

Effect of green tea catechins with or without caffeine on anthropometric measures: a systematic review and meta-analysis¹⁻³

Olivia J Phung, William L Baker, Leslie J Matthews, Michael Lanosa, Alicia Thorne, and Craig I Coleman

ABSTRACT

Background: Green tea catechins (GTCs) with or without caffeine have been studied in randomized controlled trials (RCTs) for their effect on anthropometric measures and have yielded conflicting results.

Objective: The objective was to perform a systematic review and meta-analysis of RCTs of GTCs on anthropometric variables, including body mass index (BMI), body weight, waist circumference (WC), and waist-to-hip ratio (WHR).

Design: A systematic literature search of MEDLINE, EMBASE, CENTRAL, and the Natural Medicines Comprehensive Database was conducted through April 2009. RCTs that evaluated GTCs with or without caffeine and that reported BMI, body weight, WC, or WHR were included. The weighted mean difference of change from baseline (with 95% CIs) was calculated by using a random-effects model.

Results: Fifteen studies ($n = 1243$ patients) met the inclusion criteria. On meta-analysis, GTCs with caffeine decreased BMI (-0.55 ; 95% CI: $-0.65, -0.40$), body weight (-1.38 kg; 95% CI: $-1.70, -1.06$), and WC (-1.93 cm; 95% CI: $-2.82, -1.04$) but not WHR compared with caffeine alone. GTC ingestion with caffeine also significantly decreased body weight (-0.44 kg; 95% CI: $-0.72, -0.15$) when compared with a caffeine-free control. Studies that evaluated GTCs without concomitant caffeine administration did not show benefits on any of the assessed anthropometric endpoints.

Conclusions: The administration of GTCs with caffeine is associated with statistically significant reductions in BMI, body weight, and WC; however, the clinical significance of these reductions is modest at best. Current data do not suggest that GTCs alone positively alter anthropometric measurements. *Am J Clin Nutr* 2010;91:73-81.

pressure, serum lipids, and glucose variables to ultimately decrease the risk of cardiovascular disease and diabetes (1). Therefore, body weight loss remains an important target for disease prevention.

There is a growing body of research showing that intake of green tea catechins (GTCs) may reduce BMI and body weight and suggests that the risk of cardiovascular disease may also be modified (7, 8). Catechins found in green tea include epicatechin (EC), epicatechin gallate (ECG), epigallocatechin (EGC), epigallocatechin gallate (EGCG), gallic catechin (GC), catechin gallate (CG), gallic catechin gallate (GCG), and catechin (C) (9). EGCG is believed to be the most pharmacologically active catechin and constitutes $>50\%$ of the total catechin content in most green tea products (7). Potential mechanisms by which GTCs exert these anthropometric effects involve inhibition of adipocyte differentiation and proliferation (10), reduced fat absorption (11), inhibition of catechol-*o*-methyl-transferase (10), increased energy expenditure (8), and increased utilization of fat (11).

In addition to GTCs, green tea also naturally contains caffeine (9). The use of caffeine may also contribute to changes in anthropometric measures through increased energy expenditure (12, 13) or increased thermogenesis (13). Because of caffeine's independent effects, the combination of GTCs with caffeine may be able to provide additive or even synergistic benefit over GTCs alone.

Randomized controlled trials have been conducted (14-28) to assess the effect of GTCs with or without caffeine on anthropometric variables, but yielded conflicting results and had only modest sample sizes. Therefore, we performed a systematic review and meta-analysis of randomized clinical trials to characterize the relation between GTCs with and without caffeine and changes in anthropometric variables, including BMI, body

INTRODUCTION

Being overweight or obese, defined as a body mass index (BMI; in kg/m^2) between 25 and 30 and a BMI >30 , respectively (1), is associated with a higher risk of developing cardiovascular disease and type 2 diabetes mellitus (2) and increased mortality (3, 4). Nearly two-thirds of the US adult population is overweight (5) and $\approx 26\%$ are obese, with some states reporting obesity rates as high as 33% (6). According to the clinical guidelines regarding overweight and obesity published by the National Institutes of Health, weight loss (and subsequent BMI reduction) is recommended to decrease blood

¹ From the University of Connecticut School of Pharmacy, Storrs, CT (OJP, WLB, LJM, ML, and CIC); the Department of Drug Information at Hartford Hospital, Hartford, CT (OJP and WLB); and the Cleveland Clinic, Cleveland, OH (AT).

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³ Address correspondence to CI Coleman, University of Connecticut School of Pharmacy, Pharmacoeconomics and Outcomes Studies Group, Hartford Hospital, 80 Seymour Street, Hartford, CT 06102-5037. E-mail: ccolema@harthosp.org.

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weight, waist circumference (WC), and waist-to-hip ratio (WHR).

METHODS

A systematic literature search was conducted through April 2009 in the following databases: MEDLINE (beginning 1950) (<http://www.pubmed.gov>), EMBASE (beginning 1990) (<http://www.embase.com>), Cochrane CENTRAL (indexed April 2009) (http://mrw.interscience.wiley.com/cochrane/cochrane_clcentral_articles_fs.html), and the Natural Medicines Comprehensive Database (<http://www.naturaldatabase.com/>). A search strategy was performed combining the Medical Subject Headings and the following text keywords: tea, green tea, green tea extract, catechin, EGCG, tea polyphenols, theaflavin, or *Camelia sinensis* with BMI, body weight, WC, waist-to-hip ratio, metabolic syndrome, weight loss, obesity, or overweight. No language restrictions were imposed and duplicate citations were removed. In addition, a manual search of references from primary or review articles was performed to identify additional relevant trials.

Trials were included in the analysis if they were randomized and evaluated the use of GTCs with or without caffeine and reported data on at least one of the following endpoints: 1) BMI, 2) body weight, 3) WC, or 4) WHR. Both parallel and crossover trials were eligible for inclusion, but ultimately no eligible crossover trials were identified. In trials for which there was more than one published report on the same population of patients, the data were accounted for only once but were referenced multiple times as necessary. For one study (26), for which insufficient data for a meta-analysis were provided, the author was contacted via E-mail with a request to provide additional data, to which the author responded with usable body weight data. Three investigators (OJP, LJM, and ML) reviewed potentially relevant articles independently and abstracted the necessary data with differences resolved through discussion.

Validity assessment was performed by 2 investigators (LJM and ML) using the American Dietetic Association Research Design and Implementation Checklist for primary research (29). This checklist includes 10 validity questions covering the following domains: a clear statement of the research question, bias-free subject selection, comparable groups, description of withdrawal handling, blinding, detailed description of protocol, clear definition of outcomes, appropriate statistical analysis, conclusions supported by data, and unlikely bias due to sponsorship or funding. Each of the 10 questions has a series of subquestions that aid in answering the overall question as either yes, no, or unclear. The 4 questions pertaining to bias-free subject selection, comparable groups, detailed description of protocol, and clear definition of outcomes received the most consideration when evaluating the overall study quality. The study was rated as positive if the 4 major criteria were met along with ≥ 1 other "yes," neutral if the 4 major criteria were not all "yes," and minus if most (≥ 6) questions were answered as "no."

To account for the possible confounding effect of caffeine on our results, we conducted 3 separate analyses. The first analysis evaluated trials that studied GTCs with caffeine compared with a caffeine-matched control, the second evaluated GTCs with caffeine compared with a caffeine-free control, and the third evaluated caffeine-free GTCs compared with a caffeine-free control. For each analysis, the mean change in BMI, body weight,

WC, and WHR from baseline were treated as continuous variables, and the weighted mean differences (WMDs) were calculated as the differences between the mean in the GTC and control groups. A DerSimonian and Laird random-effects model (a variation on the inverse variance method, which incorporates an assumption that the different studies are estimating different, yet related, treatment effects) was used to calculate the WMD with accompanying 95% CIs (30). Net changes in each of these study variables were calculated as the difference (catechin minus control) in the changes (baseline minus follow-up) in these mean values (also referred to as the change score). In instances in which variances for net changes were not reported directly, they were calculated from confidence intervals, *P* values, or individual variances for catechin and control groups. For trials in which variance for paired differences were reported separately for each group, we calculated a pooled variance for net change using standard methods. When the variance for paired differences was not reported, we calculated it from variances at baseline and at the end of follow-up. As suggested by Follmann et al (31), we assumed a correlation coefficient of 0.5 between initial and final values. For one study (23) in which the medians and interquartile ranges were reported, values were assumed to approximate means and 95% CIs (32). The statistical analysis was performed by using StatsDirect software (version 2.4.6, 2008; StatsDirect Ltd, Cheshire, United Kingdom). A *P* value < 0.05 was considered statistically significant for all analyses. Statistical heterogeneity was assessed by using the I^2 statistic, where values of 25%, 50%, and 75% were considered to have low, medium, and high statistical heterogeneity, respectively. Visual inspection of funnel plots and Egger's weighted regression statistics were used to determine the presence of publication bias. For analyses in which significant publication bias was detected, trim-and-fill analyses were conducted by using MIX for Meta-Analysis software (version 1.7, 2008) (33, 34) to assess its potential effect on our results.

RESULTS

Study characteristics

Of the 341 nonduplicate citations retrieved through the search strategy, 46 full-text articles were identified for detailed evaluation (**Figure 1**). Through a manual reference search of primary and review articles, 8 additional articles were retrieved for detailed evaluation. From the overall pool of full-text articles, 25 did not report relevant outcomes, 9 were not randomized controlled trials, 2 did not evaluate GTCs, and 2 repeated data from another study (35, 36). Three studies reported anthropometric outcomes (37–39) but were considered nonrelevant because both investigated weight maintenance subsequent to a low-calorie diet and exercise regimen rather than weight loss resulting from GTCs.

A total of 15 trials ($n = 1243$) met the inclusion criteria (**Table 1**). Of the 15 trials included, 7 trials ($n = 600$) evaluated GTCs with caffeine compared with a caffeine-matched control (14–20), 6 trials ($n = 524$) evaluated GTCs with caffeine compared with a caffeine-free control (21–26), and 2 trials ($n = 119$) evaluated caffeine-free GTCs compared with a caffeine-free control (27, 28). Patients were followed for 8 to 24 wk (median: 12 wk). Treatment groups received GTCs [dose range: 576–714



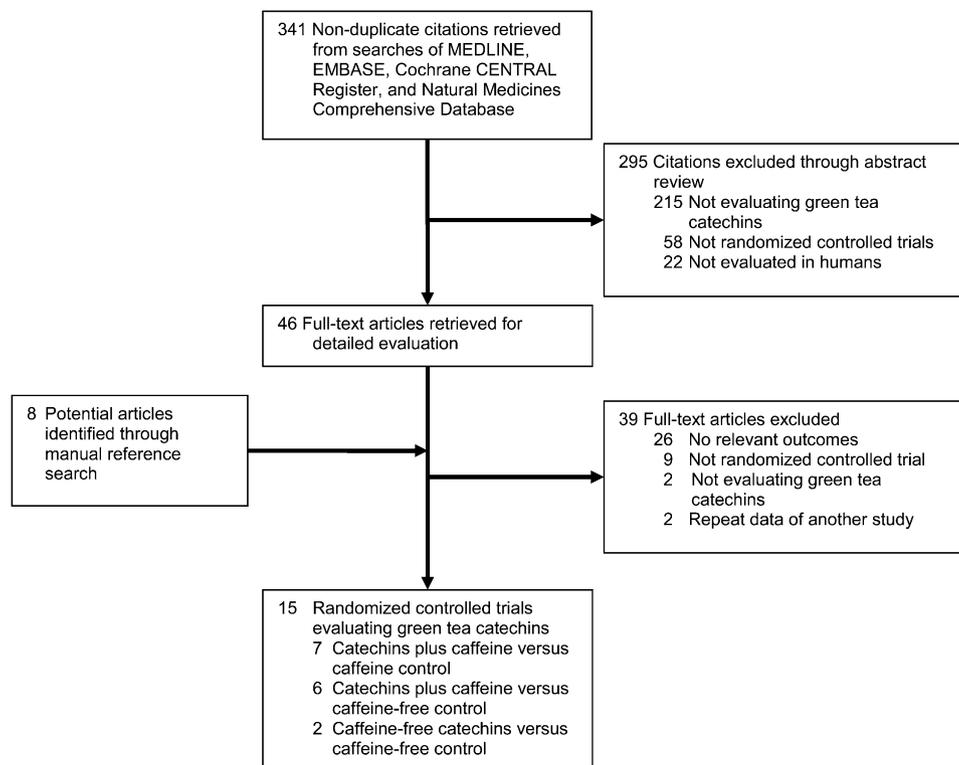


FIGURE 1. QUOROM (Quality of Reporting of Meta-analyses) flow diagram of study identification, inclusion, and exclusion of randomized controlled trials that evaluated the effect of green tea on anthropometric variables.

(median: 588) mg/d in the GTCs with caffeine compared with caffeine-matched control group trials; 141–1207 (median: 474) mg/d in the GTCs with caffeine compared with caffeine-free control group trials; and 282–548 (median: 415) mg/d in the caffeine-free trials] in various dosage forms, such as green tea extract capsules or green tea beverages. Four trials (14, 16, 17, 19) limited additional tea or catechin-rich food consumption other than study materials. Additional caffeine intake was regulated in 4 studies, with caffeine being restricted to no more than 2 or 3 beverages per day (14, 15), being completely prohibited (23), or requiring a standardized amount in both intervention and control groups (24). Two trials (15, 28) required concurrent exercise for both intervention and control groups. Results of the quality rating of trials are also presented in Table 1.

Quantitative data synthesis

On meta-analysis of studies evaluating GTCs with caffeine compared with a caffeine-matched control, the GTC group showed statistically significant reductions in BMI, body weight, and WC, with no statistically significant effect on WHR (**Figure 2**). Statistical heterogeneity was not found for BMI or body weight ($I^2 = 0\%$ for both), but a moderate degree of heterogeneity was present for WC ($I^2 = 52\%$) and WHR ($I^2 = 27\%$) analyses. Review of funnel plots and the Egger's weighted regression statistic P value suggested potential publication bias for BMI and body weight ($P < 0.06$) but a low likelihood for WC and WHR ($P > 0.55$). Trim-and-fill analyses for both BMI and body weight imputed 4 trials, with a result of -0.58 (95% CI: $-0.69, -0.46$) and -1.54 kg (95% CI: $-1.83, -1.26$), respectively (**Figure 3**).

For the analysis of studies evaluating GTCs with caffeine compared with a caffeine-free control, the GTC group showed statistically significant reductions in body weight, but no effect on BMI, WC, or WHR was observed. Statistical heterogeneity was not detected for any of the endpoints ($I^2 = 0\%$ for all). There was a low potential for presence of publication bias for all endpoints, as assessed by funnel plots and Egger's weighted regression statistic P value ($P > 0.68$).

Meta-analysis of studies evaluating GTC without caffeine compared with a caffeine-free control showed no statistical significance in any of the endpoints. Because of the small number of studies in this analysis, statistical heterogeneity and publication bias were not formally assessed.

DISCUSSION

Epidemiologic evidence has shown that habitual tea consumption of an average 434 mL/d for 10 y is associated with a lower percentage body fat and WC than no tea drinking (40). Of the tea drinkers, most (>90%) drank green tea, initially suggesting that GTCs have a role in weight loss (40). Weight reduction due to GTCs may result from increased energy expenditure and fat oxidation. In healthy men supplemented with green tea extract containing 270 mg EGCG and 150 mg caffeine, energy expenditure increased significantly by 4% compared with caffeine alone, and fat oxidation was 41% for green tea compared with 33% for caffeine alone ($P < 0.01$ for both) (8).

BMI, body weight, WC, and WHR were chosen for this analysis because they are considered important diagnostic indicators for overweight and obesity as well as independent risk factors for cardiovascular disease and diabetes (1). Statistical

TABLE 1
Characteristics of included randomized controlled trials of green tea catechins¹

Total sample size	Study design	ADA quality rating	Population	Baseline characteristics (I, C)		Follow-up wk	Tea group	Control group	Catechin components mg	Concurrent lifestyle modifications
				I	C					
Green tea catechins with caffeine compared with caffeine-matched control										
Frank et al, 2009 (14), n = 33	Double-blinded, parallel	+	Healthy men, age 18–55 y, BMI 22–32	BMI: 26.7, 25.4	3	Aqueous GTE capsule (714 mg catechins), 114 mg caffeine	Placebo (maltodextrin) capsules with 114 mg caffeine	EGC: 282; EGCG: 150; ECG:84; GC: 54; GCG: 48; EC: 30; CG: 18; C: 6	Limit daily tea and coffee consumption to ≤3 cups (711 mL) but maintain normal diet and exercise	
Maki et al, 2009 (15), n = 129	Double-blinded, parallel	+	Age 21–65 y, WC ≥90/87 (men/women), total cholesterol ≥5.2 mmol/L	BMI: 32.2, 32.2; WT: 95.1, 95.1; WC: 108.2, 108.9	12	500 mL green tea beverage (625 mg catechins), 39 mg caffeine	Placebo beverage containing 0 mg catechins, 39 mg caffeine, same number of calories	GC: 51.8; GC: 207.5; C: 19.2; EC: 53.9; EGCG: 214.4; GCG: 15.4; ECG: 56.5; CG: 6	Limit to ≤2 caffeinated beverages per day (excluding study beverage); normal diet; ≥180 min exercise weekly, including 3 supervised exercise sessions per week	
Nagao et al, 2009 (16), n = 43	Double-blinded, parallel	+	T2DM (no insulin therapy, stable medication and diet)	BMI: 25.6, 24.0; WT: 61.8, 60.0; WC: 89.8, 86.5; WHR: 0.93, 0.91	12	340 mL green tea beverage (583 mg catechins), 70 mg caffeine	340 mL green tea beverage containing 96 mg catechins and 70 mg caffeine	Enriched tea: C: 42.8; CG: 40.1; GC: 127.5; GCG: 139.7; EC: 32.3; ECG: 30.9; EGCG: 69.4; EGCG: 100.3 Control tea: C: 6.1; CG: 4.4; GC: 23.8; GCG: 24.1; EC: 4.8; ECG: 5.1; EGC: 11.2; EGCG: 16.7	Normal diet; no catechin-rich foods that might change carbohydrate or lipid metabolism	
Matsuyama et al, 2008 (17), n = 40	Double-blinded, parallel	+	Children aged 6–16 y, BMI ≥28 or diagnosis of obesity	BMI: 27.2, 27.4; WT: 65.5, 65.4; WC: 89.2, 88.9; WHR: 0.95, 0.94	24	340 mL green tea beverage (576 mg catechins), 80 mg caffeine	340 mL green tea beverage containing 75 mg catechins, 78 mg caffeine	Enriched tea: C: 39.8; CG: 36.7; GC: 128.9; GCG: 135.7; EC: 29.2; ECG: 32; EGCG: 71.4; EGCG: 102.3 Control tea: C: 5.8; CG: 3.7; GC: 20.4; GCG: 17.3; EC: 4.4; ECG: 3.7; EGC: 7.8; EGCG: 11.6	No excess lipids, sugars, or caffeine; no catechin-rich foods; no “foods that reduce excess adiposity;” maintain usual exercise	

(Continued)

TABLE 1 (Continued)

Total sample size	Study design	ADA quality rating	Population	Baseline characteristics (I, C)	Follow-up wk	Tea group	Control group	Catechin components mg	Concurrent lifestyle modifications
Nagao et al, 2007 (18), n = 240	Double-blinded, parallel	+	Age 25–55 y, BMI 24–30, and/or WC 80–94	BMI: 26.9, 26.7; WT: 73.3, 72.1; WC: 87.2, 86.5; WHR ² : 0.89, 0.89	12	340 mL green tea beverage (583 mg catechins), 70 mg caffeine	340 mL green tea beverage containing 96 mg catechins and 70 mg caffeine	Enriched tea: C: 42.8; CG: 40.1; GC: 127.5; GCG: 139.7; EC: 32.3; ECG: 30.9; EGC: 69.4; EGCG: 100.3 Control tea: C: 6.1; CG: 4.4; GC: 23.8; GCG: 24.1; EC: 4.8; ECG: 5.1; EGC: 11.2; EGCG: 16.7	Normal diet; no medications or supplements that change carbohydrate or lipid metabolism; no restrictions on tea or coffee intake
Nagao et al, 2005 (19), n = 35	Double-blinded, parallel	Ø	Healthy men, normal to overweight	BMI: 24.9, 25.0; WT: 73.9, 73.8; WC: 87.9, 87.8; WHR ² : 0.90, 0.91	12	340 mL GTE/oolong tea beverage (690 mg catechins), 75 mg caffeine	340 mL oolong tea beverage containing 22 mg catechins, 78 mg caffeine	Enriched tea: C: 45.9; EC: 44.5; CG: 32.6; ECG: 51.3; GC: 137.4; EGC: 102.7; GCG: 139.4; EGCG: 136 Control tea: C: 1.7; EC: 1; CG: 0.7; ECG: 0; GC: 5.8; EGC: 3.7; GCG: 5.8; EGCG: 3.1	2 planned meals per day at cafeteria; no tea or other foods high in catechins; <27.5 mL alcohol/d
Tsuchida et al, 2002 (20), n = 80	Double-blinded, parallel	Ø	Men and postmenopausal women, BMI 24–30	BMI: 26.4, 26.1; WT: 70.7, 70.4; WC: 85.2, 86.2; WHR: 0.87, 0.89	12	340 mL green tea beverage (588 mg catechins), 83 mg caffeine	340 mL green tea beverage with 126 mg catechins, 81 mg caffeine	Enriched tea: C: 39.4; CG: 34.7; GC: 134.3; GCG: 126.5; EC: 27.5; ECG: 30.6; EGC: 79.6; EGCG: 114.9 Control tea: C: 7.8; CG: 5.8; GC: 32; GCG: 27.2; EC: 4.8; ECG: 5.4; EGC: 18.7; EGCG: 25.2	Normal diet and exercise; no additional foods that may affect energy or metabolism; patients recorded diet and exercise 3 times/wk
Green tea catechins with caffeine compared with caffeine-free control									
Auvichayapat et al, 2008 (21), n = 60	Double-blinded, parallel	+	Men and postmenopausal women aged 40–60 y, BMI >25	BMI: 27.42, 28; WT: 69.3, 71.9; WC: 88.06, 92.23; WHR: 0.86, 0.86	12	750 mg GTE capsules (141 mg catechins), 87 mg caffeine	Placebo (cellulose) capsules	EGCG: 100.7; ECG: 27.8; C: 12.3	8374 kcal/d of hospital-prepared meals

(Continued)

TABLE 1 (Continued)

Total sample size	Study design	ADA quality rating	Population	Baseline characteristics (I, C)		Follow-up wk	Tea group	Control group	Catechin components mg	Concurrent lifestyle modifications
				I	C					
Hsu et al, 2008 (22), n = 78	Double-blinded, parallel	+	Females aged 16–60 y, BMI >27	BMI: 31.2, 30.5; WT: 78.5, 76.3; WC: 94.7, 93.0; WHR ² : 0.86, 0.85	12	1200 mg GTE capsules (491 mg catechins), 27.3 mg caffeine	Placebo (cellulose) capsules	GC: 61.6; EGC: 36.9; C: 8.3; EC: 70.3; EGCG: 377.1; GCG: 27.5; ECG: 31.8	Maintain normal diet, no other antiobesity treatment	
Chan et al, 2006 (23), n = 34	Single-blinded, parallel	+	Women aged 25–40 y with PCOS; BMI >28	BMI ¹ : 30.5, 29.7; WT ³ : 76.0, 76.6; WHR ² : 0.85, 0.86	12	Green tea capsules (661 mg catechins), 152 mg caffeine	Placebo (not specified) capsules	EGCG: 538.4; EGC: 50.6; ECG: 38.3; EC: 32	No additional caffeine; nutritional consults	
Diepvens et al, 2005 (24), n = 46	Double-blinded, parallel	+	Women aged 19–57 y, BMI 25–31, moderate caffeine use	BMI: 27.7, 27.6; WT: 76.4, 76.3; WC: 85.6, 84.0; WHR: 0.81, 0.79	12.4	GTE capsules (1207 mg catechins), 237 mg caffeine	Placebo (maltodextrin) capsules	EC: 126, EGC: 240.3, ECG: 212.4, EGCG: 595.8, C: 31.5	3 cups coffee/d, no additional caffeine, Slim Fast (Unilever, Englewood Cliffs, NJ) diet	
Fukino et al, 2005 (25, 36), n = 66	Open-label, parallel	Ø	Patients with diabetes or patients with prediabetes	BMI: 25.5, 25.9; WT: 68.2, 69.8	8	GTE powder packets (456 mg catechins), 102 mg caffeine	No intervention	NR	Both groups allowed to drink green tea as normal	
Maron et al, 2003 (26), n = 240	Double-blinded, parallel	+	Patients with mild-to-moderate hypercholesterolemia	BMI: 24.0, 24.4; WT ⁴ : 65.49, 66.09	12	Theaflavin-enriched GTE (150 mg catechins), caffeine content NR	Placebo (inert ingredients)	NR	Habitual, traditional Chinese diet, including customary intake of tea	
Caffeine-free green tea catechins compared with caffeine-free control										
Takeshita et al, 2008 (27), n = 81	Double-blinded, parallel	Ø	Healthy males, BMI ≥ 25	BMI: 27.8, 28; WT: 82.3, 82.8; WC: 93.0, 93.9; WHR ² : 0.91, 0.92	12	“Sports drink” containing decaffeinated GTE (548 mg catechins)	“Sports drink” containing no catechins or caffeine	C: 17.5; EC: 50.5; CG: 0, EGC: 18.5; GC: 39.5; EGCG: 282; GCG: 132.5	Maintain habitual lifestyle; no additional tea; coffee limited to 200 mL/d	
Hill et al, 2007 (28), n = 38	Double-blinded, parallel	+	Postmenopausal women aged 45–70 y, BMI 25–39.9	BMI: 30.65, 31.39; WT: 79.92, 81.05; WC: 102.4, 104.7; WHR: 0.909, 0.92	12	Teavigo capsules (282 mg EGCG)	Placebo (lactose) capsules	EGCG: 282	Maintain normal diet; run/walk 45 min 3 times/wk at heart rate of 75% age-predicted maximum	

¹ BMIs are provided in kg/m². ADA, American Dietetic Association; Ø, neutral; +, positive; I, intervention; C, control; WT, weight (kg); WC, waist circumference (cm); WHR, waist-to-hip ratio; GTE, green tea extract; EGCG, epigallocatechin gallate; ECG, epicatechin gallate; EGC, epigallocatechin; EC, epicatechin; CG, gallic acid; GC, gallic acid; GCG, gallic acid; PCOS, polycystic ovarian syndrome; T2DM, type 2 diabetes mellitus; NR, not reported.

² WHR not provided in the publication; value calculated from baseline WC and hip circumference.

³ Median value.

⁴ Unpublished data obtained from personal communication with the author (D Maron, 2009).

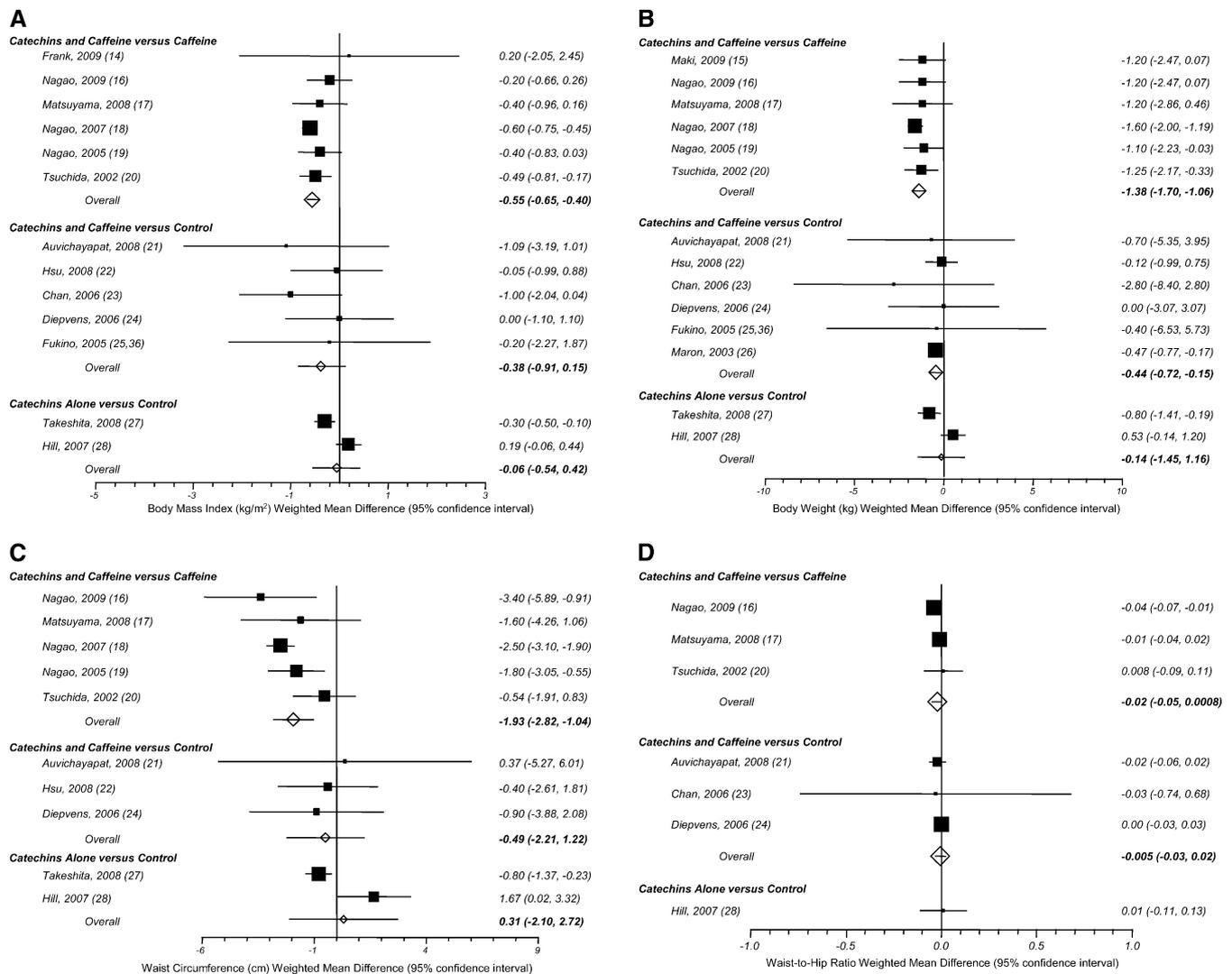


FIGURE 2. Forest plots depicting the effect of green tea on BMI (A), weight (B), waist circumference (C), and waist-to-hip ratio (D). The squares represent individual studies, and the size of the squares represents the weight given to each study in the meta-analysis. Error bars represent 95% CIs. The diamonds represent the pooled results. The solid vertical line extending upward from 0 is the null value.

pooling of data from the 7 trials in the analysis of GTCs with caffeine compared with a caffeine-matched control showed that ingesting GTCs at a dose ranging from 583 to 714 mg/d over a median of 12 wk had a statistically significant benefit on BMI, body weight, and WC, with no effect on WHR. On pooling the 6 trials in the analysis of GTCs with caffeine compared with caffeine-free control, GTC ingestion significantly reduced body weight, with no effect on BMI, WC, or WHR. Of the 2 caffeine-free trials, pooling the 2 trials showed no statistically significant effect.

The inclusion of certain study characteristics of the trials in the analysis may have contributed to clinical and statistical heterogeneity and was a limitation of this meta-analysis. The populations studied varied between children, healthy adults, and adults with comorbidities such as overweight or obesity, hyperlipidemia, or diabetes mellitus. Unfortunately, the wide variety of populations studied made it difficult to determine the population that would most benefit from GTCs. The wide range of GTC doses evaluated may also have contributed to the heterogeneous results; however, a previous trial showed no relation

between dose and BMI ($P = 0.89$) (25). Because of the small number of studies in each analysis, we could not assess a dose-response relation through meta-regression. In addition, GTC absorption increased in the fasted state (41), so variations in GTC ingestion between the trials with relation to food may also have contributed to the heterogeneous results. In our meta-analysis, some trials stated that GTCs could be consumed at any time of the day (15, 17, 18), whereas others specified either before (14, 28), during (19, 24), or after (21, 22) meals. Another consideration was the variation in catechin composition among the trials. Although we were unable to assess the effect of catechin composition on anthropometric outcomes, much of GTCs' benefits have been attributed to EGCG specifically (7, 10). Interestingly, the trial that evaluated EGCG alone (28) showed nonsignificant increases in BMI and body weight when compared with placebo. This suggests that the effect of GTCs might be due to the combination, rather than to any single catechin, and merits further investigation. The presence or absence of blinding, as well as the overall quality rating of trials, may have also contributed to the heterogeneity of the results. However, the



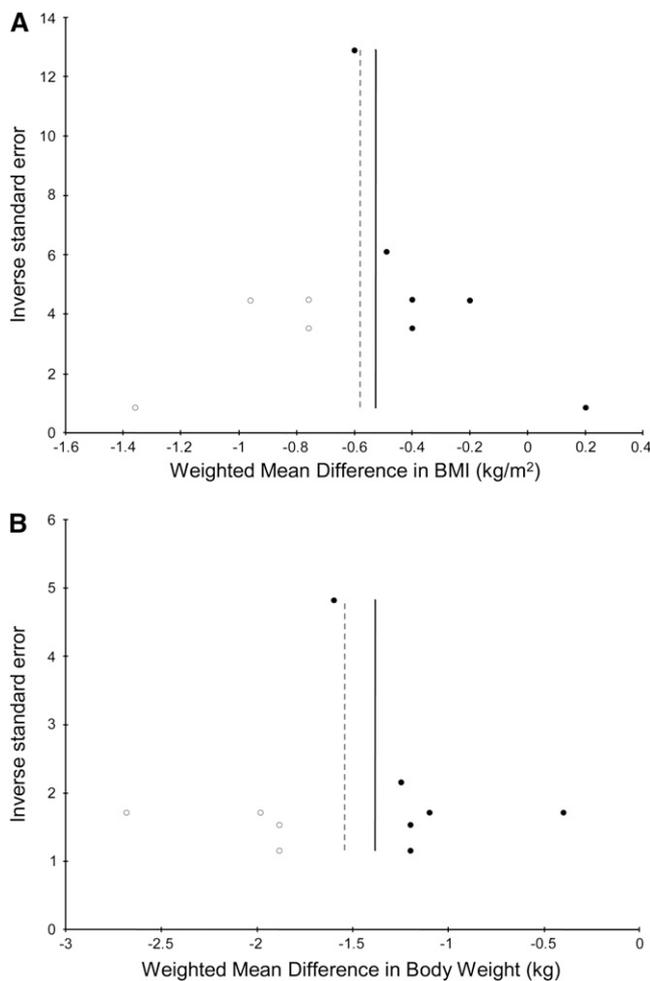


FIGURE 3. Trim-and-fill funnel plot. The solid circles represent actual identified studies, and the open circles represent imputed studies from a trim-and-fill analysis. The solid vertical lines represent the effect of green tea catechins on BMI (A) and body weight (B) in the initial analysis, whereas the dotted vertical lines represent the effect when allowing for publication bias.

effects of these characteristics were not quantified via sensitivity analyses because of the limited number of trials available.

Because of the abovementioned heterogeneous nature of the included trials, we felt it inappropriate to pool all of the studies into one single analysis; therefore, the trials were analyzed as 3 separate pools of data, and we recommend that our results be interpreted as such. Although it may be tempting to cross compare the results of the 3 separate analyses, this comparison is inherently flawed. Such indirect comparisons of separate sets of trials composed of different populations provide weak evidence for concluding that any of the treatment regimens have greater benefit than another.

Our meta-analysis did not pool safety data because it was not reported in a standard manner; however, the trials reported that patients did not experience any major adverse events (16, 18, 22, 23). Case reports of GTC consumption have brought up concerns of hepatotoxicity, and the US Pharmacopoeia Dietary Supplements Information Expert Committee has proposed that all green tea extract products bear a label that suggests consumption together with food because of the possibility of severe liver problems (42). Of the trials that evaluated liver transaminases (14–16, 26, 28), only one reported elevations in the

GTC group (16); however, transaminase concentrations were elevated at baseline, which suggests potential bias in group allocation. To assess concerns of liver damage, a randomized controlled trial using high-dose GTCs (714 mg/d) was undertaken in healthy men (14). This trial found that over 3 wk of GTC intake, there were no elevations in liver transaminases or reports of liver dysfunction (14).

As with all meta-analyses, publication bias is a concern. For most endpoints evaluated, there was a low likelihood of publication bias, as assessed by funnel plot inspection and Egger's weighted regression *P* value. In the 2 cases in which there was a significant presence of publication bias, trim-and-fill analyses did not significantly alter the results, which suggests that publication bias did not significantly affect our results.

Despite the statistical significance achieved in some of the analyses, the changes observed are not likely clinically relevant. For example, for pharmacologic weight-loss products on the market, patients are considered to have failed treatment if they have not achieved a loss of 2 kg after 4 wk of therapy (1). In our meta-analysis, GTCs with caffeine only provided an average weight loss of >1 kg compared with a caffeine-matched control, and <0.5 kg compared with a caffeine-free control taken over a median of 12 wk. Furthermore, the observed reductions in WC, although statistically significant in some cases, were smaller than potential variations in measurement. Anthropometric measurements of WC made by trained professionals can vary by 1.5 to 2.1 cm between measurements (43). Therefore, reductions in WC of <2 cm cannot be ruled out to chance and should be interpreted with caution.

Future studies should be conducted to further understand the relation between GTC intake and changes in anthropometric measures, especially with regard to caffeine intake. In addition, future studies may be able to identify the target population for catechin use and determine the ideal dose.

In conclusion, on the basis of the currently available literature, ingestion of GTCs with caffeine may positively affect BMI, body weight, and WC. However, the magnitude of effect over a median of 12 wk is small and not likely clinically relevant. Current data from a small number of studies do not suggest that GTCs alone positively alter anthropometric measurements.

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