



DIGITAL ACCESS TO SCHOLARSHIP AT HARVARD

Coffee Consumption and Risk of Cardiovascular Diseases and All-Cause Mortality Among Men With Type 2 Diabetes

The Harvard community has made this article openly available. [Please share](#) how this access benefits you. Your story matters.

Citation	Zhang, Weili, Esther Lopez-Garcia, Tricia Y. Li, Frank B. Hu, and Rob M. van Dam. 2009. Coffee Consumption and Risk of Cardiovascular Diseases and All-Cause Mortality Among Men With Type 2 Diabetes. <i>Diabetes Care</i> 32(6): 1043-1045.
Published Version	doi:10.2337/dc08-2251
Accessed	February 19, 2015 8:27:13 AM EST
Citable Link	http://nrs.harvard.edu/urn-3:HUL.InstRepos:4887120
Terms of Use	This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA

(Article begins on next page)

Coffee Consumption and Risk of Cardiovascular Diseases and All-Cause Mortality Among Men With Type 2 Diabetes

WEILI ZHANG, MD, PHD^{1,2}
ESTHER LOPEZ-GARCIA, PHD^{1,3}
TRICIA Y. LI, MD¹

FRANK B. HU, MD, PHD^{1,4,5}
ROB M. VAN DAM, PHD^{1,5}

OBJECTIVE — Coffee consumption has been linked to detrimental acute metabolic and hemodynamic effects. We investigated coffee consumption in relation to risk of CVDs and mortality in diabetic men.

RESEARCH DESIGN AND METHODS — We conducted a prospective cohort study including 3,497 diabetic men without CVD at baseline.

RESULTS — After adjustment for age, smoking, and other cardiovascular risk factors, relative risks (RRs) were 0.88 (95% CI 0.50–1.57) for CVDs (P for trend = 0.29) and 0.80 (0.41–1.54) for all-cause mortality (P for trend = 0.45) for the consumption of ≥ 4 cups/day of caffeinated coffee compared with those for non-coffee drinkers. Stratification by smoking and duration of diabetes yielded similar results. RRs for caffeine intake for the highest compared with the lowest quintile were 1.02 (0.70–1.47; P for trend = 0.96) for CVDs and 0.96 (0.64–1.44; P for trend = 0.69) for mortality.

CONCLUSIONS — These data indicate that regular coffee consumption is not associated with increased risk for CVDs or mortality in diabetic men.

Diabetes Care 32:1043–1045, 2009

Coffee drinking is widespread across the world and has been linked with both beneficial and harmful effects on biological markers of cardiovascular disease (CVD) (1). Recently, caffeine has been reported to have acute detrimental effects on glucose tolerance in diabetes (2). Whereas most prospective studies have suggested that coffee consumption is not associated with increased risk for CVD in general population (3,4), data among diabetes are sparse (5). Therefore, we prospectively examined the relationship between coffee and coronary heart disease (CHD), stroke,

and mortality among men with type 2 diabetes in the Health Professionals Follow-up Study (HPFS).

RESEARCH DESIGN AND METHODS

The HPFS is a prospective cohort study of 51,529 male health professionals aged 40–75 years in 1986. In this study, after excluding participants with CVDs or cancer at baseline, 3,497 men remained who reported a diagnosis of type 2 diabetes on any questionnaire from 1986 to 2004.

Assessment of coffee consumption

Coffee intake was assessed using a semi-quantitative frequency questionnaire sent to the participants in 1986, 1990, 1994, 1998, and 2002. The validity and reliability of the frequency questionnaire has previously been described (6). We also assessed total caffeine intake (7).

Ascertainment of end points

The end points were incident CHD (defined as nonfatal myocardial infarction or fatal CHD), stroke, and mortality. The diagnosis of outcomes has previously been described (4). Briefly, myocardial infarction was confirmed if it met the criteria of the World Health Organization of symptoms and the patient's records showed diagnostic electrocardiographic changes or elevated cardiac enzyme levels. Stroke was confirmed by medical records according to the criteria of the National Survey of Stroke, which define it as a constellation of neurological deficits, sudden or rapid in onset, lasting at least 24 h or until death. Deaths were reported by next of kin or the postal system or ascertained through the National Death Index.

Statistical analysis

Cox proportional hazards regression was used to investigate the association between coffee consumption and incidence of cardiovascular events and all-cause mortality. Multivariable models were adjusted for age, smoking status, BMI, physical activity, alcohol intake, parental history of myocardial infarction, hypertension, hypercholesterolemia, duration of diabetes, hypoglycemic therapy, and dietary factors (total energy intake; use of multivitamin and vitamin E supplements; polyunsaturated, saturated, and *trans* fat intake; glycemic load; and cereal fiber and folate intake) using categorical variables. The median value of each category of coffee consumption was modeled as a continuous variable to test for linear trends. All analyses were performed with SAS software (version 8.2; SAS Institute, Cary, NC).

From the ¹Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts; the ²Sino-German Laboratory for Molecular Medicine, FuWai Cardiovascular Hospital and Cardiovascular Institute, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing, China; ³Universidad Autónoma de Madrid, Madrid, Spain, and CIBERESP (CIBER of Epidemiology and Public Health), Madrid, Spain; the ⁴Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts; and the ⁵Channing Laboratory, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts.

Corresponding author: Rob M. van Dam, rvandam@hsph.harvard.edu.

Received 16 December 2008 and accepted 14 February 2009.

Published ahead of print at <http://care.diabetesjournals.org> on 19 February 2009. DOI: 10.2337/dc08-2251.

© 2009 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See <http://creativecommons.org/licenses/by-nc-nd/3.0/> for details.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Table 1—RRs (95% CI) for CVDs and total mortality by caffeinated coffee consumption and total caffeine intake among men with type 2 diabetes (1986–2004)

	Caffeinated coffee consumption (cups)					P for trend
	<1/month	1/month–4/week	5–7/week	2–3/day	≥4/day	
Total cardiovascular events						
Person-years	5,489	5,184	7,250	4,855	1,289	
n	110	90	144	72	19	
Age and smoking adjusted	1.0	0.83 (0.63–1.01)	0.95 (0.74–1.22)	0.73 (0.54–0.98)	0.71 (0.43–1.17)	0.07
Multivariable I†	1.0	0.72 (0.53–1.00)	0.94 (0.70–1.26)	0.65 (0.45–0.92)	0.86 (0.50–1.50)	0.27
Multivariable II‡	1.0	0.77 (0.53–1.10)	0.93 (0.67–1.28)	0.66 (0.45–0.97)	0.88 (0.50–1.57)	0.29
CHD						
n	86	64	106	54	14	
Age and smoking adjusted	1.0	0.75 (0.54–1.04)	0.88 (0.66–1.18)	0.70 (0.49–0.98)	0.67 (0.37–1.18)	0.11
Multivariable I†	1.0	0.61 (0.41–0.89)	0.89 (0.63–1.24)	0.60 (0.40–0.91)	0.73 (0.38–1.42)	0.26
Multivariable II‡	1.0	0.63 (0.41–0.97)	0.90 (0.62–1.31)	0.66 (0.42–1.02)	0.81 (0.41–1.62)	0.45
Stroke						
n	24	26	38	18	5	
Age and smoking adjusted	1.0	1.12 (0.64–1.96)	1.20 (0.72–2.02)	0.83 (0.45–1.54)	0.88 (0.33–2.35)	0.42
Multivariable I†	1.0	1.16 (0.62–2.17)	1.16 (0.63–2.13)	0.78 (0.37–1.64)	1.34 (0.48–3.78)	0.75
Multivariable II‡	1.0	1.15 (0.58–2.27)	0.97 (0.51–1.86)	0.63 (0.29–1.36)	0.97 (0.33–2.85)	0.31
All-cause mortality						
Person-years	5,555	5,240	7,334	4,901	1,301	
Deaths (n)	127	115	173	98	25	
Age and smoking adjusted	1.0	0.90 (0.70–1.16)	0.92 (0.73–1.16)	0.90 (0.69–1.17)	0.86 (0.56–1.33)	0.52
Multivariable I†	1.0	0.76 (0.55–1.06)	0.96 (0.71–1.30)	0.72 (0.50–1.04)	0.72 (0.39–1.31)	0.24
Multivariable II‡	1.0	0.69 (0.47–1.02)	0.89 (0.63–1.26)	0.71 (0.47–1.06)	0.80 (0.41–1.54)	0.45
	Quintiles of caffeine intake (mg/day)					P for trend
	<110	110–203	204–316	317–450	>450	
Median intake (mg/day)	48	160	238	379	724	
Total CVD events						
Person-years	4,768	4,835	4,801	4,845	4,818	
n	90	84	104	75	82	
Age and smoking adjusted	1.0	0.94 (0.70–1.27)	1.17 (0.88–1.55)	0.85 (0.62–1.15)	0.96 (0.71–1.30)	0.51
Multivariable I†	1.0	0.92 (0.65–1.29)	1.11 (0.80–1.54)	0.86 (0.60–1.23)	1.00 (0.71–1.42)	0.90
Multivariable II§	1.0	0.88 (0.61–1.27)	1.08 (0.76–1.54)	0.84 (0.57–1.23)	1.02 (0.70–1.47)	0.96
CHD						
n	67	62	76	55	64	
Age and smoking adjusted	1.0	0.92 (0.65–1.30)	1.13 (0.81–1.58)	0.82 (0.57–1.18)	1.00 (0.71–1.42)	0.79
Multivariable I†	1.0	0.88 (0.59–1.31)	1.03 (0.70–1.52)	0.82 (0.54–1.24)	0.98 (0.66–1.47)	0.91
Multivariable II§	1.0	0.85 (0.55–1.32)	1.07 (0.70–1.62)	0.83 (0.53–1.31)	1.03 (0.67–1.59)	0.85
Stroke						
n	23	22	28	20	18	
Age and smoking adjusted	1.0	1.01 (0.56–1.82)	1.28 (0.73–2.23)	0.93 (0.51–1.70)	0.82 (0.44–1.54)	0.38
Multivariable I†	1.0	1.04 (0.53–2.03)	1.36 (0.71–2.59)	1.00 (0.49–2.02)	1.04 (0.51–2.11)	0.92
Multivariable II§	1.0	0.97 (0.48–1.94)	1.17 (0.60–2.30)	0.84 (0.41–1.77)	0.94 (0.46–1.95)	0.73
All-cause mortality						
Person-years	4,826	4,887	4,858	4,882	4,877	
n	112	100	138	95	93	
Age and smoking adjusted	1.0	0.91 (0.69–1.19)	1.22 (0.95–1.57)	0.86 (0.65–1.13)	0.94 (0.71–1.24)	0.40
Multivariable I†	1.0	0.91 (0.65–1.29)	1.23 (0.89–1.71)	0.93 (0.65–1.32)	0.80 (0.55–1.16)	0.17
Multivariable II§	1.0	0.93 (0.63–1.38)	1.30 (0.90–1.87)	0.94 (0.63–1.41)	0.96 (0.64–1.45)	0.70

†Adjusted for age (5-year categories), smoking status (never, past, or current at 1–14 or ≥15 cigarettes/day), BMI (<23.0, 23.0–24.9, 25.0–29.9, or ≥30.0 kg/m²), alcohol intake (0, 0.1–4.9, 5.0–14.9, or ≥15 g/day), parental history of myocardial infarction, history of hypertension, hypercholesterolemia, physical activities (quintiles of METs/week), duration of diabetes (<5, 5–10, or ≥10 years), and hypoglycemic medication (yes or no). ‡Adjusted for the variables cited for model I and dietary factors, including total energy intake; multivitamin use and vitamin E supplement use; intake of polyunsaturated, saturated, and *trans* fat; long-chain n-3 fatty acids; cereal fiber; folate; glycemic load (all in quintiles); and decaffeinated coffee and tea consumption. §Adjusted for the variables cited above except for decaffeinated coffee and tea consumption.

RESULTS— Between 1986 and 2004 (24,121 person-years of follow-up), we documented 435 cases of incident CVD (324 CHD and 111 stroke) and 538 deaths from all causes (215 from CHD or stroke, 145 from cancer, and 178 from other causes).

In both age- and smoking-adjusted analyses and multivariable analyses adjusting for lifestyle and other cardiovascular risk factors, we observed no association between caffeinated coffee consumption and a higher risk of CHD, stroke, or all-cause mortality (Table 1). Additional adjustment for dietary factors did not substantially change the results. Similarly, caffeinated coffee consumption was not associated with risk of cardiovascular death (relative risks [RRs] 0.64 [95% CI 0.35–1.17] for once per month to four times per week, 0.84 [0.49–1.44] for five to seven times per week, and 0.58 [0.31–1.10] for two or more cups per day compared with the risks for those who did not consume caffeinated coffee; *P* for trend = 0.26). Caffeine intake was not substantially associated with CVD or mortality (Table 1). We also examined decaffeinated coffee consumption in relation to risk for CVD and mortality and did not observe significant associations (data not shown).

Stratified analyses showed no direct association between coffee consumption and CVD risk in any subgroups by risk factor status, including overweight, smoking status, duration of diabetes, hypertension, parental history of myocardial infarction, and aspirin use (supplemental Table 1, available in the online appendix [http://care.diabetesjournals.org/cgi/content/full/dc08-2251/DC1]).

CONCLUSIONS— In this prospective study in diabetic men, higher habitual coffee consumption was not associated with a higher risk of CVD or all-cause mortality. We did not find significant associations for decaffeinated coffee or total caffeine intake either.

Coffee is a major source of caffeine. Several studies showed that caffeine acutely impaired postprandial glucose metabolism in diabetic patients (8,9). In addition, concerns have been raised in short-term trials that caffeine increases blood pressure (10) and homocysteine levels (11). However, findings from short-term caffeine intervention studies cannot be extrapolated to the effects of chronic coffee consumption on risk of CVD. First, physiological effects of coffee can be different

from those of caffeine. It has been shown that caffeine results in a larger increase in epinephrine concentrations than intake of the same amount of caffeine in coffee (12). Moreover, coffee contains various substances such as antioxidants (i.e., chlorogenic acid) that may improve glucose metabolism and insulin sensitivity (13). Second, the acute effects of caffeine could be transient because partial tolerance to the humoral and hemodynamic effects of caffeine among habitual drinkers might develop after several days of use (14).

In this study, the availability of updated measures of coffee and covariates during the follow-up enabled us to incorporate changes in coffee consumption into the analysis. Because coffee drinking is often thought to be an unhealthy habit, people may quit or reduce the consumption of coffee to improve their health after developing hypertension or hypercholesterolemia. These changes would dilute a possible positive association between coffee and CHD or stroke. To reduce this bias, we excluded subjects with hypertension or hypercholesterolemia at baseline. We also conducted a sensitivity analysis where we used short-term caffeinated coffee consumption in relation to CVD and mortality, which yielded very similar results. As illustrated by the upper limits of 95% CIs of our RR estimates, we cannot exclude the possibility that we missed an association between coffee consumption and a modestly higher risk of CVD due to chance. However, results from a previous study in Finnish individuals with diabetes support the lack of a direct association and even suggest an inverse association between coffee and CVD mortality (5).

In conclusion, in this large prospective study of U.S. men, our findings do not support the hypothesis that habitual caffeinated coffee consumption increases risk of cardiovascular events or mortality among individuals with type 2 diabetes.

Acknowledgments— This study was supported by grants CA87969, HL60712, HL34594, and DK58845 from the National Institutes of Health. The research of W.Z. is supported by a grant (30670862) from the National Natural Science Foundation of China.

No potential conflicts of interest relevant to this article were reported.

References

- van Dam RM. Coffee consumption and coronary heart disease: paradoxical effects on biological risk factors versus disease incidence. *Clin Chem* 2008;54:1418–1420
- Lane JD, Feinglos MN, Surwit RS. Caffeine increases ambulatory glucose and postprandial responses in coffee drinkers with type 2 diabetes. *Diabetes Care* 2008;31:221–222
- Stensvold I, Tverdal A, Jacobsen BK. Cohort study of coffee intake and death from coronary heart disease over 12 years. *BMJ* 1996;312:544–545
- Lopez-Garcia E, van Dam RM, Willett WC, Rimm EB, Manson JE, Stampfer MJ, Rexrode KM, Hu FB. Coffee consumption and coronary heart disease in men and women: a prospective cohort study. *Circulation* 2006;113:2045–2053
- Bidel S, Hu G, Qiao Q, Jousilahti P, Antikainen R, Tuomilehto J. Coffee consumption and risk of total and cardiovascular mortality among patients with type 2 diabetes. *Diabetologia* 2006;49:2618–2626
- Feskanich D, Rimm EB, Giovannucci EL, Colditz GA, Stampfer MJ, Litin LB, Willett WC. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. *J Am Diet Assoc* 1993;93:790–796
- Salazar-Martinez E, Willett WC, Ascherio A, Manson JE, Leitzmann MF, Stampfer MJ, Hu FB. Coffee consumption and risk for type 2 diabetes mellitus. *Ann Intern Med* 2004;140:1–8
- Lane JD, Barkauskas CE, Surwit RS, Feinglos MN. Caffeine impairs glucose metabolism in type 2 diabetes. *Diabetes Care* 2004;27:2047–2048
- Robinson LE, Savani S, Battram DS, McLaren DH, Sathasivam P, Graham TE. Caffeine ingestion before an oral glucose tolerance test impairs blood glucose management in men with type 2 diabetes. *J Nutr* 2004;134:2528–2533
- Hartley TR, Lovallo WR, Whitsett TL. Cardiovascular effects of caffeine in men and women. *Am J Cardiol* 2004;93:1022–1026
- Verhoef P, Pasma WJ, Van Vliet T, Urgert R, Katan MB. Contribution of caffeine to the homocysteine-raising effect of coffee: a randomized controlled trial in humans. *Am J Clin Nutr* 2002;76:1244–1248
- Graham TE, Hibbert E, Sathasivam P. Metabolic and exercise endurance effects of coffee and caffeine ingestion. *J Appl Physiol* 1998;85:883–889
- van Dam RM. Coffee and type 2 diabetes: from beans to beta-cells. *Nutr Metab Cardiovasc Dis* 2006;16:69–77
- Robertson D, Wade D, Workman R, Woosley RL, Oates JA. Tolerance to the humoral and hemodynamic effects of caffeine in man. *J Clin Invest* 1981;67:1111–1117