REVIEW ARTICLE

Coffee, Decaffeinated Coffee, and Tea Consumption in Relation to Incident Type 2 Diabetes Mellitus

A Systematic Review With Meta-analysis

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Background: Coffee consumption has been reported to be inversely associated with risk of type 2 diabetes mellitus. Similar associations have also been reported for decaffeinated coffee and tea. We report herein the findings of meta-analyses for the association between coffee, decaffeinated coffee, and tea consumption with risk of diabetes.

Methods: Relevant studies were identified through search engines using a combined text word and MeSH (Medical Subject Headings) search strategy. Prospective studies that reported an estimate of the association between coffee, decaffeinated coffee, or tea with incident diabetes between 1966 and July 2009.

Results: Data from 18 studies with information on 457 922 participants reported on the association between coffee consumption and diabetes. Six (N=225 516) and 7 studies (N=286 701) also reported estimates of the association between decaffeinated coffee and tea with diabetes, respectively. We found an inverse log-linear relationship between coffee consumption and subsequent risk of diabetes such that every additional cup of coffee consumed in a day was associated with a 7% reduction in the excess risk of diabetes relative risk, 0.93 [95% confidence interval, 0.91-0.95]) after adjustment for potential confounders.

Conclusions: Owing to the presence of small-study bias, our results may represent an overestimate of the true magnitude of the association. Similar significant and inverse associations were observed with decaffeinated coffee and tea and risk of incident diabetes. High intakes of coffee, decaffeinated coffee, and tea are associated with reduced risk of diabetes. The putative protective effects of these beverages warrant further investigation in randomized trials.

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BY 2025, THE NUMBER OF IN INdividuals estimated to be affected by type 2 diabetes mellitus (DM) will increase by 65% to reach an estimated 380 million individuals worldwide, with the greatest burden being shouldered by the lower- and middle-income countries of the Asia-Pacific region.[1] Diabetes mellitus causes substantial morbidity and mortality in those affected and is associated with enormous economic, health, and societal costs.[2,3] Moreover, compared with unaffected individuals, those with DM are at greatly elevated risk of other chronic illnesses, including cardiovascular disease, in which cases DM more than doubles the risk of having a heart attack or stroke.[4,5] Therefore, the identification of modifiable risk factors for the primary prevention of DM is of considerable public health importance.

Despite considerable research attention, the role of specific dietary and lifestyle factors remains uncertain, although obesity[6,7] and physical inactivity[8] have consistently been reported to raise the risk of DM. Observational epidemiologic studies have also suggested that high dietary intakes of fat, especially *trans*-fats,[9] and red meat[10,11] are independently associated with reduced insulin sensitivity and increased risk of DM, and conversely, that high intakes of whole grains may be protective.[5,9,12] Other studies have highlighted the potential role that high intakes of coffee and tea may have on reducing the likelihood of developing DM.

An earlier meta-analysis suggested that individuals with the highest level of coffee consumption have approximately one-third the risk of DM compared with those with the lowest levels of consumption.[13] However, since that review was published, the amount of information that is now available on the relationship between coffee consumption and subse-

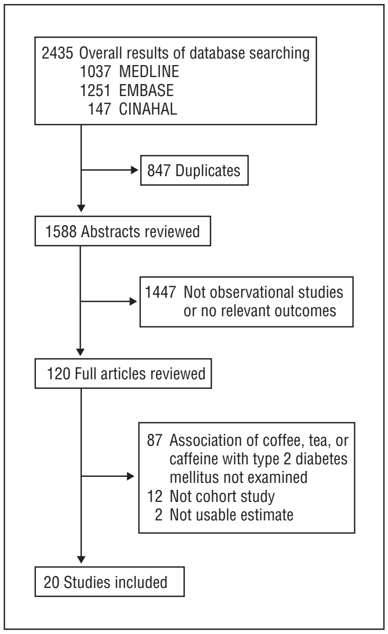

Figure 1. Flowchart for identifying eligible studies.

quent risk of DM has more than doubled.[14-24] Furthermore, several studies have also published data suggesting that decaffeinated coffee and tea may confer benefits similar to those of regular coffee consumption, although there has been no systematic evaluation of the evidence for these beverages.[16,17] Hence, the purpose of the current report is to update the previous meta-analysis of the association between coffee consumption and risk of DM and to conduct a supplementary overview of the evidence for decaffeinated coffee and tea consumption on subsequent risk.

METHODS

LITERATURE SEARCH

We performed a systematic review of available literature according to the MOOSE guidelines.[25] Relevant studies published between 1966 and July 2009 were identified from CINAHL, EMBASE, PubMed, and the Cochrane Library using a combined text and the following MeSH heading search strategies: (caffeine OR coffee OR decaffeinated OR tea) AND (diabetes OR NIDDM OR adult-onset diabetes OR glucose) AND (cohort OR case-control). References from these studies, as well from the previous reviews, were also scrutinized to identify other relevant studies. There was no language restriction.

STUDY SELECTION AND DATA EXTRACTION

Studies were included in this systematic review if they had published quantitative estimates (including variability) of the association between intake of total coffee, decaffeinated coffee, total tea (including green and black) with new-onset (incident) DM. Findings had to be adjusted for at least age and body mass index (BMI). We excluded all animal studies and, in humans, studies of type 1 DM. Given that a disease may plausibly affect dietary intake (reverse causality), we also excluded all cross-sectional studies and those case-control studies with no information on incident DM. Furthermore, we excluded studies that classified consumption only into a binary variable (ie, yes or no) without specifying the number of cups of beverage consumed per day. The literature research and data extraction were conducted by 2 of the us (C.M.Y.L. and L.T.). Where there was disagreement over the eligibility of the study, 3 more of us reviewed the article (R.H., F.B., and S.C.), and a consensus was reached.

DATA SYNTHESIS AND ANALYSIS

Given that most studies reported the association between beverage consumption and DM for more than 1 level of intake, an a priori decision was made to pool the estimates of relative risk (RR) that corresponded as closely as possible to between 3 and 4 cups of coffee, decaffeinated coffee, or tea per day, compared with none. A test for linear trend of effects across coffee consumption categories was performed by regressing each log RR on the ordered categorical variable for coffee in 5 levels using a random-effect meta-regression model. A log-linear association between cups per day and RR was fitted using generalized least squares.[26]

For studies of specific types of tea (black, green, and oolong), only 1 estimate of the association with DM was reported, and hence, we report on the association with DM comparing tea drinkers with non–tea drinkers. Summary estimates were obtained by means of a random-effects model, and studies were weighted according to an estimate of statistical size defined as the inverse of the variance of the log RR.[27] The percentage of variability across studies attributable to heterogeneity rather than chance was estimated using the I^2 statistic.[28,29] Possible sources of heterogeneity were investigated by comparing summary results obtained when studies were grouped according to statistical size, sex, method of diagnosis of DM, and level of adjustment. Publication bias was assessed taking, for each study, the RR and 95% confidence interval (CI) corresponding to the highest category of coffee consumption using the Egger test.[30] All analyses were performed using Stata software, version 10 (StataCorp LP, College Station, Texas).

RESULTS

STUDY CHARACTERISTICS

The search strategy identified a total of 2435 articles, of which 847 were duplicates. After a review of 1588 abstracts, 120 reports were reviewed in full (**Figure 1**), and 20 of these, all cohort studies, were included in our review.[14-24,31-40] The sample size ranged from 910 to 88 259 and totaled 517 325 individuals, among whom there were 21 897 cases of new-onset DM (**Table**). Cohorts were drawn from diverse populations, including Singapore,[20] Puerto Rico,[15] the United Kingdom,[17] Finland,[14,18,31,32] the United States,[16,21-23,34-36] Japan,[17,40] the Netherlands,[38,39] and Sweden[33] but included predominantly white populations, with 21% of the data derived from Asian cohorts (n=110 147). The studies represented both the general population and specific occupational groups. Age at commencement of the studies ranged from 20 to 98 years, and the median duration of follow-up ranged from 2 to 20 years.

MEASUREMENT OF EXPOSURE AND OUTCOME

Apart from 1 study, which used 24-hour dietary recall to obtain an estimate of coffee consumption,[15] all of the remaining studies used self-reported food frequency or self-administered questionnaires. Diabetes mellitus was ascertained using self-report of physician diagnoses, routinely collected hospital admission records, or direct measurement using an oral glucose tolerance test. Studies quantified the association between beverage intake and DM using RR with accom-

Table. Characteristics of Studies Reporting on the Association Between Coffee, Decaffeinated Coffee, or Tea and Subsequent Type 2 DM

Source	Sex	Age Range, y	Study Size, No. of Subjects	DM Event, No.	Follow-up, y	Assessment of DM	Variables in Multiple Adjustment	Beverage	Consumption[a]	Multivariate Adjusted RR (95% CI)
Kato et al,[40] 2009, Japan (JPHC Study Cohort)	M	40-69	24 826	1601	10	SR	Age, BMI, smoking, alcohol, family history, PA, HT, mental stress	Coffee	Almost never	1 [Reference]
									1-2/wk	0.93 (0.80-1.08)
									3-4/wk	0.84 (0.71-1.01)
									1-2	0.84 (0.73-0.97)
									3-4	0.83 (0.68-1.02)
									≥5	0.82 (0.60-1.11)
	F		31 000	1093					Almost never	1 [Reference]
									1-2/wk	0.90 (0.76-1.06)
									3-4/wk	0.95 (0.77-1.17)
									1-2	0.81 (0.69-0.96)
									3-4	0.62 (0.45-0.84)
									≥5	0.40 (0.20-0.78)
Odegaard et al,[20] 2008, Singapore (Singapore Chinese Health Study)	M and F	45-74	36 908	1889	5.7	SR	Age, year of interview, sex, dialect, education, HT, smoking, alcohol, BMI, PA, dietary variables	Coffee	Nondaily	1 [Reference]
									1	0.96 (0.86-1.08)
									2-3	0.90 (0.79-1.2)
									≥4	0.70 (0.53-0.93)
								Black tea	~0	1 [Reference]
									Weekly	0.97 (0.86-1.09)
									Daily	0.86 (0.74-1.00)
								Green tea	~0	1 [Reference]
									Weekly	1.05 (0.93-1.18)
									Daily	1.12 (0.98-1.29)
Fuhrman et al,[15] 2009, Puerto Rico (Puerto Rico Heart Health Program)	M	35-79	4685	519	2.6 (median)	SR	Age, BMI, smoking, family history of DM, education, alcohol, PA, milk and sugar intakes	Coffee	0	0.64 (0.43-0.94)
									1-2	1 [Reference]
									3	0.79 (0.69-1.00)
									≥4	0.75 (0.58-0.97)
Hamer et al,[17] 2008, United Kingdom (Whitehall II study)	M and F	35-55	5823	387	11.7	SR	Age, sex, ethnicity, employment grade, BMI, WHR, smoking, sex-specific alcohol intake, PA, family history of DM, HT, cholesterol, total energy intake, diet pattern, mutual adjustment for all beverage types	Coffee	0	1 [Reference]
									1	0.83 (0.60-1.14)
									2-3	0.85 (0.60-1.20)
									>3	0.80 (0.54-1.18)
								Decaf coffee	0	1 [Reference]
									≤1	1.13 (0.87-1.47)
									2-3	0.87 (0.58-1.30)
									>3	0.65 (0.36-1.16)
								Tea	0	1 [Reference]
									≤1	1.08 (0.75-1.56)
									2-3	0.81 (0.56-1.17)
									>3	0.77 (0.52-1.140
Bidel et al,[14] 2008, Finland	M	35-74	10 666	483		NR	Age, BMI, alcohol, smoking, PA, GGT	Coffee	0-2	1 [Reference]
									3-4	0.89 (0.68-1.18)
									5-6	0.87 (0.67-1.13)
									≥7	0.71 (0.53-0.94)
	F	35-74	11 160	379					0-2	1 [Reference]
									3-4	0.75 (0.57-0.98)
									5-6	0.63 (0.47-0.83)
									≥7	0.47 (0.33-0.69)
Smith et al,[23] 2006, United States (Rancho Bernardo Study)	M and F	≥50	910	84	8.3	OGTT	Age, sex, PA, BMI, smoking, alcohol, HT, FPG	Coffee	0	1 [Reference]
									1-2	0.66 (0.38-1.14)
									3-4	0.53 (0.26-1.08)
									≥5	0.60 (0.26-1.40)

(continued)

panying 95% CIs. With few exceptions, all studies controlled extensively for a range of potential confounders. Although some studies recruited men and women, not all reported sex-specific analyses; those that did were entered separately into the meta-analysis, resulting in a total of 37 estimates of the relationship between coffee, decaffeinated coffee, and tea with risk of DM.

ASSOCIATION BETWEEN COFFEE CONSUMPTION AND DM

A total of 23 estimates from 18 studies (5 studies reported sex-specific

Table. Characteristics of Studies Reporting on the Association Between Coffee, Decaffeinated Coffee, or Tea and Subsequent Type 2 DM (continued)

Source	Sex	Age Range, y	Study Size, No. of Subjects	DM Event, No.	Follow-up, y	Assessment of DM	Variables in Multiple Adjustment	Beverage	Consumption[a]	Multivariate Adjusted RR (95% CI)
Paynter et al,[21] 2006, United States (ARIC study)	M	45-64	5414	718	12	SR	Age, race, education, family history of DM, BMI, WHR, total caloric intake, dietary fiber, smoking, alcohol, leisure PA, HT	Coffee	Almost never	1 [Reference]
									<1	0.94 (0.74-1.18)
									1	1.04 (0.83-1.30)
									2-3	0.82 (0.66-1.03)
									≥4	0.77 (0.61-0.98)
	F	45-64	6790	719					Almost never	1 [Reference]
									<1	0.91 (0.71-1.16)
									1	1.90 (0.73-1.10)
									2-3	0.92 (0.75-1.14)
									≥4	0.89 (0.69-1.15)
Pereira et al,[22] 2006, United States (Iowa Women's Health Study)	F	55-69	28 812	1418	11	SR	Age, education, baseline HT, alcohol, smoking, BMI, WHR, PA, energy intake, total fat, Keys score, cereal fiber, tea, soda consumption, magnesium, phytate	Coffee	0	1 [Reference]
									<1	0.95 (0.77-1.18)
									1-3	1.01 (0.85-1.19)
									4-5	0.85 (0.69-1.04)
									≥6	0.79 (0.61-1.02)
								Coffee	0	1 [Reference]
									<1	0.92 (0.76-1.11)
									1-3	0.88 (0.70-1.12)
									4-5	0.89 (0.64-1.23)
									≥6	1.00 (0.84-1.19)
								Decaf coffee	0	1 [Reference]
									<1	0.98 (0.83-1.16)
									1-3	1.01 (0.84-1.21)
									4-5	0.59 (0.44-0.80)
									≥6	0.68 (0.43-1.09)
Hu et al,[18] 2006, Finland	M	35-74	10 188	517	13.4	NR	Age, study year, education, SBP, bread, vegetable, fruit, sausage, coffee, tea, alcohol, smoking, PA, BMI	Tea	0	1 [Reference]
									1-2	0.89 (0.71-1.11)
									≥3	0.83 (0.59-1.17)
	F	35-74	11 197	447	13.4	NR		Tea	0	1 [Reference]
									1-2	0.92 (0.74-1.15)
									≥3	0.85 (0.57-1.27)
Iso et al,[19] 2006, Japan (Japan Collaborative Cohort Study for Evaluation of Cancer Risk)	M	40-65	6727	231	5	SR	Age, BMI, family history of DM, smoking, alcohol, magnesium, PA, consumption of other beverages	Coffee	<1	1 [Reference]
									1-2	0.96 (0.68-1.36)
									≥3	0.54 (0.30-0.97)
								Black tea	<1	1 [Reference]
									≥1	1.43 (0.56-3.64)
								Green tea	<1	1 [Reference]
									1-2	0.82 (0.47-1.41)
									3-5	1.12 (0.71-1.76)
									≥6	0.91 (0.55-1.52)
	F	40-65	10 686	213	5	SR		Coffee	<1	1 [Reference]
									1-2	0.88 (0.61-1.25)
									≥3	0.61 (0.30-1.22)
								Black tea	<1	1 [Reference]
									≥1	0.80 (0.49-1.32)
								Green tea	<1	1 [Reference]
									1-2	0.66 (0.40-1.08)
									3-5	0.61 (0.41-0.91)
									≥6	0.49 (0.30-0.79)

(continued)

estimates) with information on 457 922 participants reported on the association between coffee consumption and subsequent risk of DM. There was evidence of a significant inverse log-linear association such that every additional cup of coffee consumed in a day was associated with a 7% reduction in the excess risk of DM (RR, 0.93 [95% CI, 0.91-0.95]) ($P < .001$) (**Figure 2**). In categorical analysis, the pooled summary estimate from these studies indicated that drinking 3 to 4 cups of coffee per day was associated with

Table. Characteristics of Studies Reporting on the Association Between Coffee, Decaffeinated Coffee, or Tea and Subsequent Type 2 DM (continued)

Source	Sex	Age Range, y	Study Size, No. of Subjects	DM Event, No.	Follow-up, y	Assessment of DM	Variables in Multiple Adjustment	Beverage	Consumption[a]	Multivariate Adjusted RR (95% CI)
van Dam et al,[24] 2006, USA (Nurses' Health Study II)	F	26-46	88 259	1263	10	SR	Age, BMI, PA, smoking, alcohol, use of hormone therapy, oral contraceptives, family history of type 2 DM, history of HT, history of hypercholesterolemia, sugar-sweetened soft drinks, punch, quintiles of processed meat, polyunsaturated to saturated fat intake ratio, total energy intake, glycemic index, cereal fiber intake	Total coffee	0	1 [Reference]
									<1	0.93 (0.80-1.09)
									1	0.87 (0.73-1.03)
									2-3	0.58 (0.49-0.68)
									≥4	0.53 (0.41-0.68)
								Coffee	0	1 [Reference]
									<1	1.00 (0.86-1.17)
									1	0.89 (0.75-1.07)
									2-3	0.62 (0.52-0.74)
									≥4	0.61 (0.43-0.81)
								Decaf coffee	0	1 [Reference]
									<1	0.86 (0.74-0.99)
									1	0.87 (0.68-1.11)
									≥2	0.52 (0.36-0.74)
								Tea	0	1 [Reference]
									<1	0.97 (0.83-1.12)
									1	1.17 (0.97-1.40)
									2-3	0.98 (0.79-1.20)
									≥4	0.88 (0.64-1.23)
Greenberg et al,[16] 2005, United States (NHANES-1)	M and F	32-88	7006	309	8.4	SR	Per capita income, education level, race, sex, PA, smoking, alcohol, BMI, age, diet	Coffee	0	1 [Reference]
									<2	0.82 (0.55-1.23)
									2-4	0.75 (0.50-1.13)
									≥4	0.37 (0.22-0.64)
								Decaf coffee	0	1 [Reference]
									<2	0.62 (0.34-1.11)
									≥2	0.43 (0.20-0.93)
								Tea	0	1 [Reference]
									<2	0.76 (0.54-1.09)
									1-2	0.67 (0.36-1.28)
									≥2	0.34 (0.15-0.76)
Song et al,[36] 2005, United States (The Woman's Health Study)	F	≥45	38 018	1614	8.8	SR	Age, BMI, total energy intake, smoking, exercise, alcohol, history of HT, history of high cholesterol, family history of DM, fiber intake, glycemic load, magnesium, and total fat intake	Tea	0	1 [Reference]
									<1	1.07 (0.95-1.21)
									1-3	1.05 (0.91-1.21)
									≥4	0.72 (0.52-1.01)

(continued)

an approximate 25% lower risk of DM than drinking none or 2 or fewer cups per day (RR, 0.76 [95% CI, 0.69-0.82]) (**Figure 3**). There was evidence of significant heterogeneity across studies ($P=.01$) that was not explained by differences in the strength of effect between men and women (RR, 0.78 [95% CI, 0.70-0.87] and 0.71 [95% CI, 0.62-0.81], respectively) ($P=.24$ for heterogeneity); the region where the study was conducted (Europe RR, 0.84 [95% CI, 0.75-0.94] vs the United States RR, 0.73 [95% CI, 0.62-0.85]) ($P=.15$ for heterogeneity); or the method of diagnosis (national register or oral glucose tolerance test RR, 0.85 [95% CI, 0.74-0.98] vs self-report RR, 0.72 [95% CI, 0.66-0.79]) ($P=.05$ for heterogeneity).

Restriction of the analysis to those 11 studies that reported both age- and sex-adjusted estimates and estimates that were adjusted for other potential confounders (Table) indicated that the observed association was unaffected by the level of adjustment in the crude model (RR,

Table. Characteristics of Studies Reporting on the Association Between Coffee, Decaffeinated Coffee, or Tea and Subsequent Type 2 DM (continued)

Source	Sex	Age Range, y	Study Size, No. of Subjects	DM Event, No.	Follow-up, y	Assessment of DM	Variables in Multiple Adjustment	Beverage	Consumption[a]	Multivariate Adjusted RR (95% CI)
Carlsson et al,[31] 2004, Finland (Finnish Twin Cohort)	M and F	30-60	10 652	408	20	NR	Age, sex, BMI, education, leisure time PA, alcohol, smoking	Coffee	≤2 3-4 5-6 ≥7	1 [Reference] 0.70 (0.48-1.01) 0.71 (0.50-1.01 0.65 (0.44-0.96)
van Dam et al,[38] 2004, the Netherlands (Hoorn Study)	M and F	50-74	1312	128	6	OGTT	Age, sex, BMI, WHR, PA, alcohol, smoking, history of CVD, use of antihypertensive medication, intake of fiber, total energy, saturated fat, polyunsaturated fat	Coffee	≤2 3-4 5-6 ≥7	1 [Reference] 0.94 (0.54-1.09) 0.92 (0.53-1.61 0.69 (0.31-1.51)
Rosengren et al,[33] 2004, Sweden (BEDA study)	F	39-65	1361	74	18	SR and NR	Age, smoking, low PA, education, BMI, serum cholesterol, triglycerides	Coffee	≤2 3-4 5-6 >6	1 [Reference] 0.56 (0.32-0.98) 0.45 (0.23-0.90) 0.57 (0.26-1.29
Salazar-Martinez et al,[34] 2004, United States (Health Professionals Follow-up Study and Nurses' Health Study)	M	40-75	41 934	1333	12	SR	Age, BMI, PA, total caloric intake, family history of DM, alcohol, smoking, intakes of glycemic load, *trans*-fat, polyunsaturated fatty acid, cereal fiber, magnesium	Coffee	0 <1 1-3 4-5 ≥6	1 [Reference] 0.98 (0.84-1.15) 0.93 (0.80-1.08) 0.71 (0.53-0.94) 0.46 (0.26-0.82)
								Decaf coffee	0 <1 1-3 ≥4	1 [Reference] 0.95 (0.84-1.08) 0.91 (0.76-1.03) 0.74 (0.48-1.12)
								Tea	0 <1 1-3 ≥4	1 [Reference] 0.92 (0.81-1.04) 0.97 (0.82-1.14) 1.02 (0.59-1.78)
	F	30-55	84 276	4085	18	SR	Age, BMI, PA, total caloric intake, family history of DM, alcohol, smoking, menopausal status and postmenopausal hormone use, intakes of glycemic load, *trans*-fat, polyunsaturated fatty acid, cereal fiber, magnesium	Coffee	0 <1 1-3 4-5 ≥6	1 [Reference] 1.16 (1.05-1.29) 0.99 (0.90-1.08) 0.70 (0.60-0.82) 0.71 (0.56-0.89)
								Decaf coffee	0 <1 1-3 ≥4	1 [Reference] 0.96 (0.88-1.05) 0.88 (0.80-0.97) 0.85 (0.61-1.17)
								Tea	0 <1 1-3 ≥4	1 [Reference] 1.05 (0.97-1.15) 1.01 (0.92-1.11) 0.91 (0.72-1.16)

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0.75 [95% CI, 0.67-0.85]) vs in the maximally adjusted model (RR, 0.76 [95% CI, 0.70-0.84]) ($P = .81$ for heterogeneity).

There was some evidence of publication bias found by the Egger test ($P = .08$) such that the smaller studies tended to report greater effect sizes than did the larger studies ($P = .01$ for trend) (**Figure 4**). The summary risk estimate from the 6 largest estimates (defined as having a statistical study weight ≥35) of drinking 3 to 4 cups of coffee per day compared with drinking none or fewer than 2 cups per day was RR, 0.85 (95% CI, 0.75-0.96), while from the 7 smallest estimates (defined as having a statistical study weight <20), it was RR, 0.62 (95% CI, 0.48-0.79).

Table. Characteristics of Studies Reporting on the Association Between Coffee, Decaffeinated Coffee, or Tea and Subsequent Type 2 DM (continued)

Source	Sex	Age Range, y	Study Size, No. of Subjects	DM Event, No.	Follow-up, y	Assessment of DM	Variables in Multiple Adjustment	Beverage	Consumption[a]	Multivariate Adjusted RR (95% CI)
Reunanen et al,[32] 2003, Finland (Mobile Clinic Health Examination Survey)	M and F	20-98	19 518	855	16	NR	Age, sex, BMI, smoking, leisure time PA	Coffee	≤2	1 [Reference]
									3-4	1.01 (0.81-1.27)
									5-6	0.98 (0.79-1.21)
									≥7	0.92 (0.73-1.16)
Saremi et al,[35] 2003, United States (Pima Indians Study)	M and F	≤15	2680	824	11	OGTT	Age, sex, BMI	Coffee	0	1 [Reference]
									1-2	0.92 (0.74-1.13)
									≥3	1.01 (0.82-1.26)
								Tea		Unrelated to incidences of DM
van Dam et al,[39] 2002, the Netherlands	M and F	30-60	17 111	306	7	SR	Age, sex, town, BMI, lifestyle, CVD, HT, hypercholesterolemia	Coffee	≤2	1 [Reference]
									3-4	0.79 (0.57-1.10)
									5-6	0.73 (0.53-1.01)
									≥7	0.50 (0.35-0.72)

Abbreviations: ARIC, Atherosclerosis Risk in Communities study; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; CVD, cardiovascular disease; decaf, decaffeinated; DM, diabetes mellitus; FPG, fasting plasma glucose level; GGT, gamma glutamyltransferase; HT, hypertension; JPHC, Japan Public Health Center–based study; NHANES, National Health and Nutrition Examination Survey; NR, national register; OGTT, oral glucose tolerance test; PA, physical activity; RR, risk ratio; SBP, systolic blood pressure; SR, self-report; WHR, waist to hip ratio.

[a] Unless otherwise indicated, consumption is measured in cups per day.

ASSOCIATION BETWEEN DECAFFEINATED COFFEE CONSUMPTION AND SUBSEQUENT RISK OF DM

Six studies (N=225 516 participants) reported on the association between decaffeinated coffee consumption and subsequent risk of DM. The pooled summary estimates from these studies indicated that individuals who drank more than 3 to 4 cups of decaffeinated coffee per day had an approximate one-third lower risk of DM than those consuming no decaffeinated coffee (RR, 0.64 [95% CI, 0.54-0.77]) (Figure 3). There was little evidence for either significant heterogeneity across included studies (*P*=.31) or publication bias (*P*=.57 for Egger test).

ASSOCIATION BETWEEN TEA CONSUMPTION AND SUBSEQUENT RISK OF DM

A total of 7 studies (N=286 701 participants) reported on the association between tea consumption and subsequent risk of DM. Pooled summary estimates indicated that individuals who drank more than 3 to 4 cups of tea per day had an approximate one-fifth lower risk of DM than those consuming no tea (RR, 0.82 [95% CI, 0.73-0.94]) (Figure 3). There was little evidence for significant heterogeneity across included studies (*P*=.46) and no evidence to indicate the presence of publication bias (*P*=.11 for Egger test). For studies of tea and decaffeinated coffee, there was insufficient data to permit examination of a dose-response relation. It was also not possible to examine the potential effect of confounding on the relationship because none of the studies reported both age- and multivariate-adjusted estimates.

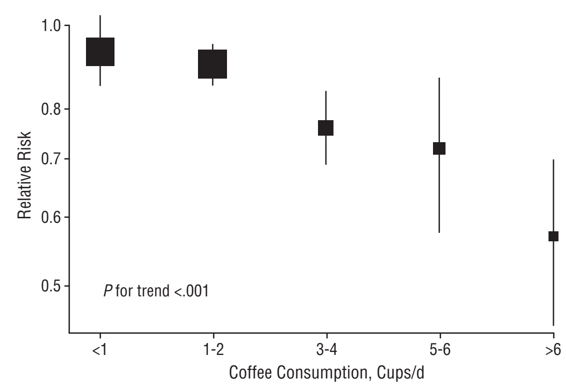

Figure 2. The relationship between coffee consumption and subsequent type 2 diabetes mellitus in different categories of coffee consumption. The center of each black square is placed at the summary point estimate; the area of the square is proportional to the statistical size; and each vertical line shows the 95% confidence interval about the summary estimate.

COMMENT

The findings from this meta-analysis, based on over 500 000 individuals with over 21 000 cases of new-onset DM, confirm an inverse association between coffee consumption and subsequent risk of DM: every additional cup of coffee consumed in a day was associated with 5% to 10% lower risk of incident DM after adjustment for potential confounders. However, this may be an overestimate of the true magnitude of the association owing to the presence of small-study bias.

Furthermore, in the first overview of which we are aware, we were able to demonstrate similar inverse associations between consumption of decaffeinated coffee and tea with risk

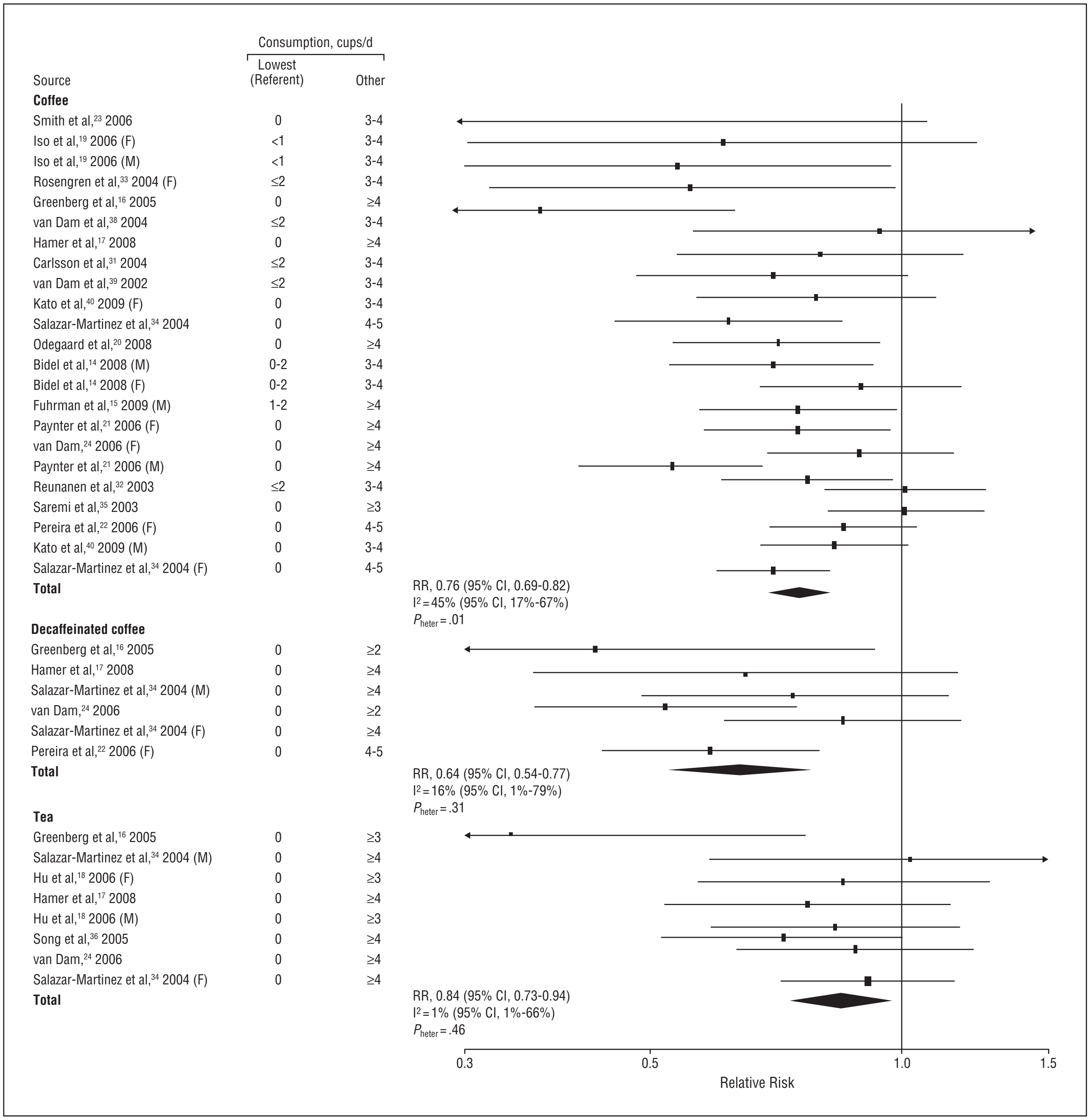

Figure 3. Association between coffee, decaffeinated coffee, and tea consumption and subsequent type 2 diabetes mellitus in published cohort studies (adjusted in all cases at least for age, sex, and body mass index). The studies are sorted by statistical size, defined by the inverse of the variance of the relative risk (RR). The center of each black square is placed at the point estimate; the area of the square is proportional to the statistical size; and each horizontal line shows the 95% confidence interval (CI) for the estimate for each study. P_{heter} indicates P value for heterogeneity.

of incident DM. For example, individuals consuming more than 3 to 4 cups of tea a day had a one-fifth lower risk of subsequent DM than non–tea drinkers; those consuming a similar amount of decaffeinated coffee had a one-third lower risk than nonconsumers. However, in the study by Greenberg and colleagues,[16] consumption of decaffeinated coffee was associated with a significant 40% reduction in the risk of DM only in those aged 60 years or younger. In older individuals, the direction of association was reversed such that there was a significant 40% increase in risk. The observed age-related effect may have been a statistical artifact driven by subgroup analysis. However, we were unable to examine the effect by age, and the possibility that the association between coffee and DM risk is age dependent warrants further investigation.

That the apparent protective effect of tea and coffee consumption appears to be independent of a number of potential confounding variables raises the possibility of direct biological effects. Our findings suggest that any protective effects of coffee and tea are unlikely to be solely effects of caffeine, but rather, as has been speculated previously, they likely involve a broader range of chemical constituents present in these beverages, such as magnesium,[41] lignans,[42] and chlorogenic acids.[43] The effects of these coffee components on glucose metabolism and insulin sensitivity from both animal studies and in vitro experiments have been extensively reviewed elsewhere.[44] While these components have been demonstrated to have beneficial effects on biological pathways intimately involved in glucose homeostasis and insulin secretion, how these findings relate to in vivo effects in humans is uncertain. Because most of the studies included in this review did not provide data on the effects of these beverages or their components on measures of hyperglycemia and insulin sensitivity, we cannot provide further evidence on the mechanisms involved. In studies that reported data on insulin sensitivity, findings were conflicting, with some suggesting that coffee use increased sensitivity to insulin,[38,45] while others reported no effect.[46] There have been few randomized trials of the effects of coffee on glucose and insulin, but 1 randomized crossover trial of 4 weeks' duration of high coffee consumption reported an increase in fasting insulin levels but no effect on fasting glucose concentration.[47]

Possible mechanisms of action for tea on DM may involve 1 or more physiologic pathways. For example, tea catechins have been shown to inhibit the carbohydrate digestive enzymes, which suggests that glucose production may be decreased in the gastrointestinal system resulting in lower levels of glucose and insulin.[48] Black, green, and oolong tea have also been reported to increase insulin sensitivity by increasing insulin-stimulated glucose uptake in adipocytes.[49] There has also been the suggestion that green tea may prevent damage to pancreatic beta cells.[50,51] There have been several small clinical intervention studies conducted that have examined the effects of tea consumption on biomarkers of glucoregulatory control, but the results from these studies have been inconsistent. Some studies have reported a significant reduction in plasma glucose and hemoglobin A_{1c} levels,[52,53] while others have reported no effect on any aspect of glucoregulatory control.[54] Given that dietary polyphenols are rapidly metabolized, one explanation for the discrepant findings between these studies may have been the measurement of the effects of tea on biomarkers at different times after its consumption. For example, catechin concentrations in human plasma reach their maximum level at 2 hours after ingestion of green tea but are undetectable after 24 hours.[55]

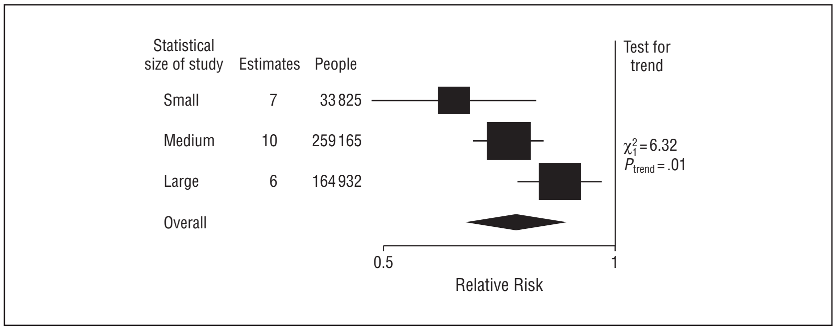

Figure 4. Impact of study size on summary estimates of the relative risk between coffee consumption and subsequent type 2 diabetes mellitus adjusted in all cases at least for age, sex, and body mass index. The center of each black square is placed at the summary point estimate; the area of the square is proportional to the statistical size; and each horizontal line shows the 95% confidence interval about the summary estimate.

That there is a causal inverse association between coffee consumption and subsequent risk of DM is further supported by the presence of a dose-response relationship. In those consuming more than 6 cups of coffee per day, the risk of new-onset DM was reduced by approximately 40% compared with non–coffee drinkers, while among those who drank less than 1 cup per day, the risk was only marginally reduced to about 4% compared with coffee abstainers. Moreover, estimates were quite similar across studies despite the diversity in populations. Of note, this similarity was presence in spite of the likely presence of marked variation between studies in types of coffee and tea and their preparation (eg, filtered vs unfiltered, cup size, cup strength, addition of milk or sugar, and other variations). Finally, the results were consistent between studies regardless of which method of diagnosis of DM was used (ie, self-report vs national register or oral glucose tolerance test).

An inherent weakness of all observational studies and meta-analyses thereof is the possibility that any association is due to the presence of confounding. However, because high levels of coffee and tea consumption have been reported to be associated with risk behaviors that are positively associated with the risk of developing DM (such as low levels of physical activity[56] and cigarette smoking[57]), it might be speculated that adjustment for such risk factors would strengthen the relationship as has been reported. We examined the impact of confounding on the relationship between coffee consumption and subsequent risk of DM by comparing crude and adjusted estimates of effect from only those studies that reported both estimates and observed that adjustment for potential confounders had no material impact (either a strengthening or a weakening) on the estimate of effect. However, we were unable to conduct a similar analysis for tea consumption because studies only reported the adjusted estimate. Tea drinkers may be more health conscious than coffee drinkers, and it is therefore plausible that some of the observed beneficial effect of tea on DM risk is due in part to other health-promoting behaviors (eg, regular physical activity, weight maintenance, and nonsmoking) that may or may not have been taken into consideration in the original studies.

A further major limitation of this analysis is the reliance on published data, which precluded more detailed analysis of the effect of adjustment for confounders at an individual level or for specific confounders separately. In this regard, it is possible that individuals who consume extreme quantities of coffee differ in other important dietary and sociologic aspects from more moderate coffee consumers, but to examine this issue any further would require an individual participant data meta-analysis. Therefore, the possibility that coffee consumption may be acting as a surrogate marker of some other dietary or lifestyle risk factor cannot be fully excluded.

Finally, although the studies included in this review were all population based, only 20% of the cohorts were from nonwhite populations, which somewhat limits the generalizability of the study findings to largely Western populations. This is an important consideration given that the pattern of beverage consumption and background risk of DM may differ across ethnic groups.

In conclusion, high intake of coffee, decaffeinated coffee, and/or tea is associated with a material reduction in the risk of new-onset DM. If such beneficial effects were observed in interventional trials to be real, the implications for the millions of individuals who have DM, or who are at future risk of developing it, would be substantial. For example, the identification of the active components of these beverages would open up new therapeutic pathways for the primary prevention of DM. It could also be envisaged that we will advise our patients most at risk for DM to increase their consumption of tea and coffee in addition to increasing their levels of physical activity and weight loss.

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