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## Coffee consumption and the incidence of type 2 diabetes in men and women with normal glucose tolerance: The Strong Heart Study

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### Abstract

**Background and aims**—It was reported that high coffee consumption was related to decreased diabetes risk. The aim of this study is to examine the association between coffee consumption and the incidence of type 2 diabetes in persons with normal glucose tolerance in a population with a high incidence and prevalence of diabetes.

**Methods and results**—In a prospective cohort study, information about daily coffee consumption was collected at the baseline examination (1989-1992) in a population-based sample of American Indian men and women 45-74 years of age. Participants with normal glucose tolerance (N=1141) at the baseline examination were followed for an average of 7.6 years. The incidence of diabetes was compared across the categories of daily coffee consumption. The hazard ratios of diabetes related to coffee consumption were calculated using Cox proportional hazards models, adjusted for potential confounders.

Levels of coffee consumption were positively related to levels of current smoking and inversely related to body mass index, waist circumference, female gender, and hypertension. Compared to those who did not drink coffee, participants who drank 12 or more cups of coffee daily had 67% less risk of developing diabetes during the follow-up (hazard ratio: 0.33, 95% confidence interval: 0.13, 0.81).

**Conclusion**—In this population, a high level of coffee consumption was associated with a reduced risk of deterioration of glucose metabolism over an average 7.6 years of follow-up. More work is needed to understand whether there is a plausible biological mechanism for this observation.

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## Keywords

coffee; Diabetes Mellitus; type 2; Indians; North American

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## Introduction

Diabetes is a huge burden for the US health care system [1], affecting about 23.6 million people or 7.8% of the population in United States. Estimated diabetes costs in the United States in 2007 were \$174 billion. The association between coffee consumption and risk of some chronic diseases including cardiovascular disease and cancer has been reported[2,3]. Several recent studies reported that coffee consumption is inversely related to the risk of type 2 diabetes [4-12]. Different components in coffee such as antioxidants, phenol chlorogenic acid, magnesium, and caffeine have been proposed to be involved in the process of developing type 2 diabetes[13]. More than 50% of Americans drink coffee, and the average per capita intake is about 2 cups per day [5]. Therefore, a protective effect of coffee could have widespread impact on the population health. Previous studies about coffee consumption and type 2 diabetes were conducted in different populations across European and US. However, data are sparse in populations with a high incidence of diabetes or in individuals with documented normal glucose tolerance.

This report presents analyses from the Strong Heart Study, a population based study of American Indians who are known to have high prevalence (range from 40% to 70% among three study centers) and incidence of diabetes (20% developed incident diabetes in a 4-year period) [14,15]. The aim of the study was to determine whether there is an association between coffee consumption and type 2 diabetes in this population.

## Methods

### Study population and the assessment of diabetes

The Strong Heart Study is a cohort study of cardiovascular disease in 13 American Indian tribes/communities in southwestern Oklahoma, central Arizona, and North and South Dakota. Participants (n = 4,549) aged 45 to 74 years underwent a baseline examination from 1989 to 1992. The design, survey methods, and laboratory techniques were described previously [16-18]. The analysis group for this study was participants with normal glucose tolerance at the baseline examination (1989-92), defined as fasting plasma glucose < 6.1 mmol/l (110mg/dl) and 2-h plasma post-glucose load < 7.8 mmol/l (140mg/dl) and those not on any oral hypoglycemic drugs or insulin. There were a total of 1141 men and women with normal glucose tolerance at the baseline examination who made up the “at risk” cohort for this analysis. Cases of incident diabetes were identified at the second (August 1993 – October 1995) and the third follow-up examinations (January 1998 – August 1999). Participants were followed for an average of 7.6 years by the end of the third follow-up examination. Diabetes was defined according to the 1998 Provisional World Health Organization Report [19] as use of an oral hypoglycemic agent or insulin, or fasting glucose  $\geq 7.0$  mmol/l (126mg/dl) or post-challenge glucose  $\geq 11.1$  mmol/l (200mg/dl) (75-g oral glucose tolerance test). Indian Health Service Institutional Review Boards, Institutional Review Boards of the participating institutions, and the participating tribes approved the study. Informed consent was obtained from all participants.

### Measurements of coffee consumption

At the baseline examination of the Strong Heart Study, a personal interview was conducted with each participant, which included a question related to coffee consumption. The

question was, “How many cups/glasses of caffeinated beverages (i.e., hot or iced coffee, tea, cocoa or chocolate milk) do you drink per day?” Although the question included beverages other than coffee, the information from the 24-h dietary recall at the second follow-up examination indicated that the proportion of participants who consumed tea, cocoa, or chocolate milk is very low in this population (2.5 % (83/3354)). Thus, the results of this question reflect primarily consumption of coffee (97.5%).

### **Assessments of medical history, anthropometry, and lifestyle**

During the Strong Heart Study, personal interview information was collected on demographic factors, medical history, medication use, and personal health habits (physical activity, smoking, and alcohol consumption). Information on leisure-time and occupation-related physical activities was collected using a physical activity questionnaire that has been validated in Pima Indians and in other populations. An estimate of the individual's self-reported physical activity level was averaged over the past year and expressed as hours per week[20]. Past smoking was defined as smoking at least 100 cigarettes in entire lifetime, smoking cigarettes regularly in the past, and not smoking currently. Current smoking was defined as smoking at least 100 cigarettes in entire lifetime, smoking cigarettes regularly, and smoking currently. Past alcohol user was defined as consuming at least 12 drinks of any kind of alcoholic beverage in entire lifetime and the last drink at least 1 year ago. Current alcohol user was defined as consuming at least 12 drinks of any kind of alcoholic beverage in entire lifetime and drinking currently. A physical examination was conducted in the morning, which included collecting fasting blood samples for laboratory tests and a 75-g oral glucose tolerance test. Glucose was measured by enzymatic methods using a Hitachi chemistry analyzer (Boehringer Mannheim Diagnostics, Indianapolis, IN)[21]. Anthropometric measurements were performed with participants in light clothing and without shoes and included weight, height, and waist and hip circumferences. Sitting blood pressure (first and fifth Korotkoff sounds) was measured three times consecutively after five minutes rest using a standard mercury sphygmomanometer (WA Baum Co) [22]. The average of the second and third systolic and diastolic blood pressure measurements was used in the analysis. The information about medication use was ascertained by interview and confirmed by review of the medications brought to the examination or by medical record review.

### **Statistical methods**

Means and percentages of baseline characteristics were calculated by categories of coffee consumption (0, 1-2, 3-4, 5-7, 8-11,  $\geq 12$  cups/glasses per day) collected at the baseline examination. Baseline characteristics included age, body mass index, waist circumference, occupational and leisure time physical activity, fasting glucose, gender, smoking, alcohol use, hypertension (yes/no), and parental history of diabetes (yes/no). The cut-points of coffee consumption categories were initially defined by quartiles. Then, those who did not consume any coffee were separated as the reference group (roughly 10%). Those who drank 12 cups/glasses per day or more comprised 8.1% of the participants and became another group. General linear models were used to test the trend of continuous variables such as age, BMI, waist circumference, fasting glucose, and occupational and leisure time physical activity according to categories of coffee consumption. Mantel-Haenszel Chi-square test was used to test the trends of categorical variables such as proportions of smokers, alcohol users, hypertensives, females, and those with a parental history of diabetes according to the categories of coffee consumption. A two-tailed  $p < 0.05$  was considered to be statistically significant.

Cumulative incidence of diabetes was calculated and presented in a graph by the six categories of daily coffee consumption. Cumulative incidence was calculated by dividing

the number of newly diagnosed diabetic participants by the third exam by the total number of participants at risk at baseline exam. Mantel-Haenszel Chi-square test was used to test the trends of incidence by the six categories of daily coffee consumption.

Cox proportional hazard models were used for multivariable analyses. The date of incident diabetes was estimated as the mid-point between the exam with the negative results and the exam with positive results. For example, for a participant who was diabetes-free at baseline examination and who became diabetic at the second examination, the time to diabetes is estimated as the midpoint of the interval between the two examinations. The covariates in the model included age, gender, smoking, alcohol use, parental history of diabetes, physical activity, and body mass index. All analyses were performed using SAS (Version 9.1, 2002, SAS Institute Inc, Cary, NC). Coffee consumption was also put in the model as continuous variable to examine linear associations between coffee consumption and risk of type 2 diabetes.

## Results

As shown in Table 1, 111 participants reported no current consumption of coffee at the baseline examination. Ninety-two participants reported drinking more than 12 cups of coffee daily. The average coffee consumption at baseline was four cups, with the first and third quartile as two and six cups, respectively. There was a significant, consistent increase in the proportion of current smokers as the category of coffee consumption increased. Coffee intake was inversely related to body mass index, waist circumference, being female, past smoking, and hypertension. There was no significant association in this univariate analysis between categories of coffee consumption and age, physical activity, fasting glucose, or alcohol use.

The crude cumulative incidence and 95% confidence intervals (CI) for diabetes (figure 1) decreased with increasing coffee consumption. For coffee consumption categories 0, 1-2, 3-4, 5-7, 8-11, and 12- cups/glasses per day, the corresponding numbers are 21.6% (14%, 29.2%), 18.9% (13.7%, 24.1%), 17.2% (12.9%, 21.6%), 14.5% (10.2%, 18.8%), 15.9% (10.5%, 21.3%), and 8.7% (2.9%, 14.5%) respectively ( $p$  for trend = 0.01). At the highest level of coffee consumption ( $\geq 12$  cups/glasses per day), the hazard ratio for diabetes was 0.33 (95% CI: 0.13, 0.81); no other level of consumption was significantly related to diabetes risk (Figure 2). The hazard ratios and 95% CI for categories as 1-2, 3-4, 5-7, and 8-11 (cups/glasses per day) are 0.93 (0.55, 1.57), 0.87 (0.53, 1.44), 0.72 (0.43, 1.23), and 0.78 (0.44, 1.37) respectively. The follow-up person-years for each coffee consumption category are as follows (from the lowest to the highest level): 714, 1374, 1873, 1676, 1144, and 623. When coffee consumption entered the model as a continuous variable, the result was consistent with the model including coffee consumption as categorical variables ( $p=0.01$ , hazard ratio and 95% confidence interval as 0.95 (0.91, 0.99)). We did the same analyses in participants with impaired fasting glucose and impaired glucose tolerance. In these participants, the association between coffee consumption and diabetes incidence was minimal.

## Discussion

In the current study, coffee consumption at baseline of 12 or more cups of coffee per day was independently associated with a significant 67% reduction in incidence of diabetes over the following 7.6 years compared to those who were not drinking coffee.

We found an association between high coffee consumption and decreased diabetes risk in a population with high prevalence and incidence of type 2 diabetes. Although such an

association was not found in Pima Indians[23], differences in the categories of coffee consumption (the highest category was 3 cups of coffee or more per day), adjusted lifestyle risk factor (the report from Pima Indian only adjusted for age, sex, and BMI), geographic location of the tribe, and tribal customs related to coffee drinking may contribute to the difference of the study results. By only including the people with normal glucose tolerance, a bias from coffee consumption behavior changes caused by diagnosis of preclinical diabetes has been avoided [5,13]. Our study adds to the existing literature concerning the association between coffee consumption and the risk of type 2 diabetes[4-8,11,12,24].

Although our study was not designed to assess by which biological mechanisms coffee was involved in reducing diabetes risk, there are several possible mechanisms. First, coffee contains compounds that are antioxidants[25,26], which may be related to the risk of diabetes because the oxidative stress may be a pathogenic mechanism linking insulin resistance with dysfunction of both beta cells and endothelium [27]. Second, phenol chlorogenic acid and its degradation products (quinides) in coffee contribute to inhibition of glucose absorption in the intestine [28,29], reducing hepatic glucose output through inhibition of glucose-6-phosphatase[30]. Third, caffeine may also contribute to the inverse association between coffee and diabetes through increasing of basal energy expenditure[31], stimulating fat oxidation and mobilization of glycogen in muscle [32], and weight loss[33]. Caffeine has also been related to acute decrease of insulin sensitivity [34], although prolonged use of caffeine may result in tolerance for such acute effect [35,36]. Finally, other components in coffee such as magnesium have been associated with a lower risk for type 2 diabetes [37,38]. We did not collect other dietary information at the baseline exam. When Exam 2 dietary data were analyzed to explore relations of dietary intake according to coffee consumption of baseline exam, we found that participants who drank 12 or more cups of coffee per day had the highest magnesium intake among all groups. Energy intake, polyunsaturated-to-saturated fat intake ratio, and fiber intake were not significantly different among coffee groups. Further studies on the biological mechanisms relating consumption are needed. Several characteristics of coffee drinkers, such as BMI, physical activity, and smoking are known to be associated with diabetes incidence; these, however, were included as covariates in all analyses.

The strength of this study is the longitudinal design, the systematic diagnosis of diabetes by using blood glucose values measured following a glucose-tolerance test instead of self-reported diabetes, and the availability of information on a wide range of potential confounders.

The limitations of this study include the lack of availability of dietary data on the participants. Given that an independent, inverse association of diabetes risk and coffee consumption was observed only for the highest consumption category ( $\geq 12$  cups/glasses per day), it may be that high coffee consumption is a marker for other factors such as energy intake, meal patterns, and food choices not measured here that are related to diabetes risk. This study was conducted in a single ethnic group; although this population has been shown to be representative of many populations in the US with high levels of obesity and diabetes, analyses in other populations must be done. In addition, analyses were limited to individuals with normal glucose tolerance.

In summary, the consumption of 12 or more cups of coffee per day was associated with a significant, 67% reduction in the incidence of diabetes compared to those who did not drink coffee. Further studies are needed to determine whether this association is causal or a result of unmeasured confounders. The potential effects of high level of coffee consumption on risk of type 2 diabetes may be important but should be considered in light of putative health

effects of coffee, such as potential detrimental effects on blood pressure and sleep quality [39,40].

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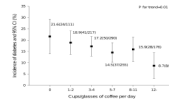
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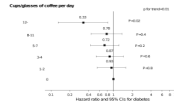
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**Figure 1.**  
Crude incidence of diabetes by daily coffee consumption categories



**Figure 2.** Hazard ratios (and 95% CIs) for incident diabetes by daily coffee consumption categories adjusted for age, gender, smoking, alcohol use, family history of diabetes, physical activity, body mass index.

**Table 1**  
Baseline characteristics by coffee drinking habits in normal glucose tolerance participants: The Strong Heart Study

Characteristics	Coffee drinking status (cups/glasses per day)						P for trend
	0 (n=111, 9.7%)	1-2 (n=217, 19%)	3-4 (n=290, 25.4 %)	5-7 (n=255, 22.3%)	8-11 (n=176, 15.4%)	12- (n =92, 8.1%)	
Age, yrs (Mean, SD)	53.8 (8.1)	55.1(8.0)	55.9(8.1)	55.1(7.6)	54.1(7.4)	52.6(6.5)	0.1
BMI, kg/m <sup>2</sup> (Mean, SD)	29.3 (5.0)	28.9(5.5)	28.6(5.3)	28.0(5.2)	28.5(5.6)	27.2(5.6)	0.004
Waist circumference, cm (Mean, SD)	99.7 (12.6)	99.8(14.0)	99.5(13.1)	97.2(12.4)	99.0(13.9)	94.2(13.8)	0.002
Physical activity, hrs/week (Median, Q <sub>1</sub> , Q <sub>3</sub> )	18.9(4.6,37.6)	16.4(3.7,31.8)	14.1(2.6, 33.3)	18.8(5.7,36.5)	17.2(6.2,33.4)	18.1(4.6,37.5)	0.3
Fasting glucose, mg/dl (Median, Q <sub>1</sub> , Q <sub>3</sub> )	99(93,104)	98(91,103)	98(92,103)	96(92,102)	99(93, 104)	96(92, 102)	0.2
Gender (% female)	63.1	59.9	51.4	47.8	47.2	48.9	0.0008
Smoking (%)							
Past	27.9	33.2	33.1	25.1	26.7	17.4	0.01
Current	30.6	24.9	40.0	53.7	60.8	77.2	0.0001
Alcohol use (%)							
Past	36.0	38.9	38.3	37.0	43.2	40.2	0.4
Current	45.1	45.8	48.6	49.6	52.3	50.0	0.2
Hypertension (%)	37.8	27.4	31.1	19.8	21.7	12.1	0.0001
Parental history of diabetes	36.9	30.9	35.2	32.6	43.2	42.4	0.05