Green tea intake lowers fasting serum total and LDL cholesterol in adults: a meta-analysis of 14 randomized controlled trials[1–4]

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ABSTRACT

Background: The effect of green tea beverage and green tea extract on lipid changes is controversial.

Objective: We aimed to identify and quantify the effect of green tea and its extract on total cholesterol (TC), LDL cholesterol, and HDL cholesterol.

Design: We performed a comprehensive literature search to identify relevant trials of green tea beverages and extracts on lipid profiles in adults. Weighted mean differences were calculated for net changes in lipid concentrations by using fixed-effects or random-effects models. Study quality was assessed by using the Jadad score, and a meta-analysis was conducted.

Results: Fourteen eligible randomized controlled trials with 1136 subjects were enrolled in our current meta-analysis. Green tea consumption significantly lowered the TC concentration by 7.20 mg/dL (95% CI: −8.19, −6.21 mg/dL; $P < 0.001$) and significantly lowered the LDL-cholesterol concentration by 2.19 mg/dL (95% CI: −3.16, −1.21 mg/dL; $P < 0.001$). The mean change in blood HDL-cholesterol concentration was not significant. Subgroup and sensitivity analyses showed that these changes were not influenced by the type of intervention, treatment dose of green tea catechins, study duration, individual health status, or quality of the study. Overall, no significant heterogeneity was detected for TC, LDL cholesterol, and HDL cholesterol; and results were reported on the basis of fixed-effects models.

Conclusion: The analysis of eligible studies showed that the administration of green tea beverages or extracts resulted in significant reductions in serum TC and LDL-cholesterol concentrations, but no effect on HDL cholesterol was observed. *Am J Clin Nutr* 2011;94:601–10.

INTRODUCTION

Cardiovascular disease (CVD) is a leading cause of morbidity, mortality, and disability worldwide (1). Hyperlipidemia, which results from abnormalities in lipid metabolism, leads to the development of atherosclerotic plaques and is one of the key risk factors of CVD (2). Risk of heart attack is 3-fold higher in subjects with hyperlipidemia than in subjects with normal lipid status (3), whereas a 1% decrease in serum cholesterol has been shown to reduce risk of CVD by 3% (1). With the increasing incidence of hyperlipidemia, more and more consumers are aware of the effects of what they eat and drink on their blood lipid profiles.

Green tea is a widely consumed beverage worldwide and is traditionally used in Asian countries as a medication. Green tea is produced from fresh leaves of *Camellia sinensis* and is not traditionally fermented. Green tea contains antioxidants and other beneficial nutrients such as protein, carbohydrates, minerals, vitamins, and flavonoid-like polyphenols (4). Epidemiologic studies have reported an inverse relation between green tea consumption and CVD risk. Subjects who drink >2 cups of green tea/d had lower plasma total cholesterol (TC) concentrations and have been shown to reduce their risk of death from CVD by 22–33% (5, 6). In vivo and in vitro studies have shown that green tea catechins (which belong to the family of flavonols and serve as an essential component of green tea), exert a cardioprotective effect via multiple mechanisms (7–10) including the inhibition of oxidation, vascular inflammation, thrombogenesis, and improvement in blood lipid concentrations.

Recent animal studies have revealed that green tea catechins could inhibit key enzymes involved in lipid biosynthesis and reduce the intestinal absorption of TC, thereby improving blood lipid profiles (9, 10). Because of promising results in preclinical models, a substantial number of clinical trials have been performed to investigate the effect of green tea beverages and extracts on lipid profiles of subjects with cardiovascular-related diseases as well as of healthy individuals (11–24). However, results of these trials were inconsistent, and sample sizes were relatively modest. As a result, the precise effect of green tea on lipid profiles has not been established to our knowledge. Therefore, we conducted a meta-analysis of all published randomized controlled trials (RCTs) that investigated the effects of green tea on blood cholesterol, including TC, LDL cholesterol, and HDL cholesterol.

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METHODS

Search strategy

According to the Quality of Reporting of Meta-analyses, we systematically searched PubMed (http://www.ncbi.nlm.nih.gov/pubmed; from 1967 to August 2010), Embase (http://www.embase.com; from December 1977 to 2010), the Cochrane Library database (http://www.cochrane.org), and reviews and reference lists of relevant articles by using the text key words tea, green tea, green tea extract, tea polyphenols, catechin, EGCG, and camelia sinensis, which were paired with the following words: blood lipid, blood cholesterol, low-density lipoprotein cholesterol, or high-density lipoprotein cholesterol. The search was restricted to English-language reports of clinical trials in adult humans. In addition, a manual search of references from reports of clinical trials or review articles was performed to identify relevant trials. Attempts were also made to contact investigators for unpublished data.

Study selection

Studies were selected for this analysis if they met the following criteria: *1*) subjects consumed a green tea beverage or extract for >2 wk, *2*) the study was an RCT in human adults with either a parallel or crossover design, *3*) the starting and endpoint lipid concentrations (TC, LDL cholesterol, and HDL cholesterol) were available, *4*) food-intake control regimens of experimental groups were consistent with those of control groups, *5*) green tea extract was not given as part of a multicomponent supplement in either experimental or control groups, and *6*) blood samples were obtained from fasting subjects.

Quality assessment

The assessment of quality characteristics used the following criteria *1*) randomization, *2*) concealment of treatment allocation, *3*) participant masking, *4*) researcher masking, *5*) reporting of withdrawals, *6*) generation of random numbers, *7*) and reporting of industry funding. The Jadad score was also introduced to evaluate the quality of the studies. Trials scored one point for each area addressed in the study design (randomization, blinding, concealment of allocation, reporting of withdrawals, and generation of random numbers) with a possible score of between 0 and 5 (highest level of quality) (25). Higher numbers represented a better quality (Jadad score $\geq$4).

Data extraction

The search, data extraction, and quality assessment were completed independently by 2 reviewers (X-XZ and Y-LX) according to inclusion criteria. Any discrepancies between the 2 reviewers were resolved through a discussion until a consensus was reached. Study characteristics (including authors, publication year, sample size, study design, study duration, dose, and type of intervention), population information (sex and initial healthy status), and baseline and final concentrations or net changes of TC, LDL cholesterol, and HDL cholesterol were extracted. Extracted data were converted to conventional units (eg, for TC concentrations, 1 mmol/L converted to 38.6 mg/dL). For multiarm studies, only intervention groups that met inclusion criteria were used in this analysis (26). If blood lipid concentrations were reported several times in different stages of the trials, only final records of lipid concentrations at the end of the trials were extracted for the meta-analysis.

Data synthesis and analysis

Net changes in each of the study variables, which were calculated from baseline and follow-up means and SDs (follow-up minus baseline) were used to estimate the principle effect. When SDs were not directly available, they were calculated from SEs or CIs. In instances in which variances for net changes were not directly reported, they were calculated from CIs, *P* values, or individual variances from the green tea group and control group. For trials in which variances for paired differences were separately reported for each group, a pooled variance for the net change was calculated by using standard methods. In addition, the change-from-baseline SDs were also imputed by using correlation coefficient methods referenced in the *Cochrane Handbook for Systematic Reviews of Interventions* (26). We assumed a correlation coefficient of 0.68 (26). For one study (12) in which medians and interquartile ranges were reported, the width of the interquartile range was $\approx$1.35 SD, and the median was approximately the mean (26).

Our meta-analysis and statistical analyses were performed with STATA (version 10; StataCorp, College Station, TX). Weighted mean differences and 95% CIs were calculated for net changes in lipid values. The statistic heterogeneity of treatment effects between studies was formally tested with Cochran's test ($P < 0.1$). The I^2 statistic was also examined, and we considered $I^2 > 50\%$ to indicate significant heterogeneity between trials (27). Results were obtained from a fixed-effects model if no significant heterogeneity was shown, and a random-effects model was selected for the analysis if significant heterogeneity was shown (28). Publication bias was assessed with funnel plots and the Egger's regression test. To examine the effects of factors on the primary outcomes and identify the possible source of heterogeneity within these studies, previously defined subgroup analyses were performed (type of intervention, catechins dose, health status, study duration, and Jadad score). Additional sensitivity analyses were also performed according to the *Cochrane Handbook for Systematic Reviews of Interventions* (26).

RESULTS

Results of literature search

The method used to select studies is shown in **Figure 1**. A total of 805 potentially eligible articles were initially identified, and 778 articles were excluded because they were not clinical trials or the interventions were not relevant to the purpose of the current meta-analysis. Therefore, 27 potentially relevant articles were selected for detailed evaluation (11–24, 29–41). From the overall pool of full-text articles, 13 articles were excluded from the analysis. The duration of the experiment was <2 wk for 5 of the trials (31, 32, 36, 39, 40), whereas 3 of the trials did not report relevant outcomes (29, 37, 38). Three articles lacked sufficient details for inclusion in meta-analysis (34, 35, 41). In one study, blood samples were collected from subjects who were not fasting (30). Another article was excluded because a low-fat

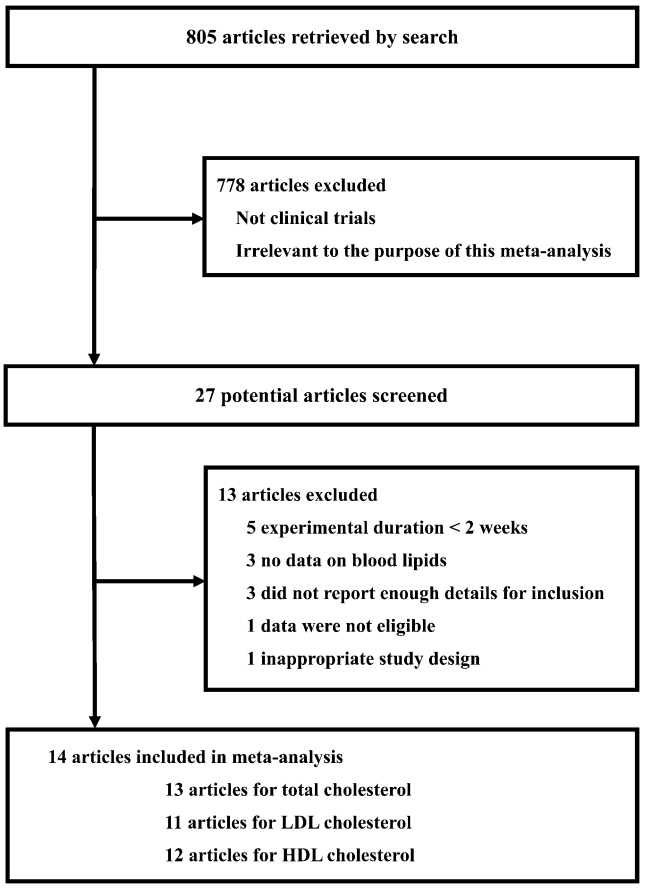

FIGURE 1. Flowchart showing the number of citations retrieved by individual searches of trials included in the review.

diet was only used in the control group, and the results may have been confounded by the inappropriate study design (33).

Study characteristics

Fourteen eligible RCTs with 1136 subjects were enrolled in the meta-analysis (11–24). Characteristics of the trials are shown in **Table 1**. The work of Princern et al (24) was separated into 2 trials (effects of green tea beverage and green tea extract on plasma lipid profiles). The trials varied in size from 20 to 240 subjects. The study duration varied from 3 wk to 3 mo (median: 12 wk). Doses of green tea catechins in the treatment group ranged from 150 to 2500 mg/d (median: 625 mg/d). Of the 14 trials used in the meta-analysis, 5 trials were conducted in healthy adults (14, 15, 22–24), and 5 trials were conducted in overweight to obese adults (12, 13, 17, 18, 21). The other studies investigated the effects of green tea consumption in patients with cardiovascular risks such as hypercholesterolemia (11, 19) or diabetes (16, 20). A green tea beverage was tested in one-half of trials (7 of 14 trials; 11, 16, 17, 19–21, 23), and a green tea extract capsule was used in the remaining 7 trials (12–15, 18, 22, 24). Most of the trials (12 trials) adopted parallel study designs (12–15, 17–24), whereas 2 trials used crossover designs (11, 16). Twelve trials were double-blinded trials (11–15, 17–23), and 10 trials were placebo-controlled trials (11–15, 17–19, 23, 24). A low-fat diet was fed in 2 trials (11, 19), and one trial used a low-energy diet (13). In the other trials, investigators attempted to maintain the usual lifestyles of participants. In 3 trials (17, 18, 23) of the included 14 trials, mild side effects were reported such as mild skin rashes, gastric upset, abdominal bloating. No side effects were reported in 7 trials (12, 14, 15, 19, 20, 22, 24). In the remaining 4 trials (11, 13, 16, 21), reports of side effects were unclear.

Data quality

Results of the validity of included trials are presented in **Table 2**. The study qualities of selected trials were diverse; 3 trials (12, 17, 20) were classified as high quality (Jadad score $\geq$4) and 11 trials (11, 13–16, 18–22, 24) were low quality (Jadad score of 2 or 3). Allocation concealment was clearly adequate in only one study (17). Two trials (12, 17) reported the generation of random numbers. Details of dropouts were reported in 12 trials (12, 14–24). Two studies (19, 20) received industry funding.

Effect of green tea on lipid concentrations

Primary outcome measures were changes in TC, LDL cholesterol, HDL cholesterol between baseline and final concentrations because of green tea beverage and green tea extract supplementation. The results for TC were reported in 14 comparisons from 13 studies that represented 949 participants, and the mean change in TC concentrations was significantly reduced in subjects supplemented with green tea ($-$7.20 mg/dL; 95% CI: $-$8.19, $-$6.21 mg/dL; $P < 0.001$) than in controls. Heterogeneity was not shown for this outcome (heterogeneity chi-square 14.30, I^2 = 9.1%, P = 0.353; **Figure 2**). The mean change in LDL-cholesterol concentrations was reported in 11 comparisons from 10 studies that represented 853 participants and was significantly decreased by 2.19 mg/dL (95% CI: $-$3.16, $-$1.21 mg/dL; $P <$ 0.001) in intervention groups than in control arms. No heterogeneity was observed for this outcome (heterogeneity chi-square = 13.41, I^2 = 25.4%, P = 0.201; **Figure 3**). The results of blood HDL cholesterol were calculated in 12 comparisons from 11 studies that included 998 subjects. For intervention groups, the mean change in blood HDL-cholesterol concentrations showed a favorable trend, but it was not significant (+0.25 mg/dL; 95% CI: $-$0.73, 1.23 mg/dL; P = 0.62). No heterogeneity was detected for this outcome (heterogeneity chi-square = 13.36, I^2 = 17.7%, P = 0.270; **Figure 4**).

Subgroup analyses were conducted to explore the dose-effect relation, study-duration effects, health-status effects, as well as differences between drinking green tea and taking green tea extracts. The consumption of catechins was divided into low dose ($<$625 mg/d) and high dose ($\geq$625 mg/d). The time to follow-up for the assessment of lipid-lowering therapy varied from 3 wk to 3 mo, and thus, a subgroup analysis was performed by dividing the follow-up duration into a shorter-term subgroup ($<$12 wk) and a longer-term subgroup ($\geq$12 wk).

Subgroup analyses showed that significant reductions of TC and LDL cholesterol were not influenced by the type of intervention (drinking green tea or taking green tea supplement). Analyses also showed that TC and LDL cholesterol were significantly decreased in the lower– and higher–catechin consumption groups. Green tea significantly reduced TC and LDL cholesterol in healthy subjects and in participants with cardiovascular risks. In the shorter- and longer-term subgroups, significant reductions in TC and LDL cholesterol were shown. We also stratified studies according to the

TABLE 1
Characteristics of 14 included randomized controlled trials[1]

Author, publication year (reference no.)	Study design	No. of subjects (M/F)	Population	Duration	Tea group	Control group	Side effect	Concurrent lifestyle modification
Batista et al, 2009 (11)	Double-blinded crossover	33 (5/28)	Hypercholesterolemic patients, 21–71 y of age	8 wk	250 mg GTE capsules (catechins NR)	Placebo capsules	NR	Maintain low-fat diet; no vitamin supplement
Chan et al, 2006 (12)	Double-blinded parallel	34 (0/34)	Obese women with PCOS, 25–40 y of age	3 mo	Green tea capsules (661 mg catechins)	Placebo capsules	No	Limit caffeine; nutritional consults
Diepvens et al, 2006 (13)	Double-blinded parallel	46 (0/46)	Overweight women, 19–57 y of age	12 wk	GTE capsules (1207 mg catechins)	Placebo (maltodextrin) capsules	NR	Maintain low-energy diet; limit 3 cups of coffee/d
Frank et al, 2009 (14)	Double-blinded parallel	33 (33/0)	Healthy men, 18–55 y of age	3 wk	Aqueous GTE capsule (714 mg catechins)	Placebo (maltodextrin) capsules	No	Maintain usual diet and exercise, limit tea and coffee $\leq$3 cups/d
Freese et al, 1999 (15)	Double-blinded parallel	20 (0/20)	Healthy nonsmoking women, 23–50 y of age	4 wk	3 g GTE capsules (810 mg catechins)	Placebo (saccharose, microcrystalline, cocoa) capsules	No	Rich in linoleic acid diet
Fukino et al, 2008 (16)	Open-label crossover	60 (51/9)	Patients with diabetes or prediabetes, 32–73 y of age	2 mo	GTE powder packets (456 mg catechins)	No intervention	NR	Maintain usual diet
Hsu et al, 2008 (17)	Double-blinded parallel	78 (0/78)	Obese women, 16–60 y of age	12 wk	1200 mg GTE capsules (491 mg catechins)	Placebo (cellulose) capsules	Yes	Maintain normal diet
Maki et al, 2009 (18)	Double-blinded parallel	128 (67/61)	Overweight or obese adults, total cholesterol $\geq$200 mg/dL, 21–65 y of age	12 wk	500 mL green tea beverage (625 mg catechins)	Placebo beverage	Yes	Maintain normal diet, limit $\leq$2 caffeinated beverages/d
Maron et al, 2003 (19)	Double-blinded parallel	220	Patients with mild-to-moderate hypercholesterolemia	12 wk	375 mg GTE capsule (150 mg catechins)	Placebo (inert ingredients) capsules	No	Maintain low–saturated fat diet
Nagao et al, 2009 (20)	Double-blinded parallel	43 (18/25)	Patients with diabetes	12 wk	340 mL green tea (583 mg catechins)	340 mL green tea (96 mg catechins)	No	Maintain usual diet and exercise
Nagao et al, 2007 (21)	Double-blinded parallel	240 (140/100)	Adults with visceral fat-type obesity, 25–55 y of age	12 wk	340 mL green tea beverage (583 mg catechins)	340 mL green tea beverage (96 mg catechins)	NR	Maintain usual diet and exercise; limit medications or supplements that influence lipid or carbohydrate metabolism
Nagao et al, 2005 (22)	Double-blinded parallel	35 (35/0)	Healthy men, 24–46 y of age	12 wk	340 mL GTE/oolong tea beverage (690 mg catechins)	340 mL oolong tea beverage (22 mg catechins)	No	2 planned meals/d; no tea or food high in catechins
Nantz et al, 2009 (23)	Double-blinded parallel	108 (44/64)	Healthy, 21–50 y of age	3 wk	400 mg GTE capsules (320 mg catechins)	Placebo (maltodextrin) capsules	Yes	Maintain normal diet and exercise; limit tea $\leq$1 cup/d
Princen et al, 1998 (24)	Single-blinded parallel	30 (15/15)	Healthy, 34 $\pm$ 12 y of age	4 wk	900 mL green tea (852 mg catechins)	Placebo (mineral water)	No	Limit milk in tea, $\leq$2 cups of fruit juice or tea, $\leq$2 oranges daily
Princen et al, 1998 (24)	Single-blinded parallel	28 (13/15)	Healthy, 34 $\pm$ 12 y of age	4 wk	9 g GTE capsules (2500 mg catechins)	Placebo (mineral water)	No	Limit milk in tea, $\leq$2 cups of fruit juice or tea, $\leq$2 oranges daily

[1] GTE, green tea extract; NR, not reported; PCOS, polycystic ovarian syndrome.

TABLE 2
Validity of included studies

Reference	Allocation concealment	Masking of participants	Masking of researchers	Generation of random number reported	Reporting of withdrawals	Industry funding	Jadad score
Batista et al (11)	Unclear	Yes	Yes	No	No	No	2
Chan et al (12)	Inadequate	Yes	Yes	Yes	Yes	No	4
Diepvens et al (13)	Unclear	Yes	Yes	No	No	No	2
Frank et al (14)	Unclear	Yes	Yes	No	Yes	No	3
Freese et al (15)	Unclear	Yes	Yes	No	Yes	No	3
Fukino et al (16)	Unclear	No	No	No	Yes	No	2
Hsu et al (17)	Adequate	Yes	Yes	Yes	Yes	No	5
Maki et al (18)	Unclear	Yes	Yes	No	Yes	No	3
Maron et al (19)	Inadequate	Yes	Yes	No	Yes	Yes	3
Nagao et al (20)	Unclear	Yes	Yes	No	Yes	Yes	3
Nagao et al (21)	Inadequate	Yes	Yes	No	Yes	No	3
Nagao et al (22)	Unclear	Yes	Yes	No	Yes	No	3
Nantz et al (23)	Unclear	Yes	Yes	Yes	Yes	No	4
Princen et al (24)	Unclear	Yes	No	No	Yes	No	2

Jadad score (<4 or ≥4). Significant reductions in TC and LDL cholesterol were shown in the low- and high-score subgroups. No significant changes in HDL cholesterol were observed in any subgroup. Results are summarized in **Table 3**.

Sensitivity analysis showed that the significance in the pooled changes in TC, LDL cholesterol, and HDL cholesterol were not altered after the imputation correlation coefficient of 0.5. Sensitivity analysis that excluded low-quality studies (11, 13–16, 18–22, 24)

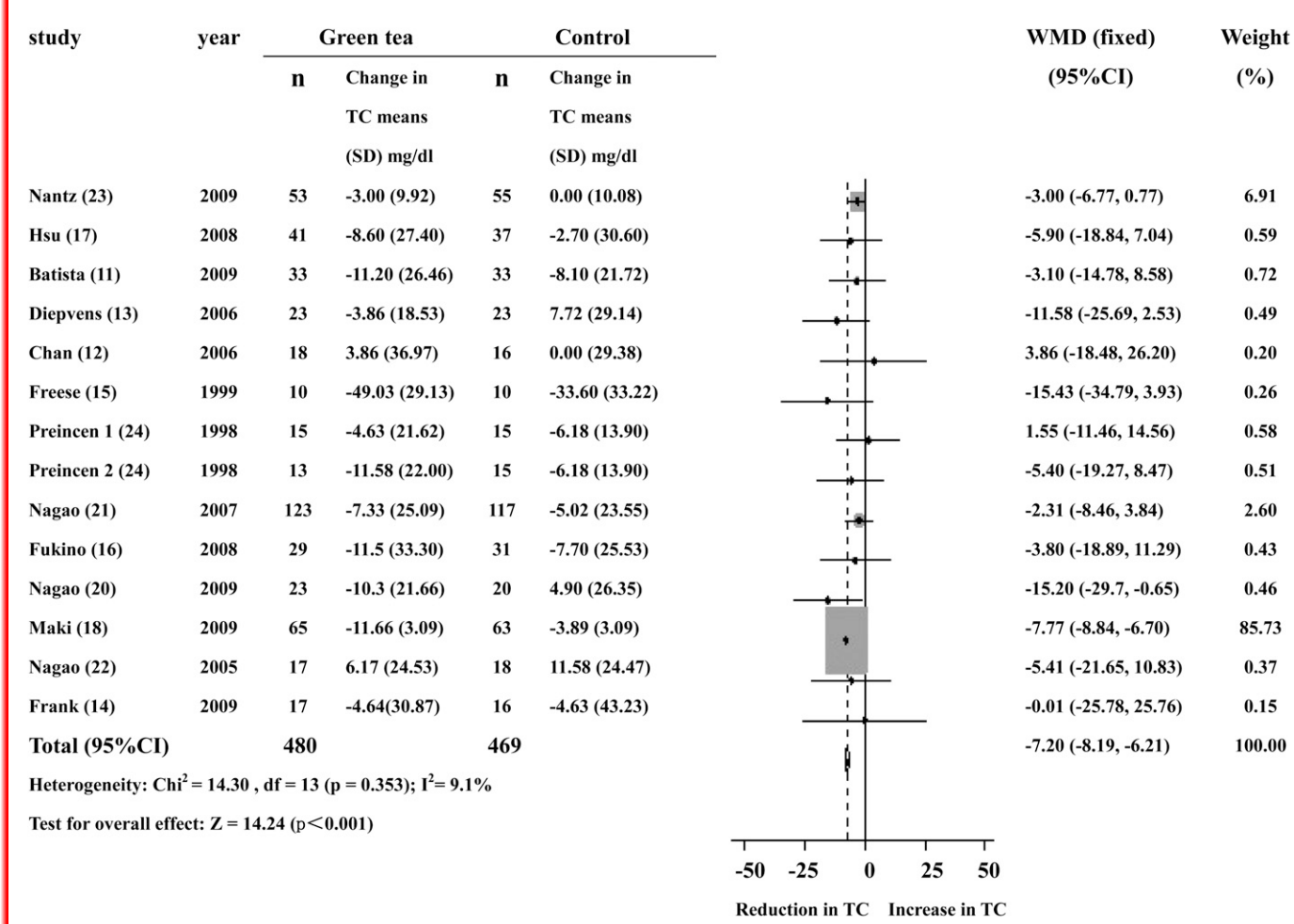

FIGURE 2. Meta-analysis of effects of green tea consumption on total cholesterol (TC) compared with control arms. Sizes of data markers indicate the weight of each study in the analysis. WMD, weighted mean difference (the result was obtained from a fixed-effects model).

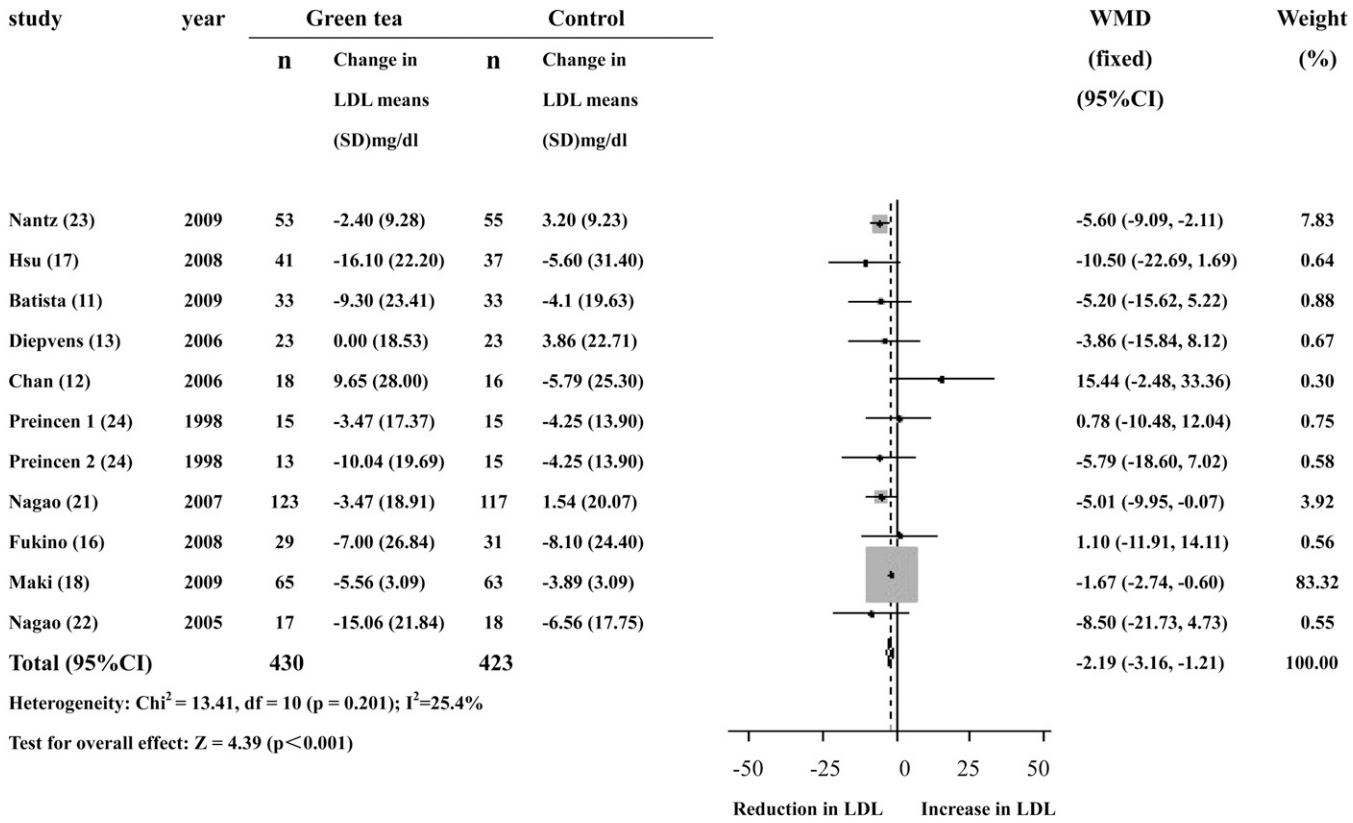

FIGURE 3. Meta-analysis of effects of green tea consumption on LDL cholesterol compared with control arms. Sizes of data markers indicate the weight of each study in the analysis. WMD, weighted mean difference (the result was obtained from a fixed-effects model).

showed that significant results were not influenced concerning TC, LDL cholesterol, and HDL cholesterol [TC concentration: −3.05 mg/dL (95% CI: −6.62, 0.53 mg/dL), *P* 0.758; LDL-cholesterol concentration: −5.25 mg/dL (95% CI: −8.54, −1.95 mg/dL), *P* = 0.053; HDL-cholesterol concentration: 2.36 mg/dL (95% CI: −0.36, 5.08 mg/dL); *P* = 0.833]. The removal of 2 trials (19, 20) with industry funding did not change the final results [TC concentration: −7.16 mg/dL (95% CI: −8.16, −6.17 mg/dL); *P* = 0.359; LDL-cholesterol concentration: −2.19 mg/dL (95% CI: −3.16, −1.21 mg/dL); *P* = 0.201; HDL-cholesterol concentration: 0.06 mg/dL (95% CI: −0.98, 1.11 mg/dL); *P* = 0.263]. The results are also shown in Table 3. Overall, no significant heterogeneity was shown for TC, LDL cholesterol, and HDL cholesterol, and the results were reported on the basis of fixed-effects models.

Publication bias

Funnel plots and Egger's tests indicated no significant publication bias in the meta-analyses of TC, LDL cholesterol, and HDL cholesterol (TC Egger's test: *P* = 0.148; LDL cholesterol Egger's test: *P* = 0.385; HDL cholesterol Egger's test: *P* = 0.679).

DISCUSSION

Our meta-analysis showed that both green tea beverages and green tea extract supplementation significantly reduce blood TC and LDL-cholesterol concentrations but did not affect HDL cholesterol concentrations. Subgroup and sensitivity analyses showed that these changes were not influenced by the type of intervention, treatment doses of green tea catechins, study duration, individual health status, or quality of the study.

A large population-based study that involved >40,000 middle-aged Japanese revealed that, compared with no tea drinking, habitual green tea consumption [an average of >2 cups (≈17 oz)/d for 10 y] was associated with a lower risk of death from CVD (5). The beneficial effects of green tea on cardiovascular health may be due to the high concentration of green tea catechins, which have been proven to favorably modulate the plasma lipid profile. These small molecules exert a variety of physiologic actions and, thus, affect lipid metabolism.

Animal experiments indicated that the inhibition of cholesterol absorption may be the mechanism to explain the cholesterol-lowering effects of green tea. Catechins with gallate esters were shown to interfere with the biliary micelle system in the lumen of the intestine by forming insoluble co-precipitates of cholesterol and increasing the fecal excretion of cholesterol (42). This apparent decrease in cholesterol absorption and reduction in liver cholesterol concentrations lead to an increase of LDL-receptor expression and activity (9). This cell-surface protein is present on the outer surface of most cells, but in particular liver cells, it can remove cholesterol-carrying LDL from the circulation. Studies in animals have provided evidence that green tea extracts and their catechin constituents can reduce plasma, liver, and thoracic aorta cholesterol and up-regulate hepatic LDL receptors (9, 10). Bursill and Roach (9) and Bursill et al (10) have concluded that the administration of green tea extract was able to significantly increase both the LDL-receptor binding activity and relative

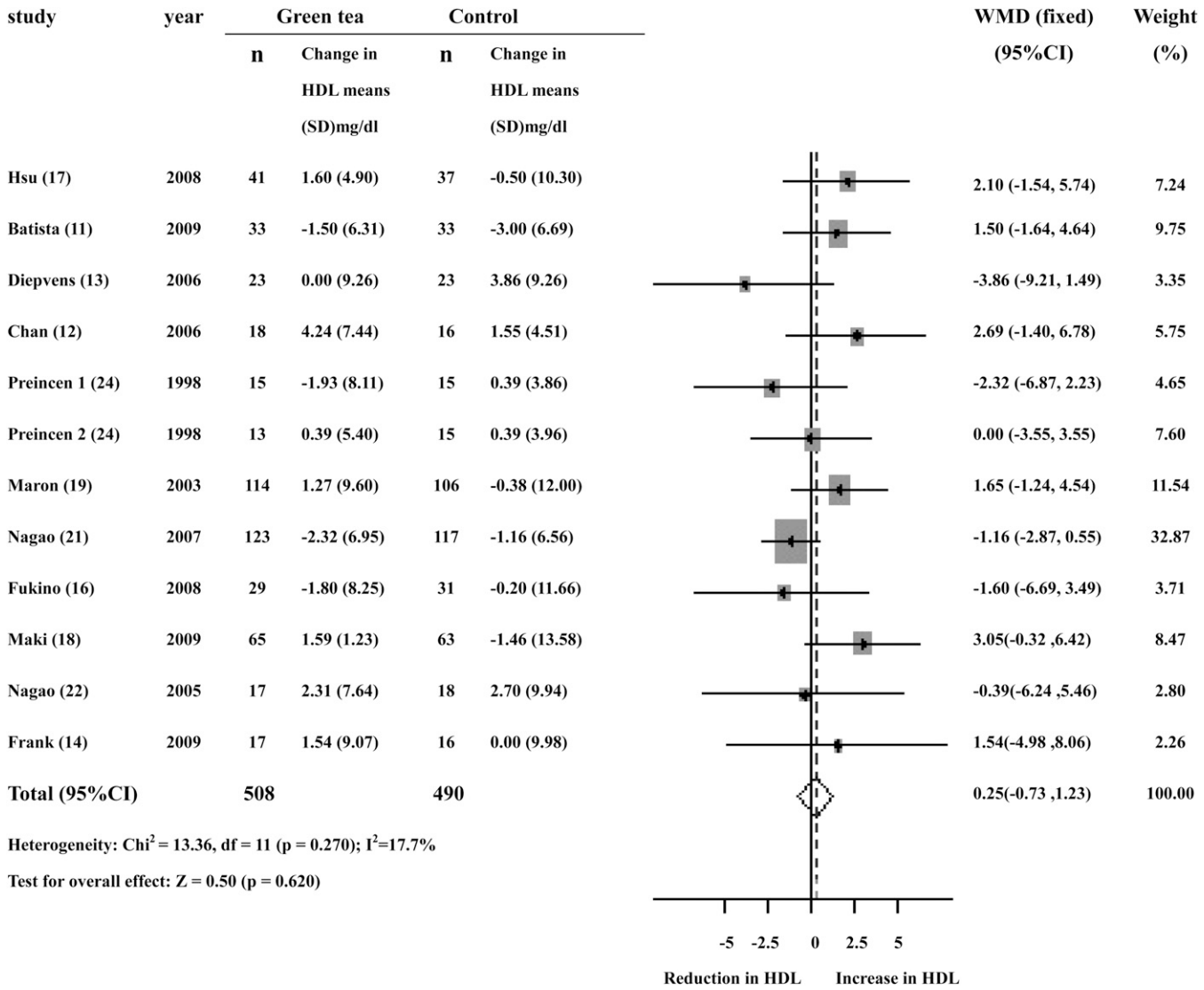

FIGURE 4. Meta-analysis of the effects of green tea consumption on HDL cholesterol as compared with the control arms. Sizes of the data markers indicate the weight of each study in the analysis. WMD, weighted mean difference (the result was obtained from a fixed-effects model).

amounts of LDL-receptor protein. In addition, there is another possible major mechanism by which green tea lowers cholesterol: catechins have direct inhibitory effects on cholesterol synthesis. A recent in vitro study has revealed that green tea catechins were potent and selective inhibitors of squalene epoxidase, which is likely a rate-limiting enzyme of cholesterol biosynthesis (43). These effects of green tea are similar to hypocholesterolemic drugs such as statins, which reduce cholesterol synthesis and increase the LDL receptor (44).

The effect of green tea beverages and green tea extract on blood lipid profiles has been investigated in vitro and in vivo, including in studies in both animals and humans, by many researchers. Hsu et al (17) have revealed that green tea intakes significantly decreased LDL-cholesterol concentrations and markedly increased concentrations of HDL cholesterol. Consistent with this study, other studies showed that green tea consumption was able to reduce serum cholesterol concentrations (11, 14, 19, 21, 23). In contrast, several studies reported that there were no positive correlations between green tea intake and reduced blood cholesterol concentrations (12, 13, 16, 24). To clarify the precise effect of green tea on serum cholesterol, we conducted the current meta-analysis of published RCTs. The results indicated that green tea beverages and green tea extract supplementation significantly reduced TC and LDL-cholesterol concentrations. The results of this study were consistent with a recently published meta-analysis that showed that green tea significantly reduced LDL-cholesterol concentrations (45). Furthermore, a recent study conducted in Japanese children showed that the consumption of a catechin-rich beverage for 24 wk significantly decreased LDL cholesterol after a 12-wk follow-up (46). To our knowledge, this study provided new evidence, which supported the conclusion of our meta-analysis, that green tea has hypocholesterolemic properties.

These results suggested that green tea may be incorporated into a targeted dietary program as part of public health policy to improve cardiovascular health. Because most Americans drink high-calorie beverages or alcohol on a daily basis, and only 20% of Americans consume low-calorie green tea (47), the potential for meaningful intervention is real.

TABLE 3
Subgroup analyses of total, LDL, and HDL cholesterol stratified by previously defined study characteristics

Variables	Total cholesterol			LDL cholesterol			HDL cholesterol		
	No. of trials	Mean difference (95% CI)	*P* for heterogeneity	No. of trials	Mean difference (95% CI)	*P* for heterogeneity	No. of trials	Mean difference (95% CI)	*P* for heterogeneity
		mg/dL			*mg/dL*			*mg/dL*	
Subgroup analysis									
Type of intervention									
Green tea beverage	6	−7.56 (−8.61, −6.52)	0.288	5	−1.82 (−2.86, −0.78)	0.549	5	−0.57 (−1.93, 0.78)	0.229
Green tea capsule	8	−3.89 (−7.05, −0.72)	0.843	6	−5.19 (−8.15, −2.23)	0.313	7	1.16 (−0.27, 2.58)	0.576
Catechins dose									
<625 mg/d (low median)	6	−3.51 (−6.41, −0.61)	0.726	5	−5.36 (−7.99, −2.73)	0.796	5	0.07 (−1.14, 1.29)	0.236
≥625 mg/d (high median)	8	−7.69 (−8.75, −6.64)	0.731	6	−1.68 (−2.73, −0.62)	0.388	7	0.57 (−1.09, 2.23)	0.270
Healthy status									
Healthy	6	−3.26 (−6.61, 0.08)	0.809	4	−5.28 (−8.14, −2.14)	0.710	4	−0.49 (−2.84, 1.87)	0.784
With cardiovascular risks	8	−7.58 (−8.62, −6.54)	0.519	7	−1.85 (−2.88, −0.83)	0.246	8	0.40 (−0.68, 1.48)	0.106
Duration									
<12 wk (low median)	7	−3.19 (−6.40, 0.02)	0.899	5	−4.77 (−7.77, −1.77)	0.742	5	0.05 (−1.80, 1.90)	0.650
≥12 wk (high median)	7	−7.63 (−8.67, −6.58)	0.489	6	−1.88 (−2.91, −0.85)	0.142	7	0.32 (−0.83, 1.48)	0.094
Jadad score									
Low (2 or 3)	11	−7.55 (−8.58, −6.52)	0.617	8	−1.89 (−2.92, −0.87)	0.789	10	−0.07 (−1.12, 0.98)	0.300
High (4 or 5)	3	−3.05 (−6.62, 0.53)	0.758	3	−5.25 (−8.54, −1.95)	0.053	3	2.36 (−0.36, 5.08)	0.833
Sensitivity analysis									
High-quality studies	3	−3.05 (−6.62, 0.53)	0.758	3	−5.25 (−8.54, −1.95)	0.053	3	2.36 (−0.36, 5.08)	0.833
Studies did not receive industry funding	13	−7.16 (−8.16, −6.17)	0.359	11	−2.19 (−3.16, −1.21)	0.201	11	0.06 (−0.98, 1.11)	0.263

Although we believe that the current meta-analysis provided useful information, some potential limitations should be addressed. First, an obvious source of conflict was that there is no general agreement on what quantity constitutes a cup of green tea. Doses of green tea catechins in the 14 trials involved in our meta-analysis ranged from 150 to 2500 mg/d (median: 625 mg/d). The wide range of green tea catechin doses made it difficult to determine the optimal dose that would most improve the blood lipid profile.

Second, caffeine is naturally contained in green tea. A newly released study showed that coffee consumption led to an increase in serum concentrations of TC and HDL cholesterol, mainly because of caffeine (48). In our meta-analysis, 11 trials stated that green tea beverages or extracts contained caffeine in the intervention groups. The independent effect of caffeine might have been a confounding factor that influenced the results of this meta-analysis.

Third, the quality of the trials included in our meta-analysis varied from low to high. Of the 14 trials, only 3 trials (12, 17, 23) were high-quality studies (Jadad score $\geq$4), whereas the other studies were low quality. Meanwhile, the study durations were short (from 3 wk to 3 mo). Therefore, more high-quality and long-term (over years) randomized studies are needed in the future.

Fourth, our meta-analysis did not pool safety data because no serious side effects were reported in these involved trials. However, concern has been raised as to the safety of supplementation with high doses of green tea polyphenols. In mice, the intraperitoneal injection of green tea catechins increased plasma concentrations of alanine transaminase (49). In addition, clinical reports have shown that green tea was the major dietary source of oxalate in some patients who presented with kidney oxalate stones (50). Daily green tea consumption in the current meta-analysis was equivalent to $\leq$18 cups, and the trials varied in length from 3 wk to 3 mo, and no subjects experienced major adverse events. This phenomenon may be attributed to the following 2 factors: *1*) the durations of studies involved in our meta-analysis were not long enough to observe serious side effects, and *2*) consumption of $<$18 cups of green tea/d may be not enough to cause adverse effects. Therefore, safety issues need to be evaluated in the future under conditions of long-term and high-dose exposure.

In conclusion, green tea significantly reduced serum total and LDL-cholesterol concentrations, and the changes were not influenced by the type of intervention, treatment doses of green tea catechins, study duration, individual health status, or quality of the study. For intervention groups, the mean change in blood HDL-cholesterol concentrations showed a favorable trend, but it was not significant.

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