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Impact of tomatoes and tomato-derived products on obesity and cardiometabolic health: a systematic review and meta-analysis

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Tomatoes and tomato-based products are central components of the Mediterranean diet and have been associated with improved cardiometabolic health, but their effects on anthropometric parameters remain unclear. This review aimed to assess the potential effects of tomato-based interventions on obesity-related and cardiometabolic outcomes in individuals with overweight or obesity. We conducted a PRISMA-compliant systematic review and meta-analysis. Eligible studies included populations with a mean BMI $\geq 25 \text{ kg m}^{-2}$, evaluated tomatoes, tomato-based products, or tomato extracts (excluding isolated lycopene) and reported at least one anthropometric outcome. The risk of bias was assessed using RoB 2 for randomized controlled trials (RCTs). Epidemiological and preclinical evidence was synthesized qualitatively. Forty-seven studies met the inclusion criteria: 11 clinical trials (RCTs), 5 epidemiological studies, and 31 preclinical studies. In the RCTs, tomato-based interventions produced a small but significant reduction in waist circumference (MD: -1.153 cm , 95% CI: -2.27 to -0.04 , $p = 0.0432$), with no consistent effects on body weight or BMI. Meta-regression analyses indicated that supplementation type influenced blood pressure-related outcomes. Epidemiological studies consistently linked higher tomato intake to more favorable cardiometabolic profiles, whereas preclinical models showed reduced visceral adiposity, inflammation, and oxidative stress, together with improved glucose and lipid homeostasis. Tomato-based interventions confer modest but biologically consistent benefits, targeting visceral adiposity and cardiometabolic pathways rather than overall weight loss. The absence of a lycopene dose response and the efficacy of lycopene-free matrices support a food-matrix synergy rather than lycopene as the primary bioactive compound. Combined clinical, epidemiological, and preclinical evidence suggests potential beneficial effects of tomatoes and tomato-based products on cardiometabolic health, which deserve further investigation. This review underscores the need to standardize tomato-derived interventions to improve comparability and strengthen the evidence base.

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Introduction

The global rise in overweight and obesity is alarming: in 2022, an estimated 2.5 billion adults worldwide were overweight and 890 million were living with obesity, representing nearly 16% of the global adult population.¹ According to the World Health Organization (WHO), obesity is defined as an abnormal or excessive accumulation of body fat that may impair health and is clinically diagnosed when the body mass index (BMI) is $\geq 30 \text{ kg m}^{-2}$, while overweight corresponds to a BMI $\geq 25 \text{ kg m}^{-2}$. Beyond this anthropometric definition, obesity is now recognized as a chronic multifactorial disease, resulting from a complex interaction among genetic, epigenetic, environmental, and nutritional factors. In addition to biological

mechanisms, behavioral and environmental factors—such as sedentary lifestyles, high-calorie diets rich in ultra-processed foods, and insufficient physical activity—contribute substantially to its global spread.^{2,3} Chronic obesity induces immune dysfunction and profound metabolic dysregulation, characterized by impaired glucose homeostasis leading to insulin resistance and by altered lipid metabolism resulting in dyslipidemia. These disturbances collectively increase the risk of cardiometabolic diseases, including type 2 diabetes mellitus (T2DM), hypertension, cardiovascular disease (CVD), and metabolic-associated fatty liver disease (MAFLD), as well as certain cancers, ultimately contributing to reduced quality of life, premature mortality, and escalating healthcare costs.^{4–7}

Given the multifactorial and inflammatory nature of obesity, nutritional strategies have emerged as fundamental approaches for both its prevention and management. Dietary patterns emphasizing whole, plant-based foods, rich in antioxidants and anti-inflammatory bioactives, have demonstrated

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substantial benefits in modulating metabolic health. Among these, the Mediterranean diet—characterized by high consumption of fruits, vegetables, legumes, whole grains, and olive oil, and moderate intake of fish and wine—has been consistently associated with reduced adiposity, improved insulin sensitivity, and lower incidence of cardiometabolic diseases.^{8–11} Within this dietary framework, the tomato (*Solanum lycopersicum*) occupies a prominent place as one of the most globally consumed vegetables, both fresh and in processed forms, such as sauces, pastes, and juices.¹² Tomatoes are a hallmark component of the Mediterranean diet and represent a major dietary source of carotenoids (particularly lycopene), vitamins (A, C and E), polyphenols, and other bioactive compounds with recognized antioxidant and anti-inflammatory properties.^{13,14}

The beneficial effects observed after tomato or tomato-based product consumption have historically been largely attributed to lycopene.^{15–19} This reductionist hypothesis, positioning lycopene as the principal “active ingredient” of tomatoes, has strongly shaped the design of clinical research over the past two decades. Early observational studies reported inverse associations between plasma lycopene or tomato intake and cardiovascular outcomes, reinforcing the assumption that lycopene alone mediated these benefits.²⁰ On this basis, numerous interventional trials have been designed to test lycopene itself as a nutrient supplement, rather than tomatoes as a complex food, administering isolated lycopene—typically in capsules or purified extracts, often at doses between 10 and 30 mg day^{−1}—to evaluate its effects on intermediate cardiometabolic endpoints. In parallel, several studies have employed lycopene-enriched or otherwise standardized tomato extracts to deliver controlled amounts of tomato-derived bioactive compounds.^{17,20} Among these, Lyc-O-Mato® is a lipid-soluble tomato extract obtained from ripe tomatoes and standardized to contain approximately 6% lycopene, alongside other naturally occurring carotenoids (including phytoene, phytofluene, and β-carotene), as well as small amounts of tocopherols and phytosterols, thereby preserving part of the native carotenoid matrix found in processed tomatoes.^{21–23} This extract has been widely used in clinical and mechanistic studies as a model of lycopene-enriched tomato bioactives.^{24–27} In contrast, Fruitflow® is a water-soluble, lycopene-free tomato extract standardized to three classes of hydrophilic compounds—nucleoside derivatives, phenolic conjugates (notably chlorogenic acid derivatives), and simple polyphenols (such as rutin and caffeic acid). Its tightly controlled composition ensures reproducible bioactivity, and it is notable for being the first natural cardio-protective functional ingredient approved by the European Food Safety Authority (EFSA).²⁸ Mechanistically, Fruitflow® exerts multiple effects, including inhibition of platelet activation, attenuation of oxidative stress through the activation of Nrf2-dependent antioxidant pathways, and suppression of NF-κB-mediated inflammatory signaling. Collectively, these actions contribute to improved endothelial function and vascular homeostasis, supporting cardiometabolic health beyond the effects of indi-

vidual compounds.²⁹ The demonstrated clinical efficacy of the lycopene-free tomato extract Fruitflow®—particularly on platelet aggregation and vascular fluidity—compared with the carotenoid-rich Lyc-O-Mato®, provides compelling evidence that the biological actions of tomatoes are not solely due to lycopene, but result from the synergistic interaction of multiple bioactives within the tomato matrix.^{30–35} However, a second wave of research involved clinical trials designed to directly compare purified lycopene with whole-tomato preparations. In the cardiometabolic domain, Landrier *et al.* reported that, although both tomato-based products and lycopene have anti-inflammatory and anti-steatotic effects in experimental models, human trials show more consistent benefits from tomato-based products.¹⁷ Similarly, Burton-Freeman and Sesso found that tomato-based products are more effective than lycopene supplements at improving oxidative stress, inflammation, and endothelial function, with comparable effects only for blood pressure.³⁶ Together with epidemiological evidence showing that high intakes of tomato products are associated with reduced cardiovascular disease (CVD) risk and mortality,²⁰ these findings support the concept of food synergy: tomato-related benefits arise from the combined actions of carotenoids, polyphenols, vitamins, minerals, and the lipid matrix rather than lycopene alone. The structural complexity of the tomato matrix modulates absorption, metabolism, and cellular signaling, producing biological effects that isolated lycopene cannot replicate. Accordingly, multiple clinical and experimental studies show greater improvements in antioxidant status, inflammation, and cardiometabolic markers with tomato-based products than with lycopene supplements.^{36–39} Thus, while lycopene contributes significantly to the biological activity of tomatoes, accumulating evidence indicates that the tomato matrix itself exerts unique metabolic and immunomodulatory effects that cannot be reproduced by the isolated compound.

A growing number of studies have examined the health effects of tomatoes, tomato-based products, and lycopene, resulting in several systematic reviews and meta-analyses on the cardiometabolic outcomes.^{20,40–45} The 2021 umbrella review by Li *et al.* reported that higher dietary intake of tomatoes or lycopene, as well as higher circulating lycopene levels, is inversely associated with CVD, stroke, and all-cause mortality, and across observational and interventional studies, these exposures are also associated with a reduced risk of CVD, stroke, metabolic syndrome (MetS), and mortality.⁴⁶ Complementing these epidemiological insights, the recent systematic review and meta-analysis conducted by Zamani *et al.* in 2023 provided further clinical clarification by highlighting that tomato and lycopene consumption led to a significant reduction in malondialdehyde (MDA), a presumed marker of oxidative stress, but reported no consistent effect on body weight, BMI, lipid profile, blood pressure, or inflammatory markers.⁴⁷ Beyond the overall cardiovascular risk, several systematic reviews have focused on cardiometabolic markers, including blood lipid profile, blood pressure, and endothelial function.^{17,36} The 2011 review by Burton-Freeman and Reimers



provided one of the first comprehensive summaries of the physiological effects of tomato consumption, highlighting contributions to antioxidant defense, inflammatory modulation, and vascular function and emphasizing that these effects arise from the combined action of tomato carotenoids, vitamins, and phenolics rather than lycopene alone.¹³ Building on this preliminary work, the 2014 review by Burton-Freeman and Sesso corroborated these findings, showing that diets rich in tomatoes and tomato-based products reliably improve endothelial function, reduce markers of oxidative stress, and attenuate inflammatory profiles.³⁶ These conclusions were reinforced by a 2017 systematic review and meta-analysis by Cheng *et al.*, which quantitatively demonstrated that tomato consumption produces significant reductions in low-density lipoprotein cholesterol (LDL-C) and systolic blood pressure (SBP), as well as an improvement in flow-mediated dilation, thus supporting the cardiometabolic benefits of tomato-based interventions.²⁰ Overall, existing studies indicate that tomatoes and tomato-based products generally have beneficial or neutral effects on key cardiometabolic parameters, but evidence specific to obesity remains limited. Although obesity is a major factor in cardiometabolic diseases, no systematic review or meta-analysis has directly examined the consequences of obesity. We therefore conducted a targeted systematic review and meta-analysis to evaluate the effects of tomatoes and tomato-based products in overweight or obese individuals on anthropometric parameters and obesity-related metabolic dysfunction, distinguishing these effects from those of isolated lycopene. This review provides an integrated synthesis of epidemiological, clinical and animal data on the impact of tomatoes and tomato-based products on obesity and associated metabolic disorders.

Methods

Literature search

A systematic search was conducted in PubMed according to PRISMA recommendations. The full PubMed search string was (((tomato) OR (Lyc-O-Mato) OR (Fruitflow)) AND ((obesity) OR (overweight) OR (type 2 diabetes) OR (metabolic syndrome) OR (cardiometabolic disease) OR (cardiovascular) OR (dyslipidemia) OR (oxidative stress) OR (high-fat diet)) NOT (review [Publication Type])). The search was performed independently by two researchers. The term “*tomato*” was used as the primary exposure keyword, as it appears systematically in all derivative expressions used in the literature. To ensure comprehensive retrieval of studies using standardized commercial tomato extracts, the terms “*Lyc-O-Mato*” and “*Fruitflow*” were also included. In addition to obesity-specific terms, more general keywords related to cardiac metabolism and inflammation were included to identify studies not listed under obesity-related headings, and the term “high-fat diet” was added to identify preclinical models of diet-induced obesity. No date restrictions were applied to allow the inclusion of earlier foundational studies. Boolean operators were used to structure the

search; reviews were excluded, and the last comprehensive search was performed on December 5, 2025.

Eligibility criteria

To be eligible for further analysis, articles needed to (1) include a nutritional intervention involving tomatoes, tomato-based products (such as tomato juice, powder, paste, sauce, puree, or concentrated preparations), or tomato extracts (either laboratory-prepared or commercially standardized); (2) report at least one morphometric outcome, including body weight, BMI or waist circumference; (3) include a population with an average BMI greater than or equal to 25 kg m⁻²; and (4) constitute original peer-reviewed research, including clinical trials, observational studies, or animal intervention studies. Conversely, studies were excluded if (1) the nutritional intervention relied solely on purified lycopene without any tomato-based products or tomato-derived extract; (2) no morphometric outcomes were reported; (3) the studied population in clinical trials had an average BMI lower than 25 kg m⁻² or the animal model was not suitable for diet-induced obesity, such as genetically induced obesity models; or (4) the publication did not qualify as an original research, including reviews, meta-analyses, theses, editorials, commentaries, or conference abstracts.

Data extraction and risk of bias assessment

The extracted data included study and participant characteristics; duration, type, and dose of supplementation; control groups; measured outcomes; and significant results observed. Risk of bias was assessed for the primary outcomes (body weight, BMI, and waist circumference) with the Cochrane Risk of Bias 2 (RoB 2) tool for randomized controlled trials (RCTs), including parallel and cross-over designs.⁴⁸ Data extraction and risk-of-bias assessment were performed independently by two researchers.

Assessment of publication bias

Potential publication bias was evaluated using funnel plots and Egger's regression test. Because fewer than 10 studies were available for most outcomes (a minimum of 7), these assessments were considered exploratory, in line with Cochrane's guidance that funnel plot asymmetry tests are unreliable when fewer than 10 studies are included.

Data synthesis

Quantitative synthesis focused on RCTs, while observational and preclinical studies were synthesized narratively. Meta-analysis was performed in RCTs comparing a tomato-based intervention to an independent control group, and effect sizes were expressed as mean differences (MD) in change from baseline between intervention and control groups, with 95% confidence intervals (CI). When standard deviations of change were not reported, they were derived from the baseline and post-intervention values assuming a pre-post correlation coefficient of $r = 0.50$. Sensitivity analyses were performed using alternative correlation coefficients ($r = 0.25$ and $r = 0.75$) to assess the robustness of the results. Pooled effect estimates were



obtained using random-effects models fitted by restricted maximum likelihood (REML). The primary outcomes were the body weight, BMI, and waist circumference, selected as key anthropometric indicators of obesity and central adiposity with established cardiometabolic relevance. Forest plots were generated exclusively for these primary outcomes, whereas all other outcomes are summarized quantitatively in Table 2. Outcomes reported in fewer than two studies were not meta-analysed. Between-study heterogeneity was assessed using τ^2 , I^2 , and Cochran's Q test, and the 95% prediction intervals were calculated. All analyses were conducted in R (4.5.1) using the *metafor* package, with statistical significance defined as a two-sided $P < 0.05$.

Meta-regression analyses

Meta-regression analyses were conducted to investigate the potential sources of between-study heterogeneity in anthropometric and cardiometabolic outcomes for RCTs of meta-analysis. Because the recommended minimum of 10 studies per outcome for reliable meta-regression was not achieved, analyses were restricted to outcomes reported by at least seven studies and were undertaken on an exploratory basis to limit model instability and potential overfitting, consistent with Cochrane methodology. Both continuous (mean baseline BMI and daily lycopene intake) and categorical moderators (type of supplementation) were examined. Random-effects meta-regression models were fitted using REML. The continuous moderators were mean-centered prior to analysis. Associations with the continuous moderators were evaluated using Wald tests of the regression coefficients, whereas between-group differences for the categorical moderator were assessed using the omnibus test of moderators (QM).

Results

Search results and trial flow

A total of 2802 records were identified through the PubMed database search. After removing duplicates, 2800 unique records remained. Following title and abstract screening, 1659 articles were excluded, and 297 full-text articles were assessed for eligibility. Of these, 250 were excluded for the following reasons: use of purified lycopene ($n = 134$), absence of morphometric outcomes ($n = 76$), unsuitable population ($n = 25$), or non-original research ($n = 15$). Ultimately, 47 studies met the inclusion criteria and were included in the systematic review and meta-analysis (Fig. 1).^{18,49–109} Among these, 5 were observational epidemiological studies, 31 were animal model studies, and 11 were RCTs included in the meta-analysis.

Characteristics of randomized controlled interventional clinical studies

Among the 11 clinical trials included (between 2000 and 2024), a total of 691 participants were included in these trials.

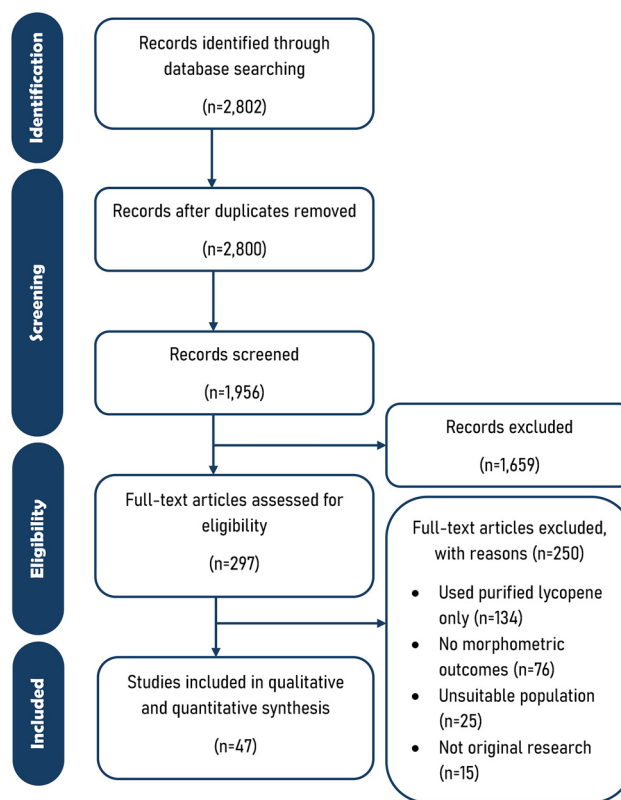


Fig. 1 PRISMA 2009 flow diagram of the study selection.

Of these, 417 individuals (60.4%) received a tomato or tomato-derived intervention (37.2% men, 62.8% women). The participants' ages ranged from 18 to 83 years, with a mean age of 49.2 years. Most studies (81.8%) recruited populations with average BMI values within the overweight range (25–30 kg m⁻²) and 18.2% within the obesity range (Table 1). Across the intervention trials, tomato-based products were administered in diverse forms, with substantial variability in both the dosage and lycopene content. The supplementation forms most frequently studied were tomato extract (33.3%), followed by fresh tomato (25.0%), tomato juice (16.7%) and combined tomato products (16.7%), with fewer studies using sofrito (8.3%) (SI Table S1). Sofrito provided the highest lycopene density, with a concentration of 215.6 mg kg⁻¹ for a daily dose of 100 g d⁻¹. Tomato juice also exhibited a high lycopene density (181.8 mg L⁻¹ for 330 mL d⁻¹), followed by fresh tomatoes (55.5 mg kg⁻¹ for 250.0 ± 50.0 g d⁻¹). Tomato extracts provided standardized doses, typically delivering 10–15 mg of lycopene per capsule (or 0 mg for Fruitflow®), corresponding to a very high lycopene density relative to the administered mass. In terms of absolute lycopene intake, tomato juice provided the highest exposure (60.0 mg d⁻¹) over a mean duration of 3.5 weeks. Combined tomato-based products and sofrito yielded intermediate intakes (20.6 and 21.6 mg d⁻¹, respectively) over 12.5 and 6 weeks. Tomato extracts (10.0 ± 7.1 mg d⁻¹, for 8.6 weeks) and fresh tomatoes (250.0 ± 50.0 g d⁻¹, for 6.7 weeks) resulted in the lowest intake of lycopene.



Table 1 Clinical trials investigating the effects of tomato and tomato-based product supplementation on anthropometric parameters and metabolic dysfunction parameters associated with obesity

Study	Study design ^a	Study population	Average BMI of the population	Number of subjects ^b	Duration ^c	Form of tomato	Tomato dosage	Outcomes	Main results ^d
Chen C.-Y. and Chien Y.-M., (2024) ⁵²	Two-arm RCT, OL	Women with MetS or moderate hypercholesterolemia (45–70 years)	26.4 kg m ⁻²	53 ♀	8 weeks	Raw tomato	200 g d ⁻¹	BW, BMI, BFM, WC, HC, BP, TG, TC, LDL-C, HDL-C serum, FBG, insulin, HOMA-IR and QUICKI indexes and IL-6 plasma	↓ BFM, WC and HC
	Control: iso-caloric and macronutrient diet with sprouts and restricted tomatoes and tomato-based products			I: 30 ♀					↓ SBP
				C: 23 ♀					↓ TC and TG serum ↑ HDL-C serum ↓ FBG plasma ↓ BW and BMI* (and after 15 d follow-up for BMI)
Yu Y. <i>et al.</i> , (2024) ⁵⁴	Two-arm RCT, DB	Adults with elevated TC levels (35–65 years)	25.1 kg m ⁻²	60 (11 ♂, 49 ♀)	45 d (follow-up for over 15 d)	Tomato extract (Fruitflow®)	1 tablet per day (150 mg extract)	BW, BMI, BFM, BP, TG, TC, LDL-C, HDL-C, FGB, CRP, Hcy serum	↓ SBP and DBP*
	Control: 300 mg placebo tablets and sugar-coated, with the same excipients as Fruitflow (microcrystalline cellulose, lactose, and magnesium stearate)			I: 30 (5 ♂, 25 ♀)					↑ HDL-C serum* ↓ FBG serum (after 15 d follow-up) ↓ CRP serum (after 15 d follow-up) ↓ Hcy serum* (and after 15 d follow-up)
				C: 30 (6 ♂, 24 ♀)					↑ DBP
López-Yerena A. <i>et al.</i> , (2023) ⁵³	Two-arm RCT crossover, OL	Overweight or obese adults (27–60 years)	31.1 kg m ⁻²	40 (27 ♂, 13 ♀)	6 weeks (2 weeks WO)	Soffritto	100 g d ⁻¹	BW, BMI, WC, WHR, BP, TG, TC, LDL-C, HDL-C, LDL-C/HDL-C ratio, FBG, AST, ALT, GGT, urea, uric acids, creatinine, TP, endothelial function and platelet aggregation	↓ Platelet aggregation
	Control: Habitual diet without tomato or tomato-based products								





Table 1 (Contd.)

Study	Study design ^a	Study population	Average BMI of the population	Number of subjects ^b	Duration ^c	Form of tomato	Tomato dosage	Outcomes	Main results ^d
Yang T. H. <i>et al.</i> , (2020) ⁵⁵	Two-arm RCT, OL Control: 1500 kcal diet (iso-macronutrients), with 5 servings of vegetables per day	Overweight or obese adults (57–61 years)	27.0 kg m ⁻²	36 ♀	8 weeks	Raw beefsteak tomato	250 g d ⁻¹	BW, BMI, BFM, WC, HC, WHR, BMR, BP, TG, TC, LDL-C, HDL-C, CRP, AST and ALT levels	↑ TC, LDL-C and HDL-C serum*
Pourahmadi Z. <i>et al.</i> , (2015) ⁵⁶	Two-arm RCT, DB Control: 330 mL water per day	Overweight or obese students, non-smokers (20–30 years)	28.3 kg m ⁻²	I: 20 ♀ C: 16 ♀ 75 ♀	20 d	Tomato juice	330 mL d ⁻¹	BW, BMI, SOD, CAT, NS GSH-Px and TAC levels	NS
Cuevas-Ramos D. <i>et al.</i> , (2013) ⁶²	Two-arm RCT, SB Control: 300 g of raw cucumber per day	Healthy adults (18–65 years)	27.1 kg m ⁻²	I: 40 ♀ C: 35 ♀ 50 (9 ♂, 41 ♀)	4 weeks (after 2 weeks of isocaloric diet)	Raw tomato	300 g d ⁻¹ (≈2 tomatoes)	BMI, WC, HC, WHR, TG, TC, LDL-C and HDL-C serum	↑ HDL-C serum with tomato intake (β = 5.79) and adherence days (β = 0.61) (R = 0.83, R ² = 0.69, p < 0.0001)
Park E. <i>et al.</i> , (2013) ¹³⁵	Two-arm RCT, OL Control: Other fruit-based products (apple or grape juice, canned fruit and boxes of raisins)	Adults at elevated risk for prostate cancer (51–83 years)	29.7 kg m ⁻²	C: 24 (5 ♂, 19 ♀) I: 21 ♂	3 months	Tomato products	≥1 serving per day	BW, BP and TC plasma	NS
Thies F. <i>et al.</i> , (2012) ⁶⁶	Triple-arm RCT, SB	Healthy adults (40–65 years)	26.8 kg m ⁻²	C: 12 ♂ 225 (93 ♂, 132 ♀)	12 weeks (after 4 weeks of control diet)	Tomato products or tomato extract (Holland and Barret)	Equivalent to ≈32.3–50.1 mg LYC per day (tomato) or 1 capsule per day (extract)	BW, BMI, WC, BP, TG, TC, LDL-C, HDL-C, ApoA-I, ApoB-100, FBG, insulin, HOMA-IR and QUICKI indexes, CRP, IL-6, ICAM-1 and Ox-LDL serum	NS

Table 1 (Contd.)

Study	Study design ^a	Study population	Average BMI of the population	Number of subjects ^b	Duration ^c	Form of tomato	Tomato dosage	Outcomes	Main results ^d
Ried K. <i>et al.</i> , (2009) ⁶⁵	Control: Low-tomato control diet (<10 mg LYC per week) Three-arm RCT, DB	Adults prehypertensive (22–73 years)	26.2 kg m ⁻²	I "Tomato": 81 (35 ♂, 46 ♀) I "Extract": 68 (28 ♂, 40 ♀) C: 76 (30 ♂, 46 ♀)	8 weeks	Tomato extract	1 capsule per day (250 mg extract)	BW, BMI, WC, BP	NS
Engelhard Y. N. <i>et al.</i> , (2006) ⁷⁰	Control: 1 placebo capsule per day with soy oil (matched to tomato extract capsules by colour, odour and size) Single-arm, RCT crossover, SB	Adults with hypertension grade 1 (30–70 years)	29.5 kg m ⁻²	C: 10 (5 ♂, 5 ♀) 31 (18 ♂, 13 ♀)	8 weeks (after 4 weeks of placebo period)	Tomato extract (Lyc-O-Mato®)	1 capsule per day (250 mg)	BMI, WC, BP, TG, TC, LDL-C, HDL-C, ApoA-I, ApoB-100, FBG, TBARS and GPx activities, urea, uric acids, creatinine and Hcy serum	↓ SBP and DBP
Upritchard J. E. <i>et al.</i> , (2000) ⁶⁸	Control: 1 placebo capsule per day (identical looking) (4 weeks) Four-arm RCT, OL	Adults with well-controlled type 2 diabetes (<75 years)	30.9 kg m ⁻²	52 (32 ♂, 20 ♀)	4 weeks (after 4 weeks of placebo period)	Tomato juice	500 mL d ⁻¹	BMI, BP, TC, FBG, CRP, ICAM-1 and VCAM-1 plasma	↑ LDL oxidation lag time by copper ions (in the Tomato group)*
	Control: Placebo gelatin capsule with starch (8 weeks)			I "Tomato": 15 (10 ♂, 5 ♀) C: 76 (30 ♂, 46 ♀)					

ApoA-I: apolipoprotein A-I, ApoB: apolipoprotein B, AST: aspartate aminotransferase, aMT6s: 6-sulfatoyxymelatonin, ALT: alanine aminotransferase, BFM: body fat mass, BMI: body mass index, BMR: basal metabolic rate, BP: blood pressure, CAT: catalase, CRP: C-reactive protein, DBP: diastolic blood pressure, FBG: fasting blood glucose, FRAP: ferric reducing antioxidant power, GGT: G-glutamyl transferase, GPx: glutathione peroxidase, GSH: reduced glutathione, HADS: hospital anxiety and depression scale, HC: hip circumference, Hcy: homocysteine, HDL-C: high-density lipoprotein cholesterol, HOMA-IR: homeostatic model assessment of insulin resistance, HR: heart rate, ICAM-1: intercellular adhesion molecule-1, IL-6: interleukin-6, LDL-C: low-density lipoprotein cholesterol, MCP-1: monocyte chemoattractant protein-1, MDA: malondialdehyde, Mets: metabolic syndrome, QUICKI: quantitative insulin sensitivity check index, REE: resting energy expenditure, SBP: systolic blood pressure, SOD: superoxide dismutase, TAC: total antioxidant capacity, TBARS: thiobarbituric acid reactive substances, TC: total cholesterol, TG: triglycerides, TP: total protein, VCAM-1: vascular cell adhesion molecule-1, WC: waist circumference, WHR: waist-to-hip ratio, and WO: wash-out. ^a Study design abbreviations: RCT, randomized controlled trial. Blinding: OL, open-label; SB, single-blind; and DB, double-blind. ^b Abbreviations for number and sex of subjects: C, number of subjects in the control group; I, number of subjects in the intervention group; ♂, males and ♀, females. ^c Duration abbreviation: d, days. ^d The results presented indicate values that differ significantly from the control group's values. When significance is observed relative to baseline, this is indicated by an asterisk *.



Risk of bias and study quality

Overall, the RCT trials were judged to have predominantly low risk of bias across domains (45.4%), whereas several parallel RCTs showed some concerns (18.2%) or high risk of bias (36.4%), mainly related to the randomization process and deviations from intended interventions (SI Fig. S1). Visual inspection of funnel plots revealed no marked asymmetry (BMI, BW, SBP, DBP, TG, TC, LDL-C and HDL-C outcomes) (SI Fig. S2). Consistently, Egger's regression tests were not significant for all outcomes (all $p > 0.1426$), providing no evidence of small-study effects or publication bias.

Metabolic effects of tomato-based interventions: qualitative and quantitative evidence

Effects of tomato-based interventions on anthropometric parameters. Among the 11 interventional trials, BMI (90.9%), body weight (72.7%), and waist circumference (63.6%) were the most frequently assessed anthropometric outcomes, whereas body fat mass (27.2%) and hip circumference (27.2%) were less commonly evaluated, among other measures. Only one study reported small but significant reductions in BMI (-0.27 kg m^{-2}) and body weight (-0.65 kg) following lycopene-free tomato extract (Fruitflow®) supplementation, and these reductions remained significant at the 15-day post-supplementation follow-up (Table 1).⁵⁴ These effects were not associated with the longest intervention duration (45 days) and were not linked to lycopene intake, as observed in the absence of lycopene in this supplementation (SI Table S1). In another study, the anthropometric parameters decreased significantly after raw-tomato supplementation *versus* the control group, during 8 weeks, notably the waist circumference ($-2.9 \pm 1.7 \text{ cm}$), hip circumference ($-1.7 \pm 1.1 \text{ cm}$), and body fat mass ($-0.8 \pm 1.3 \text{ kg}$ and $-0.3\% \pm 0.8\%$) (Table 1).⁵² This reduction was not observed in the context of a long intervention duration or a high lycopene intake (11.0 mg lycopene intake per day) (SI Table S1). Other anthropometric outcomes were unaffected.

Meta-analysis showed a significant reduction in waist circumference (MD: -1.153 cm , 95% CI: -2.27 to -0.04 , $p = 0.0432$, Fig. 2). Although the study by Chen and Chien (2024) contributed the largest statistical weight (88.4%), effect estimates were consistent across studies, with no evidence of between-study heterogeneity ($\tau^2 = 0.0$, $I^2 = 0.0\%$, Q -test $p = 0.5833$, Fig. 2).⁵² Sensitivity analysis using different assumed pre-post correlation coefficients showed that the result remained statistically significant across all tested values of r ($p = 0.0437$ for $r = 0.25$, $p = 0.0432$ for $r = 0.50$, and $p = 0.0415$ for $r = 0.75$; SI Table S2), supporting the robustness of this finding. Supplementation was associated with a non-significant reduction in body weight (MD: -0.659 kg , 95% CI: -1.94 to 0.63 , $p = 0.3149$, Fig. 3). Heterogeneity was moderate to substantial ($\tau^2 = 1.2$, $I^2 = 37.9\%$), although the Q -test was not statistically significant ($p = 0.1398$). No statistically significant pooled effects were observed for BMI (MD: -0.000 kg m^{-2} , 95% CI: -0.20 to 0.19 , $p = 0.9668$, Fig. 4), with no evidence of between-study heterogeneity ($\tau^2 = 0.0$, $I^2 = 0.0\%$, Q -test $p = 0.9621$).

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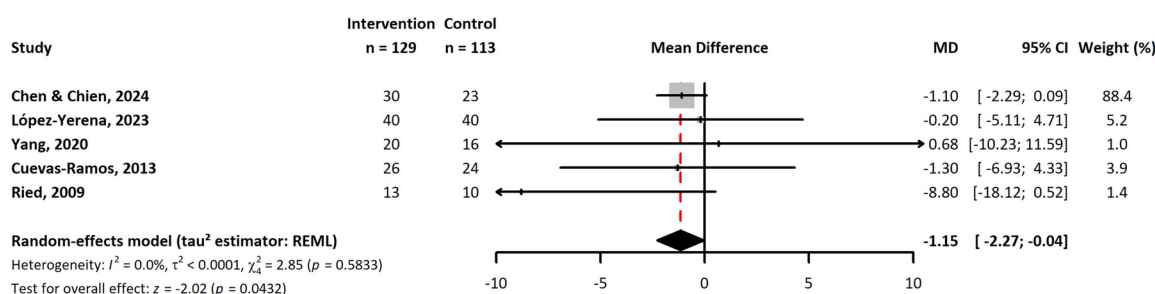


Fig. 2 Forest plots of the effect of tomato supplementation on waist circumference.

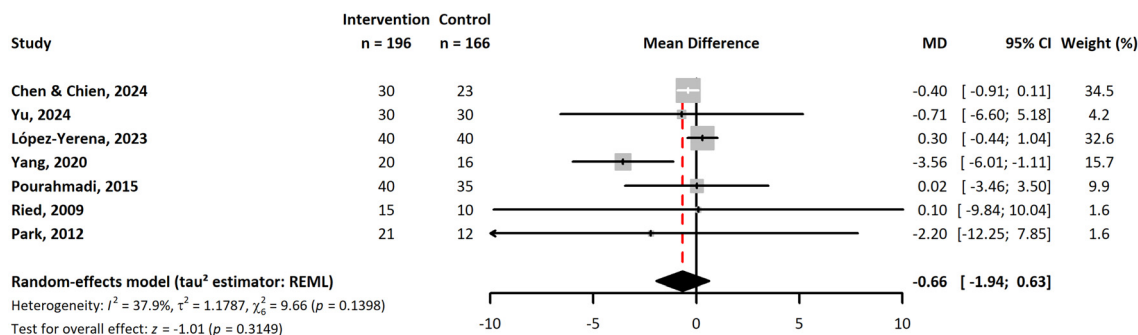


Fig. 3 Forest plots of the effect of tomato supplementation on body weight.

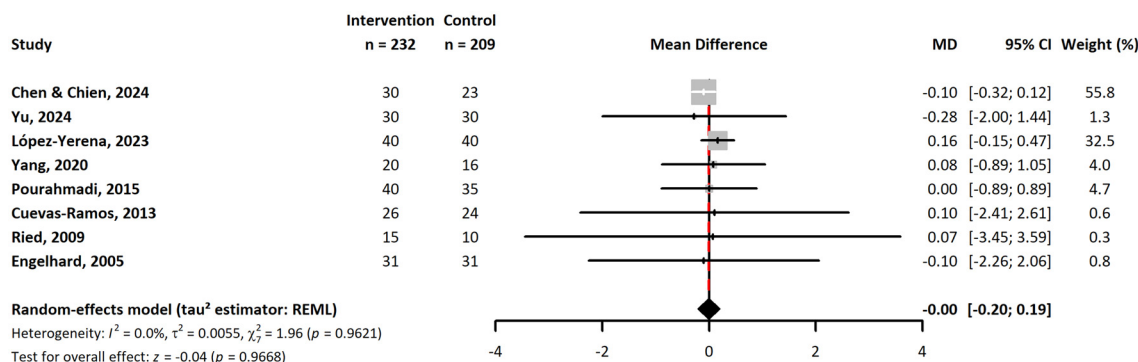


Fig. 4 Forest plots of the effect of tomato supplementation on body mass index.

Effects of tomato-based interventions on cardiometabolic parameters. Among the 9 studies assessing blood pressure, significant reductions were reported in approximately half of the trials, mainly in high cardiometabolic risk populations (hypertensive or elevated plasma cholesterol). The largest decreases were observed with tomato extracts (Fruitflow®: -5.3 mmHg SBP and -3.0 mmHg DBP⁵⁴ and Lyc-O-Mato®: -11.0 mmHg SBP and -5.5 mmHg DBP⁷⁰), whereas fresh tomato⁵² produced only modest reductions. No consistent effects were observed in normotensive individuals. López-Yerena *et al.* reported a small but significant increase in diastolic blood pressure (DBP) with sofrito ($+0.68 \pm 1.18$ mmHg, $p = 0.0400$), likely attributable to its 2% sodium content.⁵³ The meta-analysis showed no significant effect of supplementation on these parameters (MD: -2.894 mmHg, 95% CI: -6.64 to 0.85 , $p = 0.1299$ for SBP and MD: 0.077 mmHg, 95% CI: -1.91 to 2.06 , $p = 0.9391$, Table 2), but substantial heterogeneity was observed for SBP ($\tau^2 = 0.0$, $I^2 = 0.0\%$, Q -test $p = 0.9621$). Most trials evaluated lipid homeostasis parameters, with significant augmentations in the total and high-density lipoprotein-cholesterol (HDL-C) observed across different populations, including participants with hypercholesterolemia and healthy individuals, suggesting that this parameter may be particularly sensitive to supplementation-induced changes (Table 1).^{52,54,55,62} In one study, raw-tomato intake during 4 weeks was associated with an increase in HDL-C levels, with a positive association observed for both tomato intake ($\beta = 5.79$) and adherence duration ($\beta = 0.61$). The model showed a strong overall correlation ($R = 0.83$), explaining 69% of the variance in HDL-C changes ($R^2 = 0.69$), with high statistical significance ($p < 0.0001$). The meta-analysis showed a non-significant trend toward an effect (MD: 1.913 mg dL⁻¹, 95% CI: -0.65 to 4.47 , $p = 0.1428$, Table 2), with substantial between-study heterogeneity, although the Q -test for heterogeneity was not statistically significant ($\tau^2 = 4.8$, $I^2 = 45.5\%$, Q -test $p = 0.1266$, Table 2), suggesting inconsistency in effect estimates across studies. The effects on triglycerides and total cholesterol were limited. Only one study reported reductions in triglycerides (-25.9 mg dL⁻¹) and total cholesterol (-6.1 mg dL⁻¹) (Table 1),⁵² while the pooled meta-analysis did not show a statistically significant effect on either parameter (Table 2).

Glucose homeostasis outcomes were modest, with small reductions in fasting glucose reported mainly in metabolically at-risk populations (MetS or hypercholesterolemia) and limited. Chen and Chien reported that 8 weeks of raw tomato supplementation reduced fasting glucose by 5.2 mg dL⁻¹.⁵² Similarly, Yu *et al.* showed that supplementation with lycopene-free tomato extract (Fruitflow®) led to a 5.4 mg dL⁻¹ reduction in fasting glucose at the 15-day follow-up after a 45-day supplementation period.⁵⁴ No other parameters of glucose homeostasis, including insulin levels and insulin resistance indices, showed any effect in the included studies (Table 1).^{52,66} The most consistent oxidative stress-related effect was enhanced resistance of LDL particles to oxidation, evidenced by a longer copper-ion-induced LDL oxidation lag time, suggesting reduced LDL susceptibility to oxidative modification,⁶⁸ while endogenous antioxidant enzymes (SOD, CAT, and GPx) remained largely unchanged.^{52,68} Inflammatory markers showed heterogeneous but generally modest responses, with reductions in C-reactive protein (CRP)⁵⁴ observed in high-risk populations (hypercholesterolemia), alongside limited adipokine modulation. Selected studies also reported improvements in specialized cardiovascular endpoints, including reduced platelet aggregation with sofrito and modest changes in endothelial adhesion markers⁵³ (Table 1). Across all other outcomes assessed in the quantitative meta-analysis, the pooled estimates did not reach statistical significance (Table 2). Sensitivity analyses using alternative pre-post correlation coefficients confirmed the robustness of the findings, as p -values varied only minimally across the tested r values and the statistical interpretation of the results remained unchanged (SI Table S2).

Meta regression

Owing to the limited number of studies (<10 per outcome), meta-regression analyses were restricted to outcomes with at least seven studies and should be interpreted cautiously. No significant associations were observed for anthropometric outcomes (SI Table S3). For the categorical moderator, significant differences across supplement types were observed for SBP (QM = 9.47 , $p = 0.0237$, SI Fig. S3(A)) and for DBP (QM = 8.62 , $p = 0.0349$, SI Fig. S3(B)), with a more pronounced overall



Table 2 Primary meta-analysis of randomized controlled trials assessing the effects of tomato and tomato-based product interventions on anthropometric and cardiometabolic outcomes

	Description		Pooled effect estimates			Heterogeneity			Prediction interval
	N of studies	N of subjects	MD	95% CI	P-Value (effect)	τ^2	I^2 (%)	P-Value (Q-test)	
Anthropometric parameters									
BW (kg)	7	362	-0.659	[-1.94; 0.63]	0.31	1.2	37.9	0.13	[-3.14; 1.83]
BMI (kg m ⁻²)	8	441	-0.004	[-0.20; 0.19]	0.96	0.0	0.0	0.96	[-0.25; 0.24]
BFM (%)	3	149	-0.069	[-0.72; 0.59]	0.83	0.0	0.0	0.90	[-0.72; 0.59]
BFM (kg)	2	89	-0.282	[-0.91; 0.34]	0.37	0.0	0.0	0.82	[-0.91; 0.34]
HC (cm)	3	139	-0.193	[-1.01; 0.62]	0.64	0.0	0.0	0.97	[-1.01; 0.62]
WC (cm)	5	242	-1.153	[-2.27; -0.04]	0.04	0.0	0.0	0.58	[-2.27; -0.04]
WHR	4	219	-0.005	[-0.02; 0.01]	0.63	0.0	0.0	0.96	[-0.02; 0.01]
Blood pressure									
SBP (mmHg)	8	549	-2.894	[-6.64; 0.85]	0.12	14.1	56.7	0.01	[-11.15; 5.37]
DBP (mmHg)	8	549	0.077	[-1.91; 2.06]	0.93	2.9	38.4	0.16	[-3.82; 3.98]
Lipid homeostasis									
TG (mg dL ⁻¹)	7	502	0.181	[-11.23; 11.59]	0.97	70.3	31.8	0.19	[-19.82; 20.18]
TC (mg dL ⁻¹)	8	535	1.881	[-3.11; 6.87]	0.46	0.0	0.0	0.35	[-3.11; 6.87]
LDL-C (mg dL ⁻¹)	8	562	0.234	[-3.98; 4.45]	0.91	0.0	0.0	0.56	[-3.98; 4.45]
HDL-C (mg dL ⁻¹)	7	502	1.913	[-0.65; 4.47]	0.14	4.8	45.5	0.12	[-3.09; 6.91]
ApoA-I (mg dL ⁻¹)	3	287	-0.785	[-6.75; 5.18]	0.79	0.0	0.0	0.79	[-6.75; 5.18]
ApoB-100 (mg dL ⁻¹)	3	287	-3.309	[-8.22; 1.61]	0.18	0.0	0.0	0.82	[-8.22; 1.61]
Glucose homeostasis									
FBG (mg dL ⁻¹)	5	420	0.592	[-1.21; 2.39]	0.51	0.0	0.0	0.25	[-1.21; 2.39]
Insulin (μ U mL ⁻¹)	3	278	0.447	[-1.50; 2.40]	0.65	1.9	65.7	0.07	[-2.20; 3.80]
QUICKI	3	278	0.135	[-0.11; 0.38]	0.28	0.0	92.8	<0.0001	[-0.35; 0.62]
Inflammatory and oxidative stress biomarkers									
CRP (mg dL ⁻¹)	3	257	3.855	[-3.88; 11.59]	0.32	25.9	50.8	0.13	[-8.77; 16.48]
IL-6 (pg L ⁻¹)	2	225	-0.094	[-0.34; 0.15]	0.44	0.0	0.0	0.78	[-0.34; 0.15]
Ox-LDL (mmol L ⁻¹)	2	225	0.204	[-6.83; 7.24]	0.95	0.0	0.0	0.84	[-6.83; 7.24]
Renal function									
Creatinine (mg dL ⁻¹)	2	142	0.015	[-0.01; 0.04]	0.23	0.0	0.0	0.61	[-0.01; 0.04]
Urea (mg dL ⁻¹)	2	142	0.352	[-2.14; 2.85]	0.78	0.0	0.0	0.83	[-2.14; 2.85]
Uric acid (mg dL ⁻¹)	2	142	-0.154	[-0.49; 0.18]	0.36	0.0	0.0	0.72	[-0.49; 0.18]

Pooled mean differences (MD; $\Delta I - \Delta C$) with 95% confidence intervals (CI) were calculated using random-effects models (REML). When change-score standard deviations were not reported, they were derived from pre- and post-intervention standard deviations assuming a within-group correlation coefficient (r) of 0.5; sensitivity analyses using $r = 0.25$ and $r = 0.75$ showed consistent results. Heterogeneity was assessed using τ^2 , I^2 , and Cochran's Q test. Prediction intervals indicate the expected range of true effects in future studies. Outcomes reported by fewer than two studies were not pooled. ApoA-I: apolipoprotein A-I, ApoB: apolipoprotein B, BFM: body fat mass, BMI: body mass index, BW: body weight, CRP: C reactive protein, DBP: diastolic blood pressure, FBG: fasting blood glucose, HC: hip circumference, HDL-C: high-density lipoprotein cholesterol, IL: interleukin, LDL-C: low-density lipoprotein cholesterol, Ox-LDL: oxidized low-density lipoprotein, QUICKI: quantitative insulin sensitivity check index, SBP: systolic blood pressure, TC: total cholesterol, TG: triglycerides, WC: waist circumference, and WHR: waist-to-hip ratio.

decrease in this parameter for the supplementation with raw tomatoes. Additionally, the mean change in triglyceride levels showed a positive trend toward association with the mean baseline BMI as a continuous moderator ($\beta = 5.94$, $p = 0.0587$, SI Fig. S4).

Qualitative synthesis of epidemiologic and preclinical studies

Qualitative synthesis of epidemiological studies. 5 epidemiological studies published between 2012 and 2023 were included; 2 reported results from the same cohort and were thus treated as a single study. These studies assessed associations between tomato consumption and anthropometric or cardiometabolic outcomes, encompassing a total of 52 275 participants (22.4% men, 77.6% women) (Table S6). Studies were conducted in adults with excess adiposity (mean BMI > 25 kg m⁻²), with a weighted mean BMI across studies of 26.9 kg m⁻². Dietary intake was assessed using semi-quantitative food frequency questionnaires (FFQ) or repeated 24 h recalls, with tomato exposure defined as whole tomato or total

tomato-based product consumption. Participants were commonly categorized into low, moderate, and high tomato consumption groups, which were generally evenly distributed across cohorts, with comparable BMI values between intake categories. The majority of participants were free of major chronic disease at baseline (no CVD or cancer), while a substantial proportion represented populations at increased cardiometabolic risk. Large population-based cohorts accounted for the majority of participants (>95%), whereas smaller studies focused on specific subpopulations, including pregnant women (1.9%), individuals with MetS (0.1%), and HIV-positive women (0.9%).

Among the observational studies, 1 reported no association between tomato consumption and BMI or other anthropometric parameters,¹¹⁰ whereas another identified a non-linear (U-shaped) relationship across intake categories.^{111,112} A prospective cohort study in pregnant women showed that higher tomato consumption was associated with lower odds of overweight/obesity (aOR = 0.50, 95% CI: 0.30 to 0.84) and excessive



gestational weight gain (aOR = 0.48; 95% CI: 0.24–0.96).¹¹³ Among adults stratified by MetS status in 1 study, participants without MetS reported higher tomato intake than those with MetS (0.94 ± 0.76 vs. 0.58 ± 0.72 portions per day). Tomato consumption was inversely correlated with both the number of MetS criteria fulfilled ($r = -0.30$, 95% CI: -0.48 to -0.10) and MetS severity in overweight individuals ($r = -0.47$, 95% CI: -0.71 to -0.12).¹¹⁴ Cardiometabolic parameters were assessed in 3 studies. Higher tomato intake was associated with lower blood pressure, total cholesterol, LDL-C cholesterol, fasting glucose, and insulin levels, as well as higher HDL-C. However, findings for triglycerides, LDL-C, and HDL-C were inconsistent across studies. Mortality outcomes were reported in 1 study, which showed lower all-cause, cardiovascular, stroke, and cancer mortality levels across increasing categories of tomato intake.

Qualitative synthesis of preclinical studies. A total of 31 preclinical studies published between 1999 and 2024 investigated the effects of tomato-based interventions in experimental models of obesity or cardiometabolic dysfunction; two publications reported distinct outcomes derived from the same animal cohorts and were therefore considered as a single study for synthesis. Most studies relied on rodent models. Overall, 55.1% used rats (mostly males), 27.6% mice, 6.9% hamsters, 3.5% *Drosophila melanogaster*, 3.5% gerbils, and 3.5% swine. Among the studies, high-fat diet (HFD) models predominated, accounting for more than 62.1% of experimental designs. Other diet-induced models included high-sucrose diets (HSD), Western diets (WD), high-sugar-fat diets (HSF), and high-cholesterol diets (HCD) combined with HFD.

Tomato powder was the most frequently used form of supplementation, accounting for 41.4% of preclinical studies. It was typically incorporated into the diet at concentrations ranging from 3.0% to 41.7% (w/w), most commonly 5.0% (w/w), with intervention durations generally spanning 8–12 weeks (overall range: 4–24 weeks). Tomato extracts represented the second most common intervention (37.9%), followed by tomato juice (13.8%). Other formulations, including sofrito, tomato paste, and sauce, together accounted for the remaining 6.9% of studies. Among studies assessing body weight or body weight gain, tomato extract supplementation was associated with a reduction in these outcomes in 25.0% of studies. Tomato powder supplementation showed a positive effect in 57.1% of the studies, while the extract was associated with reduced body weight in 42.9% of the studies. No significant effects on body weight outcomes were reported for sofrito, paste, or sauce-based interventions. Similarly, outcomes related to adipose tissue mass or adiposity indices were significantly improved in 43.8% of studies. Among the studies reporting significant improvements, 57.1% investigated tomato extracts and 42.9% used tomato powder.

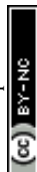
Overall, across all preclinical models of obesity and cardiometabolic dysfunction, tomato-based supplementation was consistently associated with improvements in cardiometabolic health, primarily through reductions in inflammation, oxidative stress, and hepatic lipid accumulation, whereas effects

on circulating lipid levels were more variable. Improvements in glucose homeostasis (fasting glucose, insulin, and insulin resistance indices) were observed in a substantial proportion of studies, even in the absence of significant weight loss. Among studies assessing lipid homeostasis, 72.7% reported beneficial effects. Of these studies showing improvements, 50.0% investigated tomato powder supplementation, 37.5% investigated tomato extracts, and the remaining studies used tomato juice. Similarly, among studies assessing glucose homeostasis, 62.5% reported beneficial effects. Among these, 50.0% investigated tomato powder, 30.0% investigated tomato extracts, and the remaining studies evaluated tomato juice or tomato sauce. Studies assessing inflammatory and oxidative stress biomarkers reported positive effects in nearly all cases, regardless of the form of tomato-based supplementation (SI Table S5).

Discussion

This systematic review and meta-analysis provide an integrated evaluation of clinical, epidemiological, and preclinical evidence on the effects of tomato and tomato-based interventions on obesity-related anthropometric and cardiometabolic outcomes. Collectively, the evidence indicates modest but biologically consistent effects in overweight or obese populations. Epidemiological studies reinforce these conclusions by consistently associating higher tomato consumption with more favorable cardiometabolic profiles, while preclinical studies provide mechanistic insights and demonstrate effects on adiposity, inflammation, and metabolic regulation.

From an anthropometric perspective, pooled analyses revealed a small but statistically significant reduction in waist circumference in RCTs, whereas body weight and BMI did not show significant pooled effects. Sensitivity analyses confirmed the robustness and internal consistency of these findings despite their small magnitude. This divergence suggests that tomato-based interventions may preferentially influence abdominal fat distribution rather than overall body mass, a pattern consistent with epidemiological observations and preclinical data showing reductions in visceral adiposity without marked changes in total body weight. In animal models, particularly those using tomato powder or tomato extracts, reductions in visceral white adipose tissue mass and adiposity indices were frequently reported even in the absence of body weight loss, supporting the concept of adipose tissue remodeling rather than global weight reduction. Mechanistically, growing evidence indicates that tomato-derived bioactives can directly modulate adipose tissue biology. Preclinical studies show that these effects involve key pathways regulating adipocyte function, including modulation of PPAR γ signaling and inhibition of NF- κ B-mediated inflammation, contributing to reduced adipocyte hypertrophy and lipid accumulation.^{19,115,116} While much of the evidence has focused on lycopene, complementary mechanisms have been described for dietary polyphenols, notably through activation



of thermogenic pathways, including increased brown adipose tissue (BAT) activity and induction of UCP1 and PGC-1 α expression, thereby enhancing energy expenditure and reducing adiposity.¹¹⁷ Waist circumference is a sensitive marker of visceral adiposity and cardiometabolic risk, reflecting central fat distribution and ectopic lipid accumulation. In clinical weight-loss interventions, decrements of approximately 5–10 cm have been associated with $\geq 10\%$ improvements in key cardiovascular risk markers, including total and LDL-C and DBP.¹¹⁸ Importantly, population-based evidence shows that even modest waist circumference reductions (<2 cm) confer protection against incident MetS over long-term follow-up, whereas each 1 cm increase in waist circumference is associated with an approximately 10% higher risk.¹¹⁹ Collectively, these data support the concept that even small reductions in waist circumference may yield significant metabolic benefits. The absence of consistent body weight or BMI reduction aligns with previous reviews and likely reflects the relatively short duration of most interventions and the fact that tomato-based strategies are not designed as weight-loss approaches. Instead, mechanistic evidence from preclinical studies indicates that tomato bioactives modulate adipose tissue function, resulting in reduced adipocyte hypertrophy and modulated lipid-handling pathways (e.g., *PPAR γ* , *SREBP-1c*, *ACC*).^{18,120,121} In preclinical models, the highest proportion of studies reporting reductions in body weight gain and adiposity was observed for tomato extracts and tomato powder, whereas liquid or semi-solid products generally showed limited effects on anthropometric parameters but consistent metabolic benefits. Notably, a higher lycopene content did not systematically translate into greater effects. Several studies reported substantial increases in circulating lycopene without corresponding anthropometric or metabolic improvements, and lycopene-free tomato extracts (e.g., Fruitflow®) produced comparable cardiometabolic effects.¹²² Moreover, exploratory meta-regression analyses examining different supplementation types, sorted by lycopene exposure levels, did not reveal any beneficial impact of higher lycopene intake. Although these findings are limited to a restricted set of parameters, they support the hypothesis that health effects are driven primarily by the food matrix of tomato products rather than by lycopene as an isolated nutrient. Both clinical and preclinical evidence indicate that the form of supplementation matters. Clinically, raw tomatoes generally tend to have more consistent cardiometabolic effects, with a marked impact specifically on blood pressure and plasma lipid levels. The strong association between sofrito and increased diastolic blood pressure can be explained by the presence of 2% sodium in its composition.^{53,123}

The cardiometabolic outcomes displayed a heterogeneous but coherent pattern. Qualitatively, improvements in lipid profile were more consistently observed in metabolically at-risk populations, whereas metabolically healthy individuals showed limited responsiveness. However, meta-regression analyses identified a positive association between baseline BMI and triglyceride response, indicating that the magnitude of the beneficial effect decreases with higher baseline adiposity. This

response pattern indicates that individuals with a low BMI show greater improvement in lipid metabolism than those who are overweight or obese. A similar pattern has been observed with other bioactive compounds, such as vitamin D, where overweight or obese individuals consistently show a reduced response to supplementation.¹²⁴ This may be explained by the fact that, as excessive adiposity sets in, chronic inflammation, oxidative stress, and metabolic inflexibility increase, reducing the organism's metabolic responsiveness to nutritional modulation. Therefore, these results highlight the primarily preventive rather than therapeutic effect of tomato-based dietary supplements for metabolic health, with a greater impact observed before the onset of significant adiposity and metabolic impairment. Although not all studies assessed inflammatory or oxidative stress endpoints, the most consistent effects observed were an increased LDL oxidation lag time, suggesting improved resistance of LDL particles to oxidation, and modest reductions in inflammatory markers, such as CRP and adhesion molecules. Preclinical studies consistently demonstrated the attenuation of oxidative stress pathways, reduction of lipid peroxidation, and suppression of inflammatory signaling, providing mechanistic support for clinical observations. These effects are biologically plausible and supported by known actions of tomato-derived compounds, including inhibited NF- κ B signaling, reduced expression of pro-inflammatory cytokines, improved redox balance, and enhanced resistance of lipoproteins to oxidative modification.^{13,15,17,36} These mechanisms are further supported by human intervention studies showing that tomato-derived products act through bioavailability-driven cellular effects. Notably, supplementation with Lyc-O-Mato® increased plasma and lymphocyte carotenoids (lycopene, phytoene, phytofluene, and β -carotene) and was associated with reduced oxidative stress-induced lymphocyte DNA damage, indicating improved cellular resistance to reactive species.¹²⁵ Similarly, dietary interventions with tomato-derived products were associated with reduced LDL oxidizability and lower urinary 8-iso-PGF2 α , reflecting decreased lipid peroxidation, likely mediated by carotenoid accumulation in membranes and lipoproteins with antioxidant activity.¹²⁶ Furthermore, these findings support the idea of a synergistic interaction between multiple tomato-derived bioactives, as human studies report concomitant increases in phytoene and phytofluene alongside lycopene. As shown in the human intervention study by Riso *et al.*, tomato consumption also significantly increased intracellular vitamin C levels, a well-recognized antioxidant that can regenerate oxidized lipid-phase antioxidants and enhance overall cellular redox balance, thereby contributing to improved protection against oxidative damage.¹²⁷ Beyond these intracellular effects, vitamin C has been widely associated with cardioprotective properties, including improvement of endothelial function, reduction of oxidative stress, and limitation of LDL oxidation, all of which are key processes in the development of atherosclerosis.¹²⁸ Although tomato-derived compounds are often described as antioxidants, the classical oxidative stress hypothesis has been challenged by



large-scale trials, such as ATBC and Beta-Carotene and Retinol Efficacy Trial (CARET), which reported adverse effects of β -carotene supplementation in specific high-risk populations, notably smokers and asbestos-exposed individuals.^{129,130} This highlights that antioxidant effects are context-dependent and may not systematically translate into clinical benefit, emphasizing the need for caution when interpreting oxidative stress-related outcomes.

Across all available data, sex representation was unbalanced and varied depending on the type of study. Women were over-represented in clinical trials ($\approx 63\%$) and epidemiological studies ($\approx 78\%$), while most preclinical experiments were conducted exclusively on male animals. Given the well-established sex differences in fat distribution, hormone regulation, lipid metabolism, inflammatory tone, and vascular function, men and women are likely to respond differently to tomato-based interventions. Sex hormones are known to modulate key pathways targeted by tomato bioactives, including adipogenesis, oxidative stress, and endothelial function.^{131,132} Consequently, sex-dependent responses remain poorly characterized, limiting both the generalizability and mechanistic interpretation of the findings. Future studies should systematically include both sexes and be adequately powered to explore sex-specific effects, which is essential for a comprehensive understanding of the cardiometabolic impact of tomato-based interventions.

Overall, heterogeneity was low, supporting the reliability of the observed associations despite differences in population characteristics, baseline cardiometabolic risk, intervention form, dose, duration, and study design. Importantly, outcomes reaching statistical significance generally exhibited low or negligible heterogeneity, and sensitivity analyses supported the robustness of key findings. Nevertheless, several limitations must be acknowledged. Many clinical trials had a short duration, included relatively small sample sizes, and were not specifically designed to detect changes in anthropometric outcomes. Considerable variability in tomato formulations, processing methods, and dosing further limits direct comparability across studies. Meta-regression analyses were exploratory due to the limited number of studies per outcome and should be considered hypothesis-generating rather than confirmatory. In addition, the underrepresentation of women and the predominance of male animals in preclinical research represent important sources of potential bias. Although dietary questionnaires were often used, these data were not consistently incorporated into the analyses. As a result, potential confounders (background diet, baseline tomato intake, intake of other antioxidant-rich foods, or lifestyle factors) may have influenced the observed effects. This highlights a well-recognized limitation in nutritional research, where isolating the independent impact of a single dietary component remains challenging due to the complexity of diet-lifestyle interactions. In particular, higher tomato consumption is often embedded within broader dietary patterns, such as the Mediterranean diet, characterized by high intake of plant-based foods and lower consumption of meat and processed products,¹³³ making it difficult to separate the specific effects of tomatoes from overall dietary behaviors.

Overall, converging clinical, epidemiological, and pre-clinical data suggest that tomato-based interventions have modest beneficial effects in overweight or obese individuals, primarily targeting visceral adiposity and cardiometabolic pathways rather than inducing overt weight loss, with more apparent effects in individuals with high cardiometabolic risk. One of the main contributions of this review is to support the notion that the effects of tomato-based interventions cannot be attributed to lycopene alone, as no association was observed between lycopene intake and the magnitude of anthropometric or cardiometabolic effects. Furthermore, comparable cardiometabolic and anthropometric effects were observed with tomato matrices lacking lycopene. These results contradict the assumption of a dominant role for isolated lycopene and instead highlight the importance of the tomato food matrix, supporting the concept of food synergy and reinforcing current paradigms that emphasize the benefits of whole foods and dietary habits rather than the isolated effect of nutrients. Overall, the data suggest that the consumption of tomatoes and tomato-based products may have potential as a preventive nutritional approach in the context of overweight or obesity, particularly through their beneficial effect on waist circumference. Waist circumference is a clinically relevant marker of abdominal adiposity and cardiometabolic risk, and its reduction may therefore reflect an improvement in obesity-related risk profiles. Although modest, this effect is supported by established mechanisms and is consistent with the extensive evidence linking plant-rich diets, such as the Mediterranean diet, with improved cardiometabolic health.¹³⁴ Future research should focus on long-term, sufficiently powered randomized trials using standardized interventions, clinically relevant endpoints, and sex-stratified analyses in order to better define the relevance of tomato-based interventions on cardiometabolic health.

Author contributions

JFL and LS designed the review, wrote the paper and had primary responsibility for the final content. LM participated in the writing and revision of the review. All authors have read and approved the final manuscript.

Conflicts of interest

The authors declare that there are no conflicts of interest.

Data availability

No primary research results, software or code have been included, and no new data were generated or analysed as part of this review.

Supplementary information (SI) is available. See DOI: <https://doi.org/10.1039/d6fo00495d>.



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