our findings underestimate the true strength of association. For these reasons, we cannot rule out that a true inverse association between caffeinated coffee and diabetes risk may exist in this population.

In summary, we observed an inverse association between coffee consumption, especially decaffeinated coffee consumption, and the risk of type 2 diabetes mellitus over an 11-year period in postmenopausal women residing in the state of Iowa. Although this study suggests that the causal mechanism for this association may not be caffeine, magnesium, or phytate, this study was not equipped to thoroughly explore possible causal mechanisms for this association. Although the first line of prevention for diabetes is exercise and diet, in light of the popularity of coffee consumption and high rates of type 2 diabetes mellitus in older adults, these findings may carry high public health significance.

Preventive Intervention Theme Issue

In an effort to encourage research on the topic, a special feature of the ARCHIVES will be devoted to papers on the topic of preventive interventions. Specifically, we are interested in receiving papers focused on the efficacy or effectiveness of interventions. While we will primarily concentrate on randomized controlled trials that assess efficacy, we will also consider papers that employ observational methods of investigation or economic analyses that reasonably estimate theoretical cost-effectiveness of interventions. All kinds of preventive interventions are welcomed—those in the community, in medical offices, in clinics, and in hospitals or other advanced-care settings. However, priority for this theme issue will be given to those papers that are applicable to the practicing internist.

Papers for the preventive intervention theme issue should be submitted no later than October 1, 2006. Pending completion of our peer review process, papers that are accepted for publication will appear in an issue of the Archives of Internal Medicine in the first half of 2007.