Does Coffee Consumption Reduce the Risk of Type 2 Diabetes in Individuals With Impaired Glucose?

BESA SMITH, MPH
DEBORAH L. WINGARD, PHD
TYLER C. SMITH, MS
DONNA KRITZ-SILVERSTEIN, PHD
ELIZABETH BARRETT-CONNOR, MD

OBJECTIVE — The purpose of this study was to investigate the association between coffee intake and incident diabetes based on an oral glucose tolerance test (OGTT) and examine coffee habits in those with impaired glucose separately from those with normal glucose at baseline.

RESEARCH DESIGN AND METHODS — In this prospective study, 910 adults aged ≥50 years without diabetes at baseline in 1984–1987 were followed to 1992–1996, an average of 8 years after assessment of coffee intake. Logistic regression models were adjusted for sex, age, physical activity, BMI, smoking, alcohol, hypertension, and baseline fasting plasma glucose.

RESULTS — Past and current coffee drinkers had a reduced risk of incident diabetes (odds ratio 0.38 [95% CI 0.17–0.87] and 0.36 [0.19–0.68], respectively) compared with those who never drank coffee. The 317 participants with baseline impaired glucose who were past or current coffee drinkers were also at reduced risk for incident diabetes (0.31 [0.11–0.87] and 0.36 [0.16–0.83], respectively).

CONCLUSIONS — This study confirms a striking protective effect of caffeinated coffee against incident diabetes and extends these findings to incident diabetes based on OGTT independent of multiple plausible confounders.

Diabetes Care **29:2385–2390, 2006**

The prevalence of diabetes increased 33% in the U.S. between 1990 and 1999 with 7% of the population currently affected (1,2). Estimated projections are that the global prevalence of diabetes will almost double by 2030 (3). Several recently published cohort studies suggest a significant reduced risk of type 2 diabetes in coffee drinkers (4–9). As similar results have been found with decaffeinated coffee (10,11), compounds in coffee other than caffeine have been proposed as being potentially responsible for the reduced risk (12–15). With 52% of U.S. adults consuming coffee on a daily basis (16), a coffee benefit could have widespread impact on the health of the population.

Recently published articles investigating the association between coffee and type 2 diabetes, although strong in their methodology, have relied heavily on a self-reported diagnosis of diabetes, which may be more prone to misclassification or underreporting. Presently, only two studies have used an oral glucose tolerance test (OGTT) for the classification of type 2 diabetes at follow-up (17,18). In this study, incident diabetes was defined on the basis of its absence in history and a normal OGTT at baseline with subsequent presence based largely on a repeat OGTT. Additionally, we consider coffee habits in those with impaired glucose separately from coffee habits in those with normal glucose at baseline. Associations were adjusted for sex, age, physical activity, BMI, smoking, alcohol, hypertension, and baseline fasting plasma glucose (FPG).

RESEARCH DESIGN AND METHODS

Between 1972 and 1974, 82% of all adult residents of a predominantly white middle-class community in southern California participated in a study of heart disease risk factors: the Rancho Bernardo Study (19). Between 1984 and 1987, 2,854 participants (80% of survivors) completed a baseline diabetes evaluation (20); of these individuals, 1,115 (74% of survivors) attended a follow-up evaluation in 1992–1996. Reasons for nonparticipation were death (n = 981), institutionalization, moved out of the area, or declined to participate (n = 250). In 1992, a mailed survey obtained information on current and lifetime consumption of caffeinated and decaffeinated coffee.

At each clinic visit, diagnostic and anthropometric measures along with medical, behavioral, and dietary history were obtained using identical protocols. At both the baseline and diabetes follow-up evaluation, a 75-g glucose load was administered in the morning after a 12- to 16-h fast. Blood was obtained before and 2 h after the glucose load. Fasting and 2-h postchallenge plasma glucose levels were determined by the hexokinase method in a hospital diagnostic laboratory. Height and weight were measured with participants wearing light clothing, without shoes. BMI, an estimate of obesity, was calculated as weight in kilograms divided by the square of height in meters and categorized as underweight/normal (<25.0 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (≥30.0 kg/m^2). A standard mercury sphygmomanometer was used to measure blood pressure after the participant had been seated for at least 5 min, in accord with the Hypertension Detection and Follow-up Program protocol (21). Hypertension was classified according to

From the Division of Epidemiology, Department of Family and Preventive Medicine, University of California San Diego, La Jolla, California.

Address correspondence and reprint requests to Deborah L. Wingard, PhD, Department of Family and Preventive Medicine, University of California San Diego, 9500 Gilman Dr. 0607, La Jolla, CA 92093-0607. E-mail: dwingard@ucsd.edu.

Received for publication 25 May 2006 and accepted in revised form 28 July 2006.

Abbreviations: DBP, diastolic blood pressure; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; PCG, postchallenge glucose; SBP, systolic blood pressure.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

DOI: 10.2337/dc06-1084

Table 1—*Baseline characteristics by coffee drinking habits in nondiabetic participants, Rancho Bernardo Study, 1984–1987*

Characteristic	Coffee drinking status			*P* value*
	Never	Past	Current	
n	97	153	660	
Age (years)	64.2 ± 9.0	66.2 ± 7.9	66.1 ± 8.7	0.09
Sex				0.14
Male	40 (41.2)	51 (33.3)	278 (42.1)	
Female	57 (58.8)	102 (66.7)	382 (57.9)	
Exercise ≥3 times/week				0.23
No	18 (18.6)	17 (11.1)	103 (15.6)	
Yes	79 (81.4)	136 (88.9)	557 (84.4)	
BMI (kg/m^2)				0.27
Normal (<25.0)	58 (59.8)	93 (60.8)	371 (56.2)	
Overweight (25.0–29.9)	28 (28.9)	51 (33.3)	244 (37.0)	
Obese (≥30)	11 (11.3)	9 (5.9)	45 (6.8)	
Smoking				≤0.01
Never	66 (68.0)	67 (43.8)	259 (39.2)	
Past	24 (24.7)	67 (43.8)	313 (47.4)	
Current	7 (7.2)	19 (12.4)	88 (13.3)	
Average daily alcohol intake (g)				≤0.01
None	58 (59.8)	57 (37.3)	190 (28.8)	
1–30	27 (27.8)	77 (50.3)	391 (59.2)	
>30	12 (12.4)	19 (12.4)	79 (12.0)	
Hypertension†				0.25
Normal	22 (22.7)	35 (22.9)	143 (21.7)	
Prehypertensive	41 (42.3)	45 (29.4)	221 (33.5)	
Hypertensive	34 (35.1)	73 (47.7)	296 (44.9)	

Data are means ± SD or *n* (%). **P* value for age based on ANOVA. All other *P* values based on Pearson's χ^2 test of association. †Hypertension categories were based on SBP and DBP as follows: normal (SBP <120 mmHg and DBP <80 mmHg), prehypertensive (SBP 120–139 mmHg or DBP 80–99 mmHg), or hypertensive (SBP >140 mmHg or DBP >90 mmHg). In addition, individuals taking antihypertensive medication were categorized as hypertensive.

the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (22). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were used to categorize participants' blood pressure as normal (SBP <120 mmHg and DBP <80 mmHg), prehypertensive (SBP 120–139 mmHg or DBP 80–89 mmHg), or hypertensive (SBP ≥140 mmHg or DBP ≥90 mmHg). In addition, individuals taking antihypertensive medication were categorized as hypertensive.

A specially trained interviewer obtained information on sex, age, physical activity (three or more times in the last week [no/yes]), smoking status (never, past, and current), and average daily alcohol intake (none, 1–30 g, or >30 g). Individuals were questioned about their medical history including diagnosis of diabetes and past or current use of insulin or oral hypoglycemic agents. Medication use, including insulin or oral hypoglycemic agents, was confirmed by a nurse who examined pills and prescriptions brought to the clinic.

Regular coffee and decaffeinated coffee consumption were assessed separately by mail in 1992 using a self-administered questionnaire. Participants were asked about the number of cups of caffeinated and decaffeinated coffee they drank per day from age 18–45 and after age 45, categorized as 0 cups, 1–2 cups, 3–4 cups, and ≥5 cups. Cup-years were estimated based on the age at which the participant began drinking coffee and the average cup consumption reported between ages 18 and 45 and after age 45. Participants were categorized based on lifetime coffee status (nondrinker, past drinker, or current drinker); those who did not drink coffee between 18 and 45 years of age and did not drink coffee after the age of 45 were considered nondrinkers. Those who drank coffee from 18 to 45 years of age but not after age 45 were classified as past drinkers, and the remainder (excluding 11 with missing data who were removed from analyses) were classified as current drinkers.

Individuals were classified as having normal glucose at baseline (FPG <6.1 mmol/l and postchallenge glucose [PCG] <7.8 mmol/l or missing PCG; $n = 593$) or impaired glucose at baseline. Impaired glucose was defined as either impaired fasting glucose (6.1 mmol/l ≤ FPG <7.0 mmol/l and PCG <7.8 mmol/l) or impaired glucose tolerance (FPG <6.1 and 7.8 mmol/l ≤ PCG <11.1 mmol/l).

On the basis of the 1999 World Health Organization criteria (23), individuals were classified as having type 2 diabetes if they met one of the following: FPG ≥7.0 mmol/l, PCG ≥ 11.1 mmol/l, taking oral medication for diabetes in the last 2 weeks, or having been told by a physician that they had diabetes. Because the incidence of type 2 diabetes was the focus of this investigation, those who had diabetes at baseline were excluded ($n = 127$). Eight individuals with missing glucose values and one individual with type 1 diabetes were also excluded.

After excluding an additional 11 individuals who were missing covariate data, there were 910 participants aged ≥50 years without diabetes at baseline who were followed for up to 11 years (mean 8.3) for incident type 2 diabetes.

This research was approved by the in-

Table 2—*Baseline coffee consumption by baseline glucose level in nondiabetic participants, Rancho Bernardo Study, 1984–1987*

Characteristic	Total nondiabetic	Normal glucose*	Impaired glucose*
n	910	593	317
Coffee status			
Never drank	97 (10.7)	58 (9.8)	39 (12.3)
Past drinker	153 (16.8)	93 (15.7)	60 (18.9)
Current drinker	660 (72.5)	442 (74.5)	218 (68.8)
Daily coffee consumption after age 45 years (cups)			
0	250 (27.5)	151 (25.5)	99 (31.2)
1–2	379 (41.7)	246 (41.5)	133 (42.0)
3–4	183 (20.1)	124 (20.9)	59 (18.6)
≥5	98 (10.8)	72 (12.1)	26 (8.2)
Cup-years	101.0 (98.0)	102.0 (98.5)	95.0 (100.0)

Data are *n* (%) or median (interquartile range). *Normal glucose defined as FPG <6.1 mmol/l and PCG <7.8 mmol/l or missing PCG. Impaired glucose defined as either impaired fasting glucose (6.1 mmol/l ≤ FPG < 7.0 mmol/l and PCG < 7.8 mmol/l) or impaired glucose tolerance (FPG < 6.1 mmol/l and 7.8 mmol/l ≤ PCG < 11.1 mmol/l). †Because of the missing coffee drinking start date, cup-years were based on sample sizes of 815, 536, and 279 for the total nondiabetic sample, those with normal glucose at baseline, and those with impaired glucose at baseline, respectively.

stitutional review board of the University of California, San Diego. All participants gave written informed consent at both clinic visits before participation.

Statistical analyses

After preliminary analyses using descriptive and univariate methods, multivariable logistic regression was used to model the risk of incident type 2 diabetes in relation to coffee consumption. Covariates, selected on the basis of published literature, were assessed for collinearity. Covariates were also investigated as possible confounders before removing them from further modeling. Variables were retained in all modeling if they were associated with both coffee consumption and type 2 diabetes or their removal changed measures of association by >15%. Manual backward elimination of variables was used. Analyses were conducted separately in those with normal and impaired glucose at baseline.

Incidence was defined as the number of events identified per 100 participants over an average of 8 years. Odds ratios (ORs) and 95% CIs were computed using the Wald statistic for unconditional maximum likelihood estimation. All data analyses were performed using SAS (24).

RESULTS — All 910 participants did not have diabetes at baseline; 593 had normal glucose and 317 had impaired glucose. The baseline fasting plasma glucose was 5.4 ± 0.6 mmol/l (mean ± SD). The average age was 65.9 ± years, 41% of the participants were male, and 85% reported physical activity three or more times per week. Fifty-seven percent were underweight or normal weight (BMI <25.0 kg/m^2), and 7% were obese (BMI ≥30 kg/m^2). In addition, 12–13% were current smokers, more than half drank 1–30 g of alcohol (1–2 drinks) on an average day, and 44% were hypertensive (SBP ≥140 mmHg or DBP ≥90 mmHg or taking antihypertensive medication).

As shown in Table 1, at baseline, 97 participants reported never drinking coffee, 153 were past coffee drinkers, and 660 were current coffee drinkers. Current coffee drinkers were significantly more likely to report they were current smokers ($P \leq 0.01$) and that they drank an average of 1–2 alcoholic drinks per day ($P \leq 0.01$). Age, sex, physical activity, BMI, and hypertension did not differ significantly by coffee drinking status.

Table 2 shows that the majority of participants were current drinkers of relatively small amounts of caffeinated coffee at baseline (73%). Current caffeinated coffee drinkers drank on average 2.8 cups/day (range 1–20). Participants with normal glucose had a higher median number of cup-years compared with those who had impaired glucose at baseline (102 vs. 95, respectively), drank ≥5 cups/day (12 vs. 8%, respectively), and were current coffee drinkers (75 vs. 69%, respectively); these differences, however, were not statistically significant.

Table 3 presents baseline characteristics by incident diabetes. As shown, significantly more obese and hypertensive participants developed diabetes during the course of the study ($P \leq 0.01$ and 0.04, respectively). Additionally, a proportionately higher number of participants who reported no daily alcoholic intake or who consumed an average of ≥3 drinks/day developed diabetes, compared with those who drank 1–2 drinks/day ($P = 0.03$).

In Table 4, the association of coffee consumption with the adjusted risk of incident diabetes is presented for all nondiabetic participants and separately for those with normal and impaired glucose at baseline. Current coffee drinking was significantly associated with a reduced risk of type 2 diabetes in the nondiabetic population as a whole (OR 0.36 [95% CI 0.19–0.68]) and in the subgroup with impaired glucose (0.36 [0.16–0.83]) independent of multiple covariates. Past coffee drinking was associated with a similar significantly reduced risk of type 2 diabetes in the nondiabetic population (0.38 [0.17–0.87]) and in the subgroup with impaired glucose (0.31 [0.11–0.87]). Both past (0.63 [0.12–3.21]) and current coffee drinking (0.40 [0.10–1.65]) had a reduced risk of incident type 2 diabetes in those with normal glucose at baseline; however, these findings were not significant. Daily coffee consumption (0 cups, 1–2 cups, 3–4 cups, or ≥5 cups), after the age of 45 and number of cup-years, were not significantly associated with risk of type 2 diabetes in any of the groups examined. Reduced models, eliminating nonsignificant covariates, yielded similar results.

Analyses restricted to decaffeinated coffee drinkers could not be performed because only 12 participants reported consuming decaffeinated coffee exclusively. Reanalysis of these data excluding the few participants who drank only decaffeinated coffee yielded similar results (data not shown).

CONCLUSIONS — In the present study, current or past coffee drinkers who did not have diabetes at baseline had a 60% reduced risk of type 2 diabetes during the next 8 years, when compared with those who never drank coffee. Additionally, those without diabetes who had impaired glucose at baseline were similarly protected against incident diabetes. The quantity of coffee consumed daily (cup-years) did not predict diabetes risk in ei-

Table 3—*Baseline characteristics by development of incident type 2 diabetes in nondiabetic participants, Rancho Bernardo Study, 1984–1987*

Characteristic	Incident type 2 diabetes		*P* value*
	No	Yes	
n	826	84	
Age (years)	65.9 (8.6)	66.2 (8.4)	0.73
Sex			0.25
Male	330 (40.0)	39 (46.4)	
Female	496 (60.1)	45 (53.6)	
Exercise ≥3 times/week			0.47
No	123 (14.9)	15 (17.9)	
Yes	703 (85.1)	69 (82.1)	
BMI (kg/m^2)			≤0.01
Underweight/normal (<25.0)	485 (58.7)	37 (44.1)	
Overweight (25.0–29.9)	292 (35.4)	31 (36.9)	
Obese (≥30)	49 (5.9)	16 (19.1)	
Smoking			0.12
Never	347 (42.0)	45 (53.6)	
Past	373 (45.2)	31 (36.9)	
Current	106 (12.8)	8 (9.5)	
Average daily alcohol intake (g)			0.03
None	272 (32.9)	33 (39.3)	
1–30	460 (55.7)	35 (41.7)	
>30	94 (11.4)	16 (19.1)	
Hypertension‡			0.04
Normal	190 (23.0)	10 (11.9)	
Prehypertensive	279 (33.8)	28 (33.3)	
Hypertensive	357 (43.2)	46 (54.8)	

Data are means ± SD or *n* (%).*P value for age based on *t* test. All other *P* values based on Pearson's χ^2 test of association. †Hypertension categories were based on SBP and DBP as follows: normal (SBP <120 mmHg and DBP <80 mmHg), prehypertensive (SBP 120–139 mmHg or DBP 80–99 mmHg), or hypertensive (SBP ≥140 mmHg or DBP ≥90 mmHg). In addition, individuals taking antihypertensive medication were categorized as hypertensive.

ther those with normal or impaired glucose at baseline.

A significant reduced risk of diabetes among coffee drinkers is consistent with other recent cohort studies (4–9). However, unlike those studies in which the diagnosis of diabetes was based on medical records or self-report, in the present study a glucose tolerance test was used. Diabetes is often undiagnosed in older adults; therefore, the results of the present study would be subject to less misclassification bias because both FPG and PCG were used to define incident diabetes.

Significant inverse associations between coffee consumption and type 2 diabetes including dose-response associations have been reported (5,6,9). The lack of a significant dose response association in the present study may be due to the older age of this population (average 66 years) relative to those in other studies and less coffee consumption by older adults (25).

Many published research articles investigating the biological explanation for the association between coffee and a reduced risk of type 2 diabetes have focused on the role of caffeine with contradictory results. Small placebo-controlled trials have reported that caffeine raises blood glucose levels and contributes to insulin resistance (26,27), suggesting the potential for an increased risk of type 2 diabetes. However, another small, randomized, crossover clinical trial showed that caffeinated coffee reduced FPG (28). Additionally, research has shown that elevated glucose concentrations fall 30 min after coffee consumption (29). Although some human studies reported that catecholamine activity decreases with increased tolerance to caffeine (30), studies in mice showed that caffeine promotes the release of catecholamines and stimulates an increased metabolic rate and thermogenesis of brown adipose tissue (31), which is expected to reduce obesity. Caffeine also upregulates the expression of uncoupling protein 3 (32), which has been linked to carbohydrate metabolism and type 2 diabetes (33). Specifically, uncoupling protein 3 is lower in patients with type 2 diabetes compared with healthy control

Table 4—*Adjusted* associations of coffee with incident type 2 diabetes by baseline glucose level, Rancho Bernardo Study, 1984–1987*

Coffee exposure	Total nondiabetic	Normal glucose†	Impaired glucose†
n	910	593	317
Coffee status			
Past drinker/never drank	13/18, 0.38 (0.17–0.87)	4/3, 0.63 (0.12–3.21)	9/15, 0.31 (0.11–0.87)
Current drinker/never drank	53/18, 0.36 (0.19–0.68)	14/3, 0.40 (0.10–1.65)	39/15, 0.36 (0.16–0.83)
Daily coffee consumption after age 45 years (cups)			
1–2/0	31/31, 0.66 (0.38–1.14)	8/7, 0.64 (0.22–1.89)	23/24, 0.71 (0.35–1.41)
3–4/0	13/31, 0.53 (0.26–1.08)	4/7, 0.54 (0.15–2.00)	9/24, 0.55 (0.22–1.36)
≥5/0	9/31, 0.60 (0.26–1.40)	2/7, 0.33 (0.06–1.80)	7/24, 1.01 (0.33–3.13)
Cup-years (per 20)‡	0.99 (0.93–1.05)	1.01 (0.92–1.12)	0.98 (0.90–1.06)

Data are *n*, OR (95% CI). *Models are adjusted for age, sex, exercise, BMI, smoking, daily alcohol intake, hypertension, and FPG assessed at baseline, 1984–1987. †Normal glucose defined as FPG <6.1 mmol/l and PCG <7.8 mmol/l or missing PCG. Impaired glucose defined as either impaired fasting glucose (6.1 mmol/l ≤ FPG < 7.0 mmol/l and PCG < 7.8 mmol/l) or impaired glucose tolerance (FPG < 6.1 mmol/l and 7.8 mmol/l ≤ PCG < 11.1 mmol/l). ‡Because of missing coffee drinking start date, cup-years were based on sample sizes of 815, 279, and 536 for the total nondiabetic sample, those with normal glucose at baseline, and those with impaired glucose at baseline, respectively.

subjects (34) and inversely related to BMI (35).

Geographic differences exist with respect to the coffee bean and filtration method commonly used. Although caffeine content is similar between boiled and drip-filtered coffee (36–38), diterpene content is lower in coffee that has been drip-filtered (39). A significant protective effect of coffee consumption in a Finnish population (6) refuted an earlier report from Finland that did not find a decreased risk of type 2 diabetes associated with coffee consumption (40). In the earlier report, Finns were more likely to drink boiled coffee than drip-filtered coffee (39). Diterpenes, in particular, cafestol and kahweol, have been reported to increase serum total cholesterol levels and to be associated with higher rates of coronary heart disease in coffee drinkers from Norway (41) who, like Finns, once preferred boiled coffee. Therefore, different results in the two Finnish studies may reflect a conversion from boiled to filtered coffee. Most countries, including the U.S., use arabica coffee beans, which contain about half the caffeine of robusta coffee beans (36) primarily used in France, Italy, Portugal, and the U.K., countries with slightly lower prevalence estimates of diabetes than the U.S. (42). Studies in which caffeinated beverages other than coffee were considered showed weaker correlations with fasting glycemia than for coffee per se (43,44); however, similar inverse associations with C-peptide levels have been seen in both caffeinated and decaffeinated coffee drinkers (11). Other research suggests that a reduction in risk may be due to compounds in coffee other than caffeine, including chlorogenic acid, quinides, and trigonelline (12–15).

Several potential limitations of the present study were considered. Participants were predominantly middle-class and white; results may not be applicable to other ethnicities and socioeconomic strata. Although nearly half of this older cohort died in the 8 years between baseline and follow-up, it is unlikely that survival bias explains these results as there was no significant difference in baseline coffee intake between those who did and did not participate in the follow-up visit. Coffee consumption was self-reported and may be subject to recall bias. However, validation of food frequency retrieved from questionnaires has shown strong correlation for coffee ($r = 0.92$) (45). Further, to simplify recall and minimize recall bias, early and late lifetime estimates were combined to create an overall lifetime coffee status (never, past, or current drinker). In addition, only estimates of intake from age ≥45 years were used for daily cup consumption comparisons. Information regarding coffee additives, other than milk, was not available. Although refuted in other reports (4,46), milk and sugar have been implicated as possible confounders (47); they were not considered here, but the added calories would have been expected to reduce, not create, a protective effect. Lastly, our study used results from a single OGTT at follow-up for the classification of incident type 2 diabetes, whereas clinical diagnosis is usually followed by a second, confirmatory OGTT. Research has shown that an OGTT is necessary to identify most older adults with impaired glucose levels and, thus, more people who will develop diabetes (48).

In summary, the present study shows a striking (60%) reduction in risk of incident type 2 diabetes in coffee drinkers, significantly for individuals with impaired glucose at baseline. These results were independent of age, sex, exercise, BMI, smoking status, daily alcohol intake, hypertension, and baseline fasting plasma glucose. Given the increasing prevalence of obesity, IGT, and diabetes, and the fact that the majority of adults in most of the Westernized world drink coffee daily, a coffee benefit could have widespread impact. Further investigation is warranted.

Acknowledgments— This research was supported by National Institute of Diabetes and Digestive and Kidney Diseases Grant DK-31801 and National Institute on Aging Grant AG 07181.

The authors thank Ricki Bettencourt, MS, Cedric Garland, DrPH, Frank Garland, PhD, and Ed Gorham, PhD.

References

1. Mokdad AH, Ford ES, Bowman BA, Nelson DE, Engelgau MM, Vinicor F, Marks JS: Diabetes trends in the U.S.: 1990–1998. *Diabetes Care* 23:1278–1283, 2000
2. Centers for Disease Control and Prevention: *Number of Americans with Diabetes Continues to Increase*. Atlanta, GA, Office of Communication, Centers for Disease Control and Prevention, 2005
3. Wild S, Roglic G, Green A, Sicree R, King H: Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 27:1047–1053, 2004
4. van Dam RM, Feskens EJ: Coffee consumption and risk of type 2 diabetes mellitus. *Lancet* 360:1477–1478, 2002
5. Salazar-Martinez E, Willet W, Ascherio A, Manson J, Leitzmann M, Stampfer M, Hu F: Coffee consumption and risk for type 2 diabetes mellitus. *Ann Intern Med* 140: 1–8, 2004
6. Tuomilehto J, Hu G, Bidel S, Lindstrom J, Jousilahti P: Coffee consumption and risk of type 2 diabetes mellitus among middle-aged Finnish men and women. *JAMA* 291: 1213–1219, 2004
7. Carlsson S, Hammar N, Grill V, Kaprio J: Coffee consumption and risk of type 2 diabetes in Finnish twins. *Int J Epidemiol* 33: 616–617, 2004
8. Rosengren A, Dotevall A, Wilhelmsen L, Thelle D, Johansson S: Coffee and incidence of diabetes in Swedish women: a prospective 18-year follow-up study. *J Intern Med* 255:89–95, 2004
9. van Dam RM, Willett WC, Manson JE, Hu FB: Coffee, caffeine, and risk of type 2 diabetes: a prospective cohort study in younger and middle-aged U.S. women. *Diabetes Care* 29:398–403, 2006
10. Greenberg JA, Axen KV, Schnoll R, Boozer CN: Coffee, tea and diabetes: the role of weight loss and caffeine. *Int J Obes (Lond)* 29:1121–1129, 2005
11. Wu T, Willett WC, Hankinson SE, Giovannucci E: Caffeinated coffee, decaffeinated coffee, and caffeine in relation to plasma C-peptide levels, a marker of insulin secretion, in U.S. women. *Diabetes Care* 28:1390–1396, 2005
12. van Dam RM: Coffee and type 2 diabetes: from beans to β-cells. *Nutr Metab Cardiovasc Dis* 16:69–77, 2006
13. Ross CM: Coffee consumption and development of type 2 diabetes. *JAMA* 294: 2299; author reply 2299, 2005
14. Rodriguez de Sotillo DV, Hadley M: Chlorogenic acid modifies plasma and liver concentrations of: cholesterol, triacylglycerol, and minerals in (fa/fa) Zucker rats. *J Nutr Biochem* 13:717–726, 2002
15. Shearer J, Farah A, de Paulis T, Bracy DP, Pencek RR, Graham TE, Wasserman DH: Quinides of roasted coffee enhance insulin action in conscious rats. *J Nutr* 133: 3529–3532, 2003
16. Lane JD, Pieper CF, Phillips-Bute BG, Bryant JE, Kuhn CM: Caffeine affects cardiovascular and neuroendocrine activation at work and home. *Psychosom Med* 64:595–603, 2002
17. van Dam RM, Dekker JM, Nijpels G, Stehouwer CD, Bouter LM, Heine RJ: Coffee consumption and incidence of impaired fasting glucose, impaired glucose tolerance, and type 2 diabetes: the Hoorn Study. *Diabetologia* 47:2152–2159, 2004
18. Saremi A, Tulloch-Reid M, Knowler WC: Coffee consumption and the incidence of type 2 diabetes. *Diabetes Care* 26:2211–2212, 2003
19. Criqui M, Barrett-Connor E, Austin M:

Differences between respondents and non-respondents in a population-based cardiovascular disease study. *Am J Epidemiol* 108:367–372, 1978
20. Wingard DL, Barrett-Connor E: Community-based study of prevalence of NIDDM in older adults. *Diabetes Care* 13:S3–S8, 1990
21. The hypertension detection and follow-up program: hypertension detection and follow-up program cooperative group. *Prev Med* 5:207–215, 1976
22. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 289:2560–2572, 2003
23. World Health Organization: *Definition, Diagnosis and Classification of Diabetes Mellitus and Its Complications. Report of a WHO Consultation. Part 1: Diagnosis and Classification of Diabetes Mellitus*. Geneva, World Health Org., Department of Noncommunicable Disease Surveillance, 1999
24. SAS Institute: *SAS/STAT Version 9.0*. Cary, NC, SAS Inst., 2002
25. Ferrini RL, Barrett-Connor E: Caffeine intake and endogenous sex steroid levels in postmenopausal women: the Rancho Bernardo Study. *Am J Epidemiol* 144:642–644, 1996
26. Pizziol A, Tikhonoff V, Paleari CD, Russo E, Mazza A, Ginocchio G, Onesto C, Pavan L, Casiglia E, Pessina AC: Effects of caffeine on glucose tolerance: a placebo-controlled study. *Eur J Clin Nutr* 52:846–849, 1998
27. Petrie HJ, Chown SE, Belfie LM, Duncan AM, McLaren DH, Conquer JA, Graham TE: Caffeine ingestion increases the insulin response to an oral-glucose-tolerance test in obese men before and after weight loss. *Am J Clin Nutr* 80:22–28, 2004
28. Naismith DJ, Akinyanju PA, Szanto S, Yudkin J: The effect, in volunteers, of coffee and decaffeinated coffee on blood glucose, insulin, plasma lipids and some factors involved in blood clotting. *Nutr Metab* 12:144–151, 1970
29. Johnston KL, Clifford MN, Morgan LM: Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: glycemic effects of chlorogenic acid and caffeine. *Am J Clin Nutr* 78:728–733, 2003
30. Robertson D, Wade D, Workman R, Woosley RL, Oates JA: Tolerance to the humoral and hemodynamic effects of caffeine in man. *J Clin Invest* 67:1111–1117, 1981
31. Yoshioka K, Yoshida T, Kamanaru K, Hiraoka N, Kondo M: Caffeine activates brown adipose tissue thermogenesis and metabolic rate in mice. *J Nutr Sci Vitaminol* 36:173–178, 1990
32. Kogure A, Sakane N, Takakura Y, Umekawa T, Yoshioka K, Nishino H, Yamamoto T, Kawada T, Yoshikawa T, Yoshida T: Effects of caffeine on the uncoupling protein family in obese yellow KK mice. *Clin Exp Pharmacol Physiol* 29: 391–394, 2002
33. Clapham JC, Arch JR, Chapman H, Haynes A, Lister C, Moore GB, Piercy V, Carter SA, Lehner I, Smith SA, Beeley LJ, Godden RJ, Herrity N, Skehel M, Changani KK, Hockings PD, Reid DG, Squires SM, Hatcher J, Trail B, Latcham J, Rastan S, Harper AJ, Cadenas S, Buckingham JA, Brand MD, Abuin A: Mice overexpressing human uncoupling protein-3 in skeletal muscle are hyperphagic and lean. *Nature* 406:415–418, 2000
34. Schrauwen P, Hesselink MK, Blaak EE, Borghouts LB, Schaart G, Saris WH, Keizer HA: Uncoupling protein 3 content is decreased in skeletal muscle of patients with type 2 diabetes. *Diabetes* 50:2870–2873, 2001
35. Schrauwen P, Walder K, Ravussin E: Human uncoupling proteins and obesity. *Obes Res* 7:97–105, 1999
36. Nehlig A: Are we dependent upon coffee and caffeine? A review on human and animal data. *Neurosci Biobehav Rev* 23:563–576, 1999
37. Clubley M, Bye CE, Henson TA, Peck AW, Riddington CJ: Effects of caffeine and cyclizine alone and in combination on human performance, subjective effects and EEG activity. *Br J Clin Pharmacol* 7:U57–U63, 1979
38. Colton T, Gosselin RE, Smith RP: The tolerance of coffee drinkers to caffeine. *Clin Pharmacol Ther* 9:31–39, 1968
39. Urgert R, de Groot C: Consumption of unfiltered coffee brews in elderly Europeans. *Eur J Clin Nutr* 50:S101–S104, 1996
40. Reunanen A, Heliovaara M, Aho K: Coffee consumption and risk of type 2 diabetes mellitus. *Lancet* 361:702–703, 2003
41. Urgert R, Weusten-van der Wouw MP, Hovenier R, Meyboom S, Beynen AC, Katan MB: Diterpenes from coffee beans decrease serum levels of lipoprotein(a) in humans: results from four randomized controlled trials. *Eur J Clin Nutr* 51:431–436, 1997
42. International Diabetes Federation: *Diabetes Atlas, 2005*. Available from http://www.eatlas.idf.org/. Accessed 15 April 2006
43. Tsugane S, Fahey MT, Sasaki S, Baba S: Alcohol consumption and all-cause and cancer mortality among middle-aged Japanese men: seven-year follow-up of the JPHC Study Cohort I. Japan Public Health Center. *Am J Epidemiol* 150:1201–1207, 1999
44. Tsugane S, Sobue T: Baseline survey of JPHC study—design and participation rate: Japan Public Health Center-Based Prospective Study on Cancer and Cardiovascular Diseases. *Am J Epidemiol* 11:S24–S29, 2001
45. 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* 93:790–796, 1993
46. Isogawa A, Noda M, Takahashi Y, Kadowaki T, Tsugane S: Coffee consumption and risk of type 2 diabetes mellitus. *Lancet* 361:703–704, 2003
47. Tan DS: Coffee consumption and risk of type 2 diabetes mellitus. *Lancet* 361:702, 2003
48. Sherwin RS, Anderson RM, Buse JB, Chin MH, Eddy D, Fradkin J, Ganiats TG, Ginsberg HN, Kahn R, Nwankwo R, Rewers M, Schlessinger L, Stern M, Vinicor F, Zinman B: Prevention or delay of type 2 diabetes. *Diabetes Care* 27 (Suppl. 1): S47–S54, 2004