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Original Research Article

# The effect of curcumin supplementation on weight loss and anthropometric indices: an umbrella review and updated meta-analyses of randomized controlled trials

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A B S T R A C T

**Background:** Curcumin supplementation may promote weight loss and ameliorate obesity-related complications through its antioxidative and anti-inflammatory properties.

**Objective:** An umbrella review and updated meta-analysis of randomized controlled trials (RCTs) was conducted to evaluate the effect of curcumin supplementation on anthropometric indices.

**Methods:** Systematic reviews and meta-analyses (SRMAs) of RCTs were identified from electronic databases (Medline, Scopus, Cochrane, and Google Scholar) up to 31 March, 2022, without language restriction. SRMAs were included if they assessed curcumin supplementation on any of the following: BMI, body weight (BW), or waist circumference (WC). Subgroup analyses were performed, stratifying by patient types, severity of obesity, and curcumin formula. The study protocol was a priori registered.

**Results:** From an umbrella review, 14 SRMAs with 39 individual RCTs were included with a high degree of overlap. In addition, searching was updated from the last search of included SRMAs in April 2021 up to 31 March, 2022, and we found 11 additional RCTs, bringing the total up to 50 RCTs included in the updated meta-analyses. Of these, 21 RCTs were deemed of high risk of bias. Curcumin supplementation significantly reduced BMI, BW, and WC with mean differences (MDs) of −0.24 kg/m$^2$ (95% CI: −0.32, −0.16 kg/m$^2$), −0.59 kg (95% CI: −0.81, −0.36 kg), and −1.32 cm (95% CI: −1.95, −0.69 cm), respectively. The bioavailability-enhanced form reduced BMI, BWs, and WC more, with MDs of −0.26 kg/m$^2$ (95% CI: −0.38, −0.13 kg/m$^2$), −0.80 kg (95% CI: −1.38, −0.23 kg) and −1.41 cm (95% CI: −2.24, −0.58 cm), respectively. Significant effects were also seen in subgroups of patients, especially in adults with obesity and diabetes.

**Conclusions:** Curcumin supplementation significantly reduces anthropometric indices, and bioavailability-enhanced formulas are preferred. Augmenting curcumin supplement with lifestyle modification should be an option for weight reduction.

This trial was registered at PROSPERO as CRD42022321112 (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022321112).

*Keywords*: curcumin, turmeric, umbrella review, obesity, anthropometric index, BMI, body weight, waist circumference

## Introduction

Obesity is a complex disease caused by a positive balance between the energy intake and energy expenditure, contributing to excessive fat accumulation and adipose tissue dysfunction [1]. The prevalence of obesity has been increasing worldwide, and obesity increases the risk for many diseases, particularly type 2 diabetes mellitus (T2DM), dyslipidemia, nonalcoholic fatty liver disease (NAFLD), and polycystic ovary syndrome (PCOS). One of the mechanisms linking obesity with metabolically related diseases is a proinflammatory state

*Abbreviations:* BW, body weight; CKD, chronic kidney disease; MA, meta-analyses; MetS, metabolic syndrome; NAFLD, nonalcoholic fatty liver disease; PCOS, polycystic ovary syndrome; RCT, randomized controlled trial; ROB, risk of bias; SMD, standardized mean difference; SRMA, systematic review and meta-analysis; T2DM, type 2 diabetes mellitus; WC, waist circumference; WMD, weighted mean difference.

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associated with excessive body fat, particularly visceral adipose tissue, consisting of hormonally active adipocytes accumulating around intra-abdominal organs [2]. Excessive visceral adiposity induces chronic low-grade inflammation through the production of tumor necrosis factor α and interleukin (IL)-6, along with a reduction in circulating adiponectin levels [3].

Currently, the use of medicinal herbal supplements has become popular, and ~80% of the population had used them as a part of their treatment [4]. Turmeric, or *Curcuma longa*, is a member of the ginger family cultivated in Asian countries, and it is one of the most common herbs used as a culinary ingredient or a dietary supplement [5]. It has been used as a traditional medicine for centuries in Asia because of its anti-oxidant, anti-inflammatory, anticarcinogenic, antidiabetic, and antihyperlipidemia properties [6]. Curcumin is the most bioactive compound within the turmeric rhizome [7], which has highly pleiotropic properties in multiple signaling pathways [7,8] and pharmacologic activities, such as anti-inflammatory activity and modulation of oxidative conditions [9,10]. The major limitation of its therapeutic efficacy is its low bioavailability owing to poor absorption, fast metabolism, and rapid systemic elimination [11]. Hence, there have been recent attempts to increase its oral bioavailability by developing other forms of drug delivery, such as micelles, phospholipid complexes, nanoparticles, or even by adding some ingredients [7]. It has been reported in the literature that curcumin could promote weight loss and ameliorate obesity-related complications [12]. The use of curcumin has been growing with several clinical trials reported over the past few years [13], yet the results have still been inconclusive because the formulation and doses of curcumin used may have acted differently in each type of patient.

Given the substantial body of evidence in the literature, we aimed to conduct an umbrella review to systemically summarize and assess the effect of curcumin supplementation on anthropometric indices stratified by comorbidities, severity of obesity, and forms of curcumin such as whole compound, curcumin extract, and bioavailability-enhanced forms.

## Methods

### Literature search and selection criteria

The study protocol was a priori registered in the international prospective register of systematic reviews (PROSPERO; registration code CRD42022321112). A review of systematic reviews and meta-analyses (SRMAs) was conducted in compliance with standardized procedures [14,15]. Electronic databases such as Cochrane Central, PubMed Medline, and Elsevier Scopus were searched to identify relevant studies through to 31 March, 2022, without language restriction. A 2-stage search was performed. First, SRMAs were identified since inception to 31 March, 2022. Second, individual studies published since the last search in those SRMAs to 31 March, 2022, were identified. Additional articles from Google Scholar, related articles found in reference lists of identified articles, and relevant articles suggested by the co-authors were also included. Details of the systematic search terms are described in **Supplemental Data 1**.

### Eligibility criteria and exclusion criteria

Studies were selected independently by 2 authors (CU and NP), and disagreements were resolved through consensus with a third author (PCS). Studies were eligible if they met all of the following criteria: *1*) SRMAs of randomized controlled trials (RCTs), *2*) containing a comparison of the effect of curcumin supplementation with usual or standard care, and *3*) defining outcomes as any anthropometric indices such as body weight (BW), BMI, and waist circumference (WC) measured before and after receiving interventions. Interventions of interest were any form of curcumin supplementation such as whole compound, curcumin extract, and bioavailability-enhanced formulas. Bioavailability-enhanced formulas included adding piperine, nanomicelle formation, phospholipid complexation, phytosomal formation, liposome, and amorphous dispersion. For the updated meta-analysis (MA), inclusion criteria were all of the following: *1*) a parallel-arm or crossover RCTs in adults aged 18 y or older, *2*) using any form of curcumin supplementation, and *3*) containing an assessment any of anthropometric indices such as BMI, BW, and WC. Studies using curcumin in combination with other nutritional compounds except for adding piperine were excluded. If individual articles contained duplications of registered numbers of studies, the study with the largest number of participants was chosen for updated MA.

### Outcomes of interests

The primary outcome of interest was change in BMI after supplementation. The secondary outcomes were changes in BW and WC after supplementation. The outcomes were measured at the beginning and at the end of the individual studies.

### Data extraction

Two authors (CU and NP) independently abstracted the following data from each SRMA: the first author's name, sample size, year of publication, date of the last search, country of study, study design, dosage of curcumin, type/form of curcumin, duration of supplementation, type of control, type of SRMA, the degree of heterogeneity by $I^2$ and the Cochrane Q test result, effect size along with the 95% CI, assessment of the quality of included studies, and conflict of interest and funding statements. In addition, the following data from individual RCTs included in previous or newly identified SRMAs were also directly abstracted: the first author's name, sample size, year of publication, type of study, type of patients, age, dosage of curcumin, type and form of curcumin, duration of supplementation, outcomes, and registry number. The mean and SD of outcome values were extracted at pretreatment and posttreatment measurement time points stratified by treatment groups. If a report only provided the 95% CI, SE and SD were estimated using the formula in the Cochrane Handbook for Systematic Reviews of Interventions [16].

### Quality assessment

The quality of SRMAs and individual RCTs were assessed using the Assessment of Multiple Systematic Reviews-2 (AMSTAR2) checklist [17] and the Cochrane Collaboration's tool for assessing the risk of bias (ROB) [18] by 2 authors (CU and NP). If there were any disagreements, consensus was reached in collaboration with a third author (PCS).

### Data analysis

The degree of overlap between reports was assessed by the corrected covered area method and classified as slight, moderate, high, and very high degree of overlap if the corrected covered area was $\leq$5%, 6%–10%, 11%–15%, and $>$15%, respectively [19]. For an umbrella review, effect sizes were summarized and stratified by types of patients, that is, the preplanned specific disease groups.

For updated MAs, weighted mean differences (WMDs) of continuous outcomes between curcumin and control groups were calculated, and these were pooled across studies by using a random-effects model if heterogeneity was present. Otherwise, a fixed-effects model was used. Heterogeneity was assessed using Cochrane Q test and Higgin $I^2$ statistic. Heterogeneity was adjudicated to be present if the $P$ of the Q test was $<0.1$ or $I^2 \geq 50\%$ [20,21]. A subgroup analysis was performed by patient type of comorbidity, severity of obesity, and curcumin forms such as whole compound, curcumin extract, and bioavailability-enhanced forms. Publication bias was assessed by a funnel plot along with Egger test. Sensitivity analyses were conducted by excluding studies that have high ROB and studies with small-study effects by leave-1-out crossvalidation.

All analyses were performed using Review Manager (RevMan; version 5.4.1) [22] and R (version 4.1.2; R Core Team] [23] using the forestplot package for forest plots and using the metafor package for Egger test and funnel plots. A $P$ value of $<0.05$ was considered statistical significance except for Cochrane Q test, for which a $P$ value of $<0.01$ was considered statistically significant.

## Results

A total of 193 studies were identified, of which 14 were SRMAs [24–37] eligible for the umbrella review. Within these, 39 individual RCTs were selected for repooling for the updated MA. The degree of overlap of included individual RCTs on the primary objective was 12.18%, indicating a high degree of overlap among the primary studies (Supplemental Table 1).

A total of 82 individual RCTs were identified since the last search of SRMA in April 2021, of which 9 RCTs were eligible for the updated MA. In addition, 2 RCTs were identified and eligible from the reference lists, resulting in 50 individual RCTs [38–87] for repooling for the updated MA (Figure 1).

### Characteristics of the included studies

The characteristics of the included studies are summarized in Table 1. Of the 14 SRMAs included [24–37], the number of included RCTs ($N$) ranged from 4 to 18, with sample sizes ($n$) of 198 to 1544 (Table 1). The studies were published between 2019 and 2022, with a duration of follow-up ranging from 4 to 39 wk, and the median follow-up time was 8 wk. The mean age of participants ranged from 14.7 to 70.0 y. The study population included adults with obesity ($N = 5$, $n = 252$), NAFLD ($N = 10$, $n = 634$), PCOS ($N = 5$, $n = 336$), metabolic syndrome (MetS, $N = 8$, $n = 513$), T2DM ($N = 10$, $n = 702$), chronic kidney disease (CKD) ($N = 2$, $n = 110$) and hyperlipidemia ($N = 2$, $n = 123$). Of the 50 included studies, there were 3 types of curcumin formulations such as whole compounds ($N$ of turmeric rhizome, powder, or capsules $= 5$) with dosages ranging from 2000 to 3000 mg/d, curcumin extracts with the dosages ranging from 500 to 1950 mg/d ($N = 15$), and bioavailability-enhanced formulas ($N = 27$). Bioavailability-enhanced formulas had various dosages, including curcumin ranging from 500 to 1000 mg and adding piperine 5 to 10

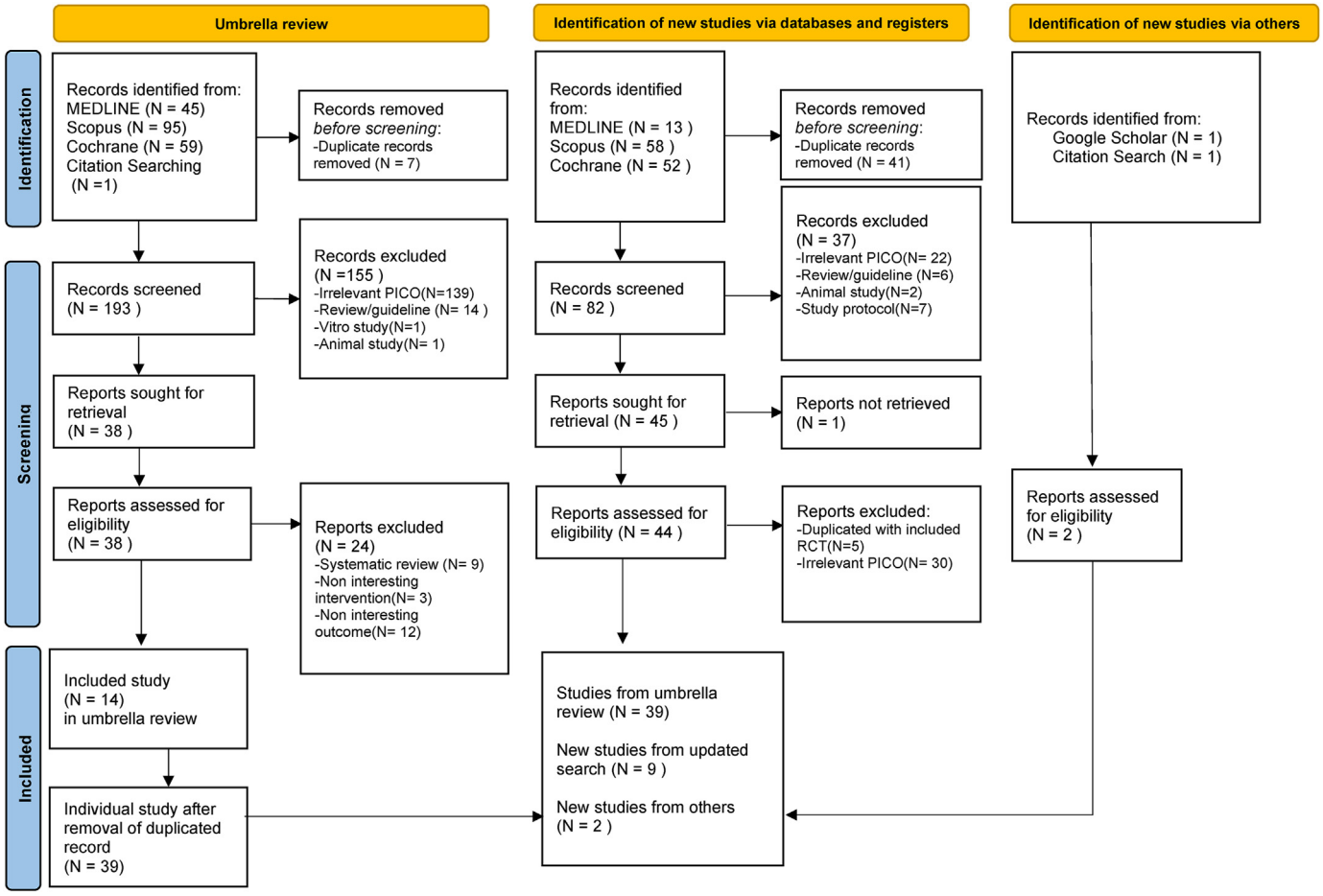



**FIGURE 1.** PRISMA flow diagram for updated systematic reviews, which included searches of databases, registers, and other sources.

**TABLE 1**
Baseline characteristics of included systematic reviews and meta-analyses in anthropometric indices

| Author, Year | Country | End search | *N* | *n* | Female (%) | Range of mean ages (y) | Patients | Intervention | Dose (mg/d) | Comparator | Outcome | Follow-up time (wk) | Conflict of interest |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Nouri et al., 2022 [24] | Iran | Feb 2021 | 4 | 198 | 198 (100) | 27.6–30.97 | PCOS | Curcumin | 93.34–1500 | Placebo | FBG, insulin level, HOMA-IR, QUICKI, BMI | 6–12 | None |
| Khalili and Nammi, 2022 [25] | Iran | April 2021 | 14 | 904 | 346 (38) | 41.8–66.72 | NAFLD | Curcumin | 80–2000 | Placebo | AST, ALT, FBG, TC, TG, LDL, HDL, BMI | 4–12 | None |
| Abdelazeem et al., 2021 [26] | USA | 5 May 2021 | 5 | 296 | 296 (100) | 27.6–30.97 | PCOS | Curcumin, highly bioavailable gel-optimized curcumin, nanomicelle | 80–1500 | Placebo | FBG, insulin level, -IR, QUICKI, TC, TG, LDL, HDL, sex hormone, BW, WC, BMI, CRP | 6–12 | None |
| Zheng et al., 2021 [27] | China | 22 Mar 2021 | 8 | 531 | 287 (54.0) | 41–70 | T2DM | Curcumin | 180–1500 | Placebo | FBG, HbA1c, TC, LDL, HDL, TG, BMI | 8–24 | NA |
| Zhang et al., 2021 [28] | China | 3 Sep 2020 | 12 | 643 | 344 (53.5) | 43–59.16 | T2DM | Curcumin, curcuminoids, turmeric, nanocurcumin | 80–1500 | Placebo | FBG, HbA1c, HOMA-IR, TC, LDL, HDL, TG, adiponectin, BMI | 8–24 | None |
| Ashtary-Larky et al., 2021 [29] | Iran | May 2021 | 9 | 337 | 195 (57.9) | 41.8–62.3 | HD, NAFLD, T2DM, MetS, migraine | Nanocurcumin | 40–120 | Placebo | FBG, HbA1c, insulin level, HOMA-IR, TC, TG, LDL, HDL, CRP, IL-6, TNF-α, BP, WC, BMI | 6–12 | None |
| Altobelli et al., 2021 [30] | Italy | 2000 to 2020 | 7 | 476 | 241 (50.6) | 55–59 | Uncomplicated T2DM | Curcumin | 80–2100 | Placebo | HbA1c, HOMA-IR, TC, TG, LDL, HDL, BMI | 8–24 | None |
| Mousavi et al., 2020 [31] | Iran | Aug 2018 | 11 | 846 | 662 (78.3) | 25.91–59.03 | Prediabetic, T2DM, obese, MetS, NAFLD | Curcumin, curcuminoids, nanomicelle, *Curcuma longa* | 70–1900 | Placebo | BW, WC, BMI | 4–39 | None |
| Jalali et al., 2020 [32] | Iran | Sep 2019 | 9 | 588 | 272 (46.3) | 37.75–48.95 | NAFLD | Curcumin | 50–1500 | Placebo | AST, ALT, FBG, HbA1c, insulin level, HOMA-IR, TC, TG, LDL, HDL, BW, WC, BMI | 8–12 | None |
| Baziar and Parohan, 2020 [33] | Iran | March 2019 | 8 | 567 | 216 (38.1) | 42–54 | NAFLD | Curcumin, turmeric, nanocurcumin | 70–3000 | Placebo | BW, WC, BMI | 8–12 | None |
| Wei et al., 2019 [34] | China | Mar 2018 | 4 | 229 | 110 (48) | 40.38–56.67 | NAFLD | Curcumin, turmeric powder | 500–3000 | Placebo | AST, ALT, FBG, HbA1c, insulin level, HOMA-IR, TC, TG, LDL, HDL, BW | 8–24 | None |

(*continued on next page*)

**TABLE 1** (*continued*)

| Author, Year | Country | End search | *N* | *n* | Female (%) | Range of mean ages (y) | Patients | Intervention | Dose (mg/d) | Comparator | Outcome | Follow-up time (wk) | Conflict of interest |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Jafarirad et al., 2019 [35] | Iran | 27 Jan 2019 | 8 | 449 | 220 (49) | 40–65 | NAFLD | Curcumin, turmeric | 80–3000 | Placebo | BW, WC, BMI | 8–24 | None |
| Azhdari et al., 2019 [36] | Iran | Sep 2018 | 7 | 503 | 224 (44.5) | 38.05–59.32 | MetS | Curcumin, turmeric, curcuminoids in capsule or powder | 800–2400 | Placebo | FBG, TG, HDL, BP, WC | 4–12 | None |
| Akbari et al., 2019 [37] | Iran | Jan 2018 | 18 | 1544 | 853 (55.2) | 14.7–60.95 | Obese, MetS, NAFLD, T2DM, DLP | Curcumin, turmeric, curcuminoids, nanocurcumin (powder and capsule) | 80–2400 | Placebo | BW, WC, BMI, hip ratio, leptin, adiponectin | 4–39 | None |

AST, aspartate transaminase; ALT, alanine transaminase; BP, blood pressure; BW, bodyweight; CRP, c-reactive protein; DLP, dyslipidemia; FBG, fasting blood glucose; HbA1c, hemoglobin A1c; HD, hemodialysis; HDL, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LDL, low-density lipoprotein cholesterol; MetS, metabolic syndrome; *N*, Number of included studies; *n*, number of subjects; NA, not available; NAFLD, nonalcoholic fatty liver disease; PCOS, polycystic ovary syndrome; QUICKI, quantitative insulin-sensitivity check index; T2DM, type 2 diabetes mellitus; TC, total cholesterol; TG, triglyceride; WC, waist circumference.

mg/d, nanocurcumin ranging from 80 to 180 mg/d, liposome as phytosomal or phospholipid ranging from 250 to 1000 mg/d, micelles at 294 mg/d, and amorphous dispersion at 500 mg/d. BMI (in kg/m$^2$) was classified according to the World Health Organization (WHO) as <25 ($N = 2$), 25–29.9 ($N = 32$), 30–34.9 ($N = 15$), and 35.0–39.9 ($N = 1$). The characteristics of the included RCTs are summarized in Supplemental Table 2.

## Quality assessment

The AMSTAR2 assessments show that 3 [26,34,37], 5 [28–31,33], 4 [25,32,35,36], and 2 [24,27] SRMAs had high, moderate, low, and critically low quality, respectively (Supplemental Table 3). For the ROB assessment, 21 of the 50 RCTs were classified as high-risk studies (Supplemental Figures 1 and 2).

## Anthropometric indices

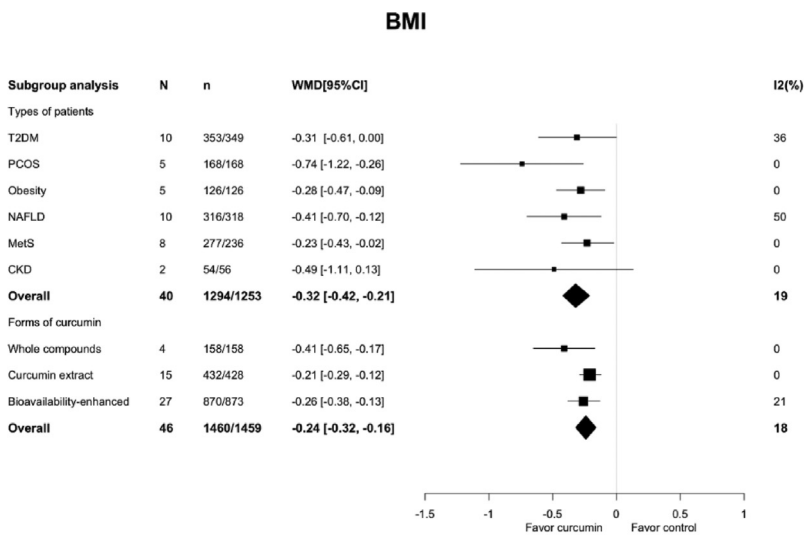
Curcumin and its active ingredients were used as treatment supplements, which were compared with either a placebo or a standard treatment. A relative MD between pretreatment and posttreatment was estimated for each treatment and compared between the treatment groups across RCTs. One SRMA by Zheng et al. [27] pooled the MD calculated to make it similar to other SRMAs. In addition, the effect size of the SRMA in the study by Zhou et al. [88] was transformed from exponentiated standard MD to standardized mean difference (SMD), which was more appropriate and presented in a forest plot. The results of repooling effect sizes on anthropometric indices and lipid parameters are described further.

### *BMI*

The effects of curcumin supplementation on BMI are displayed in Supplemental Figure 3A. Two SRMAs reported that curcumin supplementation did not show a significant effect on BMI in patients with PCOS [24,26]. Of the 4 SRMAs [25,32,33,35] in patients with NAFLD, only 1 MA [33] showed a significant lowering of BMI compared with that by placebo, with a WMD of −0.34 kg/m$^2$ (95% CI: −0.64, −0.04 kg/m$^2$; $I^2 = 63.2\%$) and a high heterogeneity. Three SRMAs [27,28,30] were conducted among patients with T2DM, but none of the SRMAs showed significant effects compared with controls. Two [31,37] of the 3 SRMAs in mixed populations (i.e., patients with MetS and related disorders) showed a significant BMI reduction with an SMD of −0.37 kg/m$^2$ (95% CI: −0.61, −0.13 kg/m$^2$; $I^2 = 69.7\%$) and WMD of −0.48 kg/m$^2$ (95% CI: −0.78, −0.17 kg/m$^2$; $I^2 = 60.2\%$), respectively, both of which had a high heterogeneity.

Our updated MA showed a reduction of BMI in the curcumin group relative to the control group with a WMD of −0.24 kg/m$^2$ (95% CI: −0.32, −0.16 kg/m$^2$; $I^2 = 18\%$) (Figure 2). Subgroup analyses according to the patient comorbidities showed significant reductions in BMI in adults with PCOS, obesity, NAFLD, and MetS with WMDs of −0.74 (95% CI: −1.22, −0.26; $I^2 = 0\%$), −0.28 (95% CI: −0.47, −0.09; $I^2 = 0\%$), −0.41 (95% CI: −0.70, −0.12; $I^2 = 50\%$), and −0.23 (95% CI: −0.43, −0.02; $I^2 = 0\%$), respectively (Figure 2A and Supplemental Figure 4A). However, subgroup analyses did not show significant reductions in BMI for adults with T2DM and CKD (Figure 2A and Supplemental Figure 4A). In addition, all forms of curcumin such as whole compounds, curcumin extract, and bioavailability-enhanced formulas significantly reduced BMI (in kg/m$^2$), with WMDs of −0.41 (95% CI: −0.65, −0.17; $I^2 = 0\%$), −0.21 (95% CI: −0.29, −0.12; $I^2 = 0\%$), and −0.27 (95% CI: −0.39, −0.15; $I^2 = 29\%$), respectively (Figure 2 and Supplemental Figure 5A). A significant effect of curcumin was seen in subjects with BMIs ranging

A

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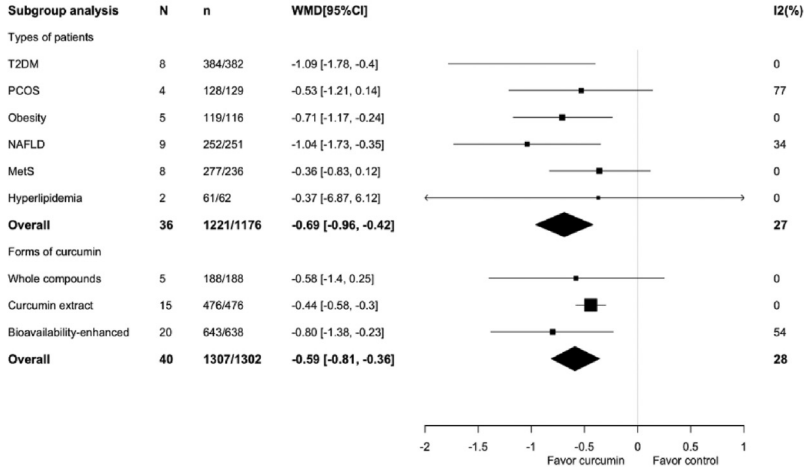


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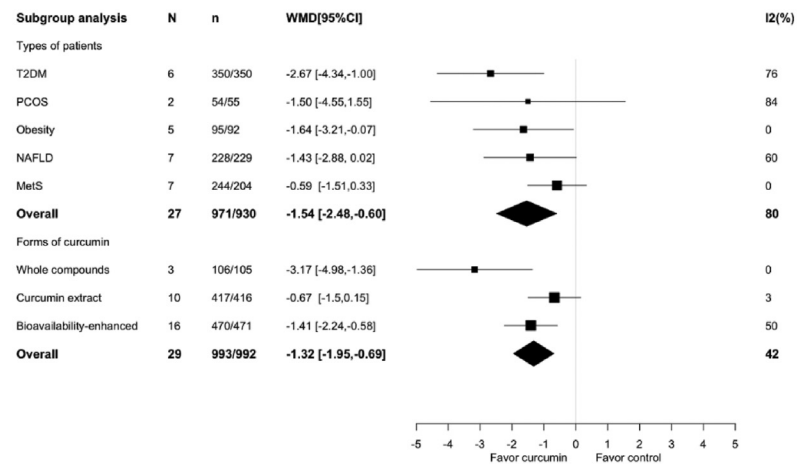


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**TABLE 2**
The subgroup analysis according to baseline BMI on anthropometric outcomes

| Outcome | *N* | *n*1/*n*0 | WMD (95% CI)[1] | Heterogeneity | |
|---|---|---|---|---|---|
| | | | | $I^2$ (%) | *P*-heterogeneity |
| BMI (kg/m$^2$) | | | | | |
| BMI <25 | 2 | 64/64 | 0.69 (−0.91, 2.29) | 51 | 0.15 |
| BMI 25–29.9 | 27 | 898/898 | −0.25 (−0.39, −0.1) | 58 | 0.0001 |
| BMI ≥30 | 16 | 498/457 | −0.12 (−0.2, −0.03) | 10 | 0.34 |
| Overall | 45 | 1460/1419 | −0.19 (−0.28, −0.1) | 49 | 0.0002 |
| Body weight (kg) | | | | | |
| BMI 25–29.9 | 23 | 800/800 | −0.68 (−0.89, −0.47) | 26 | 0.12 |
| BMI ≥30 | 16 | 507/462 | −0.51 (−0.95, −0.08) | 55 | 0.004 |
| Overall | 39 | 1307/1262 | −0.61 (−0.83, −0.40) | 43 | 0.0003 |
| Waist circumference (cm) | | | | | |
| BMI 25–29.9 | 17 | 672/675 | −1.52 (−2.20, −0.85) | 91 | <0.00001 |
| BMI ≥30 | 11 | 321/277 | −0.95 (−1.86, −.04) | 42 | 0.07 |
| Overall | 28 | 993/952 | −1.34 (−1.87, −0.81) | 86 | <0.00001 |

$I^2$, percentage degree of heterogeneity; *N*, number of included studies; *n*1, number of participants in the intervention group; *n*0, number of participants in the control group; WMD, weighted mean difference.
[1] This was performed by a random-effects model by Review Manager (RevMan), version 5.4.1.

from 25 to 29.9 and ≥30 kg/m$^2$ but not in those with normal BMI levels (Table 2).

### *Body weight*

There were no significant effects of curcumin in patients with PCOS and NAFLD [26,32,33,35] (Supplemental Figure 3B) except for those in the study by Wei et al. [34], which included only 2 studies and was a subset of another SRMA in patients with NAFLD. Two SRMAs, by Akbari et al. [37] including adults with obesity, MetS, NAFLD, T2DM, or dyslipidemia and by Mousavi et al. [31], assessed curcumin supplements in patients with prediabetes, T2DM, obesity, MetS, and NAFLD. These supplements could significantly reduce BW with an SMD of −0.23 kg (95% CI: −0.39, −0.06 kg; $I^2$ = 45.7%) and WMD of −1.14 kg (95% CI: −2.17, −0.12 kg; $I^2$ = 86.7%), but the study by Mousavi et al. had a high heterogeneity [31]. Ashtary et al. [29] included mixed populations and reported no significant results in reduction of BW, comparing nanocurcumin supplement with placebo.

Our updated MA showed a significant reduction of BW with a WMD of −0.59 kg (95% CI: −0.81, −0.36 kg; $I^2$ = 28%) (Figure 2B). Subgroup analyses also suggested a significant reduction in BW in adults with T2DM, obesity, or NAFLD, with WMDs of −1.09 kg (95% CI: −1.78, −0.4 kg; $I^2$ = 0%), −0.71 kg (95% CI: −1.17, −0.24 kg; $I^2$ = 0%), and −1.04 kg (95% CI: −1.73, −0.35 kg; $I^2$ = 34%), respectively (Figure 2B and Supplemental Figure 4B). Moreover, curcumin extract and bioavailability-enhanced formula (but not whole compound) significantly reduced BW (Figure 2B and Supplemental Figure 5B). Furthermore, a significant effect of curcumin was seen in subjects with BMI range categories of 25–29.9 and ≥30 kg/m$^2$ (Table 2).

### *Waist circumference*

In patients with NAFLD, 2 of the 4 SRMAs showed significant curcumin effects in reduction in WC with an SMD of −1.01 cm (95% CI: −1.3, −0.71 cm; $I^2$ = 96.1%) [32] and a WMD of −2.12 cm (95% CI: −3.26, −0.98 cm; $I^2$ = 27.4%) [33], of which the first MA was a subset of the second MA (Supplemental Figure 3C). There was no significant difference in WC change between curcumin supplement and placebo in patients with PCOS [26], MetS [36], or mixed populations [29,31] with the exception of those in the study by Akbari et al.[37], who reported an SMD of −0.25 cm (95% CI: −0.44, −0.05 cm; $I^2$ =42.1%).

Our repooling MA based on 29 RCTs showed a significant reduction in WC with a WMD of −1.32 cm (95% CI: −1.95, −0.69 cm; $I^2$ = 42%) (Figure 2C). Subgroup analyses showed that curcumin could significantly reduce WC with a WMD of −2.67 cm (95% CI: −4.34, −1.00 cm; $I^2$ = 76%) and −1.64 cm (95% CI: −3.21, −0.07 cm; $I^2$ = 0%) in adults with T2DM and obesity, respectively (Figure 2C and Supplemental Figure 4C), whereas whole compounds and bioavailability-enhanced forms showed significant effects in WC reduction (Figure 2C and Supplemental Figure 5C). Moreover, curcumin could reduce BMI in both BMI range categories of 25–29.9 and ≥30 kg/m$^2$ (Table 2).

## Publication bias

Funnel plots showed no evidence of asymmetry (Supplemental Figure 6), which was confirmed by Egger test *P* values: *P* = 0.27 for BMI, 0.20 for BW, and 0.89 for WC.

## Sensitivity analyses

Sensitivity analyses were performed by excluding studies with qualitatively high ROB ratings and studies showing small-study effects. For the exclusion of high ROB ratings, 20, 16, and 10 studies were excluded from pooling of BMI, BW, and WC, respectively (Table 3 and Supplemental Figure 7). The effects of curcumin on BMI, BW, and WC were still significant, with WMDs of −0.34 kg/m$^2$ (95% CI: −047, −0.21 kg/m$^2$; $I^2$ = 24%), −0.68 kg (95% CI: −1.01, −0.34 kg; $I^2$ = 31%), and −1.09 cm (95% CI: −1.74, −0.43 cm; $I^2$ = 46%), respectively. One study each was excluded in a leave-1-out cross-validation analysis for BMI [63], BW [51], and WC [45] because these analyses showed small-study effects defined as a high-effect size with a

**FIGURE 2.** Pooled effects of curcumin supplementation according to comorbidities and curcumin forms: (A) BMI (kg/m$^2$), (B) body weight (kg), and (C) waist circumference (cm). *This was performed by a random-effects model by Review Manager (RevMan), version 5.4.1. $I^2$, percentage of degree of heterogeneity; MetS, metabolic syndrome; NAFLD, nonalcoholic fatty liver disease; *N*, number of studies; *n*1, number of participants in the intervention group; *n*0, number of participants in the control group; PCOS, polycystic ovary syndrome; T2D, type 2 diabetes mellitus; WMD, weighted mean difference.

**TABLE 3**
The sensitivity analysis excluding studies with a high risk of bias and by leave-one-out crossvalidation for small-study effects pooling BMI, body weight, and waist circumference outcomes

| Outcome | No. of studies (left for the analysis) | *n*1/*n*0 | WMD (95% CI)[1] | Heterogeneity | |
|---|---|---|---|---|---|
| | | | | $I^2$ (%) | *P*-heterogeneity |
| BMI (kg/m$^2$) | | | | | |
| All studies | 46 | 1460/1459 | −0.24 (−0.32, −0.16) | 18 | 0.15 |
| Excluded high ROB | 26 | 890/890 | −0.34 (−047, −0.21) | 24 | 0.13 |
| Leave-1-out analysis (Mohammadi et al., 2013 [63]) | 45 | 1445/1444 | −0.25 (−0.33, −0.16) | 20 | 0.13 |
| Body weight (kg) | | | | | |
| All studies | 40 | 1307/1302 | −0.59 (−0.81, −0.36) | 28 | 0.05 |
| Excluded high ROB | 24 | 898/896 | −0.68 (−1.01, −0.34) | 31 | 0.08 |
| Leave-1-out analysis (Di Pierro et al., 2015 [51]) | 39 | 1285/1280 | −0.59 (−0.82, −0.36) | 30 | 0.04 |
| Waist circumference (cm) | | | | | |
| All studies | 29 | 993/992 | −1.32 (−1.95, −0.69) | 42 | 0.01 |
| Excluded high ROB | 19 | 765/768 | −1.09 (−1.74, −0.43) | 46 | 0.02 |
| Leave-1-out analysis (Campbell et al., 2017 [45]) | 28 | 982/981 | −1.33 (−1.96, −0.69) | 44 | 0.007 |

$I^2$, percentage degree of heterogeneity; *n*1, number of participants in the intervention group; *n*0, number of participants in the control group; ROB, risk of bias; WMD, weighted mean difference.
[1] This was performed by a random-effects model by Review Manager (RevMan), version 5.4.1.

high variance from funnel plots (Supplemental Figure 6). The results of curcumin effects on all anthropometric indices did not change considerably compared with those of overall pooling (Table 3 and Supplemental Figure 8).

## Discussion

We have performed an umbrella review to summarize the findings of previous SRMAs on the effect of curcumin supplementation on anthropometric indices. We have also updated pooling MAs by combining the previous and recent RCTs stratified by patient comorbidities, curcumin forms, and severity of obesity. This analysis included 50 RCTs with a pooled sample size of 2879 participants. We found that curcumin supplementation was associated with a significant reduction in BMI, BW, and WC. Our findings suggest that curcumin can significantly reduce BMI by approximately −0.74, −0.41, −0.28, and −0.23 kg/m$^2$ in adults with PCOS, NAFLD, obesity, and MetS, respectively. It can also significantly reduce BW by approximately −1.09, −1.04, and −0.71 kg in adults with T2DM, NAFLD and obesity and reduce WC by approximately −2.67 and −1.64 cm in adults with T2DM and obesity, respectively. Curcumin extract and bioavailability-enhanced formulas seem to be the most effective formulas for weight reduction.

Curcumin or diferuloylmethane is a yellow crystalline lipophilic polyphenol. It is an active ingredient of turmeric with anti-oxidant and anti-inflammatory properties. Currently, the United States Food and Drug Administration(USFDA) has approved curcumin as Generally Recognized as Safe (GRAS) [89], and the European Food Safety Authority (EFSA) has recommended an acceptable daily intake of 3 mg/kg/d [90]. Several studies have shown curcumin to have an acceptable safety profile with minimal side effects [10,91]. However, it is not recommended in patients with cholelithiasis [92].

It has been shown that curcumin has several therapeutic benefits for various diseases, such as MetS, T2DM, hyperlipidemia, and Alzheimer diseases [13,93]. However, a major limitation to curcumin as an agent with an oral route of administration is its poor bioavailability due to its poor absorption in the gastrointestinal tract, fast metabolism, and rapid elimination from the systemic circulation [7]. There may be a potential advantage in consuming turmeric as a culinary ingredient because volatile and nonvolatile oils found in turmeric enhance the bioavailability of curcumin. Moreover, when consuming turmeric with fats or oils in foods, it can be absorbed directly into blood circulation through the lymphatic system, bypassing the liver metabolism [94,95]. In addition, black pepper, which contains piperine, also enhances the bioavailability of turmeric by slowing down the metabolism of curcumin, allowing the curcumin to stay longer in the body [96,97]. Thus, to use curcumin as a dietary supplement, different delivery systems have been proposed to increase the bioavailability, such as nanomicelle formation, phospholipid complexes, liposomes, amorphous dispersion, and adding piperine [7]. Nanocurcumin, a bioavailability-enhanced form, is synthesized by ionic gelation and antisolvent precipitation, which increases the pharmacologic and biological benefits, resulting in a more efficient delivery system and better therapeutic value [39]. Moreover, combining curcumin with piperine could increase the absorption, serum concentration, and bioavailability of curcumin in animal models and human subjects [40,41]. Another formulation is curcumin–phospholipid complex, which enhances aqueous solubility of lipophilic curcumin, and this formulation can be prepared by a simple and reproducible method [42]. Previous studies have also demonstrated better pharmacokinetic profiles in bioavailability-enhanced curcumin formulations [98,99] with better outcomes [100]. This study also concords that bioavailability-enhanced forms significantly improve anthropometric indices.

Obesity is a global health problem and a major risk factor of T2DM, dyslipidemia, NAFLD, and cardiovascular disease. Our updated MAs demonstrate the beneficial effects of curcumin supplementation on reduction in BMI, BW, and WC, which confirms the conclusions of the most recent SRMAs [100]. The exact mechanisms underlying the effects of curcumin supplementation on weight reduction remain to be elucidated. Nevertheless, there are several possible mechanisms responsible for the health benefits of curcumin in treating obesity. First, curcumin suppresses adipocyte differentiation by activation of AMP-activated protein kinase, thereby downregulating peroxisome proliferator-activated receptor γ [101,102]. In addition, curcumin induces fatty acid oxidation and increases adipocyte apoptosis [101,102]. Furthermore, curcumin inhibits NF-κB in adipose tissue, resulting in a reduction in inflammatory cytokine levels, for example, tumor necrosis factor α, IL-1, IL-6, monocyte chemotactic protein 1, and plasminogen activator inhibitor type 1. High leptin levels from leptin resistance in obesity activate Janus kinase/signal transducers and activators of

transcription signaling pathways, resulting in the development of obesity. Curcumin has also been shown to increase adiponectin levels [102,103], decrease leptin levels [47,104], and inhibit Janus kinase [105]. Gut microbiota dysbiosis is also one of the pathogeneses in obesity and curcumin that acts as a prebiotic, distributing throughout the gut and influencing the composition and diversity of the microbiota. However, the effect of curcumin on obesity through gut microbiota homeostasis is still controversial [106–108]. Finally, curcumin increases energy expenditure by increasing metabolic activity in brown and white fat, which is mediated by activation of FNDC5/irisin [109]. This study demonstrated that curcumin supplementation can reduce at least one of the anthropometric indices in patients with PCOS, NAFLD, obesity, or MetS. Although the efficacy of curcumin supplementation seems to be the greatest in patients with obesity and NAFLD, there were nonsignificant health benefits in patients with CKD or hyperlipidemia. It should be noted that there were only 2 studies on CKD and 2 studies on hyperlipidemia, which were included in this analyses. This study included participants with various metabolically related diseases, and most participants were with overweight and obesity. However, some studies included participants with a normal BMI level at the baseline. This may explain the conflicting outcomes in the subgroup analysis, demonstrating the beneficial effects of curcumin supplementation on BW, BMI, and WC reduction only in adults with overweight and obesity but not in adults with a normal BMI level. Adipose tissue dysfunction is a key factor in the development of metabolically related diseases, such as insulin resistance, T2DM, NAFLD, dyslipidemia, and cardiovascular disease. Although greater weight loss provides greater benefits, as little as 2%–5% of weight loss may lead to clinically meaningful reductions in cardiovascular risk factors [110,111]. This study demonstrated that curcumin supplementation can reduce at least one of the anthropometric indices in patients with PCOS, T2DM, NAFLD, obesity, and MetS, and adults with obesity or T2DM may benefit the most because curcumin supplementation can reduce both BW and WC.

## Strengths and limitations

This review has strengths. First, the results from several sources of SRMAs were extensively combined, and repooling analyses were performed to summarize the effects of curcumin on anthropometric indices. Second, we included only RCTs with either parallel-arm or crossover designs. Third, we conducted subgroup analyses according to patient comorbidities, severity of obesity, and curcumin formulas along with their dosages based on current usage. Taken together, these strengths allow us to present an extensive and in-depth analysis of the causal effect of curcumin, to suggest the gaps of knowledge, and to suggest the way forward with future research aims.

However, this review has limitations. First, there was a significant heterogeneity across studies in many of the pooled outcomes. Thus, we used random-effects models to address heterogeneity in the repooling MAs, and we performed subgroup analyses, resolving the interpretation of most of the high heterogeneity findings. Moreover, dose–response MA was not applied in our studies, especially in bioavailability-enhanced forms, which could have given us more valuable insights.

In conclusion, this study demonstrated that curcumin supplementation reduces BMI, BW, and WC, particularly in adults with PCOS, NAFLD, obesity, or MetS. The benefit of curcumin supplementation seems to be the greatest in adults with obesity or T2DM. Bioavailability-enhanced formulas are preferred for their greater average treatment effect than either whole compounds or curcumin extracts. Curcumin supplementation should be an option for treating and managing these patients, additional to lifestyle modification.

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## Data Availability

The data described in the manuscript, code book, and analytic code will be made available on request pending application and approval.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajcnut.2023.03.006.

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