Nutritional and Related Interventions for Metabolic Markers in Polycystic Ovary Syndrome: A Systematic Review and Exploratory Meta-Analysis

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Supplementary Text S1. Detailed statistical analysis

For all endpoints, the primary outcome was the between-group difference in change from baseline, and the effect size measure was the mean difference (MD) in change scores with its 95% confidence interval (CI). For the revision, all outcome data were re-extracted from the full texts of the included reports, separately for each study arm and for baseline, follow-up and change values. Only linear unit conversions were applied, to means and SDs alike. Effect sizes were taken, in order of preference, from reported change-from-baseline means and SDs in both arms, from a baseline-adjusted between-group difference with its 95% CI reported by the trial (standard error derived as the CI width divided by 2 × 1.96), or from baseline and follow-up values with an imputed change SD. Abedini 2021 reported only arm-level ANCOVA-adjusted changes with standard errors, without a between-group contrast or its CI. The primary analysis therefore used the reported arm-level baseline and follow-up values, and a contrast derived from the adjusted arm-level changes (assuming independent arm estimates) was used only in sensitivity analysis S9. The original analyses estimated means and SDs from quantiles following Luo et al. [1] and Shi et al. [2]. In the revised analyses, medians with interquartile ranges and percentage changes were not converted into absolute changes and were described narratively (Table S3). Results are presented as experimental minus control.

Reporting of SDs for change scores was heterogeneous across studies. Reported change SDs were used when available and were not overwritten. Reported standard errors were converted to SDs as $SE \times \sqrt{n}$ using the arm-specific sample size, and within-group 95% CIs as $(upper - lower) / (2 \times t(0.975, n - 1)) \times \sqrt{n}$.

When a change SD was not reported, it was calculated from the baseline and follow-up SDs as $sqrt(SD_baseline^2 + SD_follow\text{-}up^2 - 2r \times SD_baseline \times SD_follow\text{-}up)$, assuming a correlation of r = 0.5. Sensitivity analyses repeated the calculation with r = 0, 0.25, 0.75 and 0.9.

The earlier zero-correlation and minimum-observed-correlation rules were not retained for the revised analyses. The imputed correlations are assumptions rather than patient-level estimates. The approach follows the Cochrane Handbook [3].

Each intervention–comparator pair was analyzed separately, and no estimate was pooled across interventions. Myo-inositol alone and myo-inositol with folic acid were separate comparisons. All meta-analyses used a random-effects model. The between-study variance (τ^2) was estimated

by restricted maximum likelihood (REML), and 95% CIs were calculated with the modified Hartung–Knapp method, using a t distribution with k − 1 degrees of freedom and a variance multiplier bounded below by one [4]. Analyses with two trials are exploratory, and heterogeneity estimates based on very few trials are unstable. Single trials were reported individually with normal-approximation 95% CIs and were not pooled. Shared control arms of multi-arm trials (Dastgheib 2022, Mishra 2022) contribute to different comparisons but never twice within one analysis. Companion reports of the same trial population (Rafraf 2012a, 2012b and Mohammadi 2012) were linked and contribute one effect size per outcome.

The sensitivity analyses were as follows. S1 re-included the three reports subject to a published expression or note of concern. S2 excluded all included reports sharing the common co-author of the affected reports. S3 excluded the factorial trial of Asemi 2015. S4 excluded reports with internal data inconsistencies (Table S3). S5 added the full-sample results of Javed 2019. S6 used alternative imputed correlations (r = 0, 0.25, 0.75 and 0.9) and was run for every pooled or single-trial estimate that contained an imputed change SD. S7 treated the lipid SDs of Khani 2017 as standard errors. S8 excluded results at high risk of bias. S9 used the ANCOVA-derived contrast for Abedini 2021 instead of its arm-level data. S10 re-included the two quasi-randomized trials (Bonakdaran 2012 with allocation by clinic day, and Khani 2011, described by its authors as quasi-randomized), which are not part of the primary analyses. S11 excluded the cinnamon trial in which both arms also received medroxyprogesterone acetate (Hajimonfarednejad 2018). Leave-one-out analyses omitted one trial population at a time in every comparison with at least three trials. Table S4 lists the analyses in which the conclusion about whether the 95% CI includes no difference changed, and Table S5 gives the results of every sensitivity and leave-one-out analysis, including those that left only a single trial (reported without pooling). Retracted reports were not used in any analysis (Table S7).

Absolute between-study heterogeneity was quantified using τ^2, and relative heterogeneity using the I^2 statistic [5]. Prediction intervals were planned when at least eight studies were available [6]. No comparison reached this number.

For the assessment of publication bias, Egger's tests were planned. Because no comparison included ten or more trials (k = 2–5 in the pooled analyses), neither Egger's test nor a visual judgment of funnel-plot asymmetry would be informative [3]. No test was performed. Funnel plots for the revised pooled analyses are provided for descriptive purposes only (Figures S64–S125) and are not used to infer the presence or absence of publication bias. The initial analyses were conducted in R (version 4.5.2) [7] using the meta package (version 8.5-0) [8]. The revised

analyses were implemented in Python 3.13.16 with NumPy 2.5.3 and SciPy 1.18.1. As a check, they reproduced exactly the vitamin D3 and DCI fasting-insulin estimates of the previous revision computed in R. The analysis code, the final extraction table and the output of every analysis are provided as Code S1, Data S1 and Data S2.

Certainty of evidence was rated with GRADE for each intervention–comparator–outcome estimate [3]. Risk of bias was downgraded by one level when more than 50% of the weight came from results with some concerns or high risk of bias or from reports with internal data inconsistencies, and by two levels when at least 50% came from results at high risk. Data-integrity concerns were considered only within this domain, so that the same problem was not penalized twice. Inconsistency was downgraded for I^2 of at least 50% (two levels at 75% or more), used as a guide together with the overlap of trial confidence intervals. Imprecision was judged with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224), with no difference as the threshold, because validated minimal important differences are not available for these surrogate outcomes [3]. The optimal information size was set at about 800 participants, the total sample needed to detect a small effect of 0.2 SD with a two-sided α of 0.05 and 80% power. When the 95% CI included no difference, certainty was downgraded by one level, and by two levels if the total sample was also below half of the optimal information size ($N < 400$). When the 95% CI excluded no difference, it was downgraded by one level for $N < 800$ and by two levels for $N < 400$. Each judgment and its reason are given in Table S1, and the GRADE ratings were confirmed by EZF (28–29 October 2026). Indirectness was not downgraded, and publication bias was recorded as not assessable. Risk of bias was assessed with RoB 2 for each result. Where a trial contributed an outcome without a separate earlier assessment, the judgments for the same trial and comparison were applied and confirmed by the assessor (EZF, 28–29 October 2026, § in Figures S126–S167). Each judgment, its source and its confirmation are listed in Data S1.

Table S1. GRADE evidence profiles (summary of findings) for the revised analyses

Question: Vitamin D3 compared to placebo in women with PCOS

Setting: randomized controlled trials, vitamin D3 trials enrolled women with low baseline vitamin D status (enrollment 25(OH)D <20 ng/mL in Ardabili 2013, Asemi 2015 and Abootorabi 2018, <30 ng/mL in Trummer 2019, measured baseline without an enrollment threshold in Irani 2015, low baseline group means of 10.5 and 11.0 ng/mL without a verified threshold in Dastorani 2018, see Table 2A)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	vitamin D3	placebo	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Asemi 2015, Abootorabi 2018, Trummer 2019, Dastorani 2018												
4	randomized trials	serious[a]	serious[b]	not serious	very serious[c]	publication bias not assessable[d]	146	105	-	MD **3.91 mg/dL lower** (10.7 lower to 2.87 higher)	⨁◯◯◯ **Very low**	CRITICAL
Fasting insulin (µIU/mL), trials: Asemi 2015, Abootorabi 2018, Dastorani 2018												
3	randomized trials	serious[e]	not serious	not serious	very serious[f]	publication bias not assessable[d]	65	63	-	MD **1.17 µIU/mL lower** (3.07 lower to 0.72 higher)	⨁◯◯◯ **Very low**	CRITICAL
HOMA-IR, trials: Asemi 2015, Irani 2015, Abootorabi 2018, Dastorani 2018												
4	randomized trials	serious[g]	not serious	not serious	very serious[h]	publication bias not assessable[d]	100	81	-	MD **0.21 lower** (0.46 lower to 0.036 higher)	⨁◯◯◯ **Very low**	IMPORTANT
HOMA-B, trials: Abootorabi 2018												
1	randomized trials	serious[i]	not serious[j]	not serious	very serious[k]	publication bias not assessable[d]	19	17	-	MD **81.4 higher** (0.31 lower to 163.2 higher)	⨁◯◯◯ **Very low**	IMPORTANT
QUICKI, trials: Asemi 2015, Abootorabi 2018, Dastorani 2018												
3	randomized trials	serious[l]	serious[m]	not serious	very serious[f]	publication bias not assessable[d]	65	63	-	MD **0.013 higher** (0.007 lower to 0.034 higher)	⨁◯◯◯ **Very low**	IMPORTANT
Total cholesterol (mg/dL), trials: Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018												
4	randomized trials	serious[n]	not serious	not serious	very serious[o]	publication bias not assessable[d]	105	90	-	MD **8.61 mg/dL lower** (18.4 lower to 1.18 higher)	⨁◯◯◯ **Very low**	IMPORTANT
LDL-C (mg/dL), trials: Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018												
4	randomized trials	serious[p]	not serious	not serious	very serious[o]	publication bias not assessable[d]	105	90	-	MD **4.92 mg/dL lower** (14.9 lower to 5.06 higher)	⨁◯◯◯ **Very low**	IMPORTANT
HDL-C (mg/dL), trials: Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018												
4	randomized trials	serious[q]	not serious	not serious	very serious[o]	publication bias not assessable[d]	105	90	-	MD **0.18 mg/dL lower** (2.90 lower to 2.54 higher)	⨁◯◯◯ **Very low**	IMPORTANT
Triglycerides (mg/dL), trials: Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018												
4	randomized trials	serious[r]	not serious	not serious	very serious[o]	publication bias not assessable[d]	105	90	-	MD **15.9 mg/dL lower** (45.6 lower to 13.9 higher)	⨁◯◯◯ **Very low**	IMPORTANT
VLDL-C (mg/dL), trials: Ardabili 2013, Asemi 2015, Dastorani 2018												
3	randomized trials	serious[s]	serious[t]	not serious	very serious[u]	publication bias not assessable[d]	70	72	-	MD **3.57 mg/dL lower** (12.8 lower to 5.70 higher)	⨁◯◯◯ **Very low**	IMPORTANT
Total testosterone (ng/mL), trials: Irani 2015												
1	randomized trials	very serious[v]	not serious[j]	not serious	very serious[w]	publication bias not assessable[d]	35	18	-	MD **0.037 ng/mL higher** (0.067 lower to 0.14 higher)	⨁◯◯◯ **Very low**	IMPORTANT
Free testosterone (pg/mL), trials: Irani 2015												

1	randomized trials	very serious[v]	not serious[j]	not serious	very serious[w]	publication bias not assessable[d]	35	18	-	MD **0.20 pg/mL higher** (2.06 lower to 2.46 higher)	⊕◯◯◯ **Very low**	IMPORTANT
SHBG (nmol/L), trials: Irani 2015												
1	randomized trials	very serious[v]	not serious[j]	not serious	very serious[w]	publication bias not assessable[d]	35	18	-	MD **3.00 nmol/L lower** (20.2 lower to 14.2 higher)	⊕◯◯◯ **Very low**	IMPORTANT
DHEAS (µg/mL), trials: Irani 2015												
1	randomized trials	very serious[v]	not serious[j]	not serious	very serious[w]	publication bias not assessable[d]	35	18	-	MD **0.010 µg/mL higher** (0.46 lower to 0.48 higher)	⊕◯◯◯ **Very low**	IMPORTANT
25(OH)D (ng/mL), trials: Ardabili 2013, Asemi 2015, Abootorabi 2018, Trummer 2019, Dastorani 2018												
5	randomized trials	not serious[x]	very serious[y]	not serious	very serious[z]	publication bias not assessable[d]	168	130	-	MD **15.2 ng/mL higher** (8.36 higher to 22.0 higher)	⊕◯◯◯ **Very low**	CRITICAL
BMI (kg/m²), trials: Ardabili 2013, Asemi 2015, Dastorani 2018												
3	randomized trials	serious[t]	not serious	not serious	very serious[u]	publication bias not assessable[d]	70	72	-	MD **0.026 kg/m² lower** (0.32 lower to 0.27 higher)	⊕◯◯◯ **Very low**	IMPORTANT
Body weight (kg), trials: Ardabili 2013, Asemi 2015, Dastorani 2018												
3	randomized trials	not serious[x]	not serious	not serious	very serious[u]	publication bias not assessable[d]	70	72	-	MD **0.19 kg lower** (1.06 lower to 0.68 higher)	⊕⊕◯◯ **Low**	IMPORTANT
Waist circumference (cm), trials: Asemi 2015												
1	randomized trials	not serious[x]	not serious[j]	not serious	very serious[l]	publication bias not assessable[d]	26	26	-	MD **0.50 cm lower** (1.51 lower to 0.51 higher)	⊕⊕◯◯ **Low**	IMPORTANT
Systolic BP (mmHg), trials: Irani 2015												
1	randomized trials	very serious[j]	not serious[j]	not serious	very serious[w]	publication bias not assessable[d]	35	18	-	MD **0.000 mmHg higher** (6.01 lower to 6.01 higher)	⊕◯◯◯ **Very low**	IMPORTANT
Diastolic BP (mmHg), trials: Irani 2015												
1	randomized trials	very serious[j]	not serious[j]	not serious	very serious[w]	publication bias not assessable[d]	35	18	-	MD **1.50 mmHg higher** (2.52 lower to 5.52 higher)	⊕◯◯◯ **Very low**	IMPORTANT
PTH (pg/mL), trials: Ardabili 2013												
1	randomized trials	not serious	not serious[j]	not serious	very serious[~]	publication bias not assessable[d]	24	26	-	MD **17.2 pg/mL lower** (33.0 lower to 1.48 lower)	⊕⊕◯◯ **Low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Results with some concerns or high risk contribute 54% of the weight. Downgraded once within the risk-of-bias domain.
b. Moderate heterogeneity ($I^2 = 68\%$).
c. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 251) is below 50% of the optimal information size of about 800 participants.
d. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
e. Results with some concerns or high risk contribute 96% of the weight. Downgraded once within the risk-of-bias domain.
f. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 128) is below 50% of the optimal information size of about 800 participants.
g. Results with some concerns or high risk contribute 98% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).

h. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 181) is below 50% of the optimal information size of about 800 participants.
i. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
j. Single trial, inconsistency cannot be assessed.
k. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 36) is below 50% of the optimal information size of about 800 participants.
l. Results with some concerns or high risk contribute 67% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
m. Moderate heterogeneity (I^2 = 57%).
n. Results with some concerns or high risk contribute 74% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
o. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 195) is below 50% of the optimal information size of about 800 participants.
p. Results with some concerns or high risk contribute 72% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
q. Results with some concerns or high risk contribute 68% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
r. Results with some concerns or high risk contribute 58% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
s. Results with some concerns or high risk contribute 50% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
t. Moderate heterogeneity (I^2 = 60%).
u. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 142) is below 50% of the optimal information size of about 800 participants.
v. High-risk results contribute 100% of the weight. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
w. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 53) is below 50% of the optimal information size of about 800 participants.
x. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
y. Substantial heterogeneity (I^2 = 91%).
z. 95% CI excludes no difference, but the total sample (N = 298) is below 50% of the optimal information size of about 800 participants.
{. Results with some concerns or high risk contribute 53% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
|. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 52) is below 50% of the optimal information size of about 800 participants.
}. High-risk results contribute 100% of the weight.
~. 95% CI excludes no difference, but the total sample (N = 50) is below 50% of the optimal information size of about 800 participants.

Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for $N < 800$ and two levels for $N < 400$. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Cinnamon compared to placebo in women with PCOS

Setting: randomized controlled trials, in Hajimonfarednejad 2018 both arms also received medroxyprogesterone acetate 10 mg/day for 10 days per cycle and routine lifestyle advice

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	cinnamon	placebo	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022												
3	randomized trials	not serious	very serious[a]	not serious	very serious[b]	publication bias not assessable[c]	91	94	-	MD **5.36 mg/dL lower** (21.3 lower to 10.6 higher)	⊕◯◯◯ **Very low**	CRITICAL
Fasting insulin (µIU/mL), trials: Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022												
3	randomized trials	not serious	not serious	not serious	very serious[b]	publication bias not assessable[c]	91	94	-	MD **3.28 µIU/mL lower** (6.95 lower to 0.38 higher)	⊕⊕◯◯ **Low**	CRITICAL
HOMA-IR, trials: Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022												
3	randomized trials	not serious	not serious	not serious	very serious[d]	publication bias not assessable[c]	91	94	-	MD **1.03 lower** (1.97 lower to 0.092 lower)	⊕⊕◯◯ **Low**	CRITICAL
Total cholesterol (mg/dL), trials: Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022												
3	randomized trials	not serious[e]	not serious	not serious	very serious[b]	publication bias not assessable[c]	91	94	-	MD **11.1 mg/dL lower** (28.6 lower to 6.31 higher)	⊕⊕◯◯ **Low**	IMPORTANT
LDL-C (mg/dL), trials: Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022												
3	randomized trials	not serious	not serious	not serious	very serious[b]	publication bias not assessable[c]	91	94	-	MD **11.1 mg/dL lower** (26.7 lower to 4.50 higher)	⊕⊕◯◯ **Low**	CRITICAL
HDL-C (mg/dL), trials: Borzoei 2018, Dastgheib 2022												
2	randomized trials	not serious	serious[f]	not serious	very serious[g]	publication bias not assessable[c]	62	64	-	MD **1.96 mg/dL higher** (20.6 lower to 24.5 higher)	⊕◯◯◯ **Very low**	CRITICAL
Triglycerides (mg/dL), trials: Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022												
3	randomized trials	not serious	serious[h]	not serious	very serious[b]	publication bias not assessable[c]	91	94	-	MD **1.96 mg/dL lower** (60.7 lower to 56.8 higher)	⊕◯◯◯ **Very low**	CRITICAL
Total testosterone (ng/mL), trials: Hajimonfarednejad 2018, Dastgheib 2022												
2	randomized trials	not serious[e]	not serious	not serious	very serious[i]	publication bias not assessable[c]	49	52	-	MD **0.12 ng/mL lower** (1.07 lower to 0.84 higher)	⊕⊕◯◯ **Low**	IMPORTANT

SHBG (nmol/L), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[j]	not serious	very serious[k]	publication bias not assessable[c]	20	22	-	MD **10.4 nmol/L higher** (6.65 lower to 27.4 higher)	⊕⊕◯◯ **Low**	IMPORTANT
FAI, trials: Dastgheib 2022												
1	randomized trials	not serious[e]	not serious[j]	not serious	very serious[k]	publication bias not assessable[c]	20	22	-	MD **0.43 lower** (1.58 lower to 0.72 higher)	⊕⊕◯◯ **Low**	IMPORTANT
DHEAS (µg/mL), trials: Hajimonfarednejad 2018												
1	randomized trials	serious[l]	not serious[j]	not serious	very serious[m]	publication bias not assessable[c]	29	30	-	MD **0.29 µg/mL lower** (0.90 lower to 0.32 higher)	⊕◯◯◯ **Very low**	IMPORTANT
BMI (kg/m²), trials: Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022												
3	randomized trials	not serious	not serious	not serious	very serious[b]	publication bias not assessable[c]	91	94	-	MD **0.13 kg/m² lower** (0.44 lower to 0.18 higher)	⊕⊕◯◯ **Low**	CRITICAL
Body weight (kg), trials: Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022												
3	randomized trials	not serious	not serious	not serious	very serious[b]	publication bias not assessable[c]	91	94	-	MD **0.47 kg lower** (1.19 lower to 0.24 higher)	⊕⊕◯◯ **Low**	CRITICAL
Waist circumference (cm), trials: Hajimonfarednejad 2018, Dastgheib 2022												
2	randomized trials	serious[n]	not serious	not serious	very serious[i]	publication bias not assessable[c]	49	52	-	MD **1.26 cm lower** (32.6 lower to 30.1 higher)	⊕◯◯◯ **Very low**	IMPORTANT
Waist-to-hip ratio, trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[j]	not serious	very serious[k]	publication bias not assessable[c]	20	22	-	MD **0.010 lower** (0.059 lower to 0.039 higher)	⊕⊕◯◯ **Low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Substantial heterogeneity ($I^2 = 85\%$).
b. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 185) is below 50% of the optimal information size of about 800 participants.
c. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
d. 95% CI excludes no difference, but the total sample (N = 185) is below 50% of the optimal information size of about 800 participants.
e. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
f. Moderate heterogeneity ($I^2 = 63\%$).
g. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 126) is below 50% of the optimal information size of about 800 participants.
h. Moderate heterogeneity ($I^2 = 67\%$).
i. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 101) is below 50% of the optimal information size of about 800 participants.
j. Single trial, inconsistency cannot be assessed.
k. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 42) is below 50% of the optimal information size of about 800 participants.
l. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain.

m. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 59) is below 50% of the optimal information size of about 800 participants.
n. Results with some concerns or high risk contribute 69% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for $N < 800$ and two levels for $N < 400$. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Cinnamon compared to metformin in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	cinnamon	metformin	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Dastgheib 2022, Khan 2019												
2	randomized trials	serious[a]	not serious	not serious	very serious[b]	publication bias not assessable[c]	40	40	-	MD **2.32 mg/dL lower** (48.2 lower to 43.6 higher)	⊕◯◯◯ **Very low**	CRITICAL
Fasting insulin (µIU/mL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **0.35 µIU/mL lower** (2.99 lower to 2.29 higher)	⊕⊕◯◯ **Low**	CRITICAL
HOMA-IR, trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **0.22 lower** (1.03 lower to 0.59 higher)	⊕⊕◯◯ **Low**	IMPORTANT
Total cholesterol (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious[f]	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **4.55 mg/dL higher** (13.1 lower to 22.2 higher)	⊕⊕◯◯ **Low**	IMPORTANT
LDL-C (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **1.70 mg/dL lower** (17.2 lower to 13.8 higher)	⊕⊕◯◯ **Low**	CRITICAL
HDL-C (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **0.45 mg/dL lower** (4.33 lower to 3.43 higher)	⊕⊕◯◯ **Low**	CRITICAL
Triglycerides (mg/dL), trials: Dastgheib 2022												

1	randomized trials	not serious	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **12.5 mg/dL higher** (23.3 lower to 48.3 higher)	⊕⊕◯◯ **Low**	CRITICAL
Total testosterone (ng/mL), trials: Dastgheib 2022												
1	randomized trials	not serious[f]	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **0.027 ng/mL lower** (0.21 lower to 0.15 higher)	⊕⊕◯◯ **Low**	IMPORTANT
Free testosterone (pg/mL), trials: Khan 2019												
1	randomized trials	serious[g]	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **4.00 pg/mL lower** (8.85 lower to 0.85 higher)	⊕◯◯◯ **Very low**	IMPORTANT
SHBG (nmol/L), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **1.01 nmol/L higher** (16.4 lower to 18.4 higher)	⊕⊕◯◯ **Low**	CRITICAL
FAI, trials: Dastgheib 2022												
1	randomized trials	not serious[f]	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **0.10 higher** (1.03 lower to 1.23 higher)	⊕⊕◯◯ **Low**	IMPORTANT
BMI (kg/m²), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **0.22 kg/m² higher** (2.53 lower to 2.97 higher)	⊕⊕◯◯ **Low**	CRITICAL
Body weight (kg), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **0.60 kg higher** (6.66 lower to 7.86 higher)	⊕⊕◯◯ **Low**	CRITICAL
Waist circumference (cm), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **0.40 cm lower** (10.0 lower to 9.21 higher)	⊕⊕◯◯ **Low**	IMPORTANT
Waist-to-hip ratio, trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[d]	not serious	very serious[e]	publication bias not assessable[c]	20	20	-	MD **0.010 lower** (0.062 lower to 0.042 higher)	⊕⊕◯◯ **Low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Results with some concerns or high risk contribute 66% of the weight. Downgraded once within the risk-of-bias domain.
b. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 80) is below 50% of the optimal information size of about 800 participants.
c. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
d. Single trial, inconsistency cannot be assessed.
e. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 40) is below 50% of the optimal information size of about 800 participants.
f. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
g. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals.

Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for N < 800 and two levels for N < 400. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Ginger compared to placebo in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ginger	placebo	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **6.40 mg/dL higher** (4.13 lower to 16.9 higher)	⨁⨁◯◯ **Low**	CRITICAL
Fasting insulin (µIU/mL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **1.57 µIU/mL lower** (3.86 lower to 0.72 higher)	⨁⨁◯◯ **Low**	CRITICAL
HOMA-IR, trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **0.26 lower** (0.86 lower to 0.34 higher)	⨁⨁◯◯ **Low**	CRITICAL
Total cholesterol (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious[d]	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **7.20 mg/dL higher** (15.8 lower to 30.2 higher)	⨁⨁◯◯ **Low**	IMPORTANT
LDL-C (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **7.95 mg/dL higher** (6.86 lower to 22.8 higher)	⨁⨁◯◯ **Low**	CRITICAL
HDL-C (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **2.05 mg/dL lower** (5.56 lower to 1.46 higher)	⨁⨁◯◯ **Low**	CRITICAL
Triglycerides (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **9.10 mg/dL lower** (50.4 lower to 32.2 higher)	⨁⨁◯◯ **Low**	CRITICAL
Total testosterone (ng/mL), trials: Dastgheib 2022												
1	randomized trials	not serious[d]	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **0.050 ng/mL higher** (0.098 lower to 0.20 higher)	⨁⨁◯◯ **Low**	IMPORTANT
SHBG (nmol/L), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **3.72 nmol/L lower** (19.0 lower to 11.6 higher)	⨁⨁◯◯ **Low**	IMPORTANT
FAI, trials: Dastgheib 2022												

1	randomized trials	not serious[d]	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **0.010 lower** (0.73 lower to 0.71 higher)	⊕⊕◯◯ **Low**	IMPORTANT
BMI (kg/m²), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **0.24 kg/m² lower** (3.08 lower to 2.60 higher)	⊕⊕◯◯ **Low**	CRITICAL
Body weight (kg), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **0.58 kg lower** (7.92 lower to 6.76 higher)	⊕⊕◯◯ **Low**	CRITICAL
Waist circumference (cm), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **0.65 cm higher** (7.39 lower to 8.69 higher)	⊕⊕◯◯ **Low**	IMPORTANT
Waist-to-hip ratio, trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	22	-	MD **0.000 higher** (0.041 lower to 0.041 higher)	⊕⊕◯◯ **Low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Single trial, inconsistency cannot be assessed.
b. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 43) is below 50% of the optimal information size of about 800 participants.
c. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
d. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for N < 800 and two levels for N < 400. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Ginger compared to metformin in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ginger	metformin	Relative (95% CI)	Absolute (95% CI)		

Fasting glucose (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **2.05 mg/dL lower** (12.2 lower to 8.10 higher)	⨁⨁◯◯ **Low**	CRITICAL
Fasting insulin (µIU/mL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **0.77 µIU/mL higher** (1.41 lower to 2.95 higher)	⨁⨁◯◯ **Low**	CRITICAL
HOMA-IR, trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **0.18 higher** (0.41 lower to 0.77 higher)	⨁⨁◯◯ **Low**	IMPORTANT
Total cholesterol (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious[d]	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **15.3 mg/dL higher** (5.32 lower to 36.0 higher)	⨁⨁◯◯ **Low**	IMPORTANT
LDL-C (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **9.25 mg/dL higher** (5.33 lower to 23.8 higher)	⨁⨁◯◯ **Low**	CRITICAL
HDL-C (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **2.00 mg/dL lower** (4.98 lower to 0.98 higher)	⨁⨁◯◯ **Low**	CRITICAL
Triglycerides (mg/dL), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **27.2 mg/dL lower** (70.8 lower to 16.3 higher)	⨁⨁◯◯ **Low**	CRITICAL
Total testosterone (ng/mL), trials: Dastgheib 2022												
1	randomized trials	not serious[d]	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **0.14 ng/mL higher** (0.026 lower to 0.31 higher)	⨁⨁◯◯ **Low**	IMPORTANT
SHBG (nmol/L), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **13.1 nmol/L lower** (28.8 lower to 2.59 higher)	⨁⨁◯◯ **Low**	CRITICAL
FAI, trials: Dastgheib 2022												
1	randomized trials	not serious[d]	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **0.52 higher** (0.17 lower to 1.21 higher)	⨁⨁◯◯ **Low**	IMPORTANT
BMI (kg/m²), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **0.48 kg/m² higher** (2.31 lower to 3.27 higher)	⨁⨁◯◯ **Low**	CRITICAL
Body weight (kg), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **1.32 kg higher** (5.88 lower to 8.52 higher)	⨁⨁◯◯ **Low**	CRITICAL
Waist circumference (cm), trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **0.40 cm higher** (8.59 lower to 9.39 higher)	⨁⨁◯◯ **Low**	IMPORTANT
Waist-to-hip ratio, trials: Dastgheib 2022												
1	randomized trials	not serious	not serious[a]	not serious	very serious[b]	publication bias not assessable[c]	21	20	-	MD **0.000 higher** (0.044 lower to 0.044 higher)	⨁⨁◯◯ **Low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Single trial, inconsistency cannot be assessed.

b. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 41) is below 50% of the optimal information size of about 800 participants.
c. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
d. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for N < 800 and two levels for N < 400. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Berberine compared to metformin in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	berberine	metformin	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Mishra 2022												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	43	43	-	MD **1.00 mg/dL lower** (7.48 lower to 5.48 higher)	⨁◯◯◯ **Very low**	CRITICAL
Fasting insulin (µIU/mL), trials: Mishra 2022												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	43	43	-	MD **0.64 µIU/mL higher** (0.33 lower to 1.61 higher)	⨁◯◯◯ **Very low**	CRITICAL
Total cholesterol (mg/dL), trials: Mishra 2022												
1	randomized trials	serious[e]	not serious[b]	not serious	very serious[f]	publication bias not assessable[d]	43	43	-	MD **22.0 mg/dL higher** (10.9 higher to 33.2 higher)	⨁◯◯◯ **Very low**	IMPORTANT
LDL-C (mg/dL), trials: Mishra 2022												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[f]	publication bias not assessable[d]	43	43	-	MD **18.9 mg/dL higher** (6.41 higher to 31.5 higher)	⨁◯◯◯ **Very low**	CRITICAL
HDL-C (mg/dL), trials: Mishra 2022												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[f]	publication bias not assessable[d]	43	43	-	MD **13.5 mg/dL lower** (19.0 lower to 8.03 lower)	⨁◯◯◯ **Very low**	CRITICAL
Triglycerides (mg/dL), trials: Mishra 2022												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[f]	publication bias not assessable[d]	43	43	-	MD **60.2 mg/dL higher** (37.3 higher to 83.2 higher)	⨁◯◯◯ **Very low**	CRITICAL
FAI, trials: Mishra 2022												

1	randomized trials	serious[e]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	43	43	-	MD **0.21 higher** (0.11 lower to 0.53 higher)	⊕◯◯◯ **Very low**	IMPORTANT
BMI (kg/m²), trials: Mishra 2022												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	43	43	-	MD **0.73 kg/m² higher** (0.35 lower to 1.81 higher)	⊕◯◯◯ **Very low**	CRITICAL

CI: confidence interval, **MD:** mean difference.

Explanations

a. Reports with internal data inconsistencies (Table S3) contribute 100% of the weight. Downgraded once within the risk-of-bias domain.
b. Single trial, inconsistency cannot be assessed.
c. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 86) is below 50% of the optimal information size of about 800 participants.
d. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
e. Reports with internal data inconsistencies (Table S3) contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
f. 95% CI excludes no difference, but the total sample (N = 86) is below 50% of the optimal information size of about 800 participants.
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for N < 800 and two levels for N < 400. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Myo-inositol compared to metformin in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**myo-inositol**	**metformin**	**Relative (95% CI)**	**Absolute (95% CI)**		
Fasting glucose (mg/dL), trials: Mishra 2022												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	43	43	-	MD **3.88 mg/dL lower** (9.99 lower to 2.23 higher)	⊕◯◯◯ **Very low**	CRITICAL
Fasting insulin (µIU/mL), trials: Mishra 2022												

1	randomized trials	serious[a]	not serious[b]	not serious	very serious[e]	publication bias not assessable[d]	43	43	-	MD **5.48 µIU/mL lower** (6.26 lower to 4.70 lower)	⊕◯◯◯ **Very low**	CRITICAL
Total cholesterol (mg/dL), trials: Mishra 2022												
1	randomized trials	serious[f]	not serious[b]	not serious	very serious[e]	publication bias not assessable[d]	43	43	-	MD **23.2 mg/dL higher** (12.2 higher to 34.2 higher)	⊕◯◯◯ **Very low**	IMPORTANT
LDL-C (mg/dL), trials: Mishra 2022												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[e]	publication bias not assessable[d]	43	43	-	MD **24.0 mg/dL lower** (35.7 lower to 12.2 lower)	⊕◯◯◯ **Very low**	CRITICAL
HDL-C (mg/dL), trials: Mishra 2022												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[e]	publication bias not assessable[d]	43	43	-	MD **13.5 mg/dL lower** (20.6 lower to 6.47 lower)	⊕◯◯◯ **Very low**	CRITICAL
Triglycerides (mg/dL), trials: Mishra 2022												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[e]	publication bias not assessable[d]	43	43	-	MD **54.9 mg/dL higher** (32.2 higher to 77.7 higher)	⊕◯◯◯ **Very low**	CRITICAL
FAI, trials: Mishra 2022												
1	randomized trials	serious[f]	not serious[b]	not serious	very serious[e]	publication bias not assessable[d]	43	43	-	MD **0.34 higher** (0.049 higher to 0.63 higher)	⊕◯◯◯ **Very low**	IMPORTANT
BMI (kg/m²), trials: Mishra 2022, Nehra 2017												
2	randomized trials	serious[g]	not serious	not serious	very serious[h]	publication bias not assessable[d]	73	73	-	MD **0.78 kg/m² higher** (6.20 lower to 7.75 higher)	⊕◯◯◯ **Very low**	CRITICAL
Waist circumference (cm), trials: Nehra 2017												
1	randomized trials	serious[i]	not serious[b]	not serious	very serious[j]	publication bias not assessable[d]	30	30	-	MD **0.48 cm higher** (4.07 lower to 5.03 higher)	⊕◯◯◯ **Very low**	IMPORTANT
Waist-to-hip ratio, trials: Nehra 2017												
1	randomized trials	serious[k]	not serious[b]	not serious	very serious[j]	publication bias not assessable[d]	30	30	-	MD **0.010 lower** (0.035 lower to 0.015 higher)	⊕◯◯◯ **Very low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Reports with internal data inconsistencies (Table S3) contribute 100% of the weight. Downgraded once within the risk-of-bias domain.
b. Single trial, inconsistency cannot be assessed.
c. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 86) is below 50% of the optimal information size of about 800 participants.
d. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
e. 95% CI excludes no difference, but the total sample (N = 86) is below 50% of the optimal information size of about 800 participants.
f. Reports with internal data inconsistencies (Table S3) contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
g. Results with some concerns or high risk contribute 33% of the weight. Reports with internal data inconsistencies (Table S3) contribute 67% of the weight. Downgraded once within the risk-of-bias domain.
h. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 146) is below 50% of the optimal information size of about 800 participants.

i. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain.
j. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 60) is below 50% of the optimal information size of about 800 participants.
k. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for N < 800 and two levels for N < 400. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Myo-inositol + folic acid compared to metformin in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	myo-inositol + folic acid	metformin	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Shokrpour 2019												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	26	27	-	MD **5.12 mg/dL lower** (8.09 lower to 2.16 lower)	⨁◯◯◯ **Very low**	CRITICAL
Fasting insulin (µIU/mL), trials: Shokrpour 2019												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	26	27	-	MD **1.49 µIU/mL lower** (2.28 lower to 0.70 lower)	⨁◯◯◯ **Very low**	CRITICAL
HOMA-IR, trials: Fruzzetti 2017, Shokrpour 2019												
2	randomized trials	serious[e]	not serious	not serious	very serious[f]	publication bias not assessable[d]	50	49	-	MD **0.29 lower** (1.30 lower to 0.72 higher)	⨁◯◯◯ **Very low**	IMPORTANT
QUICKI, trials: Shokrpour 2019												
1	randomized trials	serious[g]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	26	27	-	MD **0.006 higher** (0.002 higher to 0.010 higher)	⨁◯◯◯ **Very low**	IMPORTANT
Total cholesterol (mg/dL), trials: Shokrpour 2019												

1	randomized trials	serious[g]	not serious[b]	not serious	very serious[h]	publication bias not assessable[d]	26	27	-	MD **3.58 mg/dL lower** (12.5 lower to 5.37 higher)	⊕◯◯◯ **Very low**	IMPORTANT
LDL-C (mg/dL), trials: Shokrpour 2019												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[h]	publication bias not assessable[d]	26	27	-	MD **1.97 mg/dL lower** (10.4 lower to 6.43 higher)	⊕◯◯◯ **Very low**	CRITICAL
HDL-C (mg/dL), trials: Shokrpour 2019												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[h]	publication bias not assessable[d]	26	27	-	MD **1.20 mg/dL higher** (1.54 lower to 3.94 higher)	⊕◯◯◯ **Very low**	CRITICAL
Triglycerides (mg/dL), trials: Shokrpour 2019												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	26	27	-	MD **12.4 mg/dL lower** (20.5 lower to 4.37 lower)	⊕◯◯◯ **Very low**	CRITICAL
BMI (kg/m²), trials: Fruzzetti 2017, Shokrpour 2019												
2	randomized trials	serious[i]	not serious	not serious	very serious[f]	publication bias not assessable[d]	50	49	-	MD **0.10 kg/m² lower** (1.68 lower to 1.48 higher)	⊕◯◯◯ **Very low**	CRITICAL

CI: confidence interval, **MD:** mean difference.

Explanations

a. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain.
b. Single trial, inconsistency cannot be assessed.
c. 95% CI excludes no difference, but the total sample (N = 53) is below 50% of the optimal information size of about 800 participants.
d. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
e. Results with some concerns or high risk contribute 57% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
f. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 99) is below 50% of the optimal information size of about 800 participants.
g. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
h. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 53) is below 50% of the optimal information size of about 800 participants.
i. Results with some concerns or high risk contribute 99% of the weight. Downgraded once within the risk-of-bias domain.
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information

size), and, if the 95% CI excludes no difference, one level for N < 800 and two levels for N < 400. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: D-chiro-inositol compared to placebo in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	D-chiro-inositol	placebo	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Iuorno 2002, Nestler 1999												
2	randomized trials	serious[a]	serious[b]	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **2.19 mg/dL lower** (84.7 lower to 80.3 higher)	⨁◯◯◯ **Very low**	CRITICAL
Fasting insulin (µIU/mL), trials: Iuorno 2002, Nestler 1999												
2	randomized trials	serious[a]	not serious	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **14.4 µIU/mL lower** (114.8 lower to 86.0 higher)	⨁◯◯◯ **Very low**	CRITICAL
Total cholesterol (mg/dL), trials: Iuorno 2002, Nestler 1999												
2	randomized trials	serious[e]	serious[f]	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **33.2 mg/dL lower** (223.8 lower to 157.4 higher)	⨁◯◯◯ **Very low**	IMPORTANT
LDL-C (mg/dL), trials: Nestler 1999												
1	randomized trials	serious[a]	not serious[g]	not serious	very serious[h]	publication bias not assessable[d]	22	22	-	MD **1.00 mg/dL higher** (18.2 lower to 20.2 higher)	⨁◯◯◯ **Very low**	CRITICAL
HDL-C (mg/dL), trials: Nestler 1999												
1	randomized trials	serious[a]	not serious[g]	not serious	very serious[h]	publication bias not assessable[d]	22	22	-	MD **0.000 mg/dL higher** (5.45 lower to 5.45 higher)	⨁◯◯◯ **Very low**	CRITICAL
Triglycerides (mg/dL), trials: Iuorno 2002, Nestler 1999												
2	randomized trials	serious[a]	not serious	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **73.5 mg/dL lower** (291.4 lower to 144.5 higher)	⨁◯◯◯ **Very low**	CRITICAL
Total testosterone (ng/mL), trials: Iuorno 2002, Nestler 1999												
2	randomized trials	serious[e]	serious[i]	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **0.42 ng/mL lower** (2.26 lower to 1.42 higher)	⨁◯◯◯ **Very low**	IMPORTANT
SHBG (nmol/L), trials: Iuorno 2002												
1	randomized trials	serious[e]	not serious[g]	not serious	very serious[j]	publication bias not assessable[d]	10	10	-	MD **38.0 nmol/L higher** (23.6 lower to 99.6 higher)	⨁◯◯◯ **Very low**	IMPORTANT
DHEAS (µg/mL), trials: Iuorno 2002, Nestler 1999												
2	randomized trials	serious[a]	not serious	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **1.68 µg/mL lower** (7.51 lower to 4.15 higher)	⨁◯◯◯ **Very low**	IMPORTANT
BMI (kg/m²), trials: Iuorno 2002, Nestler 1999												

2	randomized trials	serious[a]	not serious	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **0.35 kg/m² higher** (4.05 lower to 4.75 higher)	⊕◯◯◯ **Very low**	CRITICAL
Waist-to-hip ratio, trials: Iuorno 2002, Nestler 1999												
2	randomized trials	serious[a]	not serious	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **0.030 lower** (0.24 lower to 0.18 higher)	⊕◯◯◯ **Very low**	IMPORTANT
Systolic BP (mmHg), trials: Iuorno 2002, Nestler 1999												
2	randomized trials	serious[a]	not serious	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **3.80 mmHg lower** (35.3 lower to 27.7 higher)	⊕◯◯◯ **Very low**	IMPORTANT
Diastolic BP (mmHg), trials: Iuorno 2002, Nestler 1999												
2	randomized trials	serious[a]	not serious	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **6.21 mmHg lower** (27.0 lower to 14.5 higher)	⊕◯◯◯ **Very low**	IMPORTANT
Androstenedione (ng/mL), trials: Iuorno 2002, Nestler 1999												
2	randomized trials	serious[a]	serious[f]	not serious	very serious[c]	publication bias not assessable[d]	32	32	-	MD **0.60 ng/mL lower** (4.97 lower to 3.78 higher)	⊕◯◯◯ **Very low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain.
b. Moderate heterogeneity ($I^2 = 53\%$).
c. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 64) is below 50% of the optimal information size of about 800 participants.
d. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
e. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
f. Moderate heterogeneity ($I^2 = 59\%$).
g. Single trial, inconsistency cannot be assessed.
h. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 44) is below 50% of the optimal information size of about 800 participants.
i. Moderate heterogeneity ($I^2 = 57\%$).
j. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 20) is below 50% of the optimal information size of about 800 participants.
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for N < 800 and two levels for N < 400. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects

model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Curcumin compared to placebo in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	curcumin	placebo	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019												
3	randomized trials	not serious	not serious	not serious	very serious[a]	publication bias not assessable[b]	78	77	-	MD **2.84 mg/dL lower** (6.05 lower to 0.38 higher)	⊕⊕◯◯ **Low**	CRITICAL
Fasting insulin (µIU/mL), trials: Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019												
3	randomized trials	not serious	not serious	not serious	very serious[a]	publication bias not assessable[b]	78	77	-	MD **1.34 µIU/mL lower** (3.33 lower to 0.65 higher)	⊕⊕◯◯ **Low**	CRITICAL
HOMA-IR, trials: Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019												
3	randomized trials	not serious	not serious	not serious	very serious[a]	publication bias not assessable[b]	78	77	-	MD **0.43 lower** (1.35 lower to 0.50 higher)	⊕⊕◯◯ **Low**	CRITICAL
QUICKI, trials: Jamilian 2020, Sohaei 2019												
2	randomized trials	not serious[c]	not serious	not serious	very serious[d]	publication bias not assessable[b]	51	50	-	MD **0.008 higher** (0.017 lower to 0.033 higher)	⊕⊕◯◯ **Low**	IMPORTANT
Total cholesterol (mg/dL), trials: Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019												
3	randomized trials	not serious[c]	not serious	not serious	very serious[a]	publication bias not assessable[b]	78	77	-	MD **11.3 mg/dL lower** (29.9 lower to 7.32 higher)	⊕⊕◯◯ **Low**	IMPORTANT
LDL-C (mg/dL), trials: Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019												
3	randomized trials	not serious	serious[e]	not serious	very serious[a]	publication bias not assessable[b]	78	77	-	MD **8.72 mg/dL lower** (38.5 lower to 21.1 higher)	⊕◯◯◯ **Very low**	CRITICAL
HDL-C (mg/dL), trials: Jamilian 2020, Sohaei 2019												
2	randomized trials	not serious	not serious	not serious	very serious[d]	publication bias not assessable[b]	51	50	-	MD **1.92 mg/dL higher** (8.62 lower to 12.5 higher)	⊕⊕◯◯ **Low**	CRITICAL
Triglycerides (mg/dL), trials: Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019												
3	randomized trials	not serious	serious[f]	not serious	very serious[a]	publication bias not assessable[b]	78	77	-	MD **4.61 mg/dL lower** (25.9 lower to 16.6 higher)	⊕◯◯◯ **Very low**	CRITICAL
VLDL-C (mg/dL), trials: Jamilian 2020												
1	randomized trials	not serious[c]	not serious[g]	not serious	very serious[h]	publication bias not assessable[b]	24	26	-	MD **1.11 mg/dL lower** (2.58 lower to 0.35 higher)	⊕⊕◯◯ **Low**	IMPORTANT
BMI (kg/m²), trials: Jamilian 2020, Sohaei 2019												
2	randomized trials	not serious	not serious	not serious	very serious[d]	publication bias not assessable[b]	51	50	-	MD **0.20 kg/m² lower** (1.47 lower to 1.08 higher)	⊕⊕◯◯ **Low**	CRITICAL
Body weight (kg), trials: Jamilian 2020, Sohaei 2019												
2	randomized trials	not serious	not serious	not serious	very serious[d]	publication bias not assessable[b]	51	50	-	MD **0.60 kg lower** (3.66 lower to 2.46 higher)	⊕⊕◯◯ **Low**	CRITICAL

CI: confidence interval, **MD:** mean difference.

Explanations

a. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 155) is below 50% of the optimal information size of about 800 participants.
b. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
c. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
d. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 101) is below 50% of the optimal information size of about 800 participants.
e. Moderate heterogeneity (I^2 = 74%).
f. Moderate heterogeneity (I^2 = 53%).
g. Single trial, inconsistency cannot be assessed.
h. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 50) is below 50% of the optimal information size of about 800 participants.
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for N < 800 and two levels for N < 400. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Omega-3 compared to placebo or control in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	omega-3	placebo or control	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Rafraf/Mohammadi 2012, Khani 2017												
2	randomized trials	serious[a]	very serious[b]	not serious	very serious[c]	publication bias not assessable[d]	73	75	-	MD **6.76 mg/dL lower** (50.7 lower to 37.2 higher)	⊕◯◯◯ **Very low**	CRITICAL
Fasting insulin (µIU/mL), trials: Rafraf/Mohammadi 2012, Mejia-Montilla 2018												
2	randomized trials	serious[e]	not serious	not serious	very serious[f]	publication bias not assessable[d]	127	129	-	MD **2.08 µIU/mL lower** (8.08 lower to 3.92 higher)	⊕◯◯◯ **Very low**	CRITICAL
HOMA-IR, trials: Rafraf/Mohammadi 2012, Mejia-Montilla 2018												

2	randomized trials	serious[g]	not serious	not serious	very serious[f]	publication bias not assessable[d]	127	129	-	MD **0.46 lower** (2.09 lower to 1.16 higher)	⊕◯◯◯ **Very low**	CRITICAL
Total cholesterol (mg/dL), trials: Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018												
3	randomized trials	serious[h]	very serious[i]	not serious	very serious[j]	publication bias not assessable[d]	170	173	-	MD **14.9 mg/dL lower** (32.7 lower to 2.79 higher)	⊕◯◯◯ **Very low**	IMPORTANT
LDL-C (mg/dL), trials: Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018												
3	randomized trials	serious[g]	very serious[k]	not serious	very serious[j]	publication bias not assessable[d]	170	173	-	MD **16.1 mg/dL lower** (36.9 lower to 4.77 higher)	⊕◯◯◯ **Very low**	CRITICAL
HDL-C (mg/dL), trials: Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018												
3	randomized trials	serious[l]	very serious[m]	not serious	very serious[j]	publication bias not assessable[d]	170	173	-	MD **4.13 mg/dL higher** (1.56 lower to 9.81 higher)	⊕◯◯◯ **Very low**	CRITICAL
Triglycerides (mg/dL), trials: Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018												
3	randomized trials	serious[g]	very serious[n]	not serious	very serious[j]	publication bias not assessable[d]	170	173	-	MD **11.2 mg/dL lower** (30.2 lower to 7.69 higher)	⊕◯◯◯ **Very low**	CRITICAL
MDA (µmol/L), trials: Rafraf/Mohammadi 2012												
1	randomized trials	serious[o]	not serious[p]	not serious	very serious[q]	publication bias not assessable[d]	30	31	-	MD **0.67 µmol/L lower** (1.14 lower to 0.20 lower)	⊕◯◯◯ **Very low**	IMPORTANT
BMI (kg/m²), trials: Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018												
3	randomized trials	serious[r]	not serious	not serious	very serious[j]	publication bias not assessable[d]	170	173	-	MD **0.89 kg/m² lower** (2.32 lower to 0.54 higher)	⊕◯◯◯ **Very low**	CRITICAL
Body weight (kg), trials: Rafraf/Mohammadi 2012												
1	randomized trials	serious[s]	not serious[p]	not serious	very serious[t]	publication bias not assessable[d]	30	31	-	MD **0.39 kg lower** (5.11 lower to 4.33 higher)	⊕◯◯◯ **Very low**	CRITICAL
Waist circumference (cm), trials: Rafraf/Mohammadi 2012, Khani 2017												
2	randomized trials	serious[u]	not serious	not serious	very serious[c]	publication bias not assessable[d]	73	75	-	MD **1.77 cm lower** (12.4 lower to 8.92 higher)	⊕◯◯◯ **Very low**	IMPORTANT
Waist-to-hip ratio, trials: Rafraf/Mohammadi 2012, Mejia-Montilla 2018												
2	randomized trials	serious[v]	not serious	not serious	very serious[f]	publication bias not assessable[d]	127	129	-	MD **0.015 higher** (0.062 lower to 0.092 higher)	⊕◯◯◯ **Very low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Results with some concerns or high risk contribute 100% of the weight. Reports with internal data inconsistencies (Table S3) contribute 54% of the weight. Downgraded once within the risk-of-bias domain.
b. Substantial heterogeneity ($I^2 = 78\%$).
c. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 148) is below 50% of the optimal information size of about 800 participants.
d. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
e. Results with some concerns or high risk contribute 100% of the weight. Reports with internal data inconsistencies (Table S3) contribute 66% of the weight. Downgraded once within the risk-of-bias domain.
f. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 256) is below 50% of the optimal information size of about 800 participants.

g. Results with some concerns or high risk contribute 100% of the weight. Reports with internal data inconsistencies (Table S3) contribute 80% of the weight. Downgraded once within the risk-of-bias domain.
h. Results with some concerns or high risk contribute 100% of the weight. Reports with internal data inconsistencies (Table S3) contribute 82% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
i. Substantial heterogeneity ($I^2 = 84\%$).
j. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 343) is below 50% of the optimal information size of about 800 participants.
k. Substantial heterogeneity ($I^2 = 96\%$).
l. Results with some concerns or high risk contribute 100% of the weight. Reports with internal data inconsistencies (Table S3) contribute 74% of the weight. Downgraded once within the risk-of-bias domain.
m. Substantial heterogeneity ($I^2 = 90\%$).
n. Substantial heterogeneity ($I^2 = 80\%$).
o. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
p. Single trial, inconsistency cannot be assessed.
q. 95% CI excludes no difference, but the total sample (N = 61) is below 50% of the optimal information size of about 800 participants.
r. Results with some concerns or high risk contribute 100% of the weight. Reports with internal data inconsistencies (Table S3) contribute 83% of the weight. Downgraded once within the risk-of-bias domain.
s. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain.
t. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 61) is below 50% of the optimal information size of about 800 participants.
u. Results with some concerns or high risk contribute 100% of the weight. Reports with internal data inconsistencies (Table S3) contribute 77% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
v. Results with some concerns or high risk contribute 100% of the weight. Reports with internal data inconsistencies (Table S3) contribute 49% of the weight. Downgraded once within the risk-of-bias domain.
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for $N < 800$ and two levels for $N < 400$. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Omega-3 + vitamin E compared to placebo in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	omega-3 + vitamin E	placebo	Relative (95% CI)	Absolute (95% CI)		
Fasting insulin (µIU/mL), trials: Jamilian 2018												
1	randomized trials	not serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	20	20	-	MD **3.40 µIU/mL lower** (6.34 lower to 0.46 lower)	⨁⨁◯◯ **Low**	CRITICAL
HOMA-IR, trials: Jamilian 2018												
1	randomized trials	not serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	20	20	-	MD **0.80 lower** (1.47 lower to 0.13 lower)	⨁⨁◯◯ **Low**	CRITICAL
BMI (kg/m²), trials: Jamilian 2018												
1	randomized trials	not serious	not serious[b]	not serious	very serious[e]	publication bias not assessable[d]	20	20	-	MD **0.100 kg/m² lower** (0.42 lower to 0.22 higher)	⨁⨁◯◯ **Low**	CRITICAL
Waist circumference (cm), trials: Jamilian 2018												
1	randomized trials	not serious[a]	not serious[b]	not serious	very serious[e]	publication bias not assessable[d]	20	20	-	MD **0.20 cm lower** (0.54 lower to 0.14 higher)	⨁⨁◯◯ **Low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
b. Single trial, inconsistency cannot be assessed.
c. 95% CI excludes no difference, but the total sample (N = 40) is below 50% of the optimal information size of about 800 participants.
d. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
e. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 40) is below 50% of the optimal information size of about 800 participants.
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for N < 800 and two levels for N < 400. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects

model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Soy isoflavones compared to placebo in women with PCOS

Setting: randomized controlled trials, baseline vitamin D status not reported or not used for enrollment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	soy isoflavones	placebo	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Jamilian 2016												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **1.70 mg/dL higher** (0.97 lower to 4.37 higher)	⨁◯◯◯ **Very low**	CRITICAL
Fasting insulin (µIU/mL), trials: Jamilian 2016												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **4.00 µIU/mL lower** (6.04 lower to 1.96 lower)	⨁◯◯◯ **Very low**	CRITICAL
HOMA-IR, trials: Jamilian 2016												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **0.90 lower** (1.39 lower to 0.41 lower)	⨁◯◯◯ **Very low**	CRITICAL
HOMA-B, trials: Jamilian 2016												
1	randomized trials	serious[f]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **15.1 lower** (22.9 lower to 7.29 lower)	⨁◯◯◯ **Very low**	IMPORTANT
QUICKI, trials: Jamilian 2016												
1	randomized trials	serious[f]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **0.011 higher** (0.000 higher to 0.021 higher)	⨁◯◯◯ **Very low**	IMPORTANT
Total cholesterol (mg/dL), trials: Jamilian 2016												
1	randomized trials	serious[f]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **3.60 mg/dL higher** (4.48 lower to 11.7 higher)	⨁◯◯◯ **Very low**	IMPORTANT
LDL-C (mg/dL), trials: Jamilian 2016												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **7.30 mg/dL higher** (1.86 lower to 16.5 higher)	⨁◯◯◯ **Very low**	CRITICAL
HDL-C (mg/dL), trials: Jamilian 2016												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **1.00 mg/dL higher** (1.20 lower to 3.20 higher)	⨁◯◯◯ **Very low**	CRITICAL
Triglycerides (mg/dL), trials: Jamilian 2016												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **23.6 mg/dL lower** (45.7 lower to 1.45 lower)	⨁◯◯◯ **Very low**	CRITICAL
Total testosterone (ng/mL), trials: Jamilian 2016												
1	randomized trials	serious[f]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **0.30 ng/mL lower** (0.47 lower to 0.13 lower)	⨁◯◯◯ **Very low**	IMPORTANT
SHBG (nmol/L), trials: Jamilian 2016												
1	randomized trials	serious[f]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **5.20 nmol/L higher** (2.84 higher to 7.56 higher)	⨁◯◯◯ **Very low**	IMPORTANT
FAI, trials: Jamilian 2016												

1	randomized trials	serious[f]	not serious[b]	not serious	very serious[e]	publication bias not assessable[d]	35	35	-	MD **0.050 lower** (0.067 lower to 0.033 lower)	⊕◯◯◯ **Very low**	IMPORTANT
DHEAS (µg/mL), trials: Jamilian 2016												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **0.60 µg/mL lower** (1.49 lower to 0.29 higher)	⊕◯◯◯ **Very low**	IMPORTANT
MDA (µmol/L), trials: Jamilian 2016												
1	randomized trials	serious[f]	not serious[b]	not serious	very serious[e]	publication bias not assessable[d]	35	35	-	MD **1.50 µmol/L lower** (2.31 lower to 0.69 lower)	⊕◯◯◯ **Very low**	IMPORTANT
hs-CRP (mg/L), trials: Jamilian 2016												
1	randomized trials	serious[f]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **0.40 mg/L lower** (1.93 lower to 1.13 higher)	⊕◯◯◯ **Very low**	IMPORTANT
BMI (kg/m²), trials: Jamilian 2016												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **0.000 kg/m² higher** (0.19 lower to 0.19 higher)	⊕◯◯◯ **Very low**	CRITICAL
Waist circumference (cm), trials: Jamilian 2016												
1	randomized trials	serious[f]	not serious[b]	not serious	very serious[c]	publication bias not assessable[d]	35	35	-	MD **0.20 cm higher** (0.53 lower to 0.93 higher)	⊕◯◯◯ **Very low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Results with some concerns or high risk contribute 100% of the weight. Reports with internal data inconsistencies (Table S3) contribute 100% of the weight. Downgraded once within the risk-of-bias domain.
b. Single trial, inconsistency cannot be assessed.
c. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 70) is below 50% of the optimal information size of about 800 participants.
d. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
e. 95% CI excludes no difference, but the total sample (N = 70) is below 50% of the optimal information size of about 800 participants.
f. Results with some concerns or high risk contribute 100% of the weight. Reports with internal data inconsistencies (Table S3) contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for N < 800 and two levels for N < 400. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Question: Pomegranate juice compared to placebo beverage or control in women with PCOS

Setting: randomized controlled trials, comparator: placebo beverage (Esmaeilinezhad 2019) or routine dietary advice without a beverage (Abedini 2021)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pomegranate juice	placebo beverage or control	Relative (95% CI)	Absolute (95% CI)		
Fasting glucose (mg/dL), trials: Esmaeilinezhad 2019, Abedini 2021												
2	randomized trials	serious[a]	not serious	not serious	very serious[b]	publication bias not assessable[c]	43	42	-	MD **1.46 mg/dL higher** (24.0 lower to 26.9 higher)	⨁◯◯◯ **Very low**	CRITICAL
Fasting insulin (µIU/mL), trials: Esmaeilinezhad 2019, Abedini 2021												
2	randomized trials	serious[d]	not serious	not serious	very serious[b]	publication bias not assessable[c]	43	42	-	MD **1.59 µIU/mL lower** (11.9 lower to 8.73 higher)	⨁◯◯◯ **Very low**	CRITICAL
HOMA-IR, trials: Esmaeilinezhad 2019, Abedini 2021												
2	randomized trials	serious[e]	not serious	not serious	very serious[b]	publication bias not assessable[c]	43	42	-	MD **0.38 lower** (3.20 lower to 2.43 higher)	⨁◯◯◯ **Very low**	CRITICAL
QUICKI, trials: Esmaeilinezhad 2019												
1	randomized trials	serious[f]	not serious[g]	not serious	very serious[h]	publication bias not assessable[c]	22	21	-	MD **0.005 higher** (0.002 higher to 0.008 higher)	⨁◯◯◯ **Very low**	IMPORTANT
Total cholesterol (mg/dL), trials: Abedini 2021												
1	randomized trials	serious[i]	not serious[g]	not serious	very serious[j]	publication bias not assessable[c]	21	21	-	MD **2.09 mg/dL higher** (11.9 lower to 16.1 higher)	⨁◯◯◯ **Very low**	IMPORTANT
LDL-C (mg/dL), trials: Abedini 2021												
1	randomized trials	serious[k]	not serious[g]	not serious	very serious[j]	publication bias not assessable[c]	21	21	-	MD **4.25 mg/dL higher** (7.26 lower to 15.8 higher)	⨁◯◯◯ **Very low**	CRITICAL
HDL-C (mg/dL), trials: Abedini 2021												
1	randomized trials	serious[k]	not serious[g]	not serious	very serious[j]	publication bias not assessable[c]	21	21	-	MD **3.28 mg/dL higher** (2.25 lower to 8.81 higher)	⨁◯◯◯ **Very low**	CRITICAL
Triglycerides (mg/dL), trials: Abedini 2021												
1	randomized trials	serious[k]	not serious[g]	not serious	very serious[j]	publication bias not assessable[c]	21	21	-	MD **23.6 mg/dL lower** (49.3 lower to 2.12 higher)	⨁◯◯◯ **Very low**	CRITICAL
Total testosterone (ng/mL), trials: Esmaeilinezhad 2019												
1	randomized trials	serious[f]	not serious[g]	not serious	very serious[h]	publication bias not assessable[c]	22	21	-	MD **0.090 ng/mL lower**	⨁◯◯◯ **Very low**	IMPORTANT

										(0.16 lower to 0.021 lower)		
BMI (kg/m²), trials: Esmaeilinezhad 2019, Abedini 2021												
2	randomized trials	serious[l]	not serious	not serious	very serious[b]	publication bias not assessable[c]	43	42	-	MD **0.26 kg/m² lower** (8.41 lower to 7.90 higher)	⨁◯◯◯ **Very low**	CRITICAL
Waist circumference (cm), trials: Esmaeilinezhad 2019												
1	randomized trials	serious[f]	not serious[g]	not serious	very serious[m]	publication bias not assessable[c]	22	21	-	MD **0.98 cm lower** (4.55 lower to 2.59 higher)	⨁◯◯◯ **Very low**	IMPORTANT
Waist-to-hip ratio, trials: Esmaeilinezhad 2019												
1	randomized trials	serious[n]	not serious[g]	not serious	very serious[m]	publication bias not assessable[c]	22	21	-	MD **0.010 lower** (0.030 lower to 0.010 higher)	⨁◯◯◯ **Very low**	IMPORTANT

CI: confidence interval, **MD:** mean difference.

Explanations

a. Results with some concerns or high risk contribute 56% of the weight. Reports with internal data inconsistencies (Table S3) contribute 44% of the weight. Downgraded once within the risk-of-bias domain.
b. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 85) is below 50% of the optimal information size of about 800 participants.
c. Fewer than 10 trials. Funnel plot and small-study tests were not performed.
d. Results with some concerns or high risk contribute 39% of the weight. Reports with internal data inconsistencies (Table S3) contribute 61% of the weight. Downgraded once within the risk-of-bias domain.
e. Results with some concerns or high risk contribute 54% of the weight. Reports with internal data inconsistencies (Table S3) contribute 46% of the weight. Downgraded once within the risk-of-bias domain.
f. Reports with internal data inconsistencies (Table S3) contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
g. Single trial, inconsistency cannot be assessed.
h. 95% CI excludes no difference, but the total sample (N = 43) is below 50% of the optimal information size of about 800 participants.
i. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain. Some judgments carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026).
j. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 42) is below 50% of the optimal information size of about 800 participants.
k. Results with some concerns or high risk contribute 100% of the weight. Downgraded once within the risk-of-bias domain.
l. Results with some concerns or high risk contribute 22% of the weight. Reports with internal data inconsistencies (Table S3) contribute 78% of the weight. Downgraded once within the risk-of-bias domain.
m. 95% CI includes no difference (null used as the threshold, no validated minimal important difference), and the total sample (N = 43) is below 50% of the optimal information size of about 800 participants.
n. Reports with internal data inconsistencies (Table S3) contribute 100% of the weight. Downgraded once within the risk-of-bias domain.

Rules applied: risk of bias downgraded one level when more than 50% of the weight comes from results with some concerns or high risk of bias or from reports with internal data inconsistencies (Table S3), and two levels when at least 50% comes from results at high risk. Data-integrity concerns are considered only within this domain, so the same problem is not penalized twice. Inconsistency downgraded for $I^2 \geq 50\%$ (two levels for $I^2 \geq 75\%$), used as a guide together with the overlap of trial confidence intervals. Imprecision assessed with the minimally contextualized approach of GRADE Guidance 34 (Zeng et al., J Clin Epidemiol 2022, 150, 216–224) using no difference as the threshold, because validated minimal important differences are not available for these outcomes, and with an optimal information size of about 800 participants (small effect of 0.2 SD, two-sided α 0.05, power 0.8). Imprecision downgraded one level if the 95% CI includes no difference, two levels if N is also below 400 (half of the optimal information size), and, if the 95% CI excludes no difference, one level for $N < 800$ and two levels for $N < 400$. Indirectness not downgraded (populations, interventions and comparators match the review question, and all outcomes are biomarkers or anthropometric measures). Publication bias not assessable (fewer than 10 trials). Effects: REML random-effects model with modified Hartung–Knapp 95% CI. Single trials with normal-approximation 95% CI. Risk of bias: RoB 2 for each result. Judgments confirmed by the assessor (EZF, 28–29 October 2026). Quasi-randomized trials (Bonakdaran 2012, Khani 2011) are not part of these profiles. They were used only in sensitivity analysis S10.

Table S2. PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract (see PRISMA 2020 for Abstracts checklist below)
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Section 1
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Section 1 (last paragraph)
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Section 2.2, Table 1
Information	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date	Section 2.1,

Section and Topic	Item #	Checklist item	Location where item is reported
sources		when each source was last searched or consulted.	Figure S1
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Section 2.1, Figure S1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Section 2.3, Figure 1
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Sections 2.3–2.4, Text S1
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Sections 2.2 and 2.4, Data S1
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Section 2.4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Section 2.5, Text S1, Data S1
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Section 2.6, Text S1

Section and Topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Sections 2.2 and 2.6, Text S1, Table S6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Section 2.6, Text S1, Table S3
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Section 2.6, Text S1
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s),	Section 2.6,

Section and Topic	Item #	Checklist item	Location where item is reported
		method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Text S1, Code S1
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Section 2.6, Text S1
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Section 2.6, Text S1, Tables S4–S5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Section 2.6, Text S1
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Section 2.5, Text S1
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Section 3.1, Figure 1, Table S6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Section 3.1, Table S7
Study characteristics	17	Cite each included study and present its characteristics.	Section 3.2, Table 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Section 3.7, Figures S126–S167, Data S1
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Section 3.3, Figures 2–4, Table 3, Figures S2–S63, Table S1
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies.	Sections 3.3 and 3.7, Figures S126–S167

Section and Topic	Item #	Checklist item	Location where item is reported
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Section 3.3, Table 3, Figures S2–S63
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Section 3.3, Table 3 (I^2), Table S1
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Section 3.3, Tables S4–S5
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Sections 2.6 and 3.6, Figures S64–S125
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Section 3.5, Table 5, Table S1
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Section 4
	23b	Discuss any limitations of the evidence included in the review.	Section 4.1
	23c	Discuss any limitations of the review processes used.	Section 4.1
	23d	Discuss implications of the results for practice, policy, and future research.	Section 4.2
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Section 2
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Section 2
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Section 2 (list of deviations)
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Funding statement
Competing interests	26	Declare any competing interests of review authors.	Conflicts of Interest

Section and Topic	Item #	Checklist item	Location where item is reported
			statement
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms, data extracted from included studies, data used for all analyses, analytic code, any other materials used in the review.	Data Availability Statement, Data S1, Data S2, Code S1

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Abstract (Background /Objectives)
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Abstract (Methods), Section 2.2
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Abstract (Methods), Section 2.1
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Abstract (Methods)
Synthesis of results	6	Specify the methods used to present and synthesise results.	Abstract (Methods), Section 2.6, Text S1
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarize relevant characteristics of studies.	Abstract (Results), Section 3.1
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favored).	Abstract (Results), Section 3.3
DISCUSSION			

Section and Topic	Item #	Checklist item	Location where item is reported
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Abstract (Results and Conclusions)
Interpretation	10	Provide a general interpretation of the results and important implications.	Abstract (Conclusions), Section 4
OTHER			
Funding	11	Specify the primary source of funding for the review.	Not reported in abstract
Registration	12	Provide the register name and registration number.	Abstract (Methods), Section 2

Table S3. Data that could not be pooled, design issues and internal data inconsistencies in the source reports

Report	Outcome(s)	Issue	Handling
Ravn 2022	All outcomes	Medians (IQR) only	Narrative only, not pooled
Trummer 2019	All outcomes except fasting glucose and 25(OH)D	Medians (IQR), analyzed on the log scale by the authors	Not pooled, baseline-adjusted MDs reported by the trial used for fasting glucose and 25(OH)D
Javed 2019	Total and HDL cholesterol, triglycerides, glucose, insulin, HOMA-IR, testosterone, SHBG, FAI, DBP	At least one arm as median (IQR), metformin-free subgroup reported only as percentage change	Not pooled, full-sample mean values used only in sensitivity analysis S5
Nestler 1999	SHBG	Reported in µg/dL	Not combined with nmol/L data
Mishra 2022	Total testosterone	Unit not stated	Not combined with other trials
Abedini 2021	Total testosterone	Baseline values only	Not estimable
Abedini 2021	All outcomes	Between-group contrast not reported, arm-level ANCOVA-adjusted changes with SEs only	Arm-level baseline and follow-up values used (imputed change SD, r = 0.5), derived ANCOVA contrast only in S9
Dastgheib 2022	DHEA	DHEA, not DHEAS	Not combined with DHEAS
Esmaeilinezhad 2019	Synbiotic juice and synbiotic beverage arms	Probiotic co-intervention	Arms not used, plain pomegranate juice vs placebo beverage analyzed
Khani 2011	All outcomes	Quasi-randomized allocation, group sizes reversed between text and table, LDL cholesterol in text differs from table, testosterone labeled pg/mL with ng/mL-range values	Not in primary analyses (quasi-randomized), re-included only in S10
Bonakdaran 2012	All outcomes	Allocation by day of clinic attendance (quasi-randomized)	Not in primary analyses, re-included only in S10
Jamilian 2016	Triglycerides, DHEAS	Placebo end-of-trial triglyceride SD 5.1 (baseline 41.0). Soy DHEAS row identical to soy free-testosterone row	Primary analysis, excluded in S4
Mejia-Montilla 2018	Glucose AUC, insulin, HOMA-IR	Identical baseline glucose AUC in both arms. Baseline SDs differ between Tables 1 and 3	Primary analysis, excluded in S4
Esmaeilinezhad 2019	All outcomes	Tables state n = 23 per arm, flow diagram shows 22 and 21 analyzed	Flow-diagram numbers used, excluded in S4
Khani 2017	Lipids	Lipid SDs of 1–6 mg/dL with n = 43–44, consistent with standard errors	Analyzed as reported, as standard errors in S7, excluded in S4
Mishra 2022	Body weight, waist circumference, waist-to-hip ratio, SHBG, lipids	Identical post-treatment body weight in two arms, text–table contradictions for waist measures, SHBG values	Body weight, waist measures and SHBG excluded. Other outcomes in primary analysis and excluded in S4

		identical to BMI values, lipid changes internally inconsistent	
Hajimonfarednejad 2018	HDL cholesterol	Baseline SD equal to the mean	HDL excluded, other outcomes retained
Hajimonfarednejad 2018	All outcomes	Both arms also received medroxyprogesterone acetate 10 mg/day for 10 days per cycle	Retained (identical in both arms), excluded in S11
Ghanbarzadeh-Ghashti 2023	HDL cholesterol, triglycerides	Placebo end-of-trial HDL identical to baseline, including SD, implausibly small end-of-trial triglyceride SDs	HDL excluded, triglycerides from the reported ANCOVA difference

IQR: interquartile range, MD: mean difference, AUC: area under the curve, S1–S11: sensitivity analyses as numbered in Text S1.

Table S4. Sensitivity and leave-one-out analyses that changed the interpretation of an estimate or left a single trial

Comparison	Outcome	Analysis	Primary: k, MD (95% CI)	Sensitivity: k, MD (95% CI)
Vitamin D3 vs placebo	Fasting insulin	S2 without all reports co-authored by the shared author	3: −1.17 (−3.07 to 0.72)	1: −0.14 (−3.90 to 3.62) (single trial, not pooled)
Vitamin D3 vs placebo	QUICKI	S1 concern-affected reports re-included	3: 0.013 (−0.007 to 0.034)	4: 0.017 (0.001 to 0.033)
Vitamin D3 vs placebo	QUICKI	S2 without all reports co-authored by the shared author	3: 0.013 (−0.007 to 0.034)	1: 0.017 (−0.003 to 0.037) (single trial, not pooled)
Vitamin D3 vs placebo	Total cholesterol	S1 concern-affected reports re-included	4: −8.61 (−18.40 to 1.18)	5: −8.87 (−16.63 to −1.11)
Vitamin D3 vs placebo	Total cholesterol	S6d r = 0.9	4: −8.61 (−18.40 to 1.18)	4: −9.28 (−18.54 to −0.015)
Vitamin D3 vs placebo	VLDL-C	S2 without all reports co-authored by the shared author	3: −3.57 (−12.83 to 5.70)	1: −6.52 (−12.99 to −0.051) (single trial, not pooled)
Vitamin D3 vs placebo	BMI	S2 without all reports co-authored by the shared author	3: −0.026 (−0.32 to 0.27)	1: −0.002 (−0.22 to 0.22) (single trial, not pooled)
Vitamin D3 vs placebo	Body weight	S2 without all reports co-authored by the shared author	3: −0.19 (−1.06 to 0.68)	1: −0.36 (−0.92 to 0.20) (single trial, not pooled)
Cinnamon vs placebo	Fasting insulin	S6d r = 0.9	3: −3.28 (−6.95 to 0.38)	3: −3.17 (−6.01 to −0.33)
Cinnamon vs placebo	HOMA-IR	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	3: −1.03 (−1.97 to −0.092)	2: −0.98 (−4.02 to 2.06)
Cinnamon vs placebo	Total testosterone	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	2: −0.12 (−1.07 to 0.84)	1: −0.12 (−0.28 to 0.044) (single trial, not pooled)
Cinnamon vs placebo	SHBG	S6d r = 0.9 (single trial)	1: 10.37 (−6.65 to 27.39)	1: 10.37 (2.27 to 18.47) (single trial, not pooled)
Cinnamon vs placebo	Waist circumference	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	2: −1.26 (−32.60 to 30.08)	1: −0.15 (−8.88 to 8.58) (single trial, not pooled)

Cinnamon vs metformin	Free testosterone	S6c r = 0.75 (single trial)	1: −4.00 (−8.85 to 0.85)	1: −4.00 (−7.51 to −0.49) (single trial, not pooled)
Cinnamon vs metformin	Free testosterone	S6d r = 0.9 (single trial)	1: −4.00 (−8.85 to 0.85)	1: −4.00 (−6.35 to −1.65) (single trial, not pooled)
Ginger vs placebo	Fasting insulin	S6d r = 0.9 (single trial)	1: −1.57 (−3.86 to 0.72)	1: −1.57 (−2.62 to −0.52) (single trial, not pooled)
Ginger vs placebo	LDL-C	S6d r = 0.9 (single trial)	1: 7.95 (−6.86 to 22.76)	1: 7.95 (0.78 to 15.12) (single trial, not pooled)
Ginger vs placebo	HDL-C	S6d r = 0.9 (single trial)	1: −2.05 (−5.56 to 1.46)	1: −2.05 (−4.08 to −0.023) (single trial, not pooled)
Ginger vs metformin	Total cholesterol	S6c r = 0.75 (single trial)	1: 15.35 (−5.32 to 36.02)	1: 15.35 (0.56 to 30.14) (single trial, not pooled)
Ginger vs metformin	Total cholesterol	S6d r = 0.9 (single trial)	1: 15.35 (−5.32 to 36.02)	1: 15.35 (5.66 to 25.04) (single trial, not pooled)
Ginger vs metformin	LDL-C	S6d r = 0.9 (single trial)	1: 9.25 (−5.33 to 23.83)	1: 9.25 (2.14 to 16.36) (single trial, not pooled)
Ginger vs metformin	HDL-C	S6d r = 0.9 (single trial)	1: −2.00 (−4.98 to 0.98)	1: −2.00 (−3.44 to −0.56) (single trial, not pooled)
Ginger vs metformin	Total testosterone	S6c r = 0.75 (single trial)	1: 0.14 (−0.026 to 0.31)	1: 0.14 (0.021 to 0.26) (single trial, not pooled)
Ginger vs metformin	Total testosterone	S6d r = 0.9 (single trial)	1: 0.14 (−0.026 to 0.31)	1: 0.14 (0.061 to 0.22) (single trial, not pooled)
Ginger vs metformin	SHBG	S6c r = 0.75 (single trial)	1: −13.08 (−28.75 to 2.59)	1: −13.08 (−25.16 to −1.00) (single trial, not pooled)
Ginger vs metformin	SHBG	S6d r = 0.9 (single trial)	1: −13.08 (−28.75 to 2.59)	1: −13.08 (−22.35 to −3.81) (single trial, not pooled)
Ginger vs metformin	FAI	S6c r = 0.75 (single trial)	1: 0.52 (−0.17 to 1.21)	1: 0.52 (0.022 to 1.02) (single trial, not pooled)
Ginger vs metformin	FAI	S6d r = 0.9 (single trial)	1: 0.52 (−0.17 to 1.21)	1: 0.52 (0.19 to 0.85) (single trial, not pooled)
Berberine vs metformin	Fasting insulin	S6d r = 0.9 (single trial)	1: 0.64 (−0.33 to 1.61)	1: 0.64 (0.16 to 1.12) (single trial, not pooled)
Berberine vs metformin	FAI	S6d r = 0.9 (single trial)	1: 0.21 (−0.11 to 0.53)	1: 0.21 (0.025 to 0.40) (single trial, not pooled)
Berberine vs metformin	BMI	S6d r = 0.9 (single trial)	1: 0.73 (−0.35 to 1.81)	1: 0.73 (0.24 to 1.22) (single trial, not pooled)
Myo-inositol vs metformin	Fasting glucose	S6d r = 0.9 (single trial)	1: −3.88 (−9.99 to 2.23)	1: −3.88 (−6.73 to −1.03) (single trial, not pooled)
Myo-inositol vs metformin	FAI	S6a r = 0 (single trial)	1: 0.34 (0.049 to 0.63)	1: 0.34 (−0.051 to 0.73) (single trial, not pooled)
Myo-inositol vs metformin	FAI	S6b r = 0.25 (single trial)	1: 0.34 (0.049 to 0.63)	1: 0.34 (−0.005 to 0.68) (single trial, not pooled)

Myo-inositol vs metformin	BMI	S4 without reports with internal data inconsistencies	2: 0.78 (−6.20 to 7.75)	1: −0.010 (−1.63 to 1.61) (single trial, not pooled)
Myo-inositol + folic acid vs metformin	HOMA-IR	S2 without all reports co-authored by the shared author	2: −0.29 (−1.30 to 0.72)	1: −0.20 (−0.42 to 0.022) (single trial, not pooled)
Myo-inositol + folic acid vs metformin	BMI	S2 without all reports co-authored by the shared author	2: −0.10 (−1.68 to 1.48)	1: −0.40 (−3.26 to 2.46) (single trial, not pooled)
D-chiro-inositol vs placebo	SHBG	S6d r = 0.9 (single trial)	1: 38.00 (−23.64 to 99.64)	1: 38.00 (2.23 to 73.77) (single trial, not pooled)
Curcumin vs placebo	QUICKI	S2 without all reports co-authored by the shared author	2: 0.008 (−0.017 to 0.033)	1: 0.010 (0.005 to 0.015) (single trial, not pooled)
Curcumin vs placebo	HDL-C	S2 without all reports co-authored by the shared author	2: 1.92 (−8.62 to 12.45)	1: 0.79 (−3.19 to 4.77) (single trial, not pooled)
Curcumin vs placebo	BMI	S2 without all reports co-authored by the shared author	2: −0.20 (−1.47 to 1.08)	1: 0.100 (−2.24 to 2.44) (single trial, not pooled)
Curcumin vs placebo	Body weight	S2 without all reports co-authored by the shared author	2: −0.60 (−3.66 to 2.46)	1: −0.050 (−6.40 to 6.30) (single trial, not pooled)
Omega-3 vs placebo/control	Fasting glucose	S4 without reports with internal data inconsistencies	2: −6.76 (−50.72 to 37.20)	1: −10.50 (−15.78 to −5.22) (single trial, not pooled)
Omega-3 vs placebo/control	Fasting insulin	S4 without reports with internal data inconsistencies	2: −2.08 (−8.08 to 3.92)	1: −1.45 (−3.04 to 0.14) (single trial, not pooled)
Omega-3 vs placebo/control	HOMA-IR	S4 without reports with internal data inconsistencies	2: −0.46 (−2.09 to 1.16)	1: −0.72 (−1.26 to −0.18) (single trial, not pooled)
Omega-3 vs placebo/control	Total cholesterol	S4 without reports with internal data inconsistencies	3: −14.94 (−32.67 to 2.79)	1: −14.80 (−29.91 to 0.31) (single trial, not pooled)
Omega-3 vs placebo/control	Total cholesterol	S7 Khani 2017 lipid SDs treated as SEs	3: −14.94 (−32.67 to 2.79)	3: −18.59 (−32.63 to −4.54)
Omega-3 vs placebo/control	LDL-C	S4 without reports with internal data inconsistencies	3: −16.08 (−36.94 to 4.77)	1: −15.65 (−30.50 to −0.80) (single trial, not pooled)
Omega-3 vs placebo/control	HDL-C	S4 without reports with internal data inconsistencies	3: 4.13 (−1.56 to 9.81)	1: 2.26 (−0.77 to 5.29) (single trial, not pooled)
Omega-3 vs placebo/control	Triglycerides	S4 without reports with internal data inconsistencies	3: −11.24 (−30.18 to 7.69)	1: −2.34 (−16.50 to 11.82) (single trial, not pooled)
Omega-3 vs placebo/control	BMI	S4 without reports with internal data inconsistencies	3: −0.89 (−2.32 to 0.54)	1: −0.15 (−1.71 to 1.41) (single trial, not pooled)
Omega-3 vs placebo/control	Waist circumference	S4 without reports with internal data inconsistencies	2: −1.77 (−12.45 to 8.92)	1: −0.21 (−3.35 to 2.93) (single trial, not pooled)
Omega-3 vs placebo/control	Waist-to-hip ratio	S4 without reports with internal data inconsistencies	2: 0.015 (−0.062 to 0.092)	1: 0.010 (−0.007 to 0.027) (single trial, not pooled)
Pomegranate juice vs control	Fasting glucose	S4 without reports with internal data inconsistencies	2: 1.46 (−23.99 to 26.91)	1: 2.15 (−3.07 to 7.37) (single trial, not pooled)
Pomegranate juice vs control	Fasting insulin	S4 without reports with internal data inconsistencies	2: −1.59 (−11.92 to 8.73)	1: −2.03 (−4.57 to 0.51) (single trial, not pooled)

Pomegranate juice vs control	HOMA-IR	S4 without reports with internal data inconsistencies	2: −0.38 (−3.20 to 2.43)	1: −0.42 (−1.01 to 0.17) (single trial, not pooled)
Pomegranate juice vs control	HDL-C	S6d r = 0.9 (single trial)	1: 3.28 (−2.25 to 8.81)	1: 3.28 (0.75 to 5.81) (single trial, not pooled)
Pomegranate juice vs control	Triglycerides	S6c r = 0.75 (single trial)	1: −23.57 (−49.26 to 2.12)	1: −23.57 (−41.81 to −5.33) (single trial, not pooled)
Pomegranate juice vs control	Triglycerides	S6d r = 0.9 (single trial)	1: −23.57 (−49.26 to 2.12)	1: −23.57 (−35.25 to −11.89) (single trial, not pooled)
Pomegranate juice vs control	Total testosterone	S6a r = 0 (single trial)	1: −0.090 (−0.16 to −0.021)	1: −0.090 (−0.19 to 0.007) (single trial, not pooled)
Pomegranate juice vs control	BMI	S4 without reports with internal data inconsistencies	2: −0.26 (−8.41 to 7.90)	1: −0.38 (−3.05 to 2.29) (single trial, not pooled)
Pomegranate juice vs control	Waist-to-hip ratio	S6d r = 0.9 (single trial)	1: −0.010 (−0.030 to 0.010)	1: −0.010 (−0.020 to −0.000) (single trial, not pooled)
Cinnamon vs placebo	HOMA-IR	Leave-one-out: without Borzoei 2018	primary: −1.03 (−1.97 to −0.092)	2: −0.89 (−5.06 to 3.27)
Cinnamon vs placebo	HOMA-IR	Leave-one-out: without Hajimonfarednejad 2018	primary: −1.03 (−1.97 to −0.092)	2: −0.98 (−4.02 to 2.06)
Cinnamon vs placebo	HOMA-IR	Leave-one-out: without Dastgheib 2022	primary: −1.03 (−1.97 to −0.092)	2: −1.17 (−4.43 to 2.08)
Omega-3 vs placebo/control	LDL-C	Leave-one-out: without Mejia-Montilla 2018	primary: −16.08 (−36.94 to 4.77)	2: −9.49 (−13.98 to −5.01)
Omega-3 vs placebo/control	Triglycerides	Leave-one-out: without Mejia-Montilla 2018	primary: −11.24 (−30.18 to 7.69)	2: −8.97 (−16.76 to −1.19)

Listed are analyses in which the 95% CI changed between including and excluding no difference, or in which only one trial remained so that no pooled estimate was possible. In the leave-one-out analyses for cinnamon HOMA-IR, omitting any one trial widened the CI to include no difference. This reflects the loss of precision with two trials and does not show that one trial drives the effect. Complete results: Table S5. MD: mean difference, CI: confidence interval.

Table S5. Results of all sensitivity and leave-one-out analyses

Comparison	Outcome	Analysis	Trials included	k	N	MD (95% CI)	τ^2	I^2 (%)
Vitamin D3 vs placebo	Fasting glucose	S1 concern-affected reports re-included	Asemi 2015, Abootorabi 2018, Trummer 2019, Dastorani 2018, Maktabi 2017	5	321	−3.64 (−7.84 to 0.56)	6.696	59
Vitamin D3 vs placebo	Fasting glucose	S2 without all reports co-authored by the shared author	Abootorabi 2018, Trummer 2019	2	159	−4.99 (−56.83 to 46.84)	29.476	88
Vitamin D3 vs placebo	Fasting glucose	S3 without the factorial trial of Asemi 2015	Abootorabi 2018, Trummer 2019, Dastorani 2018	3	199	−3.63 (−14.78 to 7.52)	15.257	77
Vitamin D3 vs placebo	Fasting insulin	S1 concern-affected reports re-included	Asemi 2015, Abootorabi 2018, Dastorani 2018, Maktabi 2017	4	198	−2.12 (−5.12 to 0.88)	1.829	55
Vitamin D3 vs placebo	Fasting insulin	S2 without all reports co-authored by the shared author	Abootorabi 2018	1	36	−0.14 (−3.90 to 3.62)	–	–

Vitamin D3 vs placebo	Fasting insulin	S3 without the factorial trial of Asemi 2015	Abootorabi 2018, Dastorani 2018	2	76	−1.06 (−6.16 to 4.04)	0.000	0
Vitamin D3 vs placebo	HOMA-IR	S1 concern-affected reports re-included	Asemi 2015, Irani 2015, Abootorabi 2018, Dastorani 2018, Maktabi 2017	5	251	−0.40 (−0.92 to 0.12)	0.074	45
Vitamin D3 vs placebo	HOMA-IR	S2 without all reports co-authored by the shared author	Irani 2015, Abootorabi 2018	2	89	−0.13 (−3.95 to 3.69)	0.000	0
Vitamin D3 vs placebo	HOMA-IR	S3 without the factorial trial of Asemi 2015	Irani 2015, Abootorabi 2018, Dastorani 2018	3	129	−0.20 (−0.53 to 0.14)	0.000	0
Vitamin D3 vs placebo	HOMA-IR	S6a r = 0	Asemi 2015, Irani 2015, Abootorabi 2018, Dastorani 2018	4	181	−0.21 (−0.46 to 0.035)	0.000	0
Vitamin D3 vs placebo	HOMA-IR	S6b r = 0.25	Asemi 2015, Irani 2015, Abootorabi 2018, Dastorani 2018	4	181	−0.21 (−0.46 to 0.035)	0.000	0
Vitamin D3 vs placebo	HOMA-IR	S6c r = 0.75	Asemi 2015, Irani 2015, Abootorabi 2018, Dastorani 2018	4	181	−0.20 (−0.45 to 0.039)	0.000	0
Vitamin D3 vs placebo	HOMA-IR	S6d r = 0.9	Asemi 2015, Irani 2015, Abootorabi 2018, Dastorani 2018	4	181	−0.19 (−0.43 to 0.044)	0.000	1
Vitamin D3 vs placebo	HOMA-IR	S8 without results at high risk of bias	Asemi 2015, Abootorabi 2018, Dastorani 2018	3	128	−0.22 (−0.57 to 0.13)	0.000	6
Vitamin D3 vs placebo	HOMA-B	S1 concern-affected reports re-included	Abootorabi 2018, Foroozanfard 2015, Maktabi 2017	3	158	−14.39 (−44.84 to 16.06)	0.000	63
Vitamin D3 vs placebo	QUICKI	S1 concern-affected reports re-included	Asemi 2015, Abootorabi 2018, Dastorani 2018, Maktabi 2017	4	198	0.017 (0.001 to 0.033)	0.000	69
Vitamin D3 vs placebo	QUICKI	S2 without all reports co-authored by the shared author	Abootorabi 2018	1	36	0.017 (−0.003 to 0.037)	–	–
Vitamin D3 vs placebo	QUICKI	S3 without the factorial trial of Asemi 2015	Abootorabi 2018, Dastorani 2018	2	76	0.008 (−0.021 to 0.038)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	S1 concern-affected reports re-included	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018, Maktabi 2017	5	265	−8.87 (−16.63 to −1.11)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	S2 without all reports co-authored by the shared author	Ardabili 2013, Irani 2015	2	103	−16.76 (−108.09 to 74.56)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	S3 without the factorial trial of Asemi 2015	Ardabili 2013, Irani 2015, Dastorani 2018	3	143	−9.86 (−24.09 to 4.37)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	S6a r = 0	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−8.43 (−18.35 to 1.50)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	S6b r = 0.25	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−8.49 (−18.37 to 1.39)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	S6c r = 0.75	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−8.87 (−18.45 to 0.72)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	S6d r = 0.9	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−9.28 (−18.54 to −0.015)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	S8 without results at high risk of bias	Ardabili 2013, Asemi 2015, Dastorani 2018	3	142	−8.19 (−21.85 to 5.46)	0.000	0

Vitamin D3 vs placebo	LDL-C	S1 concern-affected reports re-included	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018, Maktabi 2017	5	265	−5.97 (−12.84 to 0.90)	0.000	0
Vitamin D3 vs placebo	LDL-C	S2 without all reports co-authored by the shared author	Ardabili 2013, Irani 2015	2	103	−7.73 (−87.14 to 71.68)	0.000	0
Vitamin D3 vs placebo	LDL-C	S3 without the factorial trial of Asemi 2015	Ardabili 2013, Irani 2015, Dastorani 2018	3	143	−7.16 (−19.73 to 5.41)	0.000	0
Vitamin D3 vs placebo	LDL-C	S5 Javed 2019 full sample added	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018, Javed 2019 (full sample)	5	232	−2.87 (−12.65 to 6.91)	17.901	27
Vitamin D3 vs placebo	LDL-C	S6a r = 0	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−4.75 (−16.01 to 6.51)	10.608	11
Vitamin D3 vs placebo	LDL-C	S6b r = 0.25	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−4.81 (−15.57 to 5.94)	8.549	11
Vitamin D3 vs placebo	LDL-C	S6c r = 0.75	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−5.13 (−14.09 to 3.83)	0.658	12
Vitamin D3 vs placebo	LDL-C	S6d r = 0.9	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−5.05 (−13.40 to 3.31)	0.000	12
Vitamin D3 vs placebo	LDL-C	S8 without results at high risk of bias	Ardabili 2013, Asemi 2015, Dastorani 2018	3	142	−4.49 (−24.45 to 15.48)	23.683	40
Vitamin D3 vs placebo	HDL-C	S1 concern-affected reports re-included	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018, Maktabi 2017	5	265	0.12 (−1.93 to 2.17)	0.000	0
Vitamin D3 vs placebo	HDL-C	S2 without all reports co-authored by the shared author	Ardabili 2013, Irani 2015	2	103	−0.025 (−19.64 to 19.59)	0.000	0
Vitamin D3 vs placebo	HDL-C	S3 without the factorial trial of Asemi 2015	Ardabili 2013, Irani 2015, Dastorani 2018	3	143	−0.14 (−3.93 to 3.65)	0.000	0
Vitamin D3 vs placebo	HDL-C	S6a r = 0	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−0.16 (−2.92 to 2.60)	0.000	0
Vitamin D3 vs placebo	HDL-C	S6b r = 0.25	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−0.17 (−2.91 to 2.58)	0.000	0
Vitamin D3 vs placebo	HDL-C	S6c r = 0.75	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−0.22 (−2.88 to 2.45)	0.000	0
Vitamin D3 vs placebo	HDL-C	S6d r = 0.9	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−0.31 (−2.81 to 2.20)	0.000	0
Vitamin D3 vs placebo	HDL-C	S8 without results at high risk of bias	Ardabili 2013, Asemi 2015, Dastorani 2018	3	142	−0.14 (−3.91 to 3.63)	0.000	0
Vitamin D3 vs placebo	Triglycerides	S1 concern-affected reports re-included	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018, Maktabi 2017	5	265	−11.14 (−27.42 to 5.15)	49.995	23
Vitamin D3 vs placebo	Triglycerides	S2 without all reports co-authored by the shared author	Ardabili 2013, Irani 2015	2	103	−25.71 (−206.39 to 154.97)	0.000	0
Vitamin D3 vs placebo	Triglycerides	S3 without the factorial trial of Asemi 2015	Ardabili 2013, Irani 2015, Dastorani 2018	3	143	−11.12 (−53.90 to 31.66)	129.299	28
Vitamin D3 vs placebo	Triglycerides	S6a r = 0	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−16.62 (−48.09 to 14.86)	175.266	42

Vitamin D3 vs placebo	Triglycerides	S6b r = 0.25	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−16.33 (−47.13 to 14.47)	167.595	42
Vitamin D3 vs placebo	Triglycerides	S6c r = 0.75	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−14.97 (−42.72 to 12.78)	135.067	42
Vitamin D3 vs placebo	Triglycerides	S6d r = 0.9	Ardabili 2013, Asemi 2015, Irani 2015, Dastorani 2018	4	195	−13.77 (−38.92 to 11.39)	110.071	42
Vitamin D3 vs placebo	Triglycerides	S8 without results at high risk of bias	Ardabili 2013, Asemi 2015, Dastorani 2018	3	142	−17.94 (−64.88 to 28.99)	215.016	61
Vitamin D3 vs placebo	VLDL-C	S1 concern-affected reports re-included	Ardabili 2013, Asemi 2015, Dastorani 2018, Maktabi 2017	4	212	−2.42 (−6.70 to 1.85)	2.695	41
Vitamin D3 vs placebo	VLDL-C	S2 without all reports co-authored by the shared author	Ardabili 2013	1	50	−6.52 (−12.99 to −0.051)	–	–
Vitamin D3 vs placebo	VLDL-C	S3 without the factorial trial of Asemi 2015	Ardabili 2013, Dastorani 2018	2	90	−2.79 (−37.41 to 31.83)	10.438	64
Vitamin D3 vs placebo	Total testosterone	S1 concern-affected reports re-included	Irani 2015, Maktabi 2017	2	123	−0.019 (−1.07 to 1.03)	0.007	45
Vitamin D3 vs placebo	Total testosterone	S6a r = 0	Irani 2015	1	53	0.037 (−0.11 to 0.18)	–	–
Vitamin D3 vs placebo	Total testosterone	S6b r = 0.25	Irani 2015	1	53	0.037 (−0.089 to 0.16)	–	–
Vitamin D3 vs placebo	Total testosterone	S6c r = 0.75	Irani 2015	1	53	0.037 (−0.040 to 0.11)	–	–
Vitamin D3 vs placebo	Total testosterone	S6d r = 0.9	Irani 2015	1	53	0.037 (−0.017 to 0.091)	–	–
Vitamin D3 vs placebo	Total testosterone	S8 without results at high risk of bias	–	0	–	–	–	–
Vitamin D3 vs placebo	Free testosterone	S1 concern-affected reports re-included	Irani 2015, Maktabi 2017	2	123	0.29 (−4.14 to 4.72)	0.000	0
Vitamin D3 vs placebo	Free testosterone	S6a r = 0	Irani 2015	1	53	0.20 (−2.94 to 3.34)	–	–
Vitamin D3 vs placebo	Free testosterone	S6b r = 0.25	Irani 2015	1	53	0.20 (−2.54 to 2.94)	–	–
Vitamin D3 vs placebo	Free testosterone	S6c r = 0.75	Irani 2015	1	53	0.20 (−1.45 to 1.85)	–	–
Vitamin D3 vs placebo	Free testosterone	S6d r = 0.9	Irani 2015	1	53	0.20 (−0.94 to 1.34)	–	–
Vitamin D3 vs placebo	Free testosterone	S8 without results at high risk of bias	–	0	–	–	–	–
Vitamin D3 vs placebo	SHBG	S1 concern-affected reports re-included	Irani 2015, Maktabi 2017	2	123	−0.30 (−70.86 to 70.27)	0.000	0
Vitamin D3 vs placebo	SHBG	S6a r = 0	Irani 2015	1	53	−3.00 (−25.67 to 19.67)	–	–
Vitamin D3 vs placebo	SHBG	S6b r = 0.25	Irani 2015	1	53	−3.00 (−23.13 to 17.13)	–	–
Vitamin D3 vs placebo	SHBG	S6c r = 0.75	Irani 2015	1	53	−3.00 (−16.72 to 10.72)	–	–
Vitamin D3 vs placebo	SHBG	S6d r = 0.9	Irani 2015	1	53	−3.00 (−14.09 to 8.09)	–	–
Vitamin D3 vs placebo	SHBG	S8 without results at high risk of bias	–	0	–	–	–	–

Vitamin D3 vs placebo	FAI	S1 concern-affected reports re-included	Maktabi 2017	1	70	0.043 (−0.033 to 0.12)	–	–
Vitamin D3 vs placebo	DHEAS	S1 concern-affected reports re-included	Irani 2015, Maktabi 2017	2	123	0.004 (−1.97 to 1.98)	0.000	0
Vitamin D3 vs placebo	DHEAS	S6a r = 0	Irani 2015	1	53	0.010 (−0.65 to 0.67)	–	–
Vitamin D3 vs placebo	DHEAS	S6b r = 0.25	Irani 2015	1	53	0.010 (−0.57 to 0.59)	–	–
Vitamin D3 vs placebo	DHEAS	S6c r = 0.75	Irani 2015	1	53	0.010 (−0.33 to 0.35)	–	–
Vitamin D3 vs placebo	DHEAS	S6d r = 0.9	Irani 2015	1	53	0.010 (−0.21 to 0.23)	–	–
Vitamin D3 vs placebo	DHEAS	S8 without results at high risk of bias	–	0	–	–	–	–
Vitamin D3 vs placebo	25(OH)D	S1 concern-affected reports re-included	Ardabili 2013, Asemi 2015, Abootorabi 2018, Trummer 2019, Dastorani 2018, Foroozanfard 2015, Maktabi 2017	7	420	14.68 (10.42 to 18.95)	18.450	88
Vitamin D3 vs placebo	25(OH)D	S2 without all reports co-authored by the shared author	Ardabili 2013, Abootorabi 2018, Trummer 2019	3	206	17.88 (3.09 to 32.67)	32.274	91
Vitamin D3 vs placebo	25(OH)D	S3 without the factorial trial of Asemi 2015	Ardabili 2013, Abootorabi 2018, Trummer 2019, Dastorani 2018	4	246	16.18 (6.84 to 25.51)	31.657	93
Vitamin D3 vs placebo	25(OH)D	S5 Javed 2019 full sample added	Ardabili 2013, Asemi 2015, Abootorabi 2018, Trummer 2019, Dastorani 2018, Javed 2019 (full sample)	6	335	15.80 (10.34 to 21.27)	24.339	90
Vitamin D3 vs placebo	MDA	S1 concern-affected reports re-included	Foroozanfard 2015, Maktabi 2017	2	122	−0.88 (−4.47 to 2.71)	0.000	0
Vitamin D3 vs placebo	BMI	S2 without all reports co-authored by the shared author	Ardabili 2013	1	50	−0.002 (−0.22 to 0.22)	–	–
Vitamin D3 vs placebo	BMI	S3 without the factorial trial of Asemi 2015	Ardabili 2013, Dastorani 2018	2	90	−0.001 (−0.93 to 0.92)	0.000	0
Vitamin D3 vs placebo	BMI	S5 Javed 2019 full sample added	Ardabili 2013, Asemi 2015, Dastorani 2018, Javed 2019 (full sample)	4	179	−0.026 (−0.25 to 0.19)	0.000	0
Vitamin D3 vs placebo	Body weight	S2 without all reports co-authored by the shared author	Ardabili 2013	1	50	−0.36 (−0.92 to 0.20)	–	–
Vitamin D3 vs placebo	Body weight	S3 without the factorial trial of Asemi 2015	Ardabili 2013, Dastorani 2018	2	90	−0.12 (−3.04 to 2.80)	0.029	28
Vitamin D3 vs placebo	Body weight	S5 Javed 2019 full sample added	Ardabili 2013, Asemi 2015, Dastorani 2018, Javed 2019 (full sample)	4	179	−0.19 (−0.83 to 0.45)	0.019	0
Vitamin D3 vs placebo	Waist circumference	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Vitamin D3 vs placebo	Waist circumference	S3 without the factorial trial of Asemi 2015	–	0	–	–	–	–
Vitamin D3 vs placebo	Systolic BP	S5 Javed 2019 full sample added	Irani 2015, Javed 2019 (full sample)	2	90	−0.64 (−32.73 to 31.44)	0.000	0
Vitamin D3 vs placebo	Systolic BP	S6a r = 0	Irani 2015	1	53	0.00 (−8.26 to 8.26)	–	–

Vitamin D3 vs placebo	Systolic BP	S6b r = 0.25	Irani 2015	1	53	0.00 (−7.22 to 7.22)	–	–
Vitamin D3 vs placebo	Systolic BP	S6c r = 0.75	Irani 2015	1	53	0.00 (−4.48 to 4.48)	–	–
Vitamin D3 vs placebo	Systolic BP	S6d r = 0.9	Irani 2015	1	53	0.00 (−3.24 to 3.24)	–	–
Vitamin D3 vs placebo	Systolic BP	S8 without results at high risk of bias	–	0	–	–	–	–
Vitamin D3 vs placebo	Diastolic BP	S6a r = 0	Irani 2015	1	53	1.50 (−4.16 to 7.16)	–	–
Vitamin D3 vs placebo	Diastolic BP	S6b r = 0.25	Irani 2015	1	53	1.50 (−3.41 to 6.41)	–	–
Vitamin D3 vs placebo	Diastolic BP	S6c r = 0.75	Irani 2015	1	53	1.50 (−1.36 to 4.36)	–	–
Vitamin D3 vs placebo	Diastolic BP	S6d r = 0.9	Irani 2015	1	53	1.50 (−0.34 to 3.34)	–	–
Vitamin D3 vs placebo	Diastolic BP	S8 without results at high risk of bias	–	0	–	–	–	–
Calcitriol vs placebo	Fasting glucose	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	31	6.30 (0.18 to 12.42)	–	–
Calcitriol vs placebo	Fasting insulin	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	31	−0.20 (−14.94 to 14.54)	–	–
Calcitriol vs placebo	HOMA-IR	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	31	−0.60 (−3.84 to 2.64)	–	–
Calcitriol vs placebo	Total testosterone	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	31	−0.22 (−0.58 to 0.13)	–	–
Calcitriol vs placebo	DHEAS	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	31	−0.17 (−1.17 to 0.83)	–	–
Calcitriol vs placebo	25(OH)D	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	31	9.60 (−0.95 to 20.15)	–	–
Calcitriol vs placebo	Body weight	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	31	0.20 (−9.94 to 10.34)	–	–
Calcitriol vs placebo	Systolic BP	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	31	−6.60 (−14.69 to 1.49)	–	–
Calcitriol vs placebo	Diastolic BP	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	31	−2.30 (−7.53 to 2.93)	–	–
Calcitriol vs placebo	PTH	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	31	−27.10 (−43.27 to −10.93)	–	–
Calcitriol vs metformin	Fasting glucose	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	32	5.00 (−9.34 to 19.34)	–	–
Calcitriol vs metformin	Fasting insulin	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	32	10.50 (−7.89 to 28.89)	–	–
Calcitriol vs metformin	HOMA-IR	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	32	3.10 (−2.96 to 9.16)	–	–
Calcitriol vs metformin	Total testosterone	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	32	−0.068 (−0.41 to 0.28)	–	–
Calcitriol vs metformin	DHEAS	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	32	−0.18 (−1.16 to 0.81)	–	–
Calcitriol vs metformin	25(OH)D	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	32	10.20 (1.00 to 19.40)	–	–
Calcitriol vs metformin	Body weight	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	32	1.20 (−8.56 to 10.96)	–	–
Calcitriol vs metformin	Systolic BP	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	32	1.70 (−6.20 to 9.60)	–	–

Calcitriol vs metformin	Diastolic BP	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	32	0.50 (−4.82 to 5.82)	–	–
Calcitriol vs metformin	PTH	S10 quasi-randomized trials re-included	Bonakdaran 2012	1	32	−54.80 (−70.85 to −38.75)	–	–
Cinnamon vs placebo	Fasting glucose	S6a r = 0	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−5.96 (−22.12 to 10.20)	29.630	79
Cinnamon vs placebo	Fasting glucose	S6b r = 0.25	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−5.69 (−21.72 to 10.35)	30.796	82
Cinnamon vs placebo	Fasting glucose	S6c r = 0.75	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−4.98 (−20.99 to 11.02)	34.689	88
Cinnamon vs placebo	Fasting glucose	S6d r = 0.9	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−4.72 (−20.77 to 11.33)	36.531	90
Cinnamon vs placebo	Fasting glucose	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	Borzoei 2018, Dastgheib 2022	2	126	−6.15 (−87.24 to 74.94)	68.079	82
Cinnamon vs placebo	Fasting insulin	S6a r = 0	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−3.30 (−7.39 to 0.79)	0.000	0
Cinnamon vs placebo	Fasting insulin	S6b r = 0.25	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−3.30 (−7.21 to 0.62)	0.000	0
Cinnamon vs placebo	Fasting insulin	S6c r = 0.75	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−3.24 (−6.50 to 0.012)	0.000	0
Cinnamon vs placebo	Fasting insulin	S6d r = 0.9	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−3.17 (−6.01 to −0.33)	0.000	0
Cinnamon vs placebo	Fasting insulin	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	Borzoei 2018, Dastgheib 2022	2	126	−3.00 (−14.45 to 8.45)	0.000	0
Cinnamon vs placebo	HOMA-IR	S6a r = 0	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−1.07 (−2.10 to −0.034)	0.000	0
Cinnamon vs placebo	HOMA-IR	S6b r = 0.25	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−1.05 (−2.04 to −0.058)	0.000	0
Cinnamon vs placebo	HOMA-IR	S6c r = 0.75	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−1.00 (−1.85 to −0.14)	0.000	0
Cinnamon vs placebo	HOMA-IR	S6d r = 0.9	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−0.97 (−1.82 to −0.12)	0.018	9
Cinnamon vs placebo	HOMA-IR	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	Borzoei 2018, Dastgheib 2022	2	126	−0.98 (−4.02 to 2.06)	0.000	0
Cinnamon vs placebo	Total cholesterol	S6a r = 0	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−11.28 (−30.54 to 7.99)	0.000	0
Cinnamon vs placebo	Total cholesterol	S6b r = 0.25	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−11.22 (−29.80 to 7.37)	0.000	0

Cinnamon vs placebo	Total cholesterol	S6c r = 0.75	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−10.93 (−25.92 to 4.06)	0.000	0
Cinnamon vs placebo	Total cholesterol	S6d r = 0.9	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−10.42 (−25.62 to 4.78)	16.019	42
Cinnamon vs placebo	Total cholesterol	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	Borzoei 2018, Dastgheib 2022	2	126	−10.00 (−68.04 to 48.05)	0.000	0
Cinnamon vs placebo	LDL-C	S6a r = 0	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−11.19 (−29.02 to 6.64)	0.000	0
Cinnamon vs placebo	LDL-C	S6b r = 0.25	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−11.16 (−28.12 to 5.81)	0.000	0
Cinnamon vs placebo	LDL-C	S6c r = 0.75	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−10.82 (−27.26 to 5.62)	13.480	34
Cinnamon vs placebo	LDL-C	S6d r = 0.9	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−10.48 (−28.35 to 7.38)	33.548	67
Cinnamon vs placebo	LDL-C	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	Borzoei 2018, Dastgheib 2022	2	126	−8.96 (−63.49 to 45.56)	0.000	0
Cinnamon vs placebo	HDL-C	S6a r = 0	Borzoei 2018, Dastgheib 2022	2	126	2.44 (−17.06 to 21.93)	2.588	37
Cinnamon vs placebo	HDL-C	S6b r = 0.25	Borzoei 2018, Dastgheib 2022	2	126	2.20 (−19.09 to 23.49)	3.483	50
Cinnamon vs placebo	HDL-C	S6c r = 0.75	Borzoei 2018, Dastgheib 2022	2	126	1.72 (−21.62 to 25.06)	5.274	75
Cinnamon vs placebo	HDL-C	S6d r = 0.9	Borzoei 2018, Dastgheib 2022	2	126	1.58 (−22.04 to 25.19)	5.811	83
Cinnamon vs placebo	Triglycerides	S6a r = 0	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−6.97 (−55.44 to 41.50)	95.296	44
Cinnamon vs placebo	Triglycerides	S6b r = 0.25	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−4.05 (−59.16 to 51.06)	224.848	55
Cinnamon vs placebo	Triglycerides	S6c r = 0.75	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−0.30 (−61.36 to 60.76)	472.008	79
Cinnamon vs placebo	Triglycerides	S6d r = 0.9	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	0.57 (−61.53 to 62.66)	542.026	87
Cinnamon vs placebo	Triglycerides	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	Borzoei 2018, Dastgheib 2022	2	126	5.69 (−279.26 to 290.64)	843.098	83
Cinnamon vs placebo	Total testosterone	S6a r = 0	Hajimonfarednejad 2018, Dastgheib 2022	2	101	−0.12 (−1.42 to 1.19)	0.000	0
Cinnamon vs placebo	Total testosterone	S6b r = 0.25	Hajimonfarednejad 2018, Dastgheib 2022	2	101	−0.12 (−1.26 to 1.03)	0.000	0
Cinnamon vs placebo	Total testosterone	S6c r = 0.75	Hajimonfarednejad 2018, Dastgheib 2022	2	101	−0.12 (−0.82 to 0.58)	0.000	0
Cinnamon vs placebo	Total testosterone	S6d r = 0.9	Hajimonfarednejad 2018, Dastgheib 2022	2	101	−0.12 (−0.59 to 0.35)	0.000	0

Cinnamon vs placebo	Total testosterone	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	Dastgheib 2022	1	42	−0.12 (−0.28 to 0.044)	–	–
Cinnamon vs placebo	SHBG	S6a r = 0	Dastgheib 2022	1	42	10.37 (−13.49 to 34.23)	–	–
Cinnamon vs placebo	SHBG	S6b r = 0.25	Dastgheib 2022	1	42	10.37 (−10.35 to 31.09)	–	–
Cinnamon vs placebo	SHBG	S6c r = 0.75	Dastgheib 2022	1	42	10.37 (−1.86 to 22.60)	–	–
Cinnamon vs placebo	SHBG	S6d r = 0.9	Dastgheib 2022	1	42	10.37 (2.27 to 18.47)	–	–
Cinnamon vs placebo	FAI	S6a r = 0	Dastgheib 2022	1	42	−0.43 (−2.05 to 1.19)	–	–
Cinnamon vs placebo	FAI	S6b r = 0.25	Dastgheib 2022	1	42	−0.43 (−1.83 to 0.97)	–	–
Cinnamon vs placebo	FAI	S6c r = 0.75	Dastgheib 2022	1	42	−0.43 (−1.24 to 0.38)	–	–
Cinnamon vs placebo	FAI	S6d r = 0.9	Dastgheib 2022	1	42	−0.43 (−0.95 to 0.086)	–	–
Cinnamon vs placebo	DHEAS	S6a r = 0	Hajimonfarednejad 2018	1	59	−0.29 (−1.11 to 0.53)	–	–
Cinnamon vs placebo	DHEAS	S6b r = 0.25	Hajimonfarednejad 2018	1	59	−0.29 (−1.01 to 0.43)	–	–
Cinnamon vs placebo	DHEAS	S6c r = 0.75	Hajimonfarednejad 2018	1	59	−0.29 (−0.77 to 0.19)	–	–
Cinnamon vs placebo	DHEAS	S6d r = 0.9	Hajimonfarednejad 2018	1	59	−0.29 (−0.66 to 0.084)	–	–
Cinnamon vs placebo	DHEAS	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	–	0	–	–	–	–
Cinnamon vs placebo	BMI	S6a r = 0	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−0.13 (−0.44 to 0.18)	0.000	0
Cinnamon vs placebo	BMI	S6b r = 0.25	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−0.13 (−0.44 to 0.18)	0.000	0
Cinnamon vs placebo	BMI	S6c r = 0.75	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−0.14 (−0.44 to 0.17)	0.000	0
Cinnamon vs placebo	BMI	S6d r = 0.9	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−0.16 (−0.60 to 0.28)	0.006	0
Cinnamon vs placebo	BMI	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	Borzoei 2018, Dastgheib 2022	2	126	−0.13 (−1.04 to 0.78)	0.000	0
Cinnamon vs placebo	Body weight	S6a r = 0	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−0.47 (−1.19 to 0.24)	0.000	0
Cinnamon vs placebo	Body weight	S6b r = 0.25	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−0.47 (−1.19 to 0.24)	0.000	0
Cinnamon vs placebo	Body weight	S6c r = 0.75	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−0.48 (−1.19 to 0.24)	0.000	0

Cinnamon vs placebo	Body weight	S6d r = 0.9	Borzoei 2018, Hajimonfarednejad 2018, Dastgheib 2022	3	185	−0.49 (−1.19 to 0.22)	0.000	0
Cinnamon vs placebo	Body weight	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	Borzoei 2018, Dastgheib 2022	2	126	−0.47 (−2.59 to 1.65)	0.000	0
Cinnamon vs placebo	Waist circumference	S6a r = 0	Hajimonfarednejad 2018, Dastgheib 2022	2	101	−1.26 (−45.53 to 43.02)	0.000	0
Cinnamon vs placebo	Waist circumference	S6b r = 0.25	Hajimonfarednejad 2018, Dastgheib 2022	2	101	−1.26 (−39.62 to 37.10)	0.000	0
Cinnamon vs placebo	Waist circumference	S6c r = 0.75	Hajimonfarednejad 2018, Dastgheib 2022	2	101	−1.26 (−23.47 to 20.94)	0.000	0
Cinnamon vs placebo	Waist circumference	S6d r = 0.9	Hajimonfarednejad 2018, Dastgheib 2022	2	101	−1.27 (−15.40 to 12.85)	0.000	0
Cinnamon vs placebo	Waist circumference	S11 without the trial with background medroxyprogesterone (Hajimonfarednejad 2018)	Dastgheib 2022	1	42	−0.15 (−8.88 to 8.58)	–	–
Cinnamon vs placebo	Waist-to-hip ratio	S6a r = 0	Dastgheib 2022	1	42	−0.010 (−0.079 to 0.059)	–	–
Cinnamon vs placebo	Waist-to-hip ratio	S6b r = 0.25	Dastgheib 2022	1	42	−0.010 (−0.070 to 0.050)	–	–
Cinnamon vs placebo	Waist-to-hip ratio	S6c r = 0.75	Dastgheib 2022	1	42	−0.010 (−0.045 to 0.025)	–	–
Cinnamon vs placebo	Waist-to-hip ratio	S6d r = 0.9	Dastgheib 2022	1	42	−0.010 (−0.033 to 0.013)	–	–
Cinnamon vs metformin	Fasting glucose	S6a r = 0	Dastgheib 2022, Khan 2019	2	80	−1.19 (−39.50 to 37.13)	0.129	0
Cinnamon vs metformin	Fasting glucose	S6b r = 0.25	Dastgheib 2022, Khan 2019	2	80	−1.75 (−44.63 to 41.12)	7.041	24
Cinnamon vs metformin	Fasting glucose	S6c r = 0.75	Dastgheib 2022, Khan 2019	2	80	−2.88 (−50.53 to 44.76)	20.865	72
Cinnamon vs metformin	Fasting glucose	S6d r = 0.9	Dastgheib 2022, Khan 2019	2	80	−3.22 (−51.38 to 44.93)	25.012	87
Cinnamon vs metformin	Fasting insulin	S6a r = 0	Dastgheib 2022	1	40	−0.35 (−3.79 to 3.09)	–	–
Cinnamon vs metformin	Fasting insulin	S6b r = 0.25	Dastgheib 2022	1	40	−0.35 (−3.42 to 2.72)	–	–
Cinnamon vs metformin	Fasting insulin	S6c r = 0.75	Dastgheib 2022	1	40	−0.35 (−2.48 to 1.78)	–	–
Cinnamon vs metformin	Fasting insulin	S6d r = 0.9	Dastgheib 2022	1	40	−0.35 (−2.10 to 1.40)	–	–
Cinnamon vs metformin	HOMA-IR	S6a r = 0	Dastgheib 2022	1	40	−0.22 (−1.26 to 0.82)	–	–
Cinnamon vs metformin	HOMA-IR	S6b r = 0.25	Dastgheib 2022	1	40	−0.22 (−1.15 to 0.71)	–	–
Cinnamon vs metformin	HOMA-IR	S6c r = 0.75	Dastgheib 2022	1	40	−0.22 (−0.88 to 0.44)	–	–
Cinnamon vs metformin	HOMA-IR	S6d r = 0.9	Dastgheib 2022	1	40	−0.22 (−0.77 to 0.33)	–	–
Cinnamon vs metformin	Total cholesterol	S6a r = 0	Dastgheib 2022	1	40	4.55 (−20.16 to 29.26)	–	–
Cinnamon vs metformin	Total cholesterol	S6b r = 0.25	Dastgheib 2022	1	40	4.55 (−16.92 to 26.02)	–	–

Cinnamon vs metformin	Total cholesterol	S6c r = 0.75	Dastgheib 2022	1	40	4.55 (−8.15 to 17.25)	–	–
Cinnamon vs metformin	Total cholesterol	S6d r = 0.9	Dastgheib 2022	1	40	4.55 (−3.91 to 13.01)	–	–
Cinnamon vs metformin	LDL-C	S6a r = 0	Dastgheib 2022	1	40	−1.70 (−22.98 to 19.58)	–	–
Cinnamon vs metformin	LDL-C	S6b r = 0.25	Dastgheib 2022	1	40	−1.70 (−20.29 to 16.89)	–	–
Cinnamon vs metformin	LDL-C	S6c r = 0.75	Dastgheib 2022	1	40	−1.70 (−13.18 to 9.78)	–	–
Cinnamon vs metformin	LDL-C	S6d r = 0.9	Dastgheib 2022	1	40	−1.70 (−9.93 to 6.53)	–	–
Cinnamon vs metformin	HDL-C	S6a r = 0	Dastgheib 2022	1	40	−0.45 (−5.65 to 4.75)	–	–
Cinnamon vs metformin	HDL-C	S6b r = 0.25	Dastgheib 2022	1	40	−0.45 (−5.04 to 4.14)	–	–
Cinnamon vs metformin	HDL-C	S6c r = 0.75	Dastgheib 2022	1	40	−0.45 (−3.46 to 2.56)	–	–
Cinnamon vs metformin	HDL-C	S6d r = 0.9	Dastgheib 2022	1	40	−0.45 (−2.79 to 1.89)	–	–
Cinnamon vs metformin	Triglycerides	S6a r = 0	Dastgheib 2022	1	40	12.50 (−36.51 to 61.51)	–	–
Cinnamon vs metformin	Triglycerides	S6b r = 0.25	Dastgheib 2022	1	40	12.50 (−30.41 to 55.41)	–	–
Cinnamon vs metformin	Triglycerides	S6c r = 0.75	Dastgheib 2022	1	40	12.50 (−14.31 to 39.31)	–	–
Cinnamon vs metformin	Triglycerides	S6d r = 0.9	Dastgheib 2022	1	40	12.50 (−7.06 to 32.06)	–	–
Cinnamon vs metformin	Total testosterone	S6a r = 0	Dastgheib 2022	1	40	−0.027 (−0.28 to 0.22)	–	–
Cinnamon vs metformin	Total testosterone	S6b r = 0.25	Dastgheib 2022	1	40	−0.027 (−0.24 to 0.19)	–	–
Cinnamon vs metformin	Total testosterone	S6c r = 0.75	Dastgheib 2022	1	40	−0.027 (−0.15 to 0.10)	–	–
Cinnamon vs metformin	Total testosterone	S6d r = 0.9	Dastgheib 2022	1	40	−0.027 (−0.11 to 0.057)	–	–
Cinnamon vs metformin	Free testosterone	S6a r = 0	Khan 2019	1	40	−4.00 (−10.79 to 2.79)	–	–
Cinnamon vs metformin	Free testosterone	S6b r = 0.25	Khan 2019	1	40	−4.00 (−9.90 to 1.90)	–	–
Cinnamon vs metformin	Free testosterone	S6c r = 0.75	Khan 2019	1	40	−4.00 (−7.51 to −0.49)	–	–
Cinnamon vs metformin	Free testosterone	S6d r = 0.9	Khan 2019	1	40	−4.00 (−6.35 to −1.65)	–	–
Cinnamon vs metformin	SHBG	S6a r = 0	Dastgheib 2022	1	40	1.01 (−22.75 to 24.77)	–	–
Cinnamon vs metformin	SHBG	S6b r = 0.25	Dastgheib 2022	1	40	1.01 (−19.80 to 21.82)	–	–
Cinnamon vs metformin	SHBG	S6c r = 0.75	Dastgheib 2022	1	40	1.01 (−12.05 to 14.07)	–	–
Cinnamon vs metformin	SHBG	S6d r = 0.9	Dastgheib 2022	1	40	1.01 (−8.57 to 10.59)	–	–
Cinnamon vs metformin	FAI	S6a r = 0	Dastgheib 2022	1	40	0.10 (−1.49 to 1.69)	–	–

Cinnamon vs metformin	FAI	S6b r = 0.25	Dastgheib 2022	1	40	0.10 (−1.28 to 1.48)	–	–
Cinnamon vs metformin	FAI	S6c r = 0.75	Dastgheib 2022	1	40	0.10 (−0.71 to 0.91)	–	–
Cinnamon vs metformin	FAI	S6d r = 0.9	Dastgheib 2022	1	40	0.10 (−0.42 to 0.62)	–	–
Cinnamon vs metformin	BMI	S6a r = 0	Dastgheib 2022	1	40	0.22 (−3.66 to 4.10)	–	–
Cinnamon vs metformin	BMI	S6b r = 0.25	Dastgheib 2022	1	40	0.22 (−3.15 to 3.59)	–	–
Cinnamon vs metformin	BMI	S6c r = 0.75	Dastgheib 2022	1	40	0.22 (−1.73 to 2.17)	–	–
Cinnamon vs metformin	BMI	S6d r = 0.9	Dastgheib 2022	1	40	0.22 (−1.03 to 1.47)	–	–
Cinnamon vs metformin	Body weight	S6a r = 0	Dastgheib 2022	1	40	0.60 (−9.63 to 10.83)	–	–
Cinnamon vs metformin	Body weight	S6b r = 0.25	Dastgheib 2022	1	40	0.60 (−8.27 to 9.47)	–	–
Cinnamon vs metformin	Body weight	S6c r = 0.75	Dastgheib 2022	1	40	0.60 (−4.56 to 5.76)	–	–
Cinnamon vs metformin	Body weight	S6d r = 0.9	Dastgheib 2022	1	40	0.60 (−2.71 to 3.91)	–	–
Cinnamon vs metformin	Waist circumference	S6a r = 0	Dastgheib 2022	1	40	−0.40 (−13.98 to 13.18)	–	–
Cinnamon vs metformin	Waist circumference	S6b r = 0.25	Dastgheib 2022	1	40	−0.40 (−12.17 to 11.37)	–	–
Cinnamon vs metformin	Waist circumference	S6c r = 0.75	Dastgheib 2022	1	40	−0.40 (−7.21 to 6.41)	–	–
Cinnamon vs metformin	Waist circumference	S6d r = 0.9	Dastgheib 2022	1	40	−0.40 (−4.74 to 3.94)	–	–
Cinnamon vs metformin	Waist-to-hip ratio	S6a r = 0	Dastgheib 2022	1	40	−0.010 (−0.083 to 0.063)	–	–
Cinnamon vs metformin	Waist-to-hip ratio	S6b r = 0.25	Dastgheib 2022	1	40	−0.010 (−0.073 to 0.053)	–	–
Cinnamon vs metformin	Waist-to-hip ratio	S6c r = 0.75	Dastgheib 2022	1	40	−0.010 (−0.047 to 0.027)	–	–
Cinnamon vs metformin	Waist-to-hip ratio	S6d r = 0.9	Dastgheib 2022	1	40	−0.010 (−0.035 to 0.015)	–	–
Ginger vs placebo	Fasting glucose	S6a r = 0	Dastgheib 2022	1	43	6.40 (−7.65 to 20.45)	–	–
Ginger vs placebo	Fasting glucose	S6b r = 0.25	Dastgheib 2022	1	43	6.40 (−6.01 to 18.81)	–	–
Ginger vs placebo	Fasting glucose	S6c r = 0.75	Dastgheib 2022	1	43	6.40 (−1.82 to 14.62)	–	–
Ginger vs placebo	Fasting glucose	S6d r = 0.9	Dastgheib 2022	1	43	6.40 (−0.055 to 12.85)	–	–
Ginger vs placebo	Fasting insulin	S6a r = 0	Dastgheib 2022	1	43	−1.57 (−4.79 to 1.65)	–	–
Ginger vs placebo	Fasting insulin	S6b r = 0.25	Dastgheib 2022	1	43	−1.57 (−4.36 to 1.22)	–	–
Ginger vs placebo	Fasting insulin	S6c r = 0.75	Dastgheib 2022	1	43	−1.57 (−3.20 to 0.057)	–	–
Ginger vs placebo	Fasting insulin	S6d r = 0.9	Dastgheib 2022	1	43	−1.57 (−2.62 to −0.52)	–	–

Ginger vs placebo	HOMA-IR	S6a r = 0	Dastgheib 2022	1	43	−0.26 (−1.11 to 0.59)	–	–
Ginger vs placebo	HOMA-IR	S6b r = 0.25	Dastgheib 2022	1	43	−0.26 (−1.00 to 0.48)	–	–
Ginger vs placebo	HOMA-IR	S6c r = 0.75	Dastgheib 2022	1	43	−0.26 (−0.69 to 0.17)	–	–
Ginger vs placebo	HOMA-IR	S6d r = 0.9	Dastgheib 2022	1	43	−0.26 (−0.54 to 0.023)	–	–
Ginger vs placebo	Total cholesterol	S6a r = 0	Dastgheib 2022	1	43	7.20 (−25.29 to 39.69)	–	–
Ginger vs placebo	Total cholesterol	S6b r = 0.25	Dastgheib 2022	1	43	7.20 (−20.97 to 35.37)	–	–
Ginger vs placebo	Total cholesterol	S6c r = 0.75	Dastgheib 2022	1	43	7.20 (−9.18 to 23.58)	–	–
Ginger vs placebo	Total cholesterol	S6d r = 0.9	Dastgheib 2022	1	43	7.20 (−3.32 to 17.72)	–	–
Ginger vs placebo	LDL-C	S6a r = 0	Dastgheib 2022	1	43	7.95 (−12.77 to 28.67)	–	–
Ginger vs placebo	LDL-C	S6b r = 0.25	Dastgheib 2022	1	43	7.95 (−10.06 to 25.96)	–	–
Ginger vs placebo	LDL-C	S6c r = 0.75	Dastgheib 2022	1	43	7.95 (−2.74 to 18.64)	–	–
Ginger vs placebo	LDL-C	S6d r = 0.9	Dastgheib 2022	1	43	7.95 (0.78 to 15.12)	–	–
Ginger vs placebo	HDL-C	S6a r = 0	Dastgheib 2022	1	43	−2.05 (−6.80 to 2.70)	–	–
Ginger vs placebo	HDL-C	S6b r = 0.25	Dastgheib 2022	1	43	−2.05 (−6.23 to 2.13)	–	–
Ginger vs placebo	HDL-C	S6c r = 0.75	Dastgheib 2022	1	43	−2.05 (−4.73 to 0.63)	–	–
Ginger vs placebo	HDL-C	S6d r = 0.9	Dastgheib 2022	1	43	−2.05 (−4.08 to −0.023)	–	–
Ginger vs placebo	Triglycerides	S6a r = 0	Dastgheib 2022	1	43	−9.10 (−61.60 to 43.40)	–	–
Ginger vs placebo	Triglycerides	S6b r = 0.25	Dastgheib 2022	1	43	−9.10 (−56.34 to 38.14)	–	–
Ginger vs placebo	Triglycerides	S6c r = 0.75	Dastgheib 2022	1	43	−9.10 (−43.49 to 25.29)	–	–
Ginger vs placebo	Triglycerides	S6d r = 0.9	Dastgheib 2022	1	43	−9.10 (−38.56 to 20.36)	–	–
Ginger vs placebo	Total testosterone	S6a r = 0	Dastgheib 2022	1	43	0.050 (−0.16 to 0.26)	–	–
Ginger vs placebo	Total testosterone	S6b r = 0.25	Dastgheib 2022	1	43	0.050 (−0.13 to 0.23)	–	–
Ginger vs placebo	Total testosterone	S6c r = 0.75	Dastgheib 2022	1	43	0.050 (−0.056 to 0.16)	–	–
Ginger vs placebo	Total testosterone	S6d r = 0.9	Dastgheib 2022	1	43	0.050 (−0.020 to 0.12)	–	–
Ginger vs placebo	SHBG	S6a r = 0	Dastgheib 2022	1	43	−3.72 (−24.94 to 17.50)	–	–
Ginger vs placebo	SHBG	S6b r = 0.25	Dastgheib 2022	1	43	−3.72 (−22.21 to 14.77)	–	–
Ginger vs placebo	SHBG	S6c r = 0.75	Dastgheib 2022	1	43	−3.72 (−14.90 to 7.46)	–	–

Ginger vs placebo	SHBG	S6d r = 0.9	Dastgheib 2022	1	43	−3.72 (−11.46 to 4.02)	–	–
Ginger vs placebo	FAI	S6a r = 0	Dastgheib 2022	1	43	−0.010 (−1.02 to 1.00)	–	–
Ginger vs placebo	FAI	S6b r = 0.25	Dastgheib 2022	1	43	−0.010 (−0.89 to 0.87)	–	–
Ginger vs placebo	FAI	S6c r = 0.75	Dastgheib 2022	1	43	−0.010 (−0.52 to 0.50)	–	–
Ginger vs placebo	FAI	S6d r = 0.9	Dastgheib 2022	1	43	−0.010 (−0.33 to 0.31)	–	–
Ginger vs placebo	BMI	S6a r = 0	Dastgheib 2022	1	43	−0.24 (−4.24 to 3.76)	–	–
Ginger vs placebo	BMI	S6b r = 0.25	Dastgheib 2022	1	43	−0.24 (−3.71 to 3.23)	–	–
Ginger vs placebo	BMI	S6c r = 0.75	Dastgheib 2022	1	43	−0.24 (−2.27 to 1.79)	–	–
Ginger vs placebo	BMI	S6d r = 0.9	Dastgheib 2022	1	43	−0.24 (−1.56 to 1.08)	–	–
Ginger vs placebo	Body weight	S6a r = 0	Dastgheib 2022	1	43	−0.58 (−10.93 to 9.77)	–	–
Ginger vs placebo	Body weight	S6b r = 0.25	Dastgheib 2022	1	43	−0.58 (−9.55 to 8.39)	–	–
Ginger vs placebo	Body weight	S6c r = 0.75	Dastgheib 2022	1	43	−0.58 (−5.81 to 4.65)	–	–
Ginger vs placebo	Body weight	S6d r = 0.9	Dastgheib 2022	1	43	−0.58 (−3.96 to 2.80)	–	–
Ginger vs placebo	Waist circumference	S6a r = 0	Dastgheib 2022	1	43	0.65 (−10.70 to 12.00)	–	–
Ginger vs placebo	Waist circumference	S6b r = 0.25	Dastgheib 2022	1	43	0.65 (−9.18 to 10.48)	–	–
Ginger vs placebo	Waist circumference	S6c r = 0.75	Dastgheib 2022	1	43	0.65 (−5.06 to 6.36)	–	–
Ginger vs placebo	Waist circumference	S6d r = 0.9	Dastgheib 2022	1	43	0.65 (−3.01 to 4.31)	–	–
Ginger vs placebo	Waist-to-hip ratio	S6a r = 0	Dastgheib 2022	1	43	0.00 (−0.058 to 0.058)	–	–
Ginger vs placebo	Waist-to-hip ratio	S6b r = 0.25	Dastgheib 2022	1	43	0.00 (−0.050 to 0.050)	–	–
Ginger vs placebo	Waist-to-hip ratio	S6c r = 0.75	Dastgheib 2022	1	43	0.00 (−0.029 to 0.029)	–	–
Ginger vs placebo	Waist-to-hip ratio	S6d r = 0.9	Dastgheib 2022	1	43	0.00 (−0.019 to 0.019)	–	–
Ginger vs metformin	Fasting glucose	S6a r = 0	Dastgheib 2022	1	41	−2.05 (−15.93 to 11.83)	–	–
Ginger vs metformin	Fasting glucose	S6b r = 0.25	Dastgheib 2022	1	41	−2.05 (−14.21 to 10.11)	–	–
Ginger vs metformin	Fasting glucose	S6c r = 0.75	Dastgheib 2022	1	41	−2.05 (−9.68 to 5.58)	–	–
Ginger vs metformin	Fasting glucose	S6d r = 0.9	Dastgheib 2022	1	41	−2.05 (−7.64 to 3.54)	–	–
Ginger vs metformin	Fasting insulin	S6a r = 0	Dastgheib 2022	1	41	0.77 (−2.24 to 3.78)	–	–
Ginger vs metformin	Fasting insulin	S6b r = 0.25	Dastgheib 2022	1	41	0.77 (−1.85 to 3.39)	–	–

Ginger vs metformin	Fasting insulin	S6c r = 0.75	Dastgheib 2022	1	41	0.77 (−0.84 to 2.38)	–	–
Ginger vs metformin	Fasting insulin	S6d r = 0.9	Dastgheib 2022	1	41	0.77 (−0.37 to 1.91)	–	–
Ginger vs metformin	HOMA-IR	S6a r = 0	Dastgheib 2022	1	41	0.18 (−0.64 to 1.00)	–	–
Ginger vs metformin	HOMA-IR	S6b r = 0.25	Dastgheib 2022	1	41	0.18 (−0.53 to 0.89)	–	–
Ginger vs metformin	HOMA-IR	S6c r = 0.75	Dastgheib 2022	1	41	0.18 (−0.26 to 0.62)	–	–
Ginger vs metformin	HOMA-IR	S6d r = 0.9	Dastgheib 2022	1	41	0.18 (−0.13 to 0.49)	–	–
Ginger vs metformin	Total cholesterol	S6a r = 0	Dastgheib 2022	1	41	15.35 (−13.70 to 44.40)	–	–
Ginger vs metformin	Total cholesterol	S6b r = 0.25	Dastgheib 2022	1	41	15.35 (−9.86 to 40.56)	–	–
Ginger vs metformin	Total cholesterol	S6c r = 0.75	Dastgheib 2022	1	41	15.35 (0.56 to 30.14)	–	–
Ginger vs metformin	Total cholesterol	S6d r = 0.9	Dastgheib 2022	1	41	15.35 (5.66 to 25.04)	–	–
Ginger vs metformin	LDL-C	S6a r = 0	Dastgheib 2022	1	41	9.25 (−11.13 to 29.63)	–	–
Ginger vs metformin	LDL-C	S6b r = 0.25	Dastgheib 2022	1	41	9.25 (−8.47 to 26.97)	–	–
Ginger vs metformin	LDL-C	S6c r = 0.75	Dastgheib 2022	1	41	9.25 (−1.30 to 19.80)	–	–
Ginger vs metformin	LDL-C	S6d r = 0.9	Dastgheib 2022	1	41	9.25 (2.14 to 16.36)	–	–
Ginger vs metformin	HDL-C	S6a r = 0	Dastgheib 2022	1	41	−2.00 (−6.16 to 2.16)	–	–
Ginger vs metformin	HDL-C	S6b r = 0.25	Dastgheib 2022	1	41	−2.00 (−5.62 to 1.62)	–	–
Ginger vs metformin	HDL-C	S6c r = 0.75	Dastgheib 2022	1	41	−2.00 (−4.15 to 0.15)	–	–
Ginger vs metformin	HDL-C	S6d r = 0.9	Dastgheib 2022	1	41	−2.00 (−3.44 to −0.56)	–	–
Ginger vs metformin	Triglycerides	S6a r = 0	Dastgheib 2022	1	41	−27.25 (−83.77 to 29.27)	–	–
Ginger vs metformin	Triglycerides	S6b r = 0.25	Dastgheib 2022	1	41	−27.25 (−77.72 to 23.22)	–	–
Ginger vs metformin	Triglycerides	S6c r = 0.75	Dastgheib 2022	1	41	−27.25 (−62.66 to 8.16)	–	–
Ginger vs metformin	Triglycerides	S6d r = 0.9	Dastgheib 2022	1	41	−27.25 (−56.67 to 2.17)	–	–
Ginger vs metformin	Total testosterone	S6a r = 0	Dastgheib 2022	1	41	0.14 (−0.092 to 0.37)	–	–
Ginger vs metformin	Total testosterone	S6b r = 0.25	Dastgheib 2022	1	41	0.14 (−0.062 to 0.34)	–	–
Ginger vs metformin	Total testosterone	S6c r = 0.75	Dastgheib 2022	1	41	0.14 (0.021 to 0.26)	–	–
Ginger vs metformin	Total testosterone	S6d r = 0.9	Dastgheib 2022	1	41	0.14 (0.061 to 0.22)	–	–
Ginger vs metformin	SHBG	S6a r = 0	Dastgheib 2022	1	41	−13.08 (−34.18 to 8.02)	–	–

Ginger vs metformin	SHBG	S6b r = 0.25	Dastgheib 2022	1	41	−13.08 (−31.66 to 5.50)	–	–
Ginger vs metformin	SHBG	S6c r = 0.75	Dastgheib 2022	1	41	−13.08 (−25.16 to −1.00)	–	–
Ginger vs metformin	SHBG	S6d r = 0.9	Dastgheib 2022	1	41	−13.08 (−22.35 to −3.81)	–	–
Ginger vs metformin	FAI	S6a r = 0	Dastgheib 2022	1	41	0.52 (−0.45 to 1.49)	–	–
Ginger vs metformin	FAI	S6b r = 0.25	Dastgheib 2022	1	41	0.52 (−0.32 to 1.36)	–	–
Ginger vs metformin	FAI	S6c r = 0.75	Dastgheib 2022	1	41	0.52 (0.022 to 1.02)	–	–
Ginger vs metformin	FAI	S6d r = 0.9	Dastgheib 2022	1	41	0.52 (0.19 to 0.85)	–	–
Ginger vs metformin	BMI	S6a r = 0	Dastgheib 2022	1	41	0.48 (−3.45 to 4.41)	–	–
Ginger vs metformin	BMI	S6b r = 0.25	Dastgheib 2022	1	41	0.48 (−2.93 to 3.89)	–	–
Ginger vs metformin	BMI	S6c r = 0.75	Dastgheib 2022	1	41	0.48 (−1.51 to 2.47)	–	–
Ginger vs metformin	BMI	S6d r = 0.9	Dastgheib 2022	1	41	0.48 (−0.81 to 1.77)	–	–
Ginger vs metformin	Body weight	S6a r = 0	Dastgheib 2022	1	41	1.32 (−8.84 to 11.48)	–	–
Ginger vs metformin	Body weight	S6b r = 0.25	Dastgheib 2022	1	41	1.32 (−7.49 to 10.13)	–	–
Ginger vs metformin	Body weight	S6c r = 0.75	Dastgheib 2022	1	41	1.32 (−3.80 to 6.44)	–	–
Ginger vs metformin	Body weight	S6d r = 0.9	Dastgheib 2022	1	41	1.32 (−1.98 to 4.62)	–	–
Ginger vs metformin	Waist circumference	S6a r = 0	Dastgheib 2022	1	41	0.40 (−12.31 to 13.11)	–	–
Ginger vs metformin	Waist circumference	S6b r = 0.25	Dastgheib 2022	1	41	0.40 (−10.61 to 11.41)	–	–
Ginger vs metformin	Waist circumference	S6c r = 0.75	Dastgheib 2022	1	41	0.40 (−5.96 to 6.76)	–	–
Ginger vs metformin	Waist circumference	S6d r = 0.9	Dastgheib 2022	1	41	0.40 (−3.64 to 4.44)	–	–
Ginger vs metformin	Waist-to-hip ratio	S6a r = 0	Dastgheib 2022	1	41	0.00 (−0.062 to 0.062)	–	–
Ginger vs metformin	Waist-to-hip ratio	S6b r = 0.25	Dastgheib 2022	1	41	0.00 (−0.054 to 0.054)	–	–
Ginger vs metformin	Waist-to-hip ratio	S6c r = 0.75	Dastgheib 2022	1	41	0.00 (−0.032 to 0.032)	–	–
Ginger vs metformin	Waist-to-hip ratio	S6d r = 0.9	Dastgheib 2022	1	41	0.00 (−0.021 to 0.021)	–	–
Berberine vs metformin	Fasting glucose	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Berberine vs metformin	Fasting glucose	S6a r = 0	Mishra 2022	1	86	−1.00 (−10.13 to 8.13)	–	–
Berberine vs metformin	Fasting glucose	S6b r = 0.25	Mishra 2022	1	86	−1.00 (−8.92 to 6.92)	–	–

Berberine vs metformin	Fasting glucose	S6c r = 0.75	Mishra 2022	1	86	−1.00 (−5.61 to 3.61)	–	–
Berberine vs metformin	Fasting glucose	S6d r = 0.9	Mishra 2022	1	86	−1.00 (−3.96 to 1.96)	–	–
Berberine vs metformin	Fasting insulin	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Berberine vs metformin	Fasting insulin	S6a r = 0	Mishra 2022	1	86	0.64 (−0.71 to 1.99)	–	–
Berberine vs metformin	Fasting insulin	S6b r = 0.25	Mishra 2022	1	86	0.64 (−0.54 to 1.82)	–	–
Berberine vs metformin	Fasting insulin	S6c r = 0.75	Mishra 2022	1	86	0.64 (−0.065 to 1.35)	–	–
Berberine vs metformin	Fasting insulin	S6d r = 0.9	Mishra 2022	1	86	0.64 (0.16 to 1.12)	–	–
Berberine vs metformin	Total cholesterol	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Berberine vs metformin	Total cholesterol	S6a r = 0	Mishra 2022	1	86	22.04 (8.29 to 35.80)	–	–
Berberine vs metformin	Total cholesterol	S6b r = 0.25	Mishra 2022	1	86	22.04 (9.52 to 34.57)	–	–
Berberine vs metformin	Total cholesterol	S6c r = 0.75	Mishra 2022	1	86	22.04 (12.43 to 31.65)	–	–
Berberine vs metformin	Total cholesterol	S6d r = 0.9	Mishra 2022	1	86	22.04 (13.50 to 30.59)	–	–
Berberine vs metformin	LDL-C	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Berberine vs metformin	LDL-C	S6a r = 0	Mishra 2022	1	86	18.95 (1.36 to 36.54)	–	–
Berberine vs metformin	LDL-C	S6b r = 0.25	Mishra 2022	1	86	18.95 (3.67 to 34.23)	–	–
Berberine vs metformin	LDL-C	S6c r = 0.75	Mishra 2022	1	86	18.95 (9.93 to 27.96)	–	–
Berberine vs metformin	LDL-C	S6d r = 0.9	Mishra 2022	1	86	18.95 (12.98 to 24.92)	–	–
Berberine vs metformin	HDL-C	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Berberine vs metformin	HDL-C	S6a r = 0	Mishra 2022	1	86	−13.53 (−20.97 to −6.10)	–	–
Berberine vs metformin	HDL-C	S6b r = 0.25	Mishra 2022	1	86	−13.53 (−20.08 to −6.99)	–	–
Berberine vs metformin	HDL-C	S6c r = 0.75	Mishra 2022	1	86	−13.53 (−17.76 to −9.31)	–	–
Berberine vs metformin	HDL-C	S6d r = 0.9	Mishra 2022	1	86	−13.53 (−16.75 to −10.32)	–	–
Berberine vs metformin	Triglycerides	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Berberine vs metformin	Triglycerides	S6a r = 0	Mishra 2022	1	86	60.23 (27.84 to 92.62)	–	–
Berberine vs metformin	Triglycerides	S6b r = 0.25	Mishra 2022	1	86	60.23 (32.17 to 88.29)	–	–

Berberine vs metformin	Triglycerides	S6c r = 0.75	Mishra 2022	1	86	60.23 (43.97 to 76.49)	–	–
Berberine vs metformin	Triglycerides	S6d r = 0.9	Mishra 2022	1	86	60.23 (49.86 to 70.59)	–	–
Berberine vs metformin	FAI	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Berberine vs metformin	FAI	S6a r = 0	Mishra 2022	1	86	0.21 (−0.22 to 0.64)	–	–
Berberine vs metformin	FAI	S6b r = 0.25	Mishra 2022	1	86	0.21 (−0.17 to 0.59)	–	–
Berberine vs metformin	FAI	S6c r = 0.75	Mishra 2022	1	86	0.21 (−0.034 to 0.45)	–	–
Berberine vs metformin	FAI	S6d r = 0.9	Mishra 2022	1	86	0.21 (0.025 to 0.40)	–	–
Berberine vs metformin	BMI	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Berberine vs metformin	BMI	S6a r = 0	Mishra 2022	1	86	0.73 (−0.79 to 2.25)	–	–
Berberine vs metformin	BMI	S6b r = 0.25	Mishra 2022	1	86	0.73 (−0.59 to 2.05)	–	–
Berberine vs metformin	BMI	S6c r = 0.75	Mishra 2022	1	86	0.73 (−0.034 to 1.49)	–	–
Berberine vs metformin	BMI	S6d r = 0.9	Mishra 2022	1	86	0.73 (0.24 to 1.22)	–	–
Myo-inositol vs metformin	Fasting glucose	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Myo-inositol vs metformin	Fasting glucose	S6a r = 0	Mishra 2022	1	86	−3.88 (−12.48 to 4.72)	–	–
Myo-inositol vs metformin	Fasting glucose	S6b r = 0.25	Mishra 2022	1	86	−3.88 (−11.34 to 3.58)	–	–
Myo-inositol vs metformin	Fasting glucose	S6c r = 0.75	Mishra 2022	1	86	−3.88 (−8.25 to 0.49)	–	–
Myo-inositol vs metformin	Fasting glucose	S6d r = 0.9	Mishra 2022	1	86	−3.88 (−6.73 to −1.03)	–	–
Myo-inositol vs metformin	Fasting insulin	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Myo-inositol vs metformin	Fasting insulin	S6a r = 0	Mishra 2022	1	86	−5.48 (−6.54 to −4.42)	–	–
Myo-inositol vs metformin	Fasting insulin	S6b r = 0.25	Mishra 2022	1	86	−5.48 (−6.41 to −4.55)	–	–
Myo-inositol vs metformin	Fasting insulin	S6c r = 0.75	Mishra 2022	1	86	−5.48 (−6.07 to −4.89)	–	–
Myo-inositol vs metformin	Fasting insulin	S6d r = 0.9	Mishra 2022	1	86	−5.48 (−5.92 to −5.04)	–	–
Myo-inositol vs metformin	Total cholesterol	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Myo-inositol vs metformin	Total cholesterol	S6a r = 0	Mishra 2022	1	86	23.20 (7.73 to 38.67)	–	–
Myo-inositol vs metformin	Total cholesterol	S6b r = 0.25	Mishra 2022	1	86	23.20 (9.79 to 36.62)	–	–

Myo-inositol vs metformin	Total cholesterol	S6c r = 0.75	Mishra 2022	1	86	23.20 (15.36 to 31.04)	–	–
Myo-inositol vs metformin	Total cholesterol	S6d r = 0.9	Mishra 2022	1	86	23.20 (18.11 to 28.30)	–	–
Myo-inositol vs metformin	LDL-C	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Myo-inositol vs metformin	LDL-C	S6a r = 0	Mishra 2022	1	86	−23.98 (−40.52 to −7.43)	–	–
Myo-inositol vs metformin	LDL-C	S6b r = 0.25	Mishra 2022	1	86	−23.98 (−38.32 to −9.63)	–	–
Myo-inositol vs metformin	LDL-C	S6c r = 0.75	Mishra 2022	1	86	−23.98 (−32.35 to −15.60)	–	–
Myo-inositol vs metformin	LDL-C	S6d r = 0.9	Mishra 2022	1	86	−23.98 (−29.39 to −18.56)	–	–
Myo-inositol vs metformin	HDL-C	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Myo-inositol vs metformin	HDL-C	S6a r = 0	Mishra 2022	1	86	−13.53 (−23.26 to −3.81)	–	–
Myo-inositol vs metformin	HDL-C	S6b r = 0.25	Mishra 2022	1	86	−13.53 (−22.04 to −5.03)	–	–
Myo-inositol vs metformin	HDL-C	S6c r = 0.75	Mishra 2022	1	86	−13.53 (−18.79 to −8.28)	–	–
Myo-inositol vs metformin	HDL-C	S6d r = 0.9	Mishra 2022	1	86	−13.53 (−17.31 to −9.76)	–	–
Myo-inositol vs metformin	Triglycerides	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Myo-inositol vs metformin	Triglycerides	S6a r = 0	Mishra 2022	1	86	54.91 (22.80 to 87.03)	–	–
Myo-inositol vs metformin	Triglycerides	S6b r = 0.25	Mishra 2022	1	86	54.91 (27.09 to 82.74)	–	–
Myo-inositol vs metformin	Triglycerides	S6c r = 0.75	Mishra 2022	1	86	54.91 (38.77 to 71.06)	–	–
Myo-inositol vs metformin	Triglycerides	S6d r = 0.9	Mishra 2022	1	86	54.91 (44.60 to 65.23)	–	–
Myo-inositol vs metformin	FAI	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Myo-inositol vs metformin	FAI	S6a r = 0	Mishra 2022	1	86	0.34 (−0.051 to 0.73)	–	–
Myo-inositol vs metformin	FAI	S6b r = 0.25	Mishra 2022	1	86	0.34 (−0.005 to 0.68)	–	–
Myo-inositol vs metformin	FAI	S6c r = 0.75	Mishra 2022	1	86	0.34 (0.12 to 0.56)	–	–
Myo-inositol vs metformin	FAI	S6d r = 0.9	Mishra 2022	1	86	0.34 (0.17 to 0.51)	–	–
Myo-inositol vs metformin	BMI	S4 without reports with internal data inconsistencies	Nehra 2017	1	60	−0.010 (−1.63 to 1.61)	–	–
Myo-inositol vs metformin	BMI	S6a r = 0	Mishra 2022, Nehra 2017	2	146	0.88 (−6.38 to 8.14)	0.000	0
Myo-inositol vs metformin	BMI	S6b r = 0.25	Mishra 2022, Nehra 2017	2	146	0.88 (−5.49 to 7.25)	0.010	1

Myo-inositol vs metformin	BMI	S6c r = 0.75	Mishra 2022, Nehra 2017	2	146	0.68 (−6.64 to 8.00)	0.457	67
Myo-inositol vs metformin	BMI	S6d r = 0.9	Mishra 2022, Nehra 2017	2	146	0.62 (−6.80 to 8.03)	0.591	86
Myo-inositol vs metformin	Waist circumference	S6a r = 0	Nehra 2017	1	60	0.48 (−5.95 to 6.91)	–	–
Myo-inositol vs metformin	Waist circumference	S6b r = 0.25	Nehra 2017	1	60	0.48 (−5.09 to 6.05)	–	–
Myo-inositol vs metformin	Waist circumference	S6c r = 0.75	Nehra 2017	1	60	0.48 (−2.75 to 3.71)	–	–
Myo-inositol vs metformin	Waist circumference	S6d r = 0.9	Nehra 2017	1	60	0.48 (−1.58 to 2.54)	–	–
Myo-inositol vs metformin	Waist-to-hip ratio	S6a r = 0	Nehra 2017	1	60	−0.010 (−0.045 to 0.025)	–	–
Myo-inositol vs metformin	Waist-to-hip ratio	S6b r = 0.25	Nehra 2017	1	60	−0.010 (−0.040 to 0.020)	–	–
Myo-inositol vs metformin	Waist-to-hip ratio	S6c r = 0.75	Nehra 2017	1	60	−0.010 (−0.028 to 0.008)	–	–
Myo-inositol vs metformin	Waist-to-hip ratio	S6d r = 0.9	Nehra 2017	1	60	−0.010 (−0.021 to 0.001)	–	–
Myo-inositol + folic acid vs metformin	Fasting glucose	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Myo-inositol + folic acid vs metformin	Fasting insulin	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Myo-inositol + folic acid vs metformin	HOMA-IR	S2 without all reports co-authored by the shared author	Fruzzetti 2017	1	46	−0.20 (−0.42 to 0.022)	–	–
Myo-inositol + folic acid vs metformin	HOMA-IR	S6a r = 0	Fruzzetti 2017, Shokrpour 2019	2	99	−0.32 (−1.37 to 0.73)	0.000	0
Myo-inositol + folic acid vs metformin	HOMA-IR	S6b r = 0.25	Fruzzetti 2017, Shokrpour 2019	2	99	−0.31 (−1.32 to 0.70)	0.000	0
Myo-inositol + folic acid vs metformin	HOMA-IR	S6c r = 0.75	Fruzzetti 2017, Shokrpour 2019	2	99	−0.27 (−1.28 to 0.74)	0.005	37
Myo-inositol + folic acid vs metformin	HOMA-IR	S6d r = 0.9	Fruzzetti 2017, Shokrpour 2019	2	99	−0.26 (−1.24 to 0.72)	0.007	52
Myo-inositol + folic acid vs metformin	QUICKI	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Myo-inositol + folic acid vs metformin	Total cholesterol	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Myo-inositol + folic acid vs metformin	LDL-C	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Myo-inositol + folic acid vs metformin	HDL-C	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Myo-inositol + folic acid vs metformin	Triglycerides	S2 without all reports co-authored by the shared author	–	0	–	–	–	–

Myo-inositol + folic acid vs metformin	BMI	S2 without all reports co-authored by the shared author	Fruzzetti 2017	1	46	−0.40 (−3.26 to 2.46)	–	–
Myo-inositol + folic acid vs metformin	BMI	S6a r = 0	Fruzzetti 2017, Shokrpour 2019	2	99	−0.10 (−1.68 to 1.48)	0.000	0
Myo-inositol + folic acid vs metformin	BMI	S6b r = 0.25	Fruzzetti 2017, Shokrpour 2019	2	99	−0.10 (−1.68 to 1.48)	0.000	0
Myo-inositol + folic acid vs metformin	BMI	S6c r = 0.75	Fruzzetti 2017, Shokrpour 2019	2	99	−0.10 (−1.68 to 1.47)	0.000	0
Myo-inositol + folic acid vs metformin	BMI	S6d r = 0.9	Fruzzetti 2017, Shokrpour 2019	2	99	−0.11 (−1.67 to 1.45)	0.000	0
D-chiro-inositol vs placebo	Fasting glucose	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	−1.93 (−84.20 to 80.34)	7.909	9
D-chiro-inositol vs placebo	Fasting glucose	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	−2.06 (−84.46 to 80.34)	26.227	31
D-chiro-inositol vs placebo	Fasting glucose	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	−2.32 (−84.88 to 80.24)	62.864	74
D-chiro-inositol vs placebo	Fasting glucose	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	−2.40 (−84.98 to 80.18)	73.855	87
D-chiro-inositol vs placebo	Fasting insulin	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	−14.39 (−151.30 to 122.52)	0.000	0
D-chiro-inositol vs placebo	Fasting insulin	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	−14.40 (−134.46 to 105.65)	0.000	0
D-chiro-inositol vs placebo	Fasting insulin	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	−14.48 (−90.23 to 61.27)	0.000	0
D-chiro-inositol vs placebo	Fasting insulin	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	−14.60 (−70.43 to 41.22)	0.000	0
D-chiro-inositol vs placebo	Total cholesterol	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	−33.37 (−223.90 to 157.17)	88.000	20
D-chiro-inositol vs placebo	Total cholesterol	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	−33.29 (−223.85 to 157.27)	176.864	39
D-chiro-inositol vs placebo	Total cholesterol	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	−33.13 (−223.72 to 157.46)	354.591	79
D-chiro-inositol vs placebo	Total cholesterol	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	−33.08 (−223.67 to 157.51)	407.909	91
D-chiro-inositol vs placebo	LDL-C	S6a r = 0	Nestler 1999	1	44	1.00 (−23.00 to 25.00)	–	–
D-chiro-inositol vs placebo	LDL-C	S6b r = 0.25	Nestler 1999	1	44	1.00 (−20.71 to 22.71)	–	–
D-chiro-inositol vs placebo	LDL-C	S6c r = 0.75	Nestler 1999	1	44	1.00 (−15.20 to 17.20)	–	–
D-chiro-inositol vs placebo	LDL-C	S6d r = 0.9	Nestler 1999	1	44	1.00 (−13.14 to 15.14)	–	–
D-chiro-inositol vs placebo	HDL-C	S6a r = 0	Nestler 1999	1	44	0.00 (−7.59 to 7.59)	–	–
D-chiro-inositol vs placebo	HDL-C	S6b r = 0.25	Nestler 1999	1	44	0.00 (−6.61 to 6.61)	–	–
D-chiro-inositol vs placebo	HDL-C	S6c r = 0.75	Nestler 1999	1	44	0.00 (−3.96 to 3.96)	–	–
D-chiro-inositol vs placebo	HDL-C	S6d r = 0.9	Nestler 1999	1	44	0.00 (−2.71 to 2.71)	–	–

D-chiro-inositol vs placebo	Triglycerides	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	−73.38 (−377.54 to 230.78)	0.000	0
D-chiro-inositol vs placebo	Triglycerides	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	−73.41 (−338.01 to 191.18)	0.000	0
D-chiro-inositol vs placebo	Triglycerides	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	−73.66 (−231.69 to 84.37)	0.000	0
D-chiro-inositol vs placebo	Triglycerides	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	−74.14 (−180.82 to 32.54)	0.000	0
D-chiro-inositol vs placebo	Total testosterone	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	−0.42 (−2.26 to 1.42)	0.009	22
D-chiro-inositol vs placebo	Total testosterone	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	−0.42 (−2.26 to 1.42)	0.017	40
D-chiro-inositol vs placebo	Total testosterone	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	−0.42 (−2.25 to 1.42)	0.031	74
D-chiro-inositol vs placebo	Total testosterone	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	−0.42 (−2.25 to 1.42)	0.035	84
D-chiro-inositol vs placebo	SHBG	S6a r = 0	Iuorno 2002	1	20	38.00 (−45.36 to 121.36)	–	–
D-chiro-inositol vs placebo	SHBG	S6b r = 0.25	Iuorno 2002	1	20	38.00 (−35.31 to 111.31)	–	–
D-chiro-inositol vs placebo	SHBG	S6c r = 0.75	Iuorno 2002	1	20	38.00 (−9.16 to 85.16)	–	–
D-chiro-inositol vs placebo	SHBG	S6d r = 0.9	Iuorno 2002	1	20	38.00 (2.23 to 73.77)	–	–
D-chiro-inositol vs placebo	DHEAS	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	−1.68 (−8.99 to 5.62)	0.000	0
D-chiro-inositol vs placebo	DHEAS	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	−1.69 (−8.18 to 4.80)	0.000	0
D-chiro-inositol vs placebo	DHEAS	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	−1.65 (−7.53 to 4.22)	0.181	42
D-chiro-inositol vs placebo	DHEAS	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	−1.64 (−7.53 to 4.25)	0.266	62
D-chiro-inositol vs placebo	BMI	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	0.35 (−5.56 to 6.27)	0.000	0
D-chiro-inositol vs placebo	BMI	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	0.35 (−4.86 to 5.57)	0.000	0
D-chiro-inositol vs placebo	BMI	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	0.34 (−3.04 to 3.72)	0.000	0
D-chiro-inositol vs placebo	BMI	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	0.32 (−2.17 to 2.81)	0.000	0
D-chiro-inositol vs placebo	Waist-to-hip ratio	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	−0.030 (−0.32 to 0.26)	0.000	0
D-chiro-inositol vs placebo	Waist-to-hip ratio	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	−0.030 (−0.28 to 0.22)	0.000	0
D-chiro-inositol vs placebo	Waist-to-hip ratio	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	−0.030 (−0.18 to 0.12)	0.000	0
D-chiro-inositol vs placebo	Waist-to-hip ratio	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	−0.030 (−0.13 to 0.072)	0.000	0
D-chiro-inositol vs placebo	Systolic BP	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	−3.88 (−35.28 to 27.52)	0.614	5
D-chiro-inositol vs placebo	Systolic BP	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	−3.84 (−35.31 to 27.63)	3.307	26
D-chiro-inositol vs placebo	Systolic BP	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	−3.76 (−35.35 to 27.83)	8.693	70

D-chiro-inositol vs placebo	Systolic BP	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	−3.74 (−35.36 to 27.88)	10.309	82
D-chiro-inositol vs placebo	Diastolic BP	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	−6.34 (−34.97 to 22.29)	0.000	0
D-chiro-inositol vs placebo	Diastolic BP	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	−6.28 (−31.33 to 18.77)	0.000	0
D-chiro-inositol vs placebo	Diastolic BP	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	−6.13 (−21.21 to 8.96)	0.000	0
D-chiro-inositol vs placebo	Diastolic BP	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	−6.06 (−16.12 to 4.00)	0.000	0
D-chiro-inositol vs placebo	Androstenedione	S6a r = 0	Iuorno 2002, Nestler 1999	2	64	−0.52 (−4.49 to 3.45)	0.072	28
D-chiro-inositol vs placebo	Androstenedione	S6b r = 0.25	Iuorno 2002, Nestler 1999	2	64	−0.56 (−4.76 to 3.65)	0.113	44
D-chiro-inositol vs placebo	Androstenedione	S6c r = 0.75	Iuorno 2002, Nestler 1999	2	64	−0.63 (−5.13 to 3.86)	0.195	75
D-chiro-inositol vs placebo	Androstenedione	S6d r = 0.9	Iuorno 2002, Nestler 1999	2	64	−0.66 (−5.19 to 3.88)	0.220	85
Curcumin vs placebo	Fasting glucose	S2 without all reports co-authored by the shared author	Ghanbarzadeh-Ghashti 2023, Sohaei 2019	2	105	−4.10 (−31.80 to 23.59)	1.495	16
Curcumin vs placebo	Fasting insulin	S2 without all reports co-authored by the shared author	Ghanbarzadeh-Ghashti 2023, Sohaei 2019	2	105	−2.66 (−19.80 to 14.49)	0.000	0
Curcumin vs placebo	Fasting insulin	S6a r = 0	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−1.29 (−3.30 to 0.72)	0.000	0
Curcumin vs placebo	Fasting insulin	S6b r = 0.25	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−1.30 (−3.31 to 0.70)	0.000	0
Curcumin vs placebo	Fasting insulin	S6c r = 0.75	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−1.65 (−4.53 to 1.22)	0.389	4
Curcumin vs placebo	Fasting insulin	S6d r = 0.9	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−2.03 (−5.50 to 1.44)	1.002	49
Curcumin vs placebo	HOMA-IR	S2 without all reports co-authored by the shared author	Ghanbarzadeh-Ghashti 2023, Sohaei 2019	2	105	−0.81 (−5.32 to 3.70)	0.000	0
Curcumin vs placebo	HOMA-IR	S6a r = 0	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−0.30 (−0.77 to 0.18)	0.000	0
Curcumin vs placebo	HOMA-IR	S6b r = 0.25	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−0.35 (−1.06 to 0.36)	0.020	0
Curcumin vs placebo	HOMA-IR	S6c r = 0.75	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−0.52 (−1.61 to 0.56)	0.103	50
Curcumin vs placebo	HOMA-IR	S6d r = 0.9	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−0.59 (−1.74 to 0.56)	0.139	72
Curcumin vs placebo	QUICKI	S2 without all reports co-authored by the shared author	Sohaei 2019	1	51	0.010 (0.005 to 0.015)	–	–
Curcumin vs placebo	Total cholesterol	S2 without all reports co-authored by the shared author	Ghanbarzadeh-Ghashti 2023, Sohaei 2019	2	105	−4.96 (−82.95 to 73.02)	0.000	0

Curcumin vs placebo	Total cholesterol	S6a r = 0	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−11.96 (−30.83 to 6.90)	10.808	0
Curcumin vs placebo	Total cholesterol	S6b r = 0.25	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−11.73 (−30.44 to 6.98)	11.261	0
Curcumin vs placebo	Total cholesterol	S6c r = 0.75	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−10.28 (−28.81 to 8.26)	18.043	24
Curcumin vs placebo	Total cholesterol	S6d r = 0.9	Jamilian 2020, Ghanbarzadeh-Ghashti 2023, Sohaei 2019	3	155	−9.19 (−27.44 to 9.06)	25.039	45
Curcumin vs placebo	LDL-C	S2 without all reports co-authored by the shared author	Ghanbarzadeh-Ghashti 2023, Sohaei 2019	2	105	−4.31 (−129.86 to 121.25)	143.710	73
Curcumin vs placebo	HDL-C	S2 without all reports co-authored by the shared author	Sohaei 2019	1	51	0.79 (−3.19 to 4.77)	–	–
Curcumin vs placebo	Triglycerides	S2 without all reports co-authored by the shared author	Ghanbarzadeh-Ghashti 2023, Sohaei 2019	2	105	8.17 (−234.75 to 251.09)	554.450	74
Curcumin vs placebo	VLDL-C	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Curcumin vs placebo	BMI	S2 without all reports co-authored by the shared author	Sohaei 2019	1	51	0.100 (−2.24 to 2.44)	–	–
Curcumin vs placebo	BMI	S6a r = 0	Jamilian 2020, Sohaei 2019	2	101	−0.20 (−1.48 to 1.08)	0.000	0
Curcumin vs placebo	BMI	S6b r = 0.25	Jamilian 2020, Sohaei 2019	2	101	−0.20 (−1.47 to 1.08)	0.000	0
Curcumin vs placebo	BMI	S6c r = 0.75	Jamilian 2020, Sohaei 2019	2	101	−0.20 (−1.47 to 1.07)	0.000	0
Curcumin vs placebo	BMI	S6d r = 0.9	Jamilian 2020, Sohaei 2019	2	101	−0.19 (−1.45 to 1.07)	0.000	0
Curcumin vs placebo	Body weight	S2 without all reports co-authored by the shared author	Sohaei 2019	1	51	−0.050 (−6.40 to 6.30)	–	–
Curcumin vs placebo	Body weight	S6a r = 0	Jamilian 2020, Sohaei 2019	2	101	−0.60 (−3.66 to 2.47)	0.000	0
Curcumin vs placebo	Body weight	S6b r = 0.25	Jamilian 2020, Sohaei 2019	2	101	−0.60 (−3.66 to 2.47)	0.000	0
Curcumin vs placebo	Body weight	S6c r = 0.75	Jamilian 2020, Sohaei 2019	2	101	−0.59 (−3.65 to 2.46)	0.000	0
Curcumin vs placebo	Body weight	S6d r = 0.9	Jamilian 2020, Sohaei 2019	2	101	−0.59 (−3.61 to 2.44)	0.000	0
Omega-3 vs placebo/control	Fasting glucose	S4 without reports with internal data inconsistencies	Rafraf/Mohammadi 2012	1	61	−10.50 (−15.78 to −5.22)	–	–
Omega-3 vs placebo/control	Fasting glucose	S6a r = 0	Rafraf/Mohammadi 2012, Khani 2017	2	148	−6.51 (−50.10 to 37.08)	13.407	56
Omega-3 vs placebo/control	Fasting glucose	S6b r = 0.25	Rafraf/Mohammadi 2012, Khani 2017	2	148	−6.64 (−50.44 to 37.17)	16.044	67
Omega-3 vs placebo/control	Fasting glucose	S6c r = 0.75	Rafraf/Mohammadi 2012, Khani 2017	2	148	−6.89 (−50.94 to 37.17)	21.320	89
Omega-3 vs placebo/control	Fasting glucose	S6d r = 0.9	Rafraf/Mohammadi 2012, Khani 2017	2	148	−6.96 (−51.04 to 37.12)	22.902	95

Omega-3 vs placebo/control	Fasting glucose	S7 Khani 2017 lipid SDs treated as SEs	Rafraf/Mohammadi 2012, Khani 2017	2	148	−10.19 (−43.66 to 23.28)	0.000	0
Omega-3 vs placebo/control	Fasting insulin	S4 without reports with internal data inconsistencies	Rafraf/Mohammadi 2012	1	61	−1.45 (−3.04 to 0.14)	–	–
Omega-3 vs placebo/control	Fasting insulin	S6a r = 0	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	−2.08 (−10.53 to 6.38)	0.000	0
Omega-3 vs placebo/control	Fasting insulin	S6b r = 0.25	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	−2.08 (−9.41 to 5.25)	0.000	0
Omega-3 vs placebo/control	Fasting insulin	S6c r = 0.75	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	−2.01 (−7.95 to 3.94)	0.200	44
Omega-3 vs placebo/control	Fasting insulin	S6d r = 0.9	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	−1.96 (−7.98 to 4.06)	0.348	77
Omega-3 vs placebo/control	HOMA-IR	S4 without reports with internal data inconsistencies	Rafraf/Mohammadi 2012	1	61	−0.72 (−1.26 to −0.18)	–	–
Omega-3 vs placebo/control	HOMA-IR	S6a r = 0	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	−0.45 (−2.41 to 1.51)	0.000	0
Omega-3 vs placebo/control	HOMA-IR	S6b r = 0.25	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	−0.45 (−2.15 to 1.25)	0.000	0
Omega-3 vs placebo/control	HOMA-IR	S6c r = 0.75	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	−0.51 (−2.44 to 1.42)	0.028	54
Omega-3 vs placebo/control	HOMA-IR	S6d r = 0.9	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	−0.54 (−2.55 to 1.48)	0.041	80
Omega-3 vs placebo/control	Total cholesterol	S4 without reports with internal data inconsistencies	Rafraf/Mohammadi 2012	1	61	−14.80 (−29.91 to 0.31)	–	–
Omega-3 vs placebo/control	Total cholesterol	S6a r = 0	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−14.63 (−33.68 to 4.43)	35.690	68
Omega-3 vs placebo/control	Total cholesterol	S6b r = 0.25	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−14.78 (−33.30 to 3.73)	36.326	76
Omega-3 vs placebo/control	Total cholesterol	S6c r = 0.75	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−15.09 (−31.60 to 1.41)	35.439	92
Omega-3 vs placebo/control	Total cholesterol	S6d r = 0.9	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−15.18 (−30.50 to 0.15)	33.921	97
Omega-3 vs placebo/control	Total cholesterol	S7 Khani 2017 lipid SDs treated as SEs	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−18.59 (−32.63 to −4.54)	6.409	0
Omega-3 vs placebo/control	LDL-C	S4 without reports with internal data inconsistencies	Rafraf/Mohammadi 2012	1	61	−15.65 (−30.50 to −0.80)	–	–
Omega-3 vs placebo/control	LDL-C	S6a r = 0	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−15.98 (−38.48 to 6.53)	61.393	93
Omega-3 vs placebo/control	LDL-C	S6b r = 0.25	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−16.03 (−37.82 to 5.76)	59.692	94
Omega-3 vs placebo/control	LDL-C	S6c r = 0.75	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−16.12 (−35.64 to 3.39)	53.834	98
Omega-3 vs placebo/control	LDL-C	S6d r = 0.9	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−16.14 (−34.48 to 2.20)	50.798	99

Omega-3 vs placebo/control	LDL-C	S7 Khani 2017 lipid SDs treated as SEs	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−16.33 (−37.10 to 4.45)	54.463	91
Omega-3 vs placebo/control	HDL-C	S4 without reports with internal data inconsistencies	Rafraf/Mohammadi 2012	1	61	2.26 (−0.77 to 5.29)	–	–
Omega-3 vs placebo/control	HDL-C	S6a r = 0	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	4.33 (−1.56 to 10.21)	4.044	80
Omega-3 vs placebo/control	HDL-C	S6b r = 0.25	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	4.23 (−1.56 to 10.03)	4.183	85
Omega-3 vs placebo/control	HDL-C	S6c r = 0.75	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	4.01 (−1.54 to 9.56)	4.491	95
Omega-3 vs placebo/control	HDL-C	S6d r = 0.9	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	3.93 (−1.53 to 9.39)	4.602	98
Omega-3 vs placebo/control	HDL-C	S7 Khani 2017 lipid SDs treated as SEs	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	3.47 (−0.95 to 7.88)	0.729	40
Omega-3 vs placebo/control	Triglycerides	S4 without reports with internal data inconsistencies	Rafraf/Mohammadi 2012	1	61	−2.34 (−16.50 to 11.82)	–	–
Omega-3 vs placebo/control	Triglycerides	S6a r = 0	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−11.45 (−28.45 to 5.55)	27.282	61
Omega-3 vs placebo/control	Triglycerides	S6b r = 0.25	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−11.44 (−29.37 to 6.48)	32.514	70
Omega-3 vs placebo/control	Triglycerides	S6c r = 0.75	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−10.77 (−30.71 to 9.17)	52.660	90
Omega-3 vs placebo/control	Triglycerides	S6d r = 0.9	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−10.38 (−30.81 to 10.05)	62.051	96
Omega-3 vs placebo/control	Triglycerides	S7 Khani 2017 lipid SDs treated as SEs	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−11.50 (−31.65 to 8.64)	43.598	69
Omega-3 vs placebo/control	MDA	S6a r = 0	Rafraf/Mohammadi 2012	1	61	−0.67 (−1.33 to −0.009)	–	–
Omega-3 vs placebo/control	MDA	S6b r = 0.25	Rafraf/Mohammadi 2012	1	61	−0.67 (−1.24 to −0.098)	–	–
Omega-3 vs placebo/control	MDA	S6c r = 0.75	Rafraf/Mohammadi 2012	1	61	−0.67 (−1.00 to −0.34)	–	–
Omega-3 vs placebo/control	MDA	S6d r = 0.9	Rafraf/Mohammadi 2012	1	61	−0.67 (−0.88 to −0.46)	–	–
Omega-3 vs placebo/control	BMI	S4 without reports with internal data inconsistencies	Rafraf/Mohammadi 2012	1	61	−0.15 (−1.71 to 1.41)	–	–
Omega-3 vs placebo/control	BMI	S6a r = 0	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−0.89 (−2.91 to 1.13)	0.000	0
Omega-3 vs placebo/control	BMI	S6b r = 0.25	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−0.89 (−2.64 to 0.86)	0.000	0
Omega-3 vs placebo/control	BMI	S6c r = 0.75	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−0.89 (−2.30 to 0.53)	0.061	37

Omega-3 vs placebo/control	BMI	S6d r = 0.9	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−0.87 (−2.53 to 0.79)	0.329	75
Omega-3 vs placebo/control	BMI	S7 Khani 2017 lipid SDs treated as SEs	Rafraf/Mohammadi 2012, Khani 2017, Mejia-Montilla 2018	3	343	−0.74 (−2.32 to 0.84)	0.000	0
Omega-3 vs placebo/control	Body weight	S6a r = 0	Rafraf/Mohammadi 2012	1	61	−0.39 (−7.06 to 6.28)	–	–
Omega-3 vs placebo/control	Body weight	S6b r = 0.25	Rafraf/Mohammadi 2012	1	61	−0.39 (−6.17 to 5.39)	–	–
Omega-3 vs placebo/control	Body weight	S6c r = 0.75	Rafraf/Mohammadi 2012	1	61	−0.39 (−3.73 to 2.95)	–	–
Omega-3 vs placebo/control	Body weight	S6d r = 0.9	Rafraf/Mohammadi 2012	1	61	−0.39 (−2.50 to 1.72)	–	–
Omega-3 vs placebo/control	Waist circumference	S4 without reports with internal data inconsistencies	Rafraf/Mohammadi 2012	1	61	−0.21 (−3.35 to 2.93)	–	–
Omega-3 vs placebo/control	Waist circumference	S6a r = 0	Rafraf/Mohammadi 2012, Khani 2017	2	148	−1.98 (−11.92 to 7.96)	0.000	0
Omega-3 vs placebo/control	Waist circumference	S6b r = 0.25	Rafraf/Mohammadi 2012, Khani 2017	2	148	−1.98 (−10.59 to 6.63)	0.000	0
Omega-3 vs placebo/control	Waist circumference	S6c r = 0.75	Rafraf/Mohammadi 2012, Khani 2017	2	148	−1.49 (−13.77 to 10.79)	1.293	64
Omega-3 vs placebo/control	Waist circumference	S6d r = 0.9	Rafraf/Mohammadi 2012, Khani 2017	2	148	−1.33 (−14.02 to 11.37)	1.729	86
Omega-3 vs placebo/control	Waist circumference	S7 Khani 2017 lipid SDs treated as SEs	Rafraf/Mohammadi 2012, Khani 2017	2	148	−0.50 (−19.30 to 18.30)	0.000	0
Omega-3 vs placebo/control	Waist-to-hip ratio	S4 without reports with internal data inconsistencies	Rafraf/Mohammadi 2012	1	61	0.010 (−0.007 to 0.027)	–	–
Omega-3 vs placebo/control	Waist-to-hip ratio	S6a r = 0	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	0.015 (−0.094 to 0.12)	0.000	0
Omega-3 vs placebo/control	Waist-to-hip ratio	S6b r = 0.25	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	0.015 (−0.079 to 0.11)	0.000	0
Omega-3 vs placebo/control	Waist-to-hip ratio	S6c r = 0.75	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	0.015 (−0.049 to 0.078)	0.000	23
Omega-3 vs placebo/control	Waist-to-hip ratio	S6d r = 0.9	Rafraf/Mohammadi 2012, Mejia-Montilla 2018	2	256	0.015 (−0.049 to 0.079)	0.000	66
Omega-3 + vitamin E vs placebo	Fasting glucose	S1 concern-affected reports re-included	Ebrahimi 2017	1	68	−2.50 (−5.74 to 0.74)	–	–
Omega-3 + vitamin E vs placebo	Fasting insulin	S1 concern-affected reports re-included	Jamilian 2018, Ebrahimi 2017	2	108	−3.57 (−15.95 to 8.81)	0.000	0
Omega-3 + vitamin E vs placebo	Fasting insulin	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Omega-3 + vitamin E vs placebo	HOMA-IR	S1 concern-affected reports re-included	Jamilian 2018, Ebrahimi 2017	2	108	−0.80 (−3.62 to 2.02)	0.000	0
Omega-3 + vitamin E vs placebo	HOMA-IR	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Omega-3 + vitamin E vs placebo	HOMA-B	S1 concern-affected reports re-included	Ebrahimi 2017	1	68	−14.80 (−24.34 to −5.26)	–	–
Omega-3 + vitamin E vs placebo	QUICKI	S1 concern-affected reports re-included	Ebrahimi 2017	1	68	0.016 (0.001 to 0.031)	–	–
Omega-3 + vitamin E vs placebo	Total testosterone	S1 concern-affected reports re-included	Ebrahimi 2017	1	68	−0.40 (−0.69 to −0.11)	–	–

Omega-3 + vitamin E vs placebo	SHBG	S1 concern-affected reports re-included	Ebrahimi 2017	1	68	0.80 (−5.91 to 7.51)	–	–
Omega-3 + vitamin E vs placebo	FAI	S1 concern-affected reports re-included	Ebrahimi 2017	1	68	−0.010 (−0.075 to 0.055)	–	–
Omega-3 + vitamin E vs placebo	DHEAS	S1 concern-affected reports re-included	Ebrahimi 2017	1	68	−0.100 (−0.90 to 0.70)	–	–
Omega-3 + vitamin E vs placebo	BMI	S1 concern-affected reports re-included	Jamilian 2018, Ebrahimi 2017	2	108	−0.032 (−1.18 to 1.12)	0.000	0
Omega-3 + vitamin E vs placebo	BMI	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Omega-3 + vitamin E vs placebo	Waist circumference	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	Fasting glucose	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	Fasting glucose	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	Fasting insulin	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	Fasting insulin	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	HOMA-IR	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	HOMA-IR	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	HOMA-B	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	HOMA-B	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	QUICKI	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	QUICKI	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	Total cholesterol	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	Total cholesterol	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	LDL-C	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	LDL-C	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	LDL-C	S10 quasi-randomized trials re-included	Khani 2011, Jamilian 2016	2	207	−1.67 (−108.63 to 105.28)	129.569	91

Soy isoflavones vs placebo	HDL-C	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	HDL-C	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	HDL-C	S10 quasi-randomized trials re-included	Khani 2011, Jamilian 2016	2	207	0.29 (−8.66 to 9.24)	0.000	0
Soy isoflavones vs placebo	Triglycerides	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	Triglycerides	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	Triglycerides	S10 quasi-randomized trials re-included	Khani 2011, Jamilian 2016	2	207	−16.72 (−65.21 to 31.78)	0.000	0
Soy isoflavones vs placebo	Total testosterone	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	Total testosterone	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	Total testosterone	S10 quasi-randomized trials re-included	Khani 2011, Jamilian 2016	2	207	−0.16 (−1.80 to 1.49)	0.030	88
Soy isoflavones vs placebo	SHBG	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	SHBG	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	FAI	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	FAI	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	DHEAS	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	DHEAS	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	DHEAS	S10 quasi-randomized trials re-included	Khani 2011, Jamilian 2016	2	207	−0.21 (−2.18 to 1.76)	0.000	0
Soy isoflavones vs placebo	MDA	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	MDA	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	hs-CRP	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	hs-CRP	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	BMI	S2 without all reports co-authored by the shared author	–	0	–	–	–	–

Soy isoflavones vs placebo	BMI	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Soy isoflavones vs placebo	Waist circumference	S2 without all reports co-authored by the shared author	–	0	–	–	–	–
Soy isoflavones vs placebo	Waist circumference	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Pomegranate juice vs control	Fasting glucose	S4 without reports with internal data inconsistencies	Abedini 2021	1	42	2.15 (−3.07 to 7.37)	–	–
Pomegranate juice vs control	Fasting glucose	S6a r = 0	Esmaeilinezhad 2019, Abedini 2021	2	85	1.48 (−33.80 to 36.76)	0.000	0
Pomegranate juice vs control	Fasting glucose	S6b r = 0.25	Esmaeilinezhad 2019, Abedini 2021	2	85	1.47 (−29.29 to 32.24)	0.000	0
Pomegranate juice vs control	Fasting glucose	S6c r = 0.75	Esmaeilinezhad 2019, Abedini 2021	2	85	1.43 (−17.23 to 20.08)	0.000	0
Pomegranate juice vs control	Fasting glucose	S6d r = 0.9	Esmaeilinezhad 2019, Abedini 2021	2	85	1.34 (−11.52 to 14.20)	0.000	0
Pomegranate juice vs control	Fasting glucose	S9 Abedini 2021: ANCOVA-derived contrast instead of arm-level data	Esmaeilinezhad 2019, Abedini 2021	2	85	0.60 (−26.75 to 27.96)	0.000	0
Pomegranate juice vs control	Fasting insulin	S4 without reports with internal data inconsistencies	Abedini 2021	1	42	−2.03 (−4.57 to 0.51)	–	–
Pomegranate juice vs control	Fasting insulin	S6a r = 0	Esmaeilinezhad 2019, Abedini 2021	2	85	−1.60 (−16.16 to 12.97)	0.000	0
Pomegranate juice vs control	Fasting insulin	S6b r = 0.25	Esmaeilinezhad 2019, Abedini 2021	2	85	−1.59 (−14.22 to 11.03)	0.000	0
Pomegranate juice vs control	Fasting insulin	S6c r = 0.75	Esmaeilinezhad 2019, Abedini 2021	2	85	−1.59 (−8.93 to 5.75)	0.000	0
Pomegranate juice vs control	Fasting insulin	S6d r = 0.9	Esmaeilinezhad 2019, Abedini 2021	2	85	−1.58 (−6.30 to 3.14)	0.000	0
Pomegranate juice vs control	Fasting insulin	S9 Abedini 2021: ANCOVA-derived contrast instead of arm-level data	Esmaeilinezhad 2019, Abedini 2021	2	85	−1.72 (−11.88 to 8.44)	0.000	0
Pomegranate juice vs control	HOMA-IR	S4 without reports with internal data inconsistencies	Abedini 2021	1	42	−0.42 (−1.01 to 0.17)	–	–
Pomegranate juice vs control	HOMA-IR	S6a r = 0	Esmaeilinezhad 2019, Abedini 2021	2	85	−0.38 (−4.34 to 3.57)	0.000	0
Pomegranate juice vs control	HOMA-IR	S6b r = 0.25	Esmaeilinezhad 2019, Abedini 2021	2	85	−0.38 (−3.82 to 3.05)	0.000	0
Pomegranate juice vs control	HOMA-IR	S6c r = 0.75	Esmaeilinezhad 2019, Abedini 2021	2	85	−0.38 (−2.39 to 1.63)	0.000	0
Pomegranate juice vs control	HOMA-IR	S6d r = 0.9	Esmaeilinezhad 2019, Abedini 2021	2	85	−0.38 (−1.69 to 0.93)	0.000	0
Pomegranate juice vs control	HOMA-IR	S9 Abedini 2021: ANCOVA-derived contrast instead of arm-level data	Esmaeilinezhad 2019, Abedini 2021	2	85	−0.40 (−3.03 to 2.23)	0.000	0
Pomegranate juice vs control	QUICKI	S4 without reports with internal data inconsistencies	–	0	–	–	–	–

Pomegranate juice vs control	QUICKI	S6a r = 0	Esmaeilinezhad 2019	1	43	0.005 (0.000 to 0.010)	–	–
Pomegranate juice vs control	QUICKI	S6b r = 0.25	Esmaeilinezhad 2019	1	43	0.005 (0.001 to 0.009)	–	–
Pomegranate juice vs control	QUICKI	S6c r = 0.75	Esmaeilinezhad 2019	1	43	0.005 (0.003 to 0.007)	–	–
Pomegranate juice vs control	QUICKI	S6d r = 0.9	Esmaeilinezhad 2019	1	43	0.005 (0.003 to 0.007)	–	–
Pomegranate juice vs control	Total cholesterol	S6a r = 0	Abedini 2021	1	42	2.09 (−17.56 to 21.74)	–	–
Pomegranate juice vs control	Total cholesterol	S6b r = 0.25	Abedini 2021	1	42	2.09 (−14.96 to 19.14)	–	–
Pomegranate juice vs control	Total cholesterol	S6c r = 0.75	Abedini 2021	1	42	2.09 (−7.88 to 12.06)	–	–
Pomegranate juice vs control	Total cholesterol	S6d r = 0.9	Abedini 2021	1	42	2.09 (−4.40 to 8.58)	–	–
Pomegranate juice vs control	Total cholesterol	S9 Abedini 2021: ANCOVA-derived contrast instead of arm-level data	Abedini 2021	1	42	6.15 (−2.91 to 15.21)	–	–
Pomegranate juice vs control	LDL-C	S6a r = 0	Abedini 2021	1	42	4.25 (−12.01 to 20.51)	–	–
Pomegranate juice vs control	LDL-C	S6b r = 0.25	Abedini 2021	1	42	4.25 (−9.84 to 18.34)	–	–
Pomegranate juice vs control	LDL-C	S6c r = 0.75	Abedini 2021	1	42	4.25 (−3.90 to 12.40)	–	–
Pomegranate juice vs control	LDL-C	S6d r = 0.9	Abedini 2021	1	42	4.25 (−0.93 to 9.43)	–	–
Pomegranate juice vs control	LDL-C	S9 Abedini 2021: ANCOVA-derived contrast instead of arm-level data	Abedini 2021	1	42	8.01 (1.16 to 14.86)	–	–
Pomegranate juice vs control	HDL-C	S6a r = 0	Abedini 2021	1	42	3.28 (−4.51 to 11.07)	–	–
Pomegranate juice vs control	HDL-C	S6b r = 0.25	Abedini 2021	1	42	3.28 (−3.48 to 10.04)	–	–
Pomegranate juice vs control	HDL-C	S6c r = 0.75	Abedini 2021	1	42	3.28 (−0.65 to 7.21)	–	–
Pomegranate juice vs control	HDL-C	S6d r = 0.9	Abedini 2021	1	42	3.28 (0.75 to 5.81)	–	–
Pomegranate juice vs control	HDL-C	S9 Abedini 2021: ANCOVA-derived contrast instead of arm-level data	Abedini 2021	1	42	3.71 (0.66 to 6.76)	–	–
Pomegranate juice vs control	Triglycerides	S6a r = 0	Abedini 2021	1	42	−23.57 (−59.83 to 12.69)	–	–
Pomegranate juice vs control	Triglycerides	S6b r = 0.25	Abedini 2021	1	42	−23.57 (−54.99 to 7.85)	–	–
Pomegranate juice vs control	Triglycerides	S6c r = 0.75	Abedini 2021	1	42	−23.57 (−41.81 to −5.33)	–	–
Pomegranate juice vs control	Triglycerides	S6d r = 0.9	Abedini 2021	1	42	−23.57 (−35.25 to −11.89)	–	–
Pomegranate juice vs control	Triglycerides	S9 Abedini 2021: ANCOVA-derived contrast instead of arm-level data	Abedini 2021	1	42	−24.45 (−41.97 to −6.93)	–	–

Pomegranate juice vs control	Total testosterone	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Pomegranate juice vs control	Total testosterone	S6a r = 0	Esmaeilinezhad 2019	1	43	−0.090 (−0.19 to 0.007)	–	–
Pomegranate juice vs control	Total testosterone	S6b r = 0.25	Esmaeilinezhad 2019	1	43	−0.090 (−0.17 to −0.006)	–	–
Pomegranate juice vs control	Total testosterone	S6c r = 0.75	Esmaeilinezhad 2019	1	43	−0.090 (−0.14 to −0.039)	–	–
Pomegranate juice vs control	Total testosterone	S6d r = 0.9	Esmaeilinezhad 2019	1	43	−0.090 (−0.12 to −0.055)	–	–
Pomegranate juice vs control	BMI	S4 without reports with internal data inconsistencies	Abedini 2021	1	42	−0.38 (−3.05 to 2.29)	–	–
Pomegranate juice vs control	BMI	S6a r = 0	Esmaeilinezhad 2019, Abedini 2021	2	85	−0.26 (−11.79 to 11.27)	0.000	0
Pomegranate juice vs control	BMI	S6b r = 0.25	Esmaeilinezhad 2019, Abedini 2021	2	85	−0.26 (−10.24 to 9.73)	0.000	0
Pomegranate juice vs control	BMI	S6c r = 0.75	Esmaeilinezhad 2019, Abedini 2021	2	85	−0.26 (−6.02 to 5.51)	0.000	0
Pomegranate juice vs control	BMI	S6d r = 0.9	Esmaeilinezhad 2019, Abedini 2021	2	85	−0.26 (−3.91 to 3.39)	0.000	0
Pomegranate juice vs control	BMI	S9 Abedini 2021: ANCOVA-derived contrast instead of arm-level data	Esmaeilinezhad 2019, Abedini 2021	2	85	−0.27 (−2.69 to 2.16)	0.000	0
Pomegranate juice vs control	Waist circumference	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Pomegranate juice vs control	Waist circumference	S6a r = 0	Esmaeilinezhad 2019	1	43	−0.98 (−5.98 to 4.02)	–	–
Pomegranate juice vs control	Waist circumference	S6b r = 0.25	Esmaeilinezhad 2019	1	43	−0.98 (−5.32 to 3.36)	–	–
Pomegranate juice vs control	Waist circumference	S6c r = 0.75	Esmaeilinezhad 2019	1	43	−0.98 (−3.55 to 1.59)	–	–
Pomegranate juice vs control	Waist circumference	S6d r = 0.9	Esmaeilinezhad 2019	1	43	−0.98 (−2.69 to 0.73)	–	–
Pomegranate juice vs control	Waist-to-hip ratio	S4 without reports with internal data inconsistencies	–	0	–	–	–	–
Pomegranate juice vs control	Waist-to-hip ratio	S6a r = 0	Esmaeilinezhad 2019	1	43	−0.010 (−0.038 to 0.018)	–	–
Pomegranate juice vs control	Waist-to-hip ratio	S6b r = 0.25	Esmaeilinezhad 2019	1	43	−0.010 (−0.034 to 0.014)	–	–
Pomegranate juice vs control	Waist-to-hip ratio	S6c r = 0.75	Esmaeilinezhad 2019	1	43	−0.010 (−0.024 to 0.004)	–	–
Pomegranate juice vs control	Waist-to-hip ratio	S6d r = 0.9	Esmaeilinezhad 2019	1	43	−0.010 (−0.020 to −0.000)	–	–
Vitamin D3 vs placebo	Fasting glucose	Leave-one-out: without Asemi 2015	–	3	199	−3.63 (−14.78 to 7.52)	15.257	77
Vitamin D3 vs placebo	Fasting glucose	Leave-one-out: without Abootorabi 2018	–	3	215	−1.47 (−5.79 to 2.84)	0.000	0
Vitamin D3 vs placebo	Fasting glucose	Leave-one-out: without Trummer 2019	–	3	128	−5.34 (−17.58 to 6.90)	15.546	71
Vitamin D3 vs placebo	Fasting glucose	Leave-one-out: without Dastorani 2018	–	3	211	−5.14 (−17.69 to 7.41)	17.551	78

Vitamin D3 vs placebo	Fasting insulin	Leave-one-out: without Asemi 2015	–	2	76	−1.06 (−6.16 to 4.04)	0.000	0
Vitamin D3 vs placebo	Fasting insulin	Leave-one-out: without Abootorabi 2018	–	2	92	−2.00 (−19.87 to 15.87)	2.616	54
Vitamin D3 vs placebo	Fasting insulin	Leave-one-out: without Dastorani 2018	–	2	88	−2.10 (−27.88 to 23.68)	4.301	52
Vitamin D3 vs placebo	HOMA-IR	Leave-one-out: without Asemi 2015	–	3	129	−0.20 (−0.53 to 0.14)	0.000	0
Vitamin D3 vs placebo	HOMA-IR	Leave-one-out: without Irani 2015	–	3	128	−0.22 (−0.57 to 0.13)	0.000	6
Vitamin D3 vs placebo	HOMA-IR	Leave-one-out: without Abootorabi 2018	–	3	145	−0.21 (−0.58 to 0.16)	0.000	17
Vitamin D3 vs placebo	HOMA-IR	Leave-one-out: without Dastorani 2018	–	3	141	−0.32 (−1.55 to 0.92)	0.000	11
Vitamin D3 vs placebo	QUICKI	Leave-one-out: without Asemi 2015	–	2	76	0.008 (−0.021 to 0.038)	0.000	0
Vitamin D3 vs placebo	QUICKI	Leave-one-out: without Abootorabi 2018	–	2	92	0.013 (−0.065 to 0.091)	0.000	76
Vitamin D3 vs placebo	QUICKI	Leave-one-out: without Dastorani 2018	–	2	88	0.020 (−0.042 to 0.081)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	Leave-one-out: without Ardabili 2013	–	3	145	−7.35 (−21.47 to 6.78)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	Leave-one-out: without Asemi 2015	–	3	143	−9.86 (−24.09 to 4.37)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	Leave-one-out: without Irani 2015	–	3	142	−8.19 (−21.85 to 5.46)	0.000	0
Vitamin D3 vs placebo	Total cholesterol	Leave-one-out: without Dastorani 2018	–	3	155	−10.12 (−36.56 to 16.33)	22.357	8
Vitamin D3 vs placebo	LDL-C	Leave-one-out: without Ardabili 2013	–	3	145	−3.22 (−21.15 to 14.71)	19.371	29
Vitamin D3 vs placebo	LDL-C	Leave-one-out: without Asemi 2015	–	3	143	−7.16 (−19.73 to 5.41)	0.000	0
Vitamin D3 vs placebo	LDL-C	Leave-one-out: without Irani 2015	–	3	142	−4.49 (−24.45 to 15.48)	23.683	40
Vitamin D3 vs placebo	LDL-C	Leave-one-out: without Dastorani 2018	–	3	155	−2.10 (−25.57 to 21.38)	21.607	21
Vitamin D3 vs placebo	HDL-C	Leave-one-out: without Ardabili 2013	–	3	145	−0.30 (−4.58 to 3.99)	0.000	0
Vitamin D3 vs placebo	HDL-C	Leave-one-out: without Asemi 2015	–	3	143	−0.14 (−3.93 to 3.65)	0.000	0
Vitamin D3 vs placebo	HDL-C	Leave-one-out: without Irani 2015	–	3	142	−0.14 (−3.91 to 3.63)	0.000	0
Vitamin D3 vs placebo	HDL-C	Leave-one-out: without Dastorani 2018	–	3	155	−0.15 (−6.25 to 5.96)	0.000	0
Vitamin D3 vs placebo	Triglycerides	Leave-one-out: without Ardabili 2013	–	3	145	−11.11 (−53.10 to 30.89)	125.343	29
Vitamin D3 vs placebo	Triglycerides	Leave-one-out: without Asemi 2015	–	3	143	−11.12 (−53.90 to 31.66)	129.299	28
Vitamin D3 vs placebo	Triglycerides	Leave-one-out: without Irani 2015	–	3	142	−17.94 (−64.88 to 28.99)	215.016	61
Vitamin D3 vs placebo	Triglycerides	Leave-one-out: without Dastorani 2018	–	3	155	−28.28 (−73.62 to 17.06)	0.000	0
Vitamin D3 vs placebo	VLDL-C	Leave-one-out: without Ardabili 2013	–	2	92	−2.68 (−35.38 to 30.01)	9.212	63

Vitamin D3 vs placebo	VLDL-C	Leave-one-out: without Asemi 2015	–	2	90	−2.79 (−37.41 to 31.83)	10.438	64
Vitamin D3 vs placebo	VLDL-C	Leave-one-out: without Dastorani 2018	–	2	102	−6.35 (−35.20 to 22.50)	0.000	0
Vitamin D3 vs placebo	25(OH)D	Leave-one-out: without Ardabili 2013	–	4	248	15.11 (4.98 to 25.23)	37.704	93
Vitamin D3 vs placebo	25(OH)D	Leave-one-out: without Asemi 2015	–	4	246	16.18 (6.84 to 25.51)	31.657	93
Vitamin D3 vs placebo	25(OH)D	Leave-one-out: without Abootorabi 2018	–	4	262	12.81 (9.42 to 16.20)	2.609	58
Vitamin D3 vs placebo	25(OH)D	Leave-one-out: without Trummer 2019	–	4	178	15.66 (5.73 to 25.58)	36.241	94
Vitamin D3 vs placebo	25(OH)D	Leave-one-out: without Dastorani 2018	–	4	258	16.22 (6.93 to 25.51)	31.220	92
Vitamin D3 vs placebo	BMI	Leave-one-out: without Ardabili 2013	–	2	92	−0.051 (−1.36 to 1.26)	0.004	13
Vitamin D3 vs placebo	BMI	Leave-one-out: without Asemi 2015	–	2	90	−0.001 (−0.93 to 0.92)	0.000	0
Vitamin D3 vs placebo	BMI	Leave-one-out: without Dastorani 2018	–	2	102	−0.059 (−1.42 to 1.30)	0.002	6
Vitamin D3 vs placebo	Body weight	Leave-one-out: without Ardabili 2013	–	2	92	−0.11 (−4.21 to 3.98)	0.077	31
Vitamin D3 vs placebo	Body weight	Leave-one-out: without Asemi 2015	–	2	90	−0.12 (−3.04 to 2.80)	0.029	28
Vitamin D3 vs placebo	Body weight	Leave-one-out: without Dastorani 2018	–	2	102	−0.42 (−3.57 to 2.74)	0.000	0
Cinnamon vs placebo	Fasting glucose	Leave-one-out: without Borzoei 2018	–	2	101	−2.63 (−23.73 to 18.47)	0.000	0
Cinnamon vs placebo	Fasting glucose	Leave-one-out: without Hajimonfarednejad 2018	–	2	126	−6.15 (−87.24 to 74.94)	68.079	82
Cinnamon vs placebo	Fasting glucose	Leave-one-out: without Dastgheib 2022	–	2	143	−7.37 (−62.32 to 47.59)	33.982	91
Cinnamon vs placebo	Fasting insulin	Leave-one-out: without Borzoei 2018	–	2	101	−3.36 (−19.10 to 12.38)	0.038	1
Cinnamon vs placebo	Fasting insulin	Leave-one-out: without Hajimonfarednejad 2018	–	2	126	−3.00 (−14.45 to 8.45)	0.000	0
Cinnamon vs placebo	Fasting insulin	Leave-one-out: without Dastgheib 2022	–	2	143	−3.64 (−17.29 to 10.02)	0.000	0
Cinnamon vs placebo	HOMA-IR	Leave-one-out: without Borzoei 2018	–	2	101	−0.89 (−5.06 to 3.27)	0.000	0
Cinnamon vs placebo	HOMA-IR	Leave-one-out: without Hajimonfarednejad 2018	–	2	126	−0.98 (−4.02 to 2.06)	0.000	0
Cinnamon vs placebo	HOMA-IR	Leave-one-out: without Dastgheib 2022	–	2	143	−1.17 (−4.43 to 2.08)	0.000	0
Cinnamon vs placebo	Total cholesterol	Leave-one-out: without Borzoei 2018	–	2	101	−10.40 (−95.56 to 74.76)	0.000	0
Cinnamon vs placebo	Total cholesterol	Leave-one-out: without Hajimonfarednejad 2018	–	2	126	−10.00 (−68.04 to 48.05)	0.000	0
Cinnamon vs placebo	Total cholesterol	Leave-one-out: without Dastgheib 2022	–	2	143	−12.47 (−68.37 to 43.44)	0.000	0
Cinnamon vs placebo	LDL-C	Leave-one-out: without Borzoei 2018	–	2	101	−10.40 (−95.70 to 74.89)	35.971	40
Cinnamon vs placebo	LDL-C	Leave-one-out: without Hajimonfarednejad 2018	–	2	126	−8.96 (−63.49 to 45.56)	0.000	0

Cinnamon vs placebo	LDL-C	Leave-one-out: without Dastgheib 2022	–	2	143	−13.22 (−64.95 to 38.52)	0.000	0
Cinnamon vs placebo	Triglycerides	Leave-one-out: without Borzoei 2018	–	2	101	7.38 (−263.22 to 277.99)	711.975	78
Cinnamon vs placebo	Triglycerides	Leave-one-out: without Hajimonfarednejad 2018	–	2	126	5.69 (−279.26 to 290.64)	843.098	83
Cinnamon vs placebo	Triglycerides	Leave-one-out: without Dastgheib 2022	–	2	143	−13.63 (−96.69 to 69.42)	0.000	0
Cinnamon vs placebo	BMI	Leave-one-out: without Borzoei 2018	–	2	101	−0.62 (−12.29 to 11.04)	0.000	0
Cinnamon vs placebo	BMI	Leave-one-out: without Hajimonfarednejad 2018	–	2	126	−0.13 (−1.04 to 0.78)	0.000	0
Cinnamon vs placebo	BMI	Leave-one-out: without Dastgheib 2022	–	2	143	−0.13 (−1.04 to 0.78)	0.000	0
Cinnamon vs placebo	Body weight	Leave-one-out: without Borzoei 2018	–	2	101	−1.10 (−29.78 to 27.57)	0.000	0
Cinnamon vs placebo	Body weight	Leave-one-out: without Hajimonfarednejad 2018	–	2	126	−0.47 (−2.59 to 1.65)	0.000	0
Cinnamon vs placebo	Body weight	Leave-one-out: without Dastgheib 2022	–	2	143	−0.47 (−2.59 to 1.64)	0.000	0
Curcumin vs placebo	Fasting glucose	Leave-one-out: without Jamilian 2020	–	2	105	−4.10 (−31.80 to 23.59)	1.495	16
Curcumin vs placebo	Fasting glucose	Leave-one-out: without Ghanbarzadeh-Ghashti 2023	–	2	101	−2.57 (−12.43 to 7.28)	0.000	0
Curcumin vs placebo	Fasting glucose	Leave-one-out: without Sohaei 2019	–	2	104	−3.44 (−22.58 to 15.70)	2.275	35
Curcumin vs placebo	Fasting insulin	Leave-one-out: without Jamilian 2020	–	2	105	−2.66 (−19.80 to 14.49)	0.000	0
Curcumin vs placebo	Fasting insulin	Leave-one-out: without Ghanbarzadeh-Ghashti 2023	–	2	101	−1.24 (−7.25 to 4.78)	0.000	0
Curcumin vs placebo	Fasting insulin	Leave-one-out: without Sohaei 2019	–	2	104	−1.29 (−7.96 to 5.38)	0.051	2
Curcumin vs placebo	HOMA-IR	Leave-one-out: without Jamilian 2020	–	2	105	−0.81 (−5.32 to 3.70)	0.000	0
Curcumin vs placebo	HOMA-IR	Leave-one-out: without Ghanbarzadeh-Ghashti 2023	–	2	101	−0.28 (−1.70 to 1.14)	0.000	0
Curcumin vs placebo	HOMA-IR	Leave-one-out: without Sohaei 2019	–	2	104	−0.47 (−4.74 to 3.80)	0.144	51
Curcumin vs placebo	Total cholesterol	Leave-one-out: without Jamilian 2020	–	2	105	−4.96 (−82.95 to 73.02)	0.000	0
Curcumin vs placebo	Total cholesterol	Leave-one-out: without Ghanbarzadeh-Ghashti 2023	–	2	101	−12.58 (−74.19 to 49.03)	14.919	27
Curcumin vs placebo	Total cholesterol	Leave-one-out: without Sohaei 2019	–	2	104	−13.55 (−72.61 to 45.51)	7.617	11
Curcumin vs placebo	LDL-C	Leave-one-out: without Jamilian 2020	–	2	105	−4.31 (−129.86 to 121.25)	143.710	73
Curcumin vs placebo	LDL-C	Leave-one-out: without Ghanbarzadeh-Ghashti 2023	–	2	101	−6.00 (−139.80 to 127.80)	191.416	86
Curcumin vs placebo	LDL-C	Leave-one-out: without Sohaei 2019	–	2	104	−15.77 (−66.51 to 34.96)	0.000	0

Curcumin vs placebo	Triglycerides	Leave-one-out: without Jamilian 2020	–	2	105	8.17 (−234.75 to 251.09)	554.450	74
Curcumin vs placebo	Triglycerides	Leave-one-out: without Ghanbarzadeh-Ghashti 2023	–	2	101	8.36 (−214.51 to 231.24)	488.025	75
Curcumin vs placebo	Triglycerides	Leave-one-out: without Sohaei 2019	–	2	104	−5.98 (−49.95 to 37.99)	0.000	0
Omega-3 vs placebo/control	Total cholesterol	Leave-one-out: without Rafraf/Mohammadi 2012	–	2	282	−15.14 (−86.88 to 56.61)	58.766	92
Omega-3 vs placebo/control	Total cholesterol	Leave-one-out: without Khani 2017	–	2	256	−20.30 (−55.26 to 14.66)	0.000	0
Omega-3 vs placebo/control	Total cholesterol	Leave-one-out: without Mejia-Montilla 2018	–	2	148	−9.93 (−26.30 to 6.44)	0.000	0
Omega-3 vs placebo/control	LDL-C	Leave-one-out: without Rafraf/Mohammadi 2012	–	2	282	−16.27 (−104.05 to 71.52)	93.686	98
Omega-3 vs placebo/control	LDL-C	Leave-one-out: without Khani 2017	–	2	256	−22.86 (−45.93 to 0.21)	0.000	0
Omega-3 vs placebo/control	LDL-C	Leave-one-out: without Mejia-Montilla 2018	–	2	148	−9.49 (−13.98 to −5.01)	0.000	0
Omega-3 vs placebo/control	HDL-C	Leave-one-out: without Rafraf/Mohammadi 2012	–	2	282	4.76 (−16.35 to 25.88)	5.136	93
Omega-3 vs placebo/control	HDL-C	Leave-one-out: without Khani 2017	–	2	256	2.83 (−6.72 to 12.38)	0.000	0
Omega-3 vs placebo/control	HDL-C	Leave-one-out: without Mejia-Montilla 2018	–	2	148	4.58 (−21.02 to 30.18)	7.046	85
Omega-3 vs placebo/control	Triglycerides	Leave-one-out: without Rafraf/Mohammadi 2012	–	2	282	−13.45 (−75.89 to 48.98)	43.420	89
Omega-3 vs placebo/control	Triglycerides	Leave-one-out: without Khani 2017	–	2	256	−11.88 (−115.86 to 92.09)	105.811	77
Omega-3 vs placebo/control	Triglycerides	Leave-one-out: without Mejia-Montilla 2018	–	2	148	−8.97 (−16.76 to −1.19)	0.000	0
Omega-3 vs placebo/control	BMI	Leave-one-out: without Rafraf/Mohammadi 2012	–	2	282	−1.05 (−5.69 to 3.59)	0.000	0
Omega-3 vs placebo/control	BMI	Leave-one-out: without Khani 2017	–	2	256	−0.74 (−5.42 to 3.95)	0.000	0
Omega-3 vs placebo/control	BMI	Leave-one-out: without Mejia-Montilla 2018	–	2	148	−0.86 (−9.69 to 7.96)	0.362	37

Analyses are listed only where they change the set of trials or the input of a comparison. Analyses that left the input unchanged are identical to the primary result (Table 3 and Table S1). k = 1: single trial, normal-approximation CI, not pooled. S6 is shown only for analyses containing an imputed change SD. τ^2: REML between-study variance, MD: mean difference, CI: confidence interval. The same results are provided in machine-readable form in Data S2.

Table S6. Included reports, trial populations and analysis status

Report	Trial population	Analysis status
Ardabili 2013	Ardabili 2013	Primary analyses
Asemi 2015	Asemi 2015	Primary analyses
Irani 2015	Irani 2015	Primary analyses
Abootorabi 2018	Abootorabi 2018	Primary analyses
Trummer 2019	Trummer 2019	Primary analyses

Dastorani 2018	Dastorani 2018	Primary analyses
Borzoei 2018	Borzoei 2018	Primary analyses
Hajimonfarednejad 2018	Hajimonfarednejad 2018	Primary analyses, excluded in S11
Dastgheib 2022	Dastgheib 2022 (four arms)	Primary analyses
Khan 2019	Khan 2019	Primary analyses
Mishra 2022	Mishra 2022 (three arms)	Primary analyses
Nehra 2017	Nehra 2017	Primary analyses
Fruzzetti 2017	Fruzzetti 2017	Primary analyses
Shokrpour 2019	Shokrpour 2019	Primary analyses
Iuorno 2002	Iuorno 2002	Primary analyses
Nestler 1999	Nestler 1999	Primary analyses
Jamilian 2020	Jamilian 2020	Primary analyses
Ghanbarzadeh-Ghashti 2023	Ghanbarzadeh-Ghashti 2023	Primary analyses
Sohaei 2019	Sohaei 2019	Primary analyses
Mohammadi 2012	Rafraf/Mohammadi 2012	Primary analyses (companion report)
Rafraf 2012a	Rafraf/Mohammadi 2012	Primary analyses (companion report)
Rafraf 2012b	Rafraf/Mohammadi 2012	Primary analyses (companion report)
Khani 2017	Khani 2017	Primary analyses
Mejia-Montilla 2018	Mejia-Montilla 2018	Primary analyses
Jamilian 2018	Jamilian 2018	Primary analyses
Jamilian 2016	Jamilian 2016	Primary analyses
Esmaeilinezhad 2019	Esmaeilinezhad 2019 (four arms, two used)	Primary analyses
Abedini 2021	Abedini 2021	Primary analyses
Foroozanfard 2015	Foroozanfard 2015	Sensitivity only (S1, expression of concern)
Maktabi 2017	Maktabi 2017	Sensitivity only (S1, note of concern)
Ebrahimi 2017	Ebrahimi 2017	Sensitivity only (S1, note of concern)
Bonakdaran 2012	Bonakdaran 2012	Sensitivity only (S10, quasi-randomized)
Khani 2011	Khani 2011	Sensitivity only (S10, quasi-randomized)
Javed 2019	Javed 2019	Sensitivity only (S5, full sample)
Ravn 2022	Ravn 2022	Narrative only (medians)
Nadjarzadeh 2015	Nadjarzadeh 2015	Qualitative review only
Haj-Husein 2016	Haj-Husein 2016	Qualitative review only
Heidary 2018	Heidary 2018	Qualitative review only
Mombaini 2017	Mombaini 2017	Qualitative review only
Izadi 2019	Izadi 2019	Qualitative review only

40 reports of 38 trial populations: 28 reports (26 populations) contribute to the primary analyses. Three reports under an expression or note of concern, two quasi-randomized trials and the full sample of Javed 2019 are used only in sensitivity analyses. One report (Ravn 2022) is described narratively. Five reports are included in the qualitative review only. Rafraf 2012a, Rafraf 2012b and Mohammadi 2012 describe one population and contribute one effect size per outcome.

Table S7. Reports affected by post-publication notices

Report	Notice	Notice identifier	Handling
Jamilian H, et al. Comparison of myo-inositol and metformin on mental health parameters and biomarkers of oxidative stress in women with polycystic ovary syndrome. J Psychosom Obstet Gynaecol	Retraction	Statement of retraction, J Psychosom Obstet Gynaecol 2024, 45(1), doi:10.1080/0167482X.2024.2346385	Excluded from the review
Amini M, et al. The effects of fish oil omega-3 fatty acid supplementation on mental health parameters and metabolic status of patients with polycystic ovary syndrome. J Psychosom Obstet Gynaecol, doi:10.1080/0167482X.2018.1508282	Retraction	Statement of retraction, J Psychosom Obstet Gynaecol 2024, 45(1), doi:10.1080/0167482X.2024.2369455	Excluded from the review
Foroozanfard F, et al. 2015 (vitamin D3 with or without calcium)	Expression of concern	PMID 36852466	Excluded from primary analyses, re-included in S1
Maktabi M, et al. Horm Metab Res 2017, 49:493–498	Note of concern	PMID 40648761, Horm Metab Res 2017, 49(07):e6, doi:10.1055/a-1736-8400	Excluded from primary analyses, re-included in S1
Ebrahimi FA, et al. Exp Clin Endocrinol Diabetes 2017, 125:353–359	Note of concern	PMID 40872975, Exp Clin Endocrinol Diabetes 2017, 125(06):e3, doi:10.1055/a-1736-9502	Excluded from primary analyses, re-included in S1

All included and potentially eligible reports were checked for retractions, expressions of concern and notes of concern during the revision (October 2026). The reasons for the notices were not published. The affected reports share a co-author. Shared authorship is not in itself evidence of a data problem and was used only to define sensitivity analysis S2.

Figure S1. Search strategy

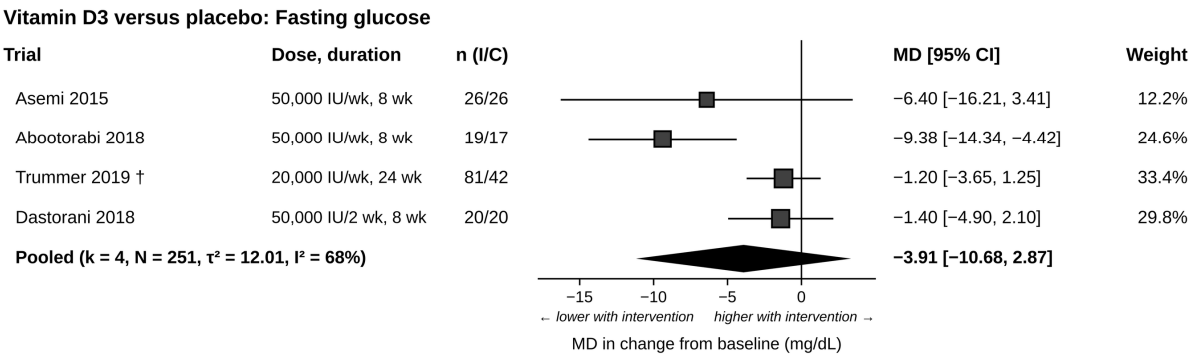
Databases: MEDLINE (via PubMed), the Cochrane Library (CENTRAL) and Embase, each searched from inception to 4 December 2025. The same search string was run in all three databases, without field tags, filters, or restrictions on language or publication date. The searches yielded 5,565 records in total (Figure 1). Reference lists of eligible articles were screened by hand (6 additional reports, none of which met the eligibility criteria). The search was not updated during the revision.

Search string, combining the population of interest with the investigated interventions:

(polycystic ovarian syndrome OR PCOS OR Stein-Leventhal syndrome) AND (foeniculum vulgare OR fennel OR cimicifuga racemosa OR actaea racemosa OR black cohosh OR grifola frondosa OR maitake OR vitex agnus-castus OR chasteberry OR berberine OR mentha spicata OR spearmint OR Cinnamomum OR cinnamon OR origanum majorana OR marjoram OR trigonella foenum-graecum OR fenugreek OR glycyrrhiza glabra OR licorice OR glycine max OR soy OR punica granatum OR pomegranate OR salvia officinalis OR sage OR panax OR ginseng OR stachys lavandulifolia OR wood betony OR linum usitatissimum OR flax OR paeonia lactiflora OR Chinese peony OR tribulus terrestris OR puncture vine OR curcuma OR turmeric OR omega-3 OR vitamin E OR myo-inositol OR folic acid OR D-chiro-inositol OR vitamin D OR phytotherapy OR medicinal plant OR herbal)

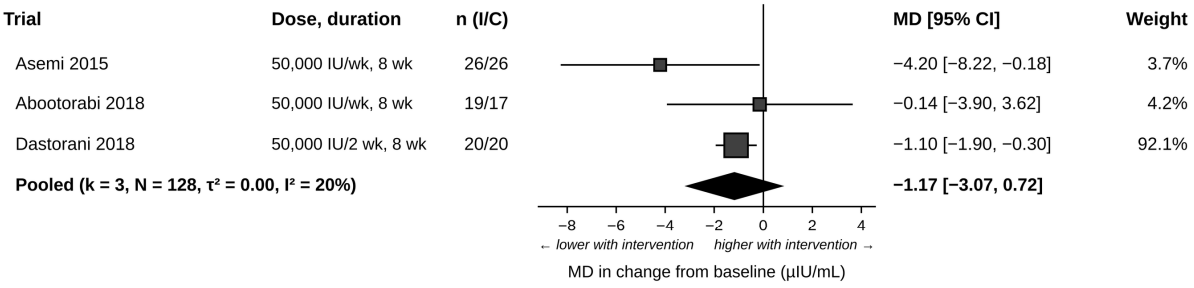
Interventions included post hoc (ginger, calcitriol, coenzyme Q10, chamomile and green tea) were not named in the search string. They were identified through the broader terms (vitamin D, herbal, medicinal plant, phytotherapy), so the search may be incomplete for these interventions.

Figure S2. Forest plot for Fasting glucose with Vitamin D3 versus placebo (revised analysis)



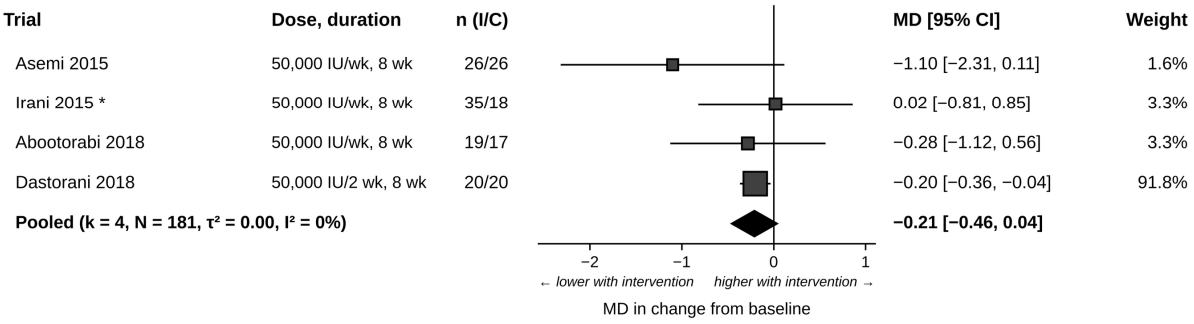
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S3. Forest plot for Fasting insulin with Vitamin D3 versus placebo (revised analysis)



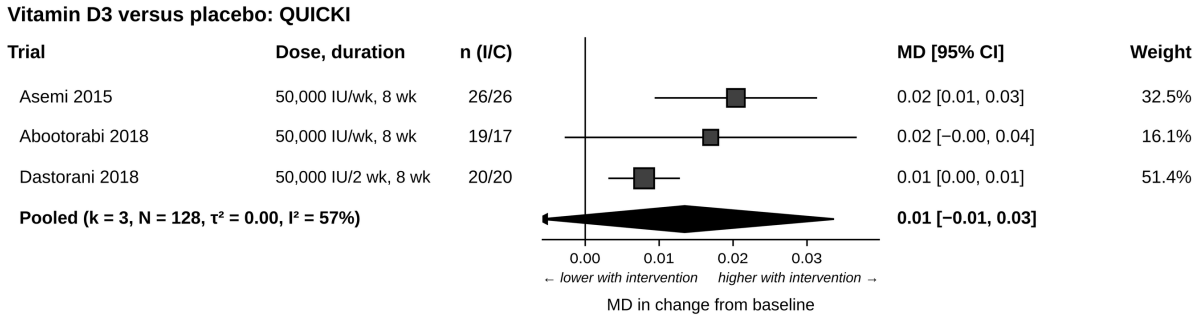
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S4. Forest plot for HOMA-IR with Vitamin D3 versus placebo (revised analysis)



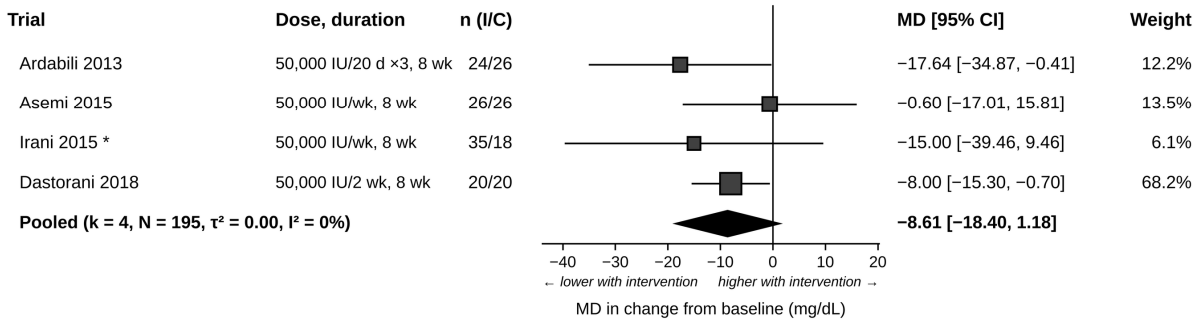
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S5. Forest plot for QUICKI with Vitamin D3 versus placebo (revised analysis)



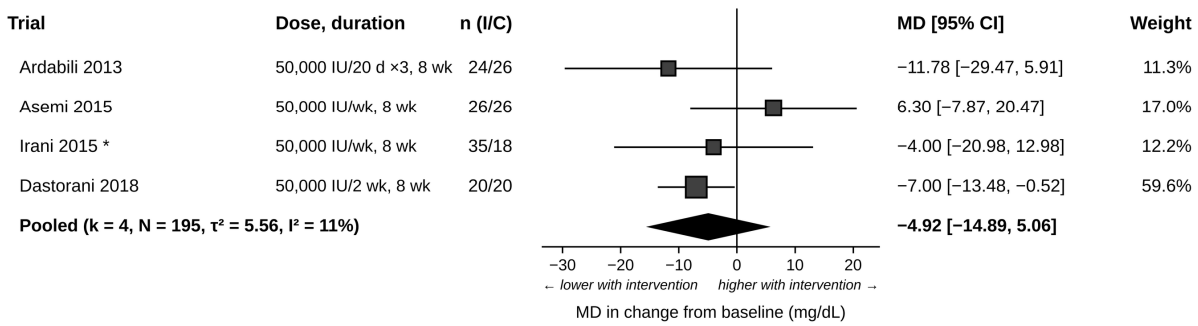
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S6. Forest plot for Total cholesterol with Vitamin D3 versus placebo (revised analysis)



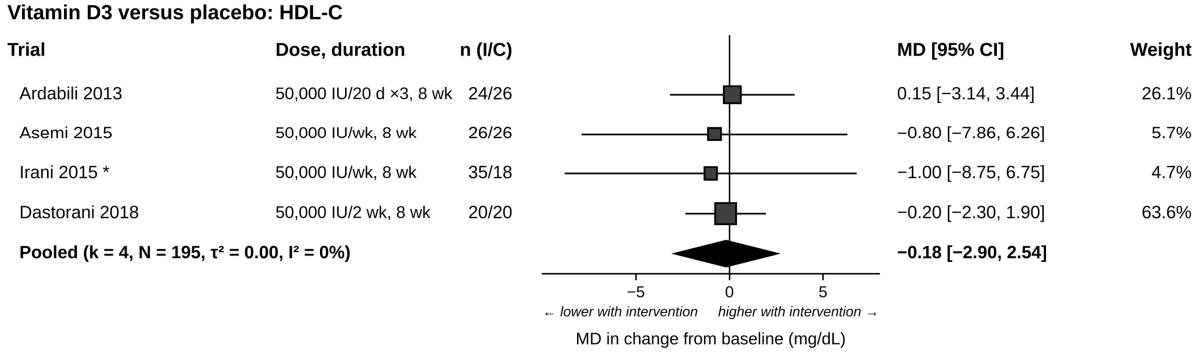
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S7. Forest plot for LDL-C with Vitamin D3 versus placebo (revised analysis)



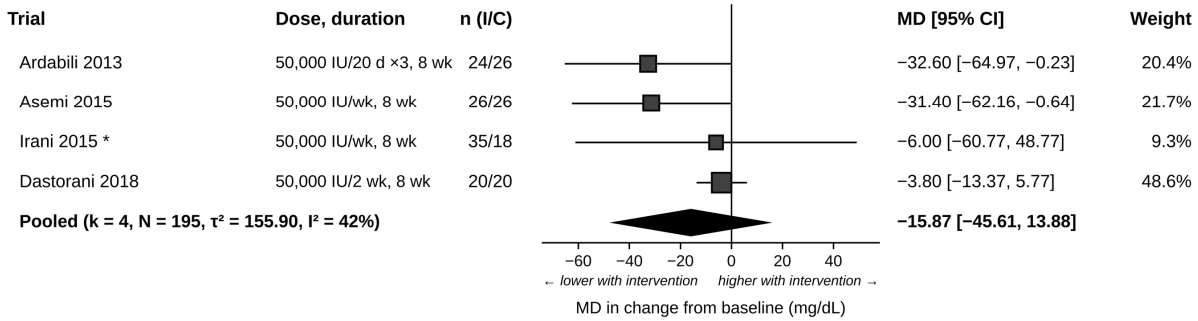
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S8. Forest plot for HDL-C with Vitamin D3 versus placebo (revised analysis)



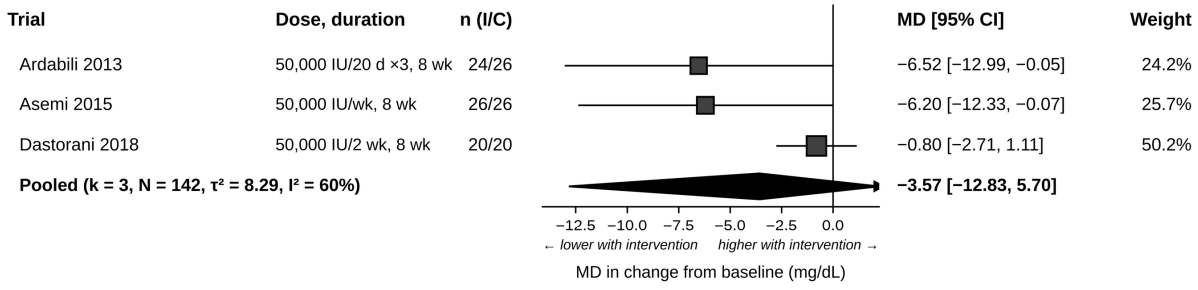
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S9. Forest plot for Triglycerides with Vitamin D3 versus placebo (revised analysis)



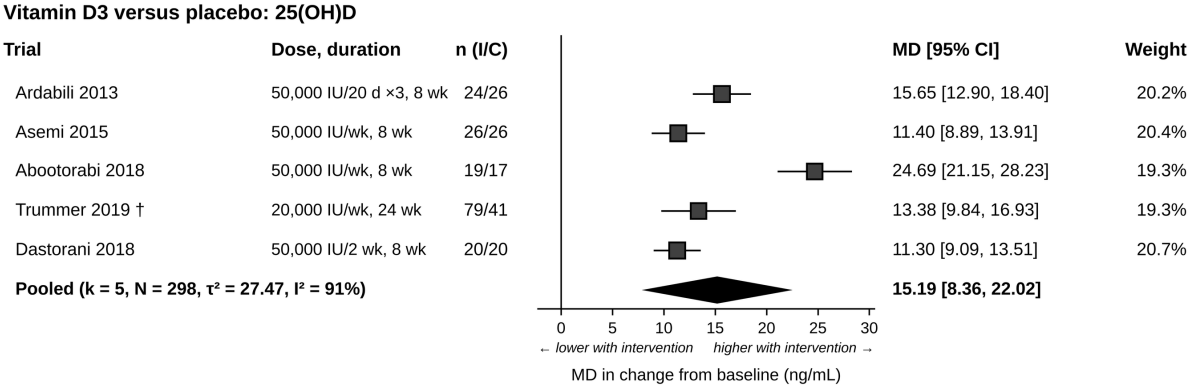
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S10. Forest plot for VLDL-C with Vitamin D3 versus placebo (revised analysis)



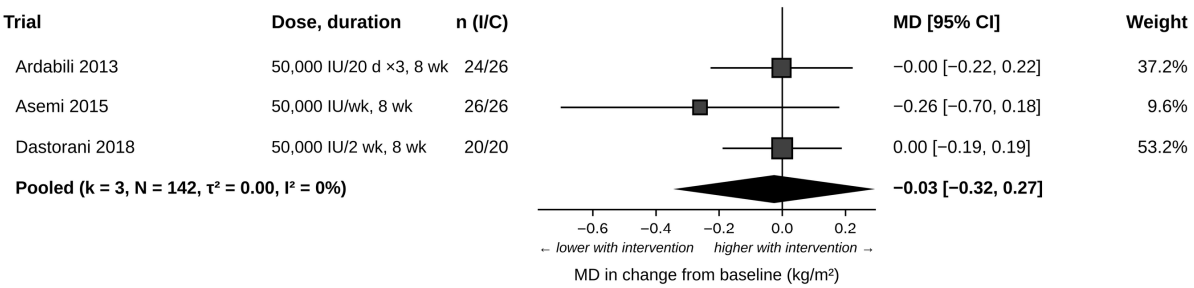
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S11. Forest plot for 25(OH)D with Vitamin D3 versus placebo (revised analysis)



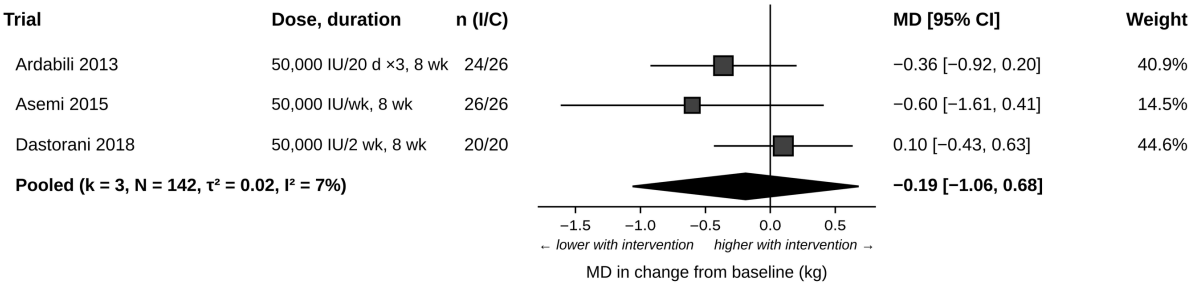
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S12. Forest plot for BMI with Vitamin D3 versus placebo (revised analysis)



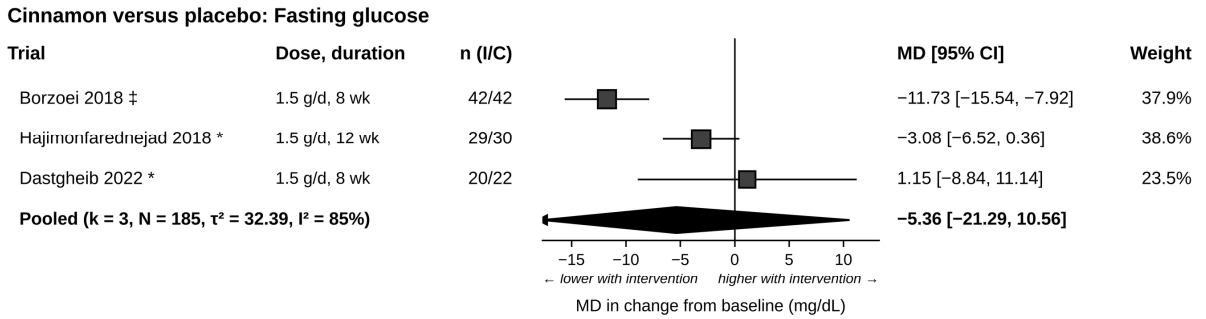
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S13. Forest plot for Body weight with Vitamin D3 versus placebo (revised analysis)



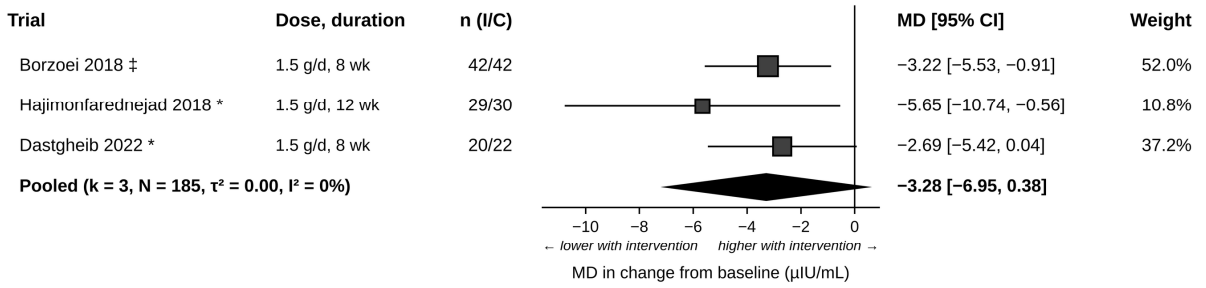
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S14. Forest plot for Fasting glucose with Cinnamon versus placebo (revised analysis)



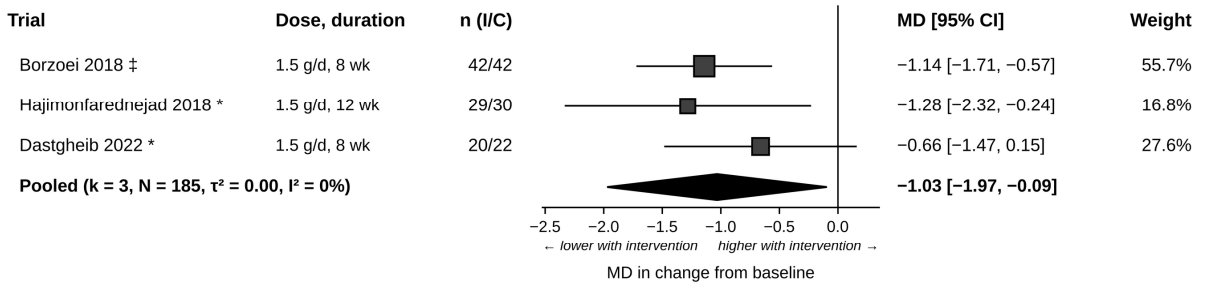
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). ‡ change SD derived from the within-group 95% CI reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S15. Forest plot for Fasting insulin with Cinnamon versus placebo (revised analysis)



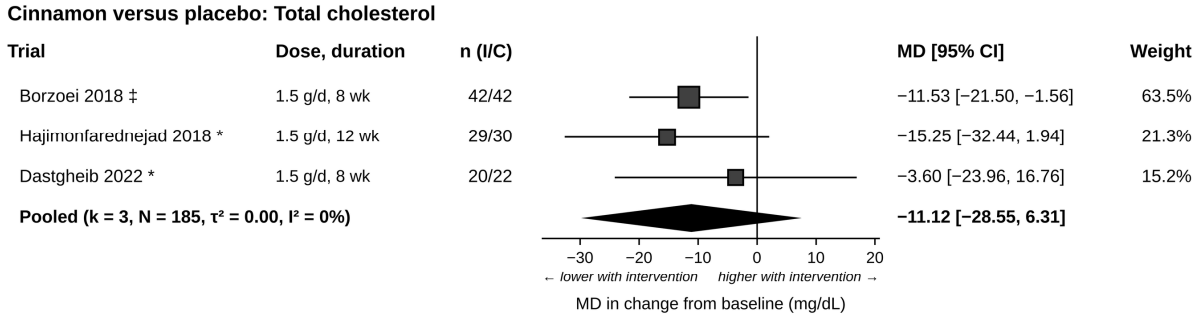
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). ‡ change SD derived from the within-group 95% CI reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S16. Forest plot for HOMA-IR with Cinnamon versus placebo (revised analysis)



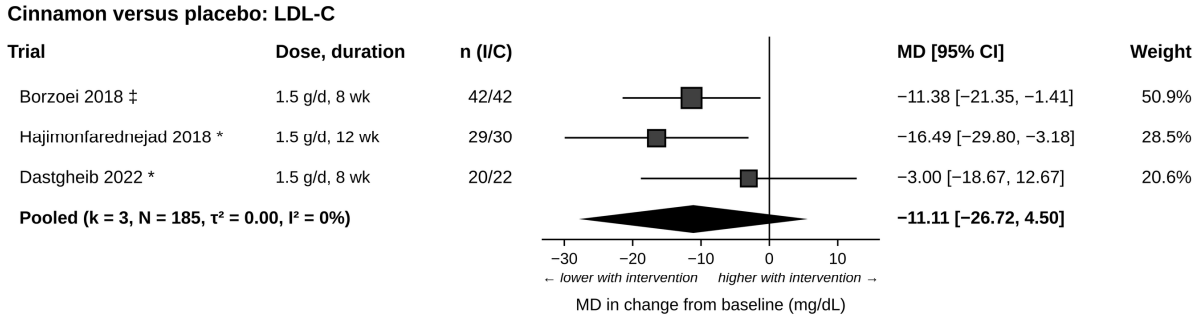
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). ‡ change SD derived from the within-group 95% CI reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S17. Forest plot for Total cholesterol with Cinnamon versus placebo (revised analysis)



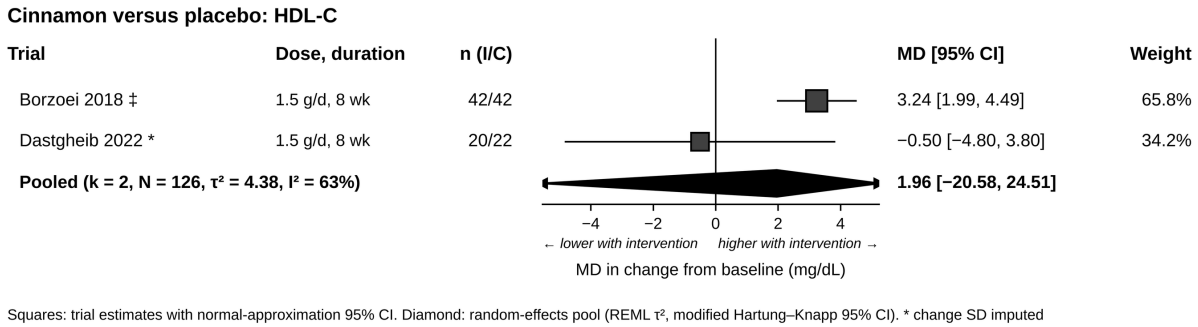
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). ‡ change SD derived from the within-group 95% CI reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S18. Forest plot for LDL-C with Cinnamon versus placebo (revised analysis)



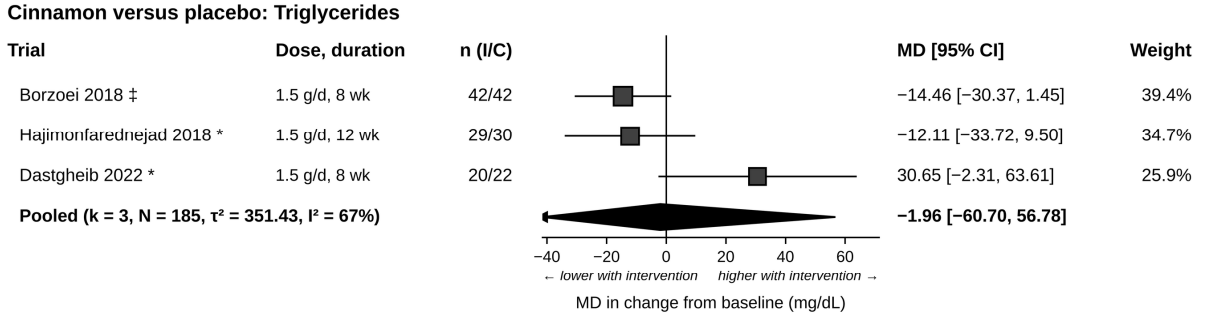
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). ‡ change SD derived from the within-group 95% CI reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S19. Forest plot for HDL-C with Cinnamon versus placebo (revised analysis)



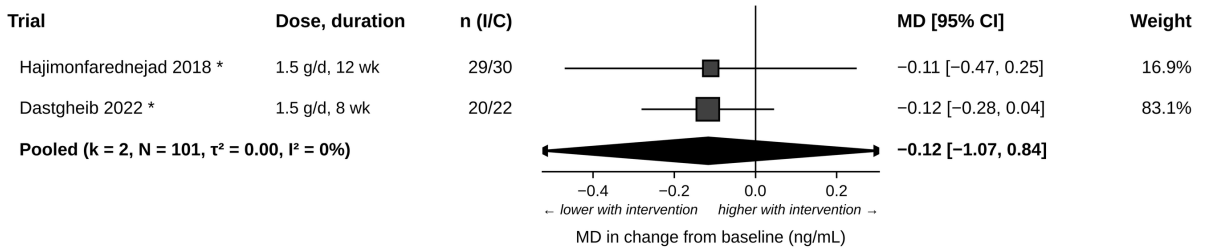
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). ‡ change SD derived from the within-group 95% CI reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S20. Forest plot for Triglycerides with Cinnamon versus placebo (revised analysis)



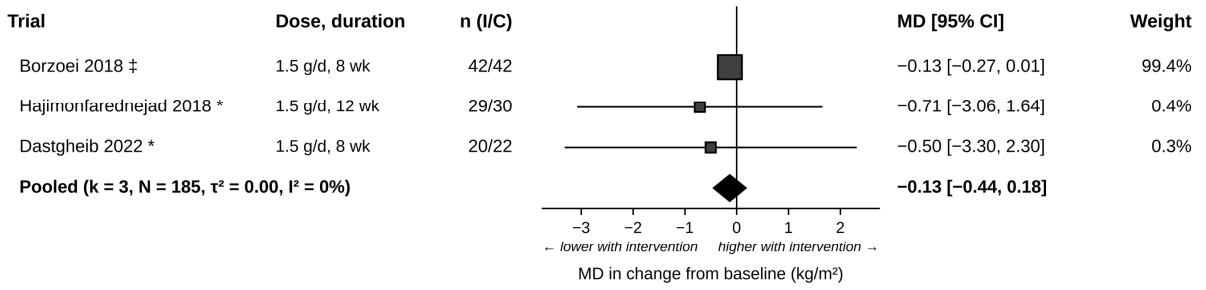
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). ‡ change SD derived from the within-group 95% CI reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S21. Forest plot for Total testosterone with Cinnamon versus placebo (revised analysis)



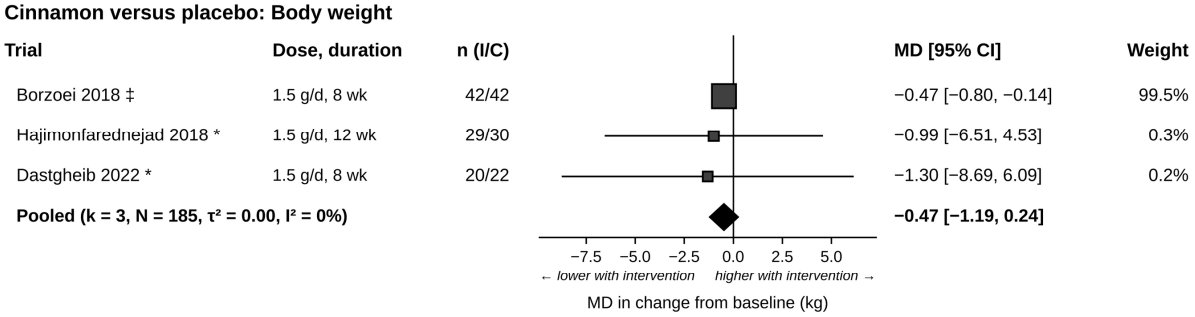
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S22. Forest plot for BMI with Cinnamon versus placebo (revised analysis)



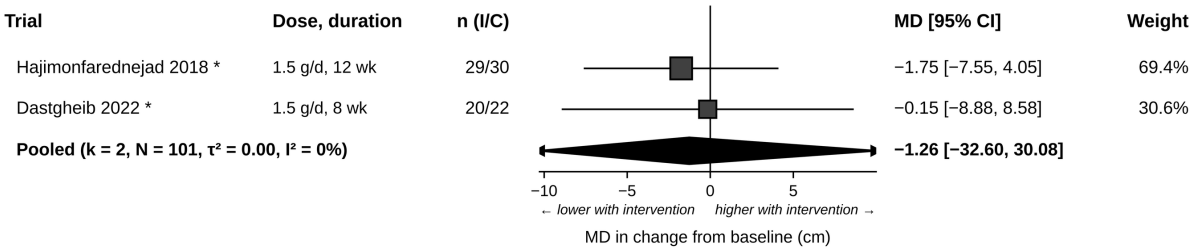
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). ‡ change SD derived from the within-group 95% CI reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S23. Forest plot for Body weight with Cinnamon versus placebo (revised analysis)



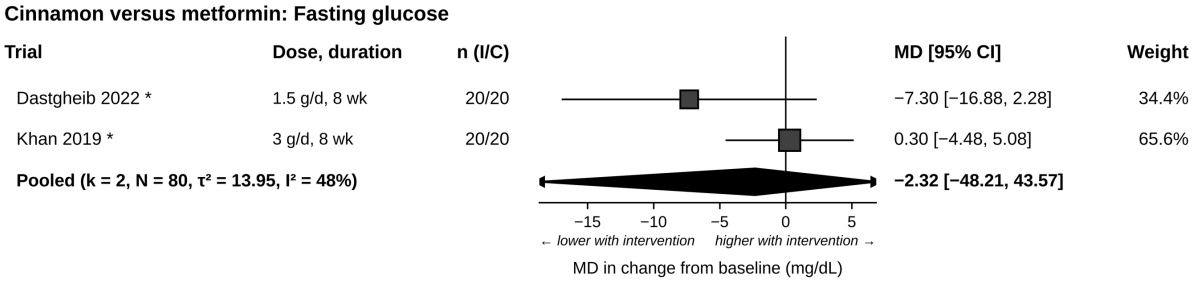
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). ‡ change SD derived from the within-group 95% CI reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S24. Forest plot for Waist circumference with Cinnamon versus placebo (revised analysis)



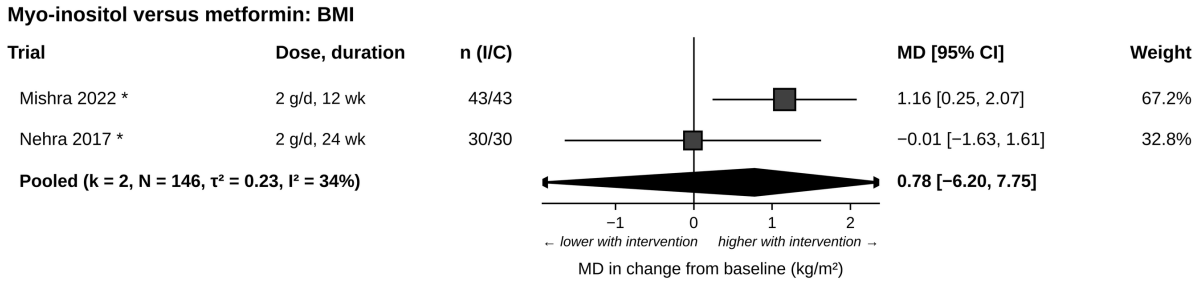
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S25. Forest plot for Fasting glucose with Cinnamon versus metformin (revised analysis)



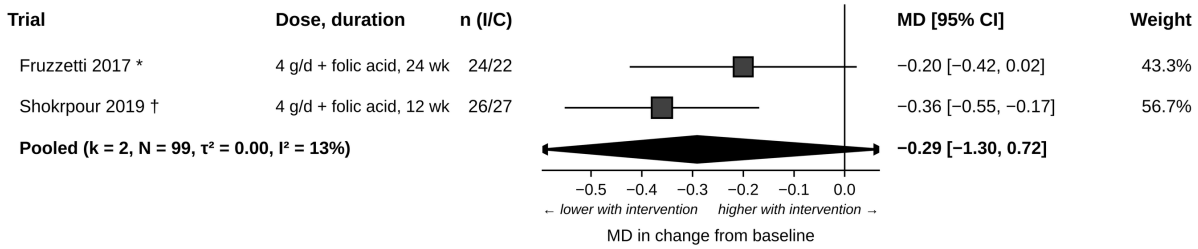
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S26. Forest plot for BMI with Myo-inositol versus metformin (revised analysis)



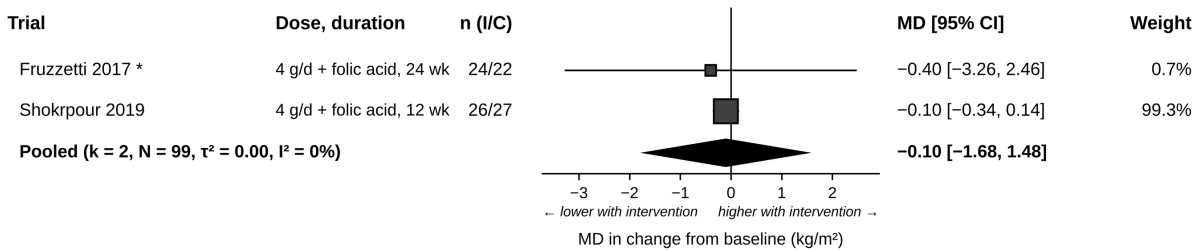
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S27. Forest plot for HOMA-IR with Myo-inositol + folic acid versus metformin (revised analysis)



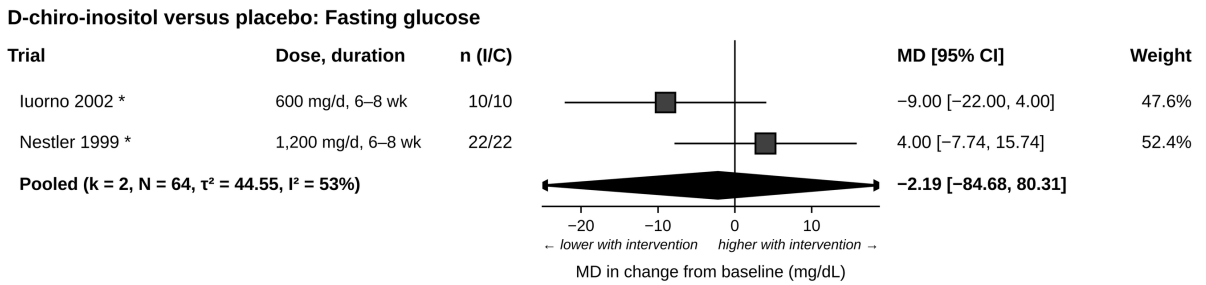
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S28. Forest plot for BMI with Myo-inositol + folic acid versus metformin (revised analysis)



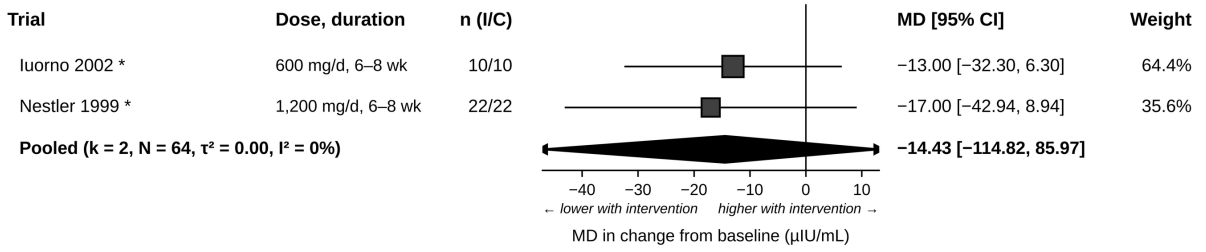
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S29. Forest plot for Fasting glucose with D-chiro-inositol versus placebo (revised analysis)



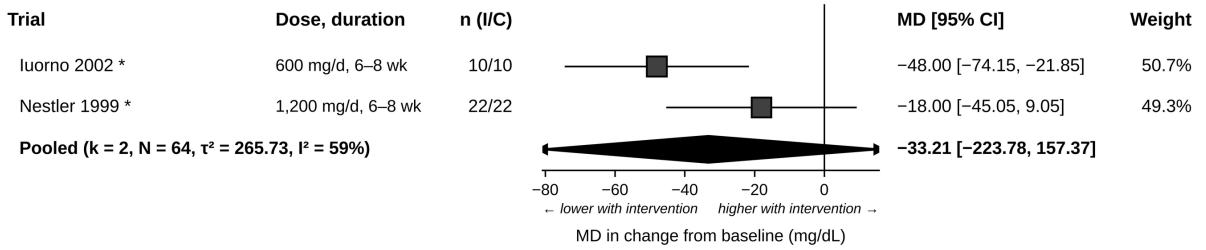
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S30. Forest plot for Fasting insulin with D-chiro-inositol versus placebo (revised analysis)



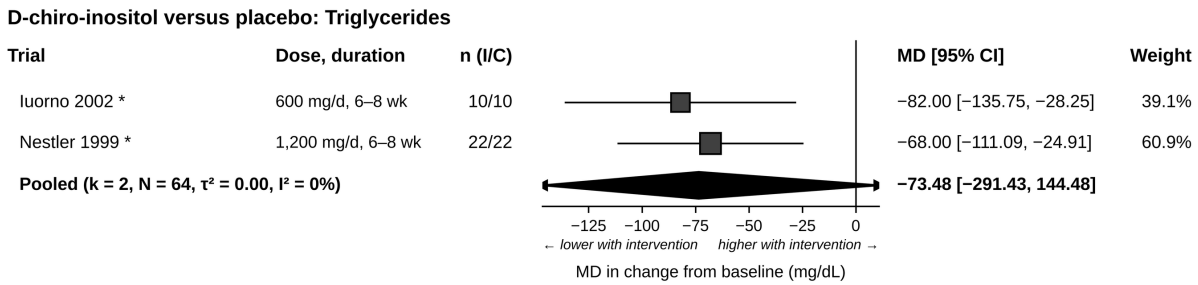
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S31. Forest plot for Total cholesterol with D-chiro-inositol versus placebo (revised analysis)



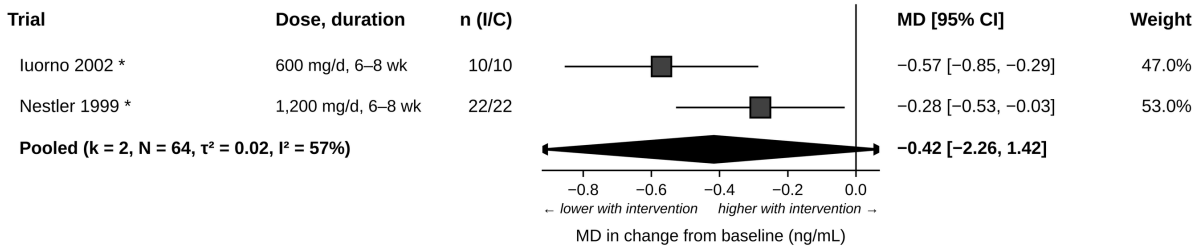
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S32. Forest plot for Triglycerides with D-chiro-inositol versus placebo (revised analysis)



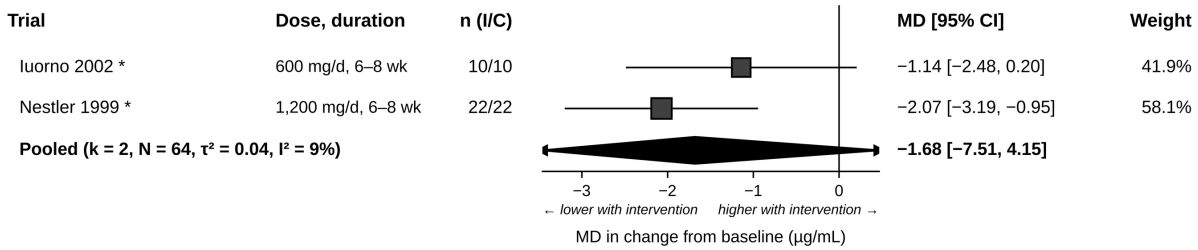
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S33. Forest plot for Total testosterone with D-chiro-inositol versus placebo (revised analysis)



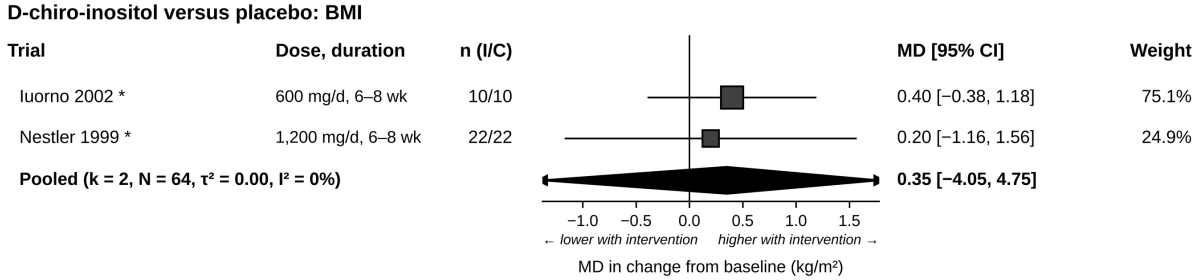
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S34. Forest plot for DHEAS with D-chiro-inositol versus placebo (revised analysis)



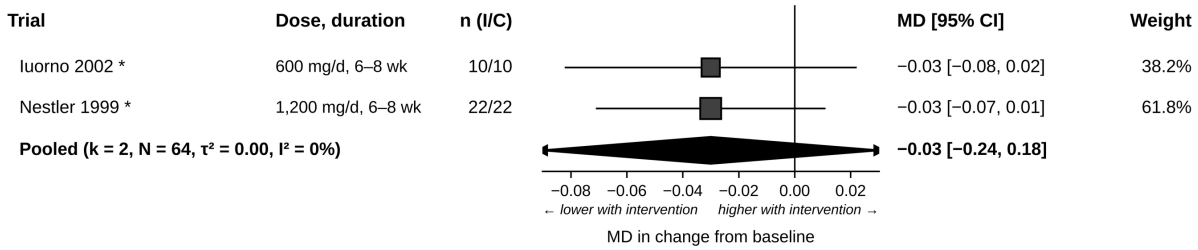
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S35. Forest plot for BMI with D-chiro-inositol versus placebo (revised analysis)



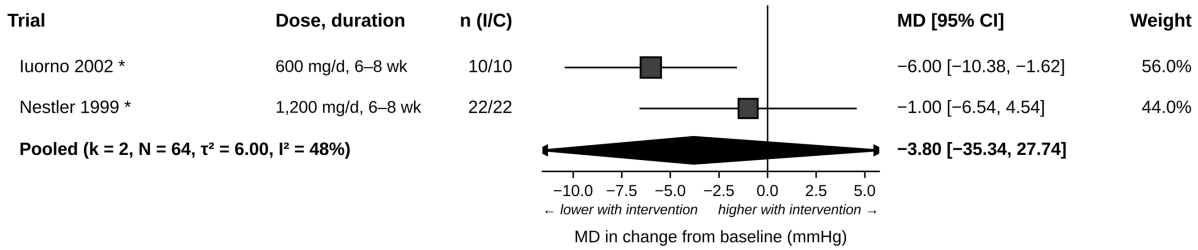
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S36. Forest plot for Waist-to-hip ratio with D-chiro-inositol versus placebo (revised analysis)



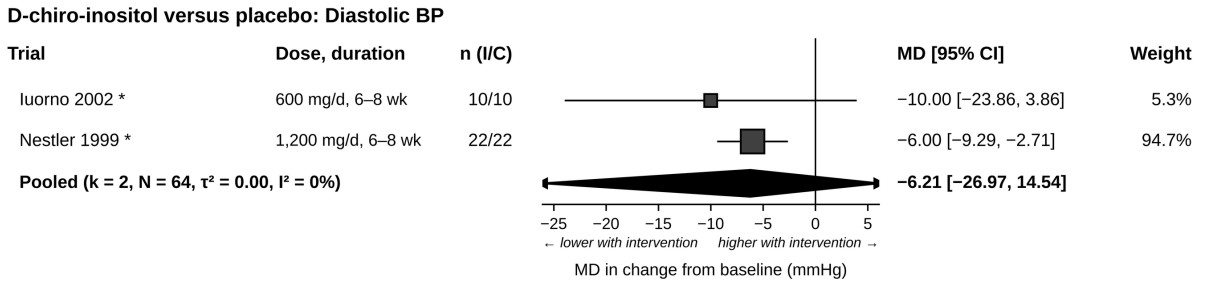
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S37. Forest plot for Systolic BP with D-chiro-inositol versus placebo (revised analysis)



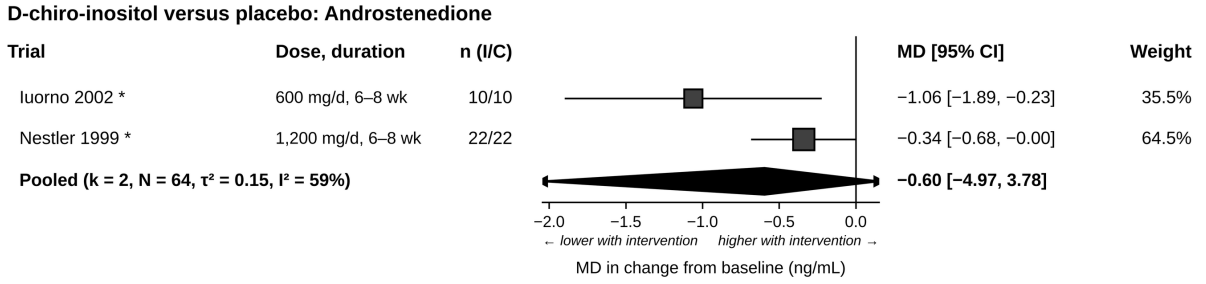
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S38. Forest plot for Diastolic BP with D-chiro-inositol versus placebo (revised analysis)



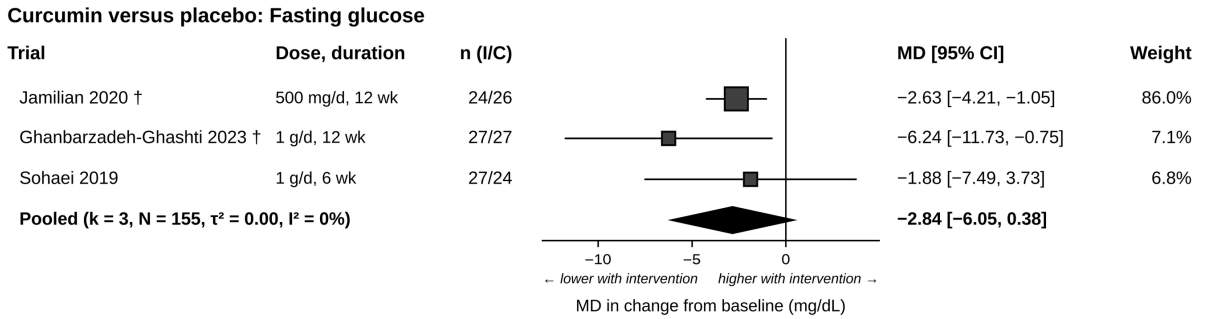
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S39. Forest plot for Androstenedione with D-chiro-inositol versus placebo (revised analysis)



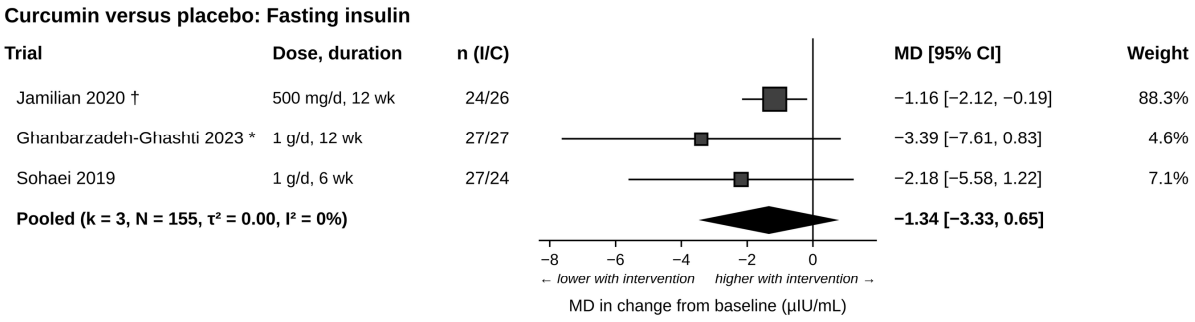
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S40. Forest plot for Fasting glucose with Curcumin versus placebo (revised analysis)



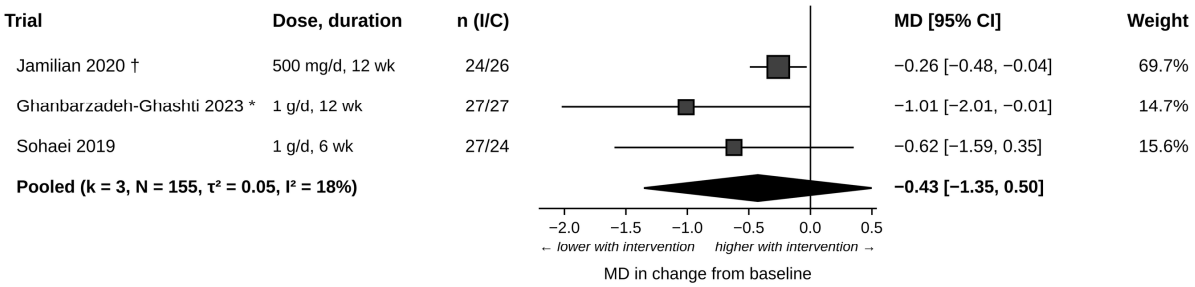
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S41. Forest plot for Fasting insulin with Curcumin versus placebo (revised analysis)



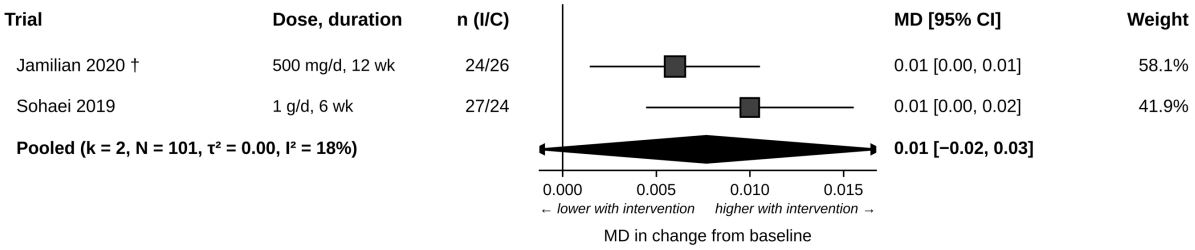
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S42. Forest plot for HOMA-IR with Curcumin versus placebo (revised analysis)



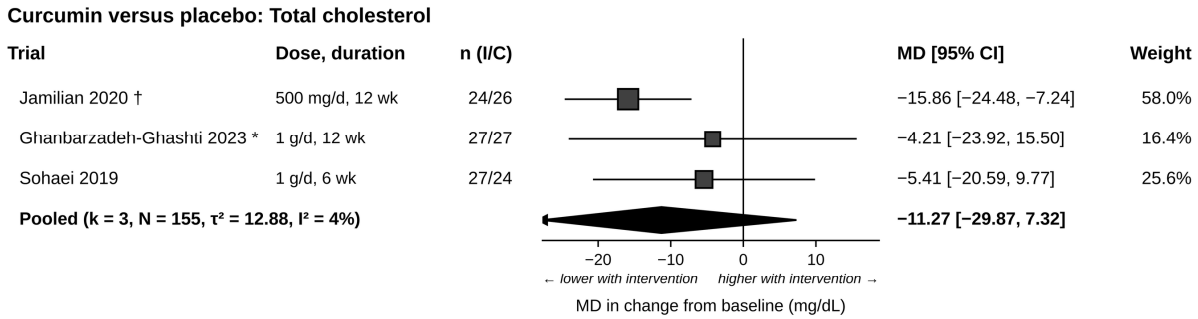
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S43. Forest plot for QUICKI with Curcumin versus placebo (revised analysis)



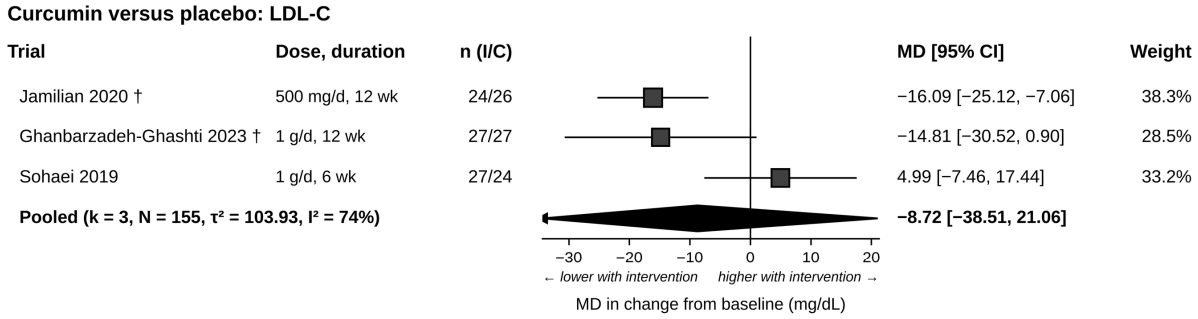
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S44. Forest plot for Total cholesterol with Curcumin versus placebo (revised analysis)



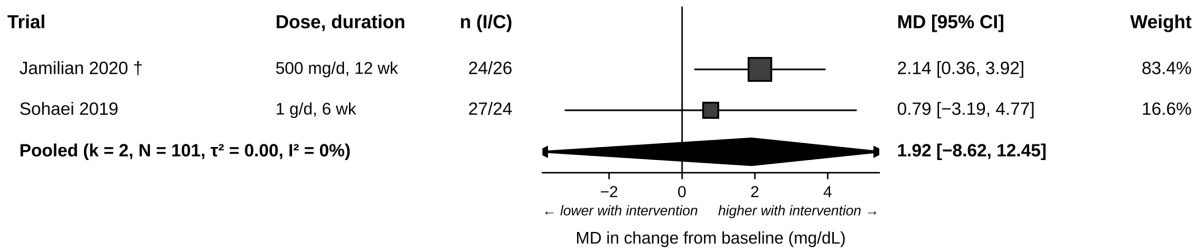
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S45. Forest plot for LDL-C with Curcumin versus placebo (revised analysis)



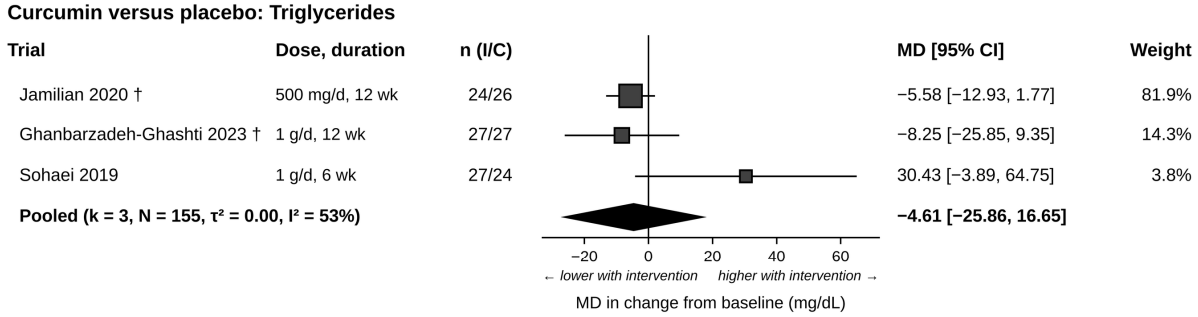
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S46. Forest plot for HDL-C with Curcumin versus placebo (revised analysis)



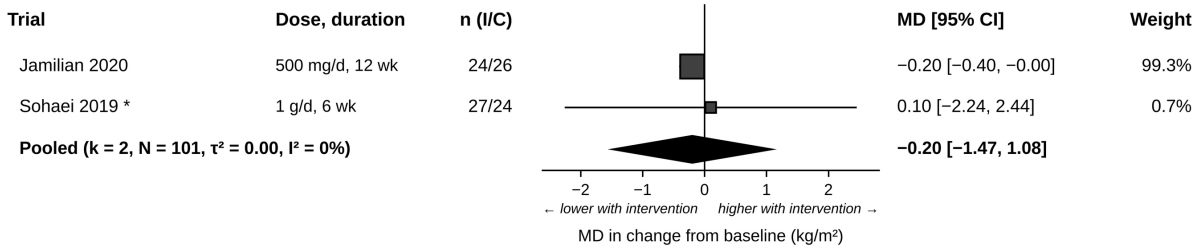
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S47. Forest plot for Triglycerides with Curcumin versus placebo (revised analysis)



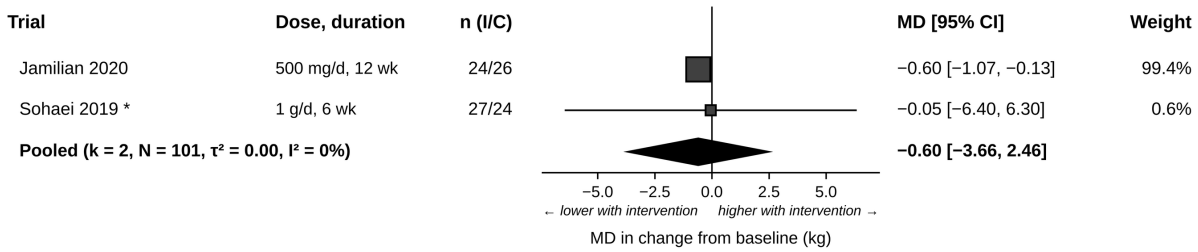
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). † baseline-adjusted between-group difference reported by the trial. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S48. Forest plot for BMI with Curcumin versus placebo (revised analysis)



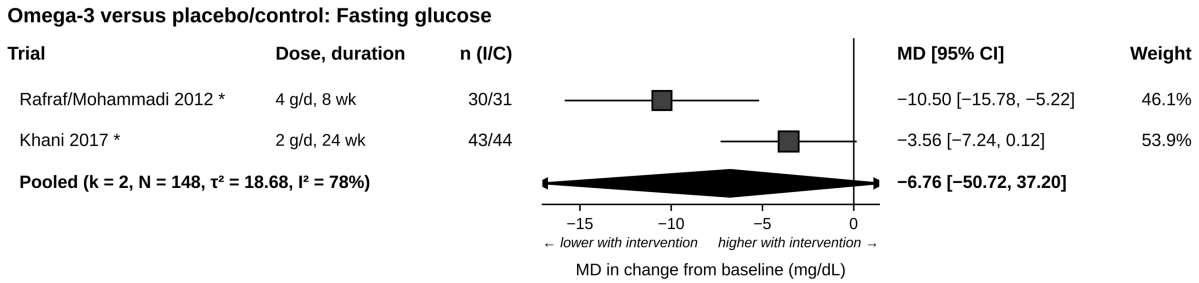
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S49. Forest plot for Body weight with Curcumin versus placebo (revised analysis)



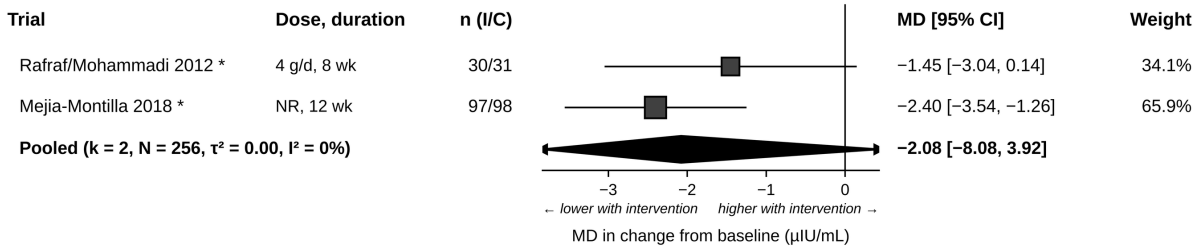
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S50. Forest plot for Fasting glucose with Omega-3 versus placebo/control (revised analysis)



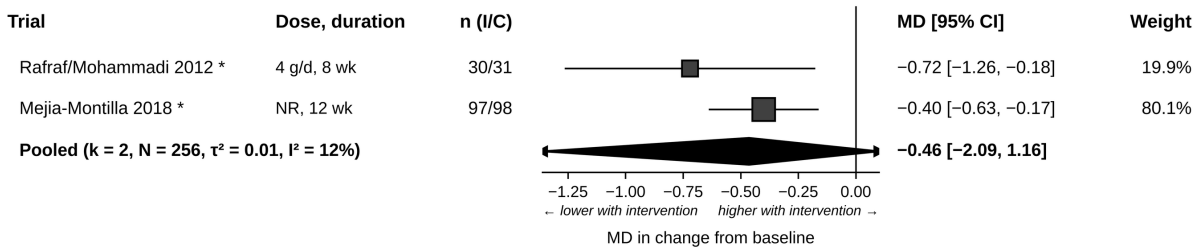
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S51. Forest plot for Fasting insulin with Omega-3 versus placebo/control (revised analysis)



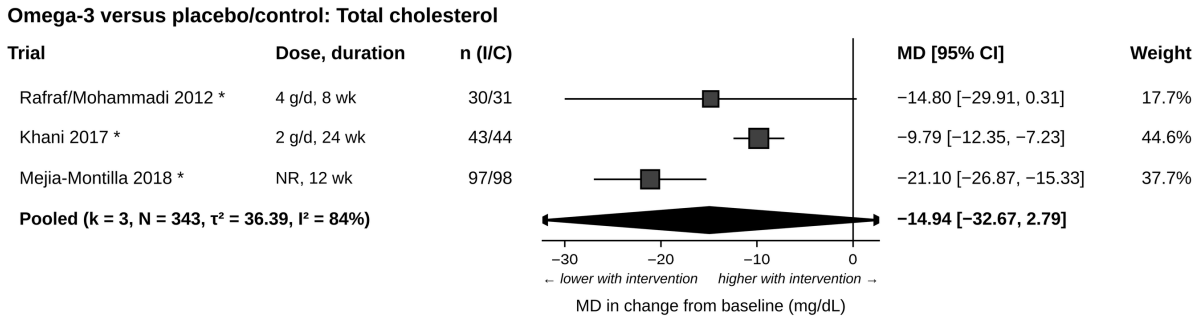
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). NR: not reported. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S52. Forest plot for HOMA-IR with Omega-3 versus placebo/control (revised analysis)



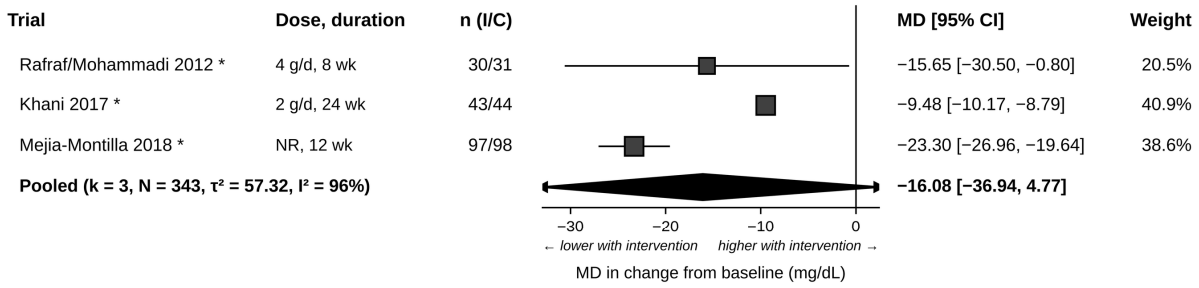
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). NR: not reported. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S53. Forest plot for Total cholesterol with Omega-3 versus placebo/control (revised analysis)



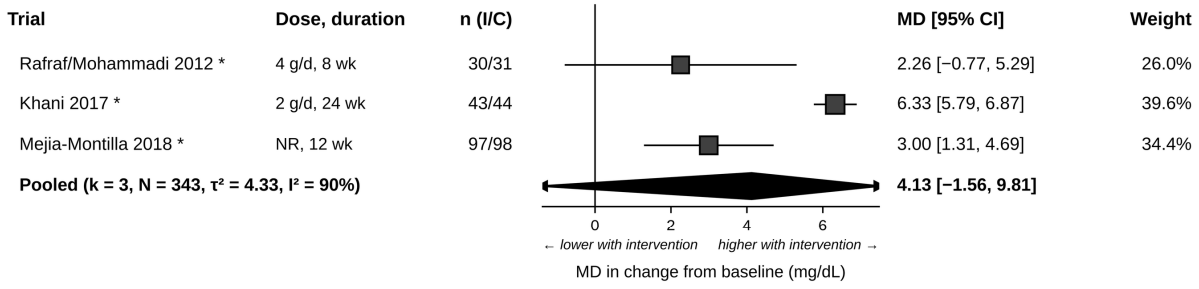
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). NR: not reported. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S54. Forest plot for LDL-C with Omega-3 versus placebo/control (revised analysis)



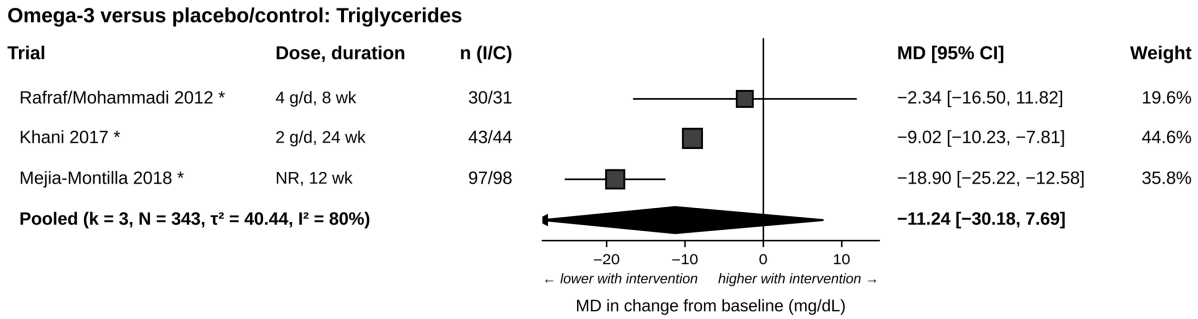
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). NR: not reported. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S55. Forest plot for HDL-C with Omega-3 versus placebo/control (revised analysis)



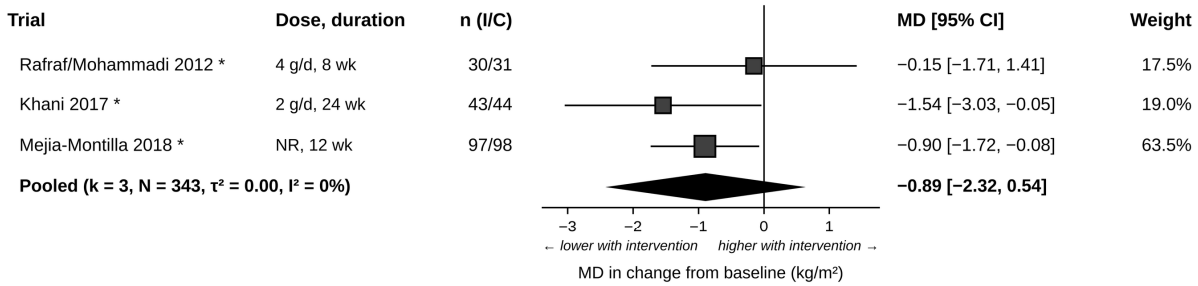
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). NR: not reported. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S56. Forest plot for Triglycerides with Omega-3 versus placebo/control (revised analysis)



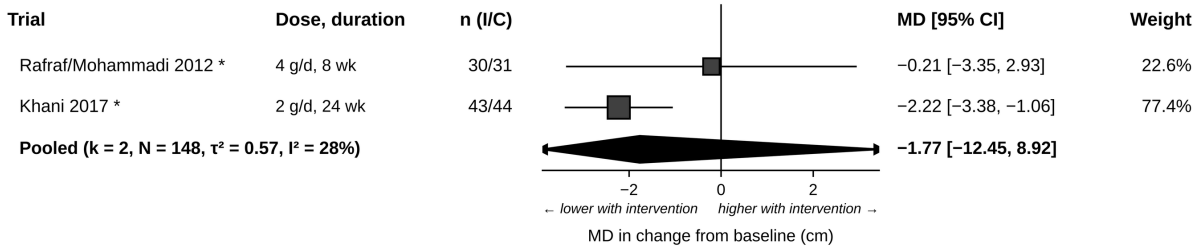
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). NR: not reported. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S57. Forest plot for BMI with Omega-3 versus placebo/control (revised analysis)



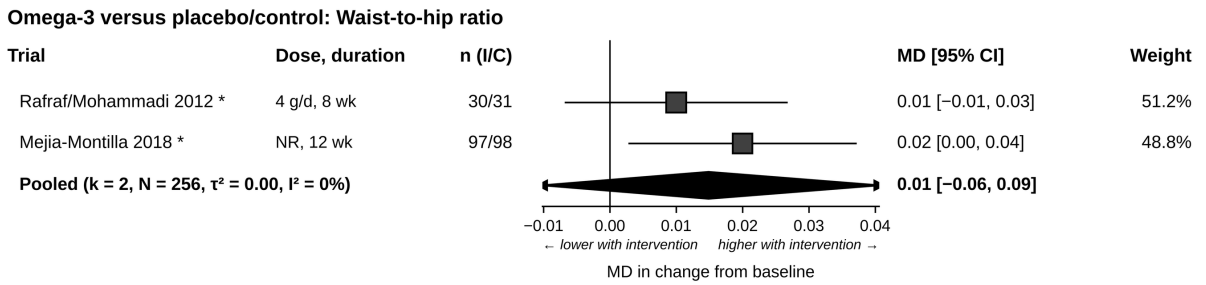
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). NR: not reported. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S58. Forest plot for Waist circumference with Omega-3 versus placebo/control (revised analysis)



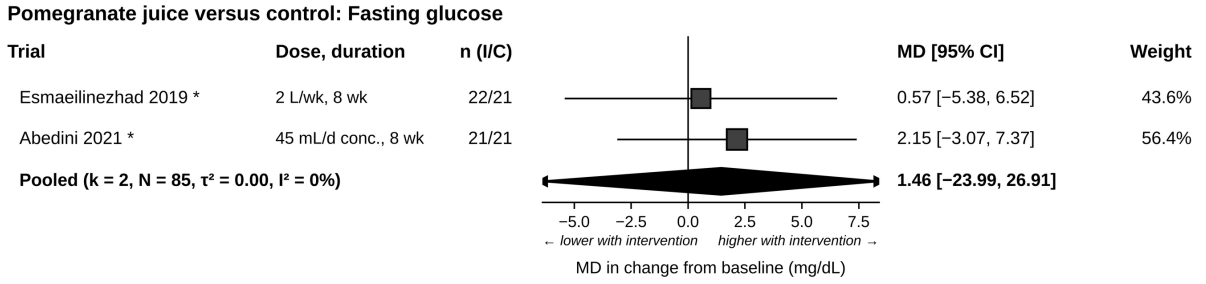
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S59. Forest plot for Waist-to-hip ratio with Omega-3 versus placebo/control (revised analysis)



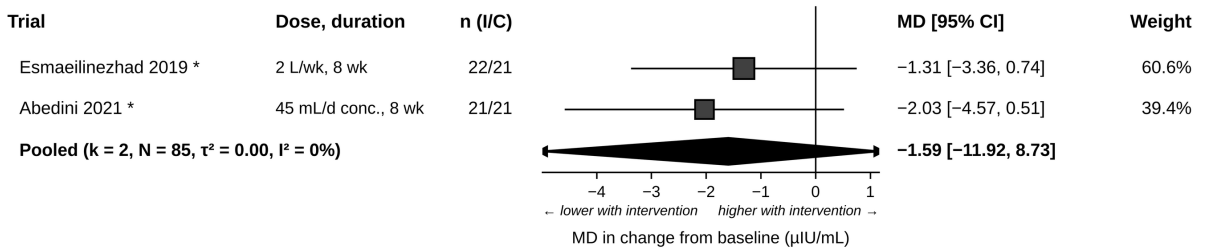
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). NR: not reported. Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S60. Forest plot for Fasting glucose with Pomegranate juice versus control (revised analysis)



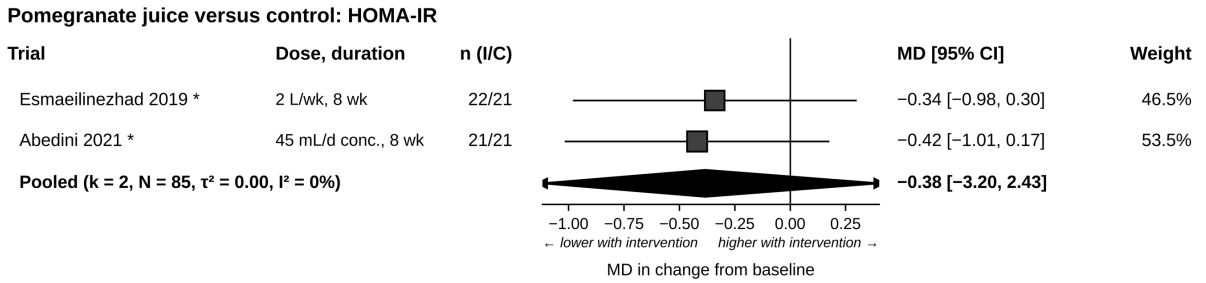
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S61. Forest plot for Fasting insulin with Pomegranate juice versus control (revised analysis)



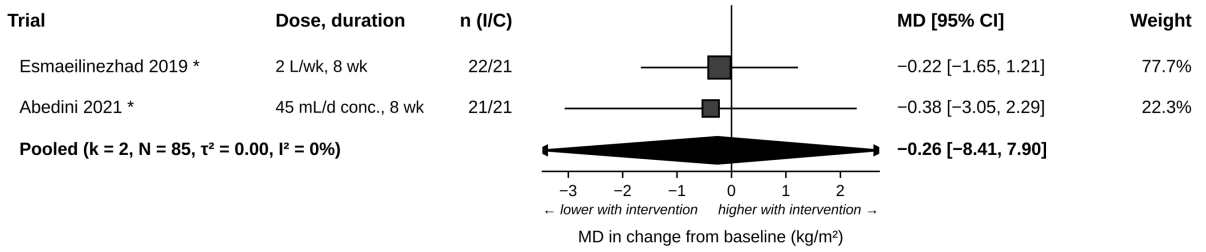
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ², modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S62. Forest plot for HOMA-IR with Pomegranate juice versus control (revised analysis)



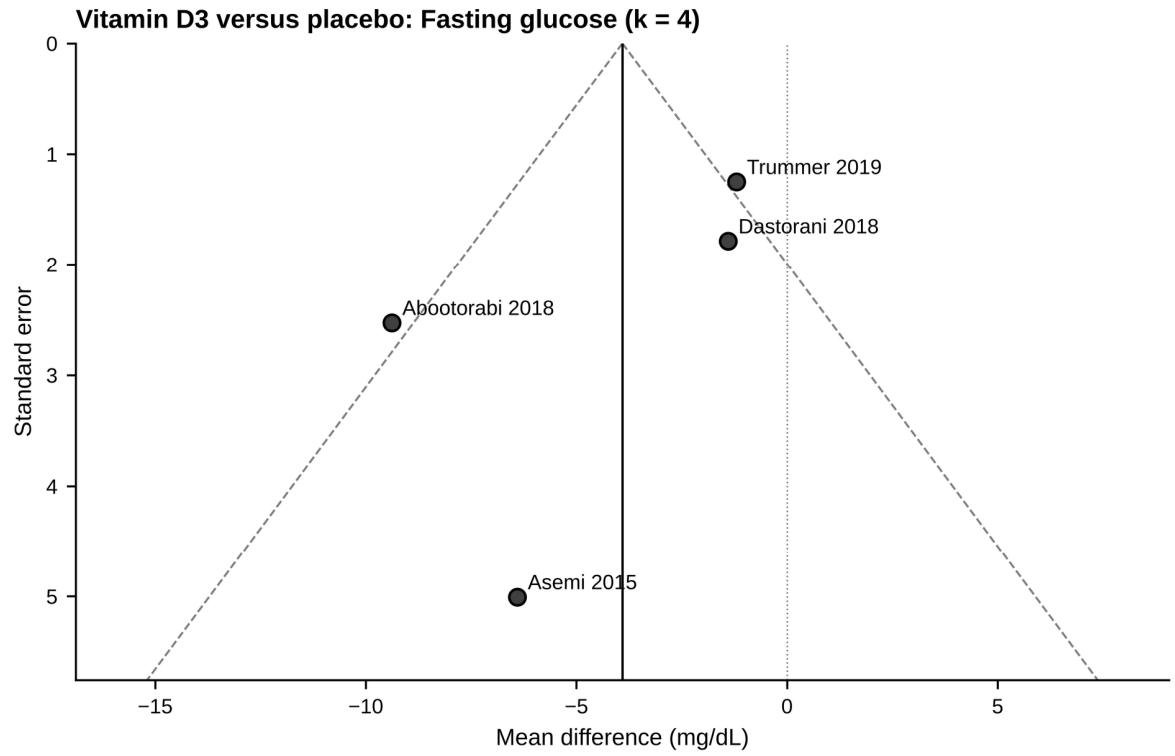
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ^2, modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S63. Forest plot for BMI with Pomegranate juice versus control (revised analysis)



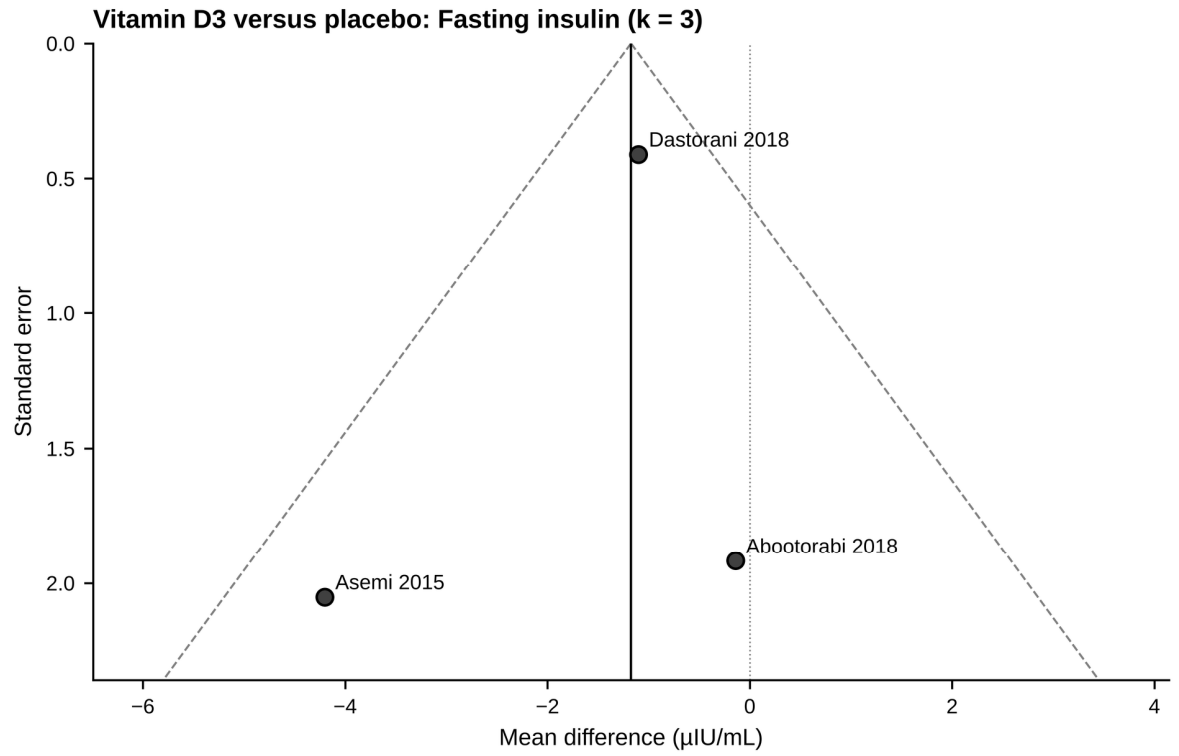
Squares: trial estimates with normal-approximation 95% CI. Diamond: random-effects pool (REML τ^2, modified Hartung–Knapp 95% CI). * change SD imputed from baseline and final SDs (r = 0.5). Arrows: CI extends beyond the plotted range. I/C: intervention/comparator, wk: weeks, d: day.

Figure S64. Funnel plot for Fasting glucose with Vitamin D3 versus placebo (descriptive only)



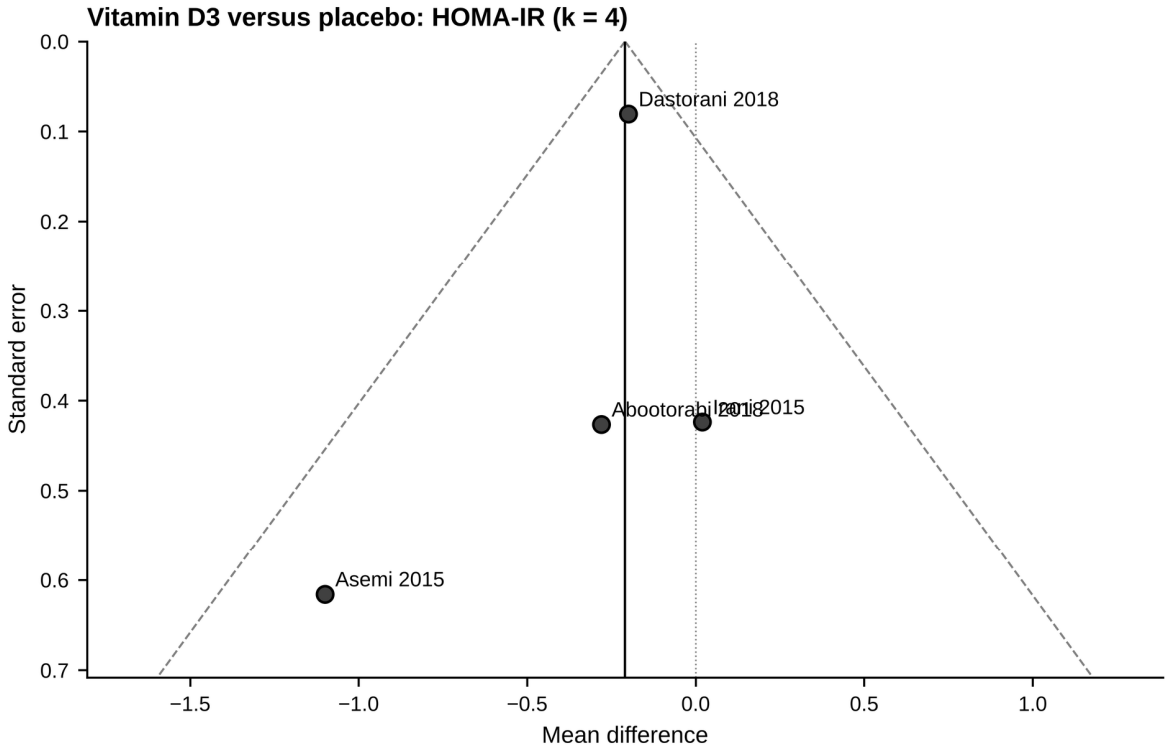
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S65. Funnel plot for Fasting insulin with Vitamin D3 versus placebo (descriptive only)



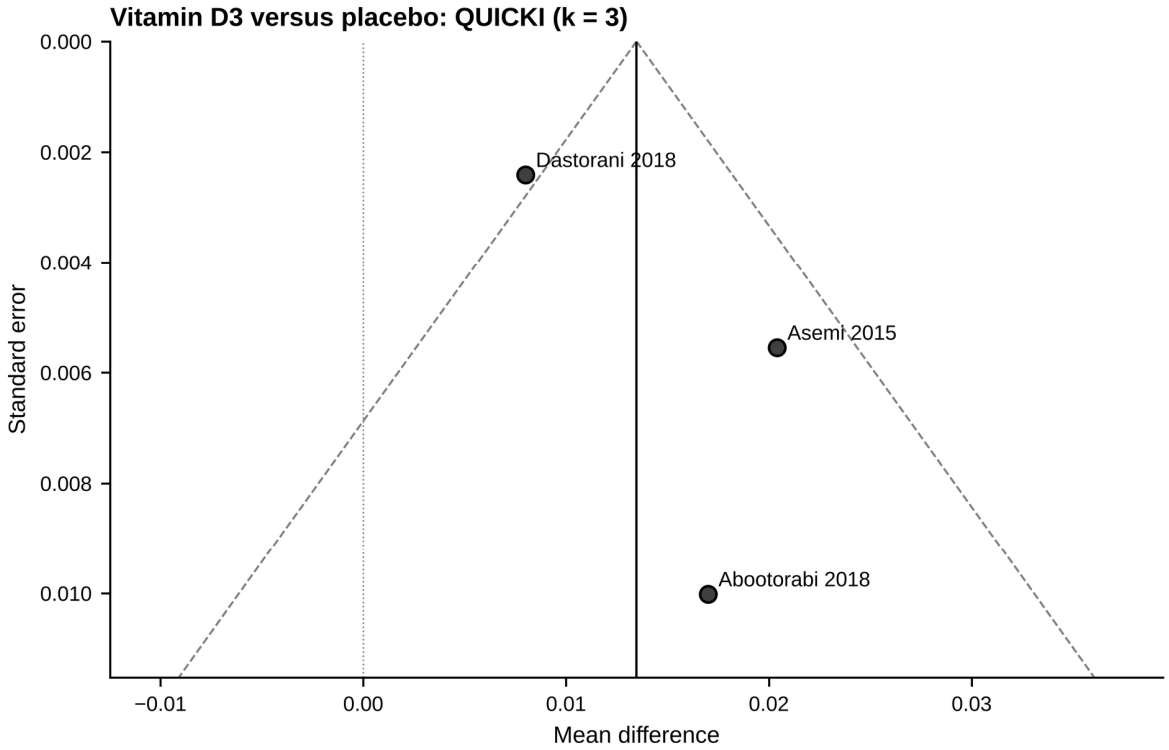
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S66. Funnel plot for HOMA-IR with Vitamin D3 versus placebo (descriptive only)



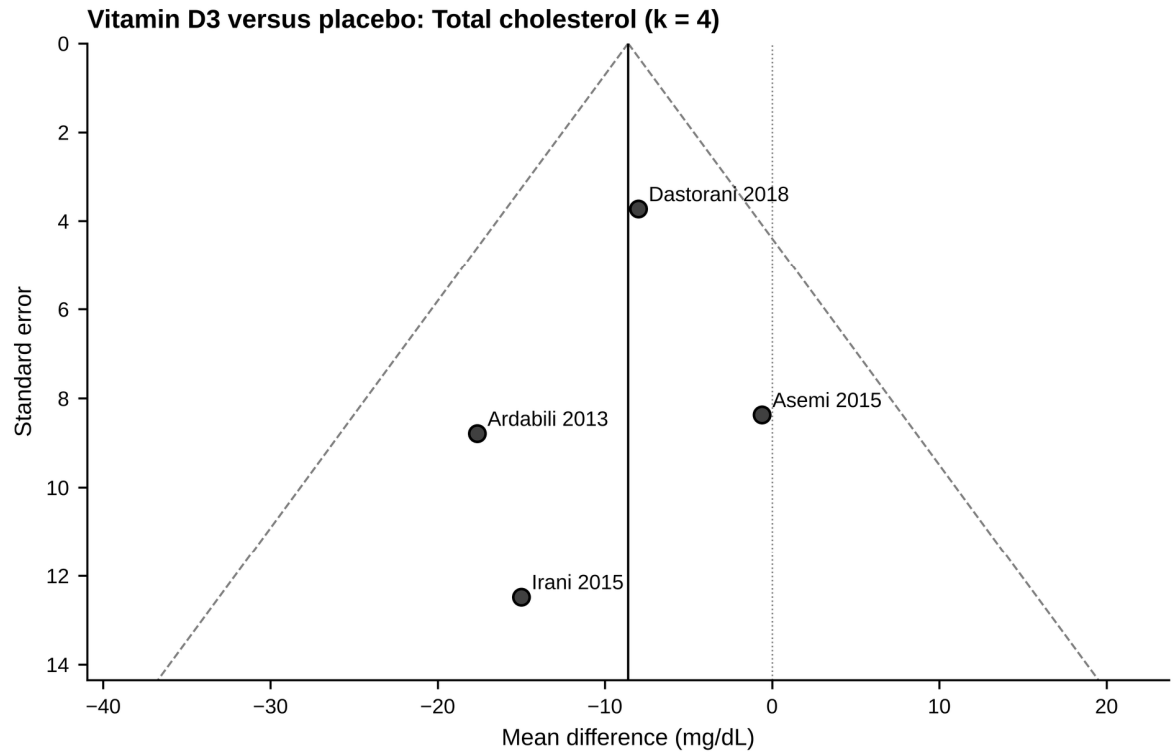
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S67. Funnel plot for QUICKI with Vitamin D3 versus placebo (descriptive only)



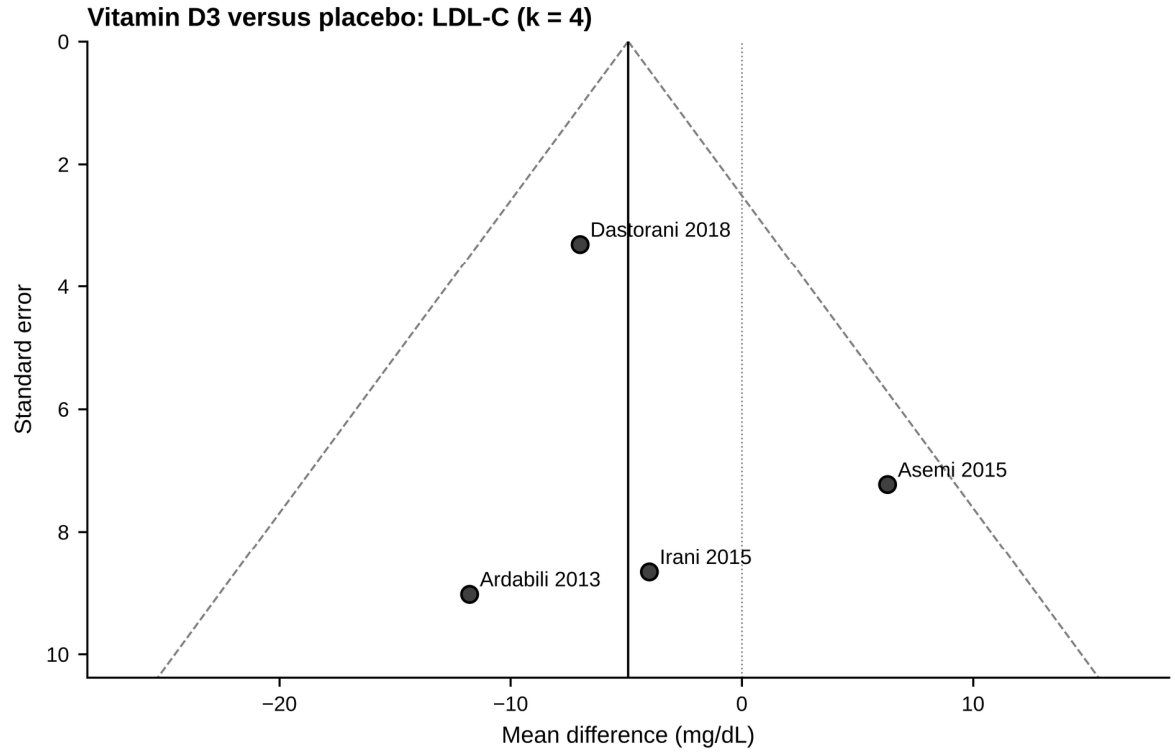
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S68. Funnel plot for Total cholesterol with Vitamin D3 versus placebo (descriptive only)



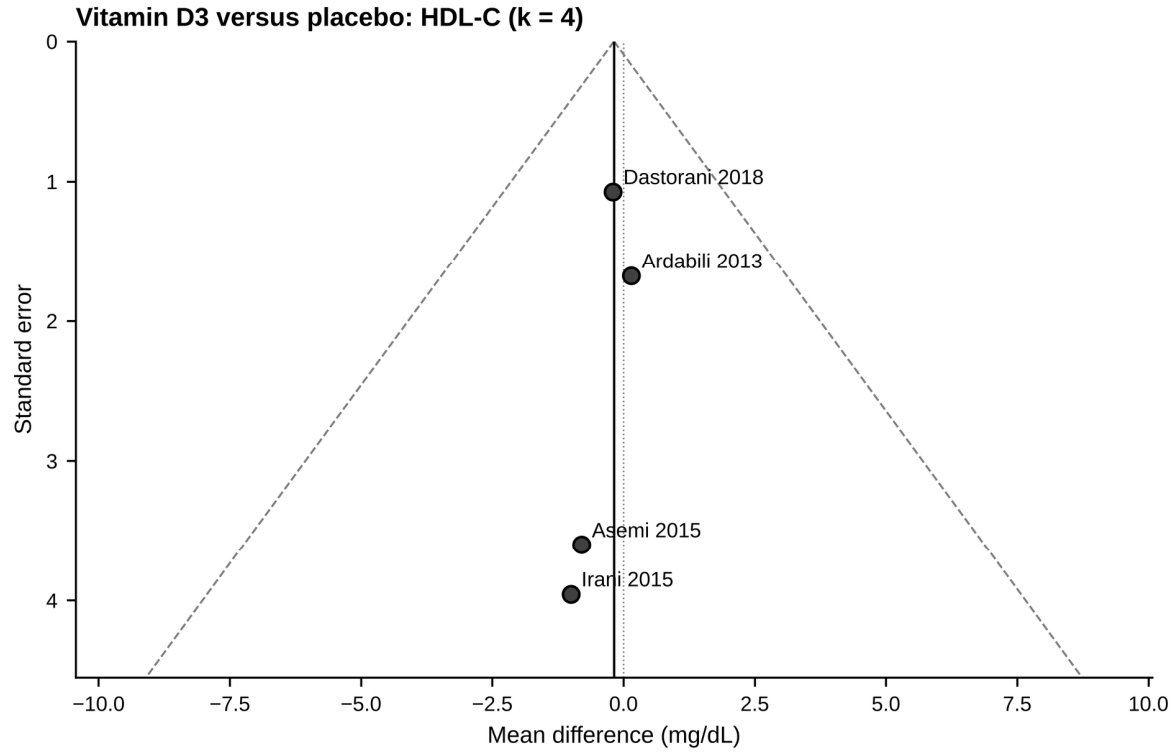
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S69. Funnel plot for LDL-C with Vitamin D3 versus placebo (descriptive only)



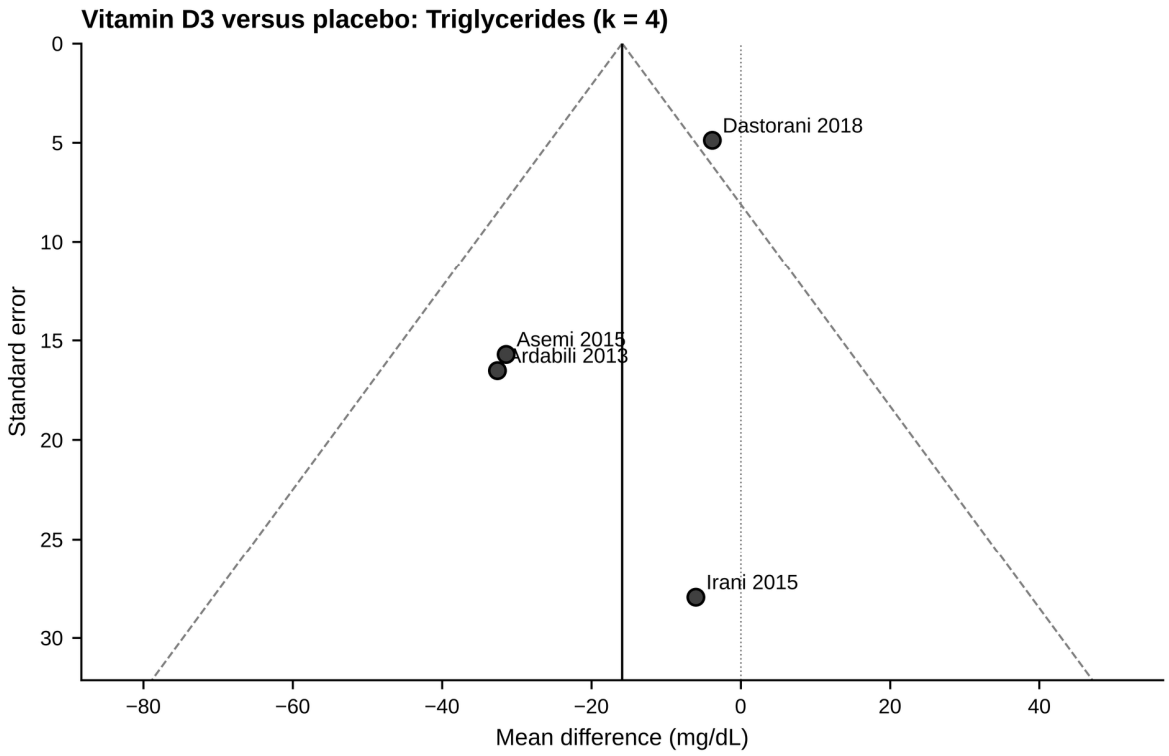
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S70. Funnel plot for HDL-C with Vitamin D3 versus placebo (descriptive only)



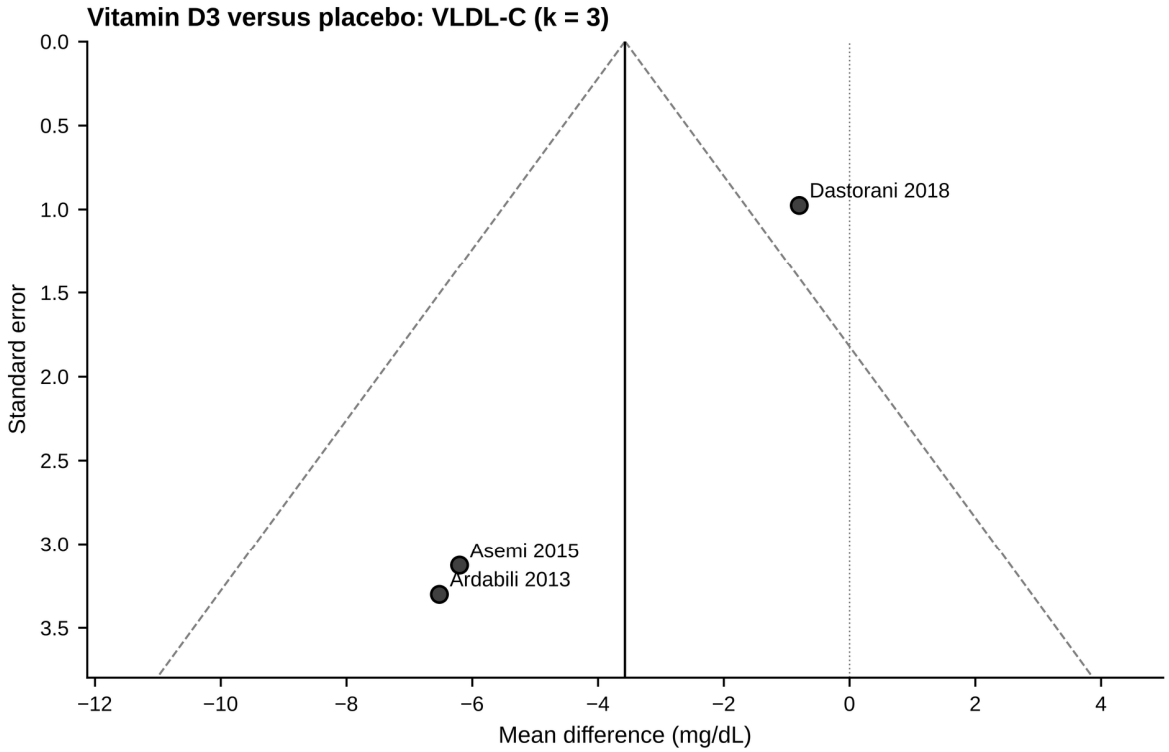
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S71. Funnel plot for Triglycerides with Vitamin D3 versus placebo (descriptive only)



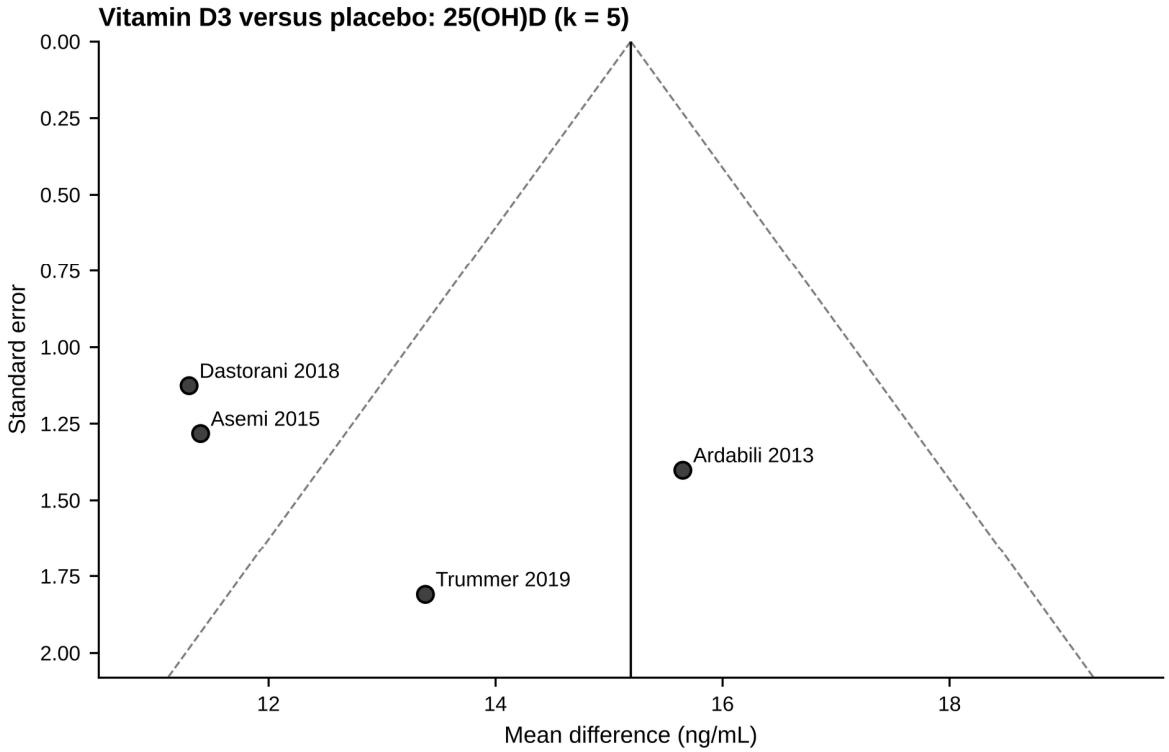
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S72. Funnel plot for VLDL-C with Vitamin D3 versus placebo (descriptive only)



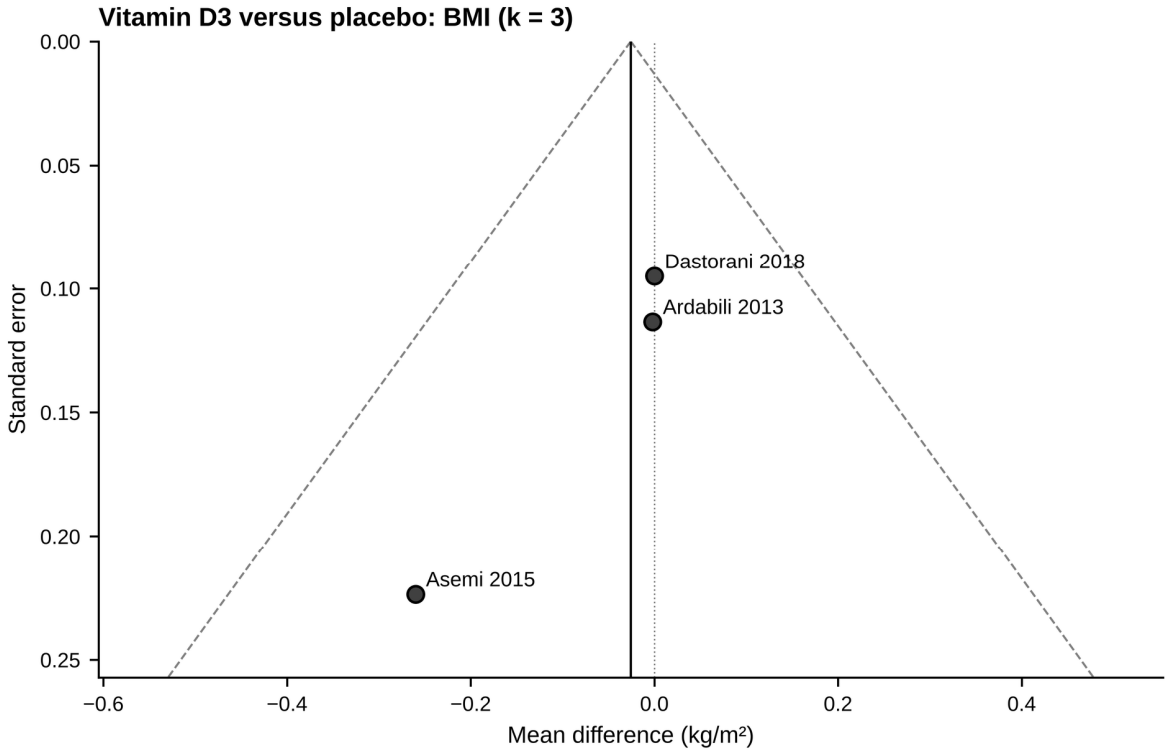
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S73. Funnel plot for 25(OH)D with Vitamin D3 versus placebo (descriptive only)



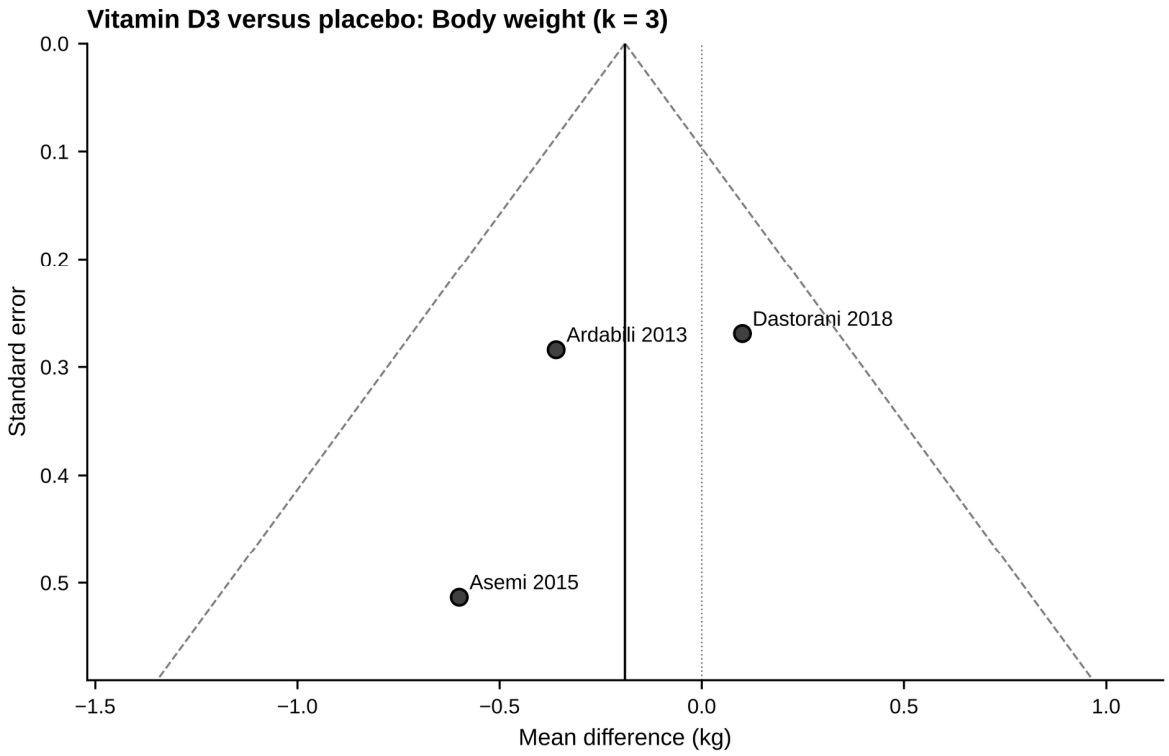
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S74. Funnel plot for BMI with Vitamin D3 versus placebo (descriptive only)



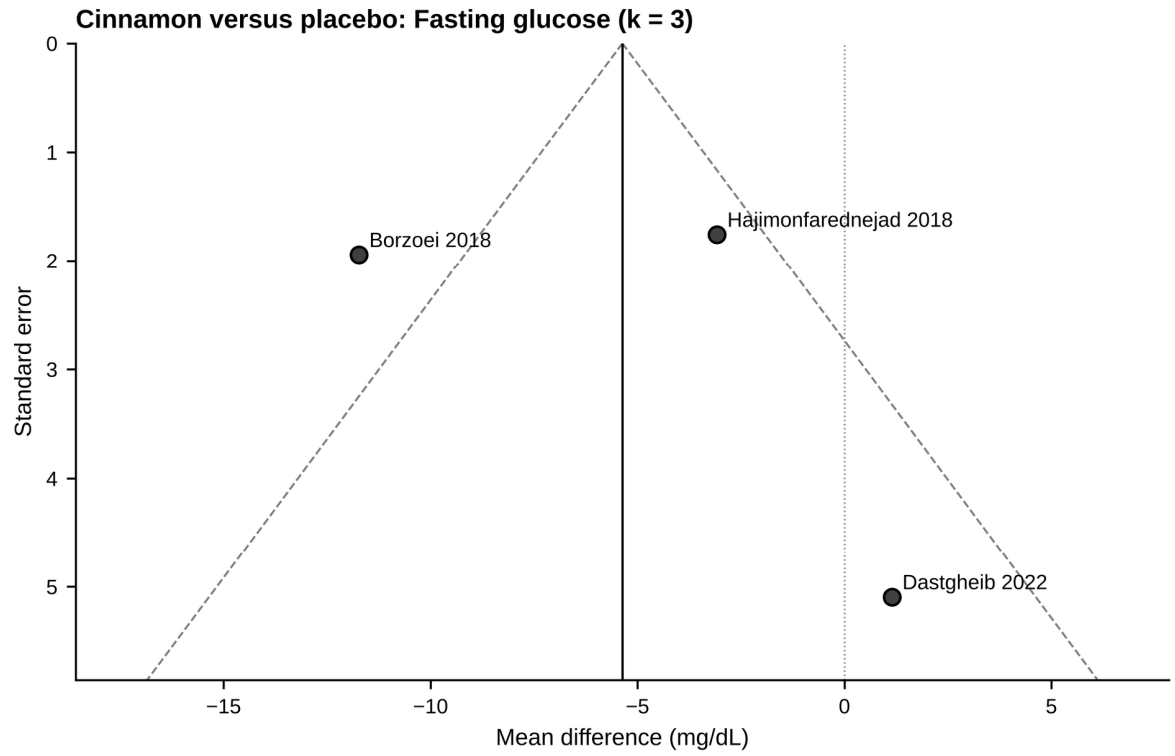
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S75. Funnel plot for Body weight with Vitamin D3 versus placebo (descriptive only)



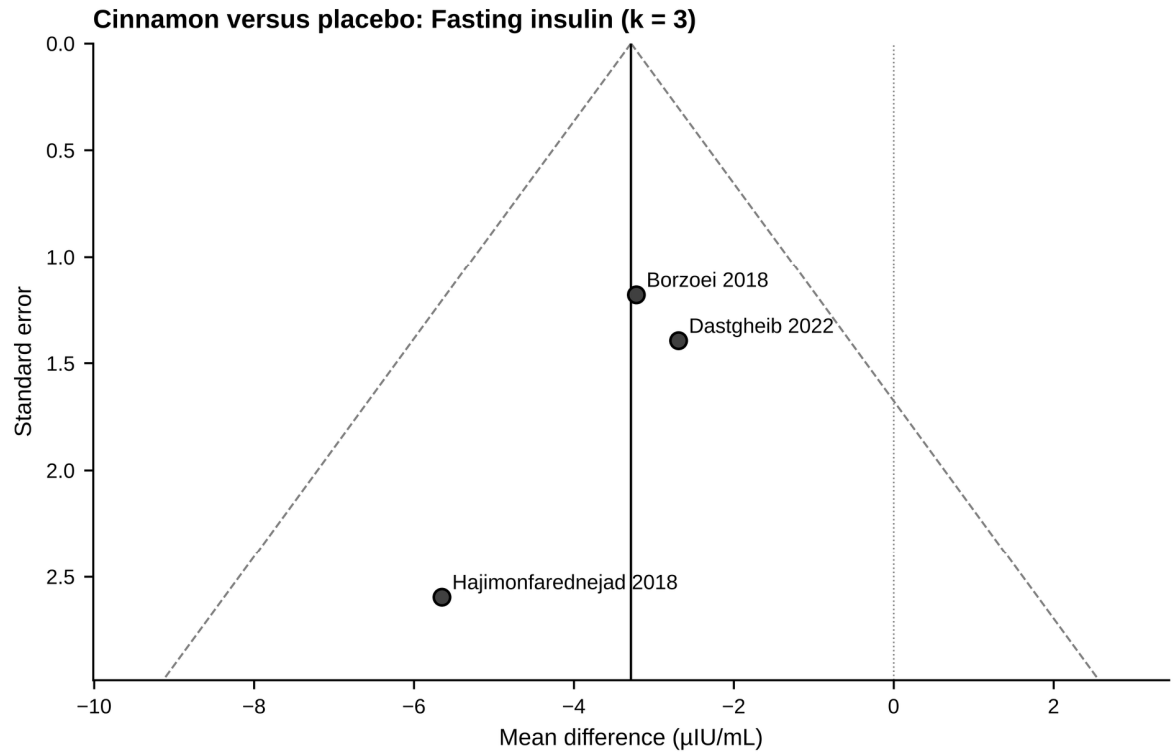
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S76. Funnel plot for Fasting glucose with Cinnamon versus placebo (descriptive only)



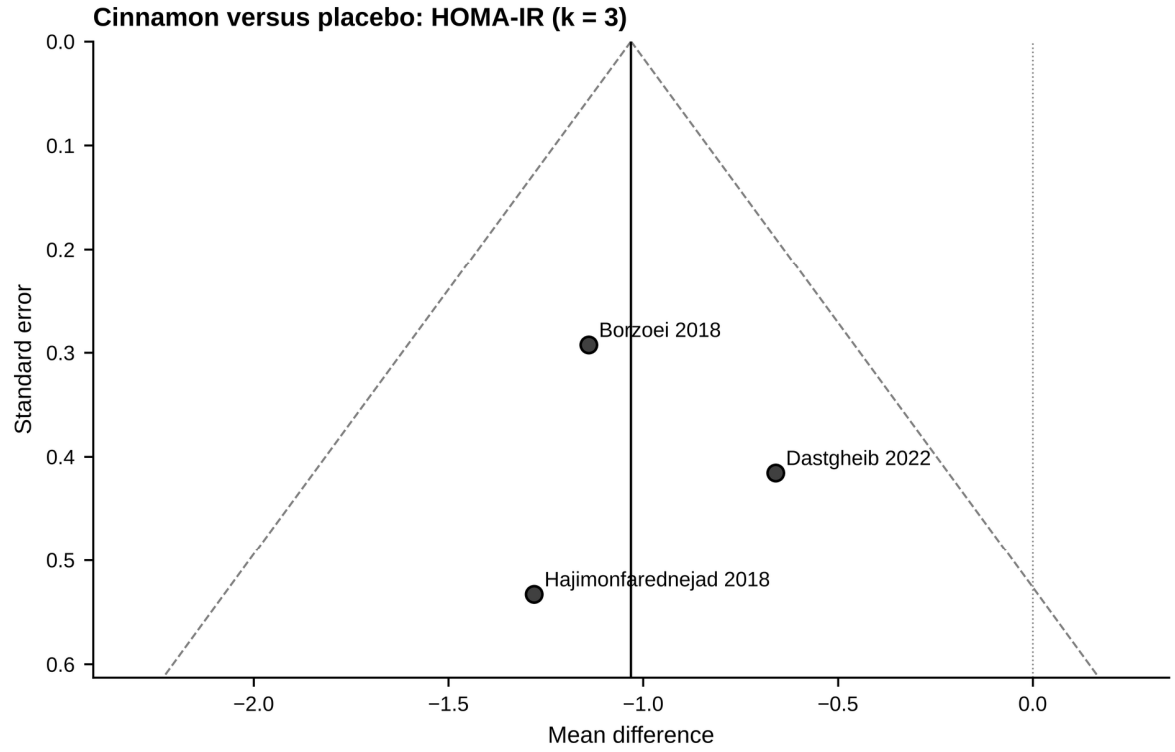
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S77. Funnel plot for Fasting insulin with Cinnamon versus placebo (descriptive only)



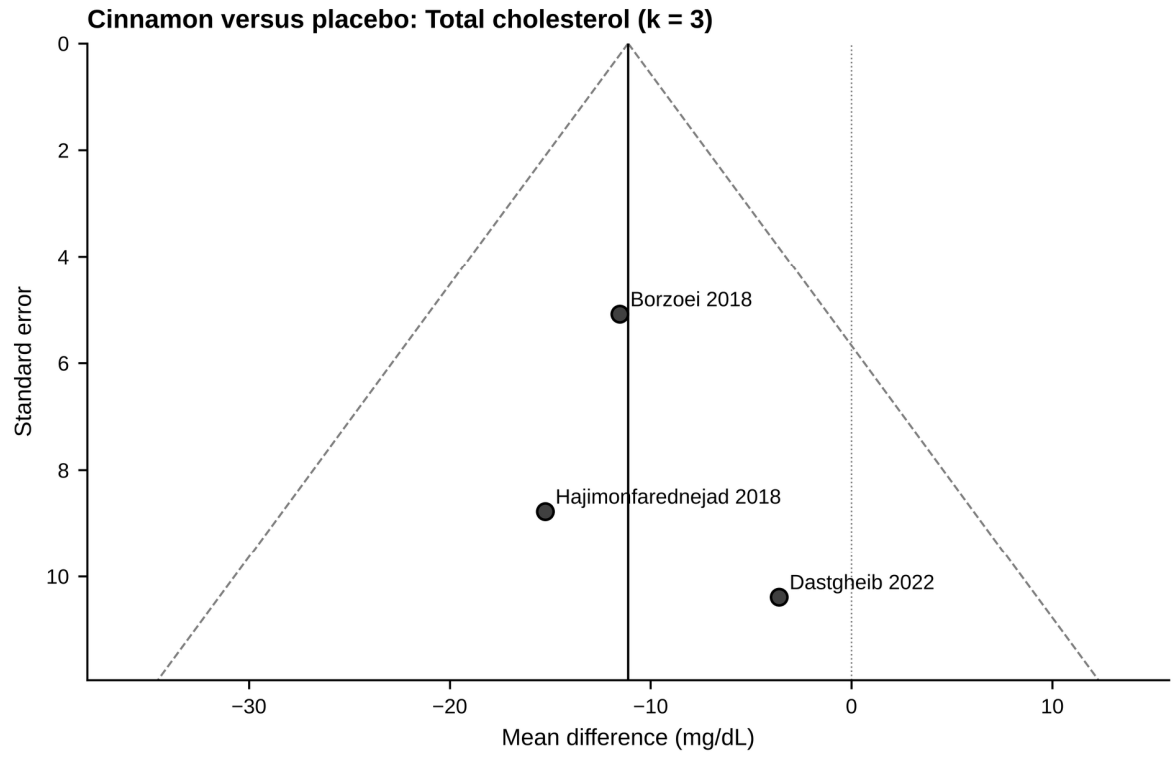
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S78. Funnel plot for HOMA-IR with Cinnamon versus placebo (descriptive only)



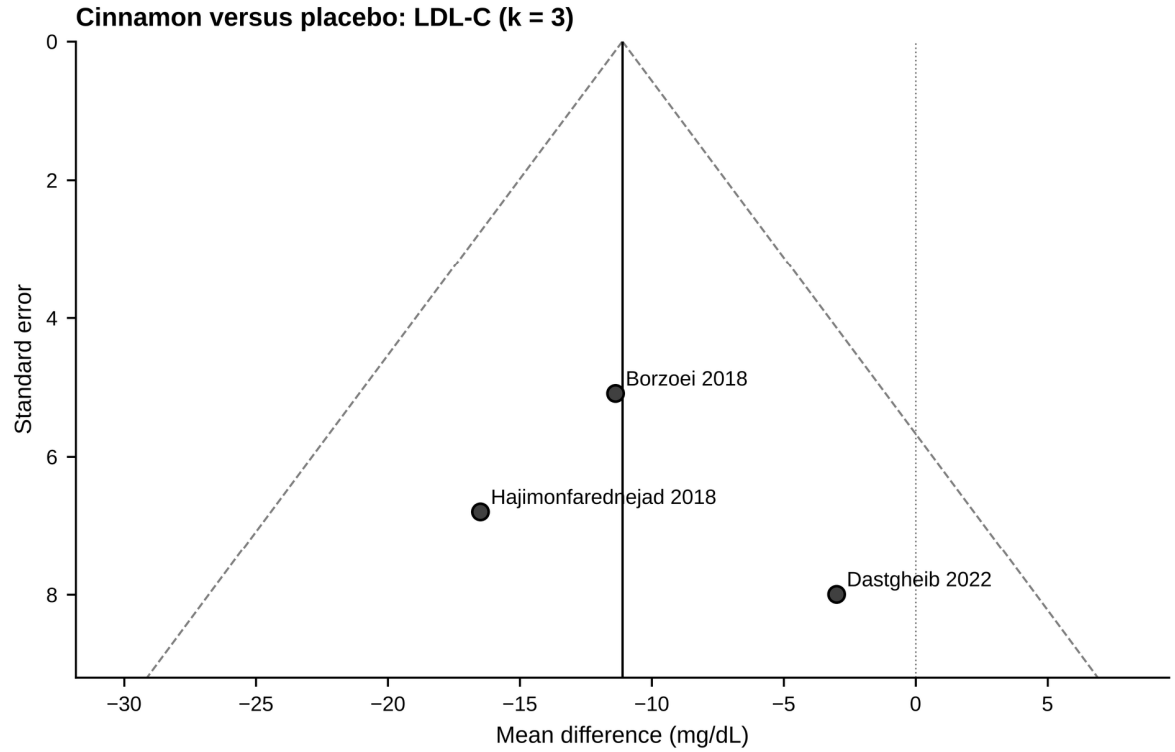
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S79. Funnel plot for Total cholesterol with Cinnamon versus placebo (descriptive only)



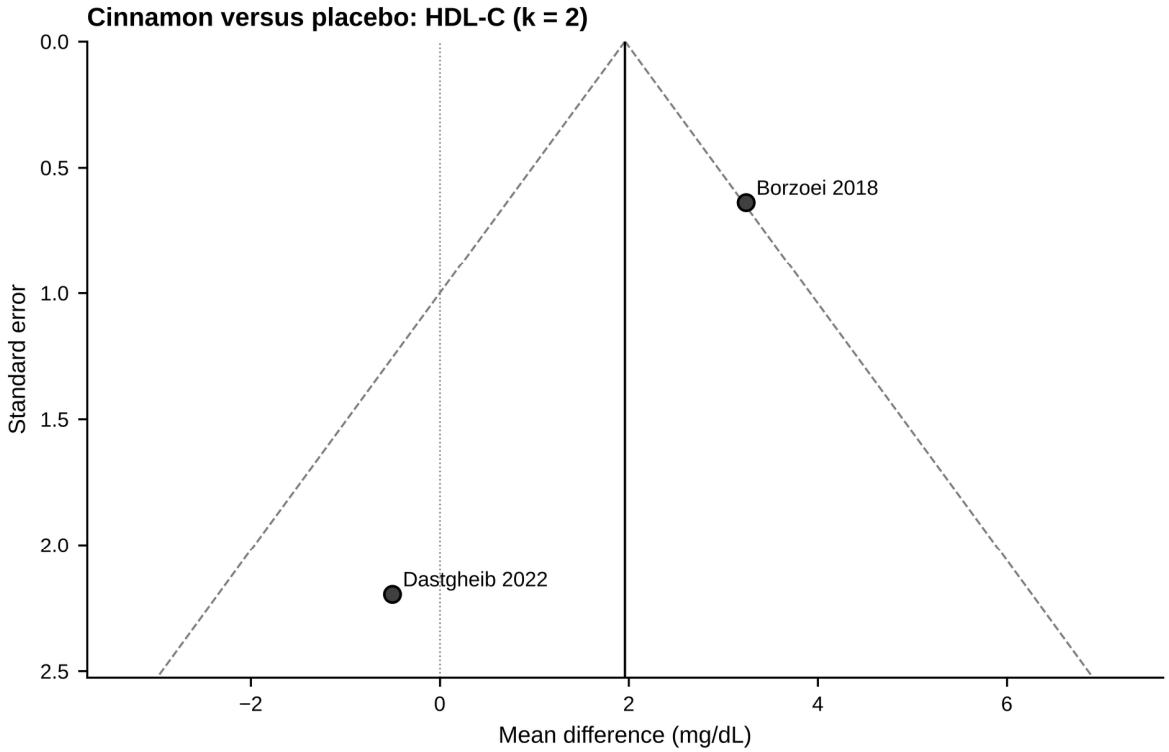
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S80. Funnel plot for LDL-C with Cinnamon versus placebo (descriptive only)



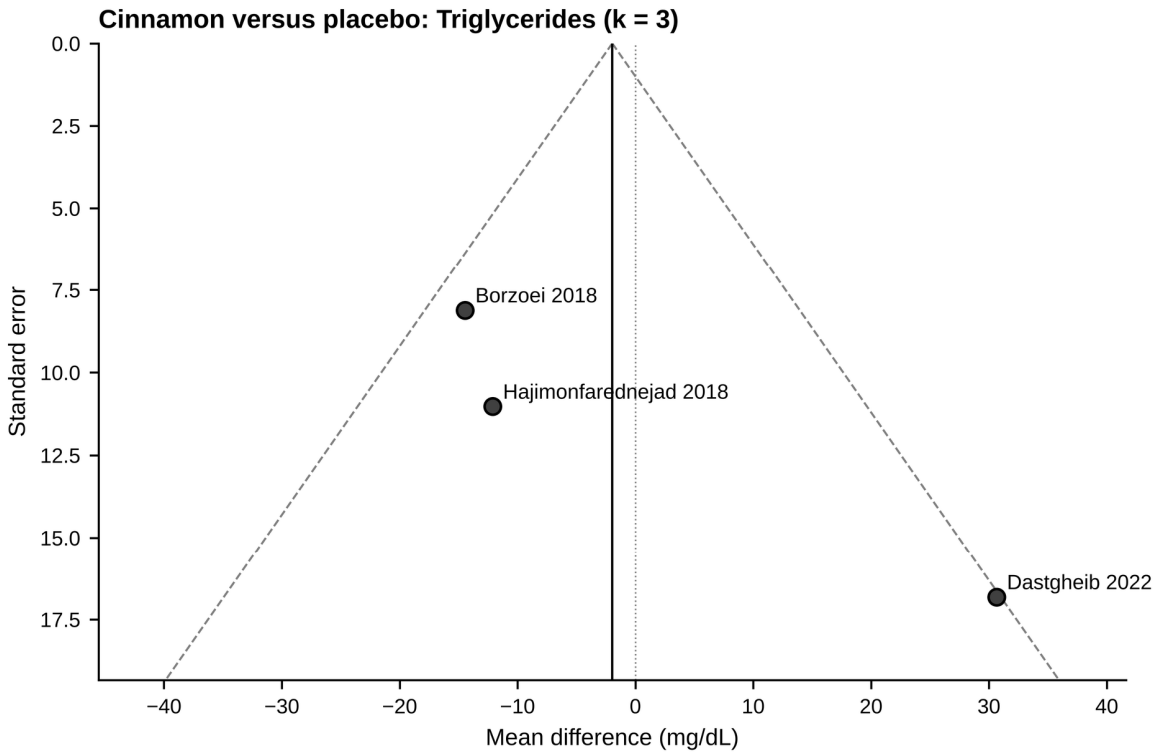
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S81. Funnel plot for HDL-C with Cinnamon versus placebo (descriptive only)



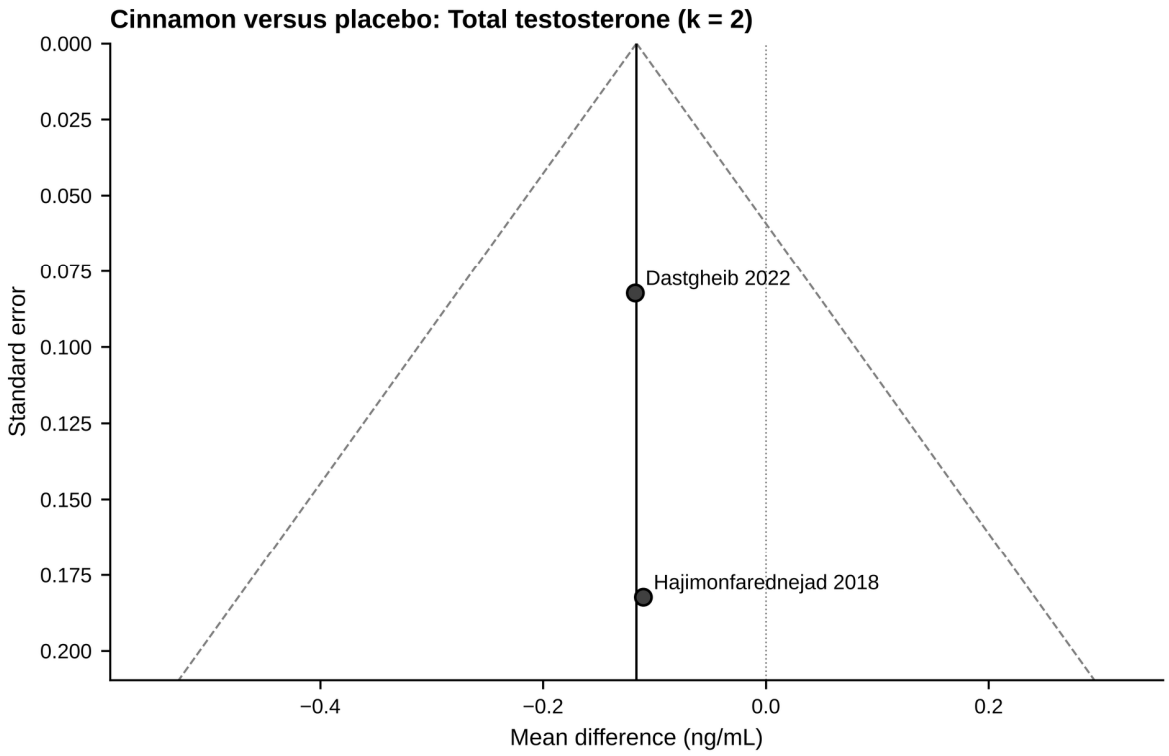
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S82. Funnel plot for Triglycerides with Cinnamon versus placebo (descriptive only)



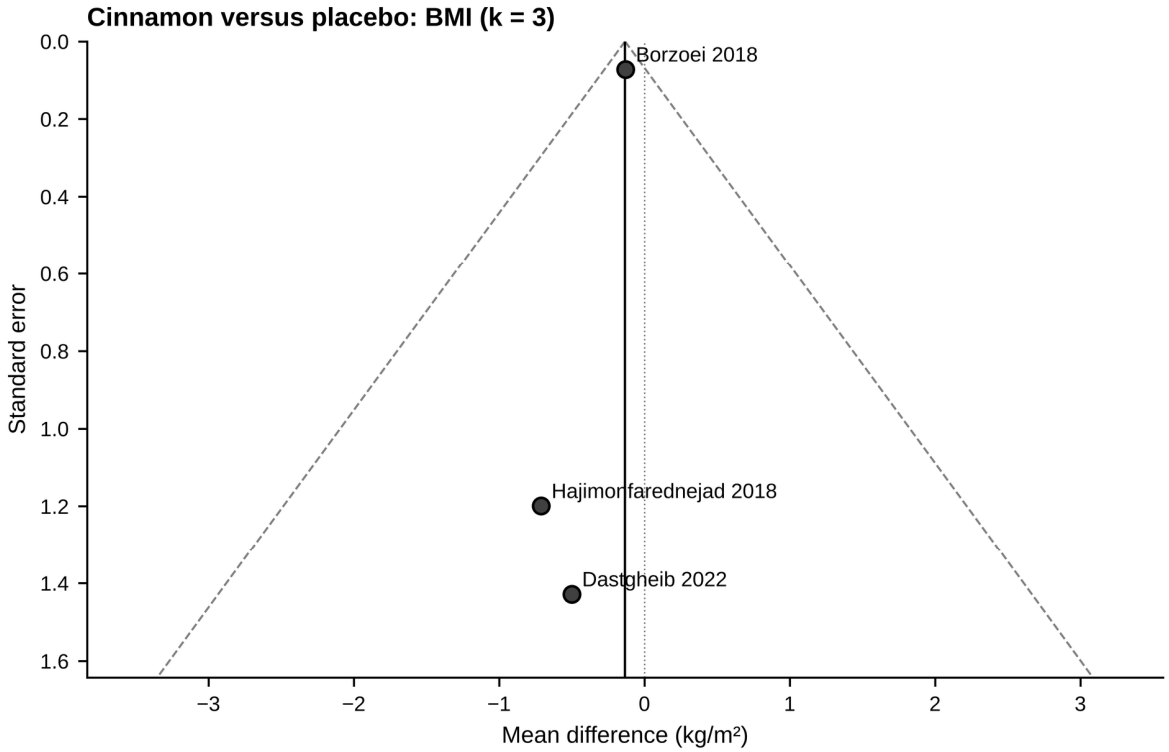
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S83. Funnel plot for Total testosterone with Cinnamon versus placebo (descriptive only)



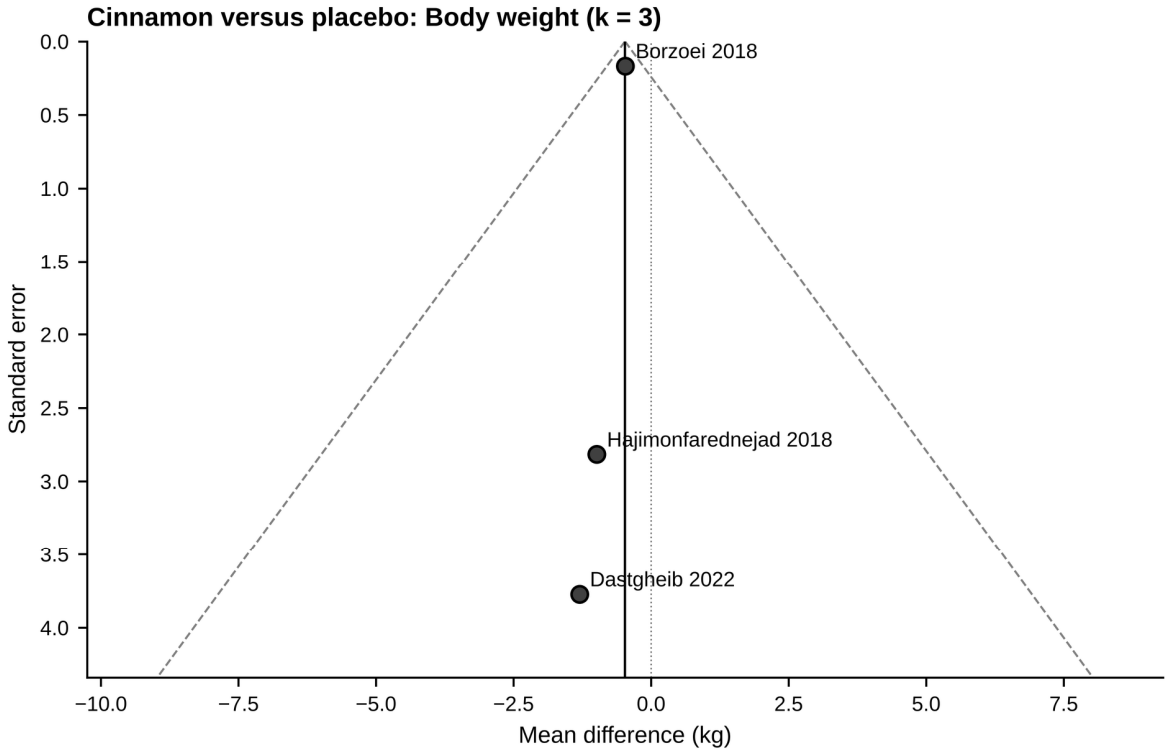
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S84. Funnel plot for BMI with Cinnamon versus placebo (descriptive only)



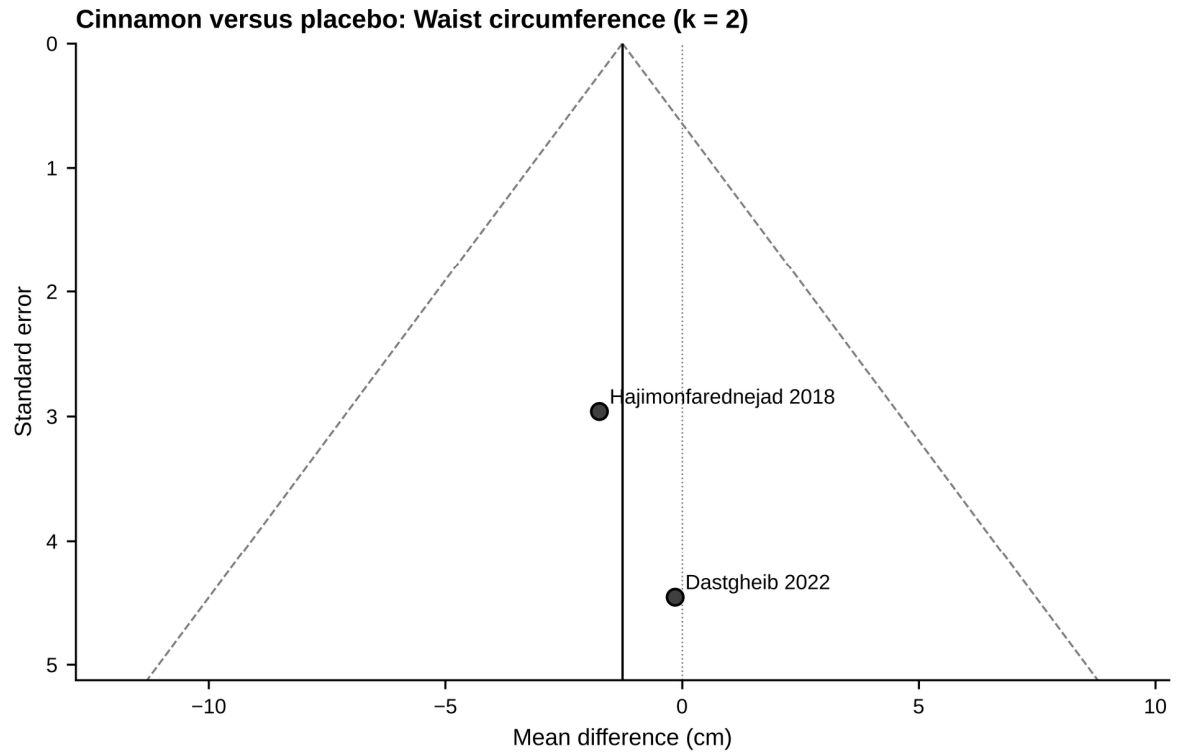
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S85. Funnel plot for Body weight with Cinnamon versus placebo (descriptive only)



Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S86. Funnel plot for Waist circumference with Cinnamon versus placebo (descriptive only)



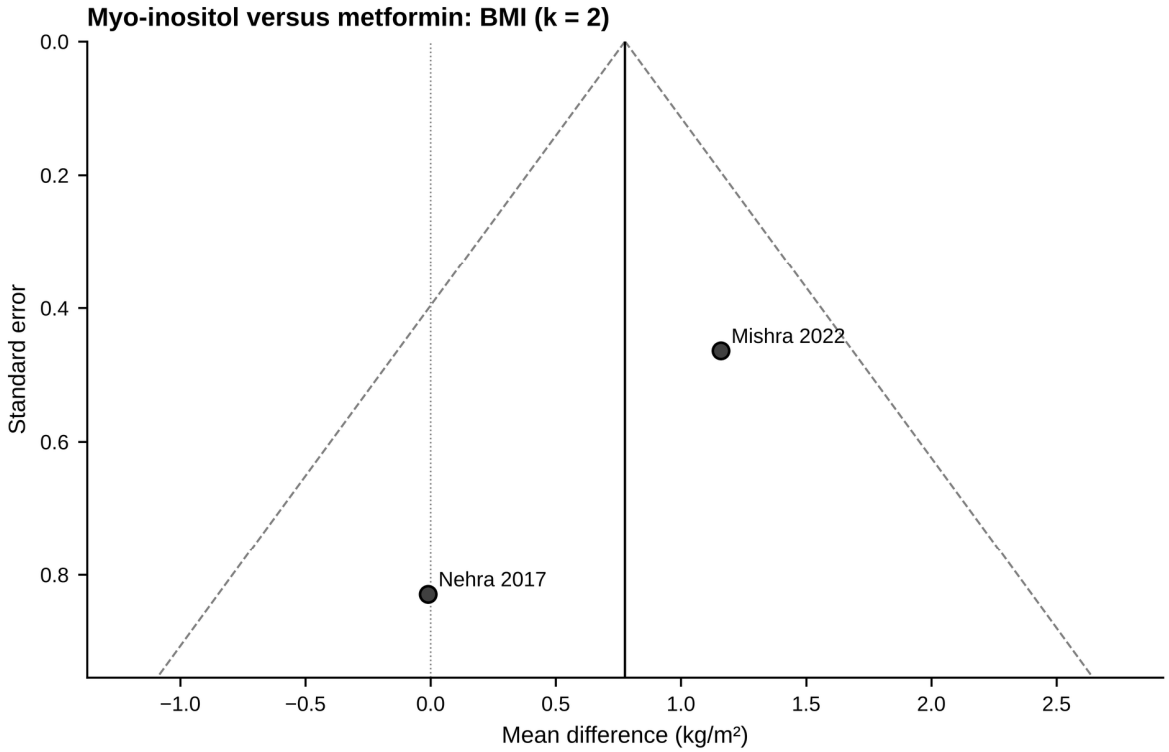
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S87. Funnel plot for Fasting glucose with Cinnamon versus metformin (descriptive only)



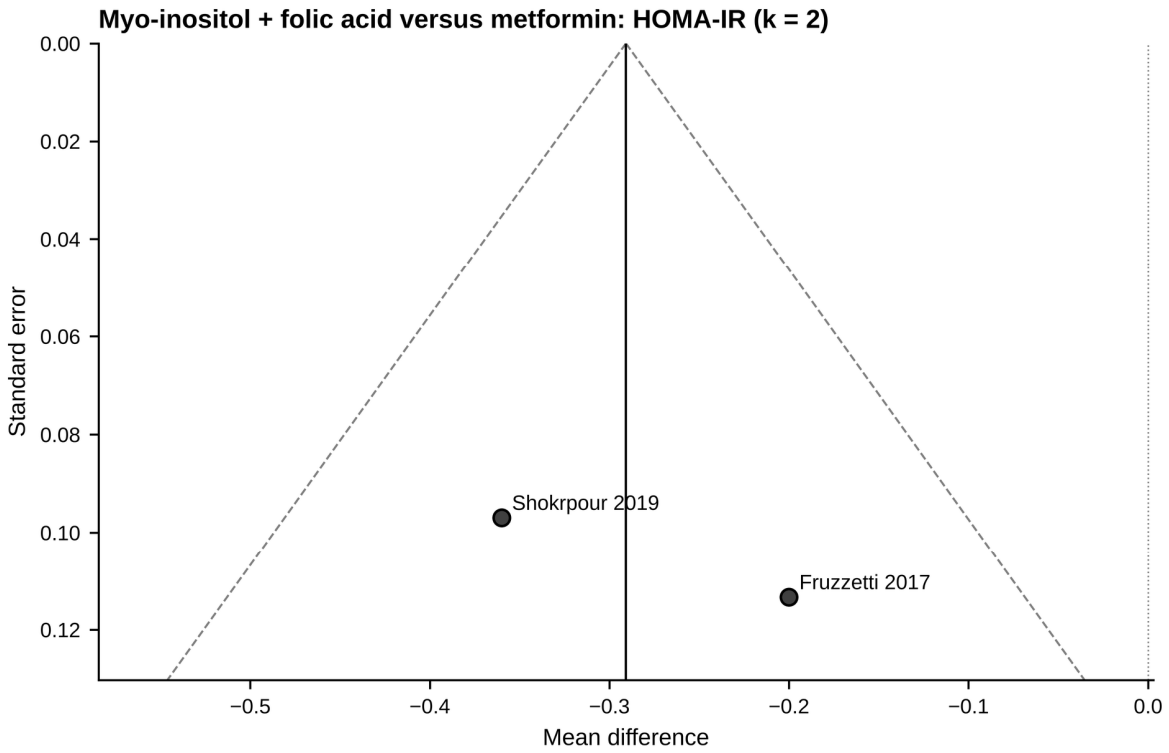
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S88. Funnel plot for BMI with Myo-inositol versus metformin (descriptive only)



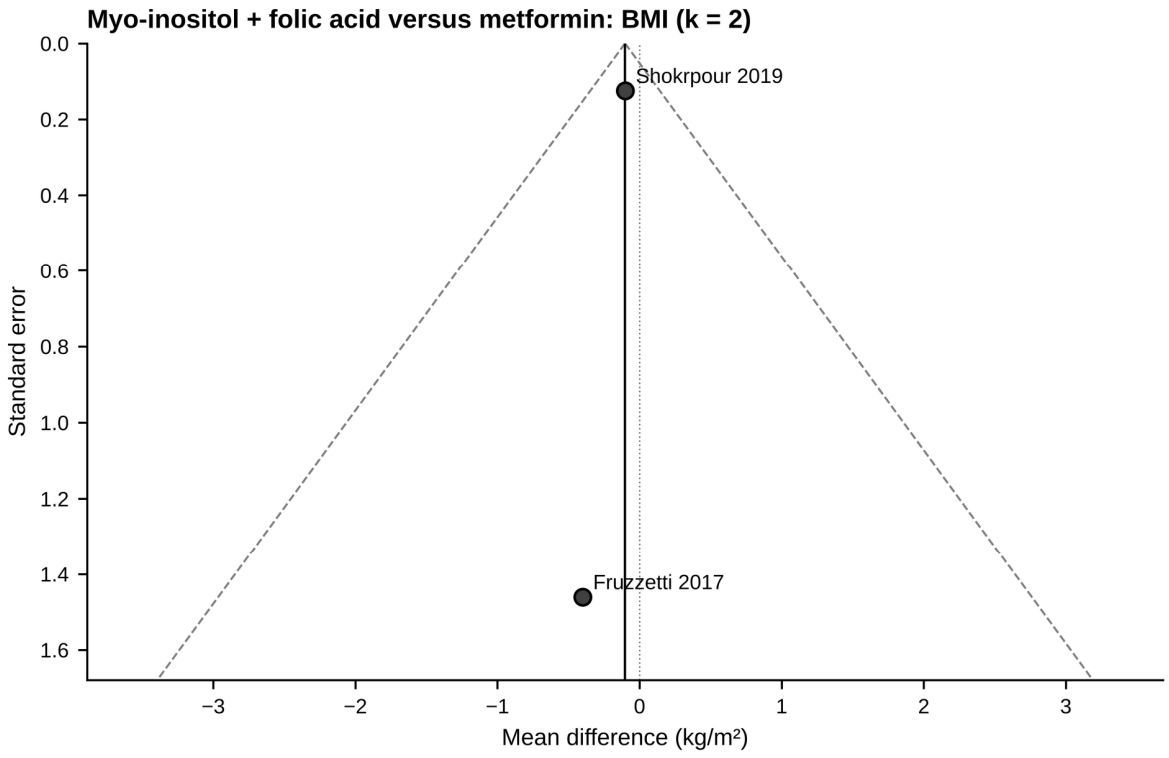
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S89. Funnel plot for HOMA-IR with Myo-inositol + folic acid versus metformin (descriptive only)



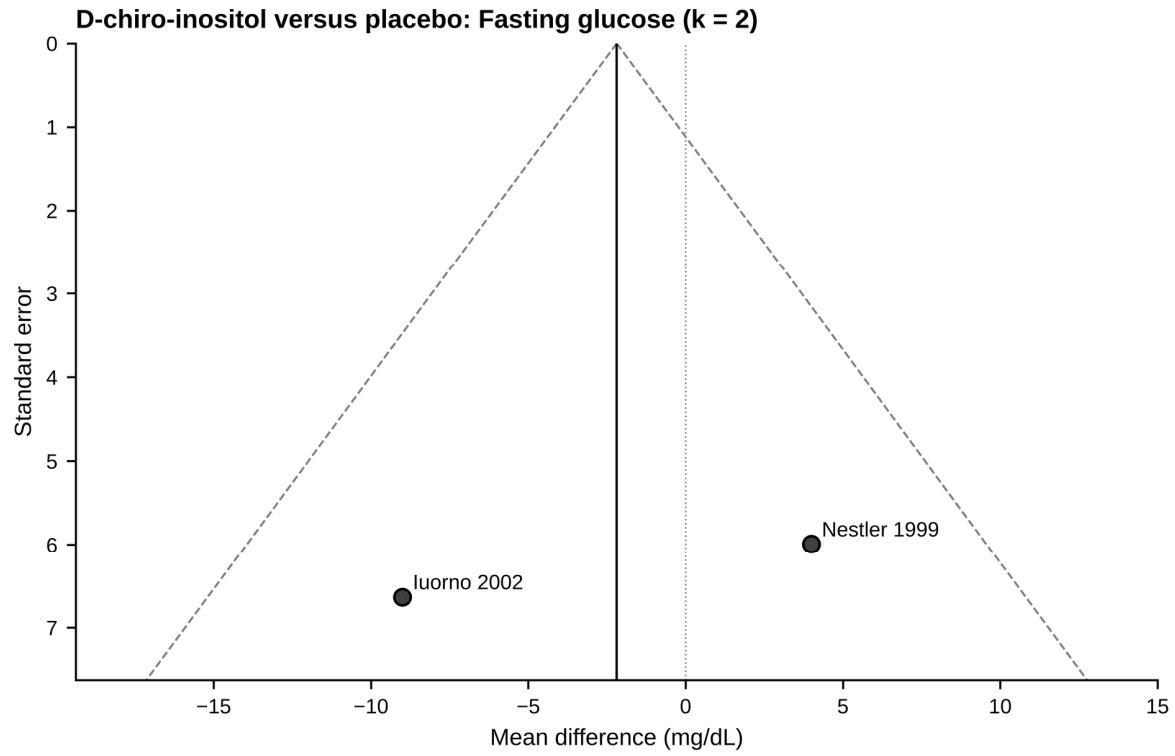
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S90. Funnel plot for BMI with Myo-inositol + folic acid versus metformin (descriptive only)



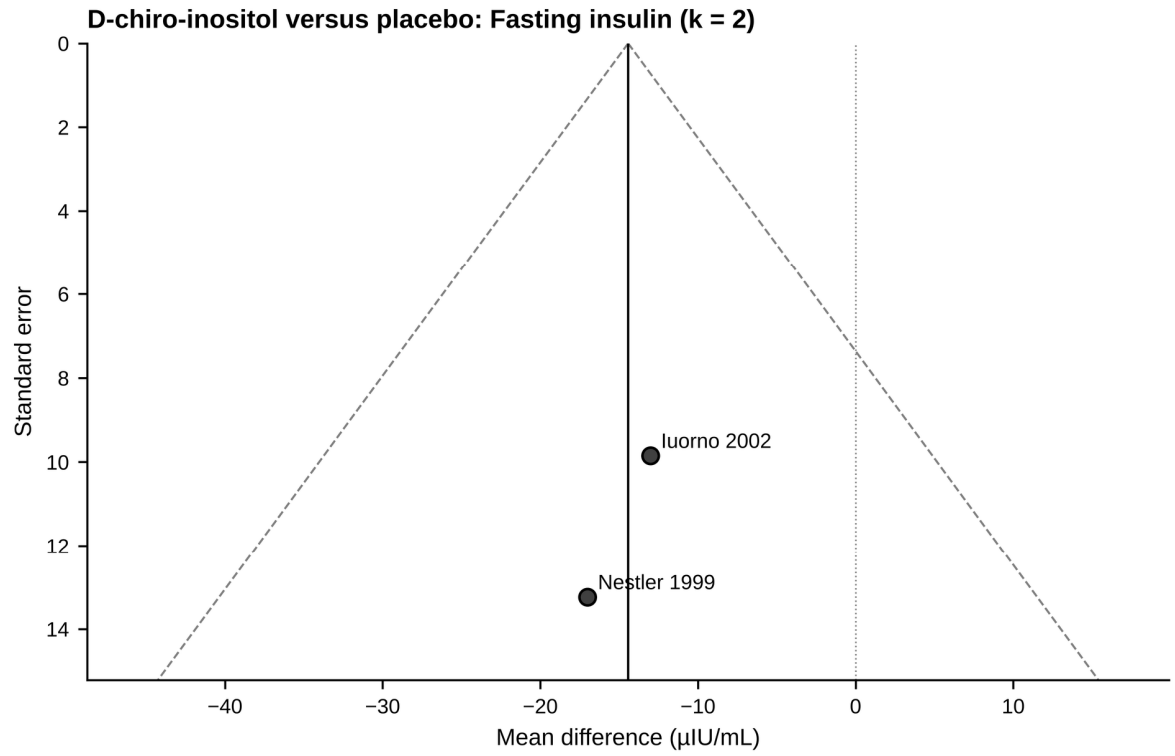
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S91. Funnel plot for Fasting glucose with D-chiro-inositol versus placebo (descriptive only)



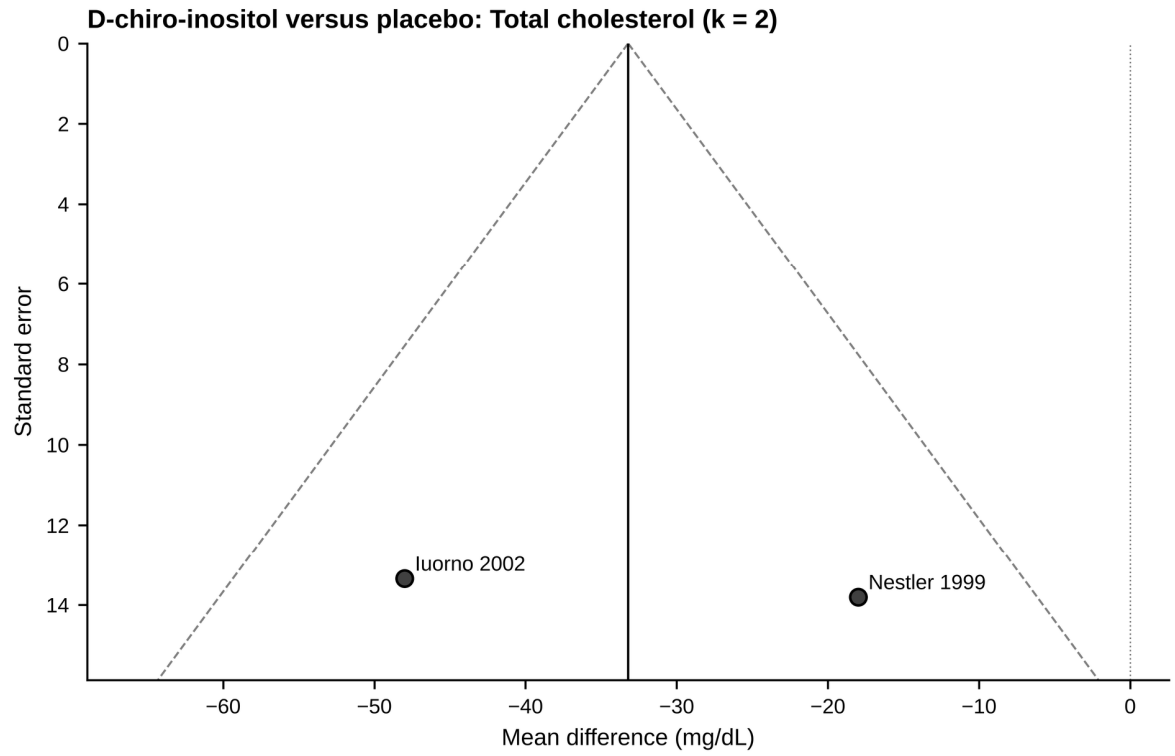
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S92. Funnel plot for Fasting insulin with D-chiro-inositol versus placebo (descriptive only)



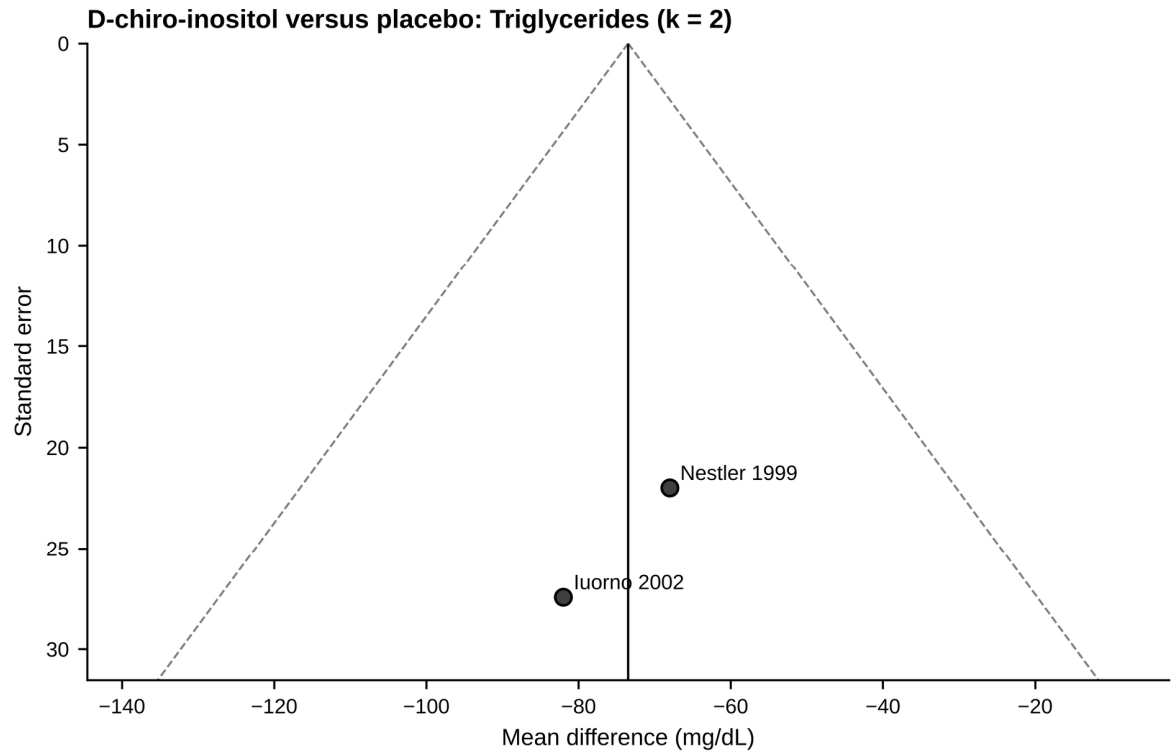
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S93. Funnel plot for Total cholesterol with D-chiro-inositol versus placebo (descriptive only)



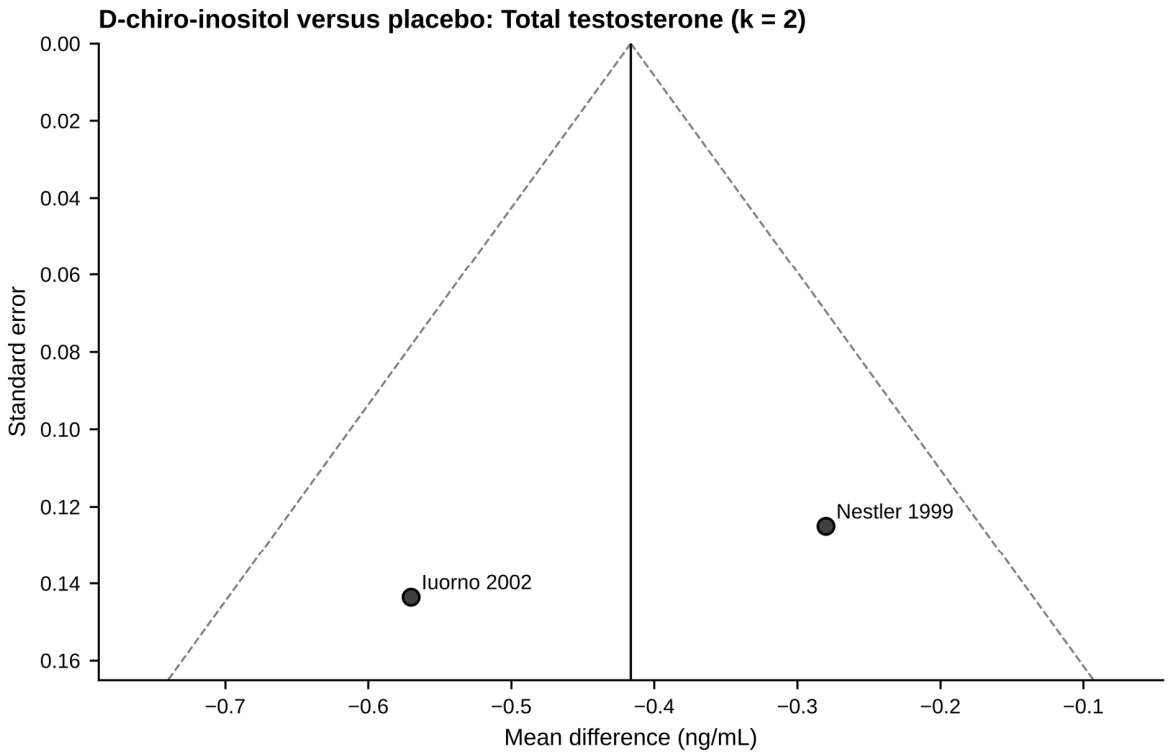
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S94. Funnel plot for Triglycerides with D-chiro-inositol versus placebo (descriptive only)



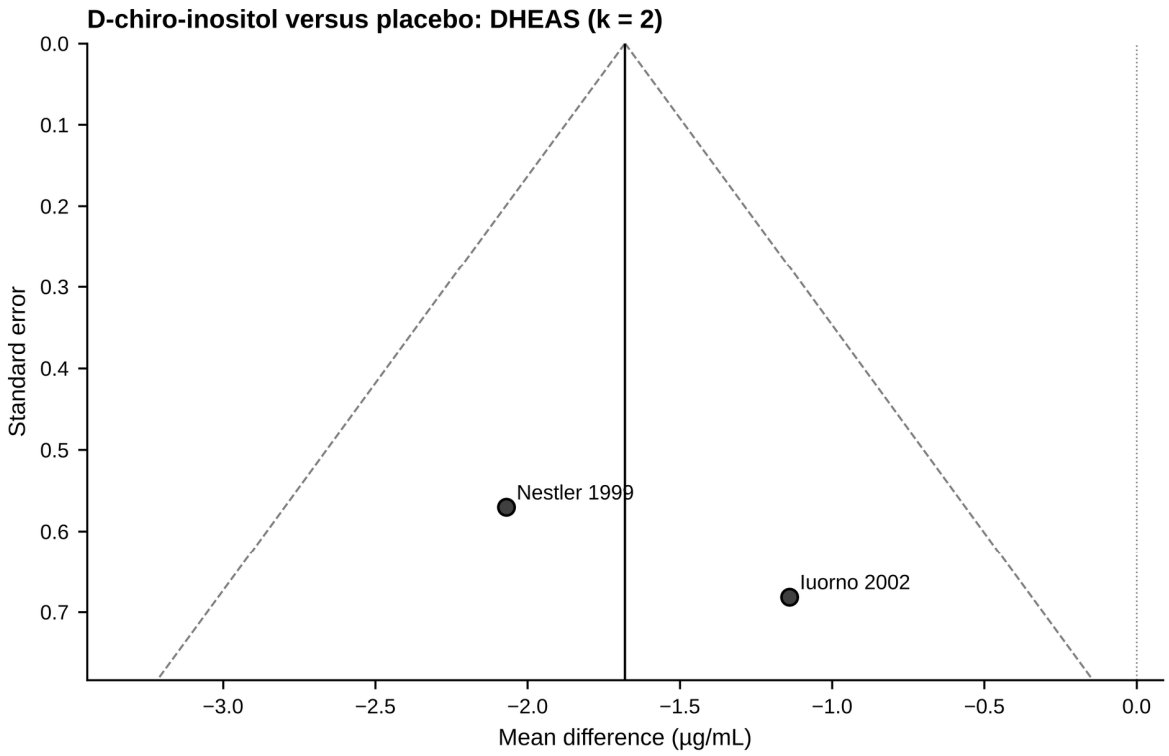
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S95. Funnel plot for Total testosterone with D-chiro-inositol versus placebo (descriptive only)



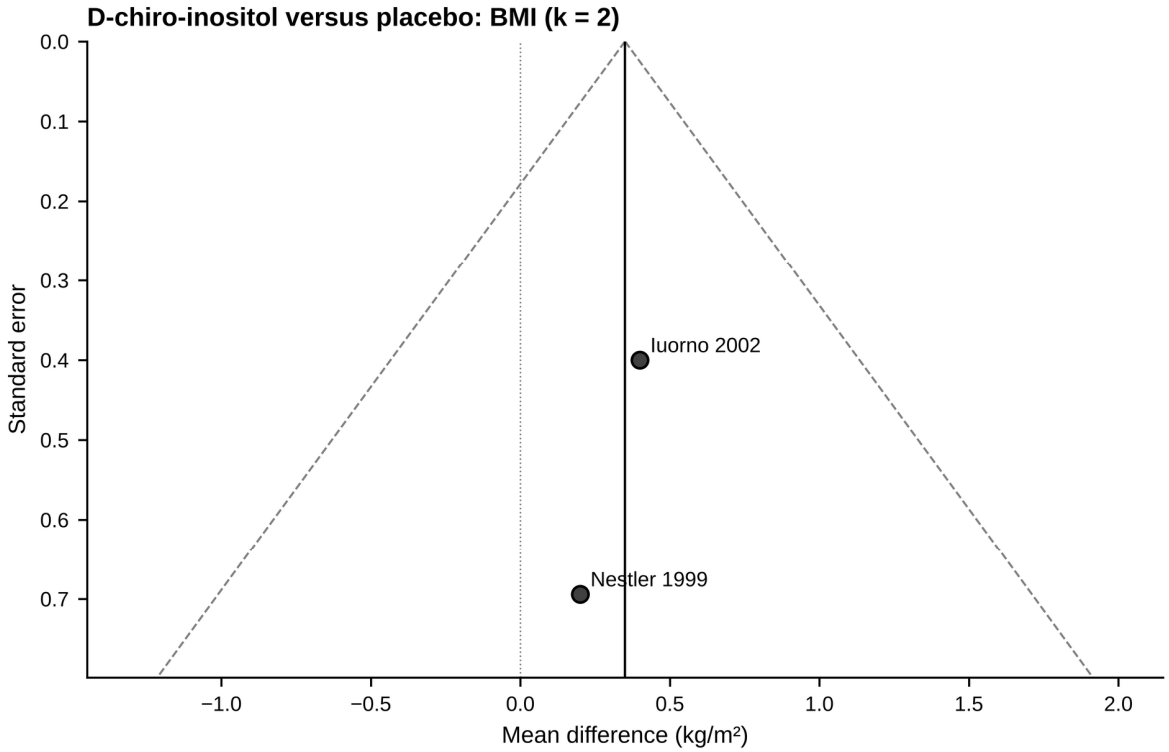
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S96. Funnel plot for DHEAS with D-chiro-inositol versus placebo (descriptive only)



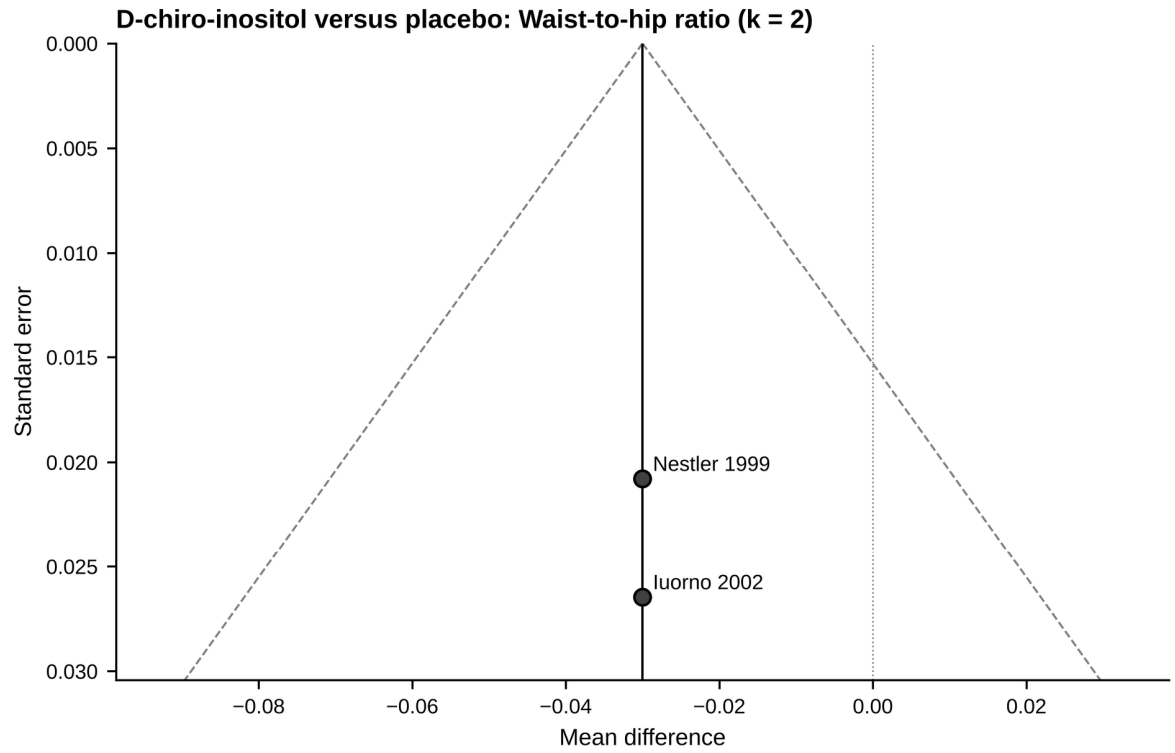
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S97. Funnel plot for BMI with D-chiro-inositol versus placebo (descriptive only)



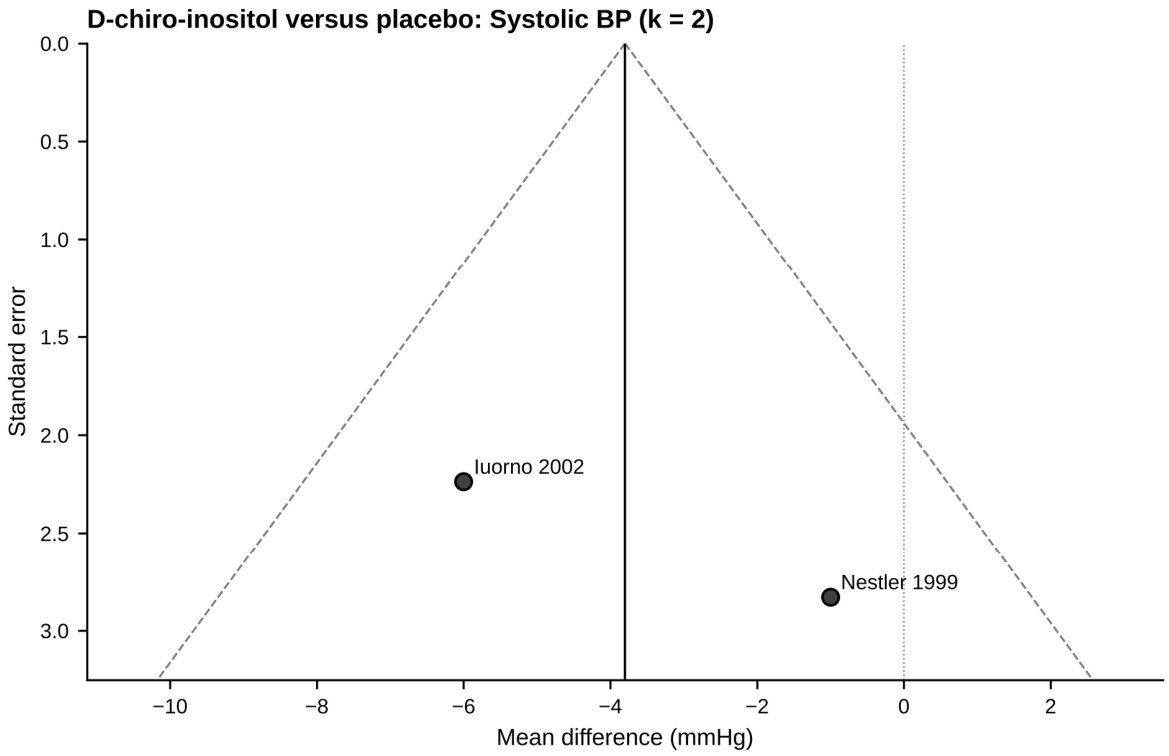
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S98. Funnel plot for Waist-to-hip ratio with D-chiro-inositol versus placebo (descriptive only)



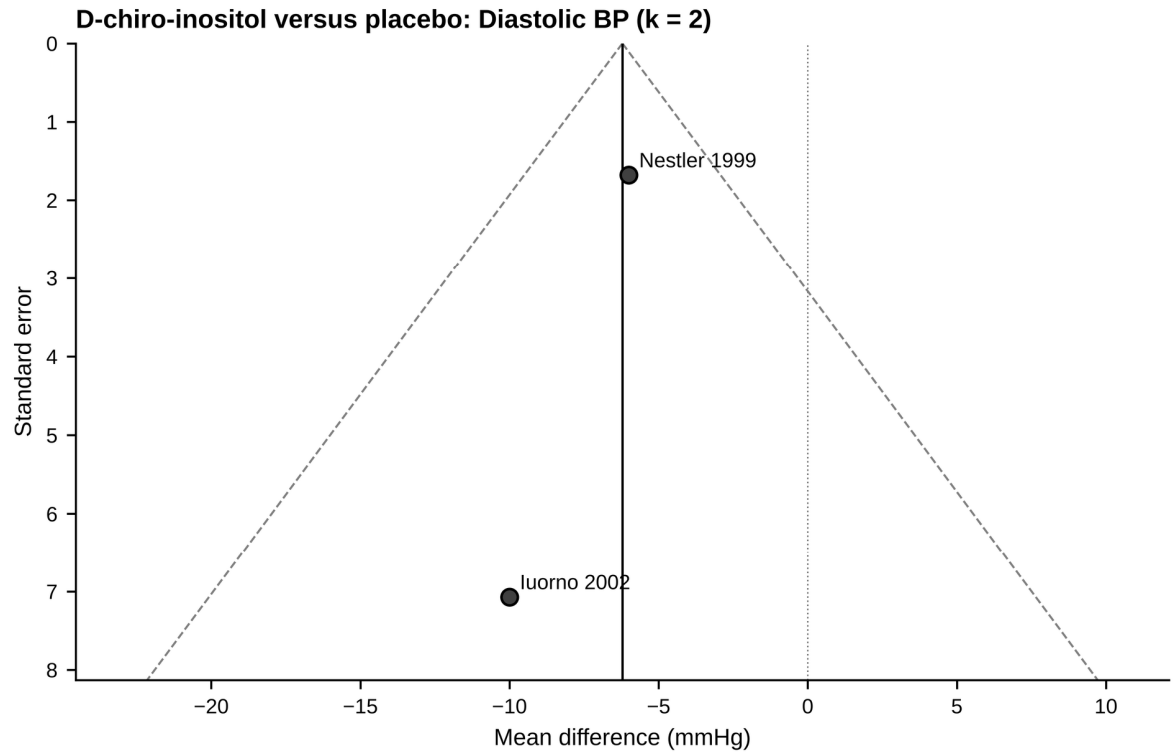
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S99. Funnel plot for Systolic BP with D-chiro-inositol versus placebo (descriptive only)



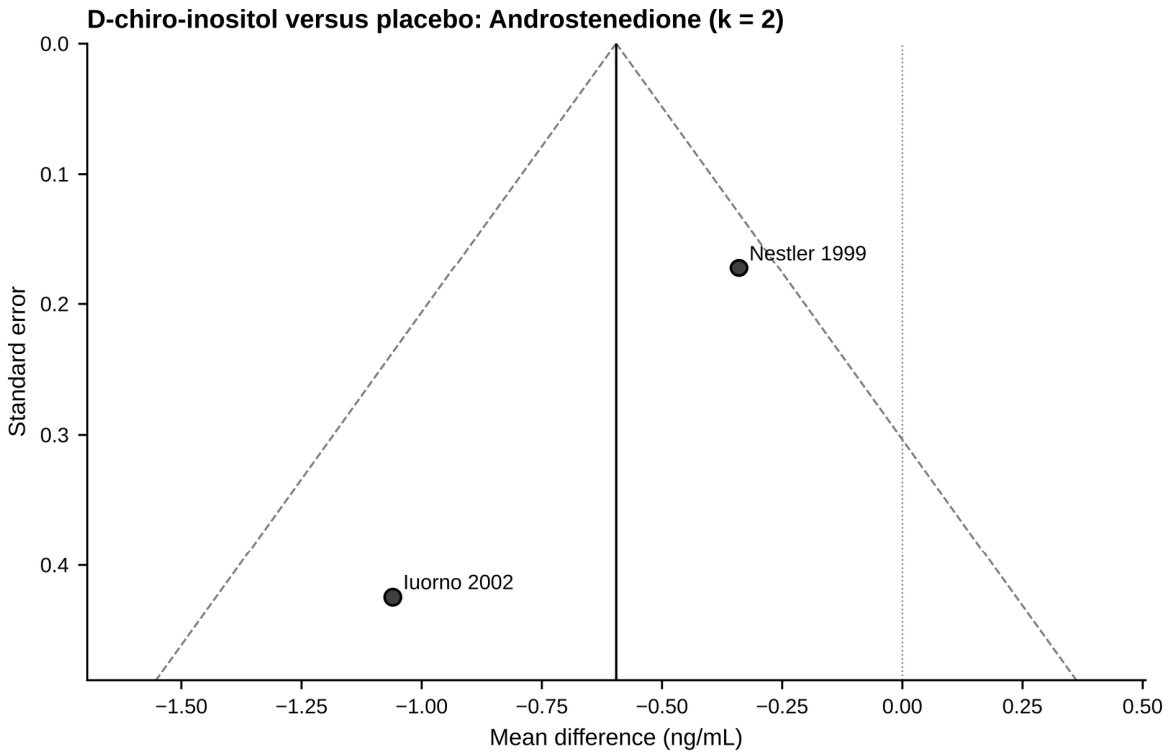
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S100. Funnel plot for Diastolic BP with D-chiro-inositol versus placebo (descriptive only)



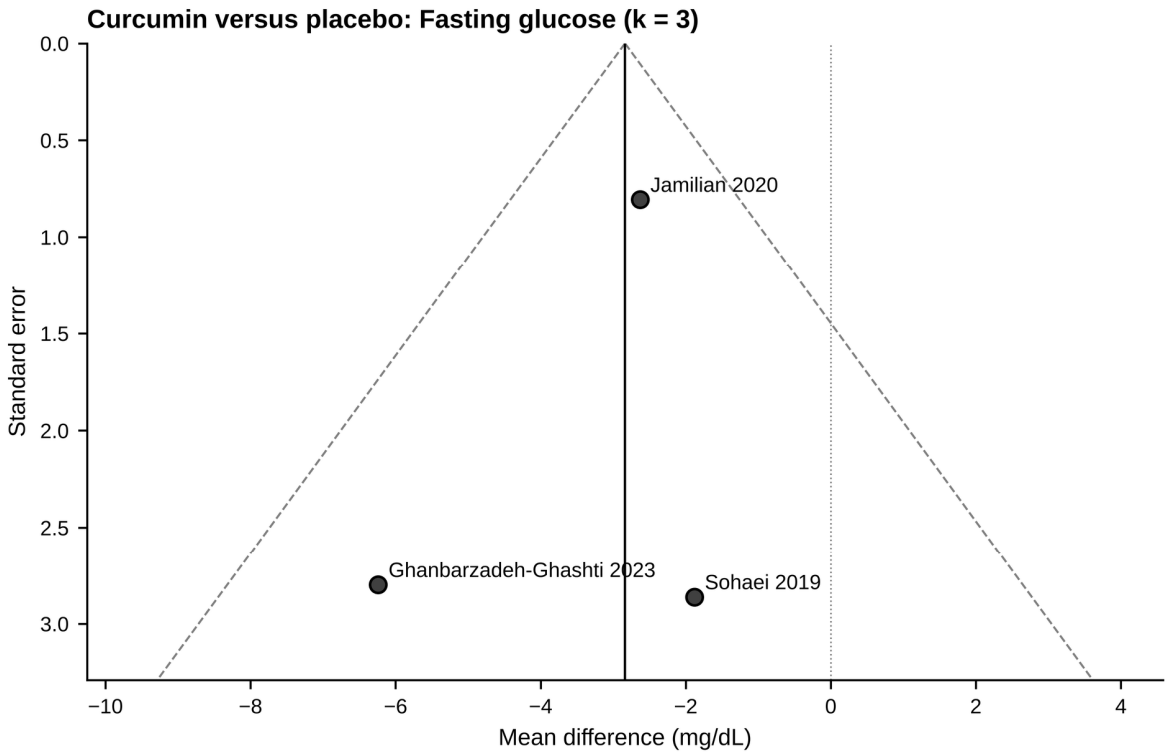
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S101. Funnel plot for Androstenedione with D-chiro-inositol versus placebo (descriptive only)



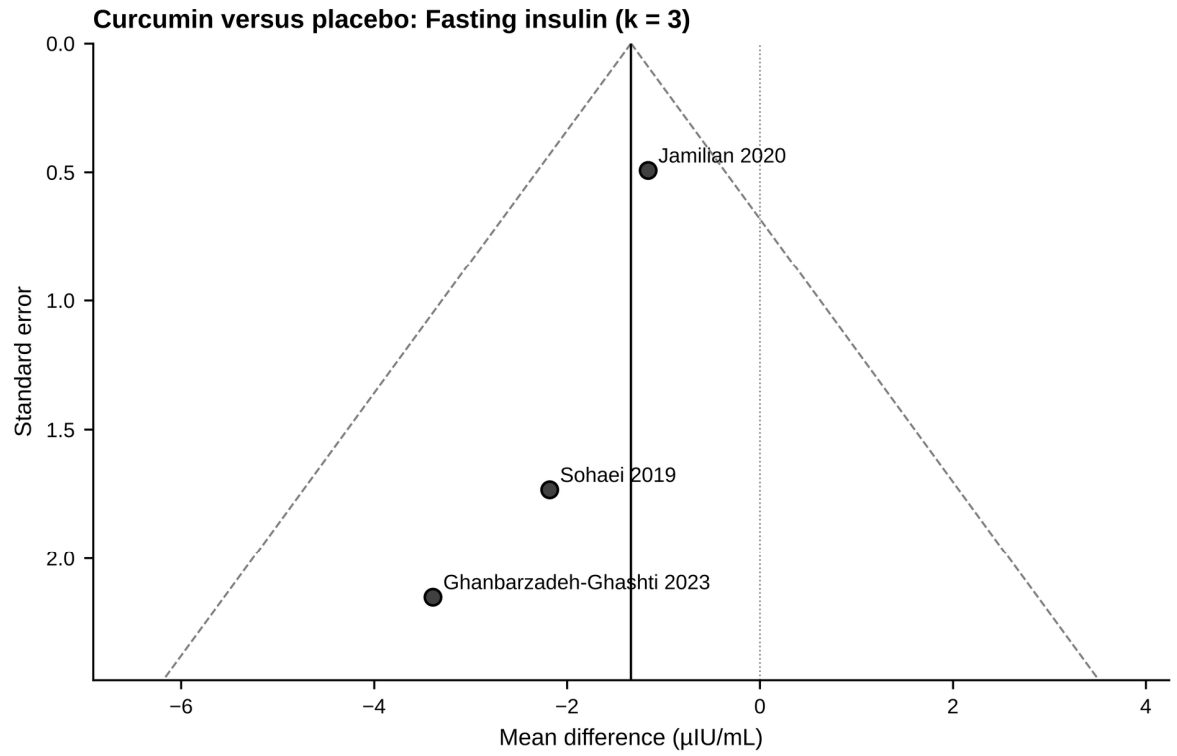
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S102. Funnel plot for Fasting glucose with Curcumin versus placebo (descriptive only)



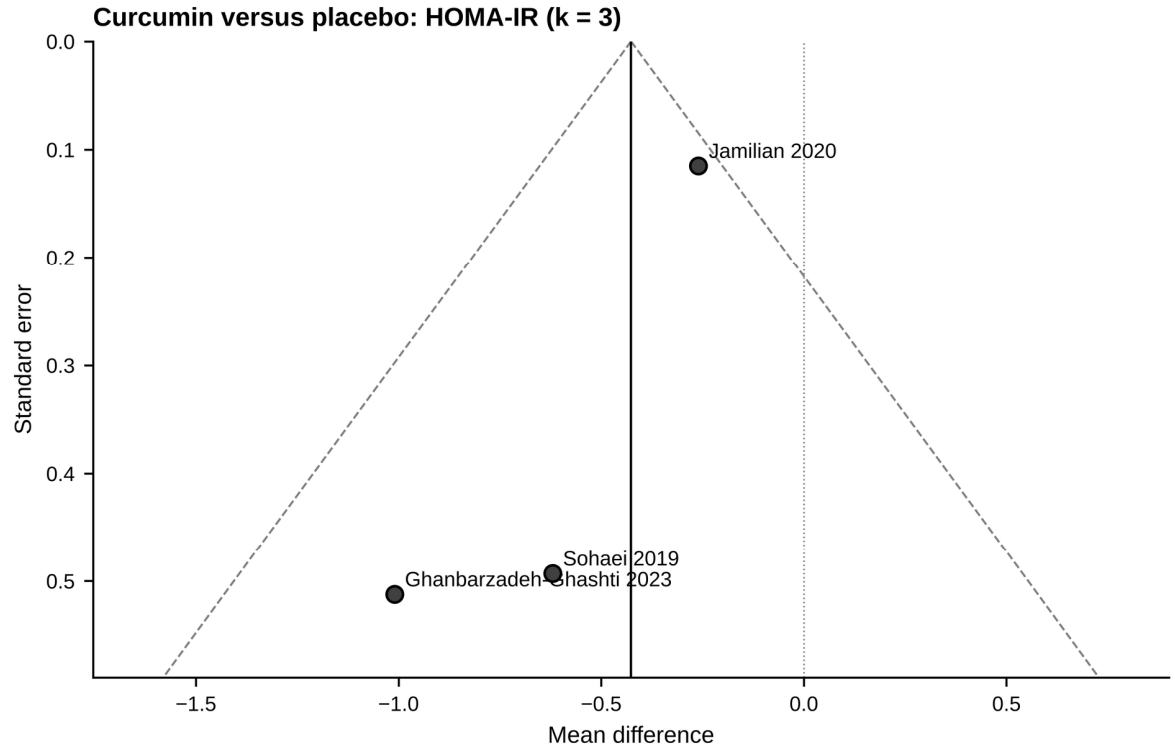
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S103. Funnel plot for Fasting insulin with Curcumin versus placebo (descriptive only)



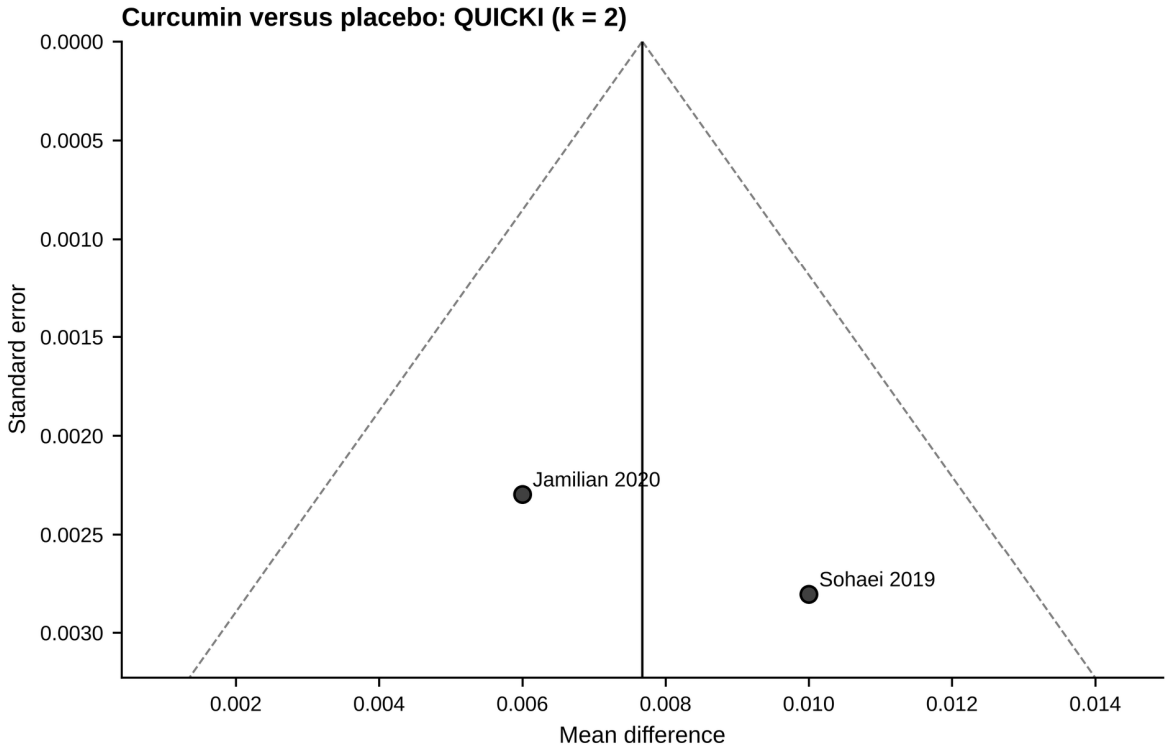
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S104. Funnel plot for HOMA-IR with Curcumin versus placebo (descriptive only)



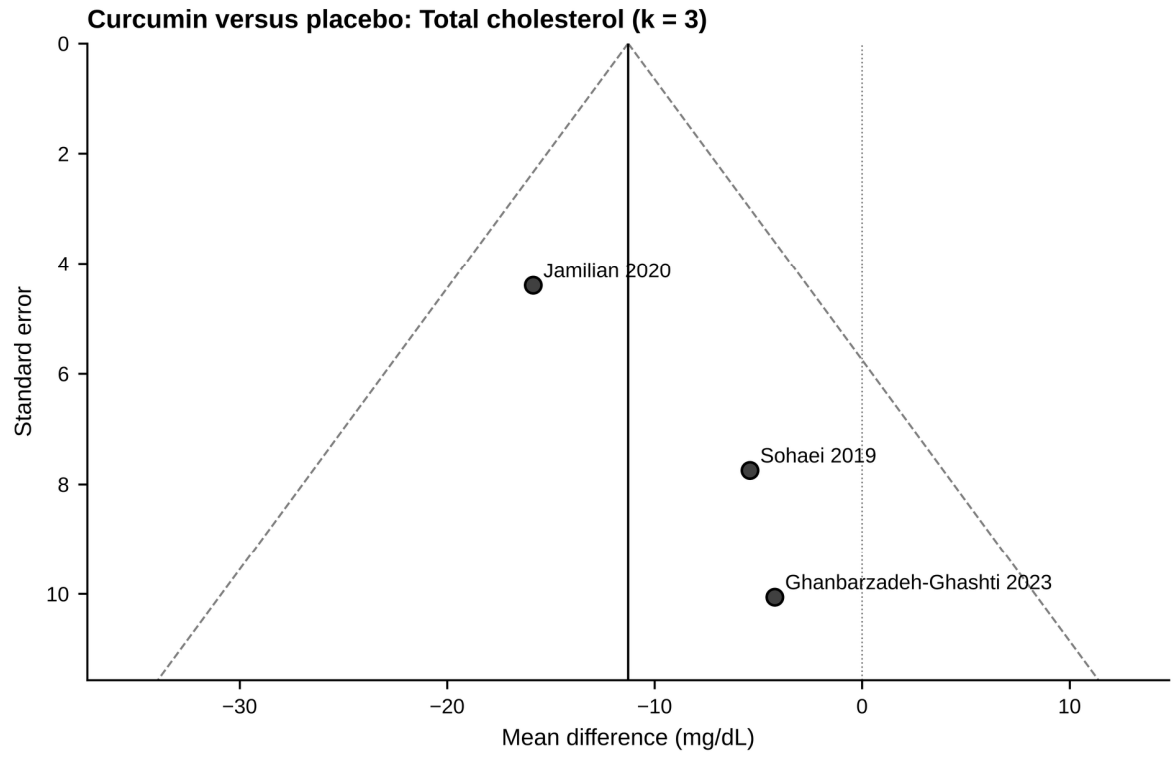
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S105. Funnel plot for QUICKI with Curcumin versus placebo (descriptive only)



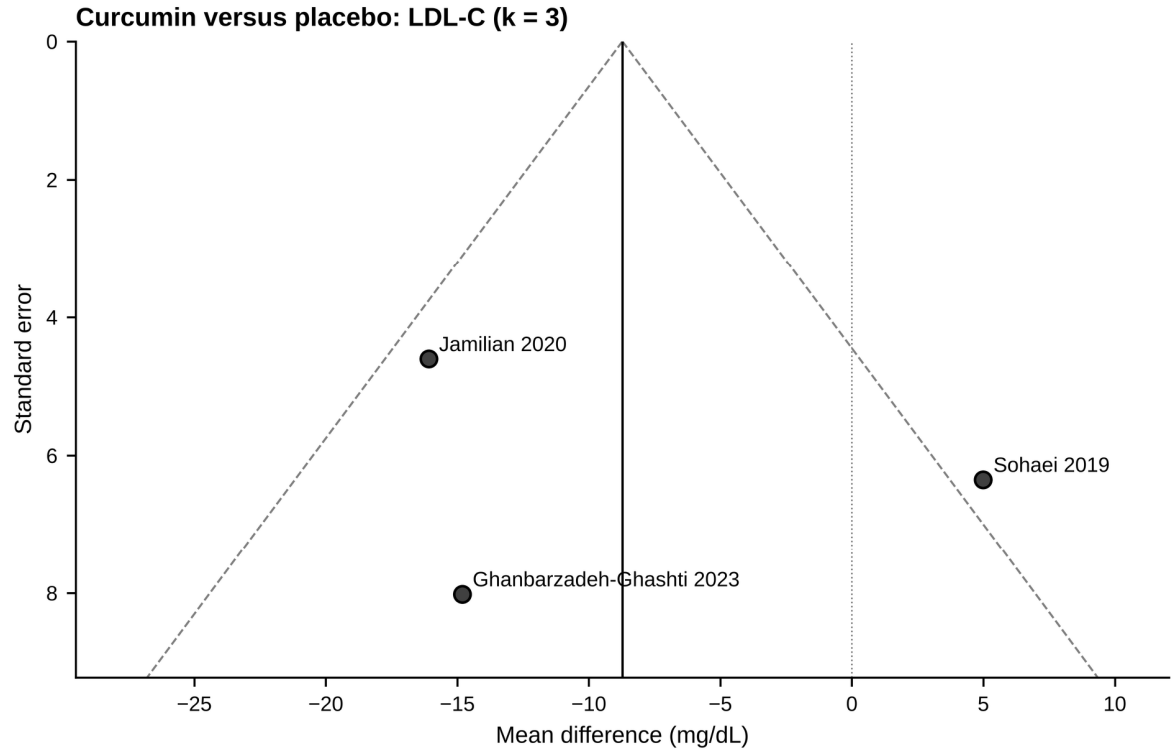
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S106. Funnel plot for Total cholesterol with Curcumin versus placebo (descriptive only)



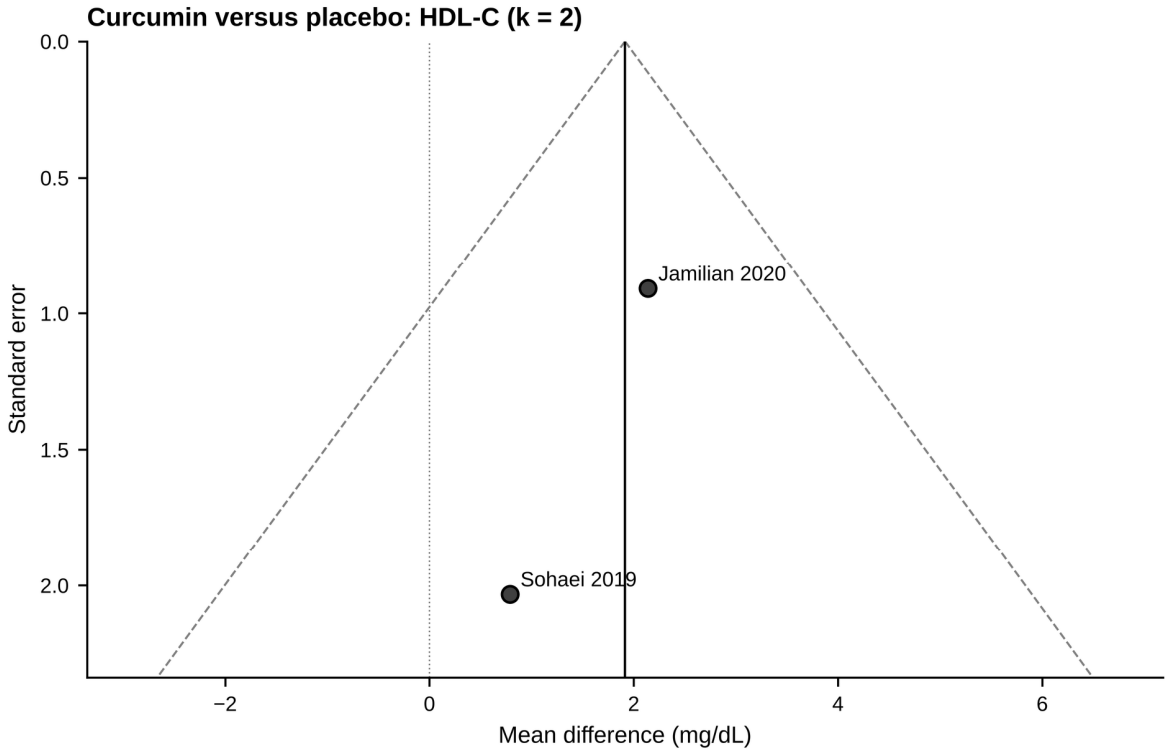
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S107. Funnel plot for LDL-C with Curcumin versus placebo (descriptive only)



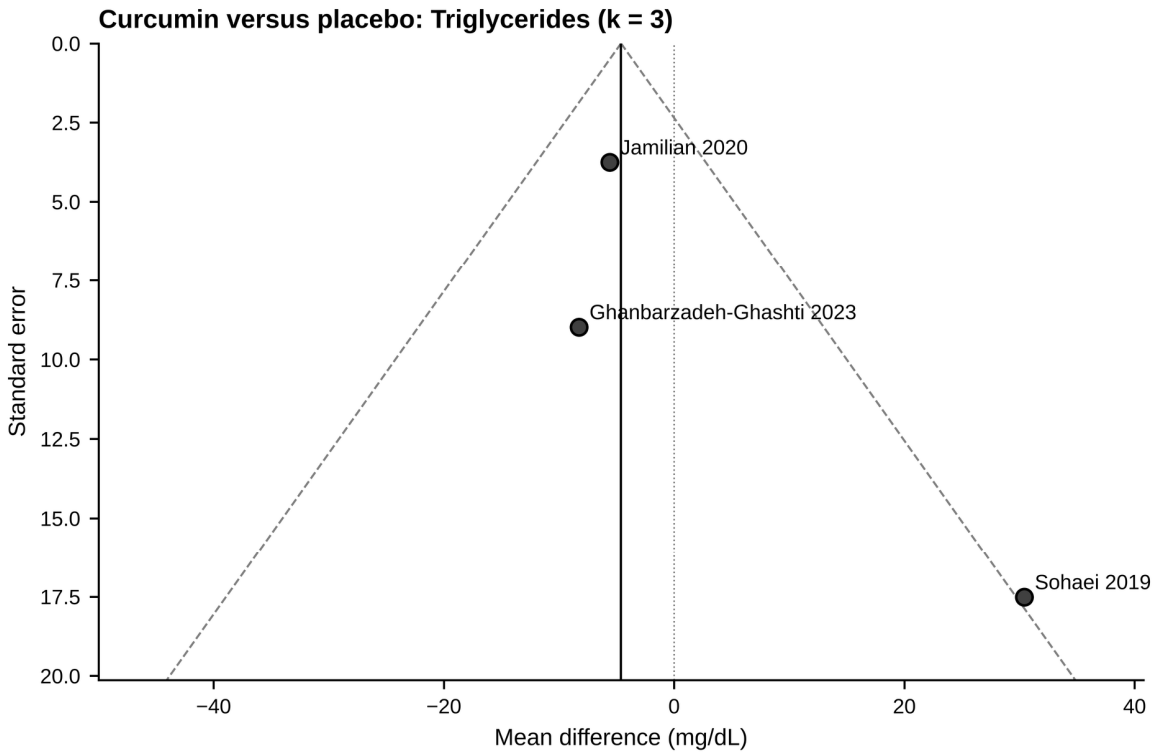
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S108. Funnel plot for HDL-C with Curcumin versus placebo (descriptive only)



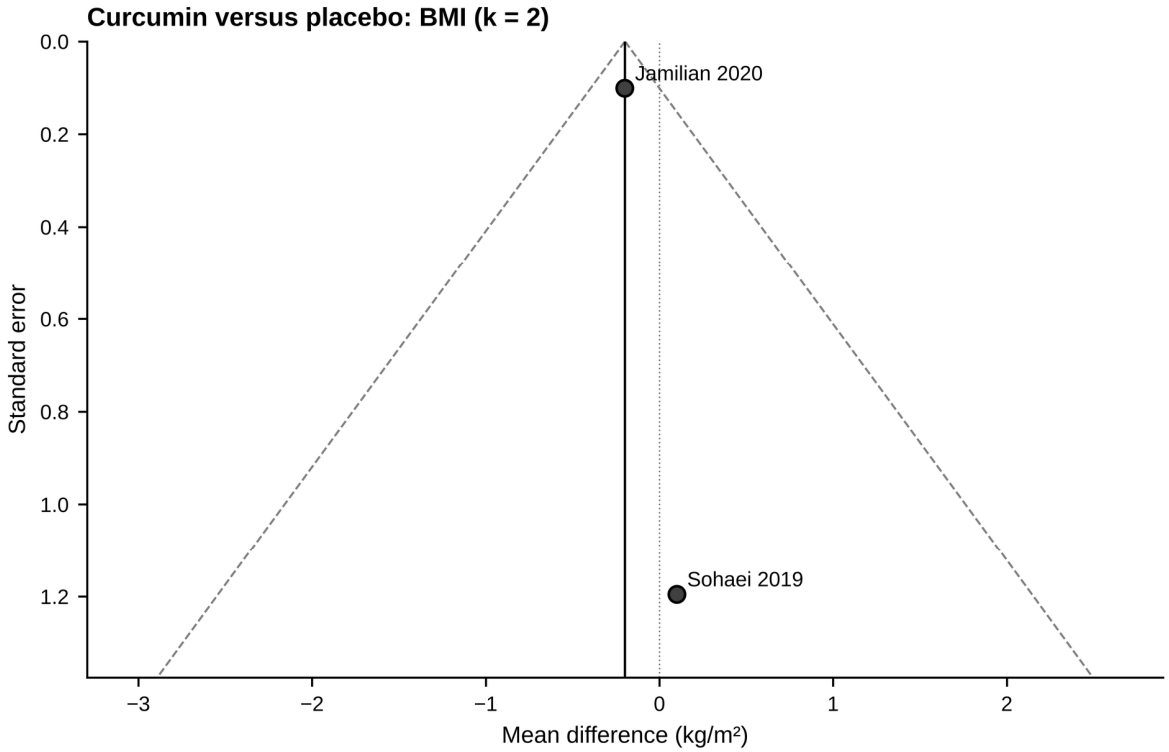
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S109. Funnel plot for Triglycerides with Curcumin versus placebo (descriptive only)



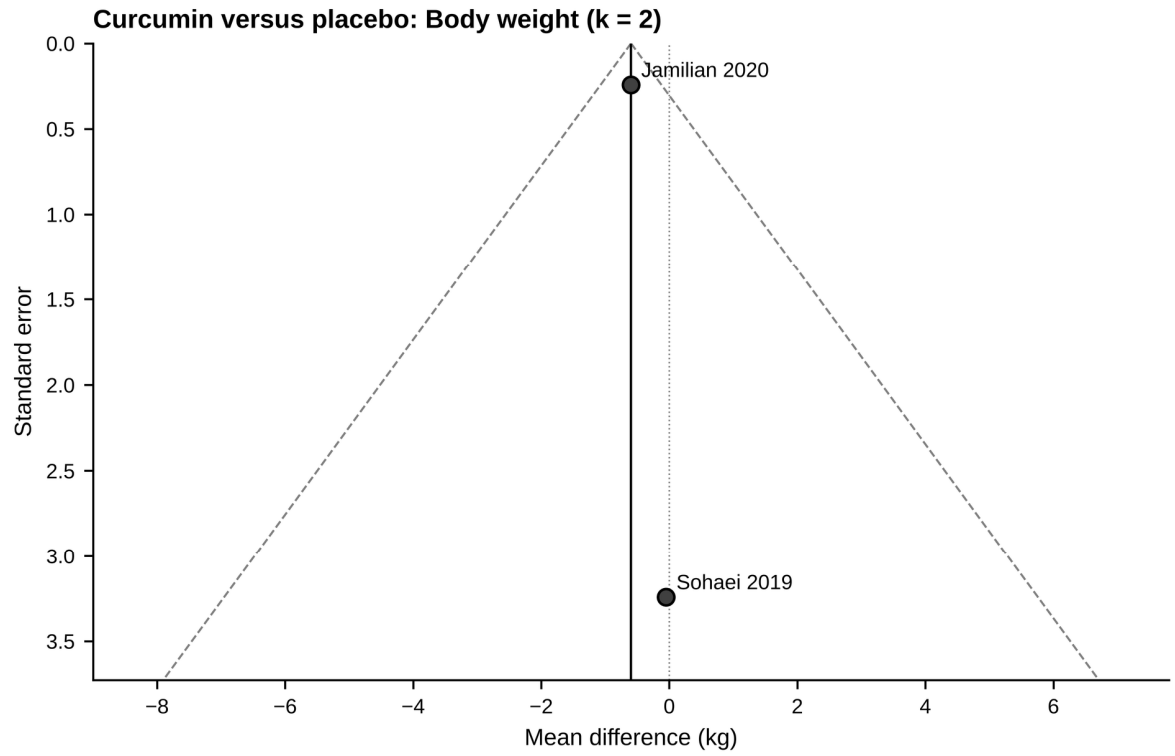
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S110. Funnel plot for BMI with Curcumin versus placebo (descriptive only)



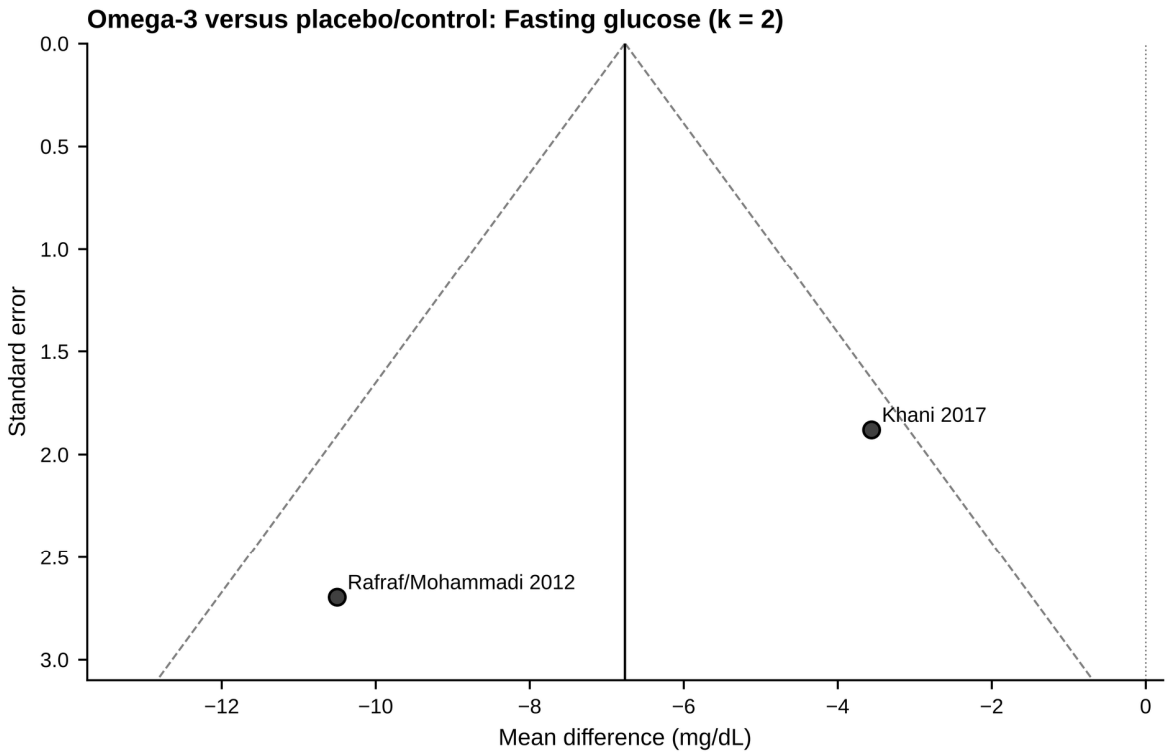
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S111. Funnel plot for Body weight with Curcumin versus placebo (descriptive only)



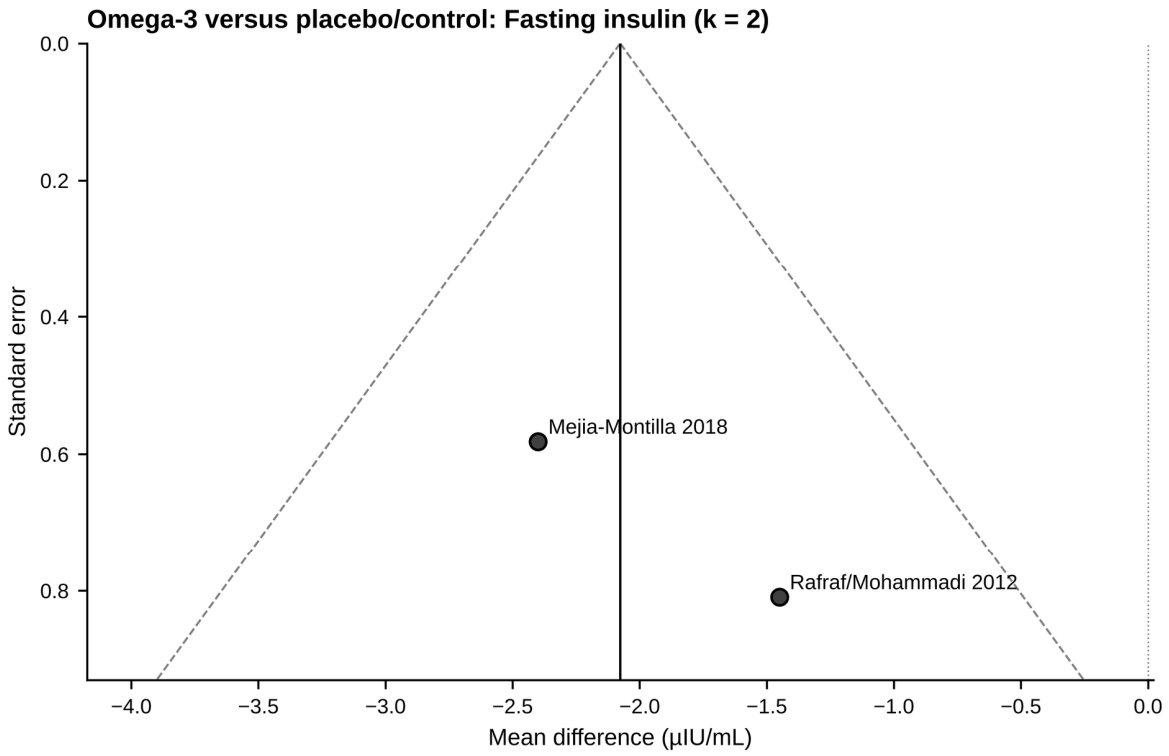
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S112. Funnel plot for Fasting glucose with Omega-3 versus placebo/control (descriptive only)



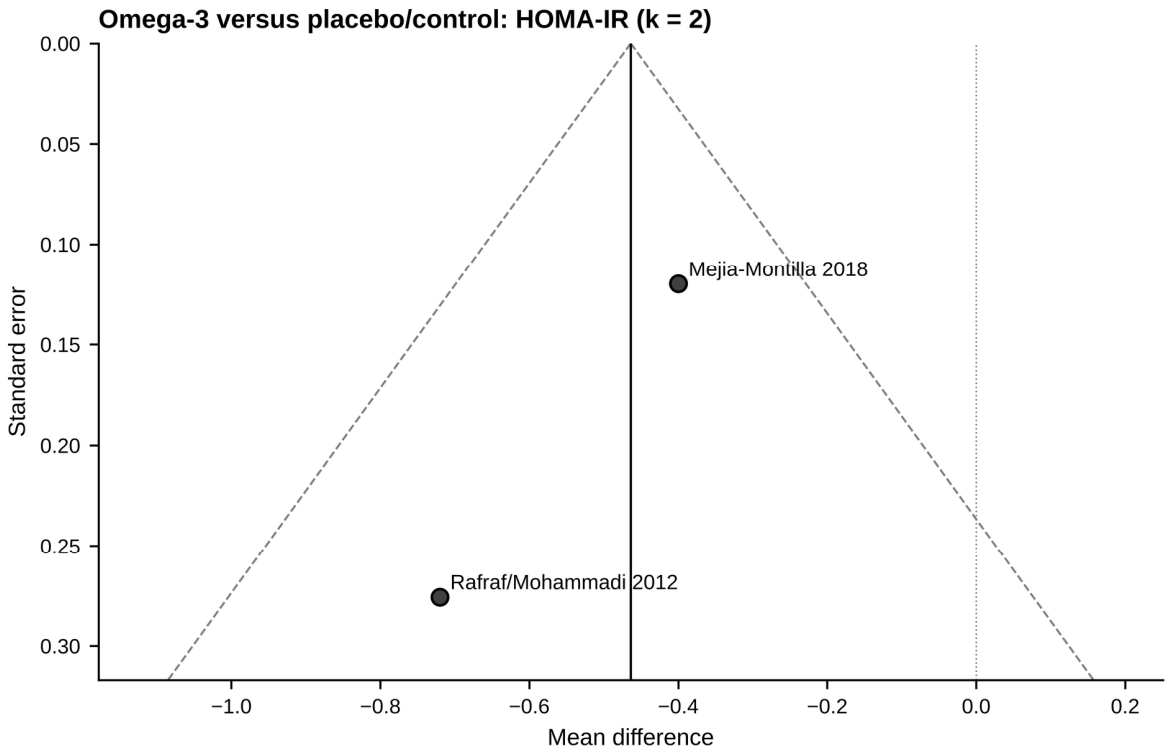
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S113. Funnel plot for Fasting insulin with Omega-3 versus placebo/control (descriptive only)



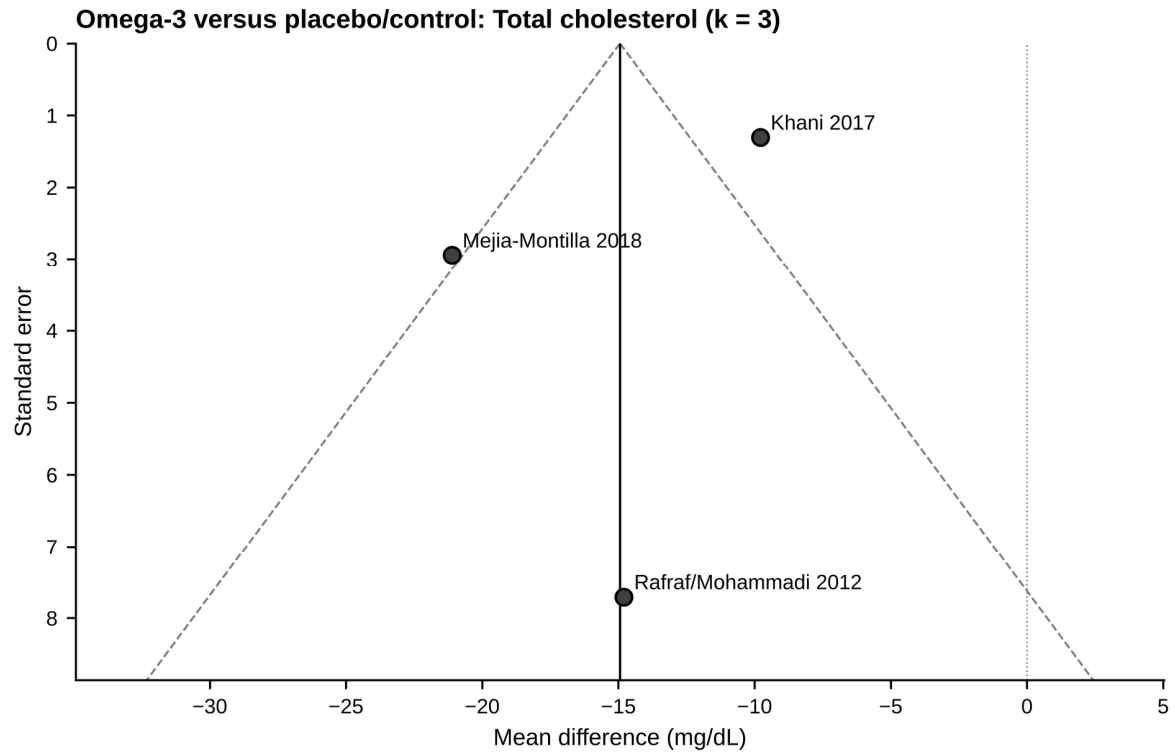
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S114. Funnel plot for HOMA-IR with Omega-3 versus placebo/control (descriptive only)



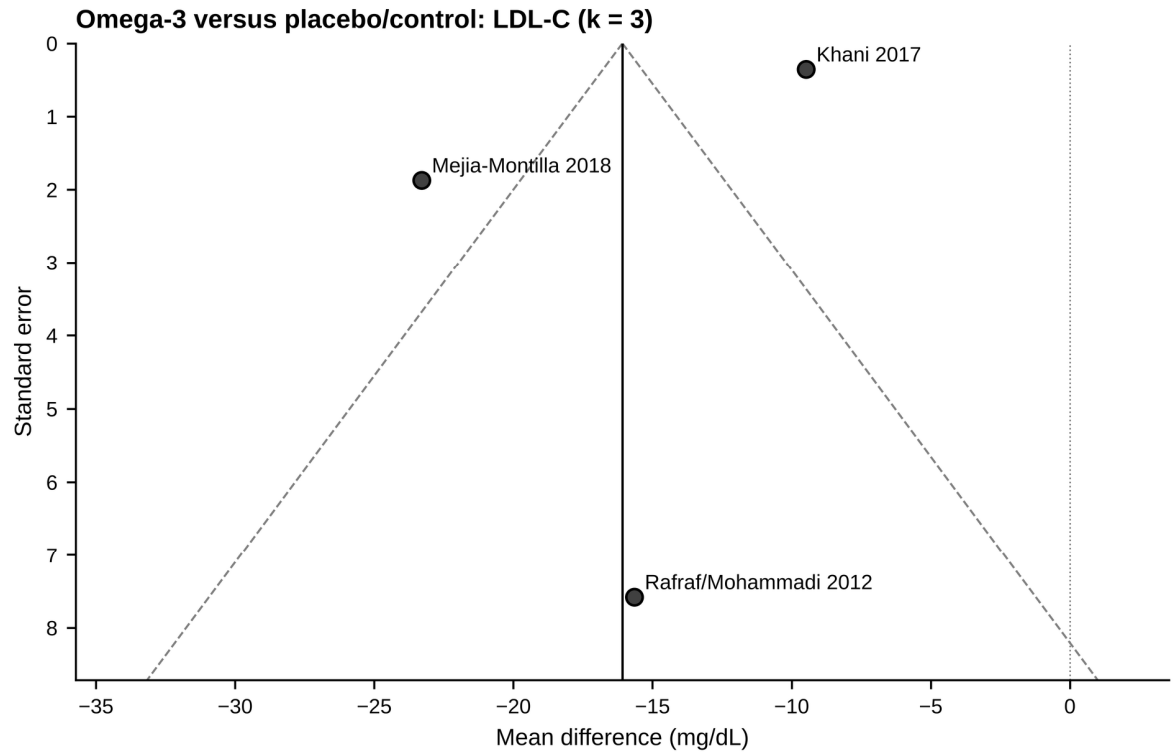
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S115. Funnel plot for Total cholesterol with Omega-3 versus placebo/control (descriptive only)



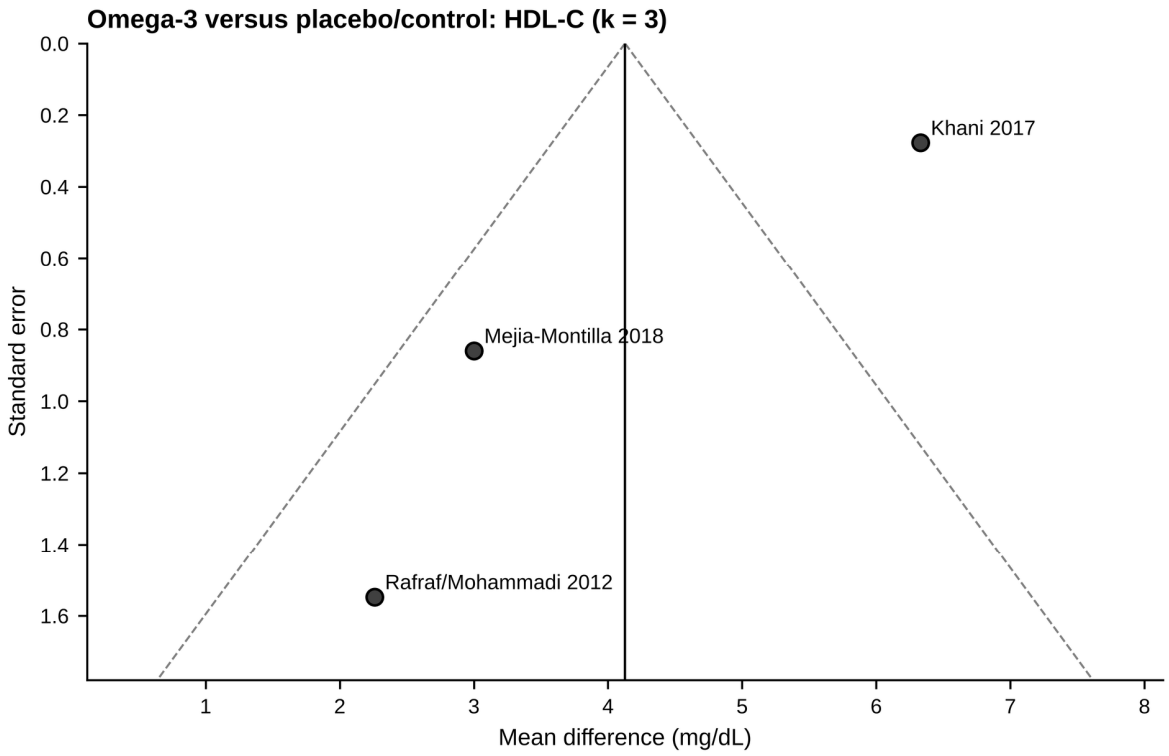
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S116. Funnel plot for LDL-C with Omega-3 versus placebo/control (descriptive only)



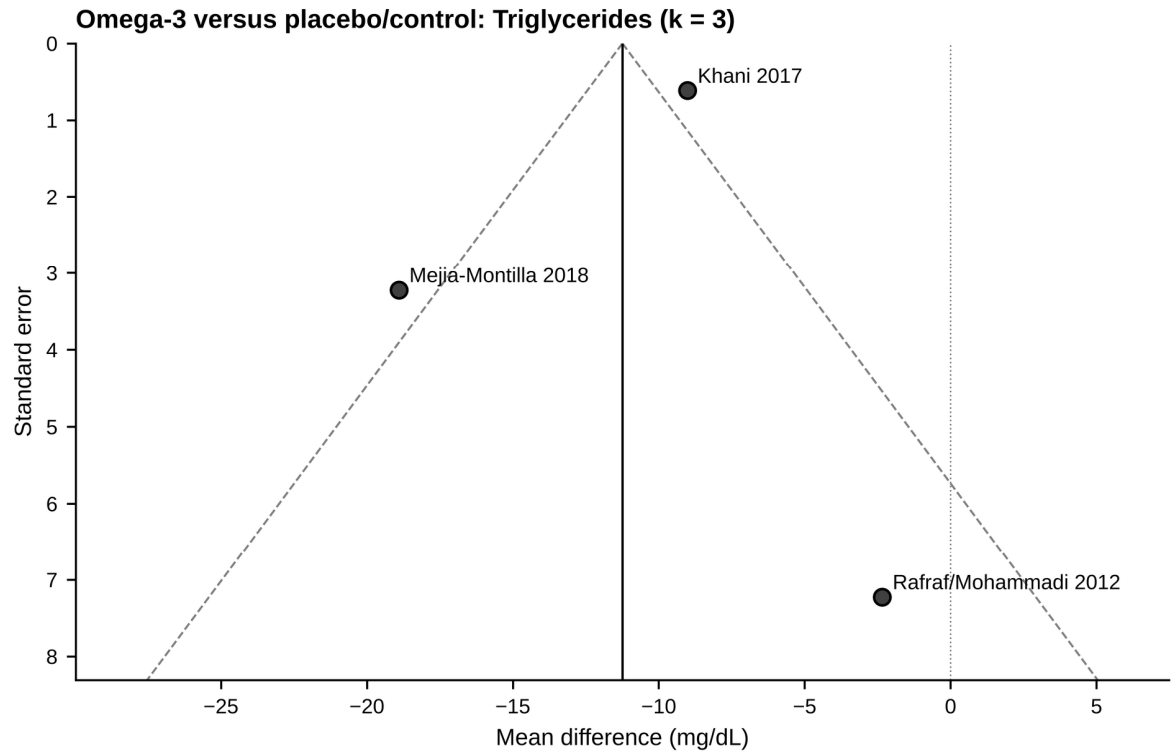
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S117. Funnel plot for HDL-C with Omega-3 versus placebo/control (descriptive only)



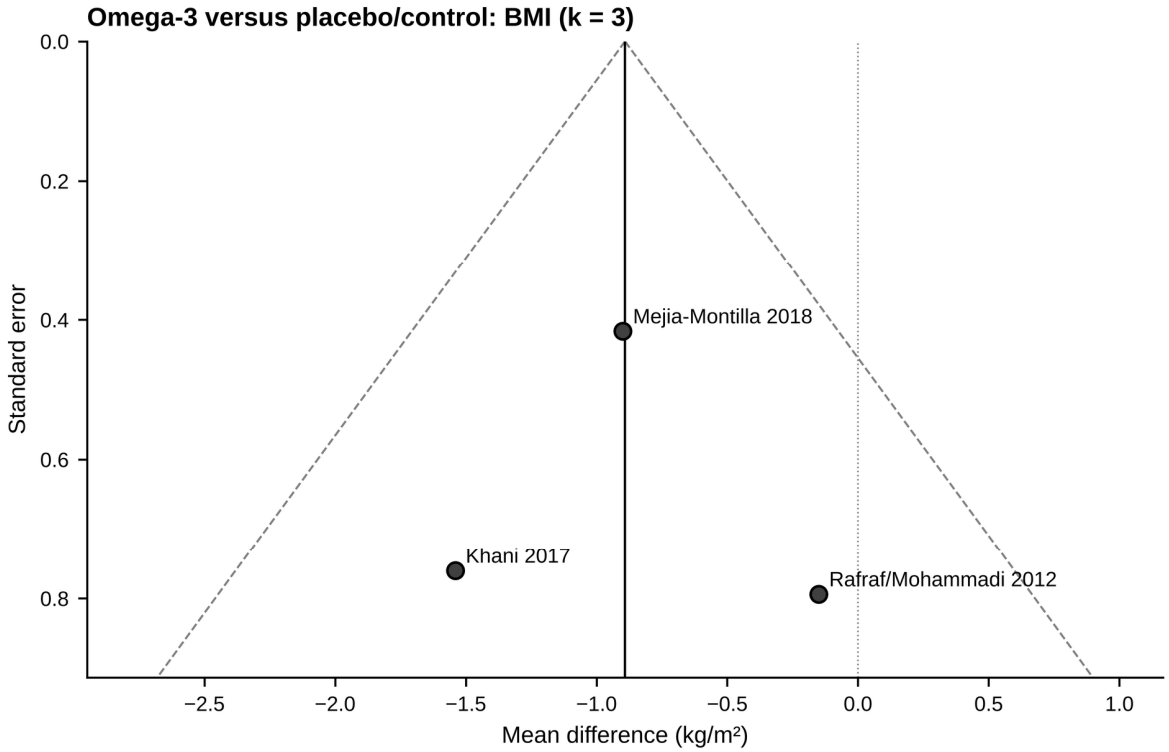
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S118. Funnel plot for Triglycerides with Omega-3 versus placebo/control (descriptive only)



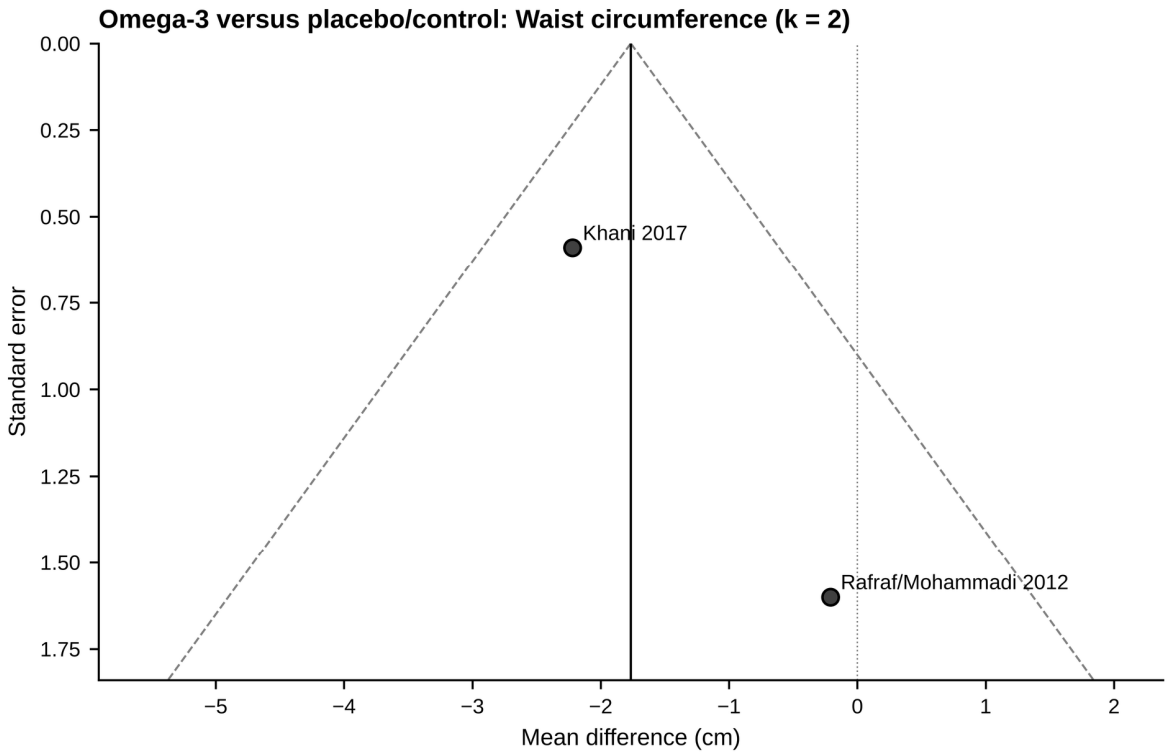
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S119. Funnel plot for BMI with Omega-3 versus placebo/control (descriptive only)



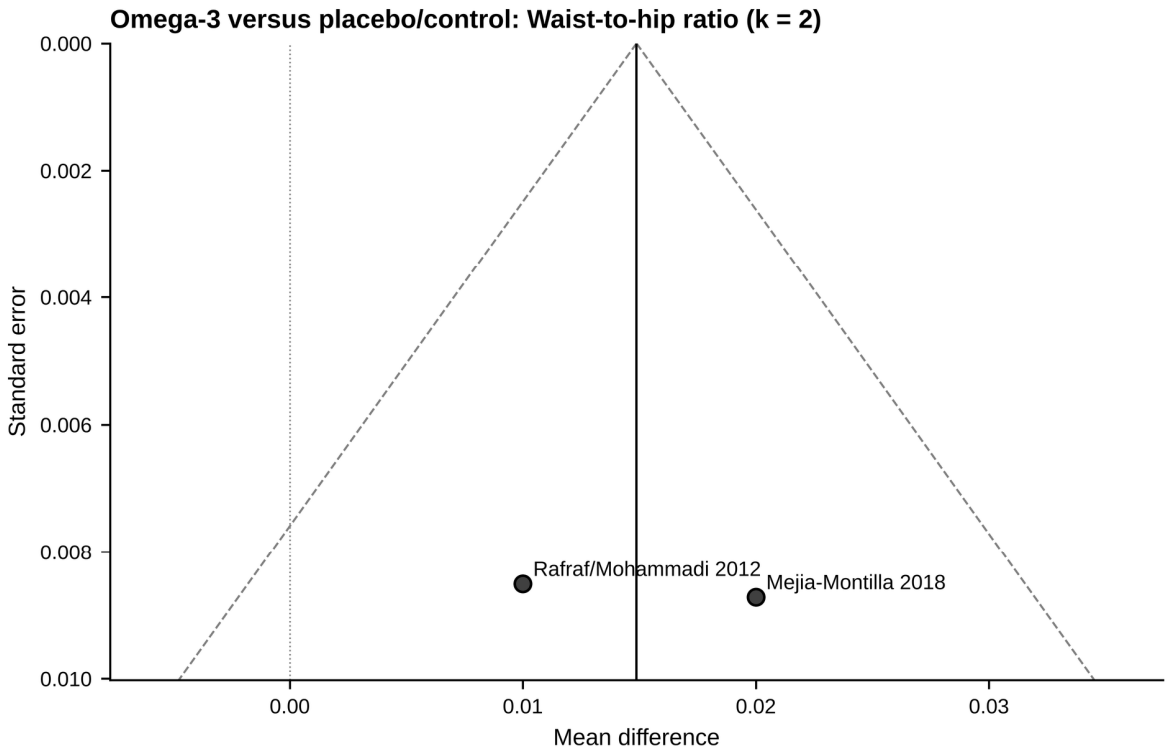
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S120. Funnel plot for Waist circumference with Omega-3 versus placebo/control (descriptive only)



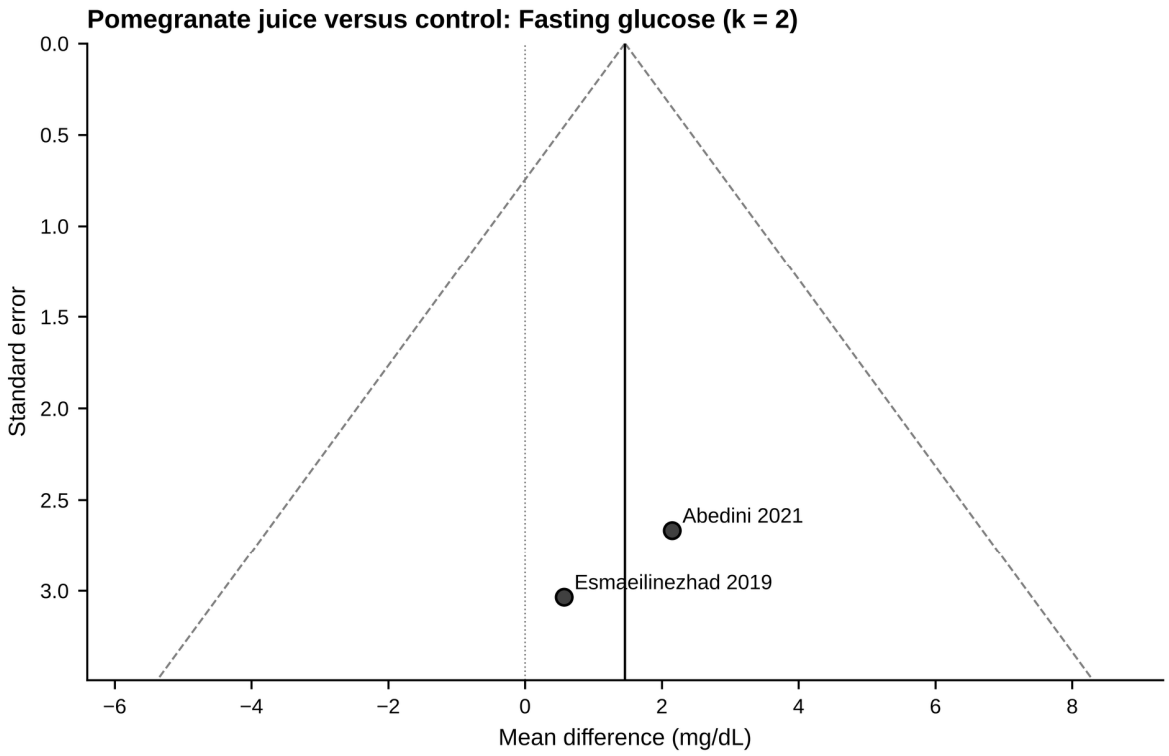
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S121. Funnel plot for Waist-to-hip ratio with Omega-3 versus placebo/control (descriptive only)



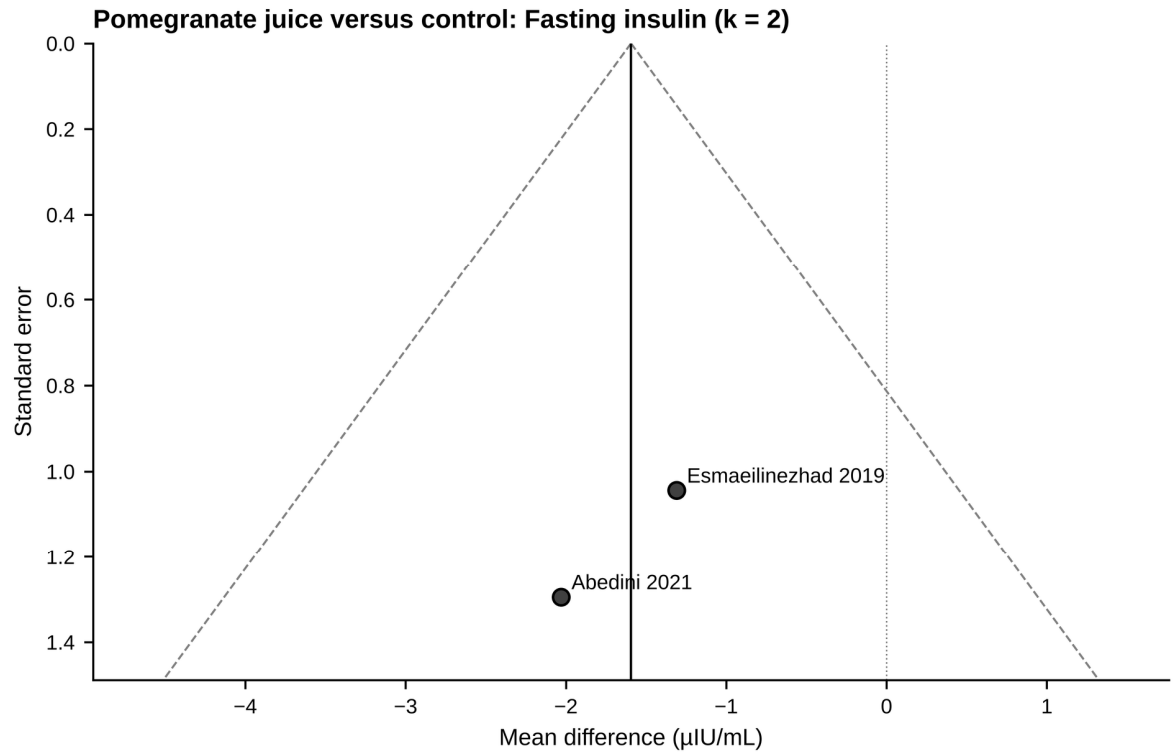
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S122. Funnel plot for Fasting glucose with Pomegranate juice versus control (descriptive only)



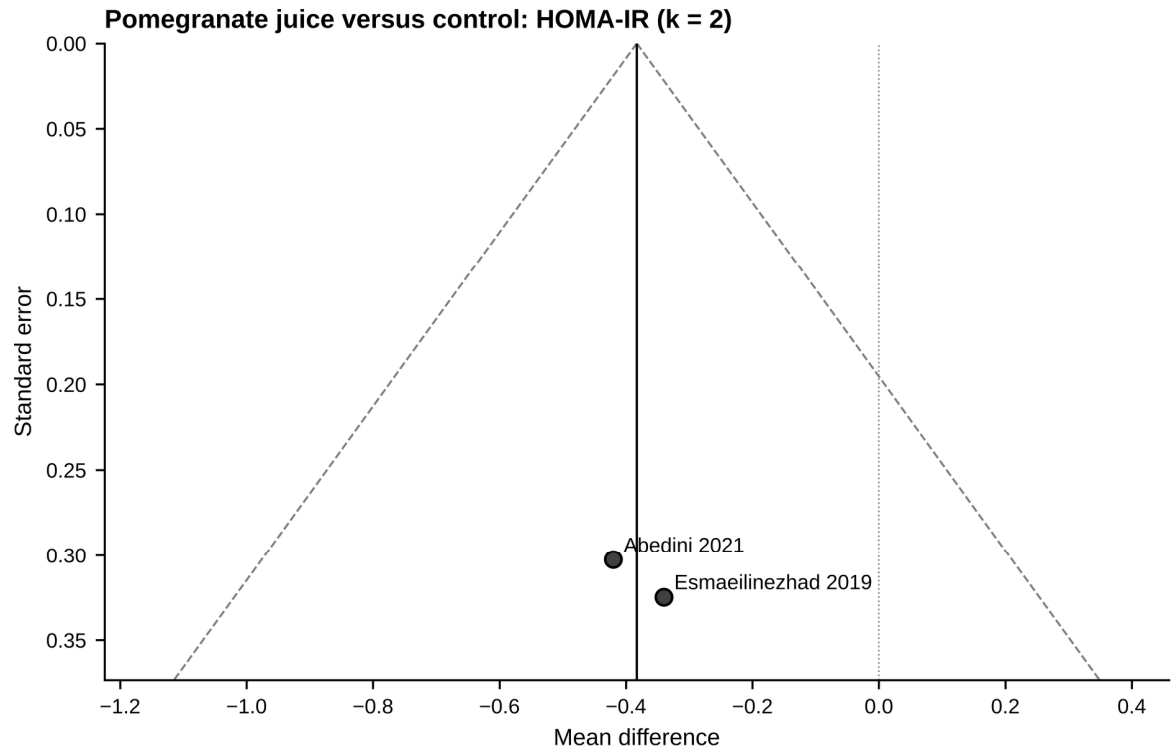
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S123. Funnel plot for Fasting insulin with Pomegranate juice versus control (descriptive only)



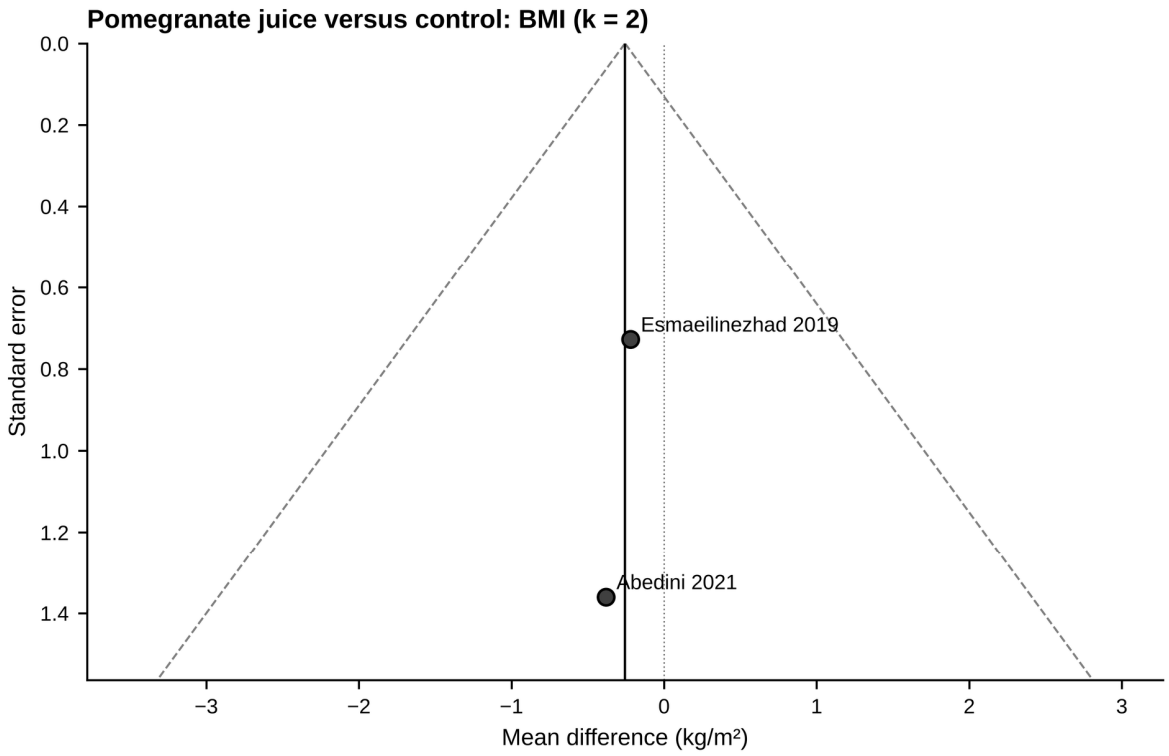
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S124. Funnel plot for HOMA-IR with Pomegranate juice versus control (descriptive only)



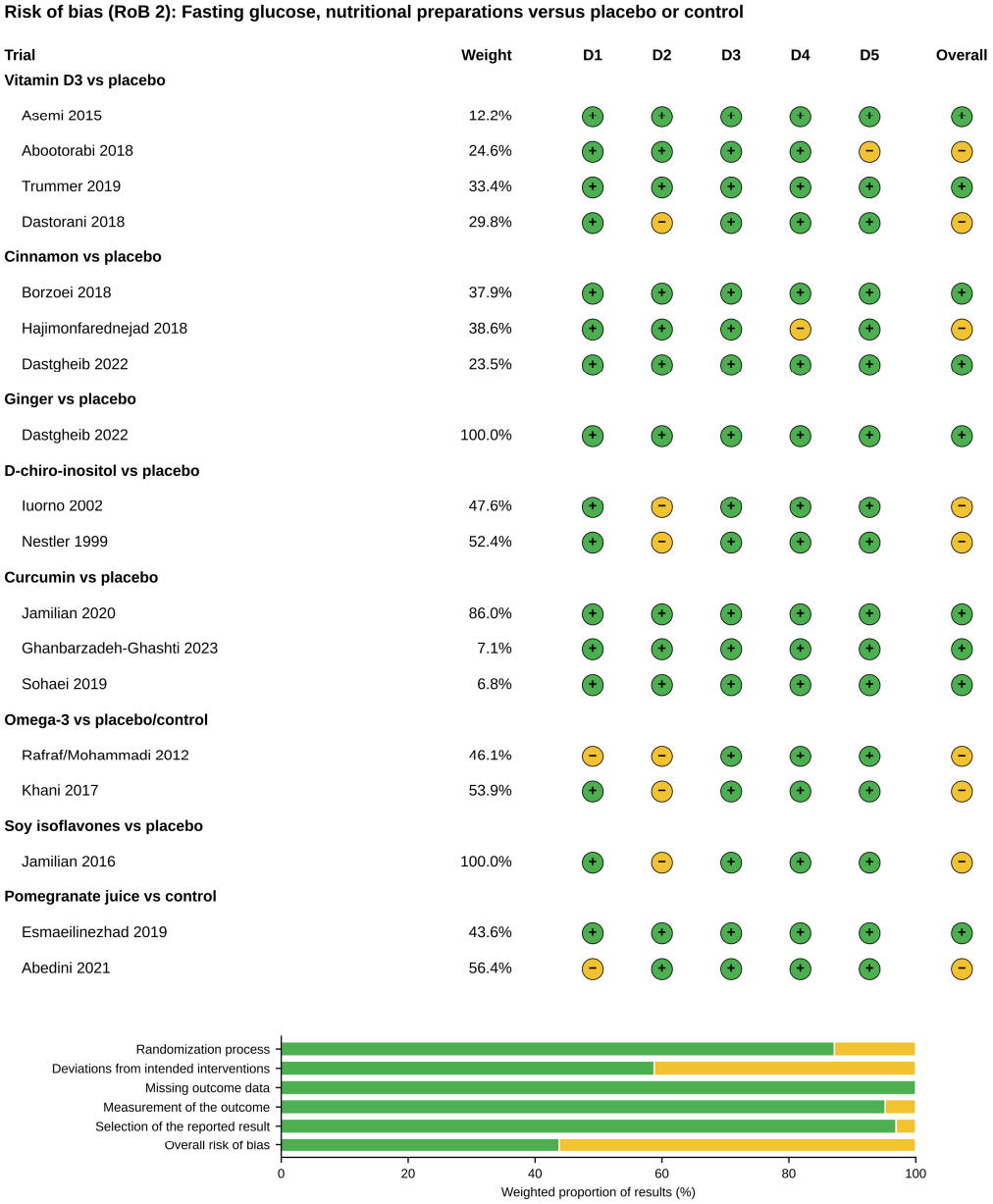
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S125. Funnel plot for BMI with Pomegranate juice versus control (descriptive only)



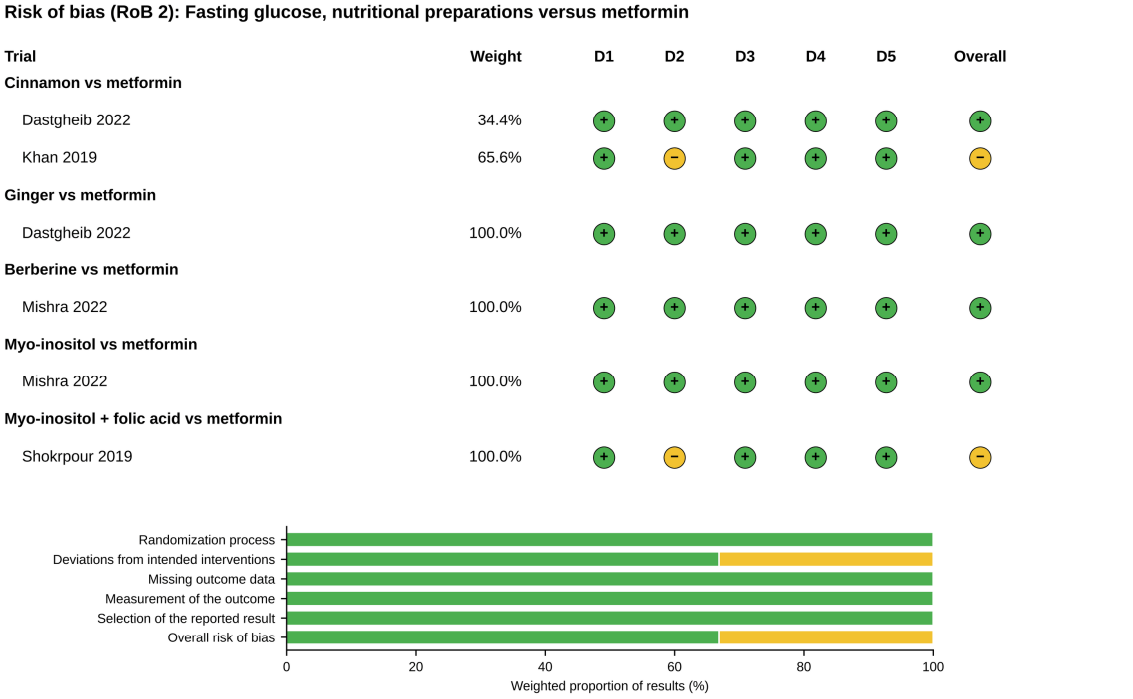
Solid line: pooled random-effects estimate. Dashed lines: pseudo 95% confidence limits. Dotted line: no difference.
Exploratory display only: fewer than 10 trials, so funnel-plot asymmetry and small-study effects cannot be assessed.

Figure S126. Risk of bias (RoB 2) of the results contributing to Fasting glucose: nutritional preparations versus placebo or control



D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S127. Risk of bias (RoB 2) of the results contributing to Fasting glucose: nutritional preparations versus metformin

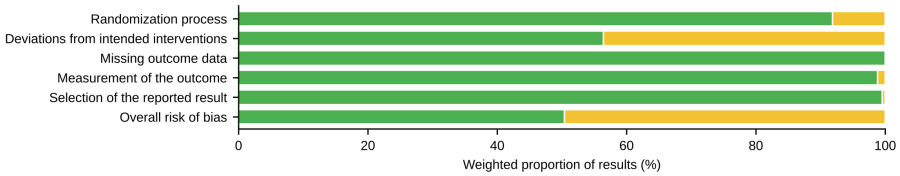


D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S128. Risk of bias (RoB 2) of the results contributing to Fasting insulin: nutritional preparations versus placebo or control

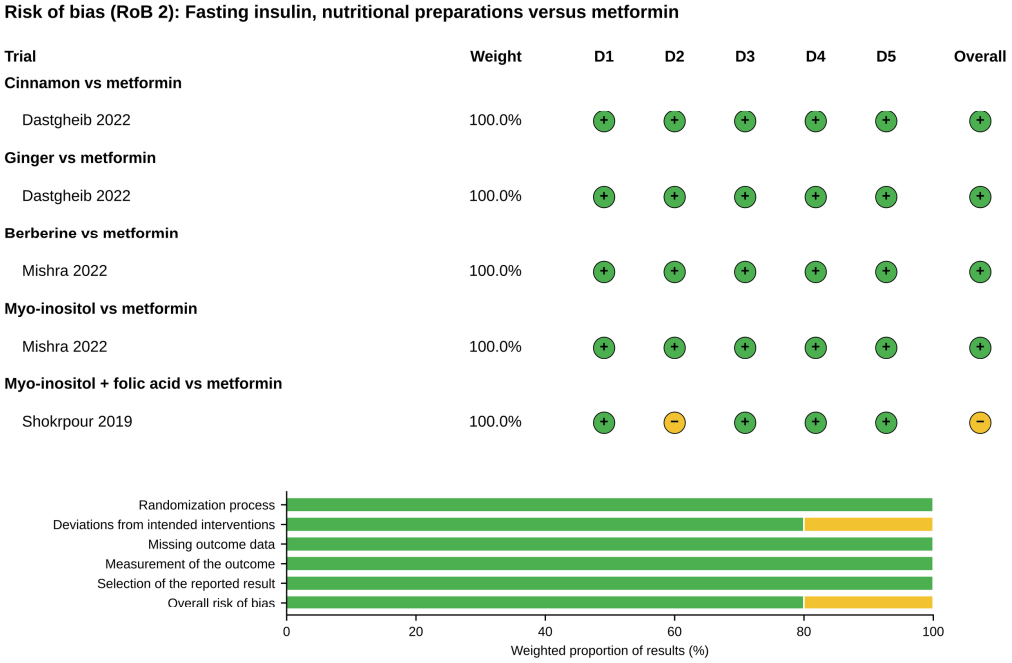
Risk of bias (RoB 2): Fasting insulin, nutritional preparations versus placebo or control

Trial	Weight	D1	D2	D3	D4	D5	Overall
Vitamin D3 vs placebo							
Asemi 2015	3.7%	+	+	+	+	+	+
Abootorabi 2018	4.2%	+	+	+	+	−	−
Dastorani 2018	92.1%	+	−	+	+	+	−
Cinnamon vs placebo							
Borzoei 2018	52.0%	+	+	+	+	+	+
Hajimonfarednejad 2018	10.8%	+	+	+	−	+	−
Dastgheib 2022	37.2%	+	+	+	+	+	+
Ginger vs placebo							
Dastgheib 2022	100.0%	+	+	+	+	+	+
D-chiro-inositol vs placebo							
Iuorno 2002	64.4%	+	−	+	+	+	−
Nestler 1999	35.6%	+	−	+	+	+	−
Curcumin vs placebo							
Jamilian 2020	88.3%	+	+	+	+	+	+
Ghanbarzadeh-Ghashti 2023	4.6%	+	+	+	+	+	+
Sohaei 2019	7.1%	+	+	+	+	+	+
Omega-3 vs placebo/control							
Rafraf/Mohammadi 2012	34.1%	−	−	+	+	+	−
Mejia-Montilla 2018	65.9%	+	−	+	+	+	−
Omega-3 + vitamin E vs placebo							
Jamilian 2018 §	100.0%	+	+	+	+	+	+
Soy isoflavones vs placebo							
Jamilian 2016	100.0%	+	−	+	+	+	−
Pomegranate juice vs control							
Esmaeilinezhad 2019	60.6%	+	+	+	+	+	+
Abedini 2021	39.4%	−	+	+	+	+	−



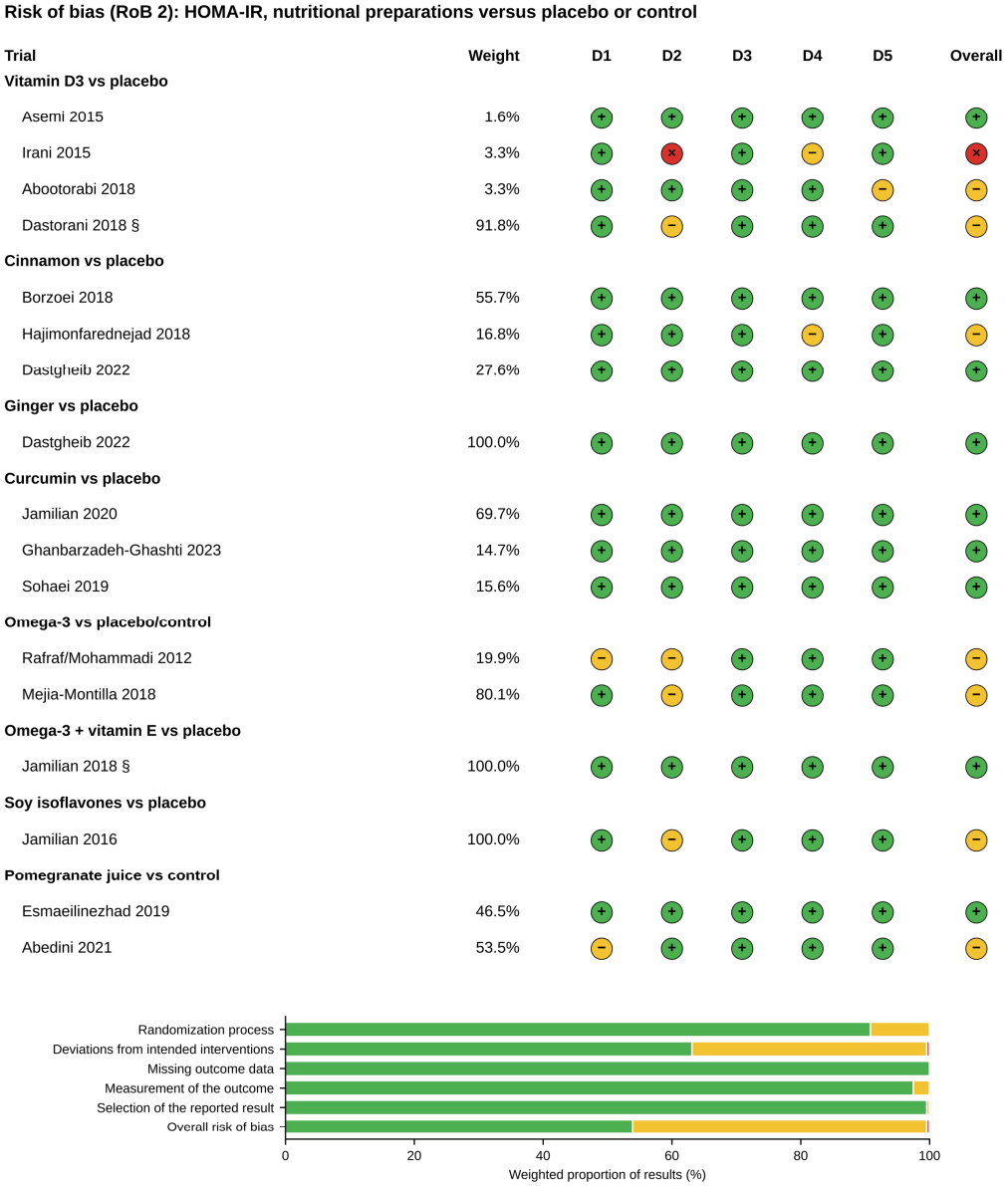
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S129. Risk of bias (RoB 2) of the results contributing to Fasting insulin: nutritional preparations versus metformin



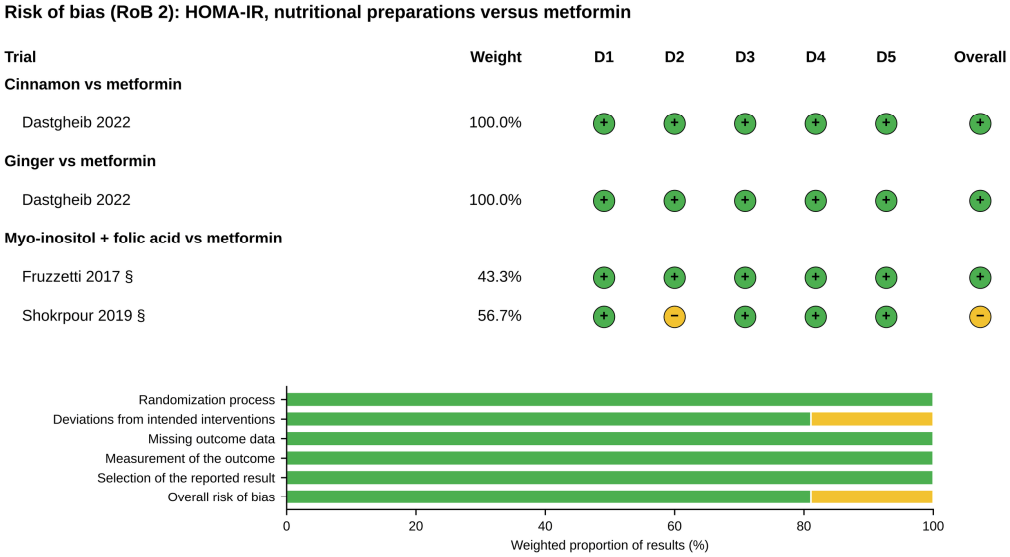
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S130. Risk of bias (RoB 2) of the results contributing to HOMA-IR: nutritional preparations versus placebo or control



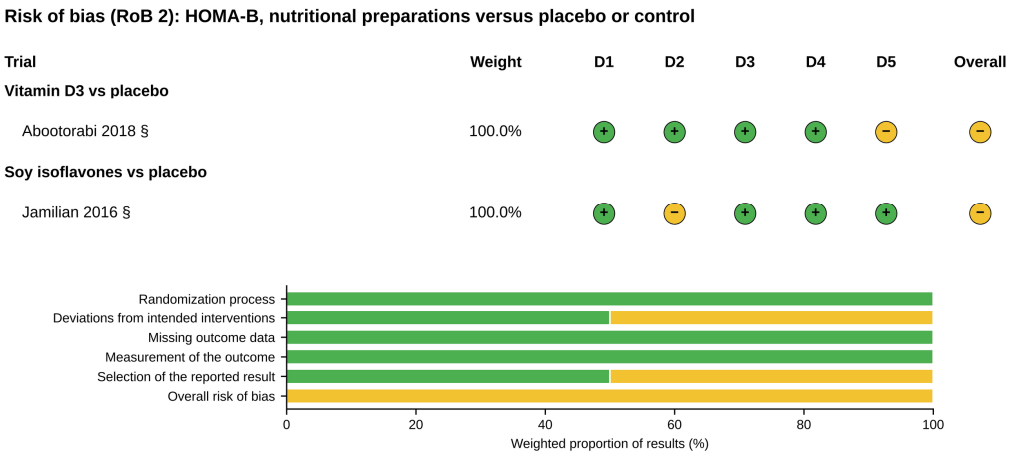
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S131. Risk of bias (RoB 2) of the results contributing to HOMA-IR: nutritional preparations versus metformin



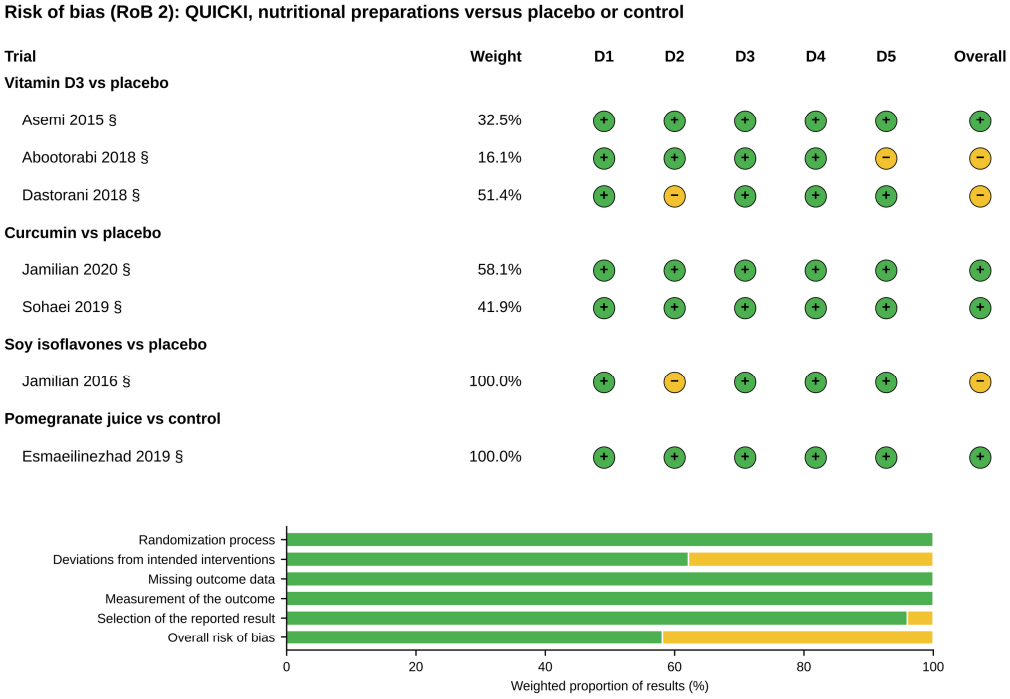
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S132. Risk of bias (RoB 2) of the results contributing to HOMA-B: nutritional preparations versus placebo or control



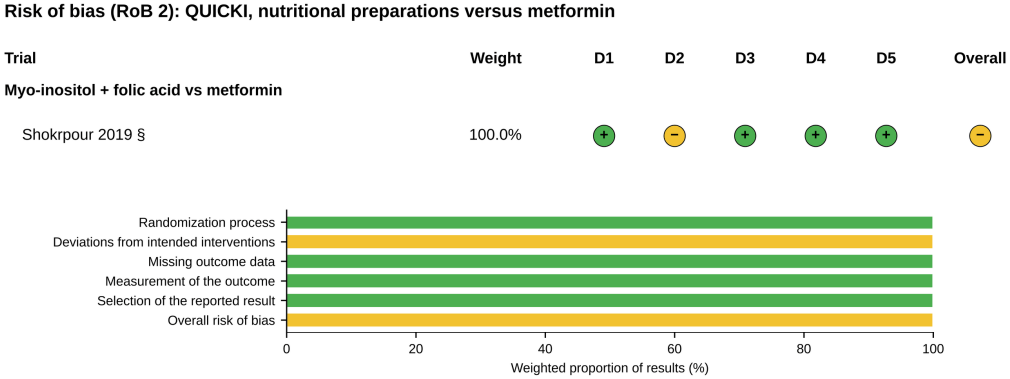
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S133. Risk of bias (RoB 2) of the results contributing to QUICKI: nutritional preparations versus placebo or control



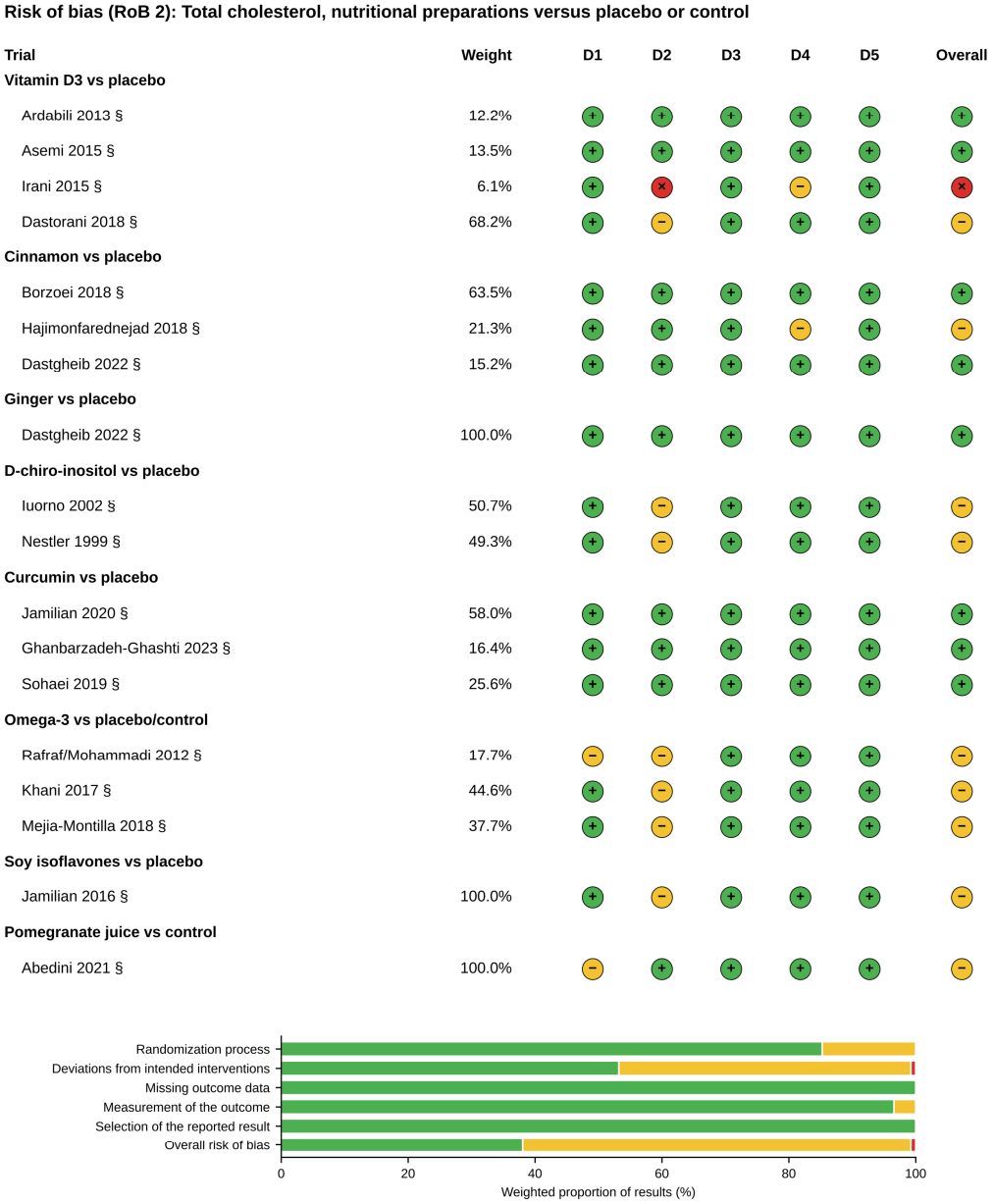
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S134. Risk of bias (RoB 2) of the results contributing to QUICKI: nutritional preparations versus metformin



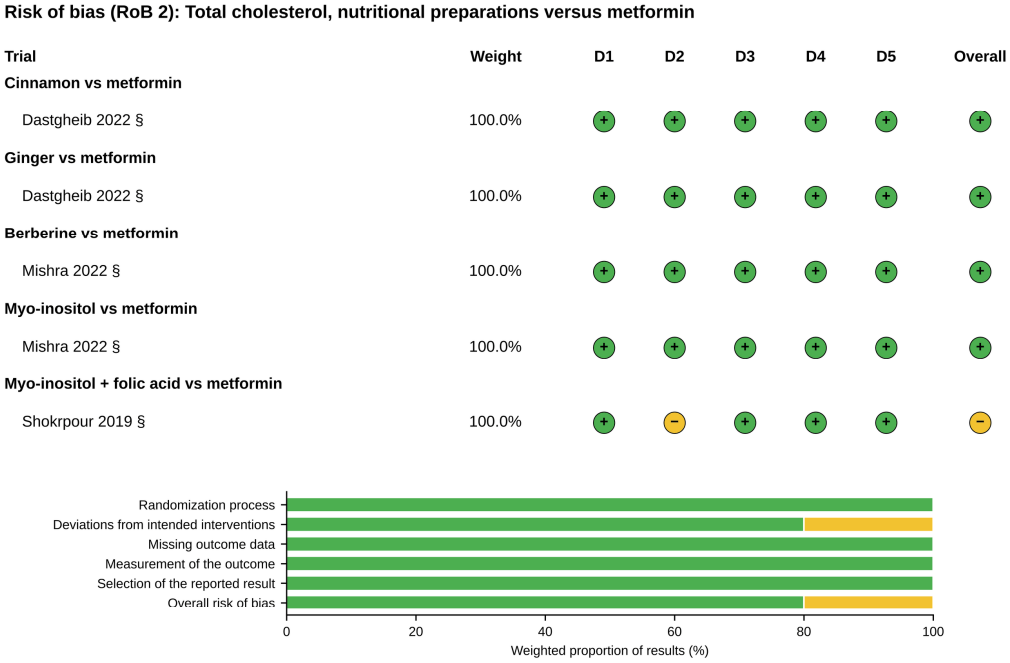
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S135. Risk of bias (RoB 2) of the results contributing to Total cholesterol: nutritional preparations versus placebo or control



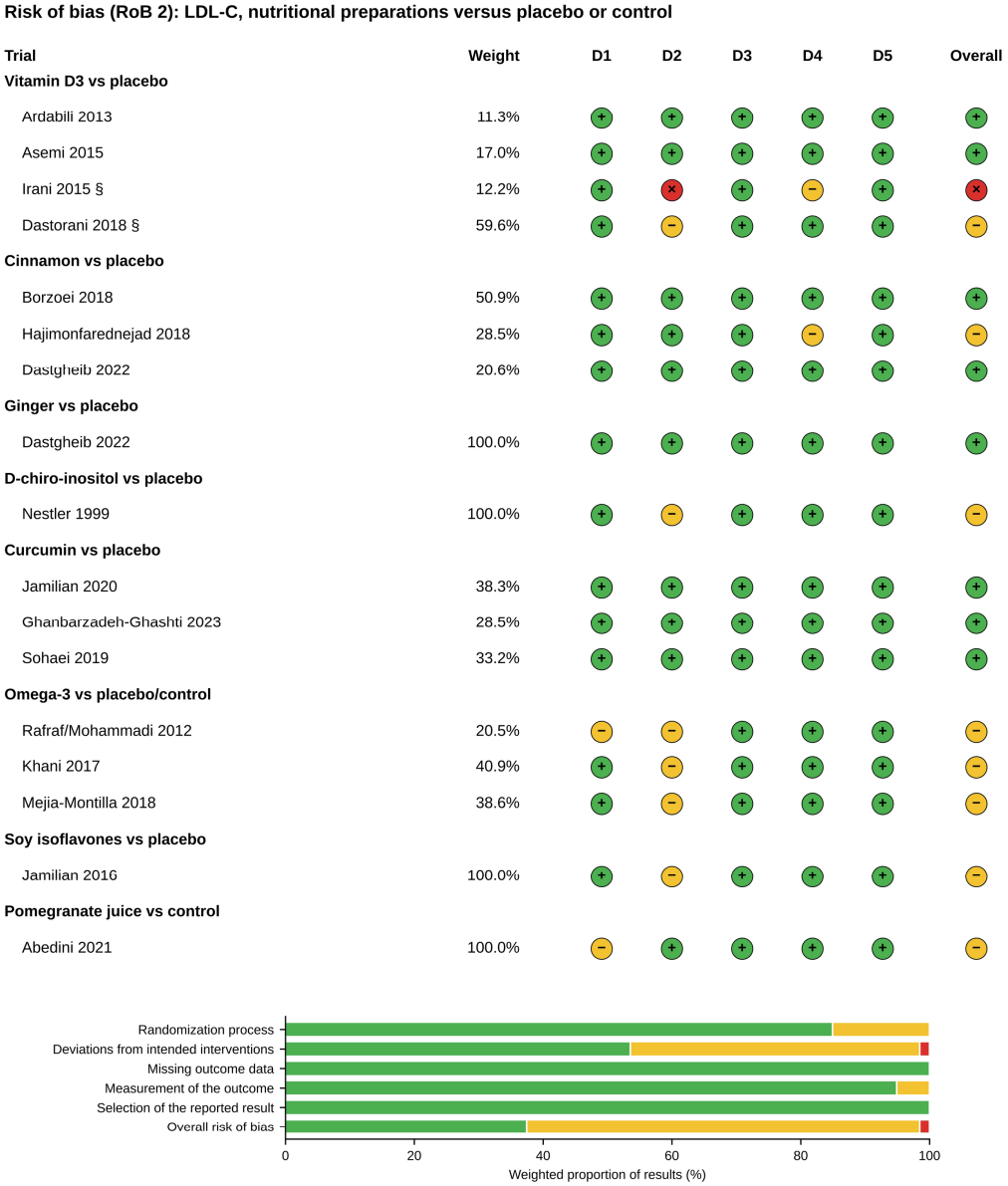
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S136. Risk of bias (RoB 2) of the results contributing to Total cholesterol: nutritional preparations versus metformin



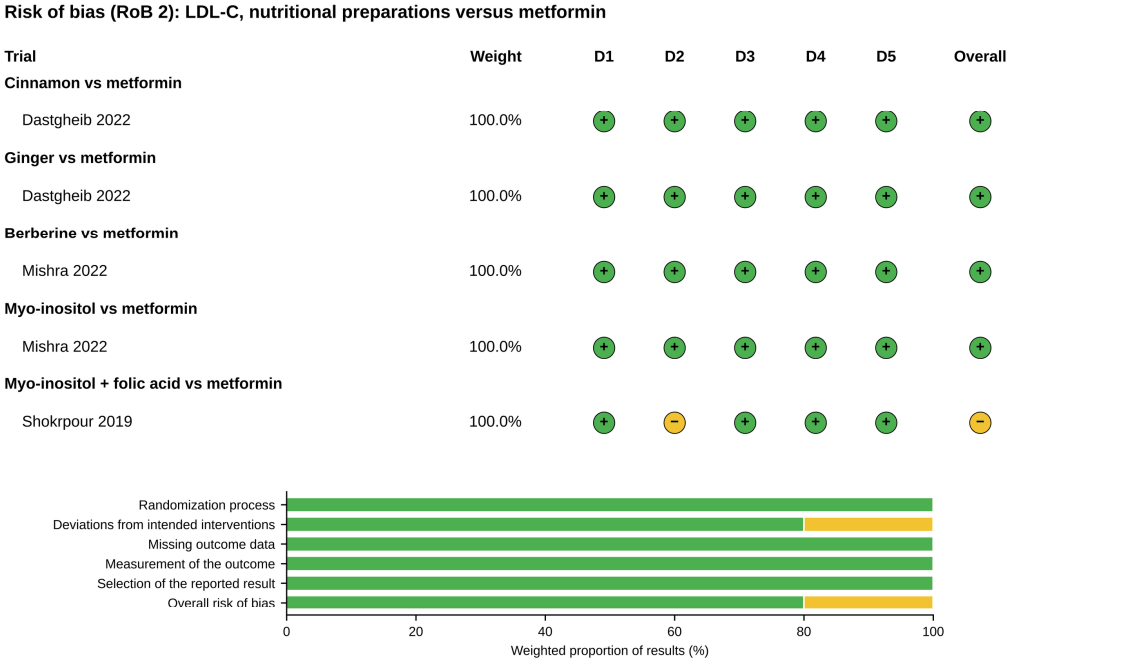
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S137. Risk of bias (RoB 2) of the results contributing to LDL-C: nutritional preparations versus placebo or control



D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S138. Risk of bias (RoB 2) of the results contributing to LDL-C: nutritional preparations versus metformin



D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
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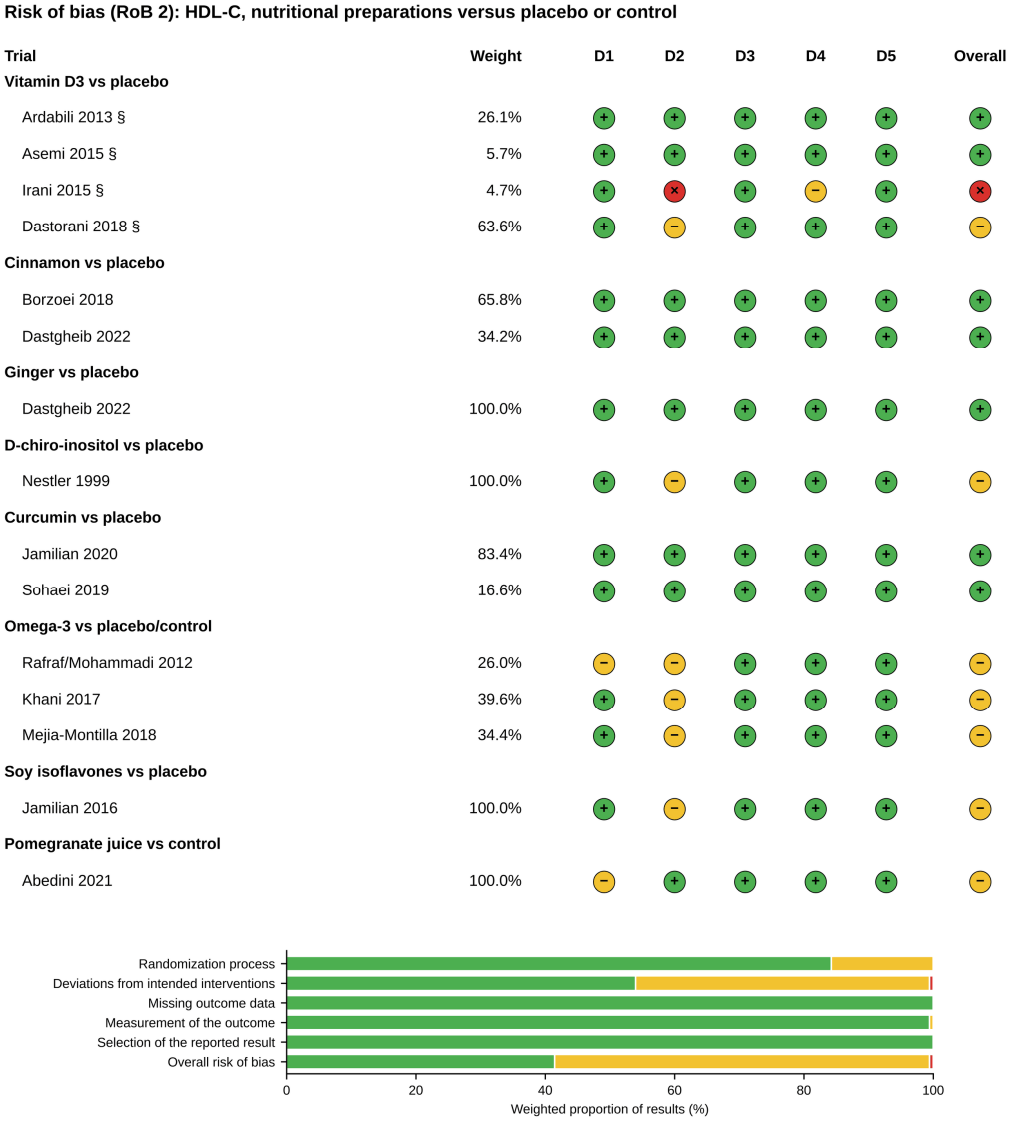
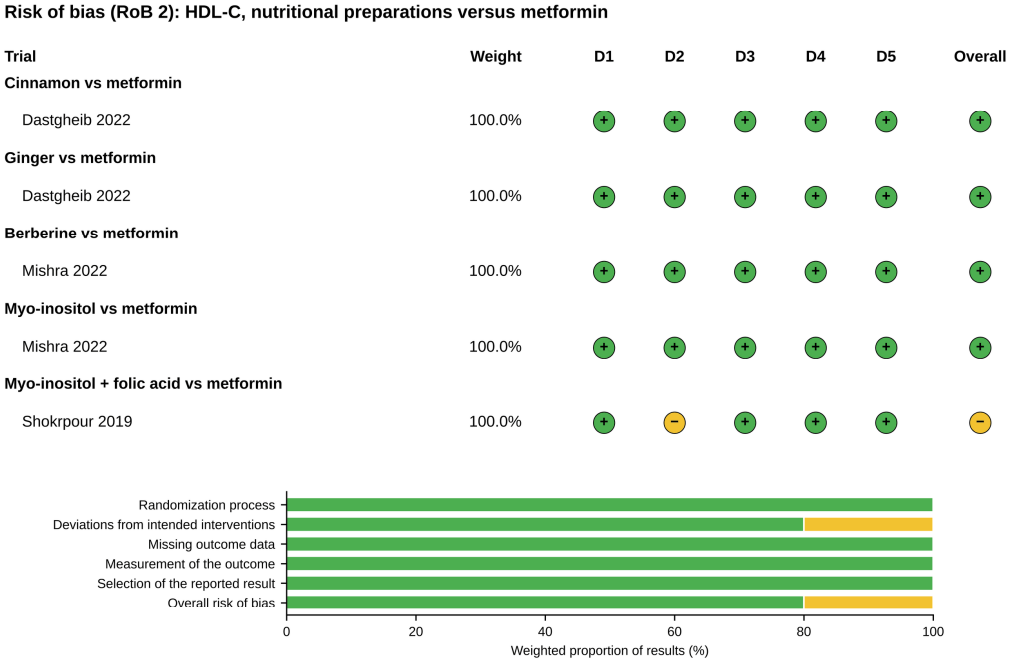
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S139. Risk of bias (RoB 2) of the results contributing to HDL-C: nutritional preparations versus placebo or control



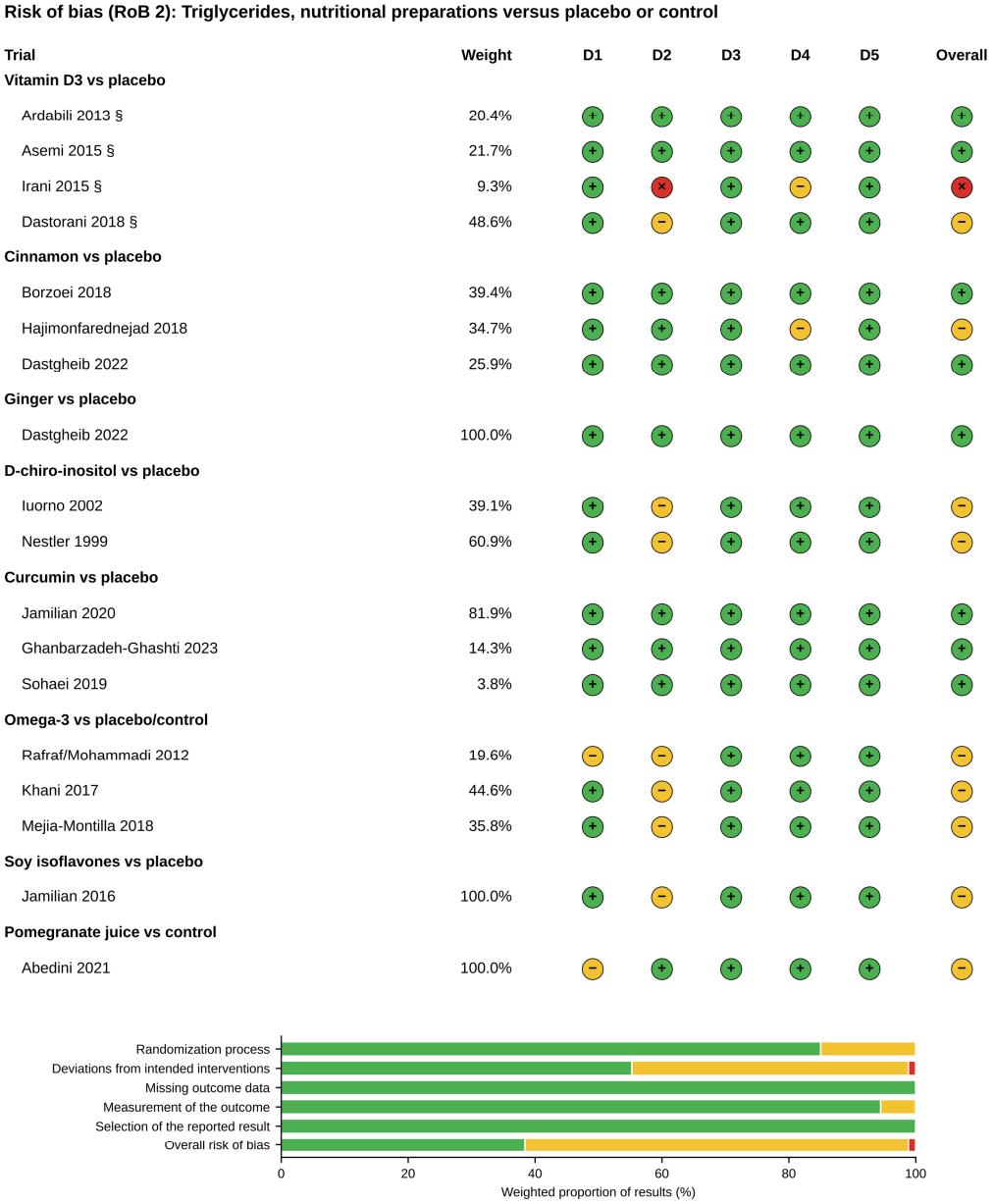
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S140. Risk of bias (RoB 2) of the results contributing to HDL-C: nutritional preparations versus metformin



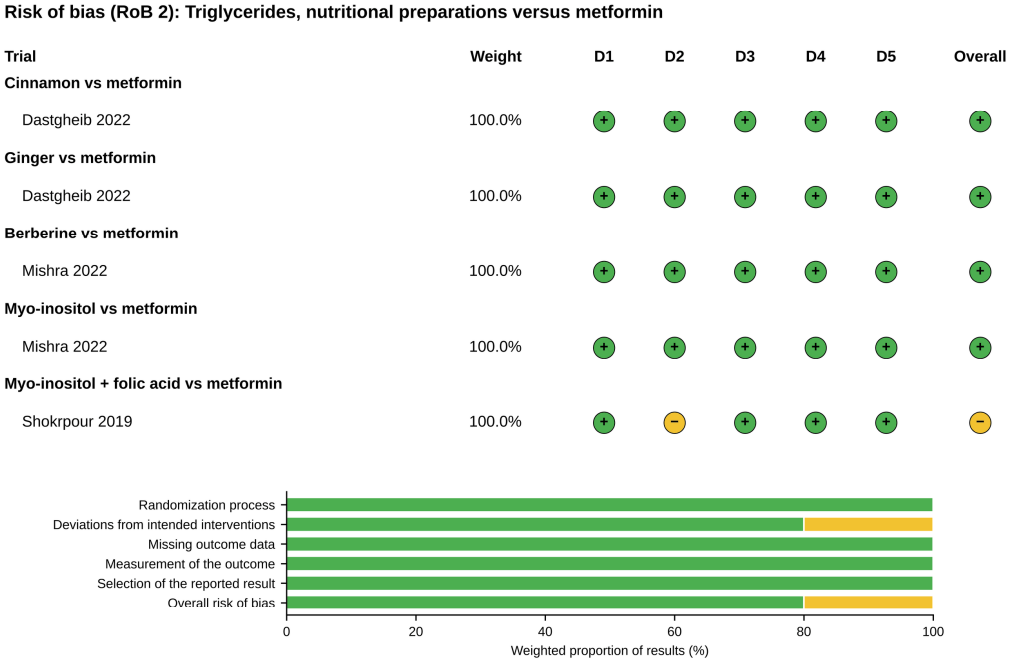
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S141. Risk of bias (RoB 2) of the results contributing to Triglycerides: nutritional preparations versus placebo or control



D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S142. Risk of bias (RoB 2) of the results contributing to Triglycerides: nutritional preparations versus metformin



D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
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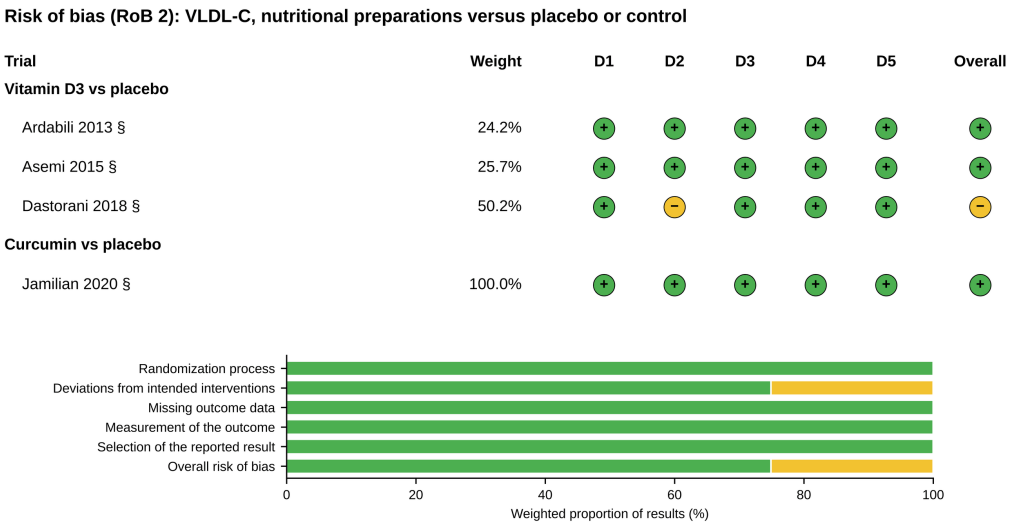
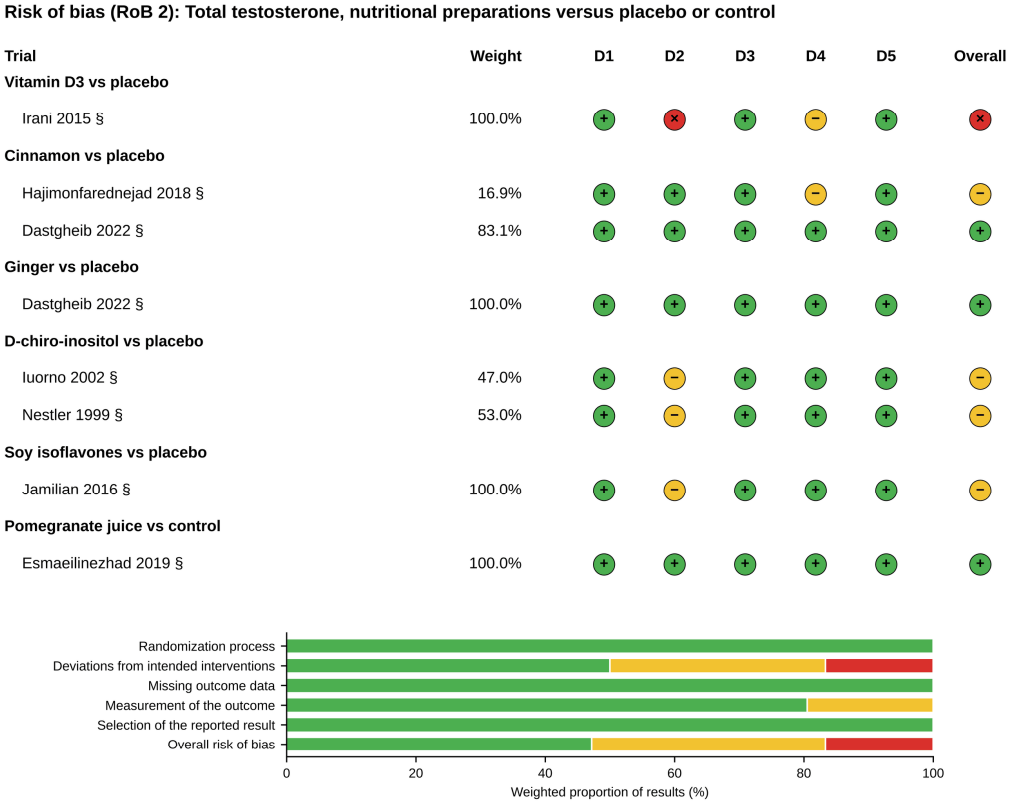
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S143. Risk of bias (RoB 2) of the results contributing to VLDL-C: nutritional preparations versus placebo or control



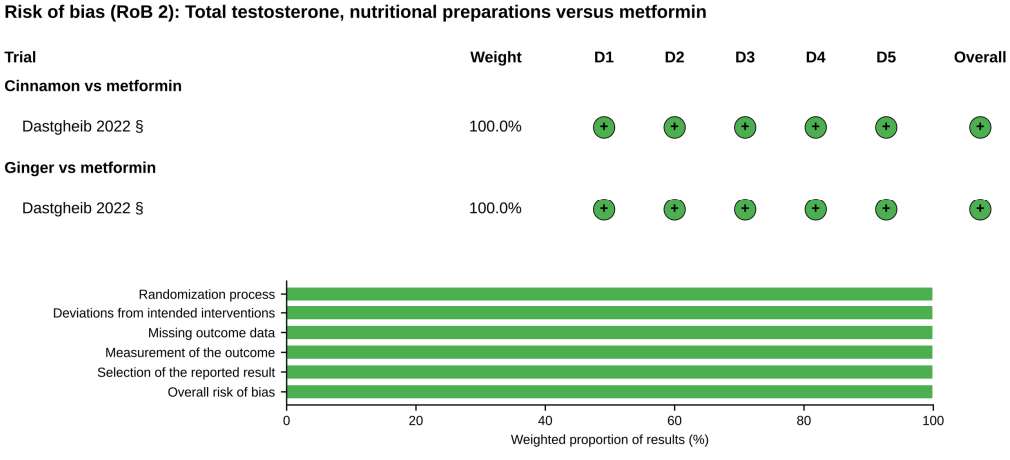
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S144. Risk of bias (RoB 2) of the results contributing to Total testosterone: nutritional preparations versus placebo or control



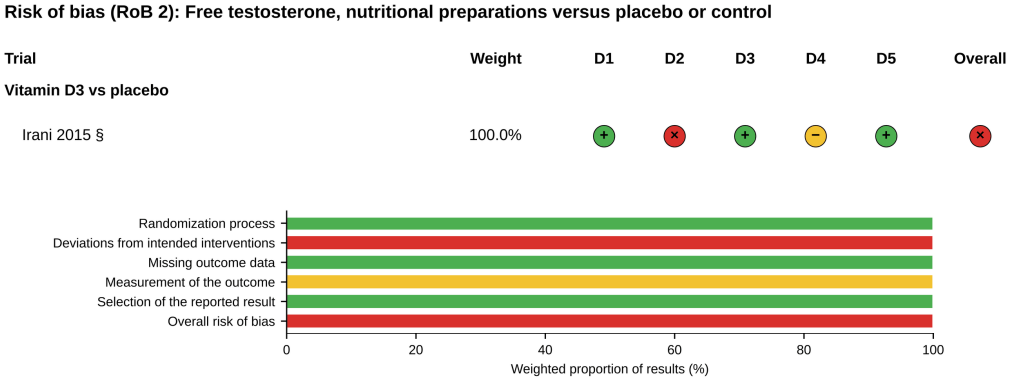
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S145. Risk of bias (RoB 2) of the results contributing to Total testosterone: nutritional preparations versus metformin



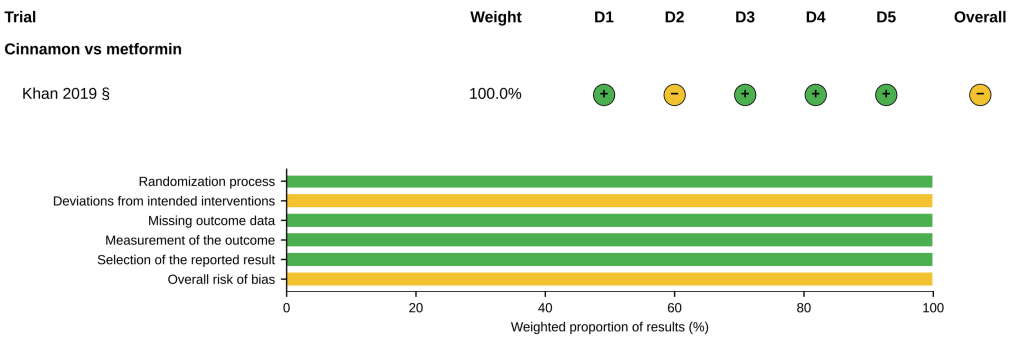
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S146. Risk of bias (RoB 2) of the results contributing to Free testosterone: nutritional preparations versus placebo or control



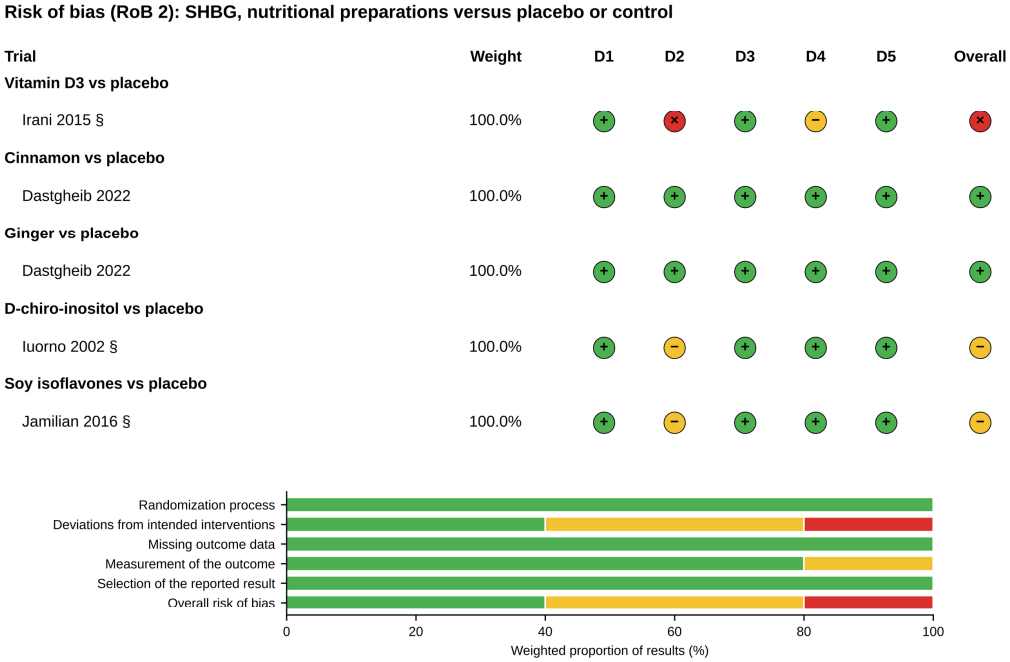
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S147. Risk of bias (RoB 2) of the results contributing to Free testosterone: nutritional preparations versus metformin



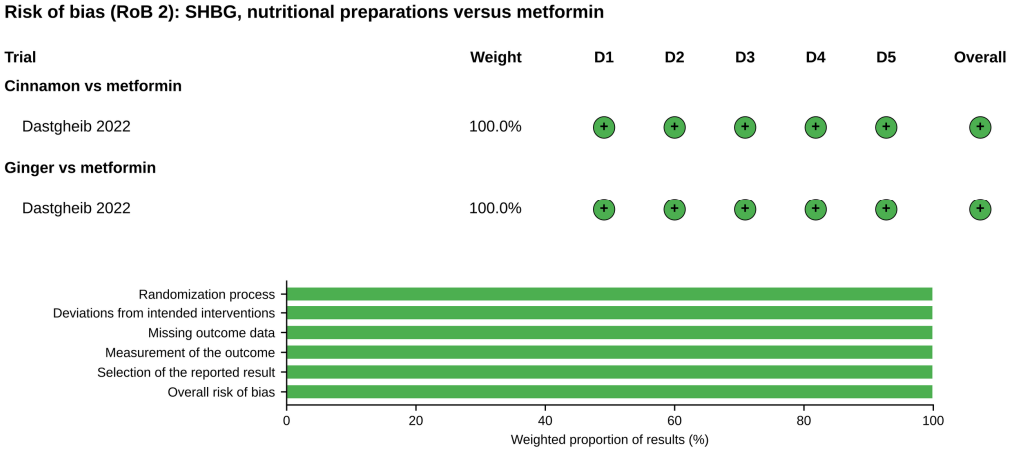
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S148. Risk of bias (RoB 2) of the results contributing to SHBG: nutritional preparations versus placebo or control



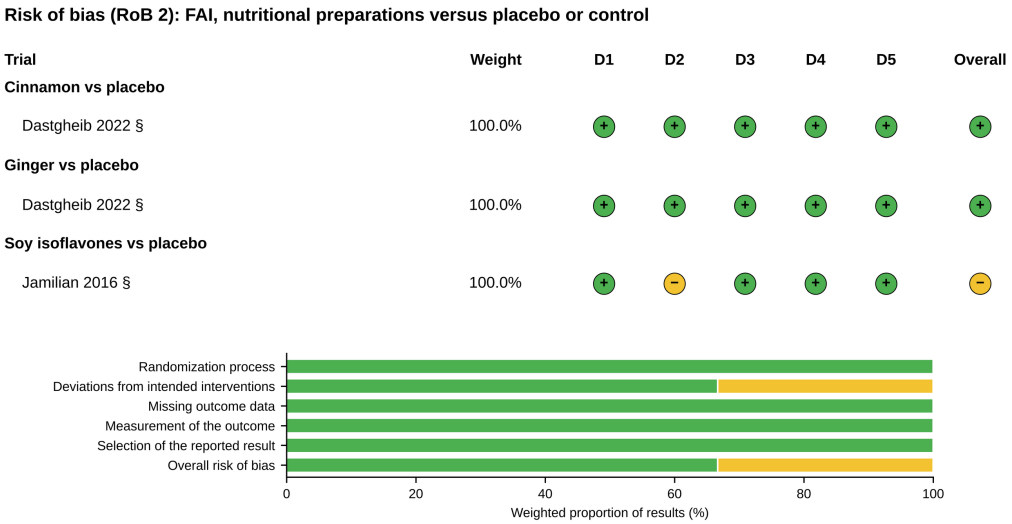
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S149. Risk of bias (RoB 2) of the results contributing to SHBG: nutritional preparations versus metformin



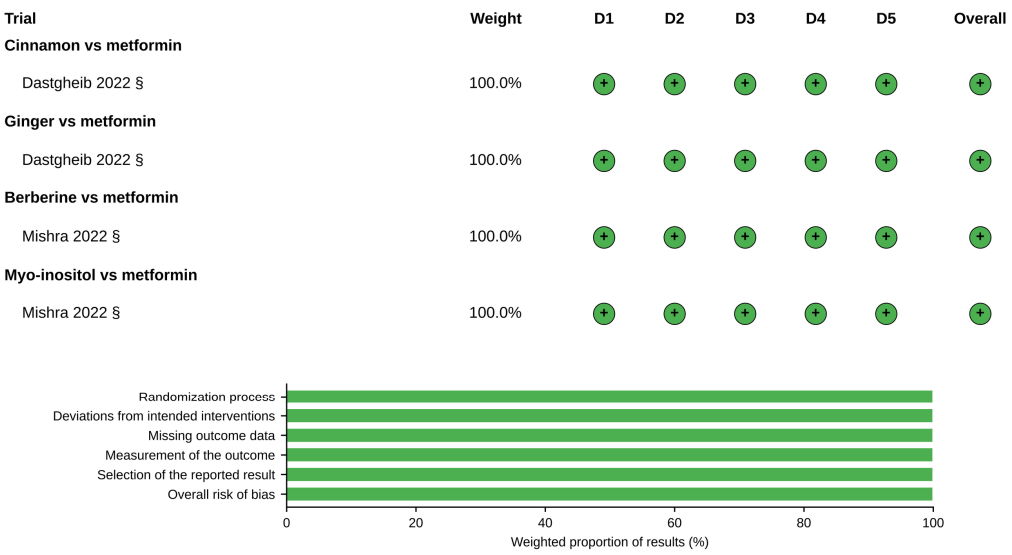
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S150. Risk of bias (RoB 2) of the results contributing to FAI: nutritional preparations versus placebo or control



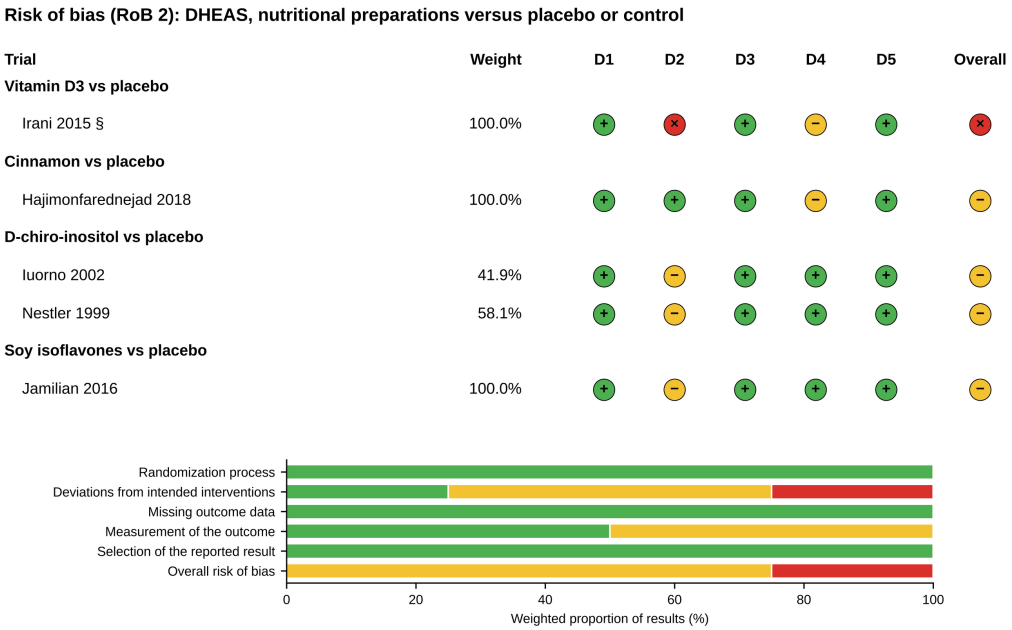
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S151. Risk of bias (RoB 2) of the results contributing to FAI: nutritional preparations versus metformin



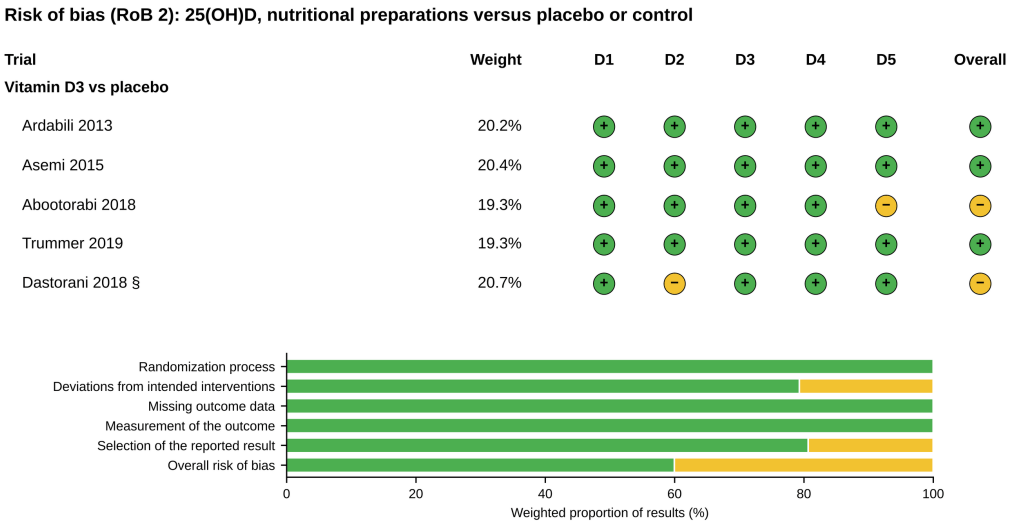
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S152. Risk of bias (RoB 2) of the results contributing to DHEAS: nutritional preparations versus placebo or control



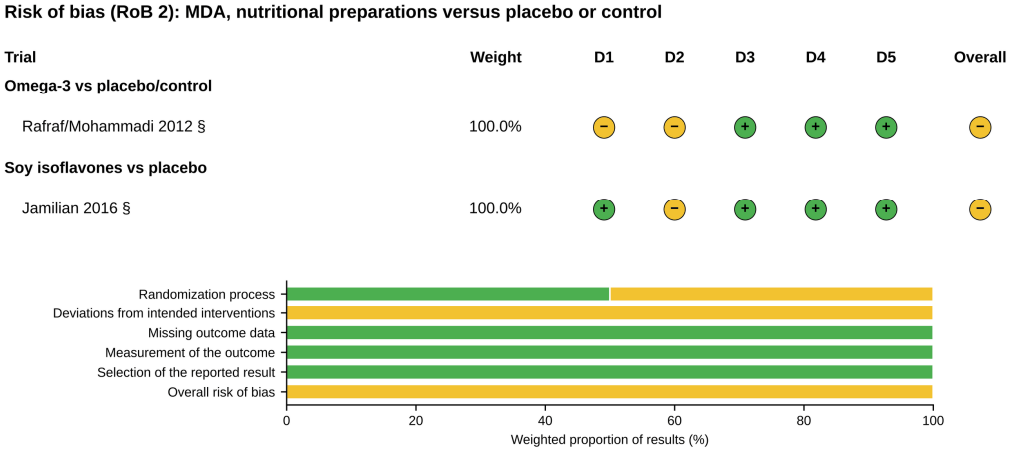
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S153. Risk of bias (RoB 2) of the results contributing to 25(OH)D: nutritional preparations versus placebo or control



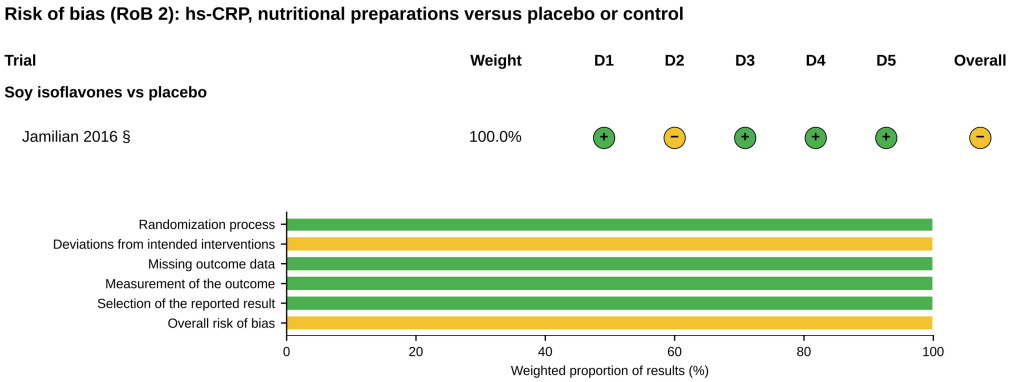
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S154. Risk of bias (RoB 2) of the results contributing to MDA: nutritional preparations versus placebo or control



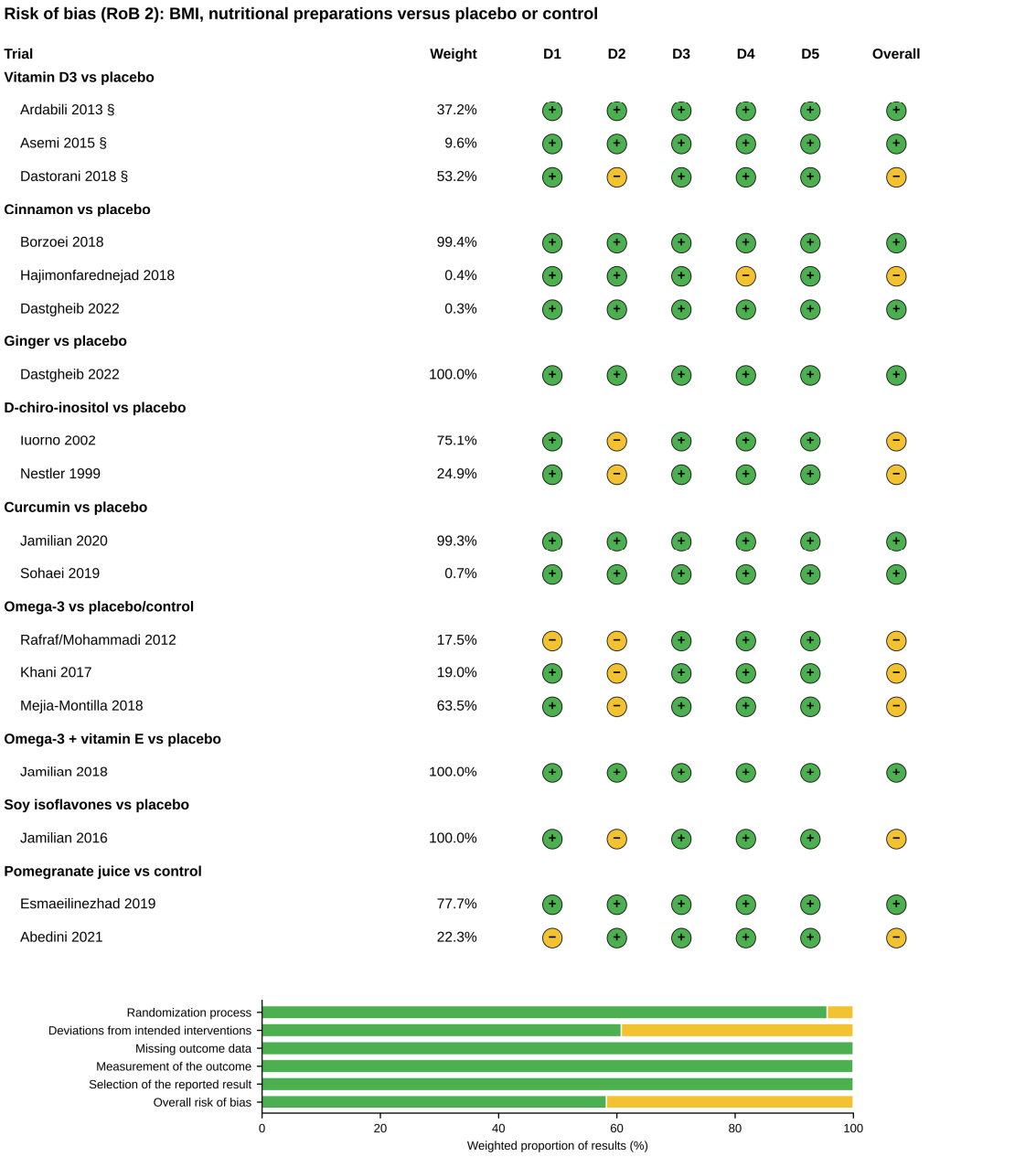
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S155. Risk of bias (RoB 2) of the results contributing to hs-CRP: nutritional preparations versus placebo or control



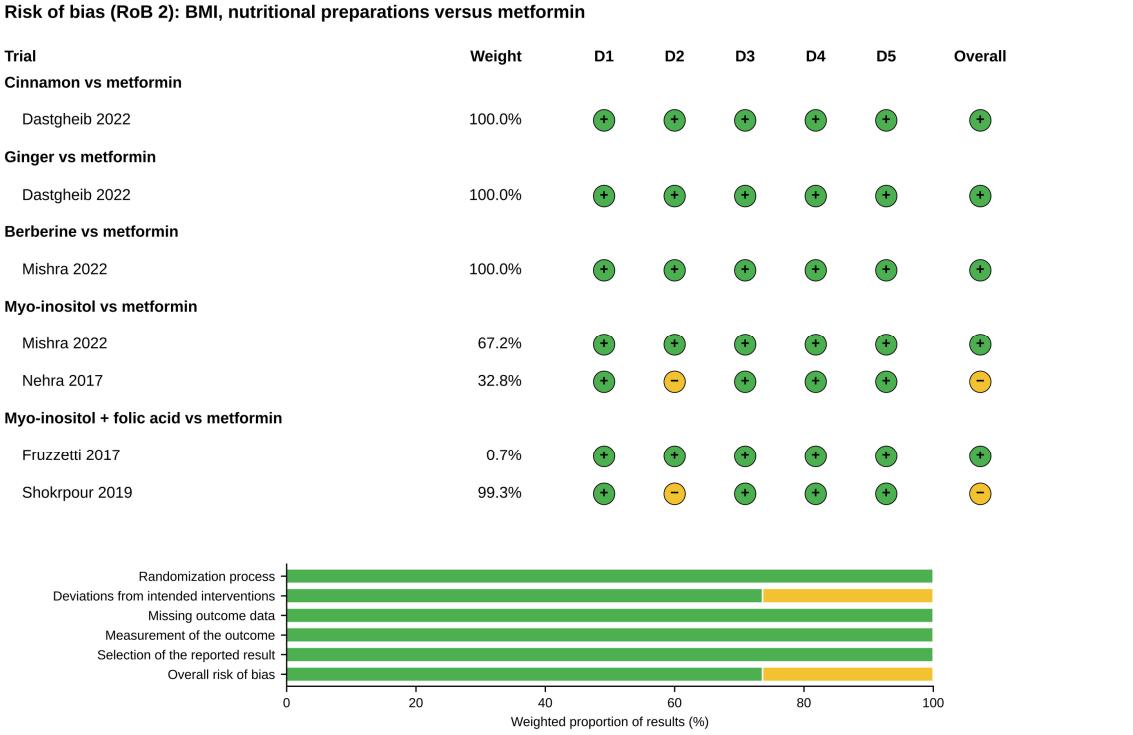
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S156. Risk of bias (RoB 2) of the results contributing to BMI: nutritional preparations versus placebo or control



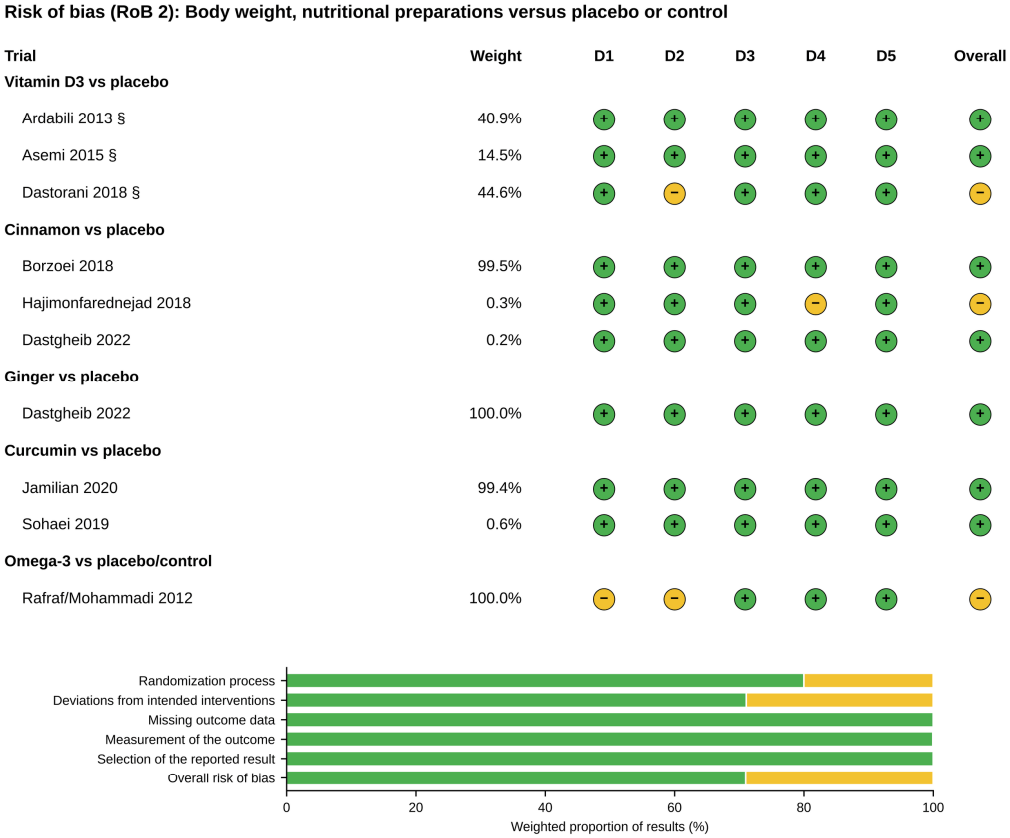
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S157. Risk of bias (RoB 2) of the results contributing to BMI: nutritional preparations versus metformin



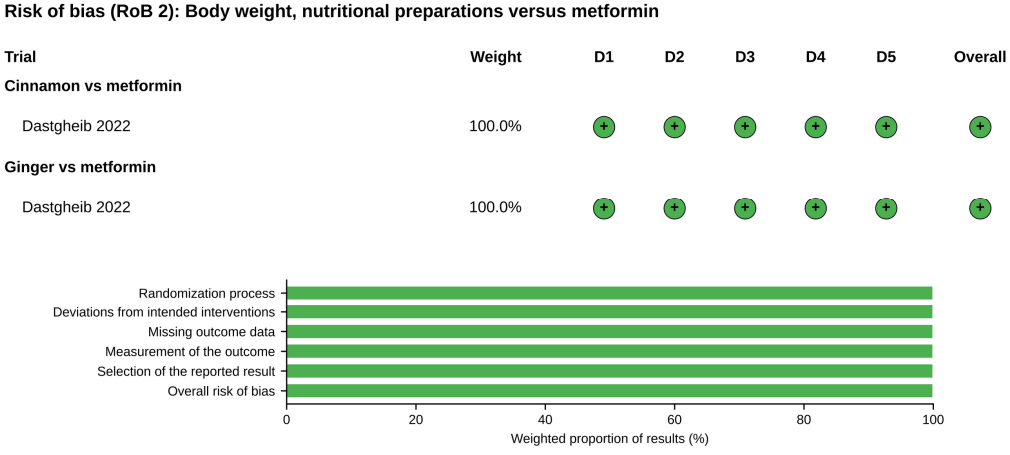
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S158. Risk of bias (RoB 2) of the results contributing to Body weight: nutritional preparations versus placebo or control



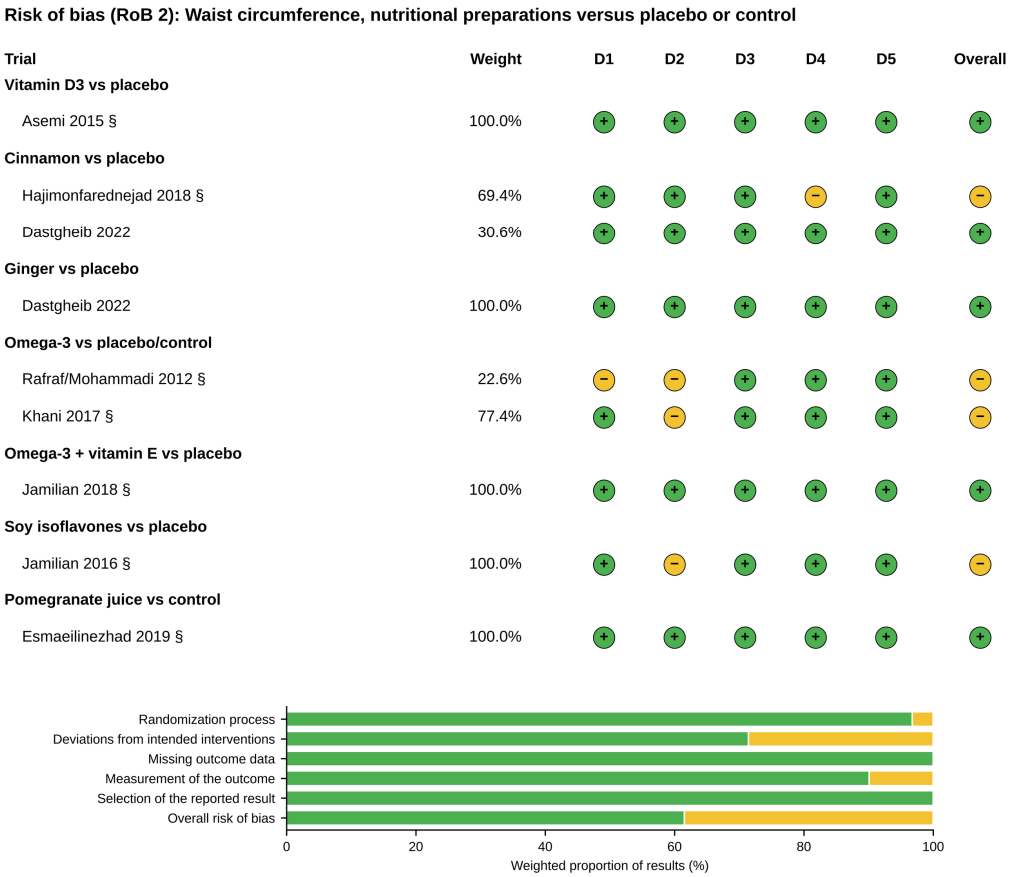
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S159. Risk of bias (RoB 2) of the results contributing to Body weight: nutritional preparations versus metformin



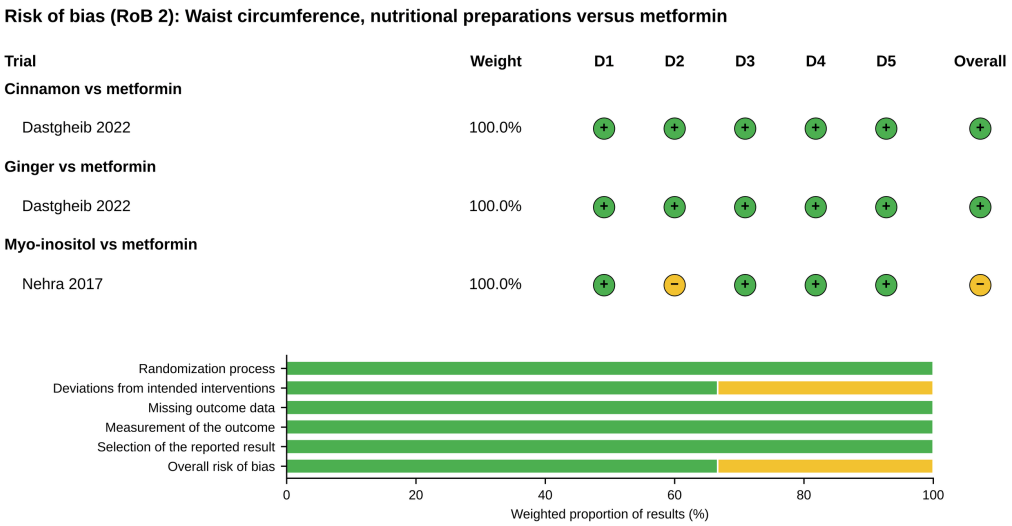
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S160. Risk of bias (RoB 2) of the results contributing to Waist circumference: nutritional preparations versus placebo or control



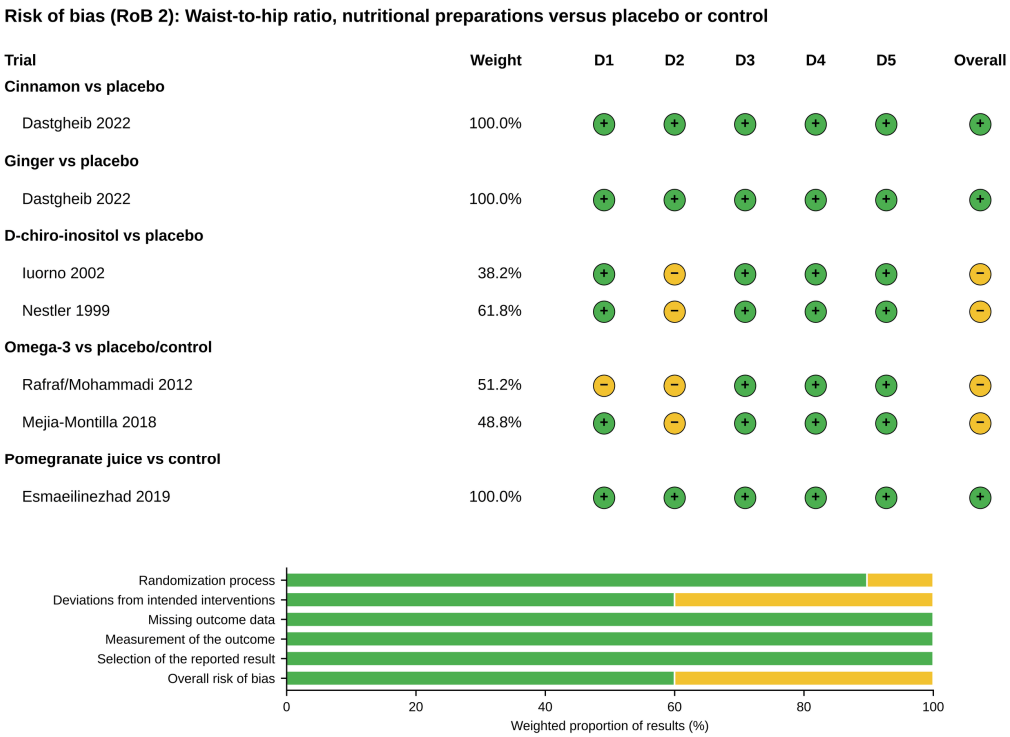
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S161. Risk of bias (RoB 2) of the results contributing to Waist circumference: nutritional preparations versus metformin



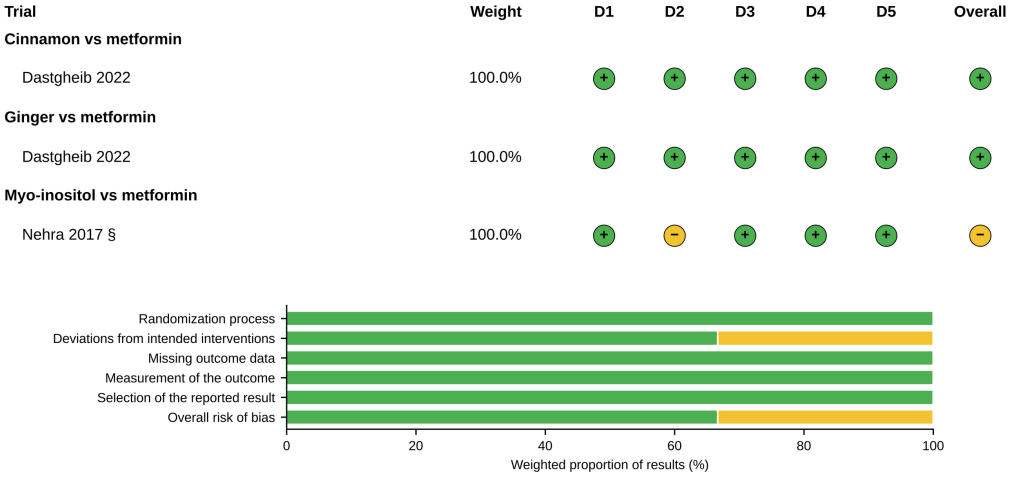
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S162. Risk of bias (RoB 2) of the results contributing to Waist-to-hip ratio: nutritional preparations versus placebo or control



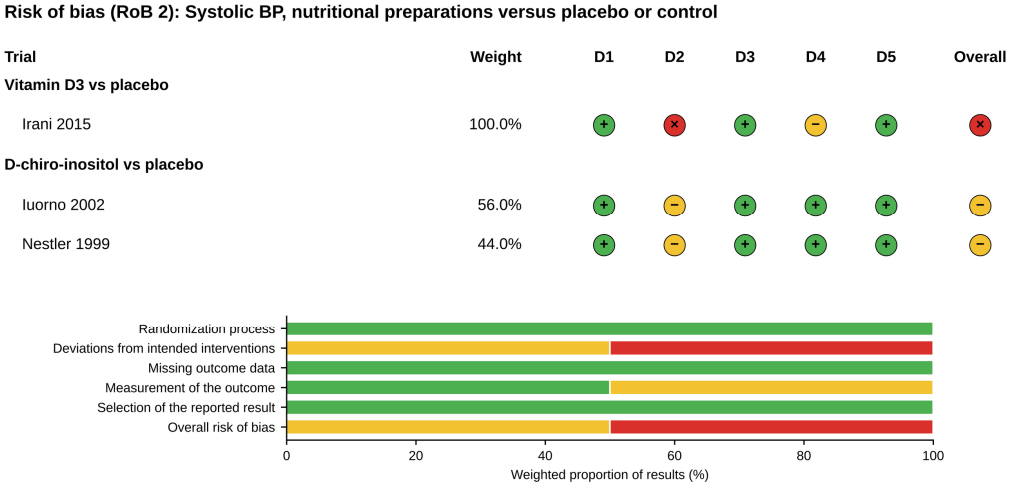
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S163. Risk of bias (RoB 2) of the results contributing to Waist-to-hip ratio: nutritional preparations versus metformin



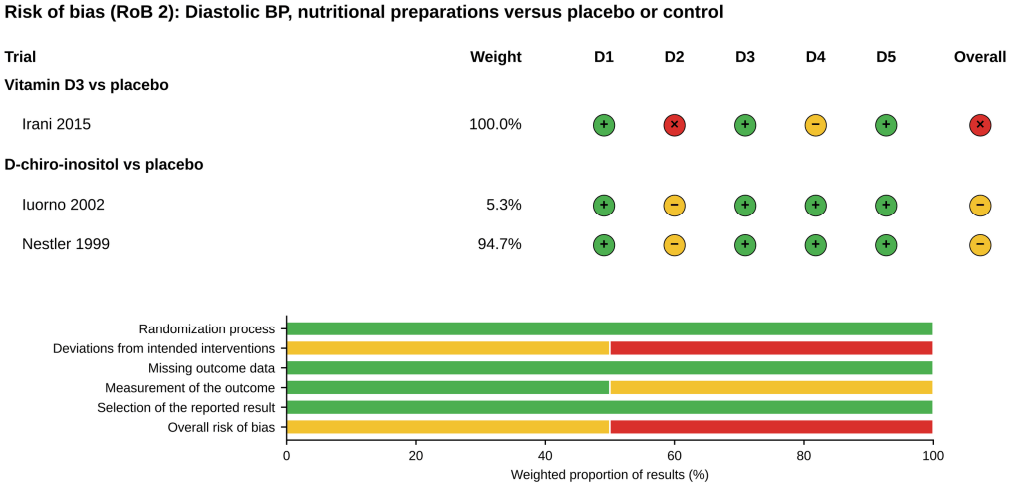
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S164. Risk of bias (RoB 2) of the results contributing to Systolic BP: nutritional preparations versus placebo or control



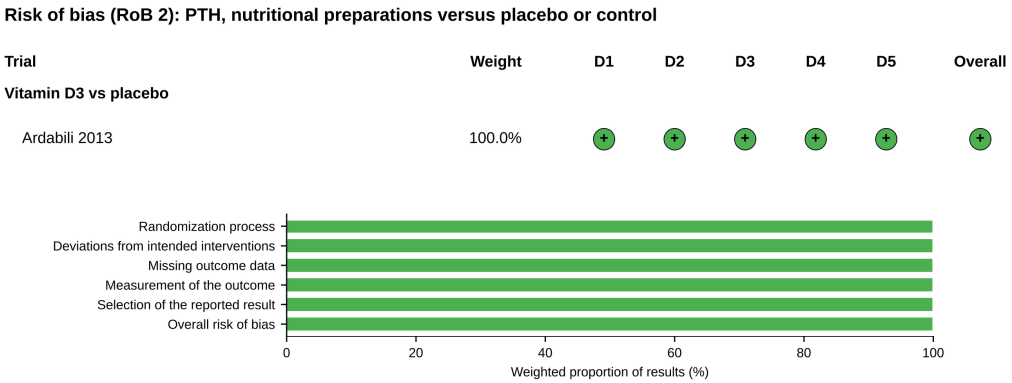
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S165. Risk of bias (RoB 2) of the results contributing to Diastolic BP: nutritional preparations versus placebo or control



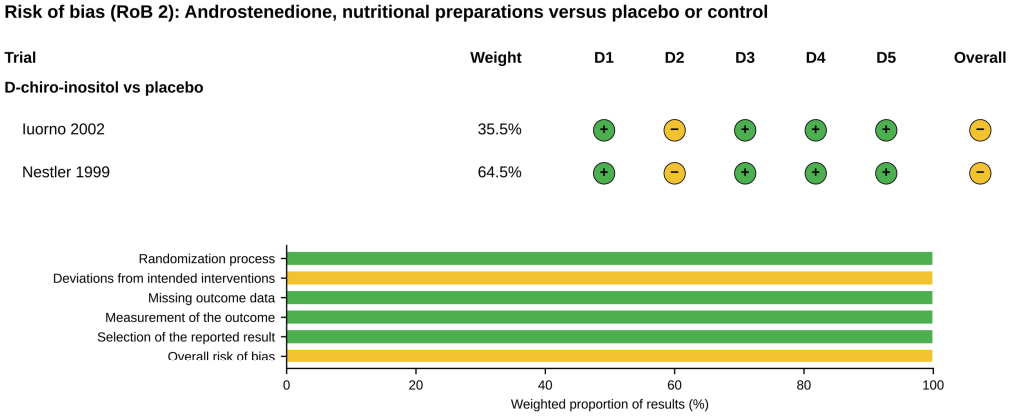
D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S166. Risk of bias (RoB 2) of the results contributing to PTH: nutritional preparations versus placebo or control



D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

Figure S167. Risk of bias (RoB 2) of the results contributing to Androstenedione: nutritional preparations versus placebo or control



D1 randomization process, D2 deviations from intended interventions, D3 missing outcome data, D4 measurement of the outcome, D5 selection of the reported result.
+ low risk, − some concerns, × high risk. Weights from the revised analyses (single-trial comparisons = 100%).
§ judgment carried over from another outcome of the same trial (confirmed by the assessor, EZF, 28–29 October 2026). ‡ domain 1 re-rated to high risk (confirmed by the assessor, EZF, 28–29 October 2026).

REFERENCES

1. Luo, D.; Wan, X.; Liu, J.; Tong, T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat Methods Med Res* **2018**, *27*, 1785-1805, doi:10.1177/0962280216669183.
2. Shi, J.; Luo, D.; Weng, H.; Zeng, X.T.; Lin, L.; Chu, H.; Tong, T. Optimally estimating the sample standard deviation from the five-number summary. *Res Synth Methods* **2020**, *11*, 641-654, doi:10.1002/jrsm.1429.
3. Higgins, J.P.T.; Thomas, J.; Chandler, J.; Cumpston, M.; Li, T.; Page, M.J.; Welch, V.A., (Eds.) *Cochrane Handbook for Systematic Reviews of Interventions*. 6.5 ed.; Cochrane: 2024.

4. Röver, C.; Knapp, G.; Friede, T. Hartung-Knapp-Sidik-Jonkman approach and its modification for random-effects meta-analysis with few studies. *BMC Med Res Methodol* **2015**, *15*, 99, doi:10.1186/s12874-015-0091-1.
5. Higgins, J.P.T.; Thompson, S.G. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* **2002**, *21*, 1539-1558, doi:10.1002/sim.1186.
6. Mátrai, P.; Kói, T.; Sipos, Z.; Farkas, N. Assessing the properties of the prediction interval in random-effects meta-analysis. *Research Synthesis Methods* **2026**, 1-21, doi:10.1017/rsm.2025.10055.
7. R Core Team *R: A Language and Environment for Statistical Computing*, R Foundation for Statistical Computing: Vienna, Austria, 2025.
8. Balduzzi, S.; Rücker, G.; Schwarzer, G. How to perform a meta-analysis with R: a practical tutorial. *Evid Based Ment Health* **2019**, *22*, 153-160, doi:10.1136/ebmental-2019-300117.