

Resveratrol Supplementation and its Potential Benefits in Obesity-related Non-communicable Diseases

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Abstract

Background/Aim: Resveratrol, a polyphenolic compound found in grapes, berries, and peanuts, has been linked to antioxidant, anti-inflammatory, and vasoprotective effects. Yet, evidence from randomized controlled trials (RCTs) remains inconsistent, and the quality, dosage, and cost of commercial resveratrol products vary considerably, raising uncertainty about their true efficacy. A comprehensive synthesis of its effects on obesity-related non-communicable diseases (NCDs) is therefore warranted. Given that obesity is a key driver of metabolic dysregulation underlying diabetes, cardiovascular disease, and fatty liver disease, clarifying resveratrol's potential in overweight and obese populations is of particular importance.

Materials and Methods: We systematically searched PubMed, Embase, the Cochrane Library, and Web of Science for RCTs published up to July 2025 that evaluated resveratrol supplementation in adults with obesity-related metabolic disorders or associated risk factors. Study selection and data extraction followed PRISMA 2020 guidelines. Pooled estimates were calculated using random-effects models, and heterogeneity was assessed with the I^2 statistic.

Results: Forty RCTs involving 2551 participants were included. Resveratrol significantly reduced the homeostatic model assessment of insulin resistance (HOMA-IR), total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL) cholesterol, systolic blood pressure (SBP) and diastolic blood pressure (DBP), high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6). No consistent changes were observed for high-density lipoprotein (HDL) cholesterol, body weight (BW), body mass index (BMI), fat mass, hip circumference (BC), waist circumference (WC), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl

continued



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transferase (GGT), or liver fat. To our knowledge, this meta-analysis includes the largest number of RCTs to date and the most comprehensive coverage of obesity-related metabolic and inflammatory endpoints. Effect sizes varied by intervention dose and duration.

Conclusion: Resveratrol supplementation shows modest benefits on selected metabolic and inflammatory parameters but does not exert broad effects across all obesity-related NCD risk factors. Its potential role may be most relevant in populations with metabolic disturbances. Large-scale, long-term RCTs are warranted to clarify optimal dosing strategies and establish its utility in the prevention and management of obesity-related non-communicable diseases.

Keywords: Lipid profile, glycemic control, polyphenols, blood pressure, inflammatory.

Introduction

Non-communicable diseases (NCDs), including cardiovascular disease, type 2 diabetes mellitus, and non-alcoholic fatty liver disease, remain the leading causes of morbidity and mortality worldwide, accounting for the majority of premature deaths and healthcare costs (1). The growing global prevalence of obesity has become a major driver of these conditions (2), as it contributes to dyslipidemia, hypertension, insulin resistance, and chronic low-grade inflammation – all key components of metabolic dysfunction (2, 3). This interconnection underscores the urgent need for safe and effective preventive and therapeutic strategies that can target multiple metabolic abnormalities simultaneously. Given the strong association between excess adiposity and the risk of NCDs, interventions capable of modulating obesity-related metabolic disturbances are of clinical interest.

Resveratrol, a naturally occurring polyphenolic stilbene found in grapes, berries, and peanuts, has attracted considerable scientific interest due to its potential cardiometabolic benefits (4, 5). Preclinical studies have demonstrated that resveratrol exerts antioxidant, anti-inflammatory, anti-atherogenic, and insulin-sensitizing effects (6), partly through activation of sirtuin-1 (SIRT1), modulation of AMP-activated protein kinase (AMPK), and suppression of pro-inflammatory cytokines such as TNF- α and IL-6 (6, 7). These molecular actions suggest a plausible role for resveratrol in

mitigating endothelial dysfunction, improving lipid metabolism, and reducing oxidative stress, which are key pathological processes underlying CVD.

Despite promising experimental evidence, findings from clinical trials on resveratrol's effects in obesity-associated metabolic disorders remain inconsistent. While some RCTs report significant improvements in lipid profile, glycemic control, blood pressure, and inflammatory biomarkers (8-10), others find minimal or no benefit (11-14). Such discrepancies may be due to variations in dosage, treatment duration, participant health status, and outcome measures across studies.

Given the heterogeneity of existing evidence, a comprehensive synthesis of clinical trial data is warranted to clarify the potential role of resveratrol in mitigating metabolic and inflammatory risk factors linked to obesity-related NCDs. Therefore, this meta-analysis systematically reviews and quantitatively evaluates randomized controlled trials investigating the effects of resveratrol supplementation on glycemic control, lipid profile, blood pressure, inflammatory markers, and anthropometric measures in adults. Special attention was given to outcomes relevant to obesity-related non-communicable diseases, aiming to provide integrated evidence that may guide clinical practice and future research.

Materials and Methods

Data sources and selection criteria. This meta-analysis synthesized data from RCTs investigating the effects of

resveratrol supplementation in individuals with cardiovascular diseases. A comprehensive search of PubMed, Embase, the Cochrane Library, and Web of Science was conducted for studies published up to July 2025. The search strategy combined Medical Subject Headings and free-text terms related to resveratrol and cardiovascular or cardiometabolic risk factors, including glycemic control, lipid profile, blood pressure, inflammatory markers, and anthropometric measures, along with terms specific to randomized controlled trial designs [Resveratrol(Mesh) OR resveratrol(tiab) OR trans-resveratrol(tiab) OR "3,5,4'-trihydroxy-trans-stilbene"(tiab)) AND ("Obesity"(Mesh) OR "Overweight"(Mesh) OR "Metabolic Syndrome"(Mesh) OR "Insulin Resistance"(Mesh) OR "Type 2 Diabetes Mellitus"(Mesh) OR Diabetes Mellitus, Type 2"(tiab) OR "Non-alcoholic Fatty Liver Disease"(Mesh) OR "Fatty Liver"(tiab) OR "Cardiovascular Diseases"(Mesh) OR "Hypertension"(Mesh) OR "Dyslipidemias"(Mesh) OR "Blood Pressure"(Mesh) OR "Glycemic Control"(tiab) OR "Glucose"(Mesh) OR cholesterol(Mesh) OR triglycerides(Mesh) OR "Inflammation"(Mesh) OR "C-Reactive Protein"(Mesh) OR "Tumor Necrosis Factor-alpha"(Mesh) OR "Interleukin-6"(Mesh) OR anthropometry(Mesh) OR "Body Mass Index"(Mesh) OR obesity(tiab) OR overweight(tiab)) AND ("Randomized Controlled Trial"(Publication Type) OR "Controlled Clinical Trial"(Publication Type) OR random*(tiab) OR placebo(tiab) OR trial(tiab)) NOT (animal(mh) NOT human(mh))]. Animal-only studies were excluded to focus on human clinical evidence. This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Reference lists of eligible studies were also screened to identify additional relevant trials. Studies such as case reports, technical papers, conference abstracts, reviews, editorials, letters, and non-clinical investigations were excluded. The study protocol was registered in PROSPERO (registration number CRD42025632701).

Selection of studies. Two independent researchers conducted the screening and evaluation of all potentially

eligible studies. A third researcher oversaw the process to ensure accuracy and consistency. Full texts of all relevant articles were obtained and carefully reviewed to confirm eligibility. The sequential selection process is presented in the PRISMA flow diagram (Figure 1).

Data extraction. Two researchers independently extracted data using a standardized form in accordance with the recommendations of the Cochrane Handbook (15). Extracted data included the study's authors and year of publication, study location, participant eligibility criteria, demographic characteristics such as sample size and age range, study design, intervention details, outcomes measured, and the methods used for outcome assessment.

Outcomes. Only RCTs with intervention durations longer than two weeks were included, while shorter trials were excluded. Primary outcomes comprised SBP, DBP, fasting blood glucose (FBG), fasting insulin, hemoglobin A1c (HbA1c), HOMA-IR, and inflammatory markers (TNF- α , hs-CRP, IL-6). Additional primary outcomes included liver enzymes (ALT, AST, GGT) and lipid parameters (TC, TG, HDL-C, LDL-C). Secondary outcomes were body weight and BMI.

Assessment of methodological quality. Two independent researchers evaluated the risk of bias in the included studies using the Cochrane Collaboration's Risk of Bias tool to determine methodological quality. Discrepancies between their assessments were resolved through discussion with a third reviewer until consensus was reached. Studies were considered to have a high risk of bias when one or more domains of the tool indicated notable concerns.

Data analysis. The quantitative analysis was performed using Standardized Mean Differences (SMDs) with corresponding 95% Confidence Intervals (CIs) to compare outcomes between intervention and control groups. A random-effects model was employed to address variability among studies. Statistical analyses were

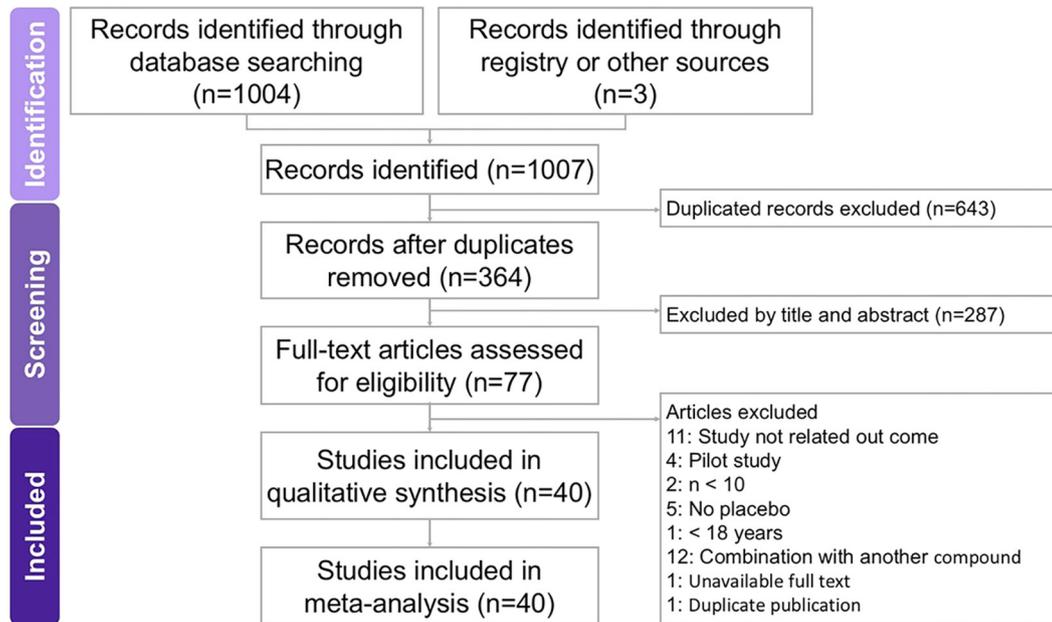


Figure 1. PRISMA flow diagram illustrating the selection process of randomized controlled trials included in the meta-analysis assessing the effects of resveratrol supplementation on non-communicable disease management.

conducted using Comprehensive Meta-Analysis software, version 3 (Biostat, Englewood, NJ, USA). Heterogeneity was assessed using the I^2 statistic, with values exceeding 50% indicating substantial heterogeneity. Publication bias was evaluated through visual inspection of funnel plots and Egger's regression test, applying a significance threshold of $p < 0.05$ for most outcomes and $p < 0.10$ for bias detection. Subgroup analyses were undertaken to identify possible sources of heterogeneity, and sensitivity analyses were conducted by sequentially excluding individual studies to examine the stability of the results.

Results

Study search and characteristics of participants. The process of identifying and selecting trials for inclusion is summarized in Figure 1. A comprehensive database search of PubMed, Embase, Web of Science, and the Cochrane Library yielded 1,007 records. After removing duplicates, 364 unique studies remained for initial screening based on titles and abstracts, leading to the

exclusion of 287 studies that did not meet the inclusion criteria. The full texts of the remaining 77 articles were assessed for eligibility, and 37 studies were subsequently excluded after detailed evaluation. Reasons for exclusion included studies enrolling participants under 18 years of age (16), pilot study (17-20), total sample size < 10 (21, 22), trials evaluating outcomes unrelated to the objectives of this analysis (23-33), no placebo (34-38), combining with other compound (39-50), unavailable full text (51), and duplicate publication (52). In total, 40 RCTs were included in the final quantitative synthesis (8-14, 53-85). All selected studies were published in English. The main characteristics of these trials are presented in Table I. The included studies, published between 2010 and 2024, enrolled a total of 2,551 participants and assessed the effects of resveratrol supplementation on glucose metabolism, lipid metabolism, and pro-inflammatory cytokines, among other related outcomes.

Quality assessment. The risk of bias for all included RCTs was evaluated using the RoB 2 tool. Forty trials were

Table I. Characteristics of included studies.

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
2~4 weeks									
Timmers (2011) / Netherlands	Obese but otherwise healthy male individuals	Obese male individuals (BMI >30), no diabetes, hypertension, or cardiovascular disease.	Diabetes, cardiovascular disease, hypertension, active smoking, and medications influencing metabolism.	P: 11 (100)/52.3±2.1 I: 10 (100)/52.3±2.1	RCT/ Double-blind/ Placebo-controlled crossover trial	Identical placebo capsules, matched in appearance and dosing schedule to resveratrol.	Resveratrol 150 mg/day for 30 days	Resveratrol significantly reduced hepatic fat, inflammatory markers, TG, ALT, and improved HOMA-IR; also decreased sleeping and resting metabolic rate.	No significant change in BW.
Voduc (2014) / Canada	Healthy, sedentary adults	Sedentary lifestyle, BMI 20-30, no significant medical conditions.	Any clinically significant abnormality, pre-existing medical conditions affecting exercise, BMI <20 or >30, current medications.	P: 12 (50)/mean age 43 I: 12 (50)/mean age 43	RCT/ Double-blind/ Placebo-controlled crossover trial	Placebo capsules, identical appearance, oral, twice daily, matched to intervention.	Resveratrol: 500 mg twice daily for 1 week, then 1000 mg twice daily for 3 weeks (total 2 g/day for 3 weeks), for 4 weeks	No significant changes in fasting glucose or inflammatory markers. Small but statistically significant increases in AST, ALT, TC, and triglycerides, all within normal limits.	No withdrawals due to side effects.
Poulsen (2013) / Denmark	Obese but otherwise healthy male individuals	BMI >30 kg/m ² , no prescription medication, no endocrine or metabolic disorders, clinically healthy by physical exam.	Overt endocrine disease, use of prescription medication, any major comorbidity, abnormal clinical biochemistry.	P: 12 (100)/31.9±2.9 I: 12 (100)/44.7±3.5	RCT/ Double-blind/ Placebo-controlled trial	Placebo tablets identical in appearance and frequency to intervention.	Resveratrol 1500 mg/day for 4 weeks	No significant effect on insulin sensitivity, fasting glucose, HOMA-IR, HbA1c, lipid profile, BMI, blood pressure, or inflammatory biomarkers.	Two participants withdrew.

Table I. Continued

Table I. *Continued*

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
van der Made (2015) / Netherlands	Overweight and slightly obese male and female individuals with low HDL	BMI 25-35, HDL <1.21 mmol/l (male individuals) or <1.53 mmol/l (female individuals), TC <8.0 mmol/l, fasting glucose <7.0 mmol/l, stable weight, non-smoker, no relevant meds.	Cholesterol-lowering or glucose-lowering medication, pregnancy/breastfeeding, high alcohol use, recent participation in other trials or blood donation.	n=45 (55.5), mean age 61±7 years; crossover design (all participants received both treatments)	RCT / Double-blind/ Placebo-controlled, crossover trial	Placebo capsules, identical appearance, 2 per day	Resveratrol 150 mg/day for 4 weeks	No significant changes in fasting lipids, fasting glucose, insulin, HOMA-IR, BW, inflammatory markers, or endothelial markers.	No significant effect on liver or kidney function, or other safety parameters.
Apostolidou (2016) / Greece	Asymptomatic hypercholesterolemia	Healthy adults, cholesterol >200 mg/dl, no medications for CVD, no other pathology.	Documented dyslipidemia, chronic liver disease, malnutrition, neoplastic/acute infectious disease, habitual supplement use, vegetarianism, alcoholism.	n=33 completed (61) / mean age 50.4±14.1. Crossover, all subjects received both treatments.	RCT / Placebo-controlled, crossover trial	Placebo capsules, identical appearance, once daily	Resveratrol 150 mg/day for 30 days	Significant increase in vitamin E (α-tocopherol, +35.7%, p<0.001), no significant change in total antioxidant capacity, no change in TC, LDL, HDL, TG, and BMI.	No adverse events; no effect on BMI, waist/hip ratio, or lifestyle factors.
Javid (2017) / Iran	T2DM	BMI 18.5-30 kg/m ² , T2DM (diagnosed <5 years), fasting glucose <22 mmol/l, moderate periodontitis.	Diabetes complications, pregnancy/lactation, travel >2 weeks, smoking immunosuppressant use, insulin therapy, periodontal treatment in last 6 months, antioxidant use.	P: 22 (18)/50±8 I: 21 (24)/49±7	RCT / Placebo-controlled, crossover trial	Placebo capsule (starch, 480 mg), 2/day	Resveratrol 240 mg/day, 4 weeks, plus standard nonsurgical periodontal treatment in both.	Resveratrol significant reduction in fasting insulin, HOMA-IR, and periodontal pocket depth compared to placebo. No significant difference in fasting glucose or TG.	No significant differences in BW, BMI, or dietary intake between groups.
van der Made (2017) / Netherlands	Overweight and slightly obese adults	BMI 25-35 kg/m ² , healthy, no disturbances in lipid or glucose metabolism, no CVD, HDL cholesterol <1.21 mmol/l (male individuals) or <1.53 mmol/l (female individuals).	Not meeting inclusion criteria, including abnormal lipid/glucose metabolism, diagnosed cardiovascular disease, outside age/BMI range.	n=45 completed (44); age 61±7 years; all received both resveratrol and placebo	RCT / Double-blind/ Placebo-controlled, crossover trial	Cellulose capsules, 2 × 58 mg/day	Resveratrol 150 mg/day, oral, for 4 weeks, with > 4 weeks washout between phases.	No effect on fasting or postprandial glucose, insulin, triglycerides.	No effect by sex, BMI category, or medication use.

Table I. *Continued*

Table I. Continued

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
Hoseini (2019) / Iran	T2DM and Coronary Heart Disease	Confirmed 2 or 3-vessel CHD	Resveratrol use within 3 months, antioxidant/anti-inflammatory supplement use, acute myocardial infarction or cardiac surgery in past 3 months, renal or hepatic failure.	P: 28 I: 28/mean age and sex not specified	RCT/ Double-blind/ Placebo-controlled trial	Placebo capsules, identical in color/ shape/ size/ package, 1 per day	Resveratrol 500 mg/day, for 4 weeks	Significant reductions in fasting glucose, insulin, HOMA-IR, total-/HDL-cholesterol ratio; significant increase in insulin sensitivity, and HDL.	No serious adverse events.
Ahmadi-Mousavi (2024) / Iran	HIV	On antiretroviral therapy	Not explicitly listed, but participants were excluded if they had acute illness, unwilling to consent, or did not meet basic study requirements.	P: 21 (38)/46.3±6.6 I: 20 (45)/44.4±10.6	RCT/ Double-blind/ Placebo-controlled trial	Identical capsule in appearance, once daily	Resveratrol 500 mg/day, for 4 weeks	Resveratrol had no significant effect on TC or TG compared to placebo. No significant effects on anxiety, depression, sleep quality, or quality of life (all $p>0.05$).	No significant adverse events; all participants completed the trial.
4~8 weeks									
Ghanim (2010) / USA	Healthy adults (no chronic disease)	Normal BMI (~21.8), similar age, no use of anti-inflammatory medication	Any history of disease, current illness, or use of anti-inflammatory agents.	P: 10/36±5 years I: 10/36±5 years	RCT/ Double-blind/ Placebo-controlled trial	Matching placebo capsules	Resveratrol, 200 mg/day for 6 weeks	Resveratrol significantly reduced inflammatory and insulin-resistance-related biomarkers. Compared to the placebo group: Improvements in lipid profiles and inflammation markers were statistically significant in intervention groups compared to control.	No participants withdrew from the study.
Militaru (2013) / Romania	Stable angina pectoris	Diagnosed with stable angina pectoris (CCS class II-IV), clinically stable at least 1 month, BMI 24-27, on standard angina treatment	Pregnancy, lactation, legal incapacity, <3 months since recent hospitalization for unstable angina/MI/ revascularization, alcohol or drug abuse, moderate/severe liver or kidney disease, anemia, chronic inflammatory disease, participation in another trial.	P: 29 (62)/64.2±7.1 I: (R): 29 (58.6)/64.9±5.8 I: (CF): 29 (62.1)/63.7±6.2 I: (CF+R): 29 (62.1)/66.3±5.5	RCT/ Double-blind/ Placebo-controlled trial	Usual care	I (R): Resveratrol 20 mg/day I (CF+R): Resveratrol 20 mg/day + CF 112 mg/day I (CF): CF 112 mg/day P: Standard medical care/ 8 weeks	No serious adverse events were reported; all treatments were well tolerated.	No serious adverse events were reported; all treatments were well tolerated.

Table I. Continued

Table I. *Continued*

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
Movahed (2013) / Iran	T2DM	Established T2DM, BMI between 25-35 kg/m ² , and stable glycemic control using oral medications.	Insulin therapy, serious liver or renal disease, thyroid disorders, recent use of anti-inflammatory or antioxidant supplements, smoking, alcohol abuse, pregnancy, or lactation.	P: 31 (45.2)/51.8 1±6.99 I: 33 (48.5)/52.45±6.18	RCT/ Double-blind/ Placebo-controlled trial	Microcellulose capsules, identical in appearance to resveratrol capsules.	I: Resveratrol 1 g/ day. P: 500 mg microcellulose twice daily. Both groups continued standard antidiabetic medications without change/ 45 days	Compared to the placebo group: FBS: ↓ 34.93 mg/dl ($p<0.0001$), HbA1c: ↓ 1.2% ($p<0.0001$), Insulin: ↓ 4.82 μIU/ml ($p<0.0001$), HOMA-IR: ↓ 2.69 ($p<0.0001$), HDL: ↑ 4.75 mg/dl ($p=0.001$), and SBP: ↓ 7.58 mmHg ($p<0.0001$).	No significant change in BMI, body weight, diastolic BP, total cholesterol, triglycerides, liver enzymes, or creatinine.
Chachay (2014) / Australia	NAFLD, overweight or obese male individuals	BMI >25 kg/m ² , waist >90 cm, hepatic steatosis by ultrasound.	Other causes of steatosis (viral hepatitis, daily ethanol >40g, steatogenic meds), cirrhosis, T2DM, chronic kidney disease, serious cardiovascular disorders.	P: 10 (100)/47.5±11.2 I: 10 (100)/48.8±12.2	RCT/ Double-blind/ Placebo-controlled trial	Placebo capsules (microcellulose), matching appearance and dose schedule to intervention.	Resveratrol 3,000 mg/day for 8 weeks	Compared to the placebo group: 1. No improvement in insulin sensitivity, 2. No reduction in energy hepatic steatosis. 3. No significant changes in fasting glucose, insulin, or lipid profile.	No significant changes in antioxidant markers or energy expenditure.
Samsami-kor (2015) / Iran	Mild to moderate active ulcerative colitis	Mild to moderate active ulcerative colitis, BMI 18.5-30, stable medication dose >1 month.	Change in drug type/dose past month, other GI/ inflammatory/ infectious diseases, cancer, pregnancy/ lactation, recent supplement or NSAID use, hospitalization or drug change during study.	P: 25 (48)/37.7±16.2 I: 24 (50)/39.0±11.8	RCT/ Double-blind/ Placebo-controlled trial	Placebo capsules, identical appearance, once daily.	Resveratrol 500 mg/day, once daily/ 6 weeks	Resveratrol significantly reduced plasma TNF-α and hs-CRP activity versus placebo; improved clinical colitis activity score and quality of life.	No adverse events.

Table I. *Continued*

Table I. Continued

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
Thazhath (2016) / Australia	T2DM	BMI ~27.7, HbA1c ~6.4%, no major comorbidities, no medications affecting GI or CV function.	Microvascular/ macrovascular complications, other significant comorbidity, medication affecting GI or CV function, smokers.	n=14 (71)/ 67.5±1.6	RCT/ Double-blind/ Placebo-controlled, crossover trial	Placebo capsules (microcrystalline cellulose), 500 mg, twice daily	Resveratrol 1000 mg/day, for 5 weeks	No significant effect of resveratrol on fasting or postprandial blood glucose, HbA1c, GLP-1 secretion, gastric emptying, body weight, or daily energy intake compared to placebo.	No reported adverse effects; excellent adherence; no withdrawals.
Khodabandehloo (2018) / Iran	T2DM	HbA1c >7, age 30-70, BMI <35 kg/m ² , on diet or oral hypoglycemic agents (not insulin), no allergy to grapes/ green tea/peanuts, provided consent.	Type 1 diabetes, pregnancy/lactation, insulin therapy, antioxidants, steroids, anti-inflammatories, anticoagulants, uncompensated diabetes, severe heart/liver/kidney disease, chronic diabetes complications, any severe or life-threatening illness, unstable weight, allergy to grapes/ green tea/peanuts.	P: 20 (50)/61.1±5.6 I: 25 (52)/56.5±6.7	RCT/ Double-blind/ Placebo-controlled trial	Microcellulose capsules, identical to intervention, 400 mg twice daily	Resveratrol 800 mg/day, for 8 weeks	Significant reduction in fasting plasma glucose and BP with resveratrol versus placebo. No significant changes in HbA1c, insulin, HOMA-IR, lipid profile, or inflammatory markers.	No significant adverse events, high compliance (>96%).
Seyyedebrahimi (2018) / Iran	T2DM	On diet or oral hypoglycemic agents (not insulin), no allergy to grapes/ green tea/peanuts, able to consent.	Type 1 diabetes, pregnancy/lactation, severe heart/hepatic/renal disease, participation in a weight loss program during study.	P: 25 (32)/58.72±6.06 I: 23 (47)/54.96±6.37	RCT/ Double-blind/ Placebo-controlled trial	Microcellulose capsules, identical to intervention, 400 mg twice daily	Resveratrol 800 mg/day, for 8 weeks	No significant effect on glycemic or lipid parameters, but weight, BMI, and BP were significantly reduced compared to placebo.	Significantly increased plasma total antioxidant capacity and total thiol content.

Table I. Continued

Table I. *Continued*

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
Abdollahi (2019) / Iran	T2DM	BMI 25-30 kg/m ² , HbA1c <8%	Other complications (cancer, renal/liver failure, GI ulcers, Alzheimer's, psychological disorders, CVD), insulin therapy, pregnancy/lactation, use of antioxidant supplements, fibrates, platelet aggregation inhibitors, anti-inflammatory drugs, red wine consumption.	P: 36 (44)/50.06±7.69 I: 35 (43)/50.14±7.38	RCT/ Double-blind/ Placebo-controlled trial	Methyl cellulose capsules, identical appearance, 500 mg twice daily	Resveratrol 1,000 mg/day, for 8 weeks	Significant reduction in fasting blood sugar, insulin, and significant increase in HDL vs: placebo (all after adjustment). No significant changes in weight, BMI, fat mass, WC, LDL, TC, TG, HbA1c, or HOMA-IR.	No significant effect on anthropometric/body composition after adjustment.
Simental-Mendia (2019) / Mexico	Dyslipidemia	Apparently healthy male and non-pregnant female patients, newly diagnosed dyslipidemia (TC >200 mg/dl and/or TG >150 mg/dl)	Smoking, alcohol intake, diabetes, acute/chronic renal or hepatic disease, malignancy, CVD, lipid-lowering drug or resveratrol supplement use, serum TG >400 mg/dL, LDL-C >190 mg/dL.	P: 36 /42.7±11.1 I: 35 /42.2±10.8	RCT/ Double-blind/ Placebo-controlled trial	Sucrose capsules (0.5 g/d), identical appearance	Resveratrol 100 mg/day, for 2 months	Resveratrol group had significant reductions in TC and TG compared to placebo. No significant differences for HDL or LDL.	No adverse effects reported.
Zhou (2023) / China	Dyslipidemia	At least two of: fasting TG >1.7 mmol/L, TC >5.2 mmol/L, LDL >3.12 mmol/L, or HDL <0.91 mmol/L	Use of lipid-lowering meds (past 6 months), phytochemical supplements (past 3 months), severe acute or chronic illness (past 1 month), pregnancy, lactation.	P: 43 (30) /61.3±8.96 I: (100 mg): 41 (27) /59.5±8.7 I: (300 mg): 43 (32.5) /61.1±9.19 I: (600 mg): 41 (31.7) /60.8±8.32	RCT/ Double-blind/ Placebo-controlled four-arm trial	Identical appearance	Resveratrol 100, 300, or 600 mg/day, for 8 weeks	No significant effect on lipid profile (TC, TG, LDL, HDL), glucose, insulin, HOMA-IR, or oxidative stress biomarkers.	No serious adverse events.
Dogan (2024) / Turkey	Ulcerative colitis	On mesalamine and/or azathioprine	Pregnancy, breastfeeding, chronic diseases (diabetes, thyroid, liver, kidney, cardiovascular), use of anti-inflammatory or antibiotics.	MD: 16 MD + Curcumin: 16 MD + Resveratrol: 16 Each group about 50% male individuals; age ~39-40 years	RCT/ Three-arm parallel trial	No true placebo group: all groups were compared on the basis of a MD	MD+R group: +Resveratrol 500 mg/day	All groups: Significant within-group reduction in CRP, waist/hip circumference, bowel frequency, and improved quality of life (p<0.05).	No serious adverse events, no withdrawals reported.

Table I. *Continued*

Table I. Continued

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
8~12 weeks									
Magyar (2012)/ Hungary	Stable coronary artery disease post-myocardial infarction.	Angiographically verified coronary artery disease; history of myocardial infarction at least 6 months prior; stable clinical condition.	Not explicitly reported.	P: 20 (65)/67.4±7.7 I: 20 (65)/65.3±9.7	RCT/ Double-blind/ Placebo-controlled trial	Matching placebo capsule, 10 mg daily, identical in appearance.	Resveratrol 10 mg/day orally, for 3 months	Resveratrol lowered LDL, while no significant changes in hs-CRP, TNF- α , total cholesterol, HDL, TG, or blood pressure.	No adverse events or dropout reported.
Faghihzadeh (2014) / Iran	NAFLD	Ultrasound-proven NAFLD, ALT >30 IU/l (men) or >19 IU/l (women), no significant alcohol use, no other liver, cardiac, respiratory, or renal disorders, not pregnant/lactating, no meds in prior 3 months.	10% weight loss during intervention, pregnancy, or voluntary withdrawal.	P: 25 (68)/46.3±9.5 I: 25 (72)/44.0±10.1	RCT/ Double-blind/ Placebo-controlled trial	Placebo capsules (medium-chain triglyceride oil), identical appearance, once daily.	Resveratrol 500 mg/day (pure trans-resveratrol), once daily for 12 weeks	Resveratrol significantly reduced ALT, improved hepatic steatosis grade (ultrasound), reduced inflammatory markers (hs-CRP, IL-6, TNF- α , NF- κ B). No significant effect on BW or BMI compared to placebo.	No significant difference in energy intake or physical activity; both groups improved anthropometric parameters (due to lifestyle advice). No serious adverse events.
Méndez-del Villar (2014) / Mexico	Metabolic syndrome, non-diabetic.	No previous medication for metabolic syndrome components, stable weight for >3 months, nonsmokers.	Morbid obesity, heavy physical activity, liver/renal/thyroid/heart disease, drugs affecting BP/ glucose/lipids in prior 6 months, pregnancy.	P: 12 (50)/40.3±5.4 I: 12 (8)/39.8±5.4	RCT/ Double-blind/ Placebo-controlled trial	Placebo capsules, identical appearance, 500 mg (three times daily).	Resveratrol 1,500 mg/day, for 90 days	Resveratrol significantly decreased BW, BMI, fat mass, WC, and insulin; no significant changes in fasting/postprandial glucose.	No significant changes in waist/hip ratio, blood pressure, or severity of liver steatosis by ultrasound.
Chen (2015) / China	NAFLD	Ultrasound-diagnosed NAFLD, BMI 20-30, fasting glucose <7.8 mmol/l, no other chronic liver/kidney disease or malignancy.	Excessive alcohol intake (>140 g/week male individuals, >70 g/week female individuals), recent use of meds affecting glucose/lipid metabolism (past 6 months).	P: 30 (67)/43.5±11.0 I: 30 (73)/45.2±10.0	RCT/ Double-blind/ Placebo-controlled trial	2 placebo capsules (pullulan + maltodextrin) twice daily, identical appearance.	Resveratrol 600 mg/day for 3 months	Significant reduction in AST, ALT, fasting glucose, HOMA-IR, TC, LDL, and TNF- α . No significant effect on BW, BMI, TG, and HDL.	No significant changes in waist/hip ratio, blood pressure, or severity of liver steatosis by ultrasound.

Table I. Continued

Table I. *Continued*

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
Imamura (2017) / Japan	T2DM	HbA1c >7.0%, on diet/exercise/ medication, no recent med changes.	HbA1c >9.0%, allergy to shellfish, pregnancy/lactation, history of cerebrovascular or vascular disease, renal or severe liver dysfunction, atrial fibrillation, fasting TG >400.	P: 25 (44)/58.2±10.1 I: 25 (60)/57.4±10.6	RCT/ Double-blind/ Placebo- controlled trial	Placebo tablet, matching appearance, 1/ day	Resveratrol tablet 100 mg/day, for 12 weeks	Resveratrol significantly decreased SBP, and oxidative stress marker compared to placebo; slight, non-significant reductions in weight and BMI. No significant effect on fasting glucose, HbA1c, TC, TG, HDL, or LDL.	No adverse events related to supplement
Asghari (2018) / Iran	NAFLD	NAFLD by ultrasound, BMI 25-35 kg/m ²	Pregnancy, breastfeeding, postmenopause, athlete, smoking, alcohol use, recent diet or weight loss, other liver disease, diabetes, thyroid dysfunction, cancer, CVD, kidney/GI/ pulmonary/ autoimmune disease, recent surgery, certain medications/ supplements within 3 months.	P: 30 (65.4)/39.3±5.5 I: 30 (72)/39.8±7.7 CR: 30 (70.8)/40.1±7.1	RCT/ Placebo- controlled parallel 3 arms clinical trial	Starch capsules, identical appearance, 2 x 300 mg/day	Resveratrol 600 mg/day, for 12 weeks	Resveratrol group: modest but significant weight loss, reduced BMI and WC vs. placebo; no significant changes in ALT, AST, hepatic steatosis, glycemic parameters, or lipid profile compared to placebo.	No serious adverse events. All groups: similar baseline and physical activity.
Kantartzis (2018) / Germany	Overweight and insulin-resistant adults	BMI >27 kg/m ² , HOMA-IR >2.0, broad liver fat content range.	Major comorbidities, advanced cardiometabolic disease, or use of medications affecting insulin sensitivity or liver fat.	P: 54 I: 54/ Age and sex balanced	RCT/ Double-blind/ Placebo- controlled trial	Placebo capsules identical in appearance, twice daily	Resveratrol 150 mg/day, for 12 weeks	No significant reduction in liver fat content with resveratrol versus placebo. No significant effects on glycaemic control, BW, total/visceral/subcutaneous adipose tissue, blood pressure, lipid profile, or inflammatory markers.	Resveratrol was safe and well tolerated; high adherence (~97%).

Table I. *Continued*

Table I. Continued

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
Farzin (2020) / Iran	NAFLD	BMI 25-35 kg/m ²	History of other liver disease, inherited liver disorders, diagnosed cardiovascular/ kidney/ diabetes/ gastrointestinal/ pulmonary/ autoimmune/ thyroid/ cancer, professional athletes, pregnant, breastfeeding, postmenopausal, alcohol/tobacco/ supplement use, recent weight loss diet, use of corticosteroids or hepatotoxic/ anticlotting/ antidiuretic/ lipid-lowering drugs.	P: 25 (68)/38.7±5.8 I: 25 (72)/39.8±8.1	RCT/ Double-blind/ Placebo-controlled trial	Corn starch capsules, identical appearance, 2 per day	Resveratrol 600 mg/day, for 12 weeks	Resveratrol group had significant reductions in BW, BMI, and WC compared to baseline; no significant effect on lipid profile, atherogenic indices, liver enzymes, HC, waist-hip ratio, or blood pressure compared to placebo.	No significant adverse events.
Batista-Jorge (2020) / Brazil	Metabolic Syndrome	BMI >30 kg/m ² , able to comply with diet and physical activity	Pregnancy, bariatric surgery, anorexigenic drug use, BMI <30, musculoskeletal/ neurologic/ vascular/ pulmonary/cardiac problems, use of hypolipidemic/ antidepressant/ anticoagulant medications, psychiatric disorder, hypothyroidism, inability to complete follow-up.	P: 12 I: 13/ mean age not reported, sex not specified	RCT/ Double-blind/ Placebo-controlled trial	Identical capsules, matched for appearance, dose not specified	Resveratrol 250 mg/day, for 12 weeks	Significant improvements in BW, BMI, WC, TC, HDL, VLDL, leptin, urea, and creatinine in the resveratrol group compared to placebo. No significant difference in fasting glucose, HBA1c, insulin, ALT, AST, triglycerides, or uric acid.	No significant adverse events.

Table I. Continued

Table I. *Continued*

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
12~24 weeks									
Arzola-Paniagua (2016) / Mexico	Obesity	BMI 30-39.9, Mexican, clinically healthy, no recent weight loss.	Fasting glucose >126 mg/dl, history of cardiovascular events, cancer, AIDS, renal/liver disease, pregnancy, smoking, substance abuse, alcohol, or any medication; recent use of hypolipidemics, antihypertensives, hypoglycemics, steroids, chemo, immuno-suppressants, anorectics.	P: 24 (12.5)/38.8±9.6 I: 15 (20)/33.7±11.9 O: 21 (23.8)/39.7±8.91 O+R: 24 (12.5)/40.9±10.0	RCT/ Double-blind/ Placebo-controlled, parallel 4-arm trial	Placebo capsules, identical appearance, 1 capsule before each meal (3/day)	Resveratrol: 300 mg/day for 6 months. Orlistat: 360 mg/day for 6 months. Orlistat + Resveratrol: 360 mg orlistat + 300 mg resveratrol daily for 6 months.	Resveratrol alone resulted in moderate weight/fat loss.	Adverse events mild and similar between groups.
Bo (2016) / Italy	T2DM	BMI <35 kg/m ² , on diet or non-insulin hypoglycemic drugs, able to provide consent and comply with study.	Insulin use, anti-inflammatory drugs (other than aspirin), liver/kidney disease, chronic complications, recent CVD event, severe comorbidities, pregnancy, allergy to relevant foods.	P: 62 (76)/65.4±8.8 I: 40 mg: 65 (59)/64.9±8.6 I: 500 mg: 65 (63)/65.0±7.6	RCT/ Double-blind/ Placebo-controlled, parallel 3-arm trial	Microcellulose capsule, identical appearance, 1 capsule/day	Resveratrol 40 mg/day or 500 mg/day, oral, 1 capsule/day for 6 months.	Resveratrol (40 mg or 500 mg) significantly reduced CRP, improved glycemic control, lipid profile, BW, fat mass, BP, or inflammatory markers versus placebo.	All doses well tolerated; no serious adverse events.
Heebøll (2016) / Aarhus	NAFLD	BMI >25 kg/m ² , transaminasemia (ALT >70 U/l male individuals, >45 U/l female individuals), histologically confirmed NAFLD, at least one metabolic syndrome component.	Diabetes, severe systemic or malignant disease, other causes of liver injury (viral, autoimmune, drug-induced, alcoholic).	P: 14/ age ~50 I: 14/age ~50	RCT/ Double-blind/ Placebo-controlled trial	Placebo capsules, identical appearance, 3/day	Resveratrol 1500 mg/day for 6 months.	Resveratrol did not significantly improve ALT, AST, GGT, or intrahepatic lipid content compared to placebo.	High-dose, long-term resveratrol was well tolerated with limited benefit in NAFLD clinical or metabolic outcomes.

Table I. *Continued*

Table I. Continued

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
Kjær (2017) / Aarhus	Metabolic syndrome	Diagnosed with metabolic syndrome, otherwise healthy.	Not specified in full text extract.	P: 24/47.8±1.3 I: (150 mg): 21/49.1±1.5 I: (1,000 mg): 21/51.9±1.3	RCT / Double-blind/ Placebo-controlled, parallel 3-arm trial	Placebo tablets, identical appearance, 2 per day	Resveratrol 150 mg/day or 1,000 mg/day, both for 16 weeks.	Neither resveratrol dose improved inflammation markers, glucose metabolism, body composition, BP, or hepatic/visceral fat (MRI). Resveratrol high group showed significant increases in TC and LDL versus placebo ($p<0.013$ and $p<0.006$, respectively).	No serious adverse events.
Bo (2018) / Italy	T2DM	BMI <35 kg/m ² , on diet or non-insulin oral hypoglycemic drugs, able to provide consent and comply with study.	Insulin therapy, use of antioxidant or anti-inflammatory drugs (except aspirin), liver/kidney disease, chronic diabetic complications, recent CVD event, severe comorbidities, pregnancy, allergy to relevant foods.	P: 62 (76) I: 65.4±8.8 I: (40 mg): 65 (59)/64.9±8.6 I: (500 mg): 65 (63)/65.0±7.6	RCT / Double-blind/ Placebo-controlled trial	Microcellulose capsule, identical appearance, 1 capsule/day	Resveratrol 40 mg/day or 500 mg/day for 6 months.	No significant changes in glycemic control, lipid profile, BW, inflammatory markers, or daily energy intake for either resveratrol dose.	Resveratrol 500 mg/day significantly prevented the decline in whole-body BMD.

Table I. Continued

Table I. *Continued*

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
de Lig (2020) / Netherlands	Overweight and obese	BMI 27-35, stable weight (± 5 kg/3 months), willing to avoid resveratrol-rich foods/supplements.	Uncontrolled hypertension, HbA1c >48 mmol/mol, diagnosed T2DM, alcohol >20 g/d, use of medications interfering with glucose metabolism, participation in other biomedical trials within 1 month.	P: 21 (57)/62 \pm 1.5 I: 20 (60)/61 \pm 1.3	RCT/ Double-blind/ Placebo-controlled trial	Capsules identical in appearance, 2 x 75 mg daily	Resveratrol 150 mg/day for 6 months.	No effect on insulin sensitivity (Matsuda index), intrahepatic lipid, body composition, blood pressure, energy metabolism, physical performance, or quality of life/sleep. HbA1c was significantly lower in the resveratrol group compared to placebo. No significant differences in fasting glucose or insulin, or lipid profile.	No serious adverse events.
Mahjabeen (2022) / Pakistan	T2DM	Diabetes duration >5 years, HbA1c 7-12%, on oral hypoglycemic agents >1 year.	Acute illness, thyroid disorders, malignancy, HIV, hepatitis B or C, uncontrolled hypertension, chronic kidney disease, BMI >35 kg/m ² , familial hyperlipidemia, pregnancy, lactation, use of insulin, statins, anti-inflammatory drugs, or vitamin supplements.	P: 55 (65)/50.0 \pm 12.6 I: 55 (56)/49.4 \pm 9.0	RCT/ Double-blind/ Placebo-controlled trial	Cellulose capsule	Resveratrol 200 mg/day, once daily for 24 weeks, in addition to standard oral hypoglycemic agents.	Resveratrol significantly reduced fasting plasma glucose, HbA1c, fasting insulin, HOMA-IR, hs-CRP, TNF- α , IL-6, and micro-albuminuria compared to placebo. No significant change in total cholesterol, LDL, HDL, or TG.	No participants withdrew due to adverse events.

Table I. *Continued*

Table I. Continued

Author (year) / Country	Diagnosis	Inclusion criteria	Exclusion criteria	Sample size (% of male)/ age	Study design	Comparator / Placebo details	Intervention/ Duration	Main results	Secondary results
García-Martínez (2023) / Mexico	T2DM	Treated with metformin and/or glibenclamide, no kidney or liver damage.	Not explicitly listed, but likely included severe renal or hepatic impairment, or not meeting above inclusion.	P: 28 I: (500 mg): 32 I: (1,000 mg): 37/ Age: 63-66 years	RCT/ Double-blind/ Placebo-controlled three-arm trial	Capsules identical to resveratrol, microcrystalline cellulose + magnesium stearate, 2 capsules daily	Resveratrol 1,000: 1,000 mg/day; Resveratrol 500: 500 mg/day/ 24 weeks	1,000 mg/day group: Significant reduction in TG; no significant change in glucose, HbA1c, TC, HDL, BW, BMI, or blood pressure.	No significant adverse events reported.
>24 weeks									
Huhn (2018) / Germany	Healthy elderly	BMI 22-40	History of stroke, psychiatric disease, diabetes, severe internal disease, antidepressant / antioxidant use, high alcohol/ caffeine/ nicotine intake, pregnancy.	P: 26 (46)/67.5±5.1 I: 27 (48)/68.6±4.9	RCT/ Double-blind/ Placebo controlled trial	Microcrystalline cellulose capsules, identical to intervention, 2 per day	Resveratrol 200 mg/day, for 26 week	Resveratrol group had a significant increase in serum cholesterol and body fat compared to placebo. No significant group difference for HbA1c, glucose, insulin, BMI, or hippocampal structure/ connectivity.	No effect on depression, sleep, stress, or lifestyle. No significant hippocampal volume or mean diffusivity changes.
Zaw (2021) / Australia	Menopausal women	Community-dwelling postmenopausal women, age 45-85, >12 months since menopause, not using hormone therapy.	Use of insulin or warfarin, history of breast/cervical cancer, major heart, kidney, or liver disease, neurological disorder, clinical depression, suspected dementia, BP >160/100 mmHg, recent critical life events.	n=125 (0) / 65±7	RCT/ Double-blind/ Placebo-crossover trial	Nert excipients, identical capsule (Veri-te™ placebo), 75 mg BID	Resveratrol 150 mg/day, for 12 months	Fasting insulin and HOMA-IR were significantly reduced (improved insulin sensitivity). No effect on fasting glucose, blood pressure, lipid profile, or arterial compliance.	Adverse events balanced between groups and mostly unrelated.

ALT: Alanine transaminase; AST: aspartate aminotransferase; BMD: bone mineral density; BMI: body mass index; BW: body weight; CF: calcium fructoborate; CR: calorie restricted; CVD: cardiovascular disease; DBP: diastolic blood pressure; FBS: fasting blood sugar; HbA1C: glycated Hemoglobin; HDL: high-density lipoprotein cholesterol; HIV: Human Immunodeficiency Virus; HOMA-IR: homeostasis model of assessment for insulin resistance; hs-CRP: high-sensitive C-reactive protein; LDL: low-density lipoprotein cholesterol; MD: mediterranean diet; NAFLD: Non-Alcoholic Fatty Liver Disease; O: orlistat; P: placebo; I: intervention; R: resveratrol; SBP: systolic blood pressure; T2DM: type 2 diabetes mellitus; TC: total cholesterol; TG: triglycerides; WC: waist circumference.

assessed across five standard domains. Overall, 57.5% of the studies were judged as having some concerns of bias, while the remainder were rated as low risk. The most frequent issue was related to the randomization process, with nearly half of the trials providing insufficient information on sequence generation or allocation concealment. Selective reporting was another common concern, observed in proximately 40% of the studies, often due to missing trial registration or the absence of a predefined analysis plan. In contrast, the risk of bias from missing outcome data was minimal in over 95% of the studies, as participant attrition was rare. Bias arising from deviations from intended interventions and outcome measurement was generally low, particularly in placebo-controlled, double-blind trials employing objective measures. Figure 2A shows the domain-level judgments for each study, and Figure 2B summarizes the proportion of studies in each risk category per domain. Taken together, the methodological quality of the included trials was moderate to high, with most studies demonstrating appropriate design and limited risk of bias.

Impact of resveratrol supplementation on fasting blood glucose. Resveratrol supplementation did not produce a statistically significant reduction in fasting blood glucose levels [SMD -0.149, 95% confidence interval (CI)=-0.257 to -0.041; $I^2=23.064\%$, $p=0.126$; Figure 3]. In subgroup analyses based on intervention duration (Figure 4), a small but significant reduction was observed in studies lasting four weeks or less (SMD -0.345, 95%CI=-0.571 to -0.119; $I^2=5.891\%$, $p=0.382$). No significant effects were detected in trials with longer durations, including those lasting 4 to 8 weeks (SMD -0.143, 95%CI=-0.407 to 0.122; $I^2=45.394\%$, $p=0.066$), 8 to 12 weeks (SMD -0.090, 95%CI=-0.317 to 0.138; $I^2<0.001\%$, $p=0.410$), 12 to 24 weeks (SMD -0.101, 95%CI=0.306 to 0.104; $I^2=24.700\%$, $p=0.232$), and more than 24 weeks (SMD -0.030, 95%CI=-0.260 to 0.201; $I^2<0.001\%$, $p=0.595$).

Analysis by daily dosage (Figure 5) showed that supplementation between 100 and 500 mg per day resulted in a small but statistically significant reduction

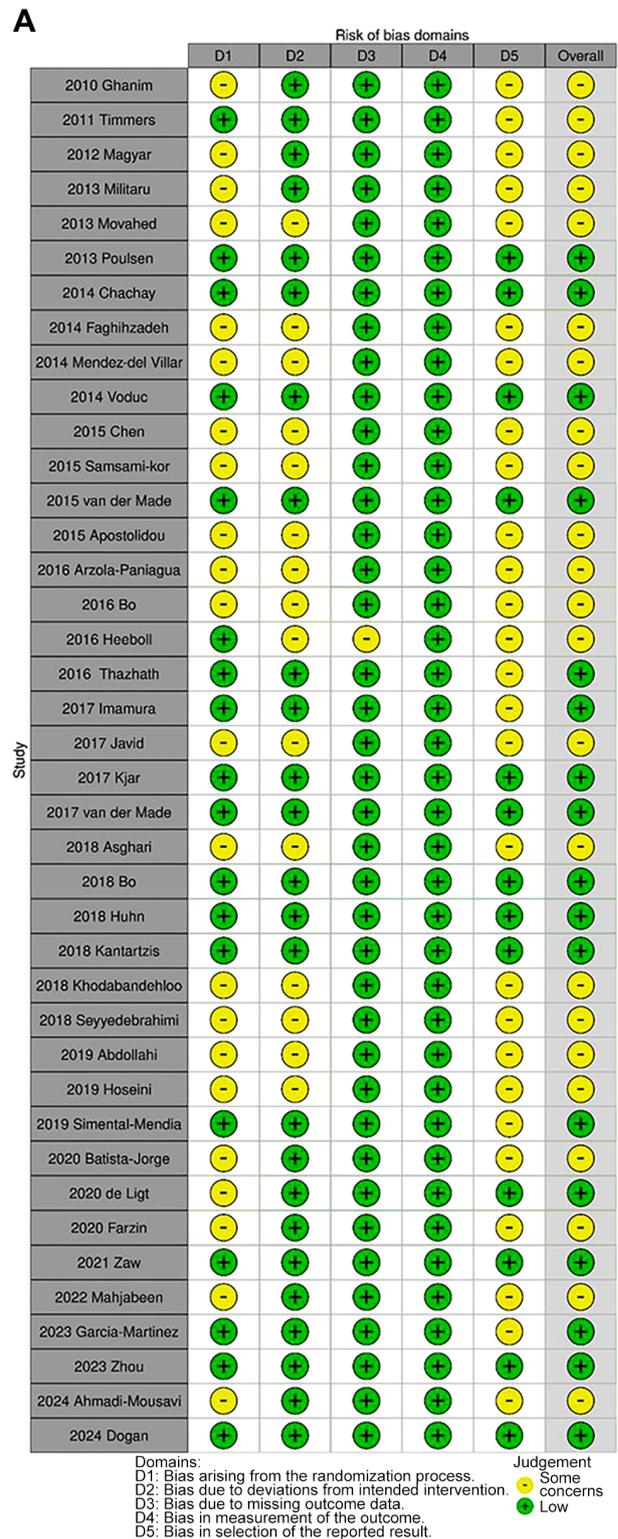


Figure 2. Continued

B

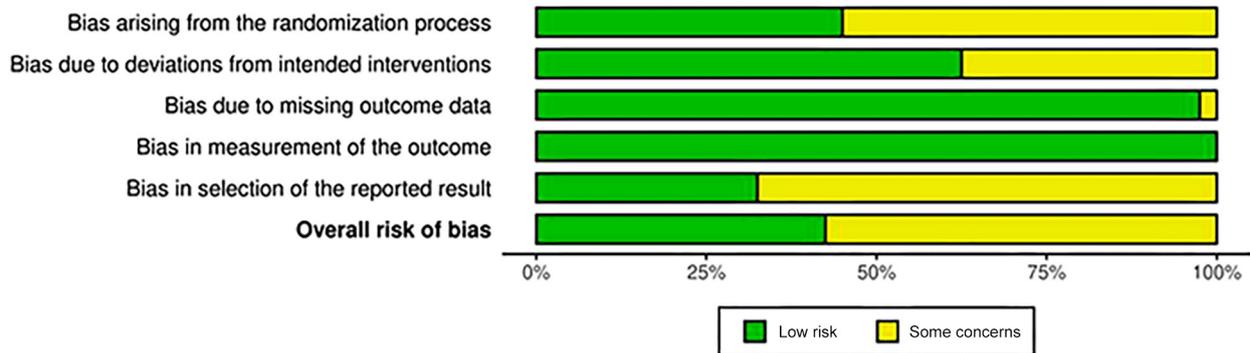


Figure 2. Evaluation of the methodological quality of the included trials. (A) Individual risk of bias assessment for each selected study, based on the Rob 2.0 tool (<https://mcguinlu.shinyapps.io/robvis/>). (B) Overall risk of bias summarized as a percentage, considering intention-to-treat and per-protocol analyses.

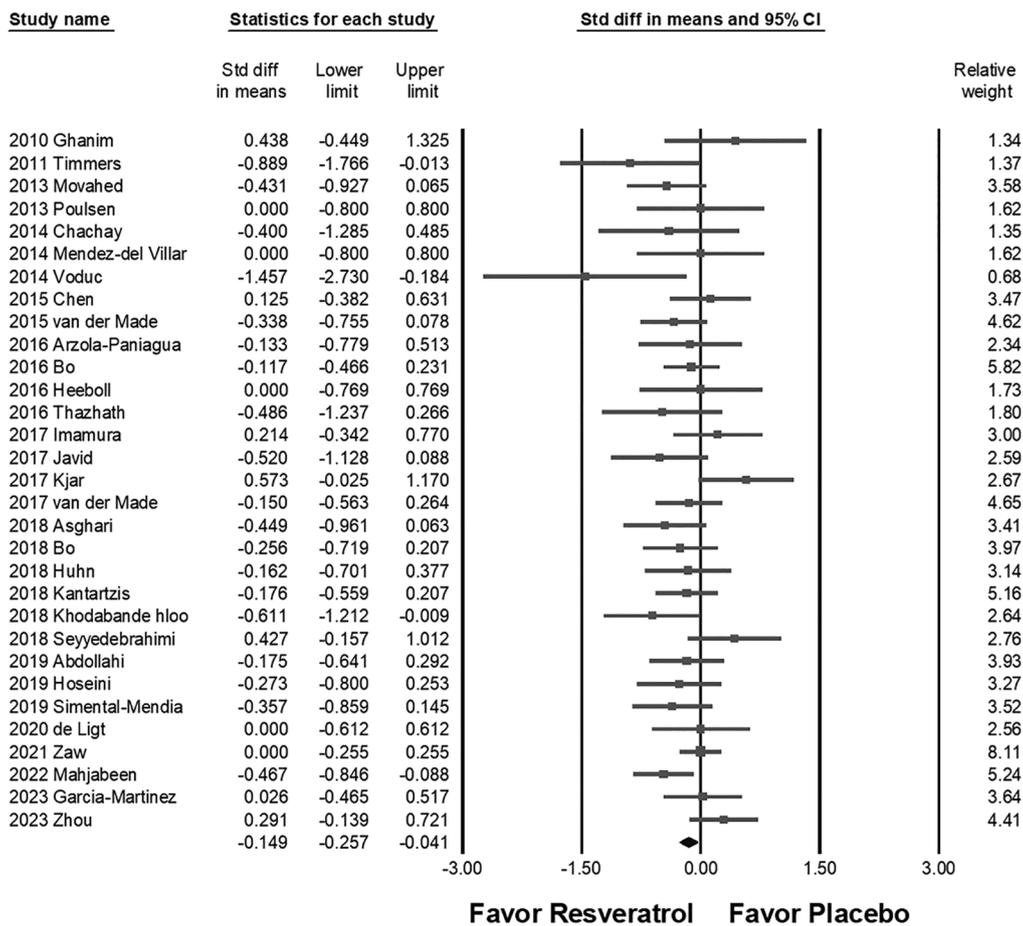


Figure 3. Forest plot presenting the effects of resveratrol supplementation on fasting blood glucose levels. Squares indicate the effect estimates of individual studies along with their 95% confidence intervals. Diamonds at the bottom of each panel represent the pooled effect size, illustrating the overall influence of resveratrol on fasting blood glucose.

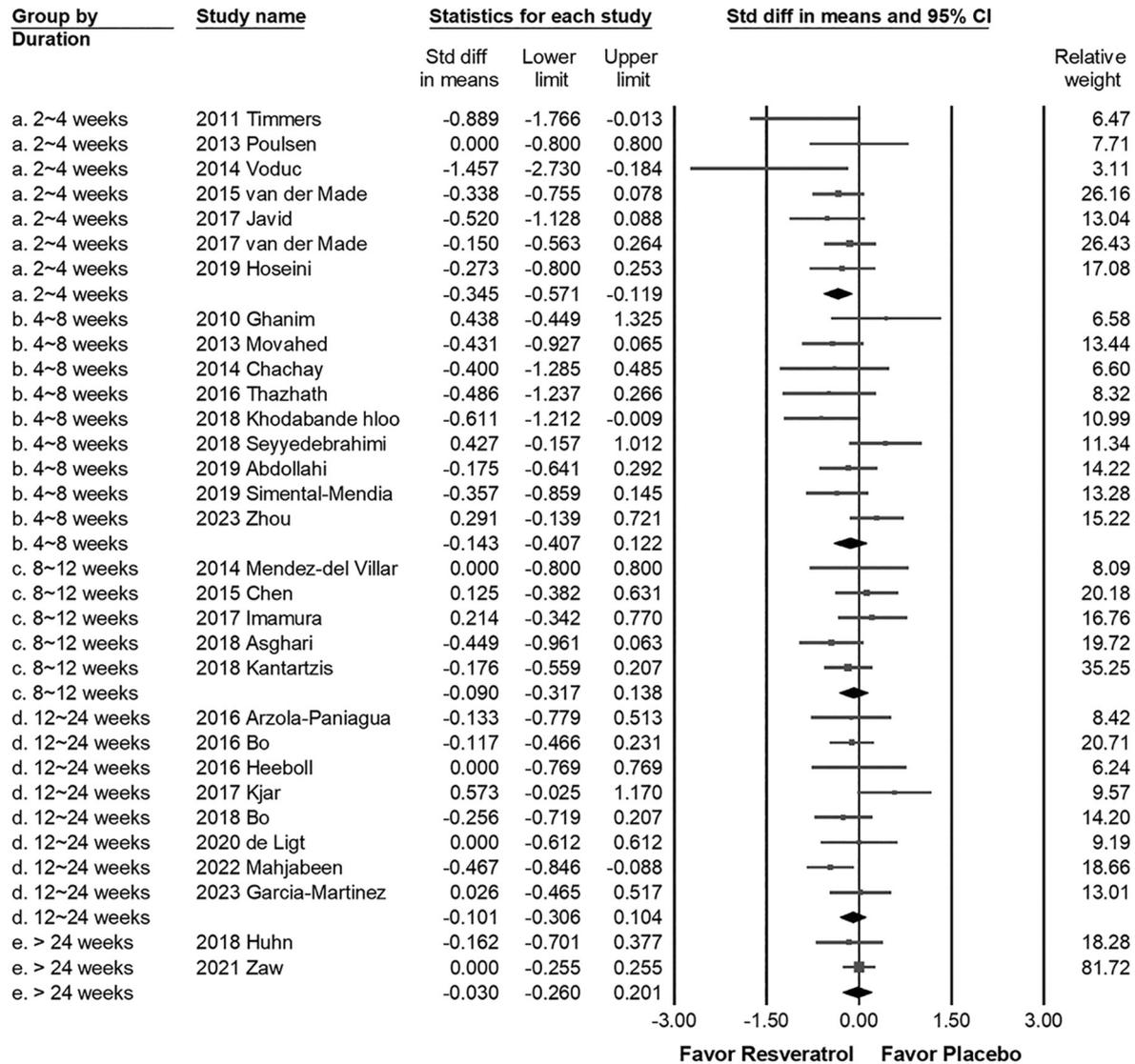


Figure 4. Forest plot showing the effects of resveratrol supplementation on fasting blood glucose levels, stratified by intervention duration. Squares display the effect estimates of individual studies with their 95% confidence intervals, and the diamonds at the bottom of each panel represent the pooled effect size, illustrating the overall impact of resveratrol on fasting blood glucose.

in fasting blood glucose (SMD -0.220, 95%CI=-0.344 to -0.097; $I^2<0.001\%$, $p=0.771$). No significant effects were found for other dosages, including less than 100 mg/day (SMD 0.033, 95%CI=-0.212 to 0.279; $I^2<0.001\%$, $p=0.362$), 501 to 999 mg/day (SMD -0.031, 95%CI=-0.417 to 0.355; $I^2=63.468\%$, $p=0.027$), exactly 1,000 mg/day (SMD -0.126, 95%CI=-0.576 to 0.324; $I^2=60.653\%$, $p=0.054$), 1,001 to 1,500 mg/day (SMD

-0.000, 95%CI=-0.456 to 0.456; $I^2<0.001\%$, $p>0.999$), and 1,501 to 3,000 mg/day (SMD -0.825, 95%CI=-1.841 to 0.190; $I^2=43.989\%$, $p=0.181$).

As shown in Figure 6, subgroup analysis combining intervention duration and dosage revealed a pronounced and statistically significant reduction in fasting blood glucose when the intervention lasted between 2 and 4 weeks with a dosage of 1,501 to 3,000 mg per day (SMD

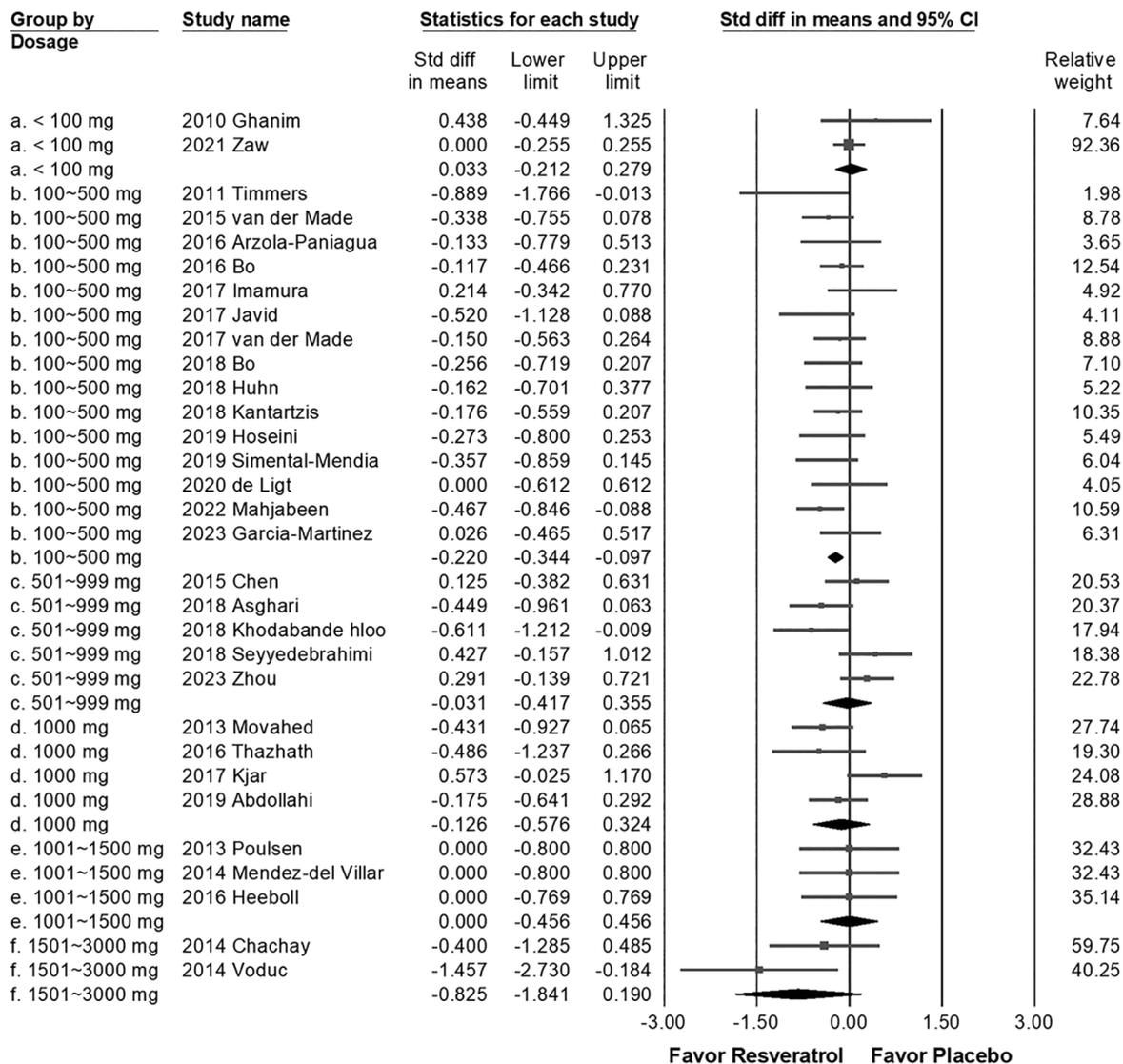


Figure 5. Forest plot illustrating the effects of resveratrol supplementation on fasting blood glucose levels, categorized by intervention dosage. Squares indicate the effect estimates of individual studies with their 95% confidence intervals, while the diamonds at the bottom of each panel represent the pooled effect size, reflecting the overall impact of resveratrol on fasting blood glucose.

-1.457; 95%CI=-2.730 to -0.184; $I^2<0.001\%$, $p>0.999$). A small reduction was observed with dosages below 500 mg per day administered for 2 to 4 weeks (SMD -0.332; 95%CI=-0.560 to -0.104; $I^2<0.001\%$, $p=0.606$), as well as with a dosage of 1,000 mg per day administered for 4 to 8 weeks (SMD -0.327; 95%CI=-0.637 to -0.018; $I^2<0.001\%$, $p=0.687$). No statistically significant effects were detected in other subgroups. These included interventions lasting

2 to 4 weeks with dosages of 1,001 to 1,500 mg per day, where a moderate effect was seen in total cholesterol (SMD 0.000; 95%CI=-0.800 to 0.800; $I^2<0.001\%$, $p>0.999$). No significant effects were observed for interventions of 4 to 8 weeks with dosages below 100 mg per day (SMD 0.438; 95%CI=-0.449 to 1.325; $I^2<0.001\%$, $p>0.999$), between 100 and 500 mg per day (SMD -0.357; 95%CI=-0.859 to 0.145; $I^2<0.001\%$, $p>0.999$), 501 to 999 mg per day (SMD

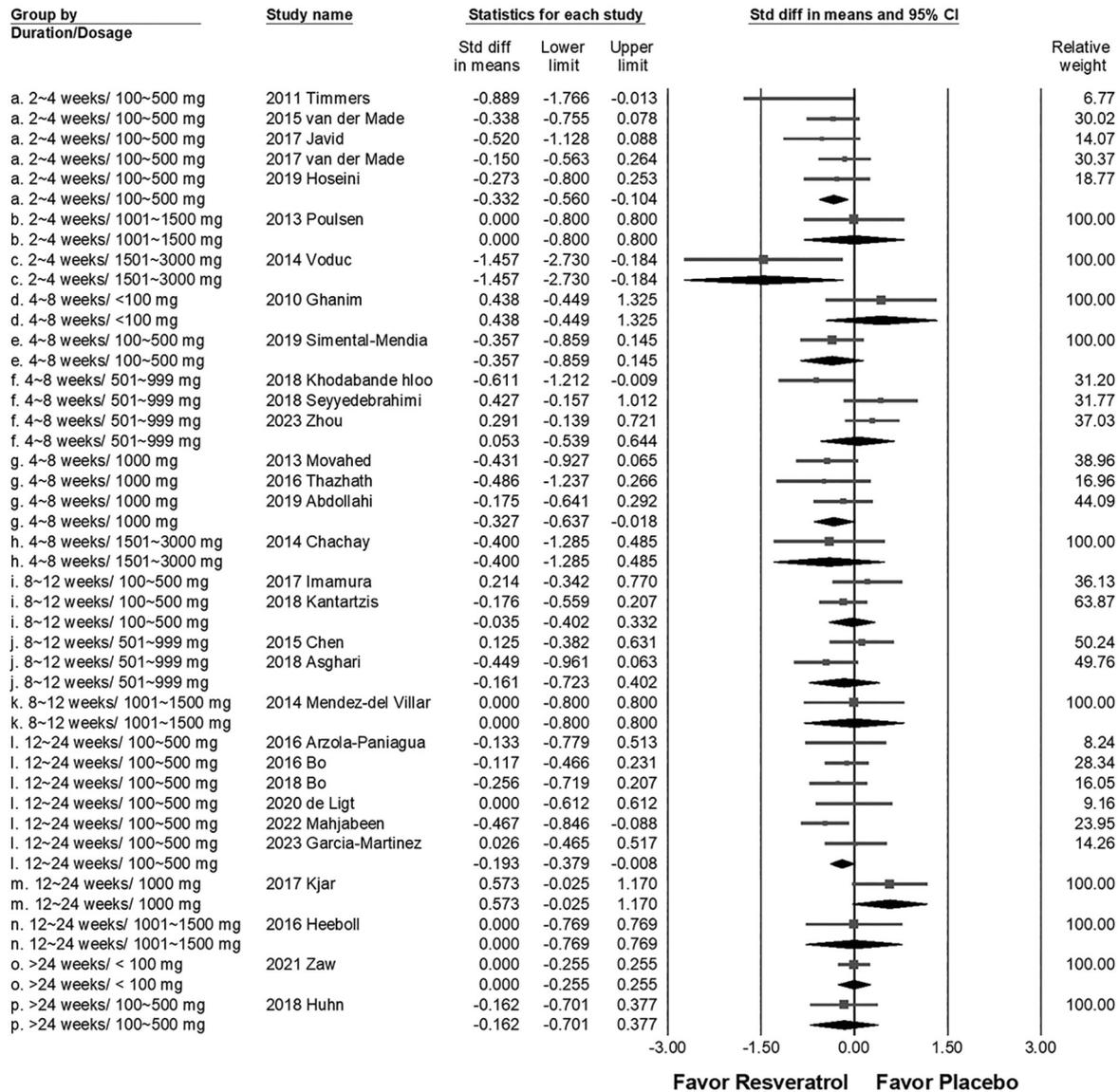


Figure 6. Forest plot showing the effects of resveratrol supplementation on fasting blood glucose levels, grouped by intervention duration and dosage. Squares represent the effect estimates of individual studies with their 95% confidence intervals, while the diamonds at the bottom of each panel indicate the pooled effect size, summarizing the overall influence of resveratrol on fasting blood glucose.

0.053; 95% CI -0.539 to 0.644; $I^2=72.687\%$, $p=0.026$), and 1,501 to 3,000 mg per day (SMD -0.400; 95%CI=-1.285 to 0.485; $I^2<0.001\%$, $p>0.999$). Similarly, no significant changes were found for dosages between 100 and 500 mg per day for 8 to 12 weeks (SMD -0.035; 95%CI=-0.402 to 0.332; $I^2=22.007\%$, $p=0.257$), 501 to 999 mg per day (SMD -0.161; 95%CI=-0.723 to 0.402; $I^2=58.968\%$, $p=0.118$), and 1,001

to 1,500 mg per day (SMD 0.000; 95%CI=-0.800 to 0.800; $I^2<0.001\%$, $p>0.999$). For 12 to 24 weeks, no significant effects were observed with dosages between 100 and 500 mg per day (SMD -0.193; 95%CI=-0.379 to -0.008; $I^2<0.001\%$, $p=0.693$), 1,000 mg per day (SMD 0.573; 95%CI=-0.025 to 1.170; $I^2<0.001\%$, $p>0.999$), or 1,001 to 1,500 mg per day (SMD 0.000; 95%CI=-0.769 to 0.769; $I^2<0.001\%$, $p>0.999$).

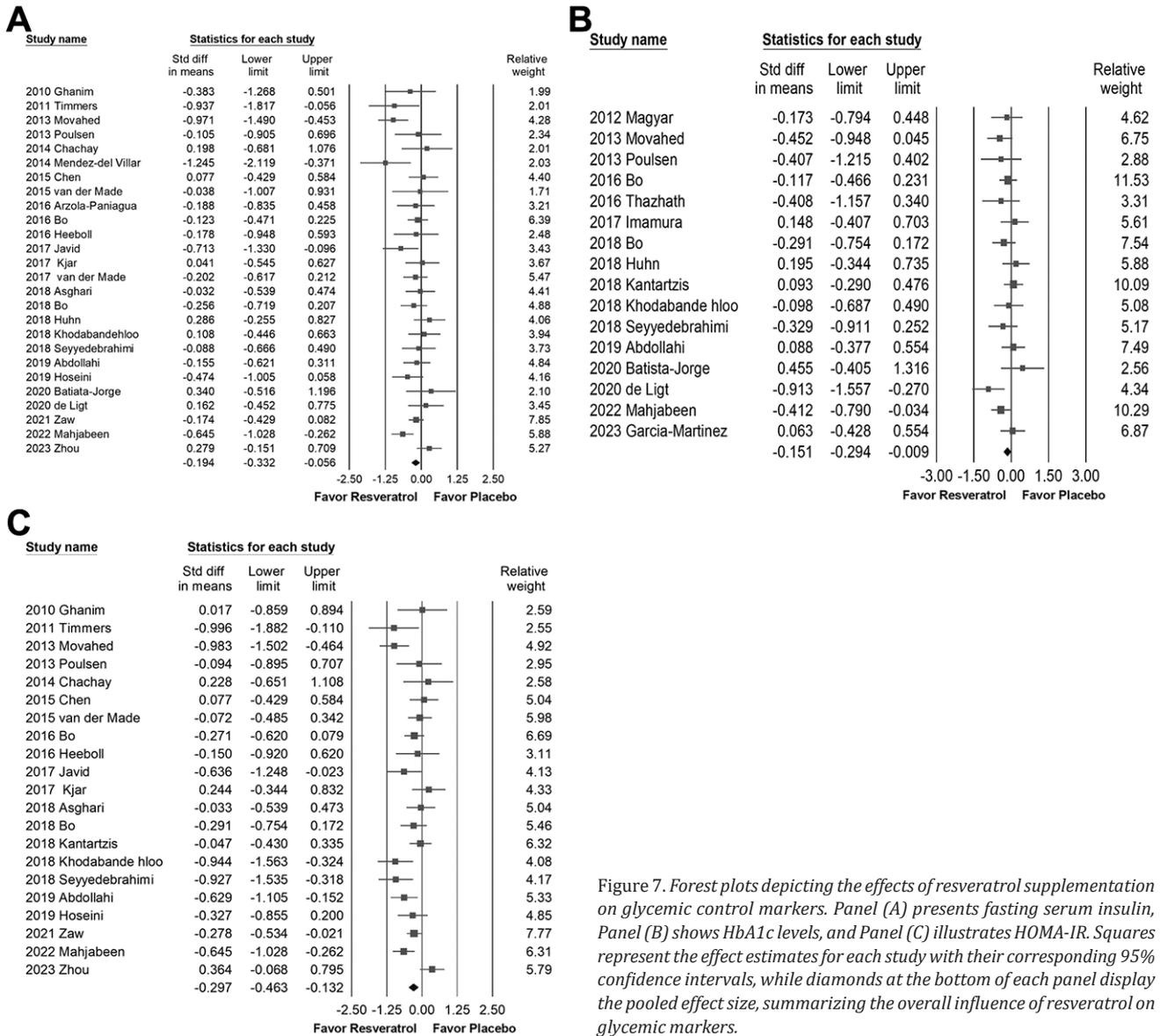


Figure 7. Forest plots depicting the effects of resveratrol supplementation on glycemic control markers. Panel (A) presents fasting serum insulin, Panel (B) shows HbA1c levels, and Panel (C) illustrates HOMA-IR. Squares represent the effect estimates for each study with their corresponding 95% confidence intervals, while diamonds at the bottom of each panel display the pooled effect size, summarizing the overall influence of resveratrol on glycemic markers.

Over periods longer than 24 weeks, no significant changes were found for dosages below 100 mg per day (SMD 0.000; 95%CI=-0.255 to 0.255; $I^2<0.001\%$, $p>0.999$) or between 100 and 500 mg per day (SMD -0.162; 95%CI=-0.701 to 0.377; $I^2<0.001\%$, $p>0.999$).

Impact of resveratrol supplementation on fasting insulin, HbA1c, and HOMA-IR. The effects of resveratrol

supplementation on glycemic markers were evaluated across several endpoints. A slight reduction in fasting insulin and HbA1c was observed, though these changes did not reach statistical significance (Figure 7A; SMD: -0.194, 95%CI=-0.332 to -0.056; $I^2=39.386\%$, $p=0.022$) and (Figure 7B; SMD: -0.151, 95%CI=-0.294 to -0.009; $I^2=17.400\%$, $p=0.254$), respectively. In contrast, a small but significant decrease in HOMA-IR was detected, indicating potential

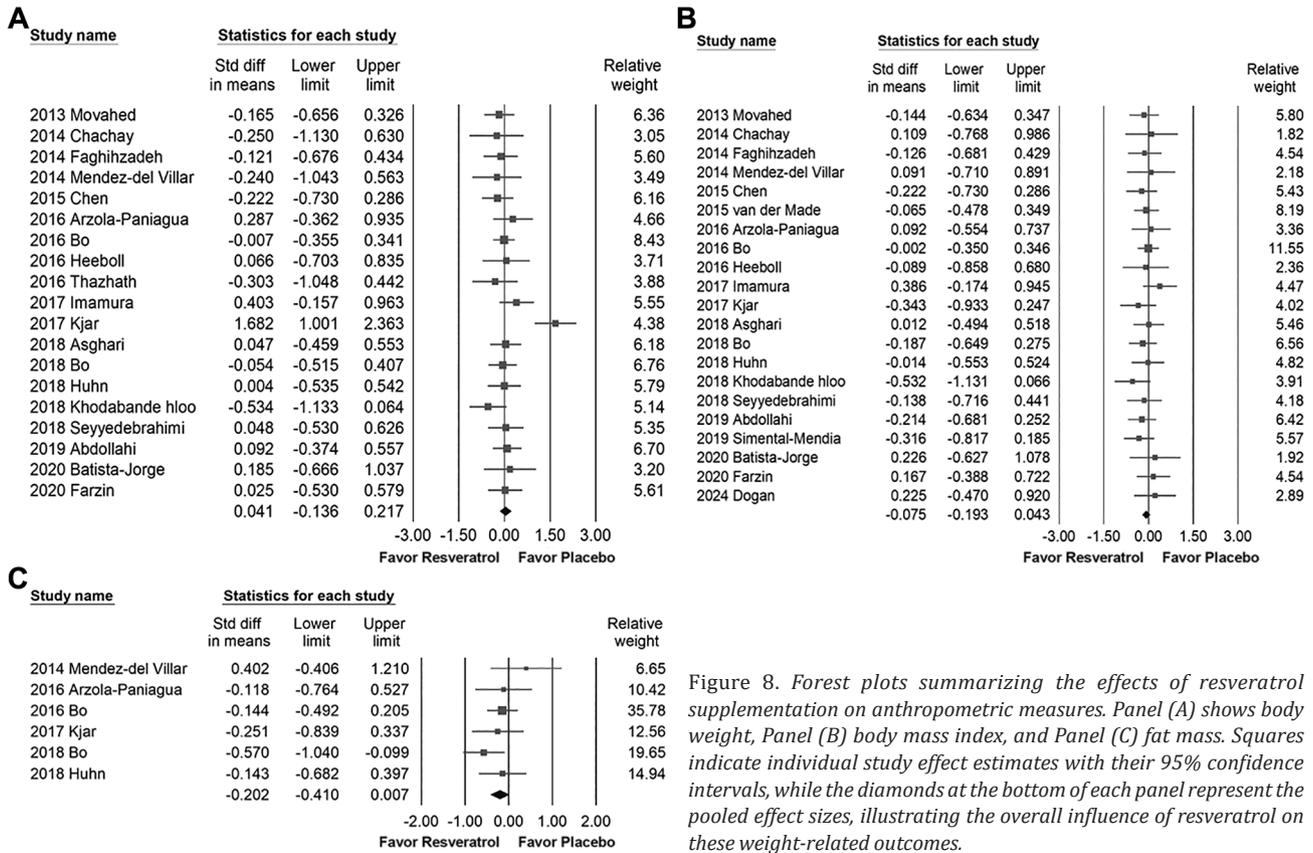


Figure 8. Forest plots summarizing the effects of resveratrol supplementation on anthropometric measures. Panel (A) shows body weight, Panel (B) body mass index, and Panel (C) fat mass. Squares indicate individual study effect estimates with their 95% confidence intervals, while the diamonds at the bottom of each panel represent the pooled effect sizes, illustrating the overall influence of resveratrol on these weight-related outcomes.

enhancements in insulin sensitivity and overall glucose homeostasis (Figure 7C; SMD: -0.297 , 95%CI= -0.463 to -0.132 ; $I^2=54.597\%$, $p=0.001$). These findings suggest that resveratrol supplementation may contribute to improved metabolic function, particularly in individuals with insulin resistance or related metabolic disorders.

Effects of resveratrol supplementation on body weight, body mass index, fat mass, hip circumference, and waist circumference. Analysis of anthropometric indicators revealed no statistically significant changes across the measured outcomes. Body weight (Figure 8A; SMD: 0.041 , 95%CI= -0.136 to 0.217 ; $I^2=44.024\%$, $p=0.021$), body mass index (Figure 8B; SMD: -0.075 , 95%CI= -0.193 to 0.043 ; $I^2<0.001\%$, $p=0.960$), and fat mass (Figure 8C; SMD: -0.202 , 95%CI= -0.410 to 0.007 ; $I^2<0.001\%$,

$p=0.448$). Similarly, hip circumference (Figure 9A; SMD: -0.037 , 95%CI= -0.270 to 0.197 ; $I^2<0.001\%$, $p=0.988$) and waist circumference (Figure 9B; SMD: -0.081 , 95%CI= -0.224 to 0.062 ; $I^2<0.001\%$, $p=0.940$) did not differ meaningfully between intervention and control groups. These findings indicate that resveratrol supplementation did not produce measurable benefits in overall or regional body composition within the study durations evaluated.

Effects of resveratrol supplementation on liver function markers and hepatic fat content. The analysis of liver-related outcomes indicated no statistically significant differences between the resveratrol and placebo groups for any of the evaluated parameters. For ALT (Figure 10A; SMD: -0.117 , 95%CI= -0.345 to -0.008 ; $I^2=32.900\%$,

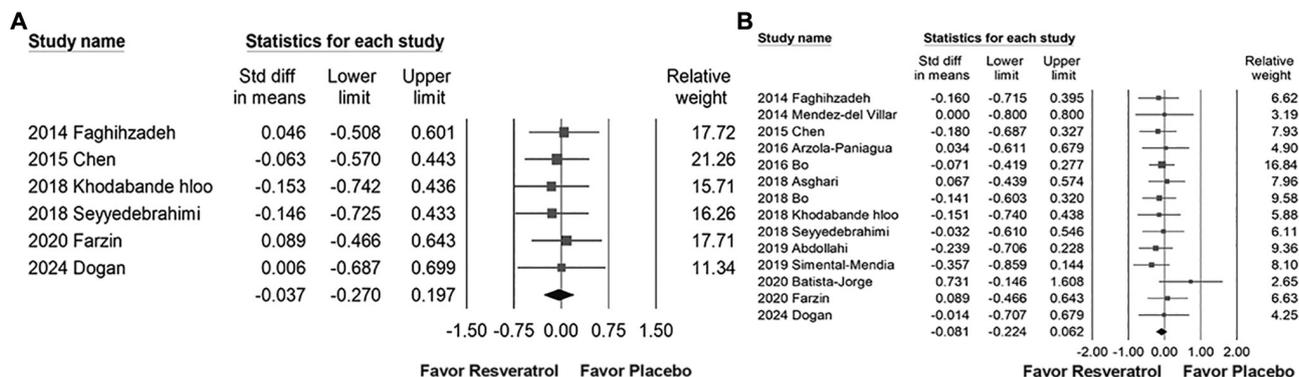


Figure 9. Forest plot illustrating the effects of resveratrol supplementation on (A) hip circumference and (B) waist circumference. Squares represent individual study effect estimates with 95% confidence intervals, and diamonds at the bottom of each panel indicate the pooled effect size, showing the overall impact on each anthropometric measure.

$p=0.093$), AST (Figure 10B; SMD: -0.162 , 95%CI= -0.382 to 0.059 ; $I^2=52.347\%$, $p=0.011$), and GGT (Figure 10C; SMD: -0.116 , 95%CI= -0.280 to 0.047 ; $I^2<0.001\%$, $p=0.809$), no meaningful improvements were observed following supplementation. Similarly, the analysis of liver fat content (Figure 10D; SMD: 0.158 , 95%CI= -0.157 to 0.474 ; $I^2<0.001\%$, $p=0.843$) revealed no significant effect. These findings suggest that, based on current evidence, resveratrol supplementation does not produce measurable changes in standard biochemical or imaging markers of hepatic function or steatosis.

Effects of resveratrol supplementation on serum lipid parameters. The influence of resveratrol supplementation on lipid metabolism was assessed by evaluating TC, TG, LDL, and HDL. Small but statistically significant reductions were observed in TC (Figure 11A; SMD: -0.253 , 95%CI= -0.357 to -0.149 ; $I^2=13.256\%$, $p=0.266$), TG (Figure 11B; SMD: -0.216 , 95%CI= -0.345 to -0.086 ; $I^2=48.555\%$, $p=0.001$), and LDL (Figure 11C; SMD: -0.242 , 95%CI= -0.355 to -0.128 ; $I^2=17.768\%$, $p=0.217$). In contrast, no significant changes were detected in HDL levels (Figure 11D; SMD: -0.158 , 95%CI= -0.253 to -0.062 ; $I^2<0.001\%$, $p=0.902$). These findings indicate that resveratrol supplementation may confer modest lipid-lowering effects, particularly in reducing TC, TG, and LDL, while its impact on HDL appears negligible.

Effects of resveratrol supplementation on blood pressure. Resveratrol supplementation was associated with a small but statistically significant reduction in systolic blood pressure, whereas no significant effect was observed for diastolic pressure. For systolic pressure, the pooled effect was SMD -0.244 (95%CI= -0.423 to -0.064 ; $I^2=55.2\%$; $p=0.003$; Figure 12A). For diastolic pressure, the pooled effect was SMD -0.183 (95%CI= -0.341 to 0.024 ; $I^2=42.9\%$; $p=0.082$; Figure 12B). These findings suggest a small antihypertensive benefit of resveratrol, primarily limited to systolic pressure, and the clinical relevance should be interpreted as supportive rather than as a standalone therapeutic effect.

Effects of resveratrol supplementation on inflammatory biomarkers. The effects of resveratrol supplementation on inflammatory biomarkers were assessed across three key markers. Small but statistically significant reductions were observed in TNF- α (Figure 13A; SMD: -0.252 , 95%CI= -0.471 to -0.033 ; $I^2=37.960\%$, $p=0.088$), IL-6 (Figure 13B; SMD: -0.316 , 95%CI= -0.459 to -0.173 ; $I^2<0.001\%$, $p=0.519$), and hs-CRP (Figure 13C; SMD: -0.272 , 95%CI= -0.391 to -0.153 ; $I^2<0.001\%$, $p=0.988$). These results suggest that resveratrol supplementation may exert a modest anti-inflammatory effect, potentially contributing to its broader benefits against non-communicable diseases.

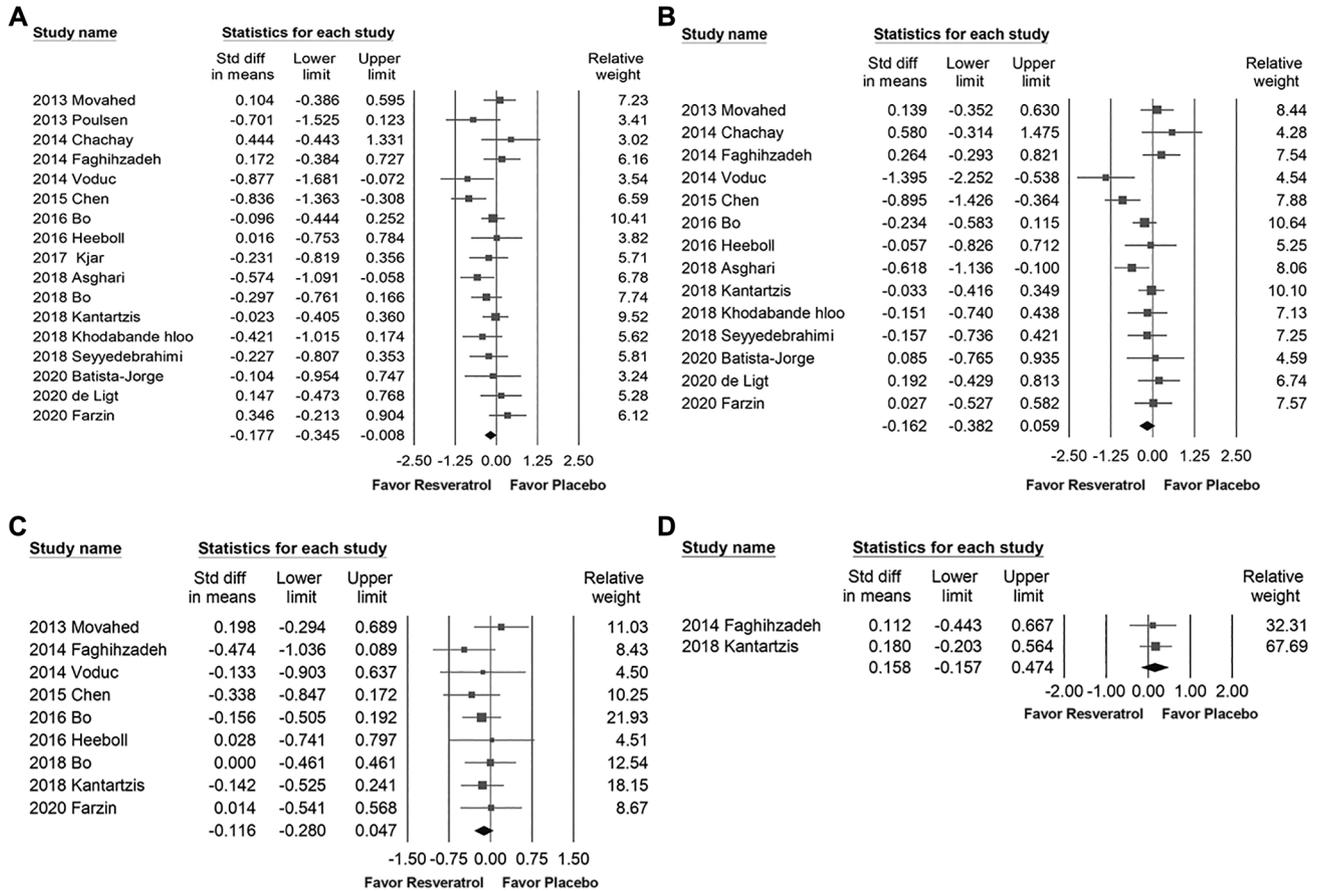


Figure 10. Forest plots summarizing the effects of resveratrol supplementation on liver-related outcomes. Panel (A) shows ALT, Panel (B) AST, Panel (C) GGT, and Panel (D) liver fat content. Squares indicate individual study effect estimates with their corresponding 95% confidence intervals, while diamonds at the bottom of each panel represent the pooled effect size, reflecting the overall impact of resveratrol supplementation on these liver parameters.

Effects of resveratrol supplementation on creatinine. No significant difference in serum creatinine was observed between the intervention and control groups (Figure 13D; SMD -0.088; 95% CI -0.334 to 0.158; $I^2 < 0.001\%$; $p = 0.817$). The pooled estimate is compatible with no meaningful effect on kidney function over the durations studied, as the confidence interval includes the null. Nevertheless, most trials were not powered for renal endpoints and primarily reported creatinine, so longer studies including estimated glomerular filtration rate (eGFR), albuminuria, and kidney injury biomarkers are needed.

Publication bias of included RCTs reporting fasting blood glucose data. Egger's regression analysis for fasting blood glucose (Figure 3) showed no statistically significant evidence of publication bias ($p = 0.379$), consistent with the overall symmetry observed in the funnel plot (Figure 13E). Visual inspection also indicated a balanced distribution on both sides, suggesting no substantial small-study effects. To further confirm this, a trim-and-fill analysis was conducted, and the adjusted effect size (point estimate: -0.149; 95%CI=-0.257 to -0.041) was identical to the original, indicating that potential publication bias had minimal influence on the pooled results.

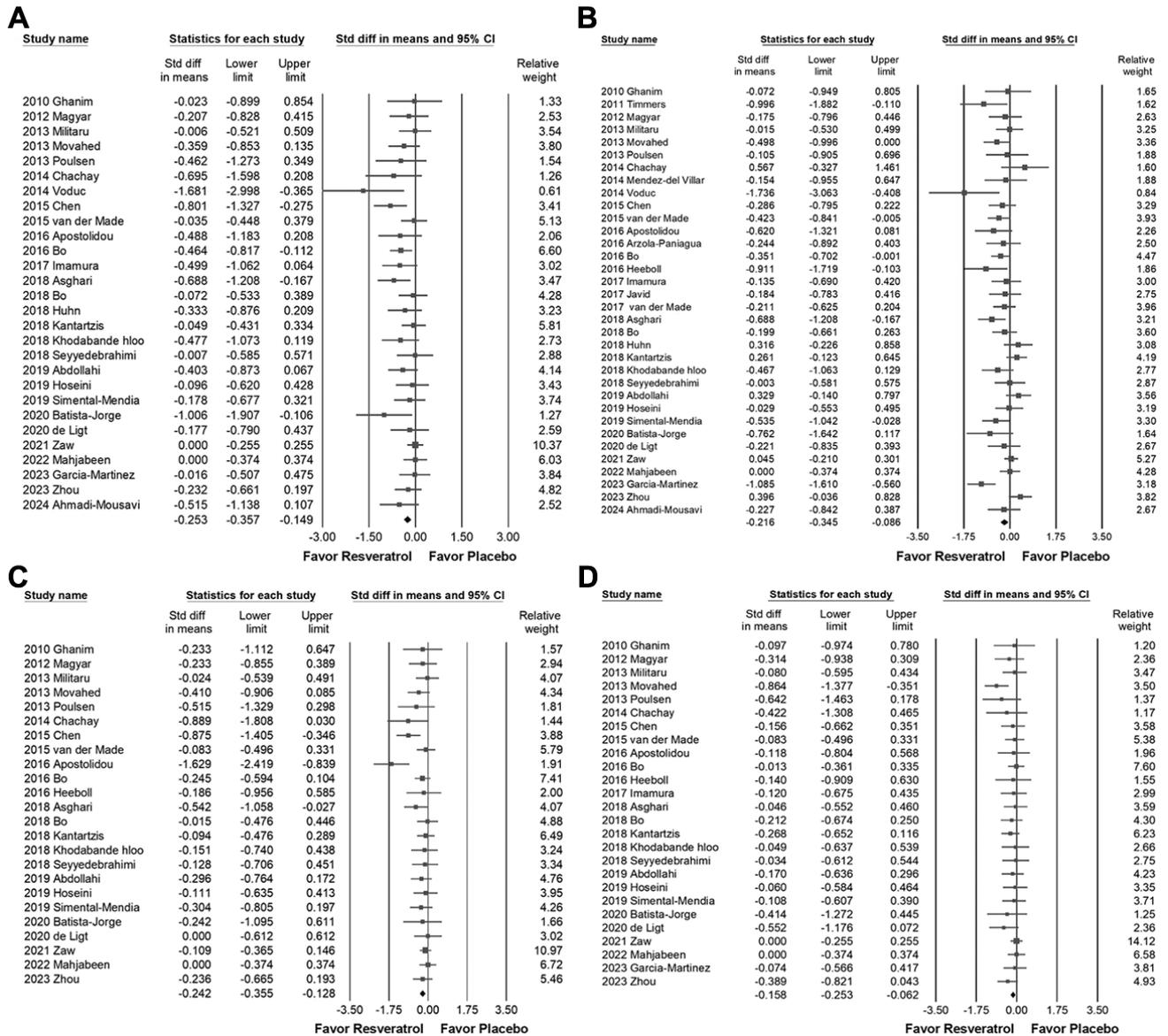


Figure 11. Forest plot illustrating the effects of resveratrol supplementation on lipid profile parameters. Panel (A) shows TC, Panel (B) TG, Panel (C) LDL, and Panel (D) HDL. Squares represent the effect estimates of individual studies with their 95% confidence intervals, while the diamonds at the bottom of each panel depict the pooled effect size, reflecting the overall influence of resveratrol on each lipid parameter.

Discussion

Resveratrol has been proposed as a promising adjunctive intervention for obesity-related non-communicable diseases owing to its antioxidant, anti-inflammatory, and metabolic regulatory properties. In this meta-analysis of

randomized controlled trials, resveratrol supplementation produced small but statistically significant improvements in insulin resistance (HOMA-IR), total cholesterol, triglycerides, LDL cholesterol, blood pressure, and key inflammatory biomarkers. Conversely, no significant changes were observed in fasting glucose, HbA1c, body

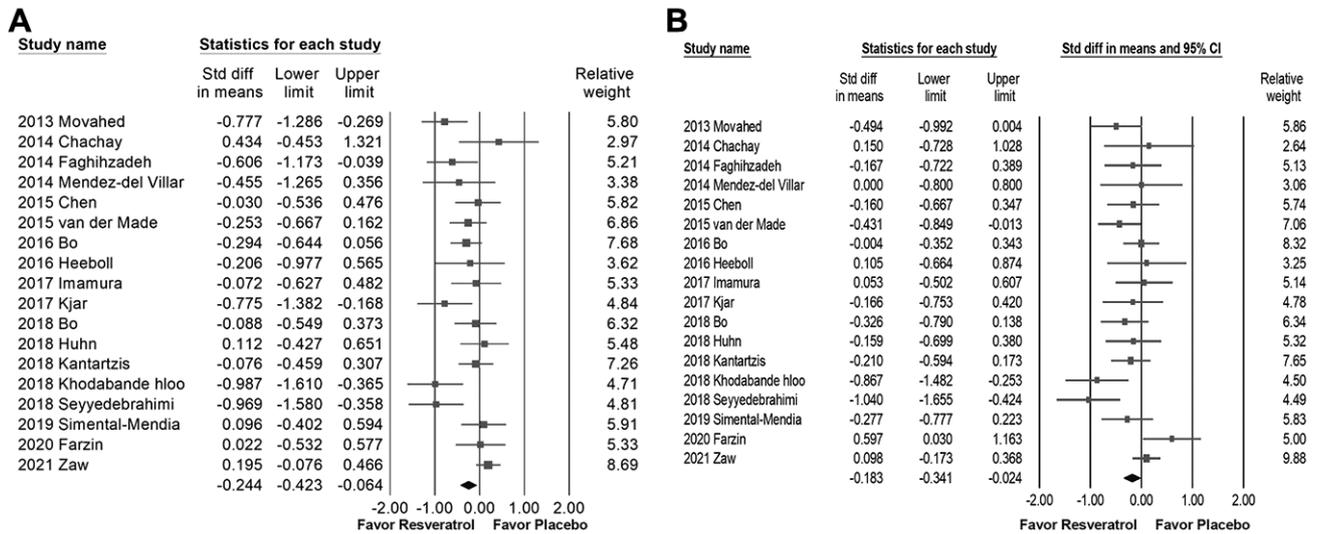


Figure 12. Forest plot illustrating the effects of resveratrol supplementation on blood pressure parameters. Panel (A) systolic blood pressure (SBP) and Panel (B) diastolic blood pressure (DBP). Squares represent the effect estimates of individual studies with their 95% confidence intervals, while the diamonds at the bottom of each panel depict the pooled effect size, reflecting the overall influence of resveratrol on each blood pressure measure.

composition, liver enzymes, or HDL cholesterol. These findings indicate that resveratrol may exert modest yet biologically relevant benefits on selected metabolic and inflammatory parameters, rather than broad or comprehensive effects across all non-communicable disease-related domains.

Comparisons with prior literature show both concordance and inconsistency. In overweight adults, Timmers *et al.* reported improvements in HOMA-IR and systolic blood pressure after 30 days of resveratrol supplementation (54). In contrast, Kjær *et al.* observed no benefits on glucose homeostasis, blood pressure, or hepatic lipid content in male patients with metabolic syndrome (68). At the evidence-synthesis level, Guo *et al.* found pooled reductions in fasting glucose, total cholesterol, and C-reactive protein, with blood-pressure benefits more apparent in type 2 diabetes subgroups (86). Teimouri *et al.*, focusing on cardiovascular cohorts, reported decreases in TNF- α and CRP but not IL-6 with low between-study heterogeneity (87). In addition, Akbari *et al.* synthesized trials in metabolic-syndrome populations and reported improvements in lipid

profiles and liver enzymes (88). Taken together, these patterns are consistent with our findings of modest improvements in insulin resistance, atherogenic lipids, systolic pressure, and inflammatory biomarkers, while the heterogeneity across participant profiles, dosing strategies, formulations, and exposure durations likely explains the variability in individual trial results.

Our subgroup analysis indicated that fasting blood glucose decreased when resveratrol was given for less than four weeks at doses below 500 mg per day, whereas longer exposure or higher doses did not improve glycemic control. This pattern is compatible with an early metabolic response that wanes over time through compensatory mechanisms or reduced bioavailability, potentially involving acute activation of AMPK and SIRT1 signaling (30, 89). Clinical evidence supports this interpretation. In patients with type 2 diabetes, Movahed *et al.* reported reductions in fasting glucose, insulin, and HOMA-IR after 45 days at 1 g per day (56). A broad clinical review similarly noted that short term, lower dose regimens showed more consistent glucose benefits, while longer term, higher dose trials often failed to replicate these

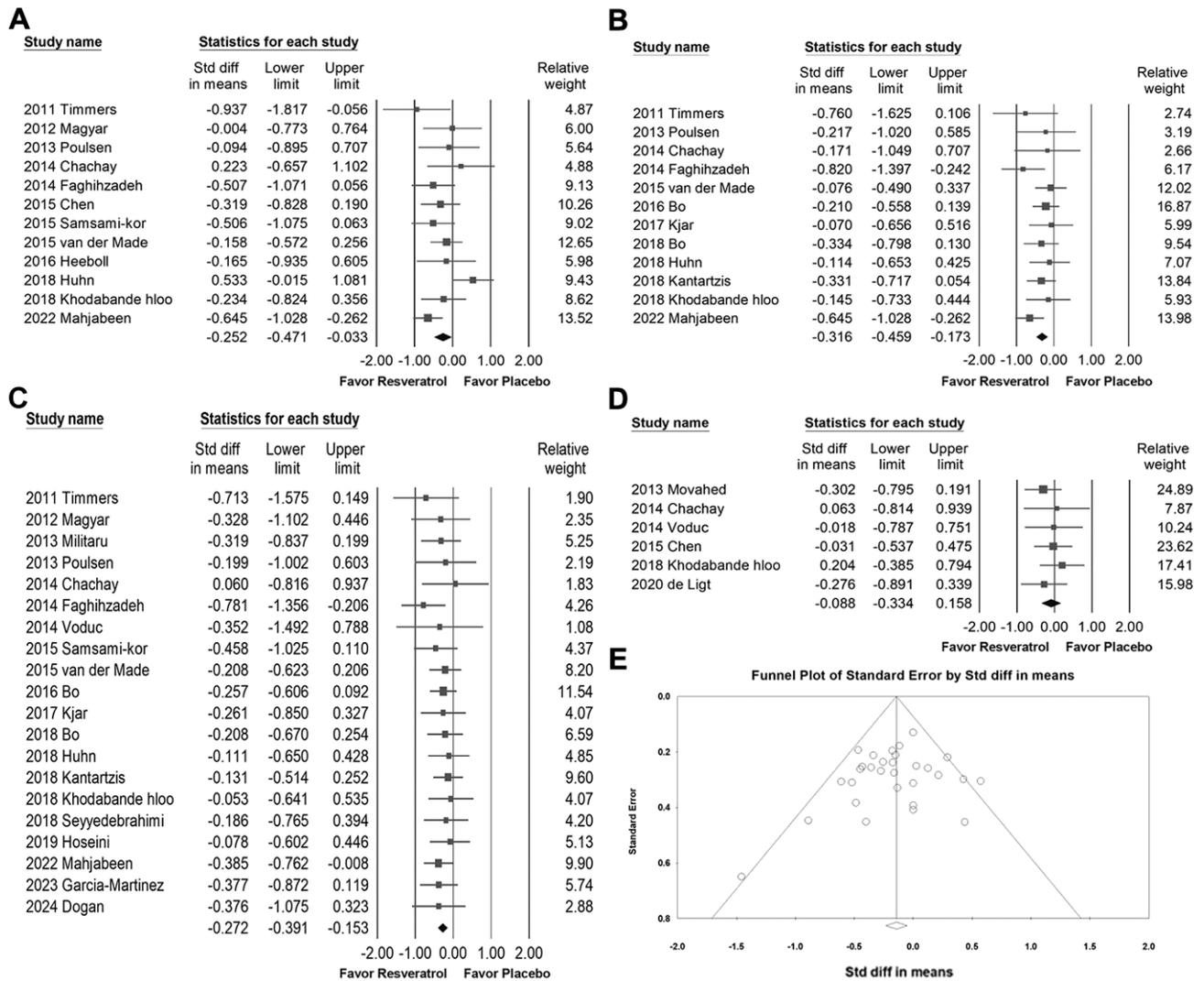


Figure 13. Forest plot illustrating the effects of resveratrol supplementation on inflammatory biomarkers. Panel (A) shows tumor necrosis factor- α (TNF- α), Panel (B) interleukin-6 (IL-6), Panel (C) high-sensitivity C-reactive protein (hs-CRP), and Panel (D) serum creatinine. Squares represent effect estimates with 95 percent confidence intervals, and diamonds indicate the pooled effect size. Panel (E) presents a funnel plot for the studies shown in Figure 3. Lines indicate confidence intervals around effect estimates. Each circle represents an individual study, with larger circles indicating greater weight or larger sample size. The diamond depicts the pooled effect size, with its center representing the overall estimate and its width indicating the corresponding confidence interval.

effects (90). Prior evidence also catalogued a wide dosing range from 8 to 3,000 mg per day and durations from 4 weeks to 12 months, and suggested that approximately three months at about 500 mg per day could be advantageous, although the optimal parameters remain uncertain (86). Taken together with our results, these observations indicate that dose and exposure time shape the magnitude and durability of glycemic effects, and that

shorter treatment periods at moderate doses appear to provide the greatest glycemic benefit.

Lipid outcomes merit nuance. Our pooled effects suggest small improvements in atherogenic lipids; however, a targeted 2025 synthesis limited to seven RCTs observed a reduction confined to triglycerides with null effects on total, LDL, and HDL cholesterol (91). Mechanistically, that article coupled network

pharmacology with molecular dynamics and identified inflammatory hubs (IL-6, IL-1 β , TNF) as plausible targets, consistent with an indirect lipid effect *via* inflammation rather than classical lipid-metabolism pathways (91). When triangulated with our small reductions in inflammatory biomarkers, this helps reconcile modest lipid changes with a stronger signal for triglycerides.

Inflammation emerges as a consistent pathway that can plausibly connect the small yet coherent biomarker changes observed in this meta-analysis. We found modest reductions in TNF- α , IL-6, and hs-CRP, indicating that resveratrol exerts a measurable anti-inflammatory effect in clinical populations with metabolic disturbances. These findings are directionally concordant with prior syntheses in cardiovascular cohorts where CRP and TNF- α decreased, although IL-6 did not consistently change, a discrepancy that likely reflects differences in baseline inflammatory burden, dosing strategies, assay platforms, and co-medications across trials (87). Convergent mechanistic evidence further supports an anti-inflammatory mode of action. Resveratrol activates SIRT1 and AMPK, attenuates NF- κ B signaling, and has been reported to influence inflammasome activity, which together can suppress transcription of pro-inflammatory cytokines and reduce oxidative stress in vascular and metabolic tissues (6). *In silico* analyses also show stable binding of resveratrol to IL-6, IL-1 β , and TNF with favorable free energy estimates, which aligns with the clinical pattern we observe (91). The clinical meaning of a small anti-inflammatory signal warrants careful interpretation. Even modest reductions in hs-CRP and TNF- α may improve endothelial function and arterial compliance, which is consistent with the small decreases in systolic blood pressure seen in the pooled analysis (87). Our results suggest that cytokine modulation can also influence hepatic lipid handling and triglyceride production, providing a plausible link between inflammatory changes and the modest improvements in atherogenic lipids. At the same time, the absence of consistent effects on anthropometric measures and hepatic fat suggests that resveratrol acts primarily on signaling and inflammatory tone rather than on energy balance or organ fat content under the tested conditions. Heterogeneity across studies remains an

important consideration. Prior reviews catalogued wide dose ranges and exposure times and emphasized that optimal parameters are uncertain, which means that anti-inflammatory benefits may be most apparent within specific dosing windows or in participants with elevated baseline inflammation (86). The CRP and TNF- α data do not suggest bias from small studies, which increases confidence in the finding. But variations in reporting and assay methods across trials can still make the overall effect look smaller or noisier (87). Taken together, our results and the external evidence suggest that resveratrol delivers a small but biologically coherent anti-inflammatory effect that likely contributes to parallel improvements in triglycerides and systolic blood pressure. Future trials should enrich for participants with higher inflammatory baselines, standardize formulations and doses, include pharmacokinetic assessments to link exposure with cytokine dynamics, and incorporate mechanistic endpoints such as NF- κ B target gene expression, SIRT1 activity readouts, and inflammasome markers. This approach will clarify whether the observed biomarker changes can be amplified or made more durable with optimized regimens and whether they translate into clinically meaningful outcomes.

Although most included trials primarily evaluated metabolic and inflammatory biomarkers, the observed patterns have broader implications for obesity-related non-communicable diseases. Small yet consistent improvements in insulin resistance, lipid profiles, and inflammatory mediators may cumulatively influence the pathophysiological pathways underlying cardiovascular disease, type 2 diabetes, and non-alcoholic fatty liver disease—conditions that collectively account for the majority of global NCD burden (2, 3). These findings align with experimental and clinical evidence showing that resveratrol modulates endothelial function, hepatic lipid metabolism, and mitochondrial bioenergetics, suggesting a potential preventive role rather than direct therapeutic efficacy (54, 92). However, the current evidence remains insufficient to establish resveratrol as a disease-modifying agent, and long-term trials with clinical endpoints such as incident diabetes, hepatic fibrosis progression, or

cardiovascular events are needed to determine its true impact on non-communicable disease trajectories (66).

This synthesis has several limitations that should be considered when interpreting the findings. First, heterogeneity across trials was considerable. Studies differed in dose, formulation, intervention duration, baseline risk, and background care, which limits precise dose response inference and likely contributes to the small pooled effects. Exposure was generally short to intermediate, and few trials extended beyond three to six months, so durability of benefit and longer-term safety remain uncertain. Formulations were not standardized, and pharmacokinetic data were rarely reported, which complicates interpretation of bioavailability and effective exposure. Second, most endpoints were surrogate biomarkers rather than clinical outcomes. The present evidence does not establish whether the observed changes translate into fewer cardiovascular events. Measurement methods for inflammatory and metabolic markers were not uniform. Differences in assay platforms, sampling schedules, and co-medications can attenuate or obscure true effects when results are combined. Third, many trials enrolled modest sample sizes and only a subset reported each outcome, which reduced power for subgroup and sensitivity analyses. Reporting of adherence and adverse events was inconsistent, limiting a balanced appraisal of benefit and risk. The meta-analysis relied on aggregated data rather than individual participant data, which restricted exploration of effect modification by baseline inflammation, insulin resistance, hepatic fat, or concomitant therapies. Fourth, some domains in the risk of bias assessment raised concerns, particularly sequence generation, allocation concealment, and selective reporting. Publication bias could not be excluded for outcomes with a small number of contributing studies, where formal tests and funnel plots were not informative. Finally, the evidence base predominantly involves adults with metabolic disturbances or related risk factors. The generalizability of these results to other populations, including older adults with frailty, patients with advanced cardiovascular disease, or younger

individuals, is uncertain. Standardized trial designs that align dose, formulation, exposure time, and outcome measurement, along with longer follow up and clinically meaningful endpoints, are needed to confirm and extend these observations.

Conclusion

Resveratrol supplementation produced small improvements in HOMA-IR, TC, TG, LDL, SBP, DBP, and inflammatory markers, but showed no significant effects on other cardiometabolic parameters, suggesting that it does not exert broad effects across CVD risk factors. These findings support a cautious, adjunctive role for resveratrol in adults with metabolic disturbances and do not justify replacement of established lifestyle or pharmacologic therapies. Future trials should standardize formulations and dosing, include pharmacokinetic assessments, and extend follow up to clinical outcomes to determine whether modest biomarker changes translate into patient benefit.

Conflicts of Interest

The Authors declare no competing interests in relation to this study.

Authors' Contributions

Chun-Yu Shen: Data curation and Investigation. Chen-Pi Li: Data curation and Investigation. Jui-Ting Yu: Data curation and Investigation. Ying-Jui Ho: Data curation and Investigation. Ru-Yin Tsai: Designed research, Conceptualization, Data curation, Investigation, Visualization, Writing-original draft, Writing-review and editing. All Authors read and approved the final manuscript.

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Artificial Intelligence (AI) Disclosure

During the preparation of this manuscript, a large language model (ChatGPT 5.1, OpenAI) was used solely for language editing and stylistic improvements in select paragraphs. No sections involving the generation, analysis, or interpretation of research data were produced by generative AI. All scientific content was created and verified by the authors. Furthermore, no figures or visual data were generated or modified using generative AI or machine learning-based image enhancement tools.

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