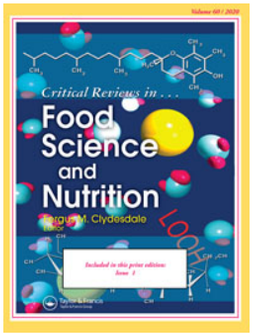

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REVIEW

The effects of curcumin supplementation on body weight, body mass index and waist circumference: a systematic review and dose-response meta-analysis of randomized controlled trials

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ABSTRACT

Background & Objectives: Inconsistent data are available about the effect of curcumin supplementation on body weight. This systematic review and meta-analysis was done to summarize data from available clinical trials on the effect of curcumin supplementation on body weight, Body Mass Index (BMI), and Waist Circumference (WC).

Methods: PubMed, SCOPUS, Cochrane Library and Google Scholar were searched to find relevant articles up to August 2018. The effect sizes were expressed as weighted mean difference (WMD) and 95% confidence intervals (CI). Between-study heterogeneity was assessed using I^2. Subgroup analysis was done to find possible sources of heterogeneity.

Results: Totally, 11 studies that enrolled 876 subjects (53% women) were included. Combining effect sizes suggested a significant effect of curcumin administration on body weight (Weighed Mean Difference (WMD): −1.14 kg, 95% CI: −2.16, −0.12, $P = 0.02$) and BMI (WMD: −0.48 kg/m^2, 95% CI: −0.78, −0.17, $P = 0.002$), respectively. However, no significant effect of curcumin supplementation on WC was found (WMD: −1.51 cm, 95% CI: −4.041, 1.003, $P = 0.23$). Based on subgroup analysis, we found that the effect of curcumin on WC was significant in studies that prescribed ≥1000 mg/d curcumin ($P \leq 0.001$), those with the intervention duration of ≥8 weeks ($P \leq 0.001$), and those that was performed on overweight subjects ($P \leq 0.001$).

Conclusions: We found a significant effect of curcumin supplementation on body weight and BMI, but not on WC. However, the effect of curcumin on WC was significant in studies done on overweight subjects, used ≥1000 mg/d curcumin, and ≥8 weeks of duration.

KEYWORDS
Curcumin; obesity; body weight; BMI; waist circumference; meta-analysis

Introduction

Obesity is one of the most important health problems worldwide (Donkin et al. 2016). According to the World Health Organization (WHO) in 2016, more than 1.9 billion adults (≥18) were overweight (Organization 2017). It affects the quality of life, increases the risk of non-communicable illnesses (e.g. cardiovascular diseases, diabetes, musculoskeletal disorders, and some cancers) and health-care costs all over the world (Heymsfield and Wadden 2017; Organization 2017). Therefore, weight management strategies are of great importance to improve the mental and physical health of obese patients (Knowler et al. 2009; Scott et al. 2008).

In recent years, the use of pharmacological interventions has been considered along with traditional methods including diet therapy and physical exercise in the weight management (Golbidi, Mesdaghinia, and Laher 2012; Dulloo 2011; Mousavi et al. 2018). Curcumin is a bioactive polyphenol component which is found in Turmeric rhizomes (*Curcuma longa*) and is commonly referred to as diferuloylmethane (Khan and Abourashed 2011; Chainani-Wu 2003). Curcumin, which accounts for 2–8% of turmeric compounds, is the main agent of yellow and golden color in turmeric and is also deemed responsible for many medical properties of turmeric (Aggarwal, Surh, and Shishodia 2007; Chattopadhyay et al. 2004). Curcumin has a low toxicity and performs a wide range of pharmacological functions including antioxidant, anti-inflammatory, anti-microbial and anti-carcinogenic effects (Maheshwari et al. 2006; Ammon and Wahl 1991). Prior studies have shown the beneficial effects of curcumin in reducing the risk of chronic diseases such as cardiovascular diseases, diabetes, several cancers and autoimmune diseases (Kunnumakkara et al. 2017). Moreover, several studies reported conflicting effects of curcumin consumption on body weight and body composition. Some clinical trials proposed a significant effect of curcumin

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intake on indicators of body composition (Chuengsamarn et al. 2012; Rahimi et al. 2016; Panahi, Khalili, et al. 2017). On the contrary, others reported no significant effect of curcumin intake on weight or body mass index (Mohammadi et al. 2013; Yang et al. 2014; Campbell et al. 2017). However, despite various studies on the effect of curcumin intake on body composition, we are aware of no prior study summarizing findings in this regard. The current study was therefore done to perform a comprehensive systematic review and meta-analysis of published randomized controlled trials (RCTs) to assess the effect of curcumin supplementation on body weight, body mass index (BMI), and waist circumference (WC) in adults.

Methods

The Preferred Reporting Items of Systematic Reviews and Meta-Analysis (PRISMA) statement guideline was used to perform and report this systematic review meta-analysis (Moher et al. 2015).

Search strategy

We did the comprehensive and systematic literature search up to August 2018 through the following online databases: PubMed/Medline, SCOPUS, Cochrane Library and Google Scholar. To find the relevant studies, we used the combination of MESH and non-MESH terms including ("Curcumin" OR "Curcuma" OR "Curcuminoid" OR "Tumeric" OR "Turmeric") AND ("Body Weight" OR "Body Weight Changes" OR "Body Mass Index" OR "Weight Loss" OR "Obesity" OR "Waist Circumference" OR "Adipose Tissue" OR "Quetelet Index" OR "BMI" OR "Weight Reduction" OR "Weight Losses" OR "Abdominal Obesity" OR "Central Obesity" OR "Visceral Obesity" OR "obes*" OR "overweight" OR "fat mass" OR "adiposity" OR "Body Fat"). In addition, all reference lists of eligible articles, related reviews, and meta-analyses were hand-searched to avoid missing any pertinent articles. Unpublished documents and gray literature such as conference papers, theses, and patents were not included in this meta-analysis.

Eligibility criteria

Studies were included if they had the following criteria: (1) full-text articles were available as English language (2) were randomized controlled trials (either parallel or crossover design) (3) carried out on adult population ($\geq$18 years) (4) reported body weight or/and BMI or/and waist circumference (WC) before and after the intervention in treatment and the placebo group (we also considered studies that reported the changes in outcome variables) (5) examined the effect of curcumin supplement only (publications which investigated the effect of turmeric were not included).

We did not include publications that had the following criteria: (i) non-clinical trials or semi-experimental studies (ii) were done on animals, children or pregnant women (iii) studies that lacked placebo group (iv) Studies that were done on the same population (only the most complete one was included) (v) those that did not report the baseline and final values of outcome variables (or changes) in both curcumin and control groups (vi) studies which examined the effect of multiple interventions plus curcumin.

Data extraction

Data extraction and study selection were done by two independent reviewers (SMM and HKV), and any controversy across selecting eligible articles were discussed and resolved by the principal investigator (AE). We contacted the authors in case of needing additional information or when the publications had not reported sufficient information. The following applicable data were extracted from each study: the general features of the study and population (first author, study location, year of publication, study design, type of study population, participants' gender, the mean age of subjects, duration of intervention and dose of curcumin supplement), results (means and standard deviation [SD] or standard error [SE] or 95% confidence interval [CI] for body weight, BMI, and WC of participants at baseline, end of the study and/or change between baseline and post-intervention were reported). When the values for outcome variable were reported in different time points, data for the end of the trial were extracted.

Quality assessment

The quality of studies was evaluated by using Jadad scoring system (Jadad et al. 1996). This scale consists of 5 questions in which 0 or 1 points were given for each of the following questions: (i) randomization (ii) appropriate method for randomization (iii) double-blinding (iv) appropriate method for double-blinding (v) description of dropouts and withdrawals. The overall score of a study according to this scale ranged between 0 and 5, with superior scores indicative of a better quality (Jadad et al. 1996). In the current study, those with a Jadad score of <3 and ≥3 were considered as low and high-quality publications, respectively (Moher et al. 1999).

Quantitative data synthesis and statistical analysis

This meta-analysis was conducted using Stata software version 12 (Stata Corp. College Station, Texas, USA) (Hamilton 2012). The mean change (SD) in body weight, BMI, and WC from the baseline was used to calculate mean difference (95% confidence interval [CI]) between the intervention and placebo groups. When the SD of the mean difference was not reported, it was calculated as follows: $SD_{change} = \text{square root } [(SD_{baseline}^2 + SD_{final}^2) - (2 \times R \times SD_{baseline} \times SD_{final})]$. The correlation coefficient of 0.9 was considered as R-value which ranges between 0 and 1 (Higgins and Green 2011). If a study reported standard error of mean (SEM), SD was estimated using this formula: $SD = SEM \times \text{square root}[n]$, in which n is the number of participants. When the publications provided medians and ranges or 95% CIs, we calculated mean (SD) by the method of Hozo, Djulbegovic, and Hozo (2005).

The random-effects model was applied to derive the overall effect size. Between-study heterogeneity was assessed using the I-square (I^2) test. In order to identify potential heterogeneity sources, we did subgroup analyses. Probable sources of heterogeneity were explored based on the following categories: intervention dosage, duration of follow up, baseline BMI, and mean age of participants. Meta-regression was conducted to evaluate the relation between the effect size and potential moderator variables including intervention dosage and duration of treatment. To explore the influence of each study on the overall effect size, a sensitivity analysis was used by the one-study remove (leave-one-out) approach (Sahebkar 2014). We also executed fractional polynominal modeling (polynomials) to explore the non-linear potential effects of curcumin dosage (mg/d) and duration of treatment (weeks). Visual evaluation of the funnel plot and Egger's regression test were used to examine publication bias. P values <0.05 were considered as statistically significant.

Results

Study selection

Out of 2532 relevant articles identified in our primary search, 596 duplicates were removed. The remaining 1936 records were screened. On the basis of title and abstract, we omitted 1874 irrelevant articles and 62 articles were chosen for further evaluation and detailed examination. An additional 51 studies were excluded for the following reasons: observational studies and conference papers ($n=9$), studies that examined the effect of curcumin in combination with other components ($n=9$), same data set with other studies ($n=5$), publications that had no placebo group ($n=2$), studies that were done on children ($n=1$) and animals ($n=1$), non-English full-texts articles ($n=2$), studies with insufficient data ($n=9$) and those that did not report outcomes of interest ($n=13$). Finally, 11 eligible studies satisfied the inclusion criteria and were included in the final meta-analysis. Out of 11 studies, 8 records examined the effect of curcumin on body weight (Chuengsamarn et al. 2012; Mohammadi et al. 2013; Yang et al. 2014; Di Pierro et al. 2015; Rahmani et al. 2016; Mohammadi et al. 2017; Panahi, Khalili, et al. 2017; Jazayeri-Tehrani et al. 2017), 10 has reported data on BMI (Mohammadi et al. 2013; Yang et al. 2014; Di Pierro et al. 2015; Panahi et al. 2016; Rahimi et al. 2016; Rahmani et al. 2016; Campbell et al. 2017; Mohammadi et al. 2017; Panahi, Khalili, et al. 2017; Jazayeri-Tehrani et al. 2017), and 6 studies had reported data on WC (Chuengsamarn et al. 2012; Mohammadi et al. 2013; Di Pierro et al. 2015; Panahi et al. 2016; Campbell et al. 2017; Mohammadi et al. 2017). The flow diagram of the study selection process is presented in Fig. 1.

Study characteristics

The general characteristics of 11 qualified studies in this systematic review and meta-analysis are summarized in Table 1. Overall, a total of 876 subjects (53% women), including 434 subjects in the intervention group and 442 subjects in the placebo group, were examined in these 11 publications. These studies were published in recent years from 2012 to 2018, and most were conducted in Iran (Mohammadi et al. 2017; Mohammadi et al. 2013; Panahi, Khalili, et al. 2017; Panahi et al. 2016; Rahimi et al. 2016; Rahmani et al. 2016; Jazayeri-Tehrani et al. 2017). The remaining studies were carried out in the United States (Campbell et al. 2017), Italy (Di Pierro et al. 2015), Taiwan (Yang et al. 2014), and Thailand (Chuengsamarn et al. 2012). Individuals' age range in these studies were between 18 and 85 years. All records examined the effect of curcumin in both genders except for one study that was restricted to men (Campbell et al. 2017). Baseline BMI of participants revealed that all trials had enrolled overweight and obese subjects (BMI$>25\,kg/m^2$). All of the nominated studies had a parallel-design, whereas Mohammadi et al (Mohammadi et al. 2013) had designed a cross-over trial. Included studies had recruited people with diabetes (Chuengsamarn et al. 2012; Rahimi et al. 2016; Panahi, Khalili, et al. 2017), nonalcoholic fatty liver disease (NAFLD) (Panahi et al. 2016; Rahmani et al. 2016; Jazayeri-Tehrani et al. 2017), metabolic syndrome (Yang et al. 2014; Di Pierro et al. 2015; Mohammadi et al. 2017), and apparently healthy obese subjects (Mohammadi et al. 2013; Campbell et al. 2017). All publications prescribed curcumin alone while Di Pierro et al assessed the effect of curcumin along with lifestyle intervention in both intervention and placebo groups (Di Pierro et al. 2015). The range of dosage of curcumin supplements varied from 70 to 1900 mg/day. The duration of intervention was between 1 and 6 months in different studies. Out of these studies, 5 records identified significant effects of curcumin intake on weight loss as compared with the placebo group (Chuengsamarn et al. 2012; Rahmani et al. 2016; Panahi, Khalili, et al. 2017; Di Pierro et al. 2015; Jazayeri-Tehrani et al. 2017), while changes in body weight were not significant in other trials (Mohammadi et al. 2013; Yang et al. 2014; Mohammadi et al. 2017). As for BMI, 6 studies had reported a significant decrease in the treatment group compared with the control group (Panahi et al. 2016; Rahimi et al. 2016; Rahmani et al. 2016; Panahi, Khalili, et al. 2017; Di Pierro et al. 2015; Jazayeri-Tehrani et al. 2017) and others failed to find such significant changes (Mohammadi et al. 2013; Yang et al. 2014; Campbell et al. 2017; Mohammadi et al. 2017). In addition, a significant reduction in WC was observed in 3 studies (Chuengsamarn et al. 2012; Panahi et al. 2016; Di Pierro et al. 2015), half other studies did not reach significant findings (Mohammadi et al. 2013; Campbell et al. 2017; Mohammadi et al. 2017).

The quality score of studies was in the range of 2–4 (Chuengsamarn et al. 2012; Yang et al. 2014; Di Pierro et al. 2015; Rahimi et al. 2016; Rahmani et al. 2016; Campbell et al. 2017; Mohammadi et al. 2013; Jazayeri-Tehrani et al. 2017) (Table 1). Three studies were categorized as low-quality publications (Jadad score <3) (Panahi et al. 2016; Mohammadi et al. 2017; Panahi, Khalili, et al. 2017). All studies were randomized trials, of them 6 records had properly explained the randomization procedure (Chuengsamarn

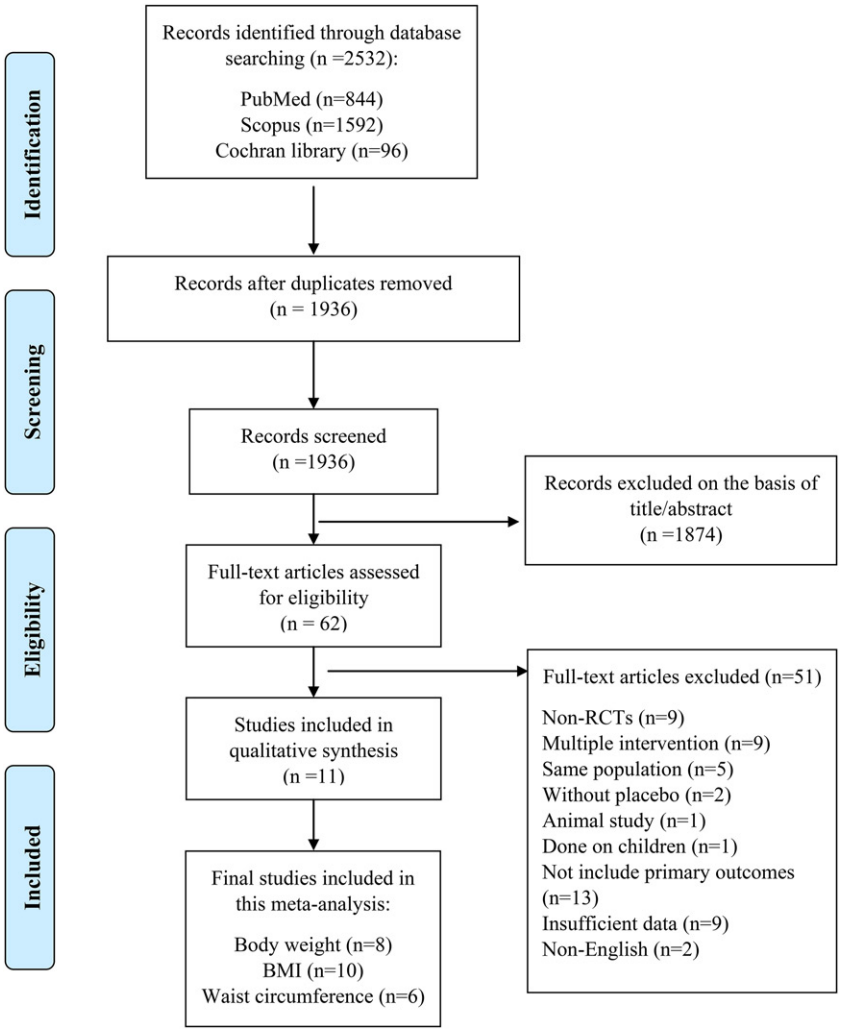

Figure 1. Flow diagram of study selection.

et al. 2012; Yang et al. 2014; Di Pierro et al. 2015; Rahimi et al. 2016; Campbell et al. 2017; Jazayeri-Tehrani et al. 2017). Among 11 included studies, 8 trials (Chuengsamarn et al. 2012; Mohammadi et al. 2013; Yang et al. 2014; Rahimi et al. 2016; Rahmani et al. 2016; Campbell et al. 2017; Panahi, Khalili, et al. 2017; Jazayeri-Tehrani et al. 2017) had mentioned blindness whereas none clearly described the blinding procedure. Details concerning a number of participants that dropped out and the reasons for this were reported in all studies except one (Panahi, Khalili, et al. 2017).

Findings for the effect of curcumin on body weight

Forest plot representing the pooled effect size of curcumin consumption on obesity indices is illustrated in Fig. 2. Combining 8 effect sizes from 8 studies based on the random-effects model, we found that curcumin administration significantly reduced body weight (Weighed Mean Difference (WMD): −1.14 kg, 95% CI: −2.16, −0.12, $P = 0.02$) (Fig. 2–A). Also, the overall effect size was robust after performing sensitivity analysis. However, there was a significant between-study heterogeneity (I^2= 86.7%, $P < 0.001$). Subgroup analysis based on different variables indicated that duration of intervention could explain the heterogeneity (I^2=46.4%, $p = 0.15$) (Table 2). However, the effect of curcumin supplementation on BW was not significant for studies with duration of intervention <8 weeks (WMD: −0.02 kg, 95% CI: −0.74, 0.69, $P = 0.94$).

Meta-regression analysis revealed that the pooled estimate is independent of curcumin dosage (slope: 0.0008; 95% CI: −0.002 to 0.004; $P = 0.55$) and duration of supplementation (slope: -0.093; 95% CI: −0.54 to 0.35; $P = 0.62$). In addition, we failed to find a significant effect of supplementation dosage on participants' body weight, as examined by non-linear dose-response meta-analysis ($P_{\text{non-linearity}} = 0.68$) (Fig. 3–A). Also, duration of curcumin administration did not display a significant non-linear relationship with body weight ($P_{\text{non-linearity}}$= 0.12) (Fig. 4–A).

Visual inspection of funnel plot revealed an asymmetry but this observation was not confirmed by Egger's linear regression ($P = 0.70$).

Findings for the effect of curcumin on BMI

Pooling effect sizes from ten studies, we reached a significant effect of curcumin intake on BMI (WMD: −0.48 kg/m^2, 95% CI: −0.78, −0.17, $P = 0.002$) (Fig. 2–B). Also, removing each individual study by sensitivity analysis did not change

Table 1. General characteristics of the included studies.

Code/ First Author (year)	Location	Design	Patient Features	Gender	Sample size	Duration (week)	Mean age (year)	Baseline BMI (kg/m^2)	Intervention		Outcome	Jadad score
									Treatment group	Control group		
1. Chuengsamarn et al. (2012)	Thailand	RCT, DB, P	Pre-diabetic subjects	Both	201	39	56.95	26.6	1500 mg/d curcuminods	Placebo	Weight, WC	4
2. Mohammadi et al. (2013)	Iran	RCT, DB, C	Obese	Both	30	4	38.43	32.6	1000 mg curcuminoids +5 mg bioperine	Placebo +5mg piperine	Weight, BMI, WC	3
3. Yang et al. (2014)	Taiwan	RCT, DB, P	Metabolic Syndrome	Both	59	12	59.03	30.6	1900 mg/d curcuminods	Placebo	Weight, BMI	4
4. Di Pierro et al. (2015)	Italy	RCT, P	Metabolic Syndrome	Both	44	4	39.1	28.6	800 mg/d Curcuma longa + lifestyle intervention	Phosphatidylserine + lifestyle intervention	Weight, BMI, WC	3
5. Panahi et al. (2016)	Iran	RCT, P	NAFLD	Both	87	8	44.98	28.9	1000 mg/d curcumin	Placebo	BMI, WC	2
6. Rahimi et al. (2016)	Iran	RCT, DB, P	diabetic subjects	Both	70	13	56.34	26.9	80 mg/d Curcumin (nano-micelle)	Placebo	BMI	4
7. Rahmani et al. (2016)	Iran	RCT, DB, P	NAFLD	Both	77	8	46.37	30.8	amorphous dispersion preparation, 70 mg/d curcuminoids	Placebo	Weight, BMI	3
8. Campbell et al. (2017)	USA	RCT, DB, P	Obese	men	22	12	25.91	33.2	200 mg/d curcuminoids + fenugreek fiber	fenugreek fiber	BMI, WC	4
9. Mohammadi et al. (2017)	Iran	RCT, P	Metabolic Syndrome	Both	72	6	37.52	30.6	200 mg/d pure curcumin	Placebo	Weight, BMI, WC	4
10. Panahi et al. (2017)	Iran	RCT, P	type 2 diabetes	Both	100	8	43	26.5	1000 mg/d curcuminoid + piperine	Placebo + piperine	Weight, BMI	2
11. Jazayeri-Tehrani et al. (2017)	Iran	RCT, DB, P	NAFLD	Both	84	12	41.8	30.6	80 mg/d nanocurcumin	Placebo	Weight, BMI	4

Abbreviations: BMI; body mass index, WC; waist circumference, RCT; randomized controlled trial , DB; double-blind, P; parallel, C; cross-over, NAFLD; nonalcoholic fatty liver disease.

the pooled effect size. As there was a significant heterogeneity ($I^2 = 60.2\%$, $P = 0.007$), we performed subgroup analysis and found that supplementation dosage ($I^2 = 49.5\%$, $P = 0.11$), duration of follow up ($I^2 = 43.8\%$, $P = 0.11$), and BMI status (overweights: $I^2 = 25.6\%$, $p = 0.25$ & obese: $I^2 = 35.2\%$, $P = 0.17$) could explain between-study heterogeneity (Table 2).

Findings from the lianear association showed that dosage of supplementation (slope: 0.0002; 95% CI: −0.001 to 0.001; $P = 0.64$) and duration of treatment (slope: −0.009; 95% CI: −0.30 to 0.28; $P = 0.94$) had no association with BMI. Non-linear dose response analysis did not show a significant effect of supplementation dosage (Fig. 3–B) and duration (Fig. 4–B) on BMI ($P_{\text{non-linearity}} = 0.17$ and 0.92, respectively).

The funnel plot indicated moderate asymmetry. In contrast, the Egger's linear regression ($P = 0.74$) provided no evidence of publication bias.

Findings for the effect of curcumin on WC

Combining findings from 6 studies revealed that curcumin supplementation had no significant effect on WC (WMD: −1.51 cm, 95% CI: −4.041, 1.003, $P = 0.23$) (Fig. 3–C). There was a considerable between-study heterogeneity ($I^2 = 84.0\%$, $P < 0.001$). Based on sensetivity analysis, no single study had a significant effect on the overall results. Subgroup analysis demonstrated that dosage of supplementation ($I^2 = 0.0\%$, $P = 0.82$), intervention duration (I^2=0.0%, $P = 0.94$), BMI status ($I^2 = 0.0\%$, $P = 0.90$), and participants' mean age (I^2=0.0%, $P = 0.52$) might help explaining heterogenity (Table 2). A signifficant reduction in WC was noticed by curcumin supplementation in studies that prescribed ≥1000 mg/d curcumin (WMD: −2.55 cm, 95% CI: −3.74, −1.35, $p \leq 0.001$) as well as in studies with ≥8 weeks of duration (WMD: −3.71 cm, 95% CI: −5.16, −2.25, $p \leq 0.001$), and in those performed on overweight subjects (WMD: −3.71 cm, 95% CI: −5.16, −2.25, $p \leq 0.001$).

To assess the influence of potential moderators on the estimated effect size, we performed random-effects meta-regression. We found that changes in WC were independent from the dosage of curcumin (slope: −.0014; 95% CI: −.014 to .011; $P = 0.768$) and duration of supplementation (slope: −.0621; 95% CI: −.562 to .437; $P = 0.747$). with regards to the non-linear dose-response analysis, we found a significant effect of duration of curcumin supplementation on WC ($P_{\text{non-linearity}} = 0.04$) (Fig. 3-C). otherwise, we failed to find such effect for curcumin dosage ($P_{\text{non-linearity}} = 0.38$) (Fig. 4-C).

Although visual inspection of the funnel plot revealed asymmetry, this was not confirmed by Egger's test ($P = 0.91$).

Discussion

In the present systematic review and meta-analysis, we summarized available data from eleven eligible RCTs which examined the effects of curcumin supplementation on body composition indices including in adults. The main results of this study were that curcumin supplementation comparing to control significantly reduced body weight and BMI.

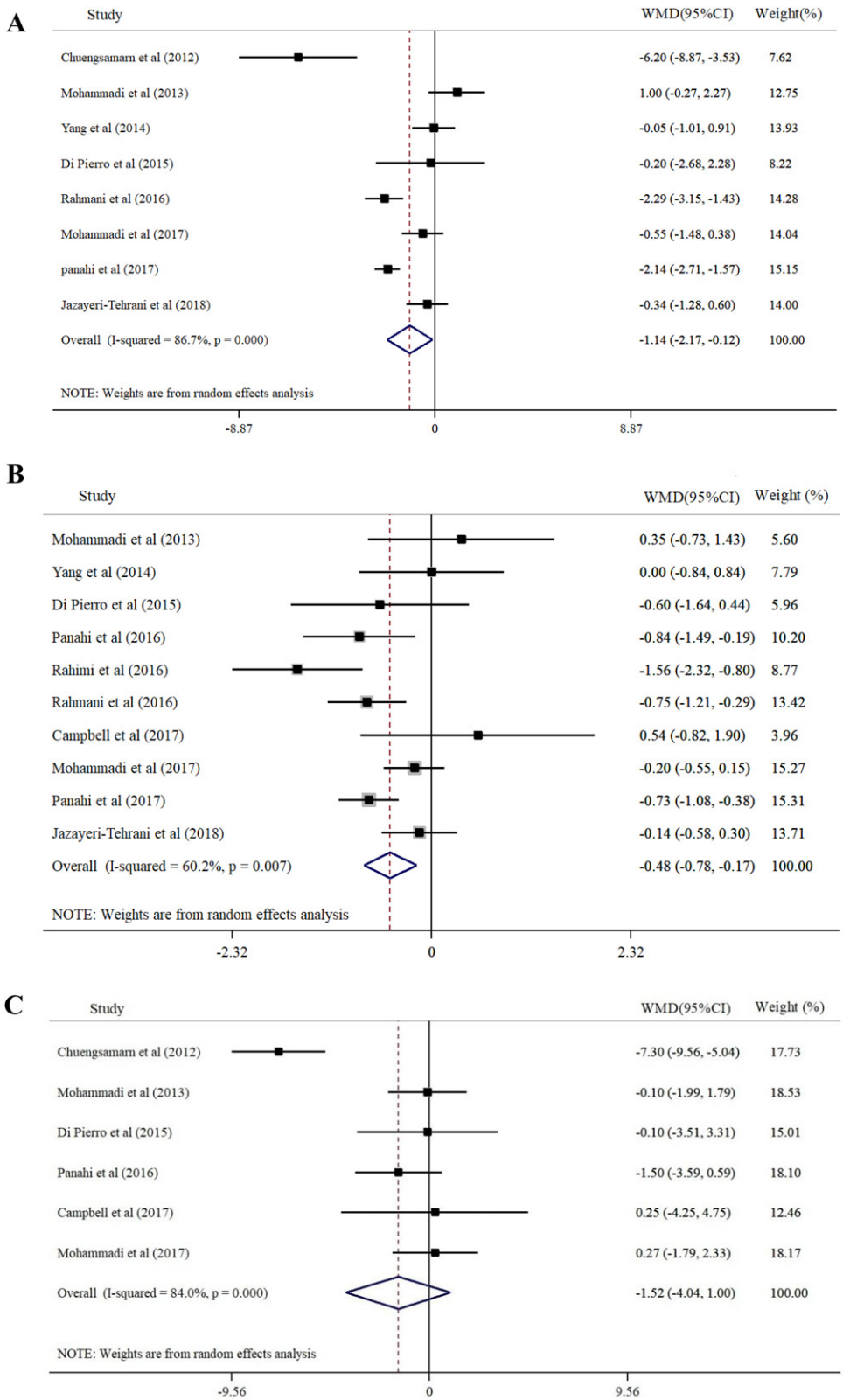

Figure 2. Forest plot detailing weighted mean difference and 95% confidence intervals (CIs) for the effect of curcumin supplementation on body weight, BMI, and waist circumference.

However, there found no significant effect of curcumin on WC.

Curcumin significantly reduced body weight and BMI in this meta-analysis. In line with our study, a systematic review of clinical trials showed that curcumin supplementation may reduce obesity and overweight in adults (Hariri and Haghighatdoost 2018). However, supplementation with curcumin in a clinical trial did not change body weight and BMI in obese adults, as compared to placebo (Mohammadi et al. 2013). In addition, curcumin did

Table 2. Results of subgroup analysis of included randomized controlled trials in meta-analysis of curcumin supplementation and body composition.

Variable	Dose (mg/d)		Duration (week)		Mean baseline BMI		Mean age (year)	
Body weight	<1000	≥1000	<8	≥8	<30	≥30	<45	≥45
No. of comparison	4	4	3	5	3	5	5	3
WMD (95% CI)	−1.09 (−1.60, −0.57)	−1.40 (−1.85, −0.95)	−0.02 (−0.74, 0.69)	−1.62 (−2.0, −1.23)	−2.21 (−2.75, −1.67)	−0.66 (−1.09, −0.23)	−1.14 (−1.54, −0.74)	−1.56 (−2.18, −0.93)
p value	<0.001	<0.001	0.94	<0.001	<0.001	0.003	<0.001	<0.001
I^2 (%)	74.3	92.5	46.4	88.3	82.1	82.1	85.5	91.6
p-heterogeneity	0.009	<0.001	0.15	<0.001	0.004	<0.001	<0.001	<0.001
BMI								
No. of comparison	6	4	6	4	4	6	7	3
WMD (95% CI)	−0.42 (−0.64, −0.20)	−0.59 (−0.87, −0.31)	−0.53 (−0.73, −0.33)	−0.35 (−0.70, −0.01)	−0.85 (−1.12, −0.57)	−0.25 (−0.48, −0.03)	−0.39 (−0.59, −0.19)	−0.79 (−1.15, −0.43)
p value	<0.001	<0.001	<0.001	0.03	<0.001	0.02	<0.001	<0.001
I^2 (%)	68.2	49.5	43.8	76.8	25.6	35.2	47.8	72.8
p-heterogeneity	0.008	0.11	0.11	0.005	0.25	0.17	0.07	0.02
WC								
No. of comparison	3	3	3	3	3	3	5	1
WMD (95% CI)	0.181 (−1.461, 1.823)	−2.551 (−3.743, −1.359)	0.045 (−1.244, 1.334)	−3.713 (−5.167, −2.258)	−3.485 (−4.886, −2.084)	0.085 (−1.245, 1.415)	−0.345 (−1.411, 0.722)	−7.300 (−9.564, −5.036)
p value	0.829	<0.001	0.946	<0.001	<0.001	0.901	0.527	<0.001
I^2 (%)	0.0	91.8	0.0	88.2	89.0	0.0	0.0	–
p-heterogeneity	0.983	<0.001	0.963	<0.001	<0.001	0.964	0.797	–

BMI; body mass index, WC; waist circumference, WMD; weight mean difference.

not show a significant effect on body weight in patients with metabolic syndrome (Yang et al. 2014). It should be noted that short-term study duration has been considered as a limitation in both of that studies. Therefore, further longitudinal studies are needed to shed light on this issue.

We failed to find a significant effect of curcumin supplementation on WC in this study. Several previous studies also could not find a significant effect of curcumin on WC (Mohammadi et al. 2013; Di Pierro et al. 2015; Campbell et al. 2017; Mohammadi et al. 2017). For instance, curcumin intake (1000 mg/day) for 30 days compared to control could not affect WC in a clinical trial in obese adults (Mohammadi et al. 2013). However, findings from another clinical trial investigating the effect of supplementation with curcumin (1000 mg/day) on patients with Non-alcoholic fatty liver disease (NAFLD) for 8 weeks, showed a significant reduction in WC after the supplementation than placebo (Panahi, Kianpour, et al. 2017). Although the effect of curcumin on WC was not significant in our meta-analysis of whole data, it was negatively significant in studies that were performed on overweight subjects, used ≥1000 mg/d curcumin, and those with ≥8 weeks of duration. It should be noted that despite body weight and BMI, WC is considered as a good indicator of abdominal obesity. It is suggested that longer intervention duration is needed to influence abdominal than general obesity (Gearon et al. 2017). Due to few available studies on the effect of curcumin supplementation on WC, further clinical trials are required to reach a firm conclusion in this area.

The exact mechanism through which curcumin might affect body weight and BMI have not been still understood. However, curcumin down-regulates Janus Kinase (JNK) enzyme which has been suggested to have a fundamental role in obesity pathogenesis (Shao-Ling et al. 2009; Hirosumi et al. 2002). Curcumin may also inhibit 11βHSD1 enzyme which activates cortisol (Hu et al. 2013). Higher concentrations of cortisol in adipocytes induces central obesity (Kumari et al. 2010). Curcumin also reduces obesity by inhibition of adipocyte differentiation in the early stages through suppression of transcription factor Peroxisome Proliferator-Activated Receptor-γ (PPAR-γ) and by enhancing monophosphate-activated protein kinase and consequently lipolysis (Lee et al. 2009; Bradford 2013). Moreover, some previous studies have shown that curcumin supplementation may reduce energy expenditure (Pu et al. 2013; Bradford 2013).

To the best of our knowledge, this study is the first meta-analysis on the effect of curcumin on body composition indices. No evidence of publication bias was seen in this meta-analysis, as examined by the Egger regression test. Moreover, an individual study or a group of studies had no significant effect on the findings, as assessed by the sensitivity analysis. Furthermore, all included studies were published in the recent years. In addition, we could find sources of between-study heterogeneity in our subgroup analyses. Beside these strengths, several limitations of this study should be considered. The main limitation of the study is that most of the included studies were conducted with unformulated curcumin, which has low bioavailability its owing because of poor absorption, rapid metabolism, and rapid removal from the body. Several methods have been made to enhance the bioavailability of curcumin including adjunct to piperine (black pepper), liposomal curcumin, nanoparticles, phospholipid complexes, and an amorphous form (Anand et al. 2007; Murdande et al. 2011). Therefore, the effect of the different dosages directly is not applicable. Also, included studies had a low to moderate methodological quality. They were done on participants with different health statuses and a wide range of age. In addition, significant heterogeneity among studies suggests that the effects of curcumin on obesity indices should be further investigated. This heterogeneity might be explained by the

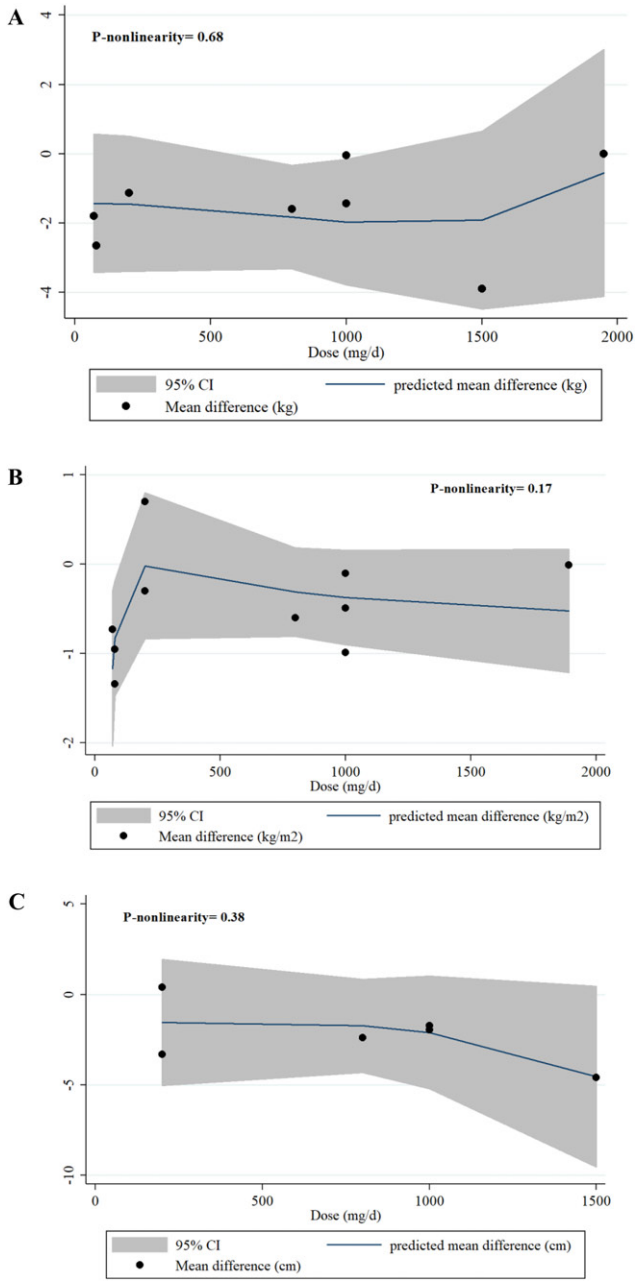

Figure 3. Dose-response relations between curcumin dosage (mg/d) and mean difference (kg) in body weight, BMI, and WC.

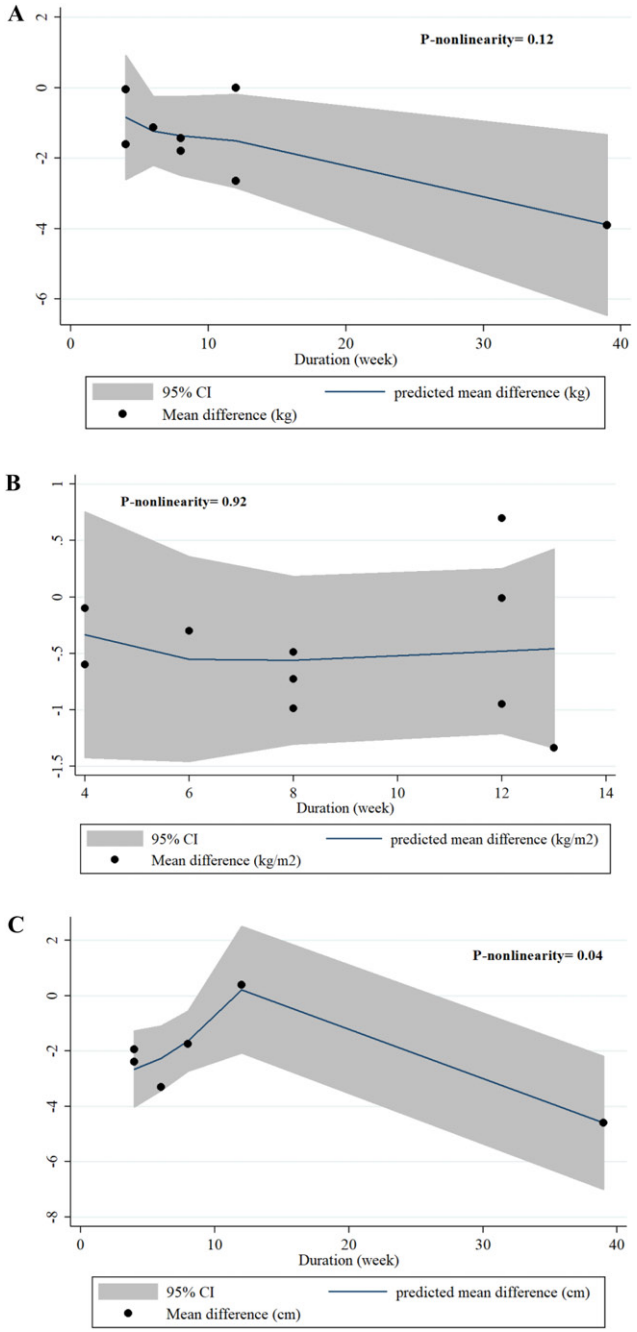

Figure 4. Dose-response relations between duration of curcumin supplementation (mg/d) and mean difference (kg) in body weight, BMI, and WC.

use of different methodologies, evaluation of different populations, using curcumin in various dosages and in different durations.

Conclusions

In conclusion, the current meta-analysis showed a significant effect of curcumin supplementation on body weight and BMI, as compared to control. However, the effect of curcumin on WC was not significant, except for studies on overweight subjects, those used $\geq$1000 mg/d curcumin, and $\geq$8 weeks of duration. Further RCTs using different doses of curcumin and a long-term intervention period are required to shed light on this issue.

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The authors' responsibilities were as follows; SMM and AE conceived the study. The literature search and screening data were done by SMM and MMG. Data extraction and quality assessment were performed independently by HKV, MMG, and SMM. SMM, AM and AE analyzed and interpreted data and wrote the manuscript. AE supervised the study. All authors read and approved the final manuscript.

Disclosure statement

The authors declared no conflicts of interest.

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