Black and green tea consumption and the risk of coronary artery disease: a meta-analysis[1–3]

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ABSTRACT

Background: Epidemiologic studies are inconsistent regarding the association between tea consumption and the risk of coronary artery disease (CAD).

Objective: The objective was to perform a meta-analysis to determine whether an association exists between tea consumption and total CAD endpoints in observational studies.

Design: We searched PUBMED and EMBASE databases for studies conducted from 1966 through November 2009. Study-specific risk estimates were combined by using a random-effects model.

Results: A total of 18 studies were included in the meta-analysis: 13 studies on black tea and 5 studies on green tea. For black tea, no significant association was found through the meta-analysis [highest compared with lowest, summary relative risk (RR): 0.92; 95% CI: 0.82, 1.04; an increment of 1 cup/d, summary RR: 0.98; 95% CI: 0.94, 1.02]. For green tea, the summary RR indicated a significant association between the highest green tea consumption and reduced risk of CAD (summary RR: 0.72; 95% CI: 0.58, 0.89). Furthermore, an increase in green tea consumption of 1 cup/d was associated with a 10% decrease in the risk of developing CAD (summary RR: 0.90; 95% CI: 0.82, 0.99).

Conclusions: Our data do not support a protective role of black tea against CAD. The limited data available on green tea support a tentative association of green tea consumption with a reduced risk of CAD. However, additional studies are needed to make a convincing case for this association. *Am J Clin Nutr* 2011;93:506–15.

INTRODUCTION

Tea is one of the most popular beverages consumed in the world. With a per capita worldwide consumption of ≈0.12 L/y (1), habitual tea drinking has long been associated with health benefits. It is produced from the leaves of the plant *Camellia sinensis*, but differences in processing techniques result in several types of tea. According to the level of fermentation, tea can be classified into 3 major types: black tea (fermented), green tea (unfermented), and oolong tea (partially fermented) (2–4). Approximately 76–78% of the tea produced and consumed worldwide is black, 20–22% is green, and <2% is oolong. Black tea is mainly drunk in Europe, North America, and North Africa (except Morocco), whereas green tea is consumed principally in Asia; oolong tea is popular in southeast China (5).

Coronary artery disease (CAD) is still the most common cause of death worldwide; an estimated 7.2 million people died of the disease in 2004 (6). Recently, interest in the relation between tea consumption and the risk of CAD has increased. In 2001, on the basis of a meta-analysis, Peters et al (7) estimated that the incidence rate of myocardial infarction (MI) decreased by 11% with each increase in tea consumption of 3 cups/d, but the study-specific effect estimates for CAD were too heterogeneous to be summarized. To date, many epidemiologic studies have been conducted to investigate the association between tea consumption and the risk of CAD, but the results remain controversial. Hence, we chose to conduct a meta-analysis to summarize the results from the available epidemiologic studies, both case control and prospective, to evaluate whether routine tea consumption is associated with CAD risk.

METHODS

Search strategy

We performed a literature search of the PUBMED (//www.ncbi.nlm.nih.gov/pubmed) and EMBASE (www.embase.com) databases that included the years 1966 through November 2009. We used the search terms "tea," "black tea," "green tea," "flavonoid," "catechin," "thearubigin," or "theaflavin" combined with "coronary artery disease," "coronary heart disease," "myocardial infarction," "ischemic heart disease," "CAD," and "CAD" in the full-text option. The search was limited to English-language articles. The titles and abstracts were scanned to exclude any studies that were clearly irrelevant. We read the full text of the remaining articles to determine whether they contained information on the topic of our interest. Furthermore, we searched all references cited in original studies and in all reviews identified. Two authors (Z-MW and BZ) conducted all of the searches independently.

Studies were included in the meta-analysis if they met the following criteria: *1*) case control or cohort study design; *2*) the exposure of interest was tea consumption and the outcome of

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interest was total CAD incidence or mortality (including MI, CAD, nonstroke cardiovascular disease, and other coronary events); *3*) odds ratio (OR) or relative risk (RR) estimates with corresponding 95% CIs (or sufficient information to calculate them) were reported; and *4*) some adjustments were made for potential CAD risk. If the data were duplicated in more than one study, the most recent and complete study was eligible for inclusion in the meta-analysis.

Our literature search identified 23 potentially relevant studies concerning tea consumption and CAD risk (8–30). One report (8) was excluded because the OR and 95% CI provided were for each additional cup of tea consumed per day. Two studies (9, 10) were excluded because the endpoint was cardiovascular disease including stroke events. The study by Rimm et al (11) was excluded because it was updated by Lopez-Garcia et al (25) in 2006. The study by Lin et al (12) was excluded because it used the same cohort as the report by Lopez-Garcia et al (25), and the latter provided information with a longer period of follow-up. The study by Wang et al (28) is our own case-control study, which was recently accepted by the Journal; we have used the information ahead of publication. Thus, our meta-analysis on tea consumption and CAD risk included 18 articles in total: 13 studies (13–25) on black tea and 5 studies (26–30) on green tea.

Data extraction

Information from the studies was extracted independently by 2 investigators (Z-MW and BZ) using a predefined data-extraction form. The following data were sought from each article: the first author's name, the year of publication, the study design (case control or cohort), the country of origin, study period, years of follow-up, sex, outcomes, the number of participants (cases and controls, or cases and cohort size), measurements of tea consumption, OR and RR estimates and their corresponding 95% CIs, and adjustment factors in the statistical analysis. For each study, we extracted the risk estimates that reflected the greatest degree of control for potential confounders. The results were compared, and any questions or discrepancies were resolved by consensus.

Statistical analysis

Statistical analyses were performed for black tea and green tea consumption separately, and the case control studies and cohort studies were considered together and as subgroups. The measure of effect of interest was the OR for case-control studies and the RR for cohort studies and their corresponding 95% CI. We considered the hazard ratio as the RR directly in prospective studies. Study-specific risk estimates were extracted from each article, and log-risk estimates were weighted by the inverse of their variances to obtain a pooled risk estimate. Studies were combined by using the DerSimonian and Laird random-effects model, which considers both within- and between-study variations (31). First, we calculated the study-specific estimates for the highest compared with the lowest level of tea consumption. Second, we compared the risk of total CAD in routine drinkers with nondrinkers/occasional drinkers. Several studies did not report a risk estimate for routine drinking; for these studies, a summary estimate for routine drinking was generated by using reported risk estimates for each drinking category. In addition, we conducted subgroup analyses to analyze the potential interactions.

To normalize the variation between studies in the difference in exposure categories, we calculated a risk estimate for an increment of tea consumption of 1 cup/d for each study. For this analysis, we used the method proposed by Greenland and Longnecker (32) and Orsini et al (33), which were used in our previous meta-analysis (34) to estimate study-specific slopes from the natural logarithm of the RR across categories of tea consumption, assigning to each class the dose corresponding to the midpoint of upper and lower boundaries. Because this method requires the risk estimates with their variance estimates for $\geq$3 quantitative exposure categories, the studies with only 2 categories (15, 17, 22, 26, 27) were not included in this analysis. In studies that did not provide the number of cases and controls/person-years in each exposure category (14, 18–20, 24, 29), the variance-weighted least-squares regression model was used to estimate the slopes. The study by Sano et al (8) was re-included in the dose-response analysis because it provided the OR and 95% CI for every additional cup of tea consumed in a day. In our previous study (28), tea consumption was indicated by grams of tea leaves; we rescaled tea drinking to the number of cups per day assuming that 125 g of tea leaves per month is approximately equivalent to 2 cups/d. Because the higher category of consumption was usually open, we considered it of the same amplitude as the preceding category. Then, we obtained the summary RR estimates by pooling the study-specific slopes using the inverse of the corresponding variances as weights.

We examined the possible heterogeneity in results across studies by using the Q and I^2 statistics (35). To avoid type II errors resulting from low power, we set the significance level at 0.10 instead of the more conventional level of 0.05 (36). When statistical heterogeneity was detected, the sources of heterogeneity were explored and a subgroup analysis was performed. A sensitivity analysis was conducted to evaluate the robustness of our results. Publication bias was evaluated with Egger's regression asymmetry test in which a P value < 0.10 was considered representative of statistically significant publication bias (37). The present meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (38). Statistical analyses were carried out with Stata 9.2 software (STATA Corp, College Station, TX). All statistical tests were 2-sided.

RESULTS

Black tea

A total of 13 studies (13–25), consisting of 3 case-control studies (13–15) and 10 prospective cohort studies (16–25), were included in the meta-analysis on black tea consumption in relation to CAD risk (**Table 1**). Six studies were conducted in the United States (13, 14, 16, 21, 24, 25), 2 in the United Kingdom (19, 20), 2 in the Netherlands (18, 23), 1 in Italy (15), 1 in Norway (17), and 1 in Finland (22).

The RR estimates of CAD for the highest black tea consumption compared with the lowest black tea consumption for individual studies and all studies combined are shown in **Table 2** and **Figure 1**. The overall results did not show an association between the highest black tea consumption and the risk of CAD (summary RR: 0.92; 95% CI: 0.82, 1.04). However, the analysis showed a significant heterogeneity across all studies ($P = 0.039$,

TABLE 1
Epidemiologic studies on black tea consumption in association with coronary artery disease (CAD) risk[1]

Study	Country	Design	Study period	Follow-up	Sex	Outcome	Sample size[2]	Tea consumption	RR/OR (95% CI)	Adjustment factor
Rosenberg et al, 1988 (13)	USA	C-C	1980–1983		M	MI	146/205	0 cups/d	1.00	Age, smoking, hypertension, diabetes, BMI, type A personality, physical activity, alcohol, coffee, family history of MI, religion, education, year of interview, region, number of visits to a physician
								1–2 cups/d	1.2 (0.6, 2.4)	
								3–4 cups/d	0.5 (0.2, 1.3)	
								≥5 cups/d	1.7 (0.6, 4.9)	
Sesso et al, 1999 (14)	USA	C-C	1982–1983		M/F	MI	335/335	None	1.00	Age, sex, smoking, hypertension, type A personality, family history of MI, diabetes, aspirin, BMI, physical activity, percentage of calories from saturated fat, total calories, alcohol
								1–3 cups/mo	0.70 (0.44, 1.13)	
								1–6 cups/wk	0.77 (0.47, 1.27)	
								≥1 cup/d	0.56 (0.35, 0.90)	
Tavani et al, 2001 (15)	Italy	C-C	1995–1999		M/F	MI	507/478	Nondrinkers	1.0	Age, sex, education, BMI, cholesterol, smoking, alcohol, physical activity, coffee, hyperlipidemia, diabetes, hypertension, family history of MI
								Drinkers	1.0 (0.7, 1.3)	
Klatsky et al, 1990 (16)	USA	Cohort	1978–1986	5 y	M/F	MI	740/101,774	0 cups/d	1.00	Age, sex, race, smoking, alcohol, baseline disease, education
								<1 cup/d	1.07 (0.90, 1.28)	
								1–3 cups/d	1.05 (0.85, 1.30)	
								4–6 cups/d	0.90 (0.49, 1.64)	
								>6 cups/d	1.11 (0.52, 2.36)	
						Other coronary cases	1174/101,774	0 cups/d	1.00	
								<1 cup/d	0.96 (0.83, 1.12)	
								≥1 cup/d	1.03 (0.88, 1.20)	
Stensvold et al, 1992 (17)	Norway	Cohort	1976–1988	12 y	M	CHD	141/9857	<1 cup/d	1.00	Age, total cholesterol, SBP, smoking
								≥1 cup/d	0.64 (0.38, 1.07)	
Hertog et al, 1993 (18)	Netherlands	Cohort	1985–1990	5 y	M	CHD	43/805	0–250 mL/d	1.00	Age, diet, history of MI, total energy, saturated fatty acids, physical activity, BMI, smoking, serum total and HDL cholesterol, SBP
								251–500 mL/d	0.38 (0.18, 0.82)	
								>500 mL/d	0.45 (0.22, 0.93)	
Hertog et al, 1997 (19)	UK	Cohort	1979–1993	14 y	M	IHD	131/1900	0–300 mL/d	1.00	Age, smoking, baseline IHD, social class, BMI, SBP, total cholesterol, energy intake, alcohol, fat, vitamin C, vitamin E, β-carotene
								450–750 mL/d	1.7 (0.8, 3.4)	
								900–1200 mL/d	2.1 (1.0, 4.1)	
								>1200 mL/d	2.3 (1.0, 5.1)	
Woodward and Tunstall-Pedoe, 1999 (20)	UK	Cohort	1984–1993	7.7 y	M	CHD	159/5724	0 cups/d	1.00	Age, housing tenure, activity at work, activity in leisure, smoking, BMI, Bortner score, cotinine, SBP, fibrinogen, total cholesterol, HDL cholesterol, triglycerides, alcohol, vitamin C, coffee
								1–2 cups/d	1.83 (0.92, 3.63)	
								3–4 cups/d	1.09 (0.52, 2.28)	
								≥5 cups/d	1.10 (0.51, 2.37)	
					F	CHD	47/5843	0 cups/d	1.00	
								1–2 cups/d	1.32 (0.36, 4.80)	
								3–4 cups/d	1.10 (0.28, 4.31)	
								≥5 cups/d	1.06 (0.28, 4.05)	

(Continued)

TABLE 1 (*Continued*)

Study	Country	Design	Study period	Follow-up	Sex	Outcome	Sample size[2]	Tea consumption	RR/OR (95% CI)	Adjustment factor
Yochum et al, 1999 (21)	USA	Cohort	1986–1995	10 y	F	CHD	438/34,492	0 times/wk	1.00	Age, energy intake, fiber, grains, BMI, vitamin E, waist-to-hip ratio, hypertension, diabetes, estrogen replacement, alcohol, education, marital status, smoking, physical activity, cholesterol, saturated fat
								0.5 times/wk	0.86 (0.64, 1.17)	
								1–4 times/wk	0.98 (0.74, 1.29)	
								5–42 times/wk	0.89 (0.67, 1.17)	
Hirvonen et al, 2001 (22)	Finland	Cohort	1987–1993	6.1 y	M	Coronary death	815/25,372	<1cup/d	1.00	Age, supplementation group, SBP, DBP, serum total cholesterol, HDL cholesterol, BMI, smoking, histories of diabetes and CHD, marital status, education, physical activity
								≥1cup/d	1.09 (0.91, 1.30)	
						MI	1122/25,372	<1cup/d	1.00	
								≥1cup/d	0.94 (0.81, 1.11)	
Geleijnse et al, 2002 (23)	Netherlands	Cohort	1990–1997	5.6 y	M/F	MI	146/4807	0 mL/d	1.00	Age, sex, BMI, smoking, education, alcohol, coffee, fiber, polyunsaturated fat, saturated fat, vitamin E, total energy
								1–375 mL/d	0.77 (0.48, 1.25)	
								>375 mL/d	0.57 (0.33, 0.98)	
Sesso et al, 2003 (24)	USA	Cohort	1977–1995	15 y	M/F	CHD	1613/17,228	None	1.00	Age, sex, BMI, physical activity, hypertension, diabetes, smoking, alcohol, early parental death
								<1 cup/d	0.97 (0.85, 1.11)	
								1 cup/d	0.98 (0.89, 1.09)	
								2 cups/d	0.93 (0.83, 1.04)	
								3 cups/d	0.85 (0.69, 1.06)	
								≥4 cups/d	0.98 (0.82, 1.18)	
Lopez-Garcia et al, 2006 (25)	USA	Cohort	1986–2000	14 y	M	CHD	2173/44,005	<1 cup/mo	1.00	Age, smoking, BMI, physical activity, alcohol, parental history of MI, menopausal status, hormone therapy, multivitamin, aspirin, hypercholesterolemia, vitamin E, hypertension, diabetes
								1/mo to 4 cups/wk	1.01 (0.92, 1.11)	
								5–7 cups/wk	1.07 (0.94, 1.21)	
								2–3 cups/d	1.08 (0.89, 1.32)	
								≥4 cups/d	1.17 (0.76, 1.78)	
			1980–2000	20 y	F	CHD	2254/84,488	<1 cup/mo	1.00	
								1/mo to 4 cups/wk	0.88 (0.79, 0.99)	
								5–7 cups/wk	0.95 (0.85, 1.07)	
								2–3 cups/d	0.86 (0.72, 1.02)	
								≥4 cups/d	0.80 (0.58, 1.12)	

[1] RR/OR, relative risk or odds ratio; C-C, case-control; MI, myocardial infarction; CHD, coronary heart disease; SBP, systolic blood pressure; IHD, ischemic heart disease; DBP, diastolic blood pressure.
[2] Cases/controls or cohort size.

TABLE 2
Summary risk estimates of the association between black tea consumption and coronary artery disease risk[1]

Black tea consumption	Sample size	RR (95% CI)[3]	Heterogeneity test[2] Q	P	I^2
					%
Highest vs lowest drinkers					
All studies	13	0.92 (0.82, 1.04)	24.54	0.039	42.9
Case control	3	0.88 (0.53, 1.47)	5.68	0.058	64.8
Cohort	10	0.94 (0.83, 1.06)	18.29	0.075	39.8
Routine vs non-/occasional drinkers					
All studies	13	0.95 (0.87, 1.03)	47.34	0.000	70.4
Case control	3	0.84 (0.62, 1.14)	4.05	0.132	50.6
Cohort	10	0.96 (0.89, 1.05)	40.43	0.000	72.8
Increment of 1 cup/d					
All studies	9	0.98 (0.94, 1.02)	39.72	0.000	74.8
Case control	2	0.90 (0.72, 1.12)	4.08	0.043	75.5
Cohort	7	0.99 (0.95, 1.03)	31.66	0.000	74.7
Sex					
Male	8	0.95 (0.72, 1.25)	14.91	0.037	53.0
Female	4	0.83 (0.67, 1.02)	2.15	0.541	0.0
Origin					
United States	6	0.94 (0.82, 1.08)	9.38	0.153	36.0
European	7	0.88 (0.68, 1.14)	15.15	0.034	53.8
Follow-up					
<10 y	5	0.92 (0.76, 1.11)	8.97	0.110	44.3
≥10 y	5	0.94 (0.78, 1.15)	9.04	0.107	44.7

[1] RR, relative risk.
[2] Heterogeneity was examined by using the Q and I^2 statistics; all statistical tests were 2-sided.
[3] Summary RR was based on the DerSimonian and Laird random-effects model.

I^2 = 42.9%). The summary result of the association between routine black tea drinking and risk of CAD also indicated a lack of association (summary RR: 0.95; 95% CI: 0.87, 1.03; P for heterogeneity = 0.000; I^2 = 70.4%). Subgroup analyses were carried out to identify sources of heterogeneity. The results for the stratified analysis of the highest black tea consumption by study design, sex, geographic region, and years of follow-up are shown in Table 2; however, we noted no significant results from

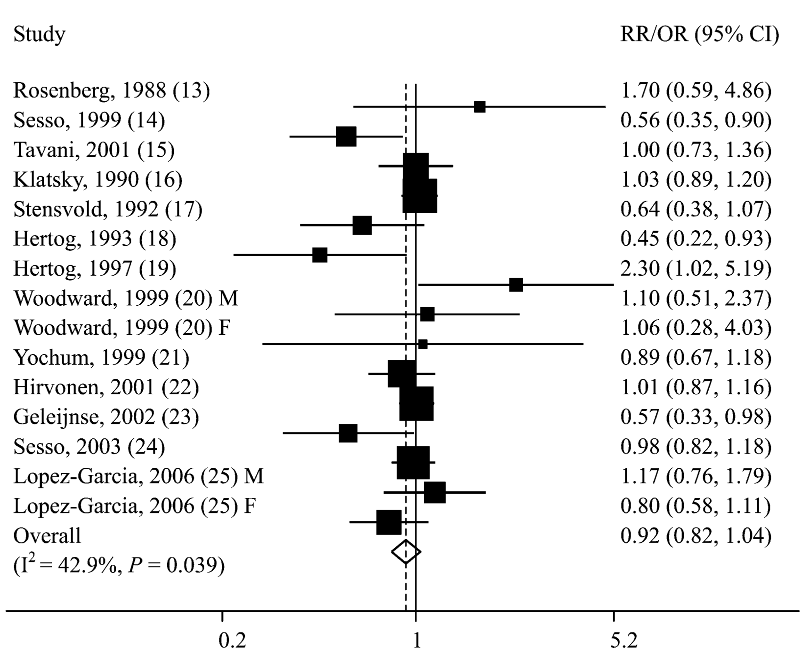

FIGURE 1. Summary relative risks (RRs) of coronary artery disease for the comparison of the highest black tea consumption with the lowest black tea consumption. The squares indicate study-specific risk estimates (size of square reflects the study's statistical weight), the horizontal lines indicate the 95% CIs, and the diamond indicates the summary RR estimate with its corresponding 95% CI. Study-specific risk estimates were combined by using the DerSimonian and Laird random-effects model. OR, odds ratio.

those analyses. The result of the sensitivity analysis in which one study was removed at a time confirmed the stability of the meta-analysis; the summary RR ranged from 0.90 [after exclusion of the study by Klatsky et al (16); 95% CI: 0.78, 1.03; P for heterogeneity = 0.038; I^2 = 44.3%] to 0.95 [after exclusion of the study by Sesso et al (14); 95% CI: 0.85, 1.06; P for heterogeneity = 0.111; I^2 = 33.0%]. In addition, the Egger's test for publication bias was not statistically significant (P = 0.380).

Our dose-response analysis did not indicate any statistically significant inverse association between an increase in black tea consumption of 1 cup/d and risk of CAD (summary RR: 0.98; 95% CI: 0.94, 1.02; P for heterogeneity = 0.000; I^2 = 74.8%) (**Figure 2**).

Green tea

A total of 5 studies (26–30) containing 3 case-control studies (26–28) and 2 prospective cohort studies (29, 30) were included in the meta-analysis on green tea consumption in relation to CAD risk (**Table 3**). Three of the 5 studies were conducted in Japan (26, 29, 30), and the remaining 2 were conducted in China (27, 28).

RR estimates of CAD for the highest green tea consumption vs the lowest green tea consumption for individual studies and all studies combined are shown in **Table 4** and **Figure 3**. The overall results showed a statistically significant 28% reduction in risk of CAD with the highest green tea consumption (summary RR: 0.72; 95% CI: 0.58, 0.89). We found no statistically significant heterogeneity among the study results (P = 0.314, I^2 = 15.5%). The summary result of the association between routine green tea drinking and risk of CAD indicated a statistically significant 17% reduction (summary RR: 0.83; 95% CI: 0.71, 0.97; P for heterogeneity = 0.482; I^2 = 0.0%). The results of subgroup analyses by study design and sex are shown in Table 4; we noted that the protective effect of green tea consumption on CAD was observed in case-control studies and male drinkers but not in cohort studies and female drinkers. In a sensitivity analysis in which one study at a time was removed and the rest analyzed, the summary RR ranged from 0.67 [after exclusion of the study by Wen et al (27); 95% CI: 0.53, 0.86; P for heterogeneity = 0.304; I^2 = 17.3%] to 0.77 [after exclusion of the study by Wang et al (28); 95% CI: 0.63, 0.94; P for heterogeneity = 0.585; I^2 = 0.0%]. In addition, no indication of publication bias was found from the Egger's test (P = 0.105).

The dose-response analysis of green tea indicated that an increase in green tea consumption of 1 cup/d was statistically significantly associated with a 10% decrease in the risk of developing CAD (summary RR: 0.90; 95% CI: 0.82, 0.99; P for heterogeneity = 0.000; I^2 = 86.1%), (**Figure 4**).

DISCUSSION

The present meta-analysis evaluated the association between black tea consumption, green tea consumption, and the risk of CAD based on published results from 6 case control studies and 12 cohort studies. The results suggest that black tea consumption is not associated with a decreased risk of CAD, and green tea is equivocally associated with a decreased risk of CAD. However, the data available are so limited that we could not confirm our findings.

In our study, we did not observe a statistically significant association between black tea consumption and risk of CAD. Despite the significant heterogeneity among the 13 studies available for the analysis, the results were strengthened by the dose-response analysis and sensitivity analysis. When the subgroup analysis was conducted by country, we found that the studies from the United States became homogenous, whereas statistically significant heterogeneity was still observed among the European countries. Within the European studies, the results of the 2 studies (19, 20) reported from the United Kingdom were associated with an increased risk of CAD, whereas the 2 studies (18, 23) from the Netherlands indicated a significant reduction in risk. This may have been due to differences in black tea drinking habits. For example, the English prefer to drink black tea with

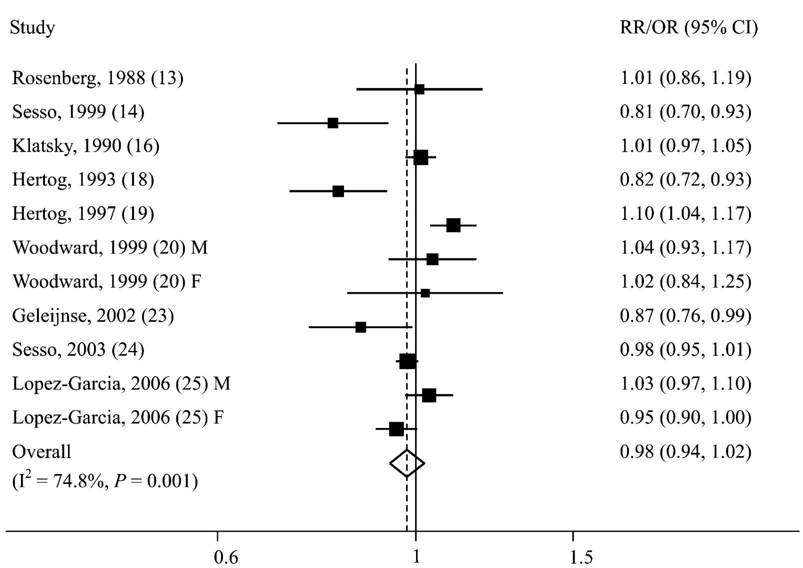

FIGURE 2. Summary relative risks (RRs) of coronary artery disease for an increase in black tea intake of 1 cup/d. The squares indicate study-specific risk estimates (size of square reflects the study's statistical weight), the horizontal lines indicate the 95% CIs, and the diamond indicates the summary RR estimate with its corresponding 95% CI. Study-specific risk estimates were combined by using the DerSimonian and Laird random-effects model. OR, odds ratio.

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TABLE 3
Epidemiologic studies on green tea consumption in association with coronary artery disease (CAD) risk[1]

Study	Country	Design	Study period	Follow-up	Sex	Outcome	Sample size[2]	Tea consumption	RR/OR (95% CI)	Adjustment factor
Hirano et al, 2002 (26)	Japan	C-C	1999–2001		M/F	MI	128/265	$<$1 cup/d	1.00	Age, sex, coffee, hypertension, green tea, fruit, diabetes, smoking, hyperlipidemia, HDL
								$\geq$1 cup/d	0.58 (0.34, 0.98)	
Wen et al, 2008 (27)	China	C-C	2002–2006		M	MI	518/2590	No	1.00	Family history of CHD, income, lifestyle factors
								Yes	0.87 (0.59, 1.28)	
Wang et al, 2010 (28)	China	C-C	2008–2009		M	CAD	246/133	No	1.00	Age, smoking, alcohol, physical activity, diabetes, hypertension, hyperlipidemia, education, BMI, residence, family history of CAD
								$<$125 g/mo	1.09 (0.61, 1.96)	
								125–249 g/mo	0.36 (0.19, 0.71)	
								$\geq$250 g/mo	0.36 (0.17, 0.73)	
								Yes	0.62 (0.38, 1.01)	
					F	CAD	79/62	No	1.00	
								Yes	0.65 (0.27, 1.57)	
Nakachi et al, 2000 (29)	Japan	Cohort	1986–1999	13 y	M/F	Nonstroke CVD	274/8552	$\leq$3 cups/d	1.00	Age, smoking, alcohol, meat, relative body weight
								4–9 cups/d	1.02 (0.76, 1.36)	
								$\geq$10 cups/d	0.72 (0.50, 1.04)	
Kuriyama et al, 2006 (30)	Japan	Cohort	1995–2001	7 y	M/F	CHD	209/40,530	$<$1 cup/d	1.00	Age, sex, job status, education, BMI, exercise, walking, hypertension, diabetes, gastric ulcer, smoking, alcohol, total energy intake, rice, miso soup, soybean products, meat, fish, dairy products, fruit, vegetables, oolong tea, black tea, coffee
								1–2 cups/d	1.04 (0.70, 1.56)	
								3–4 cups/d	0.90 (0.60, 1.36)	
								$\geq$5 cups/d	0.86 (0.59, 1.26)	

[1] RR/OR, relative risk or odds ratio; C-C, case-control; MI, myocardial infarction; CHD, coronary heart disease; CVD, cardiovascular disease.
[2] Cases/controls or cohort size.

TABLE 4
Summary risk estimates of the association between green tea consumption and coronary artery disease risk[1]

Green tea consumption	Sample size	RR (95% CI)[3]	Heterogeneity test[2] Q	P	I^2
					%
Highest vs lowest drinkers					
All studies	5	0.72 (0.58, 0.89)	5.92	0.314	15.5
Case control	3	0.63 (0.43, 0.92)	4.83	0.185	37.9
Cohort	2	0.78 (0.60, 1.02)	0.44	0.509	0.0
Routine vs non-/occasional drinkers					
All studies	5	0.83 (0.71, 0.97)	4.48	0.482	0.0
Case control	3	0.71 (0.55, 0.91)	1.95	0.582	0.0
Cohort	2	0.91 (0.75, 1.10)	0.09	0.770	0.0
Increment of 1 cup/d					
All studies	4	0.90 (0.82, 0.99)	21.51	0.000	86.1
Case control	2	0.82 (0.76, 0.88)	1.03	0.309	3.3
Cohort	2	0.98 (0.96, 1.00)	0.16	0.688	0.0
Sex					
Male	4	0.69 (0.48, 0.99)	5.91	0.116	49.2
Female	3	0.77 (0.54, 1.11)	0.20	0.905	0.0

[1] RR, relative risk.
[2] Heterogeneity was examined by using the Q and I^2 statistics; all statistical tests were 2-sided.
[3] Summary RR was based on the DerSimonian and Laird random-effects model.

milk, which may reduce the bioavailability of flavonoids. In contrast, it is unusual for black tea to be drunk with milk in the Netherlands (19). However, we were unable to carry out an analysis to examine the effect of adding milk to black tea, and it warrants further investigation.

In contrast with black tea, the findings suggest an inverse association between green tea consumption and subsequent risk of CAD. Furthermore, every additional cup of green tea consumed in a day was associated with a 10% decrease in the risk of CAD. However, this may be an overestimate of the true magnitude of the association because of the limited number of studies. When the various studies were stratified by study design, we noted discrepancies between the summary results of prospective and case-control studies regarding the association between green tea consumption and CAD risk; the inverse association was evident among case-control studies. It is possible that the inverse associations reported from the case-control studies may have been overstated because of recall or selection bias, which could be of concern in retrospective studies. However, the cohort study meta-analysis showed no significant inverse relation. One of the cohort studies that controlled well for dietary factors showed no significance (30), and another study that looked at "nonstroke CVD" found that only persons reporting >10 cups/d had an inverse relation to the outcome (29). Considering these results, the finding of reduced CAD risk in green tea drinkers is not robustly supported by these data.

It is biologically plausible that black tea and green tea might have an inconsistent effect on CAD risk. Green tea catechins have

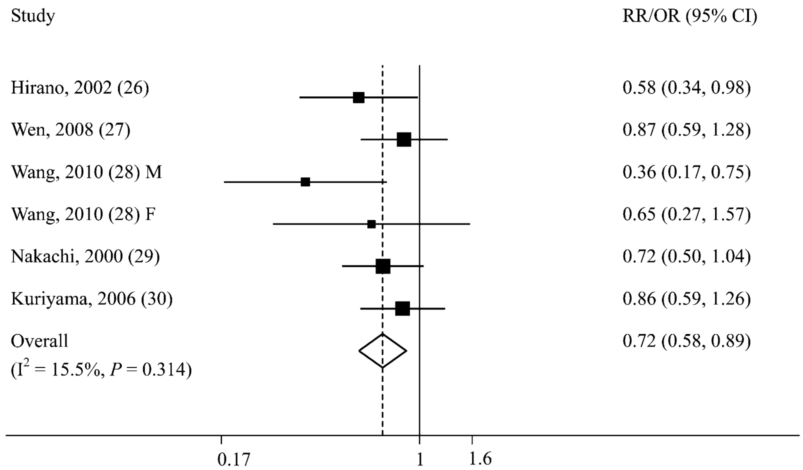

FIGURE 3. Summary relative risks (RRs) of coronary artery disease for the comparison of the highest green tea consumption with the lowest green tea consumption. The squares indicate study-specific risk estimates (size of square reflects the study's statistical weight), the horizontal lines indicate the 95% CIs, and the diamond indicates the summary RR estimate with its corresponding 95% CI. Study-specific risk estimates were combined by using the DerSimonian and Laird random-effects model. OR, odds ratio.

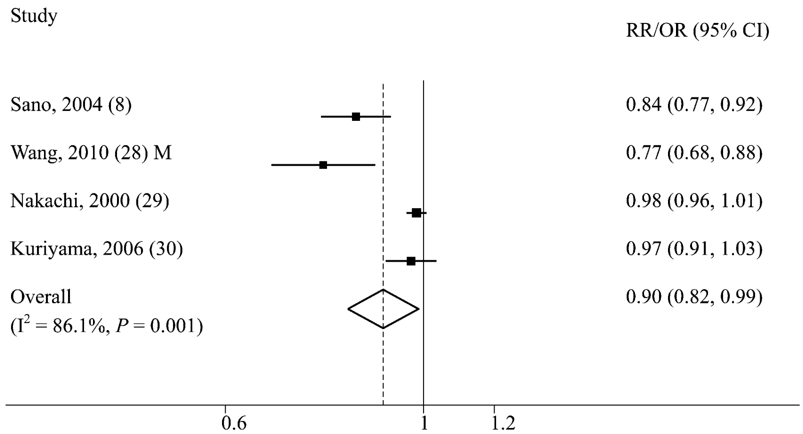

FIGURE 4. Summary relative risks (RRs) of coronary artery disease for an increase in green tea intake of 1 cup/d. The squares indicate study-specific risk estimates (size of square reflects the study's statistical weight), the horizontal lines indicate the 95% CIs, and the diamond indicates the summary RR estimate with its corresponding 95% CI. Study-specific risk estimates were combined by using the DerSimonian and Laird random-effects model. OR, odds ratio.

been shown to inhibit oxidation, vascular inflammation, atherogenesis, and thrombogenesis and to favorably modulate the plasma lipid profile and vascular reactivity, which suggests a wide spectrum of beneficial effects on CAD (4, 39, 40). Because of the different degrees of fermentation, the content and composition of catechins vary substantially between green and black tea. In green tea, catechins constitute 80–90% of total flavonoids, with epigallocatechin gallate being the most abundant (48–55%), followed by epigallocatechin (9–12%), epicatechin gallate (9–12%), and epicatechin (5–7%) (4, 41). However, during the oxidative process that occurs in the production of black tea, flavanols are converted primarily into thearubigins and theaflavins, which are complex condensation products of tea polyphenols. In black tea, the catechin content is only 20–30% (42). Therefore, if catechins are the most important contributor to the beneficial effect of green tea on CAD risk, the relative lack of association between black tea consumption and CAD risk is reasonable.

Several potential limitations of our meta-analysis must be considered when interpreting the results. First, the articles included were all published in English; limited resources prevented us from including articles published in other languages. Second, our meta-analysis was based on observational studies that were susceptible to various biases, and we cannot exclude uncontrolled confounders as a potential explanation for the observed association between tea consumption and risk of CAD; such confounders could include coffee consumption, fruit and vegetable intake, socioeconomic status, and education. Third, some of the articles that we included were not originally designed to test the association between tea consumption and risk of CAD. Therefore, the methods for measuring tea consumption differed across studies, such that the exposure of tea was assessed mostly by the number of cups consumed daily or weekly. However, the size of cups may have varied, even though we tried rescaling to account for such. Finally, the studies included in our meta-analysis were mainly conducted in the United States, Europe, China, and Japan; therefore, the results should be extrapolated to other populations with caution.

In conclusion, results from the present meta-analysis indicate that black tea consumption has no association with risk of CAD. Our limited data support a tentative protective role of green tea against CAD. However, additional large prospective cohort studies are needed to provide a more definitive conclusion concerning whether the routine consumption of green tea can guard against CAD.

The authors' responsibilities were as follows—L-SW and Z-MW: conceived the idea and designed the study; and Z-MW and BZ: conducted the literature search, extracted the data, and conducted the data analyses. All of the authors helped interpret the results and to write and revise the manuscript. The authors declared no conflicts of interest.

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