Received: 26 December 2019 | Revised: 3 March 2020 | Accepted: 22 March 2020

DOI: 10.1002/ptr.6697

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REVIEW

The effect of green tea supplementation on obesity: A systematic review and dose–response meta-analysis of randomized controlled trials

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The effects of green tea (GT) in obese subjects have been evaluated in different studies, but no consensus has been obtained due to the heterogeneity of the results. The dosage, the type of extract, and the duration of the intervention are the main contributors to the heterogeneity of the results. Therefore, the present systematic review and meta-analysis aimed to evaluate the efficacy and dose–response relationship of GT. Several databases were searched from inception to September 2019 to identify clinical trials that examined the influence of GT supplements on obesity indices in humans. Combined results using the random-effects model indicated that body weight (WMD: −1.78 kg, 95% CI: −2.80, −0.75, p = .001) and body mass index (BMI) (WMD: −0.65 kg/m^2, 95% CI: −1.04, −0.25, p = .001) did change significantly following GT administration. The reduction in waist circumference (WC) after GT consumption was significant in subjects in trials employing GT ≥800 mg/day (WMD: −2.06 cm) and with a treatment duration <12 weeks (WMD: −2.39 cm). Following the dose–response evaluation, GT intake did alter body weight, with a more important reduction when the GT dosage was <500 mg/day and the treatment duration was of 12 weeks. The results of present meta-analysis study support the use of GT for the improvement of obesity indices. Thus, we suggest that the use of GT can be combined with a balanced and healthy diet and regular physical exercise in the management of obese patients.

KEYWORDS
body mass index, dose–response, green tea, meta-analysis, obesity, weight

1 | INTRODUCTION

Obesity is an important public health problem and a major contributor to the health burden globally (OECD, 2019). The presence of obesity significantly increases one's risk of non-communicable diseases, for example, diabetes mellitus, cardiovascular disease and cancer (Gaman, Epingeac, & Gaman, 2019; Goossens, 2017). According to the World Health Organization (WHO), obesity is characterized by an abnormal or excessive fat accumulation and is diagnosed clinically based on values of the body mass index (BMI) (kg/m^2) > 30 kg/m^2 (WHO, 2018). Since 1975, the prevalence of obesity has nearly tripled, with almost one-third of the world population being obese (Forse & Kissee, 2020). In 2016, 39% of the adults aged >18 years were reportedly overweight and 13% were obese (WHO, 2018).

Obesity is a multifactorial chronic disease whose development results from an imbalance between the energy intake and expenditure

(Chrissini, Sifaki-Pistolla, Tzanakis, & Tsiligianni, 2019). In consequence, dietary and lifestyle changes are the main factors recommended in the treatment of obesity (Bluher, 2019; Vincek, White, & Feinn, 2018). The Political Declaration of the High Level Meeting of the United Nations General Assembly on the Prevention and Control of Noncommunicable Diseases supports the "WHO Global Strategy on Diet, Physical Activity and Health", in which physical exercise and healthy eating are promoted (WHO, 2018). Although the importance of diet and physical activity is well-known, it has become widespread that supportive herbal therapies may become a part of the treatment of obesity in upcoming years (Yinji Liang, Huang, & Xu, 2019). Among these, green tea (GT) supplementation has been intensely researched in the last decade (Sabu, Chacko, Kuttan, & Nishigaki, 2010).

GT is one of the major types of tea (*Camelia sinensis*) and belongs to the non-fermented tea class (Gordona & David, 2010). Among all of the tea types, the most significant effects on human health have been observed with the consumption of GT (Sabu et al., 2010). GT has hailed importance due to its health benefits on obesity (Chen, Liu, Chiu, & Hsu, 2016; Janssens, Hursel, & Westerterp-Plantenga, 2016), microbiota (Zhang et al., 2018), cancer (Liu et al., 2016; Miyata, Shida, Hakariya, & Sakai, 2019; Tofolean et al., 2016), blood pressure (Li et al., 2014; Li et al., 2015), osteoarthritis (Hashempur, Sadrneshin, Mosavat, & Ashraf, 2018), hypercholesterolemia, hyperglycemia (Ahmad et al., 2015), and neurodegenerative diseases (Pervin et al., 2018). The health benefits of GT are probably linked to its antioxidant properties, which are related to the high content in polyphenols, mainly catechins and flavonols, of GT (Li et al., 2015).

The positive effects of GT on obesity have been discussed in several studies (Ahmad et al., 2015; Chen et al., 2016; Heber et al., 2014). Human studies reported that GT has anti-obesity effects by ghrelin secretion inhibition, increase in adiponectin levels, substrate oxidation, appetite control, decrease in nutrient absorption, and inhibiting of adipogenesis (Chen et al., 2016; Huang et al., 2014). Animal studies have concluded that the possible anti-obesity mechanisms of GT are based on the activation of the brown adipose tissue, reduction in food intake, inhibition of the absorption of fatty acids, alteration of the microbiota, and increased hepatic adenosine monophosphate-activated protein kinase (AMPK) phosphorylation (Heber et al., 2014; Henning et al., 2018; Neyrinck et al., 2017; Seo et al., 2015; Xu et al., 2015). However, several clinical trials have reported no association between obesity indices and GT supplementation (Janssens, Hursel, & Westerterp-Plantenga,-2015; Quinhoneiro et al., 2018). Based on data regarding adverse events in humans, Hu, Webster, Cao, and Shao (2018) reported an observed safe level (OSL) of 704 mg epigallocatechin-gallate (EGCG)/day in tea preparations (Hu et al., 2018).

The effects of GT supplementation have been evaluated in different studies, but no consensus has been obtained due to the heterogeneity of the results. Study design, dosage, type of extract, duration, and sample selection are the main contributors to the aforementioned heterogeneity. Therefore, the present systematic review and meta-analysis aimed to evaluate the efficacy and dose–response relationship of GT supplementation on obesity indices in humans.

2 | MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline was applied in writing the current Systematic Review and Dose–Response Meta-Analysis (Moher, Liberati, Tetzlaff, Altman,, & Group, 2009).

2.1 | Search strategy

The literature search was executed in four databases including PubMed, Web of Sciences, Embase, Scopus, and Google Scholar from inception to September 2019 to identify clinical trials that examined the influence of GT supplements on obesity indices. The following combinations of Medical Subject Headings (MeSH) and non-MeSH terms were used: ("green tea" OR "green tea extract" OR "green tea extract AR25" OR catechin OR "catechins" OR "EGCG" OR "*Camellia sinensis*" OR "tea polyphenols" OR "Catechinic Acid" OR "epigallocatechin gallate") AND ("Obesity" OR "Weight Loss" OR "weight reduce" OR "weight decrease" OR "Body Weight" OR "Obesity, Abdominal" OR "Body Mass Index" OR "BMI" OR "Waist Circumference" OR obes* OR "central obesity " OR "overweight" OR "adipose tissue" OR "fat mass" OR "adiposity" OR " weight change"). Furthermore, we implemented a search of all the reference lists of the qualified articles and related reviews in order to avoid neglecting any relevant publications.

2.2 | Eligibility criteria

We considered trials that were (a) randomized placebo-controlled trials (crossover or parallel design); (b) studies that were executed on adults>18 years of age; (c) publications that reported sufficient data on baseline and post-intervention body weight (BW) or/and body mass index (BMI) or/and weight circumference (WC) in both GT and control groups. We excluded articles if they (a) involved children, pregnant women or animals; (b) were not placebo-controlled studies; (c) did not comprise enough data on the outcomes in GT or control groups; (d) or explored the effects of GT in combination with other substances; (e) studies that did not use whole GT in intervention. Grey literature, for example, dissertations, conference papers and patents, was excluded as well.

2.3 | Data extraction

Two reviewers independently extracted all trial data; the third researcher resolved disagreements when necessary. Data were extracted into separate Excel spreadsheets and then imported into STATA where they were compared for mean differences. Once all inconsistencies were resolved, a single dataset was created. For each eligible study, we extracted: author's first name, study design, year of publication, mean and standard deviations of performance for the GT

and placebo groups, intervention duration, mean age, sample size of each group, gender, GT dose in mg/kg, and type of study population.

2.4 | Quality assessment

Methodological quality and risk of bias of eligible arms were assessed by combining the Cochrane scoring system (Moher et al., 2009). This tool measures probable causes of bias in randomized trials, which include: (a) random sequence generation, (b) concealment of allocation to conditions, (c) inhibition of awareness of the allocated intervention, (d) blinding of outcome assessment, (e) incomplete outcome data, (f) selective reporting, and other biases. Three marks of yes, no, and unclear could be assigned to each abovementioned point, which are stated as high risk, low risk, and unknown risk, respectively (Supplementary Table 1).

2.5 | Data synthesis and statistical analysis

Mean modification and *SD* of the outcome measures were applied to assess the mean differences between the GT group and the control group at follow-up. If the information was described in a diverse format, standard calculations were accomplished to derive the mean and *SD* (Higgins, 2011; Hozo, Djulbegovic, & Hozo, 2005). For instance, if the *SD* of the mean change was not provided in the studies, we obtained it using the next formula: SD_{change} = square root $[(SD_{baseline}^2 + SD_{end}^2) - (2 \times R \times SD_{baseline} \times SD_{end})]$. We calculated effect sizes using the random-effects model (using DerSimonian-Laird method), and results were derived across weighted mean difference (WMD) and 95% confidence interval (95% CI). Subgroup analysis was applied to explore possible sources of heterogeneity among the trials. The non-linear dose response potential effects of GT dosage (mg/day) and length of intervention (weeks) were evaluated by fractional polynomial modeling. We performed the sensitivity analysis by the one-study omission (leave-one-out) approach, to determine the influence of each study on the combined effect size. Publication bias was calculated by means of visual interpretation of funnel plots and Egger's test (Egger, Smith, Schneider, & Minder, 1997). If any publication bias was noticed, it was confirmed via the "trim and fill" test (Palmer, Peters, Sutton, & Moreno, 2008). All statistical analyses were executed using Stata software (Stata Corp. College Station, TX).

3 | RESULTS

3.1 | Study selection

The initial database search in PubMed/MEDLINE, EMBASE, Web of Science, Scopus, and Google Scholar returned 10,112 articles; after the duplicates were removed, 4,807 articles remained. After screening based on the title and abstract, 451 articles were selected for full-text review. During the full-text review stage, 426 articles were excluded based on the following reasons: non-clinical trials, whole GT was not employed in the intervention (the studies employed decaffeinated green tea extract or green tea catechin), animal study, GT was employed in combination with other components, the studies were performed in children, insufficient data, lack of appropriate control groups, duplicate datasets. Finally, 25 articles with 26 arms were included in this meta-analysis (Afzalpour, Ghasemi, & Zarban, 2017; Al-Naggar, Osman, & Abdulghani, 2013; Amozadeh, Shabani, & Nazari, 2018; Auvichayapat et al., 2008; Basu et al., 2011; Bogdanski et al., 2012; Cardoso, Salgado, Cesar Mde, & Donado-Pestana, 2013; Chan et al., 2006; Di Pierro, Menghi, Barreca, Lucarelli, & Calandrelli, 2009; Diepvens, Kovacs, Nijs, Vogels, & Westerterp-Plantenga, 2005; Hovanloo, Fallah Huseini, Hedayati, & Teimourian, 2016; Hsu et al., 2008; Hsu et al., 2011; Hussain, Habib Ur, & Akhtar, 2017; Janssens et al., 2016; Kovacs, Lejeune, Nijs, & Westerterp-Plantenga, 2004; Mombaini, Jafarirad, Husain, Haghighizadeh, & Padfar, 2017; Nabi et al., 2018; Rostamian & Bijeh, 2017; Soeizi et al., 2017; Suliburska et al., 2012; Tabatabaee et al., 2017; Toolsee et al., 2013; Venkatakrishnan et al., 2018; Vieira Senger, Schwanke, Gomes, & Valle Gottlieb, 2012) (Supplemental Figure 1).

3.2 | Characteristics of the included studies

The features of the selected studies are provided in Table 1. These studies were published between 2004 and 2018. Eligible studies were performed in: Taiwan (Hsu et al., 2008; Hsu et al., 2011; Venkatakrishnan et al., 2018), Iran (Afzalpour et al., 2017; Amozadeh et al., 2018; Hovanloo et al., 2016; Hussain et al., 2017; Mombaini et al., 2017; Nabi et al., 2018; Rostamian & Bijeh, 2017; Soeizi et al., 2017), Pakistan (Hussain et al., 2017), China (Chan et al., 2006), The Netherlands (Diepvens et al., 2005; Janssens, Penders, et al., 2016; Kovacs et al., 2004), Malaysia (Al-Naggar et al., 2013), the United States of America (Basu et al., 2011), Toolsee et al., 2013), Brazil (Cardoso et al., 2013; Vieira Senger et al., 2012), Poland (Bogdanski et al., 2012; Suliburska et al., 2012), Italy (Di Pierro et al., 2009), and Thailand (Auvichayapat et al., 2008). The follow-up period ranged from 2 weeks to 5 months. The daily recommended dose of GT varied between 99 and 20,000 mg. Of the selected studies, all were done on both sexes with the exception of 11 trials, which involved exclusively females (Afzalpour et al., 2017; Al-Naggar et al., 2013; Amozadeh et al., 2018; Cardoso et al., 2013; Chan et al., 2006; Diepvens et al., 2005; Hovanloo et al., 2016; Hsu et al., 2008; Mombaini et al., 2017; Rostamian & Bijeh, 2017; Toolsee et al., 2013). The studies involved a range of 18 to 104 participants. The participants included in these studies suffered from: overweight or obesity, hypercholesterolemia, fatty liver disease, postmenopause status, polycystic ovary syndrome, thalassemia major, prediabetes or type 2 diabetes mellitus (Afzalpour et al., 2017; Al-Naggar et al., 2013; Amozadeh et al., 2018; Auvichayapat et al., 2008; Basu et al., 2011; Bogdanski et al., 2012; Cardoso

TABLE 1 Characteristics of eligible studies

Author	Year	Country	Clinical trial design	Population	Sex	Sample size green tea/ placebo	Duration	Outcome	Green tea dosage (mg/day)
Amozade et al.	2018	Iran	Parallel	Overweight and obese females	Female	13/13	8 week	Weight, BMI, WC	99
Bahram Naderi Nabi et al.	2018	Iran	Parallel	Obese subjects	Both	41/43	12 week	Weight, BMI, WC	300
Kamesh Venkatakrishnan et al.	2018	Taiwan	Parallel	Subjects with hypercholesterolemia	Both	20/20	12 week	Weight	780
Mazhar Hussain et al.	2017	Pakistan	Parallel	Fatty liver disease patients	Both	40/40	12 week	Weight, BMI	1,000
Marjan Rostamian et al.	2017	Iran		Sedentary postmenopausal women	Female	12/12	2 week	BMI	
SeyedMohammadTabatabaee et al.	2017	Iran	Parallel	Patients with non-alcoholic fatty liver disease	Both	21/21	3 month	Weight, BMI	550
Esmat Mombaini et al.	2017	Iran	Parallel	Women with polycystic ovary syndrome	Female	22/22	45 days	Weight, BMI, WC	2000
Ehsan Soeizi et al.	2017	Iran	Parallel	Patients with thalassemia major	Both	26/26	8 week	Weight, BMI	450
Afzalpour et al.	2016	Iran	Parallel	Overweight women	Female	10/10	10 week	Weight, BMI	1,500
Hovanloo et al.	2016	Iran	Parallel	Elderly women	Female	18/18	5 month	Weight, BMI	1,500
Pilou LHR Janssens et al.	2015	The Netherlands	Parallel	Adults	Both	30/30	12 week	Weight, BMI	2,380
Redhwan Ahmed Al-Naggar et al.	2013	Malaysia	Parallel	Young obese female	Female	15/15	25 days	Weight, BMI, WC	1,500
NaushadAliToolsee et al.	2013	United States	Parallel	Prediabetics	Both	33/30	14 week	Weight, BMI	600
NaushadAliToolsee et al.	2013	United States	Parallel	Prediabetics	Female	32/28	14 week	Weight, BMI	600
Gabrielle Aparecida Cardoso et al.	2012	Brazil	Parallel	Overweight + obese women	Female	9/9	4 week	Weight, BMI, WC	20,000
Pawel Bogdanski et al.	2012	Poland	Parallel	Obese, hypertensive patients	Both	28/28	3 month	WC	379
Vieira Senger, A. E. et al.	2012	Brazil	Parallel	Elderly with metabolic syndrome	Both	24/24	60 days	Weight, BMI, WC	600
Chung-Hua Hsu et al.	2012	Taiwan	Parallel	Obese patients with type 2 diabetes	Both	35/33	16 week	BMI, WC	1,200
Arpita Basu et al.	2011	United States	Parallel	Obesity + metabolic syndrome	Both	13/12	8 week	Weight, WC	800
Joanna Suliburska et al.	2011	Poland	Parallel	Obese patients	Both	23/23	3 month	BMI, WC	379
Francesco Di Pierro et al.	2009	Italy	Parallel	Overweight subjects	Both	50/50	90 days	Weight	300
Auvichayapat et al.	2008	Thailand	Parallel	Obese subjects	Both	30/30	12 week	Weight, BMI, WC	750
Chung Hsu et al.	2008	Taiwan	Parallel	Obese women	Female	41/37	12 week	Weight, BMI, WC	1,200
Canrna C.W. Chan et al.	2006	China	Parallel	Obese patients with polycystic ovary syndrome	Female	18/16	3 month	Weight, BMI	1,770
K Diepvens et al.	2005	The Netherlands	Parallel	Overweight Females	Female	23/23	87 days	Weight, BMI	1,350
Eva M. R. Kovacs et al.	2004	The Netherlands	Parallel	Overweight and moderately obese subjects	Both	51/53	13 week	Weight, BMI, WC	677

Note: BMI, body mass index; WC, waist circumference.

et al., 2013; Chan et al., 2006; Di Pierro et al., 2009; Diepvens et al., 2005; Hovanloo et al., 2016; Hsu et al., 2008; Hsu et al., 2011; Hussain et al., 2017; Janssens, Penders, et al., 2016; Kovacs et al., 2004; Mombaini et al., 2017; Nabi et al., 2018; Rostamian & Bijeh, 2017; Soeizi et al., 2017; Suliburska et al., 2012; Tabatabaee et al., 2017; Toolsee et al., 2013; Venkatakrishnan et al., 2018; Vieira Senger et al., 2012). Most studies were rated as good quality across the Cochrane items. For some trials, the risk of bias derived from the "blinding of participants" item (Di Pierro et al., 2009; Toolsee et al., 2013) and from "the incomplete outcome data" item (Chan et al., 2006; Hsu et al., 2008; Mombaini et al., 2017; Nabi et al., 2018; Tabatabaee et al., 2017; Venkatakrishnan et al., 2018). The assessment of the risk of bias of the qualified trials is provided in Supplementary Table 1.

3.3 | Meta-analysis results

3.3.1 | Effect of GT supplementation on body weight (BW)

A total of 22 studies, including a number of 2,357 participants (case = 1,197, and control = 1,160) reported body weight as an outcome measure. Combined results from the random-effects model indicated that body weight did change significantly following GT administration (Weighted Mean Difference (WMD): −1.78 kg, 95% CI: −2.80, −0.75, p = .001) with no significant heterogeneity among the studies (I^2 = 19%, p = .203) (Figure 1). In the subgroup analysis, studies that were conducted on a baseline BMI ≥30 kg/m^2 revealed a greater reduction in body weight (WMD: −2.53 kg, 95% CI: −4.07, −0.99) than those performed on a baseline BMI of 25–29.9 kg/m^2 (WMD: −1.07 kg, 95% CI: −2.13, −0.01). In addition, based on the GT dosage, a significant reduction in body weight was found in trials that were performed with GT <800 mg/day (WMD: −1.87 kg, 95% CI: −3.25, −0.48) compared with those conducted with GT ≥800 mg/day (WMD: −1.32 kg, 95% CI: −2.33, −0.31). Moreover, based on the duration of the intervention (weeks), a significant reduction in body weight was found in trials that exceeded a duration of 12 weeks (WMD: −2.63 kg, 95% CI: −3.85, −1.42) versus studies lasting <12 weeks (WMD: −2.34 kg, 95% CI: −4.16, −0.52). All these findings are provided in Supplementary Table 2.

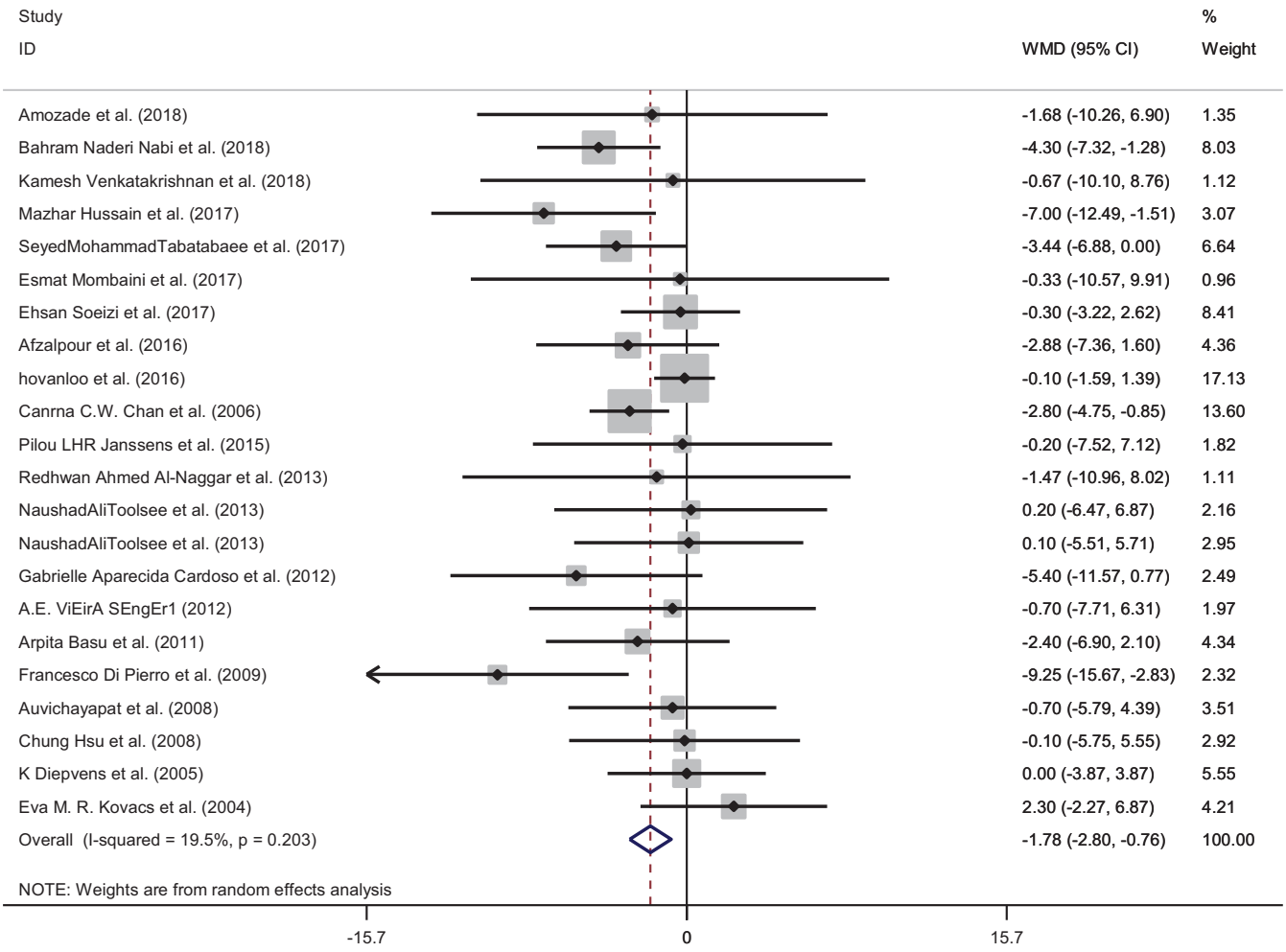

FIGURE 1 Forest plot of randomized controlled trials investigating the effects of green tea administration on body weight. WMD, weighted mean difference (WMD). 95% CI = 95% confidence interval [Colour figure can be viewed at wileyonlinelibrary.com]

3.3.2 | Effect of GT supplementation on body mass index (BMI)

In total, 22 studies including a total of 1,124 participants (case = 567 and control = 557) reported BMI as an outcome measure. Overall results from the random-effects model indicated that GT administration did result in a significant change in BMI after GT supplementation (WMD: −0.65 kg/m^2, 95% CI: −1.04, −0.25, p = .001) with a moderate heterogeneity among the studies (I^2 = 48%, p = .006) (Figure 2). However, the baseline BMI, GT dosage, and intervention duration could explain the heterogeneity. Reduction in BMI after GT consumption was significant, with a more pronounced decline, in subjects with a baseline BMI ≥30 kg/m^2 (WMD: −0.89 kg/m^2, 95% CI: −1.29, −0.48) compared with a baseline BMI 25–29.9 kg/m^2 (WMD: −0.43 kg/m^2, 95% CI: −0.75, −0.12). In addition, based on the GT dosage, a significant reduction in BMI was found in trials that were performed with GT <800 mg/day (WMD: −0.72 kg/m^2, 95% CI: −1.13, −0.31) compared with those conducted with GT ≥800 mg/day (WMD: −0.50 kg/m^2, 95% CI: −0.80, −0.21). Moreover, based on the duration of the intervention (weeks), a significantly higher reduction in BMI was found in trials that lasted more than 12 weeks duration (WMD: −1.06 kg/m^2, 95% CI: −1.42, −0.70) versus trials lasting <12 weeks (WMD: −0.55 kg/m^2, 95% CI: −1.08, −0.02). All these findings are provided in Supplementary Table 2.

3.3.3 | Effect of GT supplementation on waist circumference (WC)

Overall, 13 studies involving a total of 685 (case = 345, and control = 340) participants provided information for WC as an outcome measure. Pooled results from the random-effects model indicated that WC following GT consumption did not change significantly (mean difference: WMD: −1.50 cm, 95% CI: −3.19, 0.18, p = .081) with low heterogeneity among studies (I^2 = 37%, p = .084) (Figure 3). However, baseline BMI, GT dosage, and intervention duration could explain the heterogeneity. Reduction in WC after GT consumption was significant in the trials that employed GT ≥800 mg/day (WMD: −2.06 cm, 95% CI: −4.01, −0.11) and with a treatment duration <12 weeks (WMD: −2.39 cm, 95% CI: −4.38, −0.41). All these findings are provided in Supplementary Table 2.

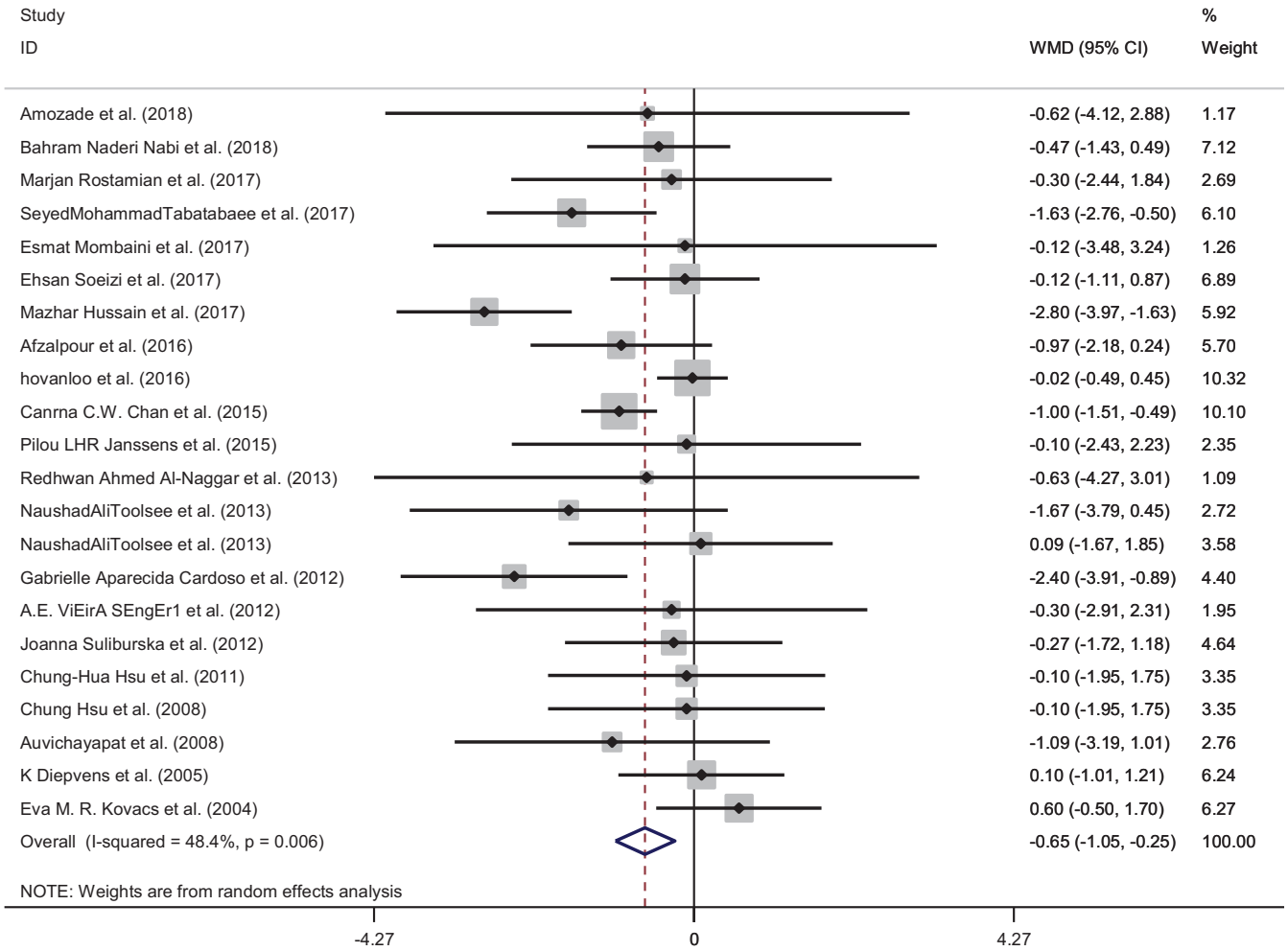

FIGURE 2 Forest plot of randomized controlled trials investigating the effects of green tea administration on the body mass index. WMD, weighted mean difference (WMD). 95% CI = 95% confidence interval [Colour figure can be viewed at wileyonlinelibrary.com]

3.3.4 | Non-linear dose–responses between dose and duration of GT supplementation and outcomes

Following the dose–response evaluation, GT intake did result in alteration of the body weight ($p < .001$), with a more pronounced reduction when the GT dosage was <500 mg/day and the supplementation lasted 12 weeks (Figure 4).

3.4 | Sensitivity analysis

To discover the impact of each single study on the combined effect size, we removed each trial from the analysis, step by step. We observed no significant effect of any individual study on the combined effect sizes of BW, BMI, and WC.

3.5 | Publication bias

We evaluated the publication bias by visual inspection of the funnel plot, which demonstrated no evidence of publication bias in the meta-analysis of GT supplementation on BW, BMI, and WC (Supplementary Figure 2). Egger's linear regression test also revealed the same result (BW: $p = .430$, BMI: $p = .742$, and WC: $p = .794$).

4 | DISCUSSION

In this meta-analysis of 26 randomized controlled trials (1,344 patients), subjects who were administered GT experienced a significant decline in BW (WMD: −1.78 kg, 95% CI: −2.80, −0.75, $p = .001$), as well as a lower BMI (WMD: −0.65 kg/m^2, 95% CI: −1.04, −0.25, $p = .001$). On the other hand, our results did not show any statically significant difference in terms of WC change following GT supplementation (WMD: −1.50 cm, 95% CI: −3.19, 0.18, $p = .081$). The current study is the most up-to-date dose–response meta-analysis on previous published articles conducted to assess the effects of GT supplementation on the reduction of anthropometric indices (Hursel, Viechtbauer, & Westerterp-Plantenga, 2009; Jurgens et al., 2012). In addition, we perceived that GT follows a dose–response pattern for BW, considering dose and treatment duration ($p < .001$), with prominent outcomes for dosages <500 mg/day and a treatment duration of 12 weeks.

An important factor to take into account is that the distribution of fat in obese patients (i.e., abdominally or affecting mainly the lower limbs) is a more important risk factor for the development of diseases rather

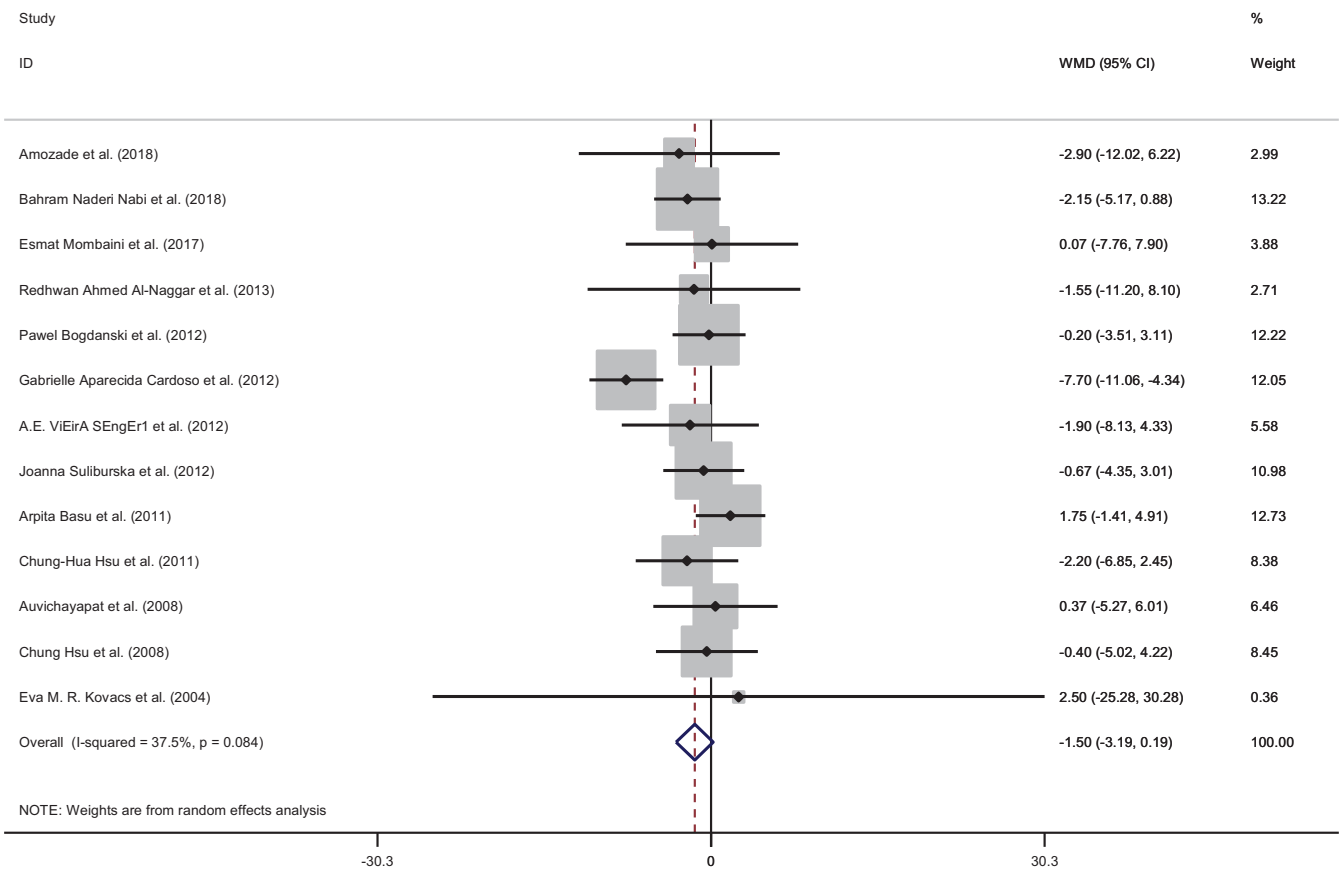

FIGURE 3 Forest plot of randomized controlled trials investigating the effects of green tea administration on weight circumference. WMD, weighted mean difference (WMD). 95% CI = 95% confidence interval [Colour figure can be viewed at wileyonlinelibrary.com]

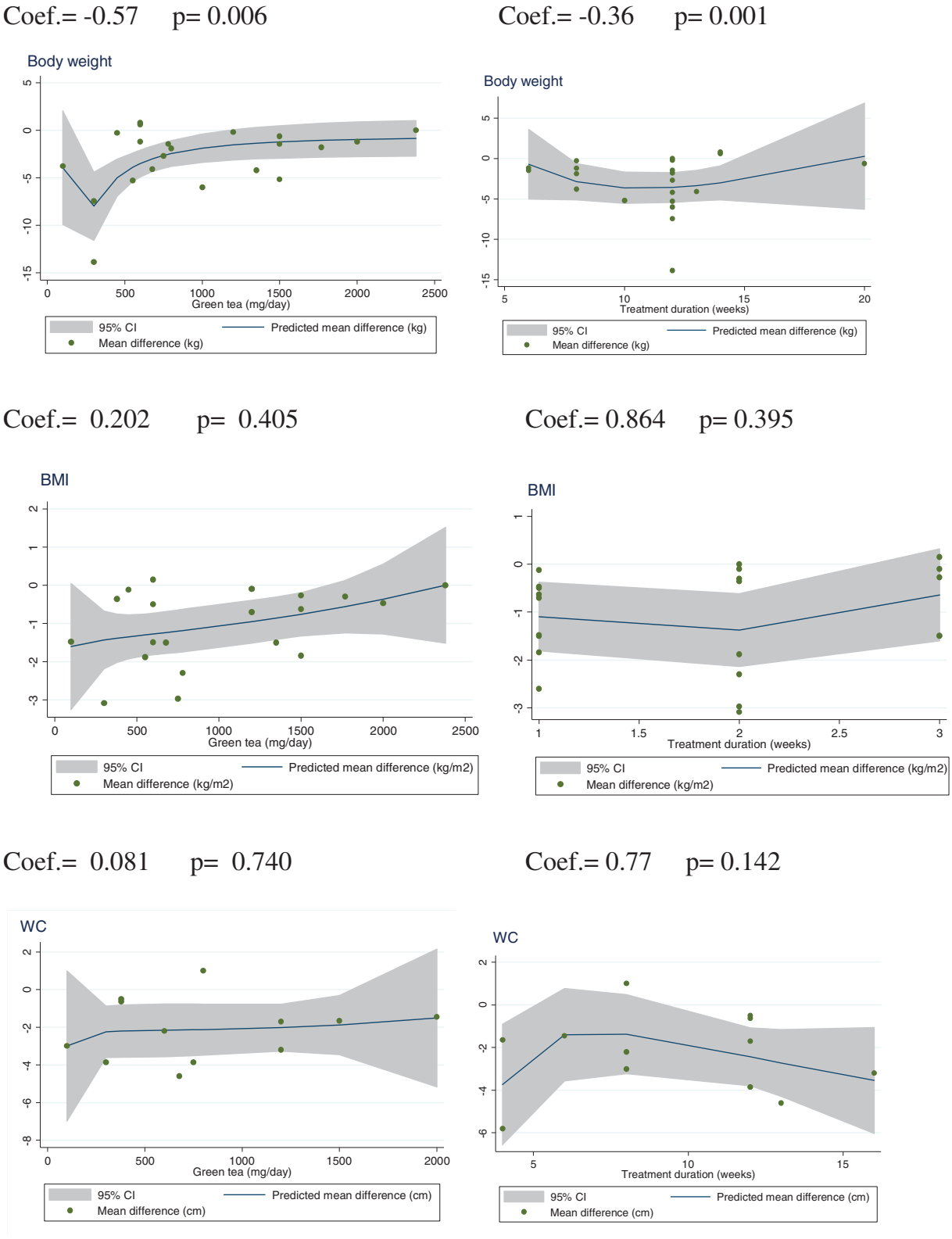

FIGURE 4 Non-linear dose-responses between green tea and unstandardized mean difference in body weight (kg) and body mass index (kg/m^2). The 95% confidence interval (CI) is depicted in the shaded regions [Colour figure can be viewed at wileyonlinelibrary.com]

than total body fat (Peiris et al., 1989). Abdominal fat is composed of both subcutaneous and visceral deposits and is more likely to be associated with cardiovascular and metabolic diseases, such as stroke, myocardial infarction, and deep vein thrombosis (Björntorp, 1997; Blüher & Laufs, 2019; Kissebah et al., 1982). Visceral abdominal fat is regarded as a prominent risk factors in obese patients due to the severe

metabolic dysfunctions encountered in these subjects: increased production of very low density lipoprotein (VLDL), stimulation of gluconeogenesis and reduction of glucose uptake into the muscle, which contribute to a hyperglycemic, hyperlipemic, and hyperinsulinemic status, which is a vicious promoter of promoter of atherosclerosis (Gastaldelli & Basta, 2010; Lohman, Roche, & Martorell, 1988; Macor et al., 1997; Sacks & Fain, 2007; Zamboni et al., 1994). Future studies should also focus on assessing the effects of GT supplementation on the distribution of fat in obese patients, in order to address the current gap of knowledge regarding this topic and in order to complement this systematic review.

Another important factor to be considered is the fact that WC has been used in different studies as a relevant predictor of visceral abdominal fat compared to the waist-hip ratio. Considering the findings of this meta-analysis, we observed that WC did not significantly change after GT supplementation in obese patients. This result can be caused by the lack of a standardized protocol regarding the assessment of this anthropometric variable, as well as intra- and inter-researcher effects and errors regarding its measurement (Medina-Gaona et al., 2018; Nadas, Putz, Kolev, Nagy, & Jermendy, 2008). This anthropometric variable is commonly affected by the location and position of the examiner and the subject during the measurement, especially in in obese and elderly individuals. Slight differences in measurement can lead to important misinterpretations of the results. Thus, a standardized assessment protocol is needed. The evaluation should be done with the patient in orthostatism, around the median point between the last rib and the iliac crest, using a measuring tape (Jelliffe & World Health, 1966; Organization, 1995). In addition, the measurement should be performed during expiration rather than inspiration.

Our results showed that BW and BMI significantly changed after GT administration, specifically for periods longer than 12 weeks and a dosage <800 mg/day. Epidemiological studies involving 1,103 subjects have shown that subjects who consumed tea habitually in an average volume of 434 mL/day for 10 years associated a lower percentage of body fat and a lower WC versus than non-obese subjects who drank no tea (Wu et al., 2003). However, we believe that a higher decrease of body indices (mostly in anthropometric indices) can be observed in longer periods of intervention with GT. This concept of a long-period requirement for weight loss in obesity has been recently discussed in the literature (Glandt & Raz, 2011). Conventional pharmacological treatments, such as sympathomimetic drugs and lipase inhibitors, also require a long-term use to achieve better outcomes. Orlistat, a lipase inhibitor, requires a treatment duration >12 weeks in order to effectively reduce the dietary fat absorption (Hauptman, Lucas, Boldrin, Collins, & Segal, 2000). Sibutramine, whose mechanism of action is related to the noradrenaline and serotonin pathways, also demonstrates benefits when administered >24 weeks (Li et al., 2005). Statins are lipid-lowering drugs, which are employed in the management of obesity and obesity-related dyslipidemia that also require a long-term administration (Horodinschi et al., 2019).

In consonance to our research findings and especially the dosage of GT needed to decrease BW and body fat, we need to consider standardization of the therapeutic dose of nutraceuticals and phytochemicals (Găman, Egbuna, & Găman, 2020). High dosages of GT can be potentially harmful for human beings and might cause toxic effect, such as headaches, nausea and vomiting, gastrointestinal dysfunction, and tachycardia (Chacko, Thambi, Kuttan, & Nishigaki, 2010; Sinija & Mishra, 2008). Furthermore, nutrient-nutrient interactions need to be taken into consideration with the supplementation of green tea, as GT is a significant source of tannin, which disrupts iron absorption (Hambidge, 2010).

A major strength of this meta-analysis is that the subgroup analysis was performed to examine the possible dose duration, and baseline BMI and WC profile of participants. In addition, we only included randomized controlled trials in our analysis and we excluded papers with a lower quality of evidence. Moreover, the existence of heterogeneity for the analyzed variables were reported. Additionally, we conducted this systematic review and meta-analysis with a minimum risk of bias in accordance to the PRISMA guidelines.

However, the present meta-analysis has some limitations that must be considered. The analysis included patients who had been diagnosed with various conditions or diseases. Consequently, this allowed more studies and participants to be included in the analysis. In addition, the current research allowed for a more nuanced guidance for further studies, since this is the first dose response meta-analysis to assess the influence of GT on obesity indices. Moreover, the presence of a low number of trials and a moderate heterogeneity in some subgroups were other limitations of the current study.

5 | CONCLUSIONS

Considering the results obtained in our systematic review and meta-analysis, GT supplementation is likely to be associated with a decrease in BW and BMI in obese patients. Although GT supplementation cannot guarantee a definitive change of these variables, we suggest that GT supplementation can be used as a complimentary measure, together with a balanced and healthy diet and the regular practice of physical exercise, in the therapeutic approach of obese patients.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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REFERENCES

Afzalpour, M. E., Ghasemi, E., & Zarban, A. (2017). Effects of 10 weeks of high intensity interval training and green tea supplementation on serum levels of Sirtuin-1 and peroxisome proliferator-activated receptor gamma co-activator 1-alpha in overweight women. *Science and Sports*, *32*(2), 82–90. https://doi.org/10.1016/j.scispo.2016.09.004

Ahmad, R. S., Butt, M. S., Sultan, M. T., Mushtaq, Z., Ahmad, S., Dewanjee, S., … Zia-Ul-Haq, M. (2015). Preventive role of green tea catechins from obesity and related disorders especially hypercholesterolemia and hyperglycemia. *Journal of Translational Medicine*, *13*, 79. https://doi.org/10.1186/s12967-015-0436-x

Al-Naggar, R. A., Osman, M. T., & Abdulghani, M. (2013). Effects green tea on the body weight of Malaysian young obese females: Single blinded

clinical trail study. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, *4*(2), 1649–1655.

Amozadeh, H., Shabani, R., & Nazari, M. (2018). The effect of aerobic training and green tea supplementation on cardio metabolic risk factors in overweight and obese females: A randomized trial. *International Journal of Endocrinology and Metabolism*, *16*(4), e60738-e60738. https://doi.org/10.5812/ijem.60738

Auvichayapat, P., Prapochanung, M., Tunkamnerdthai, O., Sripanidkulchai, B. O., Auvichayapat, N., Thinkhamrop, B., … Hongprapas, P. (2008). Effectiveness of green tea on weight reduction in obese Thais: A randomized, controlled trial. *Physiology & Behavior*, *93*(3), 486–491. https://doi.org/10.1016/j.physbeh.2007.10.009

Basu, A., Du, M., Sanchez, K., Leyva, M. J., Betts, N. M., Blevins, S., … Lyons, T. J. (2011). Green tea minimally affects biomarkers of inflammation in obese subjects with metabolic syndrome. *Nutrition*, *27*(2), 206–213. https://doi.org/10.1016/j.nut.2010.01.015

Björntorp, P. (1997). Body fat distribution, insulin resistance, and metabolic diseases. *Nutrition*, *13*(9), 795–803.

Bluher, M. (2019). Obesity: Global epidemiology and pathogenesis. *Nature Reviews. Endocrinology*, *15*(5), 288–298. https://doi.org/10.1038/s41574-019-0176-8

Blüher, M., & Laufs, U. (2019). New concepts for body shape-related cardiovascular risk: Role of fat distribution and adipose tissue function. *European Heart Journal.*, *40*, 2856–2858.

Bogdanski, P., Suliburska, J., Szulinska, M., Stepien, M., Pupek-Musialik, D., & Jablecka, A. (2012). Green tea extract reduces blood pressure, inflammatory biomarkers, and oxidative stress and improves parameters associated with insulin resistance in obese, hypertensive patients. *Nutrition Research*, *32*(6), 421–427.

Cardoso, G. A., Salgado, J. M., Cesar Mde, C., & Donado-Pestana, C. M. (2013). The effects of green tea consumption and resistance training on body composition and resting metabolic rate in overweight or obese women. *Journal of Medicinal Food*, *16*(2), 120–127. https://doi.org/10.1089/jmf.2012.0062

Chacko, S. M., Thambi, P. T., Kuttan, R., & Nishigaki, I. (2010). Beneficial effects of green tea: A literature review. *Chinese Medicine*, *5*(1), 13.

Chan, C. C. W., Koo, M. W. L., Ng, E. H. Y., Tang, O. S., Yeung, W. S. B., & Ho, P. C. (2006). Effects of Chinese green tea on weight, and hormonal and biochemical profiles in obese patients with polycystic ovary syndrome—a randomized placebo-controlled trial. *Journal of the Society for Gynecologic Investigation*, *13*(1), 63–68. https://doi.org/10.1016/j.jsgi.2005.10.006

Chen, I. J., Liu, C. Y., Chiu, J. P., & Hsu, C. H. (2016). Therapeutic effect of high-dose green tea extract on weight reduction: A randomized, double-blind, placebo-controlled clinical trial. *Clinical Nutrition*, *35*(3), 592–599. https://doi.org/10.1016/j.clnu.2015.05.003

Chrissini, M., Sifaki-Pistolla, D., Tzanakis, N., & Tsiligianni, I. (2019). Family and individual dietary and lifestyle habits as predictors of BMI and KIDMED score in Greek and immigrant preschoolers. *Arch Balk Med Union*, *53*(4), 659–671.

Di Pierro, F., Menghi, A. B., Barreca, A., Lucarelli, M., & Calandrelli, A. (2009). GreenSelect® Phytosome as an adjunct to a low-calorie diet for treatment of obesity: A clinical trial. *Alternative Medicine Review*, *14*(2), 154–160.

Diepvens, K., Kovacs, E. M. R., Nijs, I. M. T., Vogels, N., & Westerterp-Plantenga, M. S. (2005). Effects of green tea on resting energy expenditure and substrate oxidation during weight loss in overweight females. *British Journal of Nutrition*, *94*(6), 1026–1034. https://doi.org/10.1079/BJN20051580

Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ*, *315*(7109), 629–634.

Forse, R. A., & Kissee, M. C. (2020). Epidemiology and discrimination in obesity. In N. Nguyen, J. Morton, J. Ponce, & R. Rosenthal (Eds.), *The ASMBS textbook of bariatric surgery*. Cham, Switzerland: Springer.

Găman, A. M., Egbuna, C., & Găman, M. A. (2020). Chapter 6 - Natural bioactive lead compounds effective against haematological malignancies. In C. Egbuna, S. Kumar, J. C. Ifemeje, S. M. Ezzat, & S. Kaliyaperumal (Eds.), Phytochemicals as Lead Compounds for New Drug Discovery (pp. 95–115). Amsterdam, Netherlands: Elsevier.

Gaman, M. A., Epingeac, M. E., & Gaman, A. M. (2019). The relationship between oxidative stress markers, age, neutrophil-to-lymphocyte ration and obesity. *HemaSphere*, *3*(S1), 1015–1015.

Gastaldelli, A., & Basta, G. (2010). Ectopic fat and cardiovascular disease: What is the link? *Nutrition, Metabolism and Cardiovascular Diseases*, *20*(7), 481–490.

Glandt, M., & Raz, I. (2011). Present and future: Pharmacologic treatment of obesity. *Journal of Obesity*, *2011*, 1–13.

Goossens, G. H. (2017). The metabolic phenotype in obesity: Fat mass, body fat distribution, and adipose tissue function. *Obesity Facts*, *10*(3), 207–215. https://doi.org/10.1159/000471488

Gordona, N. C., & David, W. W. (2010). Antimicrobial activity of the green tea polyphenol (–)-epigallocatechin-3-gallate (EGCG) against clinical isolates of Stenotrophomonas maltophilia. *International Journal of Antimicrobial Agents*, *36*, 129–131.

Hambidge, K. M. (2010). Micronutrient bioavailability: Dietary reference intakes and a future perspective. *The American Journal of Clinical Nutrition*, *91*(5), 1430S–1432S.

Hashempur, M. H., Sadrneshin, S., Mosavat, S. H., & Ashraf, A. (2018). Green tea (*Camellia sinensis*) for patients with knee osteoarthritis: A randomized open-label active-controlled clinical trial. *Clinical Nutrition*, *37*(1), 85–90. https://doi.org/10.1016/j.clnu.2016.12.004

Hauptman, J., Lucas, C., Boldrin, M. N., Collins, H., & Segal, K. R. (2000). Orlistat in the long-term treatment of obesity in primary care settings. *Archives of Family Medicine*, *9*(2), 160–167.

Heber, D., Zhang, Y., Yang, J., Ma, J. E., Henning, S. M., & Li, Z. (2014). Green tea, black tea, and oolong tea polyphenols reduce visceral fat and inflammation in mice fed high-fat, high-sucrose obesogenic diets. *The Journal of Nutrition*, *144*(9), 1385–1393. https://doi.org/10.3945/jn.114.191007

Henning, S. M., Yang, J., Hsu, M., Lee, R. P., Grojean, E. M., Ly, A., … Li, Z. (2018). Decaffeinated green and black tea polyphenols decrease weight gain and alter microbiome populations and function in diet-induced obese mice. *European Journal of Nutrition*, *57*(8), 2759–2769. https://doi.org/10.1007/s00394-017-1542-8

Higgins, J. (2011). GSe. *Cochrane Handbook for Systematic Reviews of Interventions Version*, *5(0)*.

Horodinschi, R. N., Stanescu, A., Bratu, O. G., Pantea Stoian, A., Radavoi, D. G., & Diaconu, C. C. (2019). Treatment with statins in elderly patients. *Medicina (Kaunas, Lithuania)*, *55*(11), 721. https://doi.org/10.3390/medicina55110721

Hovanloo, F., Fallah Huseini, H., Hedayati, M., & Teimourian, M. (2016). Effects of aerobic training combined with green tea extract on leukocyte telomere length, quality of life and body composition in elderly women. *Journal of Medicinal Plants*, *15*(59), 47–57.

Hozo, S. P., Djulbegovic, B., & Hozo, I. (2005). Estimating the mean and variance from the median, range, and the size of a sample. *BMC Medical Research Methodology*, *5*(1), 13.

Hsu, C. H., Liao, Y. L., Lin, S. C., Tsai, T. H., Huang, C. J., & Chou, P. (2011). Does supplementation with green tea extract improve insulin resistance in obese type 2 diabetics? A randomized, double-blind, and placebo-controlled clinical trial. *Alternative Medicine Review*, *16*(2), 157–163.

Hsu, C. H., Tsai, T. H., Kao, Y. H., Hwang, K. C., Tseng, T. Y., & Chou, P. (2008). Effect of green tea extract on obese women: A randomized, double-blind, placebo-controlled clinical trial. *Clinical Nutrition*, *27*(3), 363–370. https://doi.org/10.1016/j.clnu.2008.03.007

Hu, J., Webster, D., Cao, J., & Shao, A. (2018). The safety of green tea and green tea extract consumption in adults—results of a systematic review. *Regulatory Toxicology and Pharmacology*, *95*, 412–433. https://doi.org/10.1016/j.yrtph.2018.03.019

Huang, J., Wang, Y., Xie, Z., Zhou, Y., Zhang, Y., & Wan, X. (2014). The anti-obesity effects of green tea in human intervention and basic molecular studies. *European Journal of Clinical Nutrition*, *68*(10), 1075–1087. https://doi.org/10.1038/ejcn.2014.143

Hursel, R., Viechtbauer, W., & Westerterp-Plantenga, M. S. (2009). The effects of green tea on weight loss and weight maintenance: A meta-analysis. *International Journal of Obesity*, *33*(9), 956–961.

Hussain, M., Habib Ur, R., & Akhtar, L. (2017). Therapeutic benefits of green tea extract on various parameters in non-alcoholic fatty liver disease patients. *Pakistan Journal of Medical Sciences*, *33*(4), 931–936. https://doi.org/10.12669/pjms.334.12571

Janssens, P. L., Hursel, R., & Westerterp-Plantenga, M. S. (2015). Long-term green tea extract supplementation does not affect fat absorption, resting energy expenditure, and body composition in adults. *The Journal of Nutrition*, *145*(5), 864–870. https://doi.org/10.3945/jn.114.207829

Janssens, P. L., Hursel, R., & Westerterp-Plantenga, M. S. (2016). Nutraceuticals for body-weight management: The role of green tea catechins. *Physiology & Behavior*, *162*, 83–87. https://doi.org/10.1016/j.physbeh.2016.01.044

Janssens, P. L., Penders, J., Hursel, R., Budding, A. E., Savelkoul, P. H., & Westerterp-Plantenga, M. S. (2016). Long-term green tea supplementation does not change the human gut microbiota. *PLoS One*, *11*(4), e0153134. https://doi.org/10.1371/journal.pone.0153134

Jelliffe, D. B., & World Health, O. (1966). *The assessment of the nutritional status of the community (with special reference to field surveys in developing regions of the world / Derrick B. Jelliffe; prepared in consultation with twenty-five specialists in various countries*. In. Geneva: World Health Organization.

Jurgens, T. M., Whelan, A. M., Killian, L., Doucette, S., Kirk, S., & Foy, E. (2012). Green tea for weight loss and weight maintenance in overweight or obese adults. *Cochrane Database of Systematic Reviews*, *12*, Cd008650. https://doi.org/10.1002/14651858.CD008650.pub2

Kissebah, A. H., Vydelingum, N., Murray, R., Evans, D. J., Kalkhoff, R. K., & Adams, P. W. (1982). Relation of body fat distribution to metabolic complications of obesity. *The Journal of Clinical Endocrinology & Metabolism*, *54*(2), 254–260.

Kovacs, E. M., Lejeune, M. P., Nijs, I., & Westerterp-Plantenga, M. S. (2004). Effects of green tea on weight maintenance after body-weight loss. *The British Journal of Nutrition*, *91*(3), 431–437. https://doi.org/10.1079/bjn20041061

Li, G., Zhang, Y., Mbuagbaw, L., Holbrook, A., Levine, M. A., & Thabane, L. (2014). Effect of green tea supplementation on blood pressure among overweight and obese adults: A protocol for a systematic review. *BMJ Open*, *4*(4), e004971. https://doi.org/10.1136/bmjopen-2014-004971

Li, G., Zhang, Y., Thabane, L., Mbuagbaw, L., Liu, A., Levine, M. A., & Holbrook, A. (2015). Effect of green tea supplementation on blood pressure among overweight and obese adults: A systematic review and meta-analysis. *Journal of Hypertension*, *33*(2), 243–254. https://doi.org/10.1097/hjh.0000000000000426

Li, Z., Maglione, M., Tu, W., Mojica, W., Arterburn, D., Shugarman, L. R., … Shekelle, P. G. (2005). Meta-analysis: Pharmacologic treatment of obesity. *Annals of Internal Medicine*, *142*(7), 532–546.

Liu, Z., Chen, Z., Guo, H., He, D., Zhao, H., Wang, Z., … Ni, L. (2016). The modulatory effect of infusions of green tea, oolong tea, and black tea on gut microbiota in high-fat-induced obese mice. *Food & Function*, *7*(12), 4869–4879. https://doi.org/10.1039/c6fo01439a

Lohman, T. G., Roche, A. F., & Martorell, R. (1988). *Anthropometric standardization reference manual* (Vol. 177). Champaign, IL: Human Kinetics Books.

Macor, C., Ruggeri, A., Mazzonetto, P., Federspil, G., Cobelli, C., & Vettor, R. (1997). Visceral adipose tissue impairs insulin secretion and insulin sensitivity but not energy expenditure in obesity. *Metabolism*, *46*(2), 123–129.

Medina-Gaona, L. A., Enríquez-Sánchez, N., Mejía-Ramírez, C. E., de Jesús Orueta-Mondragón, N., Medina-Franco, H., Sandoval-Morales, Y., & Plett-Torres, T. (2018). Frequency and correlation of body mass index and waist-hip ratio with fasting glycemia and blood pressure in high school students from Mexico. *International Journal of Medical Students*, *6*(2), 38–46. https://doi.org/10.5195/ijms.2018.4

Miyata, Y., Shida, Y., Hakariya, T., & Sakai, H. (2019). Anti-cancer effects of green tea polyphenols against prostate cancer. *Molecules*, *24*(1), 193. https://doi.org/10.3390/molecules24010193

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & Group, P. (2009). Reprint—Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Physical Therapy*, *89*(9), 873–880.

Mombaini, E., Jafarirad, S., Husain, D., Haghighizadeh, M. H., & Padfar, P. (2017). The impact of green tea supplementation on anthropometric indices and inflammatory cytokines in women with polycystic ovary syndrome. *Phytotherapy Research*, *31*(5), 747–754. https://doi.org/10.1002/ptr.5795

Nabi, B. N., Sedighinejad, A., Haghighi, M., Farzi, F., Rimaz, S., Atrkarroushan, Z., & Biazar, G. (2018). The anti-obesity effects of green tea: A controlled, randomized, clinical trial. *Iranian Red Crescent Medical Journal*, *20*(1), e55950. https://doi.org/10.5812/ircmj.55950

Nadas, J., Putz, Z., Kolev, G., Nagy, S., & Jermendy, G. (2008). Intraobserver and interobserver variability of measuring waist circumference. *Medical Science Monitor*, *14*(1), CR15–CR18.

Neyrinck, A. M., Bindels, L. B., Geurts, L., Van Hul, M., Cani, P. D., & Delzenne, N. M. (2017). A polyphenolic extract from green tea leaves activates fat browning in high-fat-diet-induced obese mice. *The Journal of Nutritional Biochemistry*, *49*, 15–21. https://doi.org/10.1016/j.jnutbio.2017.07.008

OECD. (2019). *The heavy burden of obesity: The economics of prevention, OECD health policy studies*. Paris: OECD Publishing. https://doi.org/10.1787/67450d67-en

Organization, W. H. (1995). *Physical status: The use of and interpretation of anthropometry*, Report of a WHO Expert Committee. Geneva: World Health Organization.

Palmer, T. M., Peters, J. L., Sutton, A. J., & Moreno, S. G. (2008). Contour-enhanced funnel plots for meta-analysis. *Stata Journal*, *8*(2), 242–254.

Peiris, A. N., Sothmann, M. S., Hoffmann, R. G., Hennes, M. I., Wilson, C. R., Gustafson, A. B., & Kissebah, A. H. (1989). Adiposity, fat distribution, and cardiovascular risk. *Annals of Internal Medicine*, *110*(11), 867–872.

Pervin, M., Unno, K., Ohishi, T., Tanabe, H., Miyoshi, N., & Nakamura, Y. (2018). Beneficial effects of green tea catechins on neurodegenerative diseases. *Molecules*, *23*(6), 1297. https://doi.org/10.3390/molecules23061297

Quinhoneiro, D. C. G., Nicoletti, C. F., Pinhel, M. A. S., Noronha, N. Y., Braga, C. B. M., Oliveira, B. A. P., … Nonino, C. B. (2018). Green tea supplementation upregulates uncoupling protein 3 expression in severe obese women adipose tissue but does not promote weight loss. *International Journal of Food Sciences and Nutrition*, *69*(8), 995–1002. https://doi.org/10.1080/09637486.2018.1442819

Rostamian, M., & Bijeh, N. (2017). Effect of short-term aerobic exercise and green tea consumption on MFO, fat(max), body composition and lipid profile in sedentary postmenopausal women. *International Journal of Applied Exercise Physiology*, *6*(1), 22–32.

Sacks, H. S., & Fain, J. N. (2007). Human epicardial adipose tissue: A review. *American Heart Journal*, *153*(6), 907–917.

Seo, D. B., Jeong, H. W., Cho, D., Lee, B. J., Lee, J. H., Choi, J. Y., … Lee, S. J. (2015). Fermented green tea extract alleviates obesity and related complications and alters gut microbiota composition in diet-induced obese mice. *Journal of Medicinal Food*, *18*(5), 549–556. https://doi.org/10.1089/jmf.2014.3265

Sinija, V., & Mishra, H. (2008). Green tea: Health benefits. *Journal of Nutritional & Environmental Medicine*, *17*(4), 232–242.

Soeizi, E., Rafraf, M., Asghari-Jafarabadi, M., Ghaffari, A., Rezamand, A., & Doostan, F. (2017). Effects of green tea on serum iron parameters and

antioxidant status in patients with beta-thalassemia major. *Pharmaceutical Sciences*, *23*(1), 27–36. https://doi.org/10.15171/ps.2017.05

Suliburska, J., Bogdanski, P., Szulinska, M., Stepien, M., Pupek-Musialik, D., & Jablecka, A. (2012). Effects of green tea supplementation on elements, total antioxidants, lipids, and glucose values in the serum of obese patients. *Biological Trace Element Research*, *149*(3), 315–322. https://doi.org/10.1007/s12011-012-9448-z

Tabatabaee, S. M., Alavian, S. M., Ghalichi, L., Miryounesi, S. M., Mousavizadeh, K., Jazayeri, S., & Vafa, M. R. (2017). Green tea in non-alcoholic fatty liver disease: A double blind randomized clinical trial. *Hepatitis Monthly*, *17*(12), e14993. https://doi.org/10.5812/hepatmon.14993

Tofolean, I. T., Ganea, C., Ionescu, D., Filippi, A., Garaiman, A., Goicea, A., … Baran, I. (2016). Cellular determinants involving mitochondrial dysfunction, oxidative stress and apoptosis correlate with the synergic cytotoxicity of epigallocatechin-3-gallate and menadione in human leukemia Jurkat T cells. *Pharmacological Research*, *103*, 300–317. https://doi.org/10.1016/j.phrs.2015.12.013

Toolsee, N. A., Aruoma, O. I., Gunness, T. K., Kowlessur, S., Dambala, V., Murad, F., … Bahorun, T. (2013). Effectiveness of green tea in a randomized human cohort: Relevance to diabetes and its complications. *BioMed Research International*, *2013*, 412379–412312. https://doi.org/10.1155/2013/412379

Venkatakrishnan, K., Chiu, H.-F., Cheng, J.-C., Chang, Y.-H., Lu, Y.-Y., Han, Y.-C., … Wang, C.-K. (2018). Comparative studies on the hypolipidemic, antioxidant and hepatoprotective activities of catechin-enriched green and oolong tea in a double-blind clinical trial. *Food & Function*, *9*(2), 1205–1213.

Vieira Senger, A. E., Schwanke, C. H., Gomes, I., & Valle Gottlieb, M. G. (2012). Effect of green tea (*Camellia sinensis*) consumption on the components of metabolic syndrome in elderly. *The Journal of Nutrition, Health & Aging*, *16*(9), 738–742. https://doi.org/10.1007/s12603-012-0081-5

Vincek, E., White, D. A., & Feinn, R. (2018). Assessment of healthful lifestyle behaviors between graduate programs. *International Journal of Medical Students*, *6*(3), 98–101. https://doi.org/10.5195/ijms.2018.300

WHO. (2018). World Health Organization. Retrieved from https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.

Wu, C. H., Lu, F. H., Chang, C. S., Chang, T. C., Wang, R. H., & Chang, C. J. (2003). Relationship among habitual tea consumption, percent body fat, and body fat distribution. *Obesity Research*, *11*(9), 1088–1095.

Xu, Y., Zhang, M., Wu, T., Dai, S., Xu, J., & Zhou, Z. (2015). The anti-obesity effect of green tea polysaccharides, polyphenols and caffeine in rats fed with a high-fat diet. *Food & Function*, *6*(1), 297–304. https://doi.org/10.1039/c4fo00970c

Yinji Liang, C. L., Huang, S., & Xu, Y. (2019). Traditional Chinese medicine and intestinal microbiota a complementary and integrative health approach to ameliorate obesity-related diseases. *Holistic Nursing Practice*, 33(5), 259–265. https://doi.org/10.1097/HNP.0000000000000311

Zamboni, M., Armellini, F., Cominacini, L., Turcato, E., Todesco, T., Bissoli, L., … Bosello, O. (1994). Obesity and regional body-fat distribution in men: Separate and joint relationships to glucose tolerance and plasma lipoproteins. *The American Journal of Clinical Nutrition*, *60*(5), 682–687.

Zhang, X., Zhang, M., Ho, C.-T., Guo, X., Wu, Z., Weng, P., … Cao, J. (2018). Metagenomics analysis of gut microbiota modulatory effect of green tea polyphenols by high fat diet-induced obesity mice model. *Journal of Functional Foods*, *46*, 268–277. https://doi.org/10.1016/j.jff.2018.05.003

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Lin Y, Shi D, Su B, et al. The effect of green tea supplementation on obesity: A systematic review and dose–response meta-analysis of randomized controlled trials. *Phytotherapy Research*. 2020;34:2459–2470. https://doi.org/10.1002/ptr.6697