Läkemedelsbehandling av polycystiskt ovarialsyndrom-hälsa och livskvalitet på kort och lång sikt
Pharmacological treatment of polycystic ovary syndrome - health and quality of life in the short and long term, report 394 (2025)

Appendix 7 Sensitivity analyses

Table of contents

1 Sensitivity analyses regarding combined oral contraceptives

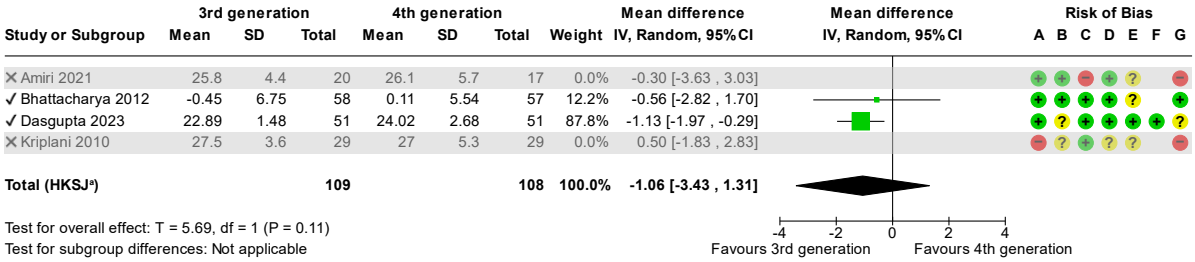
1.1 Sensitivity analyses for different kinds of combined oral contraceptives

First generation compared to fourth generation

No sensitivity analyses.

Third generation compared to fourth generation

BMI (kg/m^2) – high risk of bias

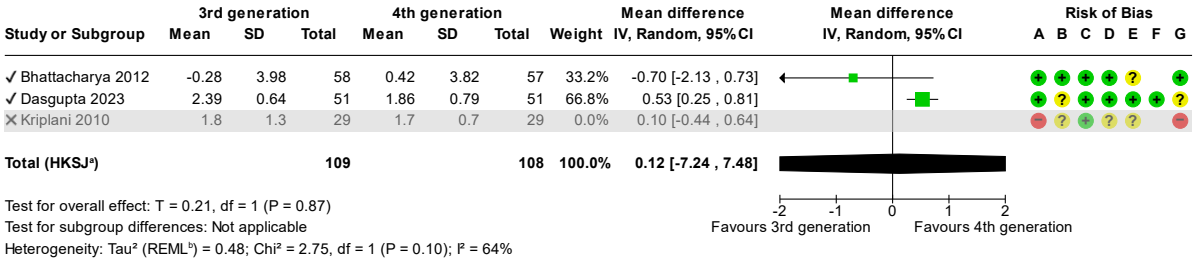


Test for overall effect: T = 5.69, df = 1 (P = 0.11)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 0.22, df = 1 (P = 0.64); I² = 0%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

HOMA-IR – high risk of bias



Test for overall effect: T = 0.21, df = 1 (P = 0.87)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.48; Chi² = 2.75, df = 1 (P = 0.10); I² = 64%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
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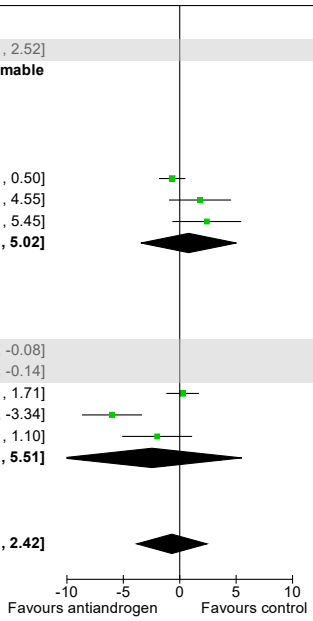
(F) Conflict of interest
(G) Overall risk of bias

2 Analyses regarding antiandrogens

2.1 Sensitivity analyses for antiandrogens+

BMI (kg/m^2) – without high risk of bias

Study or Subgroup	Antiandrogen Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.1.1 finasteride									
✕ Diri 2017[a]	26.6	4.4	17	26.9	4.2	19	0.0%	-0.30 [-3.12 , 2.52]	
Subtotal			**0**			**0**		**Not estimable**	
Test for overall effect: Not applicable									
Heterogeneity: Not applicable									
1.1.2 spironolactone									
✓ Ganie 2013[b]	24.07	3.36	62	24.74	3.11	56	19.3%	-0.67 [-1.84 , 0.50]	
✓ Mazza 2014[b]	29.5	5.4	26	27.7	4.7	26	15.8%	1.80 [-0.95 , 4.55]	
✓ Vieira 2012[c]	26.2	5.7	20	23.8	4.1	21	15.0%	2.40 [-0.65 , 5.45]	
Subtotal (HKSJ[d])			**108**			**103**	**50.2%**	**0.79 [-3.44 , 5.02]**	
Test for overall effect: T = 0.80, df = 2 (P = 0.51)									
Heterogeneity: Tau² (REML[e]) = 2.02; Chi² = 5.28, df = 2 (P = 0.07); I² = 60%									
1.1.3 flutamide									
✕ Amiri 2014 a[f]	2.8	1.9	27	3.9	1.9	26	0.0%	-1.10 [-2.12 , -0.08]	
✕ Amiri 2014 b[b]	3	1.9	27	4.2	2	25	0.0%	-1.20 [-2.26 , -0.14]	
✓ Dumesic 2023	0.3	1.2	5	0.04	1.24	6	18.8%	0.26 [-1.19 , 1.71]	
✓ Gambineri 2006 a[f]	29	3	17	35	5	19	16.0%	-6.00 [-8.66 , -3.34]	
✓ Gambineri 2006 b[b]	31	5	20	33	5	20	14.9%	-2.00 [-5.10 , 1.10]	
Subtotal (HKSJ[d])			**42**			**45**	**49.8%**	**-2.47 [-10.44 , 5.51]**	
Test for overall effect: T = 1.33, df = 2 (P = 0.31)									
Heterogeneity: Tau² (REML[e]) = 9.04; Chi² = 16.64, df = 2 (P = 0.0002); I² = 86%									
Total (HKSJ[d])			**150**			**148**	**100.0%**	**-0.70 [-3.82 , 2.42]**	
Test for overall effect: T = 0.57, df = 5 (P = 0.59)									
Test for subgroup differences: Chi² = 2.41, df = 1 (P = 0.12), I² = 58.5%									
Heterogeneity: Tau² (REML[e]) = 6.90; Chi² = 24.57, df = 5 (P = 0.0002); I² = 87%									



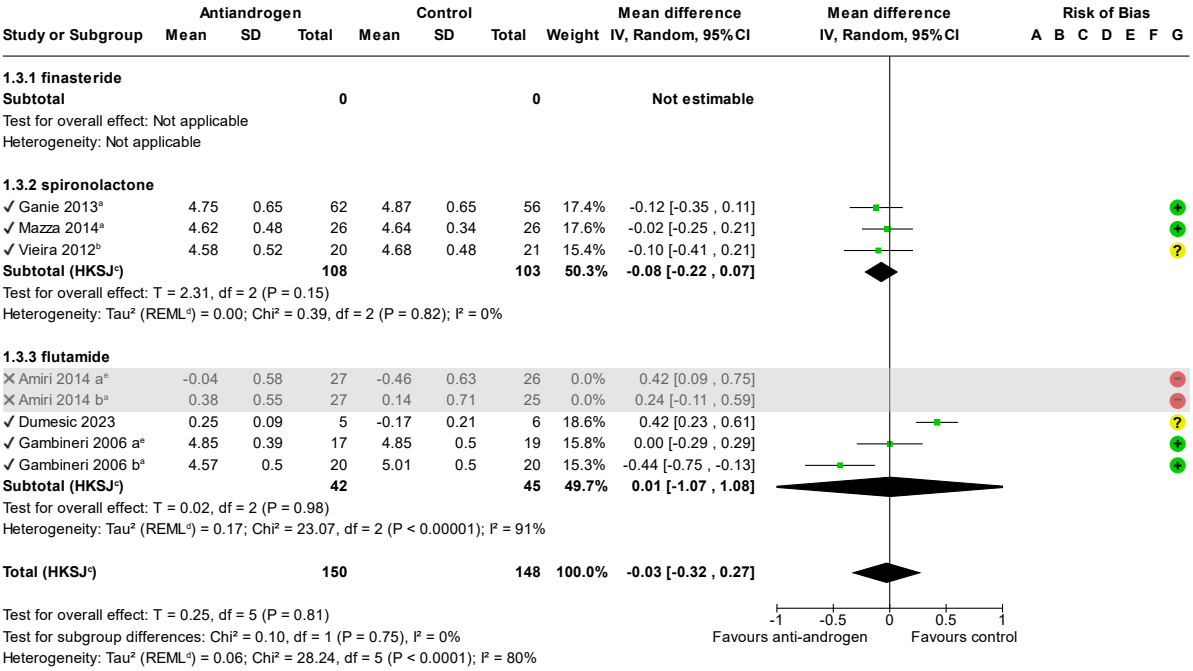
Footnotes

[a]with metformin for both groups
[b]with metformin and lifestyle intervention for both groups
[c]with oral contraceptives for both groups
[d]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[e]Tau² calculated by Restricted Maximum-Likelihood method.
[f]with lifestyle intervention for both groups

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Fasting glucose (mmol/l) – without high risk of bias



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[c]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
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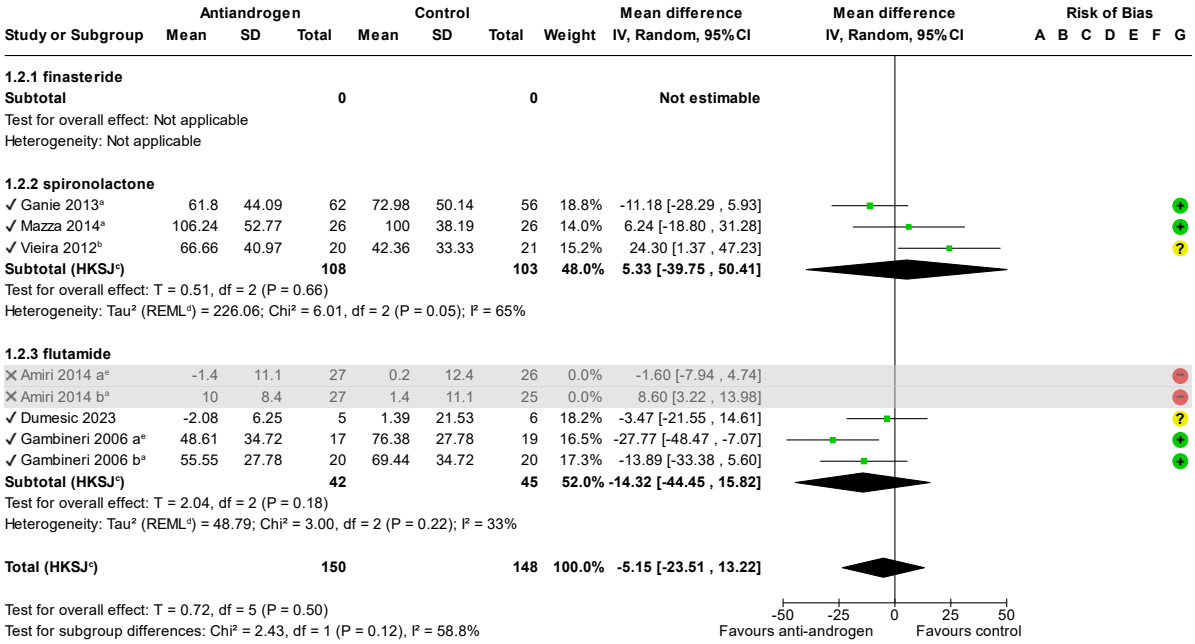
(F) Selective reporting (reporting bias)
(G) Other bias

Fasting insulin (pmol/l) – without high risk of bias



Footnotes

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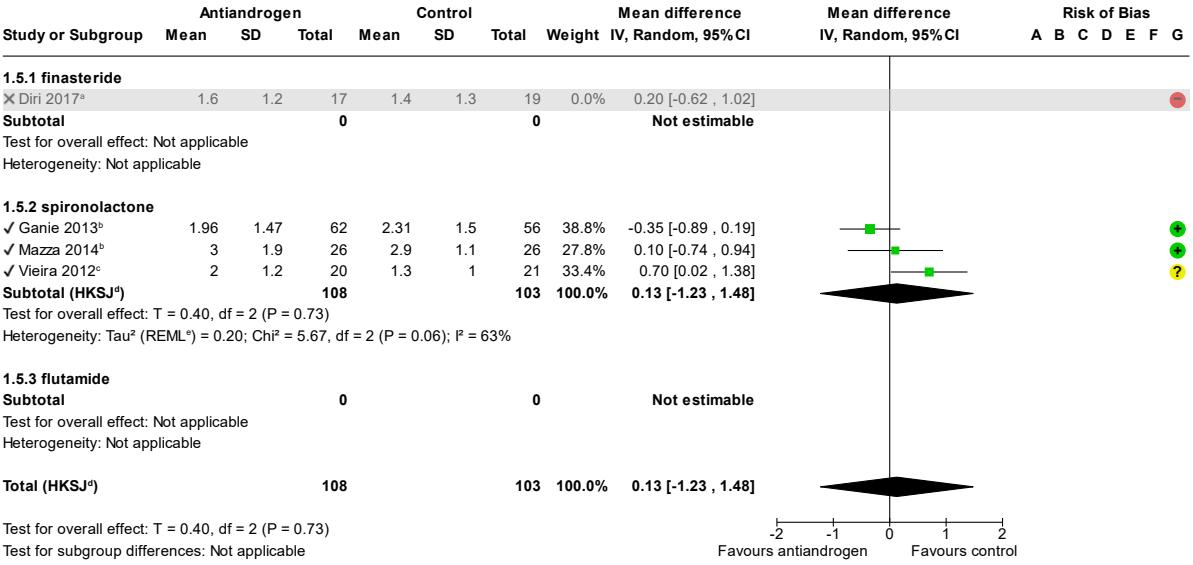
HOMA-IR – without high risk of bias



Footnotes

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[e]Tau² calculated by Restricted Maximum-Likelihood method.

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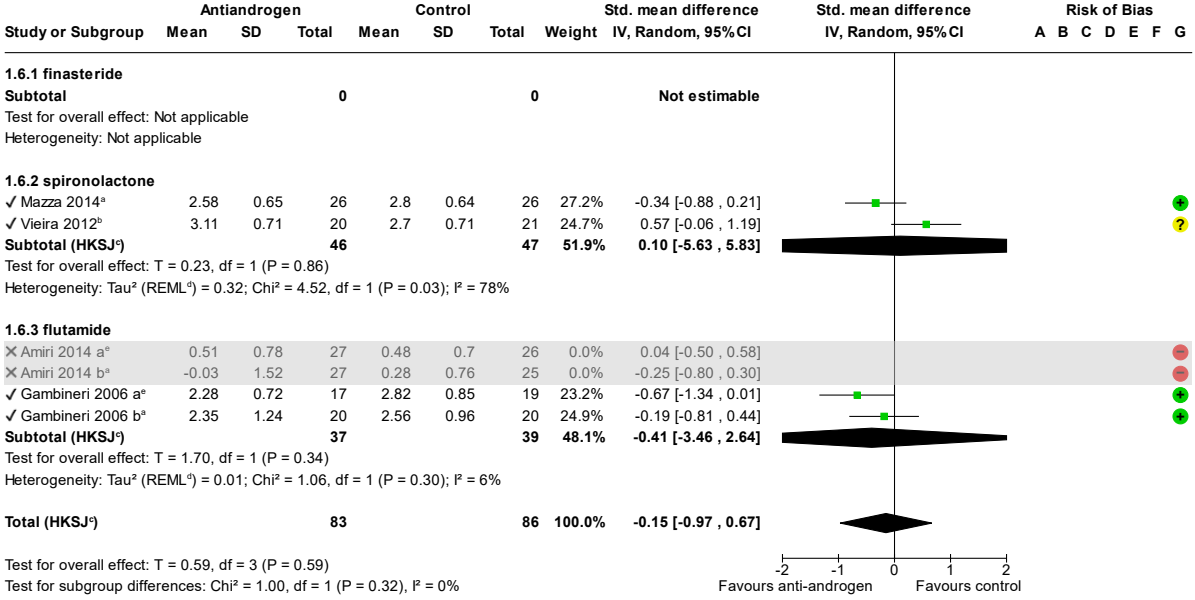
(G) Other bias

LDL (mmol/l) – without high risk of bias



Footnotes

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[c]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
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Risk of bias legend

(A) Random sequence generation (selection bias)
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(E) Incomplete outcome data (attrition bias)
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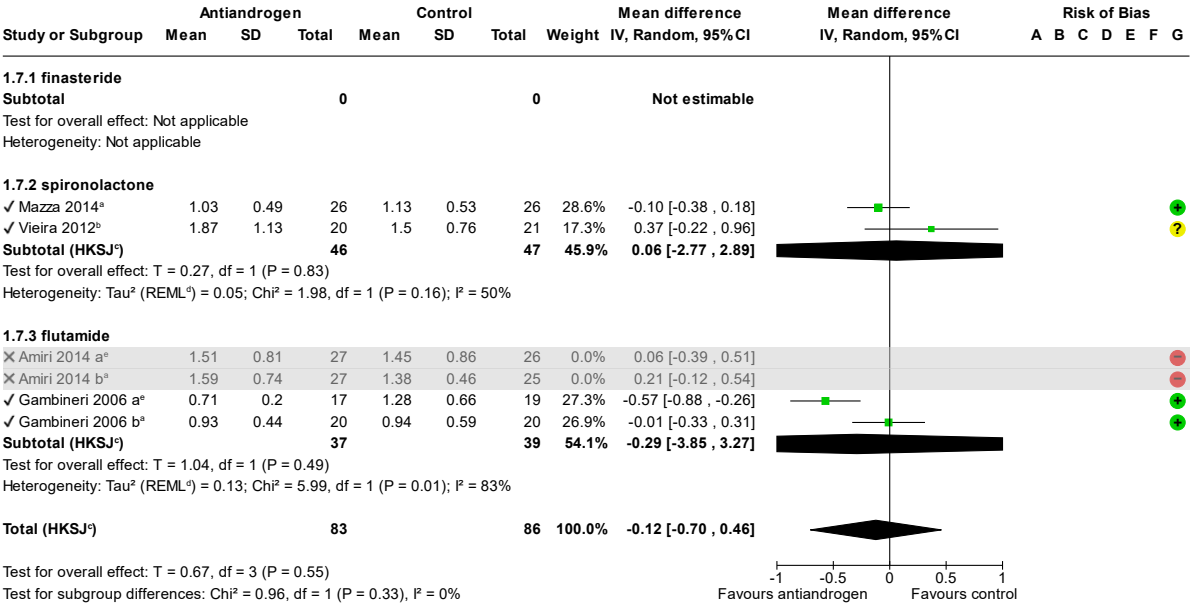
(G) Other bias

Triglycerides (mmol/l) – without high risk of bias



Footnotes

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Risk of bias legend

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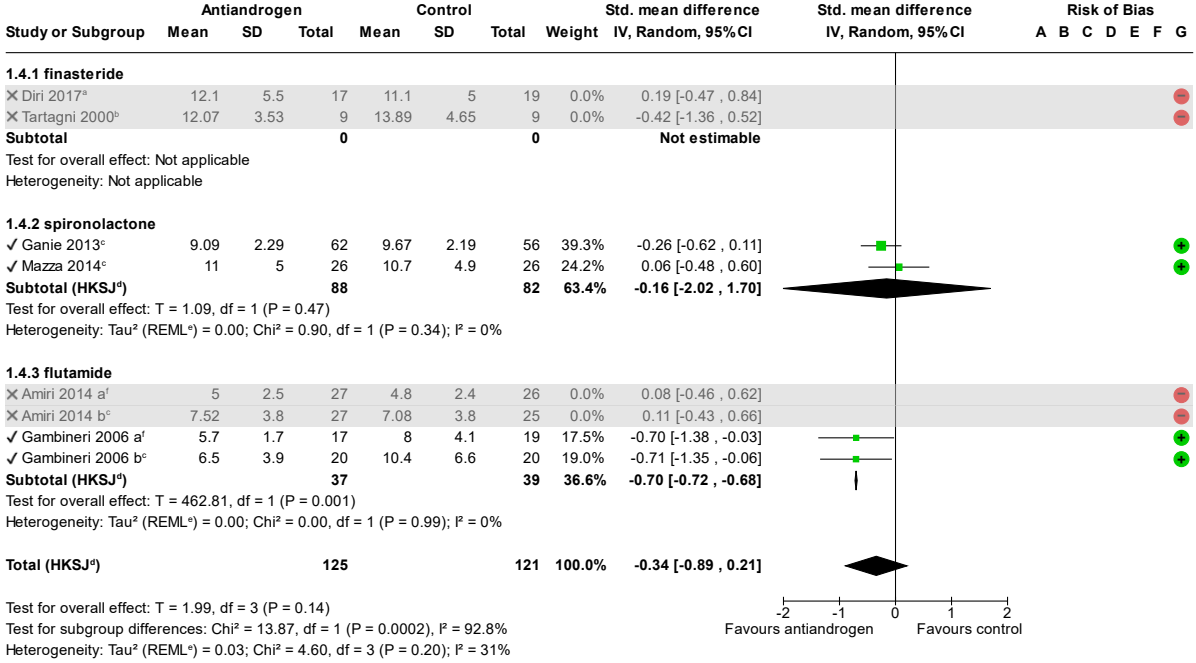
Hirsutism – without high risk of bias



Footnotes

[a]with metformin for both groups
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[c]with metformin and lifestyle intervention for both groups
[d]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[e]Tau² calculated by Restricted Maximum-Likelihood method.
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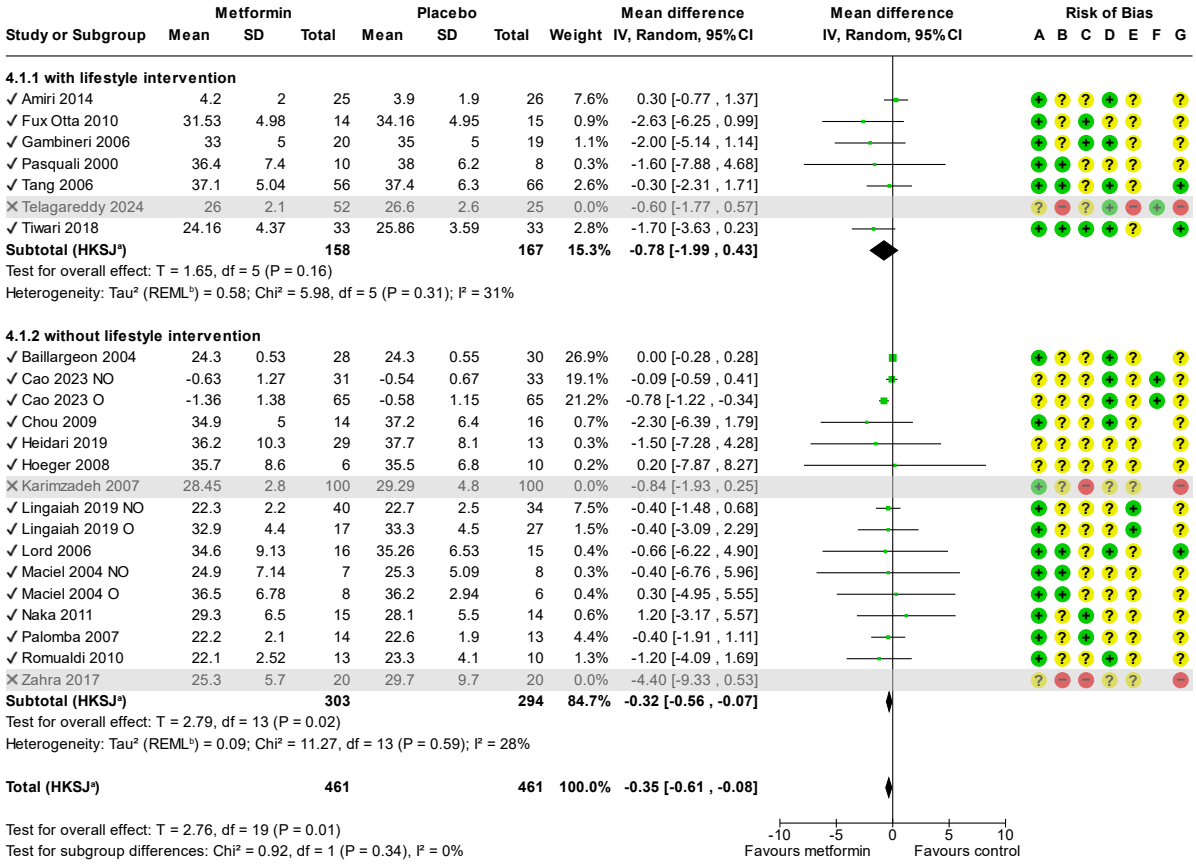
(G) Other bias

3 Analyses regarding metformin

3.1 Sensitivity analyses for metformin+

BMI all

BMI (kg/m²) – without high risk of bias



Study or Subgroup	Metformin Mean	Metformin SD	Metformin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A B C D E F G
4.1.1 with lifestyle intervention									
✓ Amiri 2014	4.2	2	25	3.9	1.9	26	7.6%	0.30 [-0.77 , 1.37]	+ ? ? + ? ?
✓ Fux Otta 2010	31.53	4.98	14	34.16	4.95	15	0.9%	-2.63 [-6.25 , 0.99]	+ ? + ? ? ?
✓ Gambineri 2006	33	5	20	35	5	19	1.1%	-2.00 [-5.14 , 1.14]	+ ? + + ? ?
✓ Pasquali 2000	36.4	7.4	10	38	6.2	8	0.3%	-1.60 [-7.88 , 4.68]	+ + ? ? ? ?
✓ Tang 2006	37.1	5.04	56	37.4	6.3	66	2.6%	-0.30 [-2.31 , 1.71]	+ + ? + ? +
✗ Telagareddy 2024	26	2.1	52	26.6	2.6	25	0.0%	-0.60 [-1.77 , 0.57]	? − ? + − + −
✓ Tiwari 2018	24.16	4.37	33	25.86	3.59	33	2.8%	-1.70 [-3.63 , 0.23]	+ + + + ? +
Subtotal (HKSJ[a])			**158**			**167**	**15.3%**	**-0.78 [-1.99 , 0.43]**	
Test for overall effect: T = 1.65, df = 5 (P = 0.16)									
Heterogeneity: Tau² (REML[b]) = 0.58; Chi² = 5.98, df = 5 (P = 0.31); I² = 31%									
4.1.2 without lifestyle intervention									
✓ Baillargeon 2004	24.3	0.53	28	24.3	0.55	30	26.9%	0.00 [-0.28 , 0.28]	+ ? ? + ? ?
✓ Cao 2023 NO	-0.63	1.27	31	-0.54	0.67	33	19.1%	-0.09 [-0.59 , 0.41]	? ? ? + ? + ?
✓ Cao 2023 O	-1.36	1.38	65	-0.58	1.15	65	21.2%	-0.78 [-1.22 , -0.34]	? ? ? + ? + ?
✓ Chou 2009	34.9	5	14	37.2	6.4	16	0.7%	-2.30 [-6.39 , 1.79]	+ ? ? + ? ?
✓ Heidari 2019	36.2	10.3	29	37.7	8.1	13	0.3%	-1.50 [-7.28 , 4.28]	? ? ? ? ? ?
✓ Hoeger 2008	35.7	8.6	6	35.5	6.8	10	0.2%	0.20 [-7.87 , 8.27]	? ? ? ? ? ?
✗ Karimzadeh 2007	28.45	2.8	100	29.29	4.8	100	0.0%	-0.84 [-1.93 , 0.25]	+ ? − ? ? −
✓ Lingaiah 2019 NO	22.3	2.2	40	22.7	2.5	34	7.5%	-0.40 [-1.48 , 0.68]	+ ? ? ? + ?
✓ Lingaiah 2019 O	32.9	4.4	17	33.3	4.5	27	1.5%	-0.40 [-3.09 , 2.29]	+ ? ? ? + ?
✓ Lord 2006	34.6	9.13	16	35.26	6.53	15	0.4%	-0.66 [-6.22 , 4.90]	+ + ? + ? +
✓ Maciel 2004 NO	24.9	7.14	7	25.3	5.09	8	0.3%	-0.40 [-6.76 , 5.96]	+ + ? ? ? ?
✓ Maciel 2004 O	36.5	6.78	8	36.2	2.94	6	0.4%	0.30 [-4.95 , 5.55]	+ + ? ? ? ?
✓ Naka 2011	29.3	6.5	15	28.1	5.5	14	0.6%	1.20 [-3.17 , 5.57]	+ ? + ? ? ?
✓ Palomba 2007	22.2	2.1	14	22.6	1.9	13	4.4%	-0.40 [-1.91 , 1.11]	+ ? + ? ? ?
✓ Romualdi 2010	22.1	2.52	13	23.3	4.1	10	1.3%	-1.20 [-4.09 , 1.69]	+ ? ? + ? ?
✗ Zahra 2017	25.3	5.7	20	29.7	9.7	20	0.0%	-4.40 [-9.33 , 0.53]	? − − ? ? −
Subtotal (HKSJ[a])			**303**			**294**	**84.7%**	**-0.32 [-0.56 , -0.07]**	
Test for overall effect: T = 2.79, df = 13 (P = 0.02)									
Heterogeneity: Tau² (REML[b]) = 0.09; Chi² = 11.27, df = 13 (P = 0.59); I² = 28%									
Total (HKSJ[a])			**461**			**461**	**100.0%**	**-0.35 [-0.61 , -0.08]**	
Test for overall effect: T = 2.76, df = 19 (P = 0.01)									
Test for subgroup differences: Chi² = 0.92, df = 1 (P = 0.34), I² = 0%									
Heterogeneity: Tau² (REML[b]) = 0.09; Chi² = 17.54, df = 19 (P = 0.55); I² = 24%									

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process

(B) Bias due to deviations from intended interventions

(C) Bias due to missing outcome data

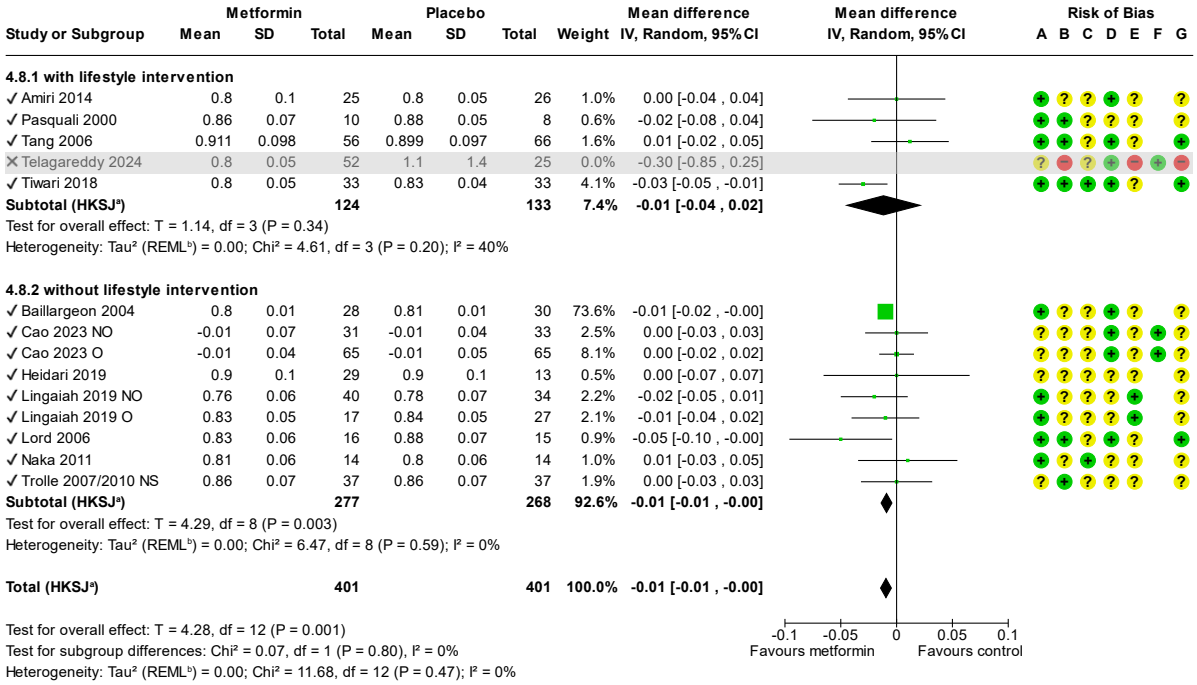
(D) Bias in measurement of the outcome

(E) Bias in selection of the reported result

(F) Conflict of interest

(G) Overall risk of bias

WHR – without high risk of bias



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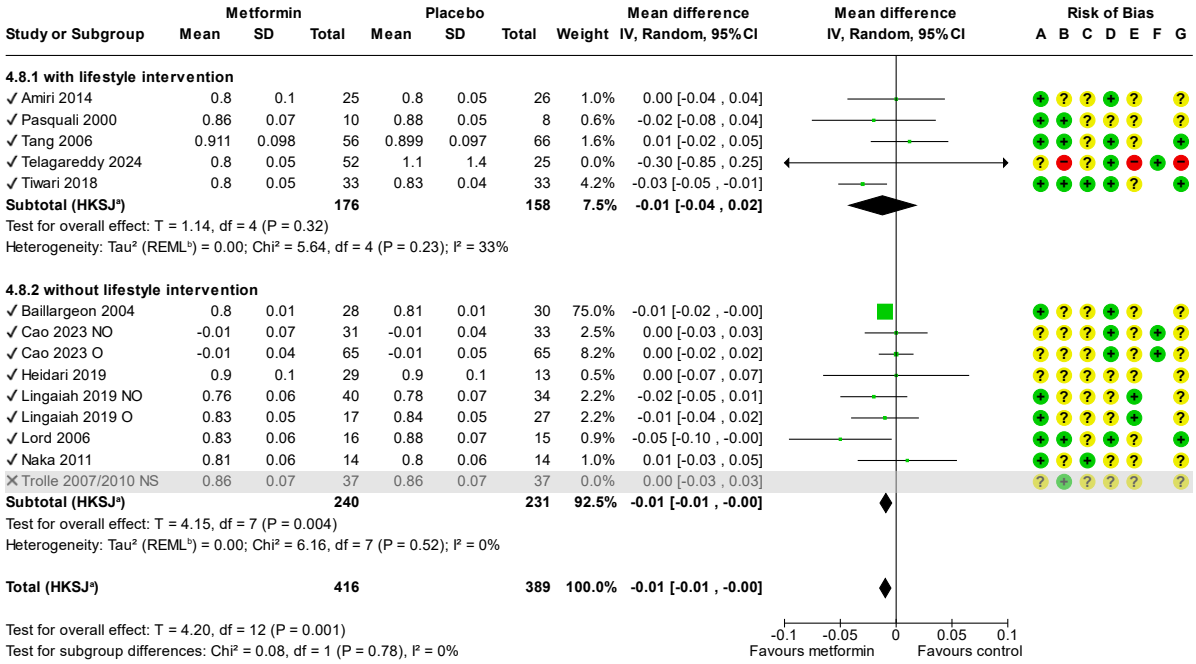
WHR – without Trolle 2007 (crossover-study)



Footnotes

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Risk of bias legend

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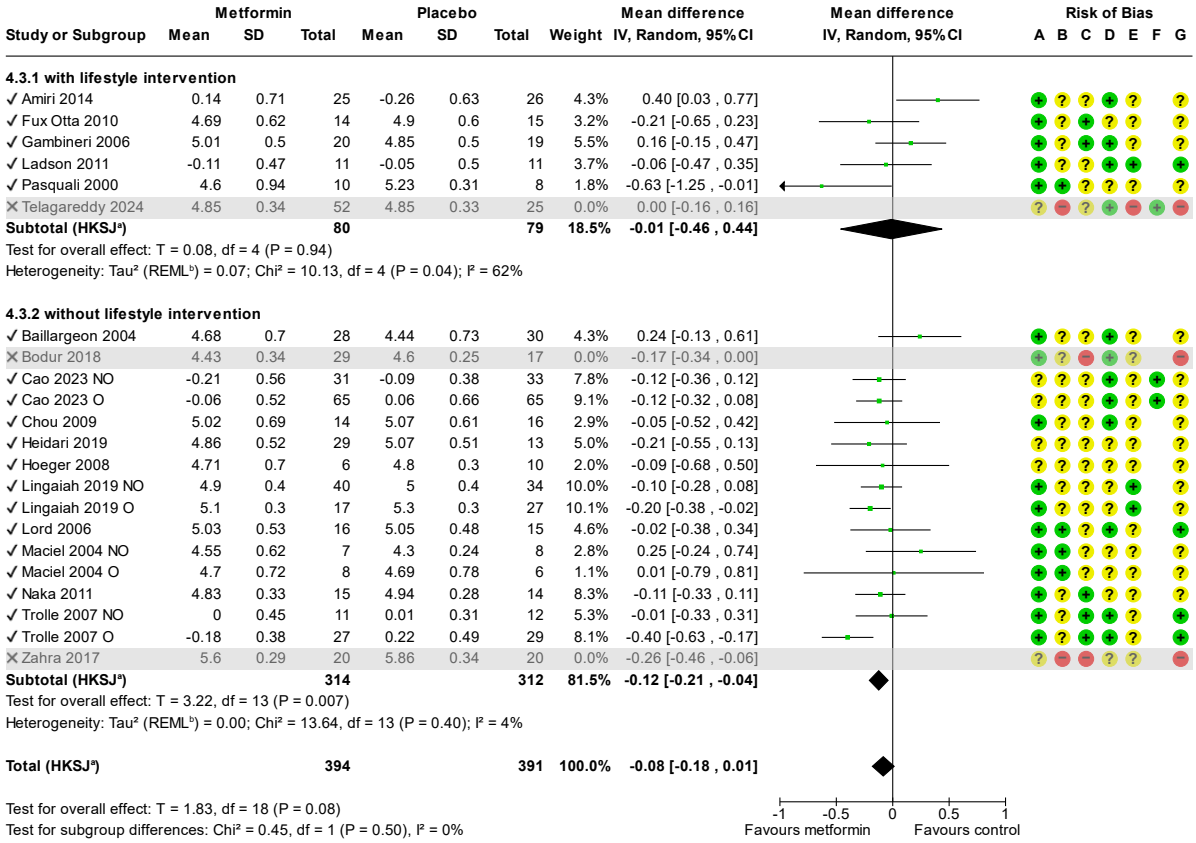
(G) Overall risk of bias

Fasting glucose (mmol/l) – without high risk of bias



Footnotes

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Risk of bias legend

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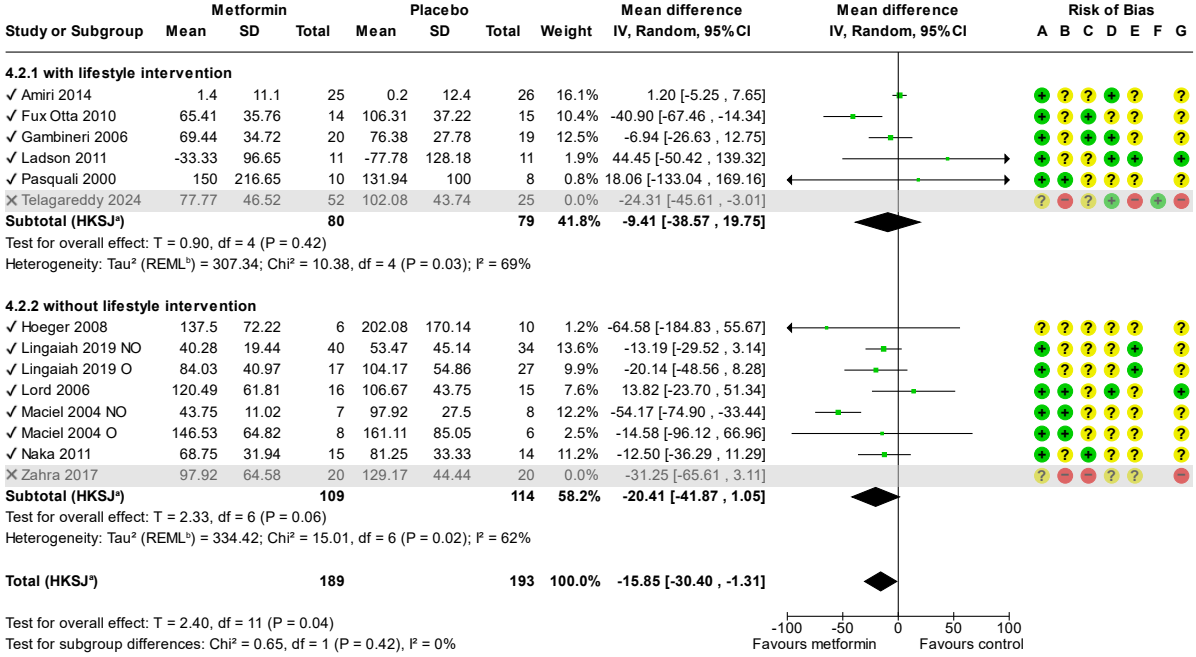
(G) Overall risk of bias

Fasting insulin (pmol/l) – without high risk of bias



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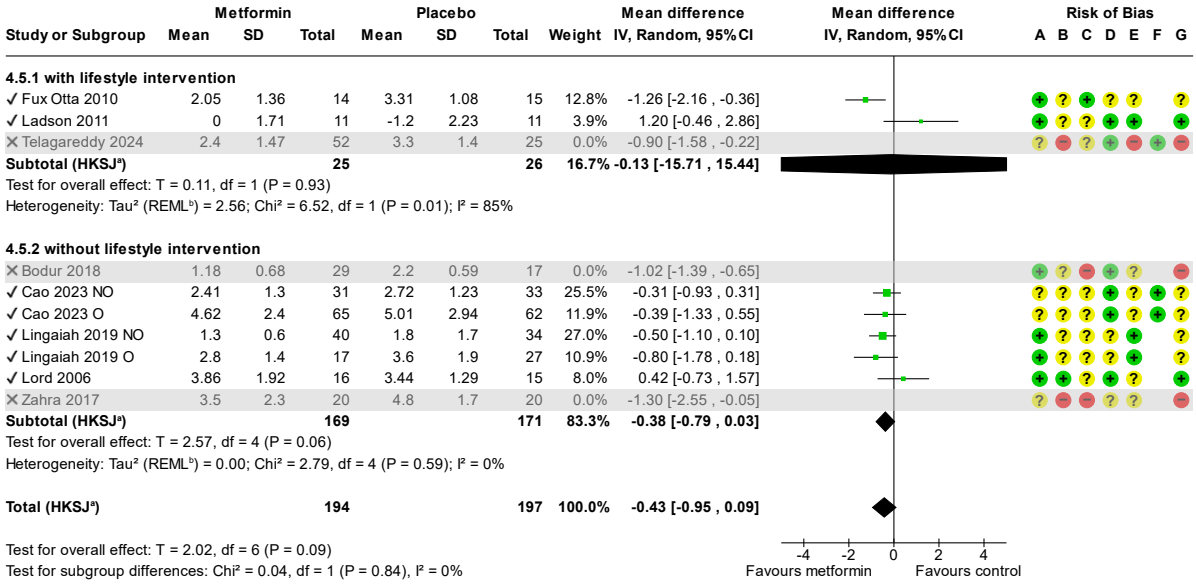
HOMA-IR – without high risk of bias



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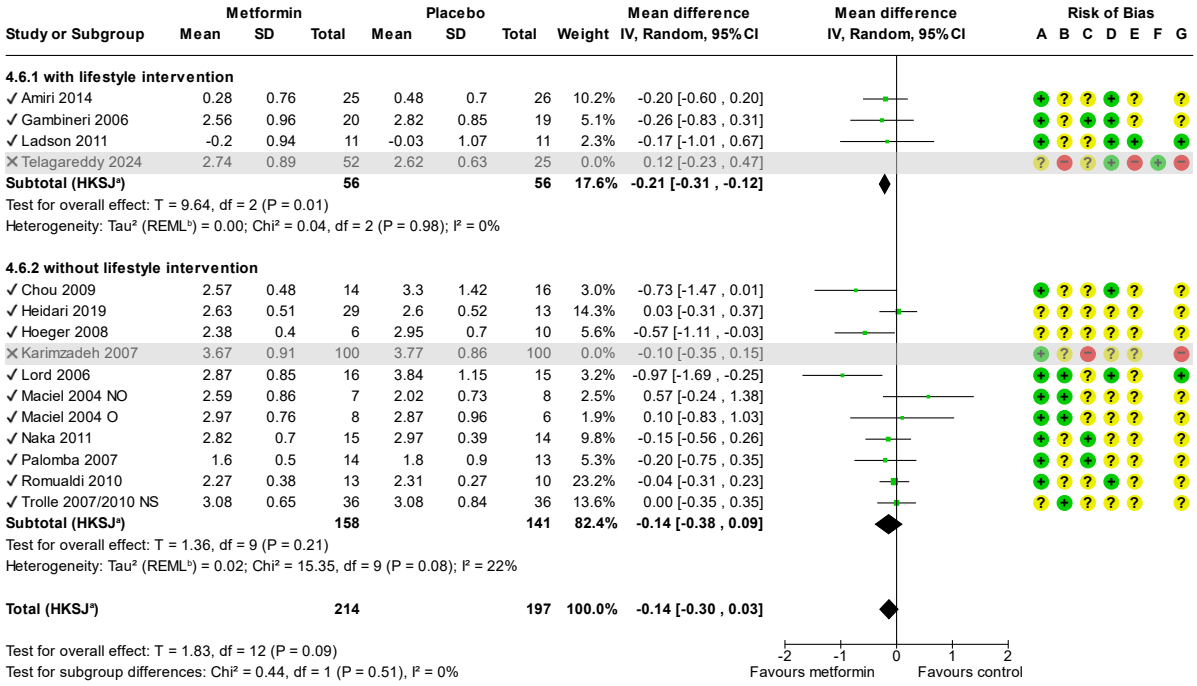
LDL (mmol/l) – without high risk of bias



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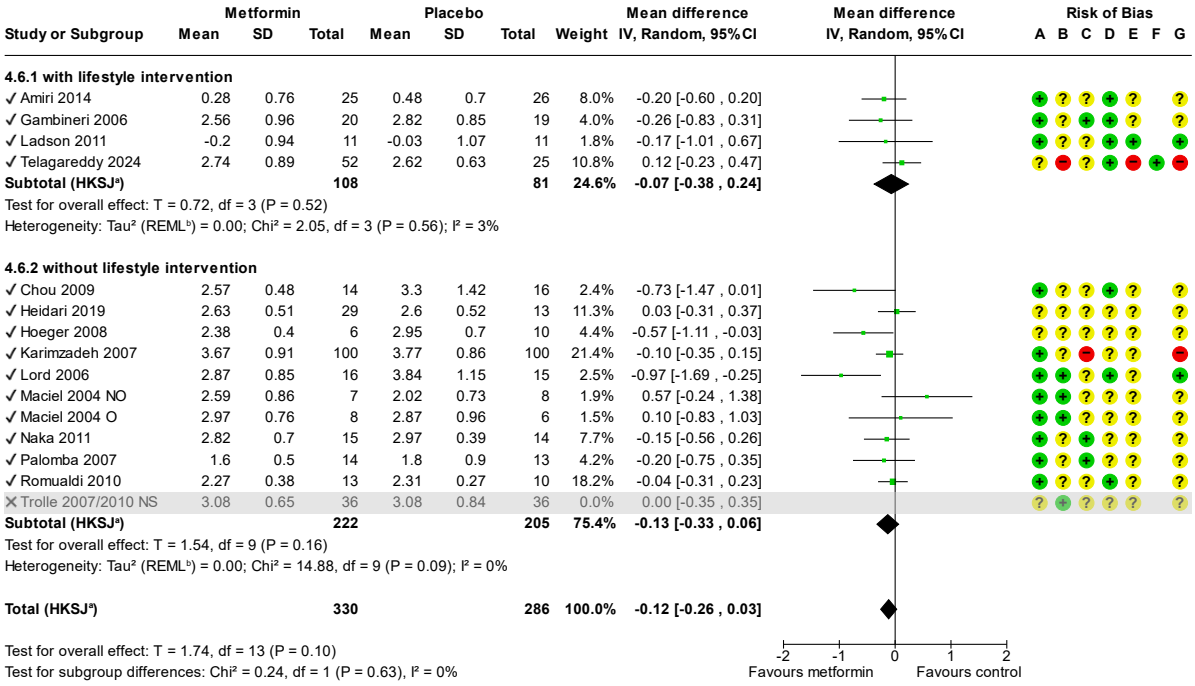
LDL (mmol/l) – without Trolle 2007 (crossover study)



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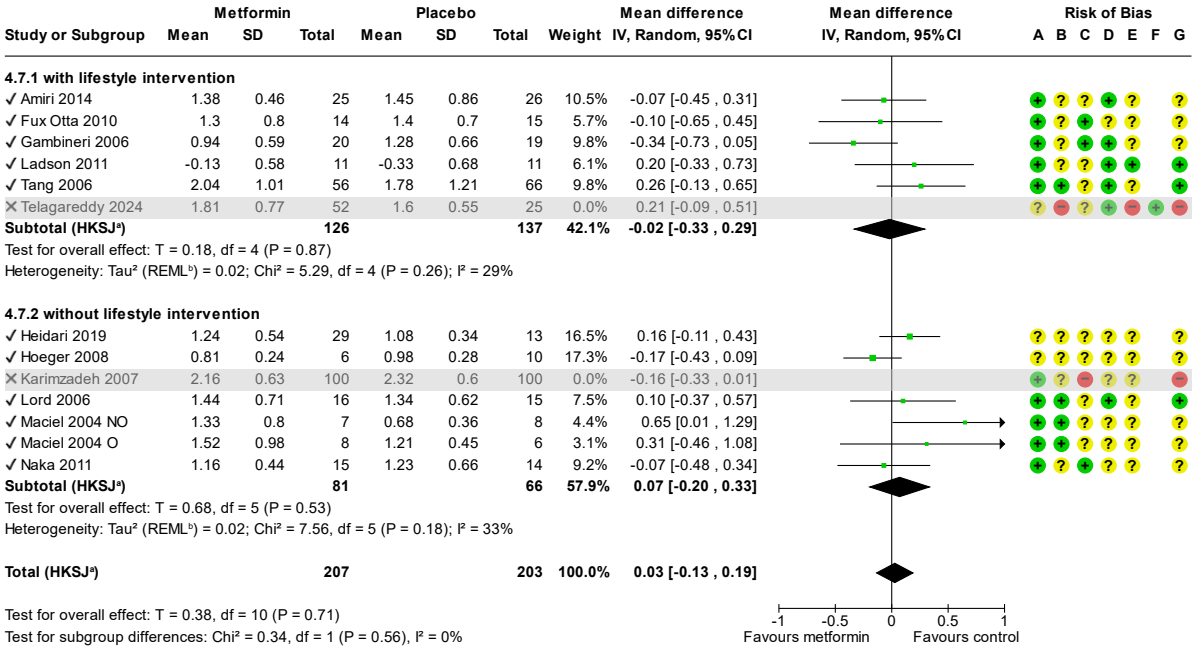
(G) Overall risk of bias

Triglycerides (mmol/l) – without high risk of bias



Study or Subgroup	Metformin Mean	Metformin SD	Metformin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
4.7.1 with lifestyle intervention															
✓ Amiri 2014	1.38	0.46	25	1.45	0.86	26	10.5%	-0.07 [-0.45 , 0.31]	+	?	?	+	?		?
✓ Fux Otta 2010	1.3	0.8	14	1.4	0.7	15	5.7%	-0.10 [-0.65 , 0.45]	+	?	+	?	?		?
✓ Gambineri 2006	0.94	0.59	20	1.28	0.66	19	9.8%	-0.34 [-0.73 , 0.05]	+	?	+	+	?		?
✓ Ladson 2011	-0.13	0.58	11	-0.33	0.68	11	6.1%	0.20 [-0.33 , 0.73]	+	?	?	+	+		+
✓ Tang 2006	2.04	1.01	56	1.78	1.21	66	9.8%	0.26 [-0.13 , 0.65]	+	+	?	+	?		+
✕ Telagareddy 2024	1.81	0.77	52	1.6	0.55	25	0.0%	0.21 [-0.09 , 0.51]	?	−	?	+	−	+	−
Subtotal (HKSJ[a])			**126**			**137**	**42.1%**	**-0.02 [-0.33 , 0.29]**							
Test for overall effect: T = 0.18, df = 4 (P = 0.87)															
Heterogeneity: Tau² (REML[b]) = 0.02; Chi² = 5.29, df = 4 (P = 0.26); I² = 29%															
4.7.2 without lifestyle intervention															
✓ Heidari 2019	1.24	0.54	29	1.08	0.34	13	16.5%	0.16 [-0.11 , 0.43]	?	?	?	?	?		?
✓ Hoeger 2008	0.81	0.24	6	0.98	0.28	10	17.3%	-0.17 [-0.43 , 0.09]	?	?	?	?	?		?
✕ Karimzadeh 2007	2.16	0.63	100	2.32	0.6	100	0.0%	-0.16 [-0.33 , 0.01]	+	?	−	?	?		−
✓ Lord 2006	1.44	0.71	16	1.34	0.62	15	7.5%	0.10 [-0.37 , 0.57]	+	+	?	+	?		+
✓ Maciel 2004 NO	1.33	0.8	7	0.68	0.36	8	4.4%	0.65 [0.01 , 1.29]	+	+	?	?	?		?
✓ Maciel 2004 O	1.52	0.98	8	1.21	0.45	6	3.1%	0.31 [-0.46 , 1.08]	+	+	?	?	?		?
✓ Naka 2011	1.16	0.44	15	1.23	0.66	14	9.2%	-0.07 [-0.48 , 0.34]	+	?	+	?	?		?
Subtotal (HKSJ[a])			**81**			**66**	**57.9%**	**0.07 [-0.20 , 0.33]**							
Test for overall effect: T = 0.68, df = 5 (P = 0.53)															
Heterogeneity: Tau² (REML[b]) = 0.02; Chi² = 7.56, df = 5 (P = 0.18); I² = 33%															
Total (HKSJ[a])			**207**			**203**	**100.0%**	**0.03 [-0.13 , 0.19]**							
Test for overall effect: T = 0.38, df = 10 (P = 0.71)															
Test for subgroup differences: Chi² = 0.34, df = 1 (P = 0.56), I² = 0%															
Heterogeneity: Tau² (REML[b]) = 0.01; Chi² = 13.12, df = 10 (P = 0.22); I² = 23%															

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

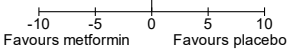
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

BMI ≥25

BMI (kg/m^2) – without high risk of bias

Study or Subgroup	Metformin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.1.1 with lifestyle intervention									
✓ Gambineri 2006	33	5	20	35	5	19	1.7%	-2.00 [-5.14 , 1.14]	+ ? + + ? ?
✓ Pasquali 2000	36.4	7.4	10	38	6.2	8	0.4%	-1.60 [-7.88 , 4.68]	+ + ? ? ? ?
✓ Tang 2006	37.1	5.04	56	37.4	6.3	66	4.2%	-0.30 [-2.31 , 1.71]	+ + ? + ? +
Subtotal (HKSJ[a])			**86**			**93**	**6.3%**	**-0.85 [-3.20 , 1.50]**	
Test for overall effect: T = 1.56, df = 2 (P = 0.26)									
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 0.86, df = 2 (P = 0.65); I² = 0%									
1.1.2 without lifestyle intervention									
✓ Cao 2023 O	-1.36	1.38	65	-0.58	1.15	65	88.4%	-0.78 [-1.22 , -0.34]	? ? ? + ? + ?
✓ Chou 2009	34.9	5	14	37.2	6.4	16	1.0%	-2.30 [-6.39 , 1.79]	+ ? ? + ? ?
✓ Heidari 2019	36.2	10.3	29	37.7	8.1	13	0.5%	-1.50 [-7.28 , 4.28]	? ? ? ? ? ?
✓ Hoeger 2008	35.7	8.6	6	35.5	6.8	10	0.3%	0.20 [-7.87 , 8.27]	? ? ? ? ? ?
✗ Karimzadeh 2007	28.45	2.8	100	29.29	4.8	100	0.0%	-0.84 [-1.93 , 0.25]	+ ? − ? ? −
✓ Lingaiah 2019 O	32.9	4.4	17	33.3	4.5	27	2.3%	-0.40 [-3.09 , 2.29]	+ ? ? ? + ?
✓ Lord 2006	34.6	9.13	16	35.26	6.53	15	0.5%	-0.66 [-6.22 , 4.90]	+ + ? + ? +
✓ Maciel 2004 O	36.5	6.78	8	36.2	2.94	6	0.6%	0.30 [-4.95 , 5.55]	+ + ? ? ? ?
Subtotal (HKSJ[a])			**155**			**152**	**93.7%**	**-0.78 [-0.98 , -0.58]**	
Test for overall effect: T = 9.37, df = 6 (P < 0.0001)									
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 0.89, df = 6 (P = 0.99); I² = 0%									
Total (HKSJ[a])			**241**			**245**	**100.0%**	**-0.78 [-0.99 , -0.58]**	

Test for overall effect: T = 8.49, df = 9 (P < 0.0001)
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.90), I² = 0%
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 1.75, df = 9 (P = 0.99); I² = 0%



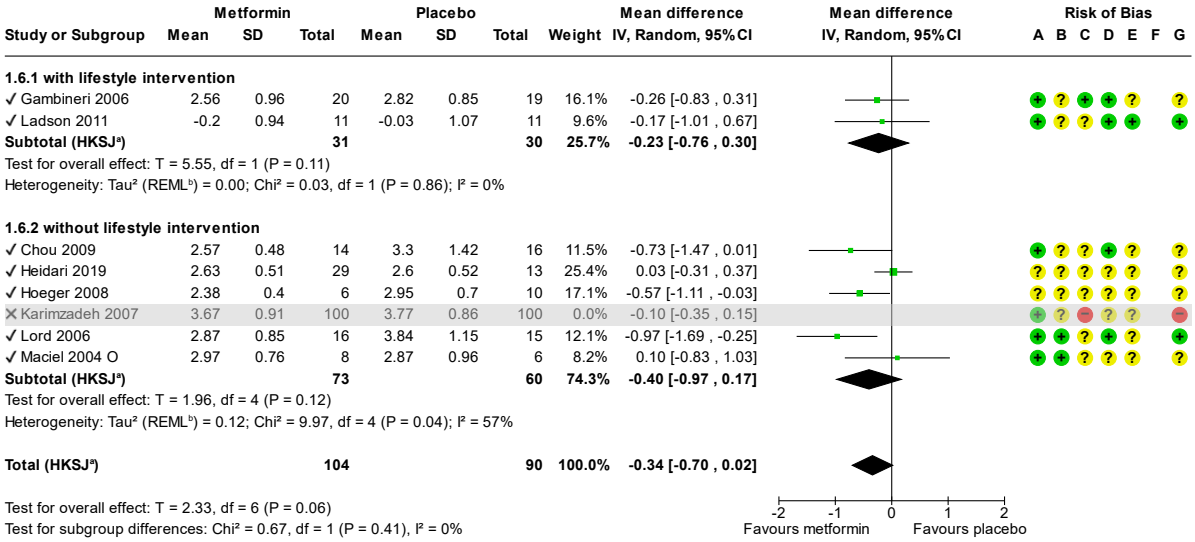
Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

LDL (mmol/l) – without high risk of bias



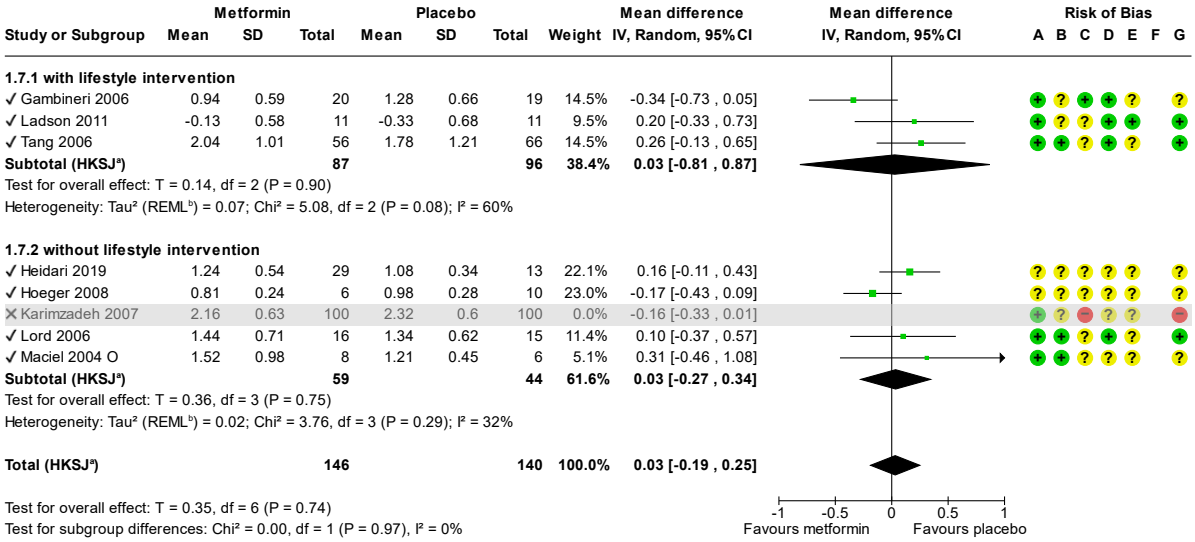
Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Triglycerides (mmol/l) – without high risk of bias



Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

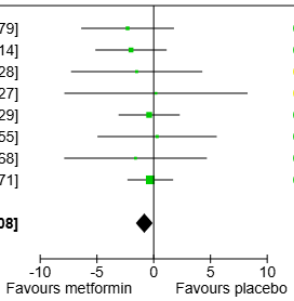
BMI <25

No sensitivity analyses.

BMI >30

BMI (kg/m^2)

Study or Subgroup	Metformin Mean	Metformin SD	Metformin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean difference IV, Random, 95% CI
Chou 2009	34.9	5	14	37.2	6.4	16	9.2%	-2.30 [-6.39 , 1.79]
Gambineri 2006	33	5	20	35	5	19	15.5%	-2.00 [-5.14 , 1.14]
Heidari 2019	36.2	10.3	29	37.7	8.1	13	4.6%	-1.50 [-7.28 , 4.28]
Hoeger 2008	35.7	8.6	6	35.5	6.8	10	2.4%	0.20 [-7.87 , 8.27]
Lingaiah 2019 O	32.9	4.4	17	33.3	4.5	27	21.1%	-0.40 [-3.09 , 2.29]
Maciel 2004 O	36.5	6.78	8	36.2	2.94	6	5.5%	0.30 [-4.95 , 5.55]
Pasquali 2000	36.4	7.4	10	38	6.2	8	3.9%	-1.60 [-7.88 , 4.68]
Tang 2006	37.1	5.04	56	37.4	6.3	66	37.8%	-0.30 [-2.31 , 1.71]
Total (HKSJ[a])			**160**			**165**	**100.0%**	**-0.83 [-1.57 , -0.08]**



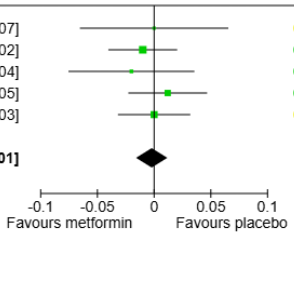
Test for overall effect: T = 2.63, df = 7 (P = 0.03)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 1.74, df = 7 (P = 0.97); I² = 0%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

WHR

Study or Subgroup	Metformin Mean	Metformin SD	Metformin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean difference IV, Random, 95% CI
Heidari 2019	0.9	0.1	29	0.9	0.1	13	6.8%	0.00 [-0.07 , 0.07]
Lingaiah 2019 O	0.83	0.05	17	0.84	0.05	27	31.4%	-0.01 [-0.04 , 0.02]
Pasquali 2000	0.86	0.07	10	0.88	0.05	8	9.4%	-0.02 [-0.08 , 0.04]
Tang 2006	0.911	0.098	56	0.899	0.097	66	24.0%	0.01 [-0.02 , 0.05]
Trolle 2007/2010 NS	0.86	0.07	37	0.86	0.07	37	28.4%	0.00 [-0.03 , 0.03]
Total (HKSJ[a])			**149**			**151**	**100.0%**	**-0.00 [-0.02 , 0.01]**



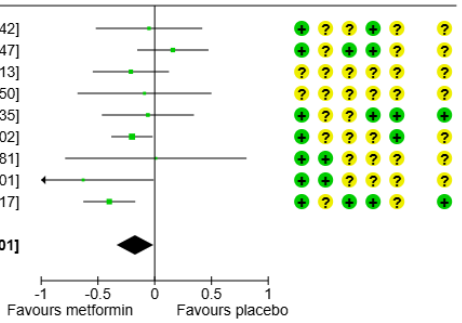
Test for overall effect: T = 0.43, df = 4 (P = 0.69)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 1.31, df = 4 (P = 0.86); I² = 0%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Fasting glucose (mmol/l)

Study or Subgroup	Metformin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
Chou 2009	5.02	0.69	14	5.07	0.61	16	7.8%	-0.05 [-0.52 , 0.42]	+	?	?	+	?		?
Gambineri 2006	5.01	0.5	20	4.85	0.5	19	13.7%	0.16 [-0.15 , 0.47]	+	?	+	+	?		?
Heidari 2019	4.86	0.52	29	5.07	0.51	13	12.6%	-0.21 [-0.55 , 0.13]	?	?	?	?	?		?
Hoeger 2008	4.71	0.7	6	4.8	0.3	10	5.4%	-0.09 [-0.68 , 0.50]	?	?	?	?	?		?
Ladson 2011	-0.11	0.47	11	-0.05	0.5	11	9.7%	-0.06 [-0.47 , 0.35]	+	?	?	+	+		+
Lingaiah 2019 O	5.1	0.3	17	5.3	0.3	27	23.3%	-0.20 [-0.38 , -0.02]	+	?	?	?	+		?
Maciel 2004 O	4.7	0.72	8	4.69	0.78	6	3.1%	0.01 [-0.79 , 0.81]	+	+	?	?	?		?
Pasquali 2000	4.6	0.94	10	5.23	0.31	8	4.9%	-0.63 [-1.25 , -0.01]	+	+	?	?	?		?
Trolle 2007 O	-0.18	0.38	27	0.22	0.49	29	19.4%	-0.40 [-0.63 , -0.17]	+	?	+	+	?		+
Total (HKSJ[a])			**142**			**139**	**100.0%**	**-0.17 [-0.34 , -0.01]**							



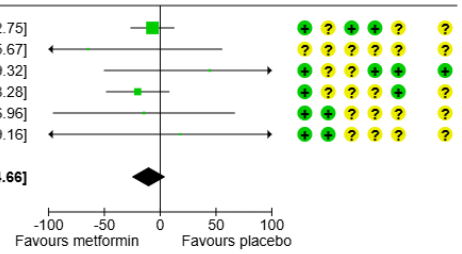
Test for overall effect: T = 2.47, df = 8 (P = 0.04)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.02; Chi² = 11.05, df = 8 (P = 0.20); I² = 34%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Fasting insulin (pmol/l)

Study or Subgroup	Metformin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
Gambineri 2006	69.44	34.72	20	76.38	27.78	19	61.5%	-6.94 [-26.63 , 12.75]	+	?	+	+	?		?
Hoeger 2008	137.5	72.22	6	202.08	170.14	10	1.6%	-64.58 [-184.83 , 55.67]	?	?	?	?	?		?
Ladson 2011	-33.33	96.65	11	-77.78	128.18	11	2.6%	44.45 [-50.42 , 139.32]	+	?	?	+	+		+
Lingaiah 2019 O	84.03	40.97	17	104.17	54.86	27	29.5%	-20.14 [-48.56 , 8.28]	+	?	?	?	+		?
Maciel 2004 O	146.53	64.82	8	161.11	85.05	6	3.6%	-14.58 [-96.12 , 66.96]	+	+	?	?	?		?
Pasquali 2000	150	216.65	10	131.94	100	8	1.0%	18.06 [-133.04 , 169.16]	+	+	?	?	?		?
Total (HKSJ[a])			**72**			**81**	**100.0%**	**-10.44 [-25.54 , 4.66]**							

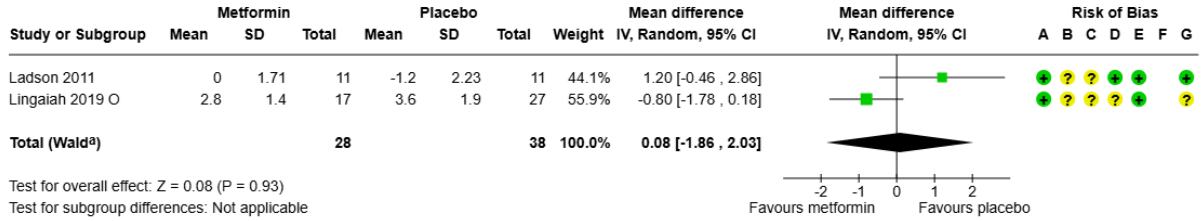


Test for overall effect: T = 1.78, df = 5 (P = 0.14)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 2.78, df = 5 (P = 0.73); I² = 0%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

HOMA-IR



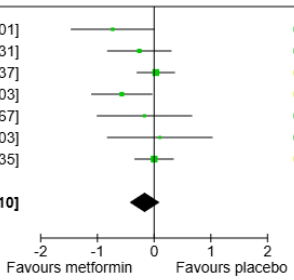
Test for overall effect: Z = 0.08 (P = 0.93)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 1.52; Chi² = 4.14, df = 1 (P = 0.04); I² = 76%

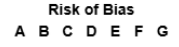
Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

LDL (mmol/l)

Study or Subgroup	Metformin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
Chou 2009	2.57	0.48	14	3.3	1.42	16	8.0%	-0.73 [-1.47 , 0.01]
Gambineri 2006	2.56	0.96	20	2.82	0.85	19	12.7%	-0.26 [-0.83 , 0.31]
Heidari 2019	2.63	0.51	29	2.6	0.52	13	27.3%	0.03 [-0.31 , 0.37]
Hoeger 2008	2.38	0.4	6	2.95	0.7	10	13.8%	-0.57 [-1.11 , -0.03]
Ladson 2011	-0.2	0.94	11	-0.03	1.07	11	6.4%	-0.17 [-1.01 , 0.67]
Maciel 2004 O	2.97	0.76	8	2.87	0.96	6	5.3%	0.10 [-0.83 , 1.03]
Trolle 2007/2010 NS	3.08	0.65	36	3.08	0.84	36	26.4%	0.00 [-0.35 , 0.35]
Total (HKSJ[a])			**124**			**111**	**100.0%**	**-0.17 [-0.43 , 0.10]**





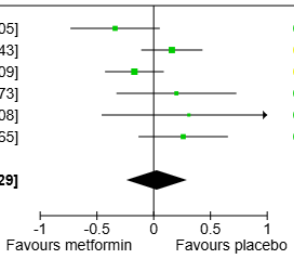
Test for overall effect: T = 1.55, df = 6 (P = 0.17)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.02; Chi² = 6.91, df = 6 (P = 0.33); I² = 19%

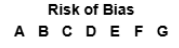
Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Triglycerides (mmol/l)

Study or Subgroup	Metformin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
Gambineri 2006	0.94	0.59	20	1.28	0.66	19	16.7%	-0.34 [-0.73 , 0.05]
Heidari 2019	1.24	0.54	29	1.08	0.34	13	24.1%	0.16 [-0.11 , 0.43]
Hoeger 2008	0.81	0.24	6	0.98	0.28	10	24.9%	-0.17 [-0.43 , 0.09]
Ladson 2011	-0.13	0.58	11	-0.33	0.68	11	11.4%	0.20 [-0.33 , 0.73]
Maciel 2004 O	1.52	0.98	8	1.21	0.45	6	6.3%	0.31 [-0.46 , 1.08]
Tang 2006	2.04	1.01	56	1.78	1.21	66	16.7%	0.26 [-0.13 , 0.65]
Total (HKSJ[a])			**130**			**125**	**100.0%**	**0.03 [-0.24 , 0.29]**





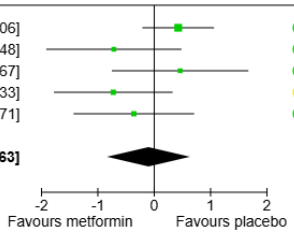
Test for overall effect: T = 0.24, df = 5 (P = 0.82)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.03; Chi² = 8.71, df = 5 (P = 0.12); I² = 45%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Hirsutism

Study or Subgroup	Metformin Mean	Metformin SD	Metformin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. mean difference IV, Random, 95% CI
Gambineri 2006	10.4	6.6	20	8	4.1	19	32.6%	0.43 [-0.21 , 1.06]
Hoeger 2004-	13.09	2.04	5	14.47	1.58	7	15.4%	-0.72 [-1.92 , 0.48]
Hoeger 2004+	13.29	4.14	5	11.78	1.58	6	15.2%	0.46 [-0.75 , 1.67]
Hoeger 2008	8.2	3.4	6	11.6	4.9	10	18.6%	-0.73 [-1.78 , 0.33]
Maciel 2004 O	7.3	1.9	8	9.1	6.86	6	18.2%	-0.36 [-1.43 , 0.71]
Total (HKSJ[a])			**44**			**48**	**100.0%**	**-0.10 [-0.84 , 0.63]**



Test for overall effect: T = 0.39, df = 4 (P = 0.72)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.14; Chi² = 5.91, df = 4 (P = 0.21); I² = 35%

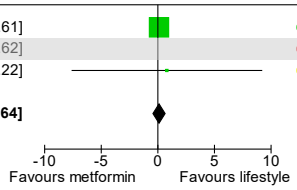
Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

3.2 Sensitivity analyses for metformin compared to lifestyle intervention

BMI (kg/m^2) – without high risk of bias

Study or Subgroup	Metformin Mean	Metformin SD	Metformin Total	Lifestyle Mean	Lifestyle SD	Lifestyle Total	Weight	Mean difference IV, Random, 95% CI
✓ Dilimulati 2024	-0.85	1.11	40	-0.95	1.22	40	99.6%	0.10 [-0.41 , 0.61]
✕ Esfahanian 2013	30.3	3.5	17	30.1	5.5	13	0.0%	0.20 [-3.22 , 3.62]
✓ Hoeger 2008	35.7	8.6	6	34.9	7	8	0.4%	0.80 [-7.62 , 9.22]
Total (HKSJ[a])			**46**			**48**	**100.0%**	**0.10 [-0.44 , 0.64]**



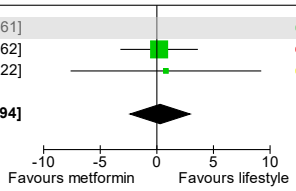
Test for overall effect: T = 2.42, df = 1 (P = 0.25)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

BMI (kg/m^2) – without Dilimulati 2024 (least squares mean)

Study or Subgroup	Metformin Mean	Metformin SD	Metformin Total	Lifestyle Mean	Lifestyle SD	Lifestyle Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A B C D E F G
✕ Dilimulati 2024	-0.85	1.11	40	-0.95	1.22	40	0.0%	0.10 [-0.41 , 0.61]	+ ? + ? + ? ?
✓ Esfahanian 2013	30.3	3.5	17	30.1	5.5	13	85.8%	0.20 [-3.22 , 3.62]	− ? − ? ? −
✓ Hoeger 2008	35.7	8.6	6	34.9	7	8	14.2%	0.80 [-7.62 , 9.22]	? ? ? ? ? ?
Total (HKSJ[a])			**23**			**21**	**100.0%**	**0.29 [-2.37 , 2.94]**	



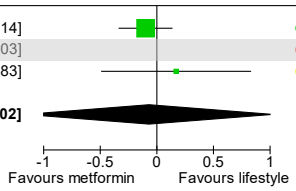
Test for overall effect: T = 1.36, df = 1 (P = 0.40)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Fasting glucose (mmol/l) – without high risk of bias

Study or Subgroup	Metformin Mean	Metformin SD	Metformin Total	Lifestyle Mean	Lifestyle SD	Lifestyle Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A B C D E F G
✓ Dilimulati 2024	-0.28	0.65	40	-0.18	0.41	40	88.5%	-0.10 [-0.34 , 0.14]	+ ? + ? + ? ?
✕ Esfahanian 2013	4.74	0.38	17	5.07	0.58	13	0.0%	-0.33 [-0.69 , 0.03]	− ? − ? ? −
✓ Hoeger 2008	4.71	0.7	6	4.54	0.51	8	11.5%	0.17 [-0.49 , 0.83]	? ? ? ? ? ?
Total (HKSJ[a])			**46**			**48**	**100.0%**	**-0.07 [-1.16 , 1.02]**	



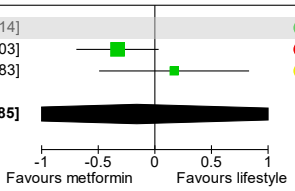
Test for overall effect: T = 0.80, df = 1 (P = 0.57)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 0.57, df = 1 (P = 0.45); I² = 0%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Fasting glucose (mmol/l) – without Dilimulati 2024 (least squares mean)

Study or Subgroup	Metformin Mean	SD	Total	Lifestyle Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A B C D E F G
✕ Dilimulati 2024	-0.28	0.65	40	-0.18	0.41	40	0.0%	-0.10 [-0.34 , 0.14]	+ ? + ? + ? ?
✓ Esfahanian 2013	4.74	0.38	17	5.07	0.58	13	66.0%	-0.33 [-0.69 , 0.03]	− ? − ? ? −
✓ Hoeger 2008	4.71	0.7	6	4.54	0.51	8	34.0%	0.17 [-0.49 , 0.83]	? ? ? ? ? ?
Total (HKSJ[a])			**23**			**21**	**100.0%**	**-0.16 [-3.17 , 2.85]**	



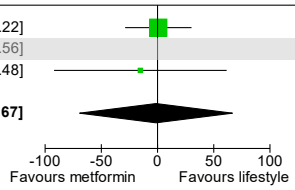
Test for overall effect: T = 0.67, df = 1 (P = 0.62)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.05; Chi² = 1.68, df = 1 (P = 0.19); I² = 41%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Fasting insulin (pmol/l) – without high risk of bias

Study or Subgroup	Metformin Mean	SD	Total	Lifestyle Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI	Risk of Bias A B C D E F G
✓ Dilimulati 2024	-23.4	72.7	40	-24.1	61.56	40	87.1%	0.70 [-28.82 , 30.22]	+ ? + ? + ? ?
✕ Esfahanian 2013	79.86	43.06	17	63.19	29.17	13	0.0%	16.67 [-9.22 , 42.56]	− ? − ? ? −
✓ Hoeger 2008	137.5	72.22	6	152.78	72.92	8	12.9%	-15.28 [-92.04 , 61.48]	? ? ? ? ? ?
Total (HKSJ[a])			**46**			**48**	**100.0%**	**-1.36 [-69.38 , 66.67]**	

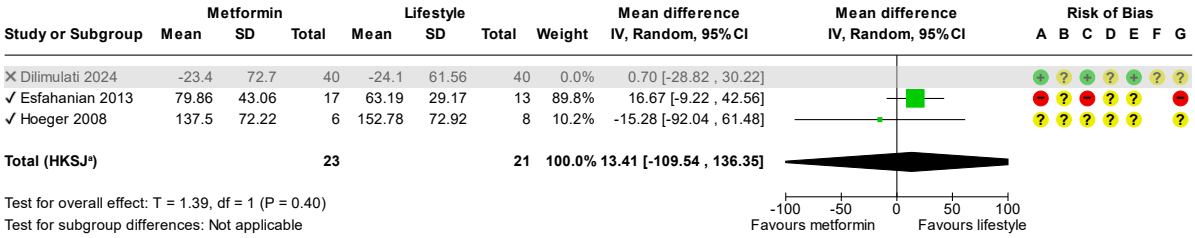


Test for overall effect: T = 0.25, df = 1 (P = 0.84)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Fasting insulin (pmol/l) – without Dilimulati 2024 (least squares mean)

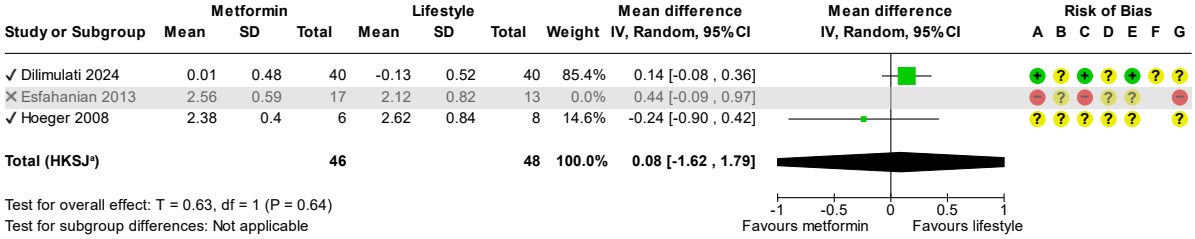


Test for overall effect: T = 1.39, df = 1 (P = 0.40)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 0.60, df = 1 (P = 0.44); I² = 0%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

LDL (mmol/l) – without high risk of bias

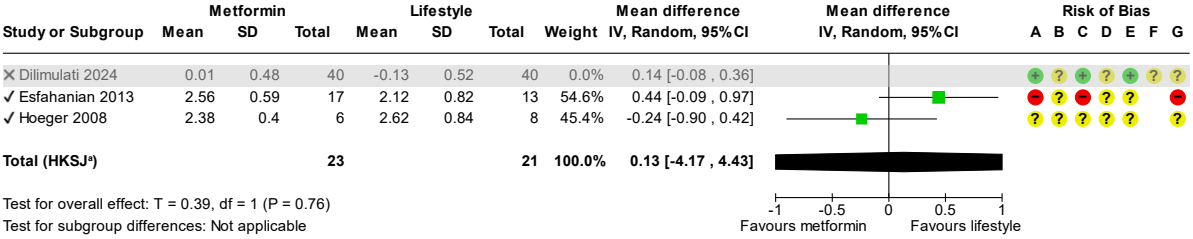


Test for overall effect: T = 0.63, df = 1 (P = 0.64)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.01; Chi² = 1.13, df = 1 (P = 0.29); I² = 12%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

LDL (mmol/l) – without Dilimulati 2024 (least squares mean)

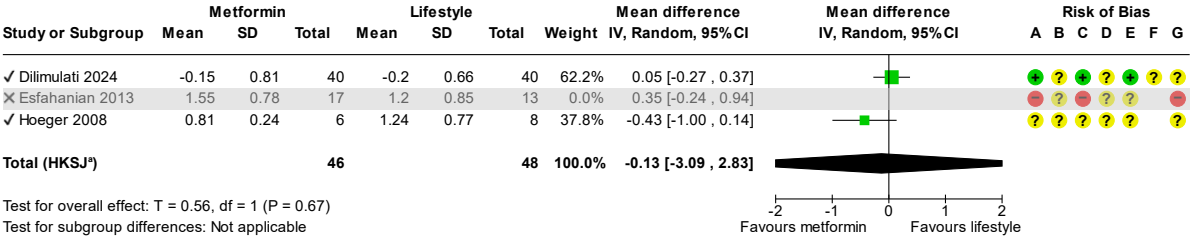


Test for overall effect: T = 0.39, df = 1 (P = 0.76)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.14; Chi² = 2.47, df = 1 (P = 0.12); I² = 60%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Triglycerides (mmol/l) – without high risk of bias

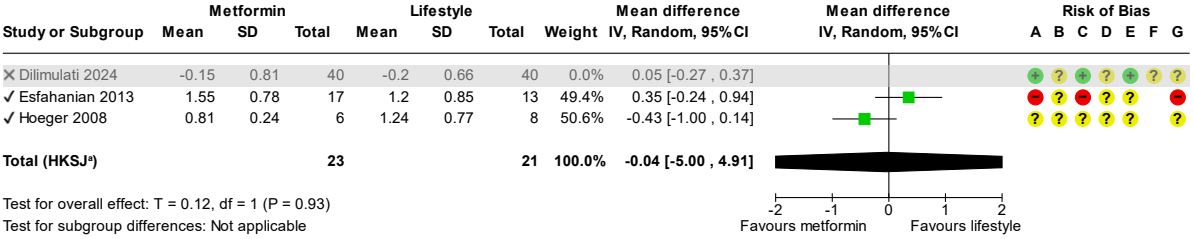


Test for overall effect: T = 0.56, df = 1 (P = 0.67)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.06; Chi² = 2.08, df = 1 (P = 0.15); I² = 52%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Triglycerides (mmol/l) – without Dilimulati 2024 (least squares mean)



Test for overall effect: T = 0.12, df = 1 (P = 0.93)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.22; Chi² = 3.48, df = 1 (P = 0.06); I² = 71%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended intervention
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

4 Analyses regarding GLP-1 analogues

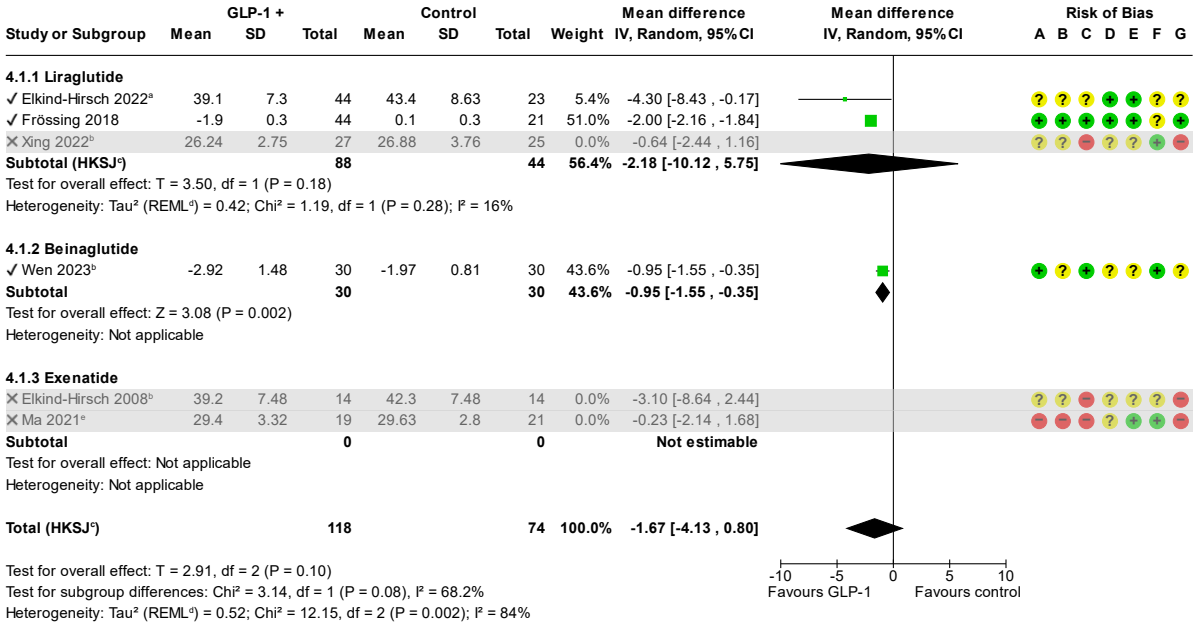
Liraglutide compared to placebo

No sensitivity analyses.

Exenatide compared to metformin

No sensitivity analyses.

Sensitivity analyses for GLP-1 + *BMI (kg/m^2) – without high risk of bias*



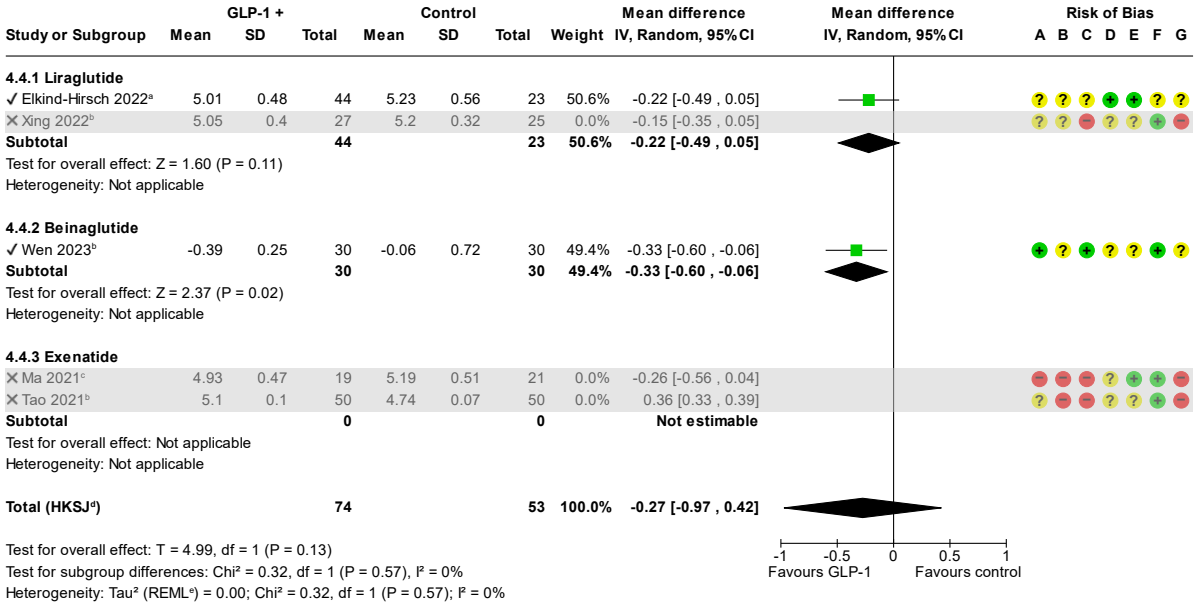
Footnotes

[a]with lifestyle intervention for both groups
[b]with metformin for both groups
[c]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[d]Tau² calculated by Restricted Maximum-Likelihood method.
[e]with metformin and CPA/EE for both groups

Risk of bias legend

(A) Risk of bias arising from the randomization process
(B) Risk of bias due to deviations from the intended interventions
(C) Missing outcome data
(D) Risk of bias in measurement of the outcome
(E) Risk of bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

Fasting glucose (mmol/l) – without high risk of bias



Test for overall effect: T = 4.99, df = 1 (P = 0.13)
Test for subgroup differences: Chi² = 0.32, df = 1 (P = 0.57), I² = 0%
Heterogeneity: Tau² (REML[e]) = 0.00; Chi² = 0.32, df = 1 (P = 0.57); I² = 0%

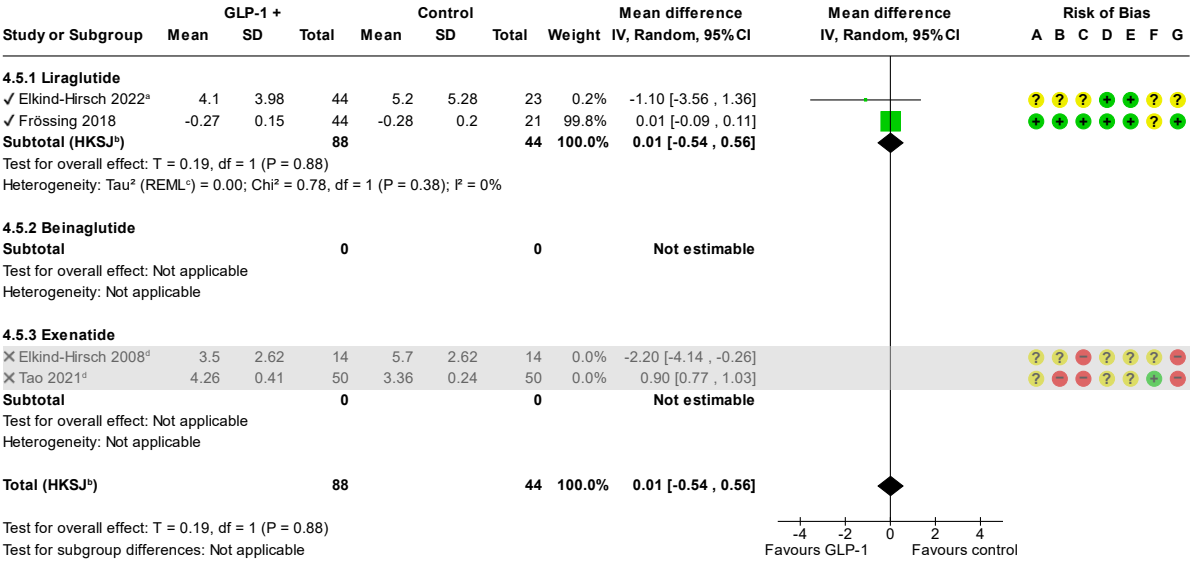
Footnotes

[a]with lifestyle intervention for both groups
[b]with metformin for both groups
[c]with metformin and CPA/EE for both groups
[d]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[e]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Risk of bias arising from the randomization process
(B) Risk of bias due to deviations from the intended interventions
(C) Missing outcome data
(D) Risk of bias in measurement of the outcome
(E) Risk of bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

HOMA-IR – without high risk of bias



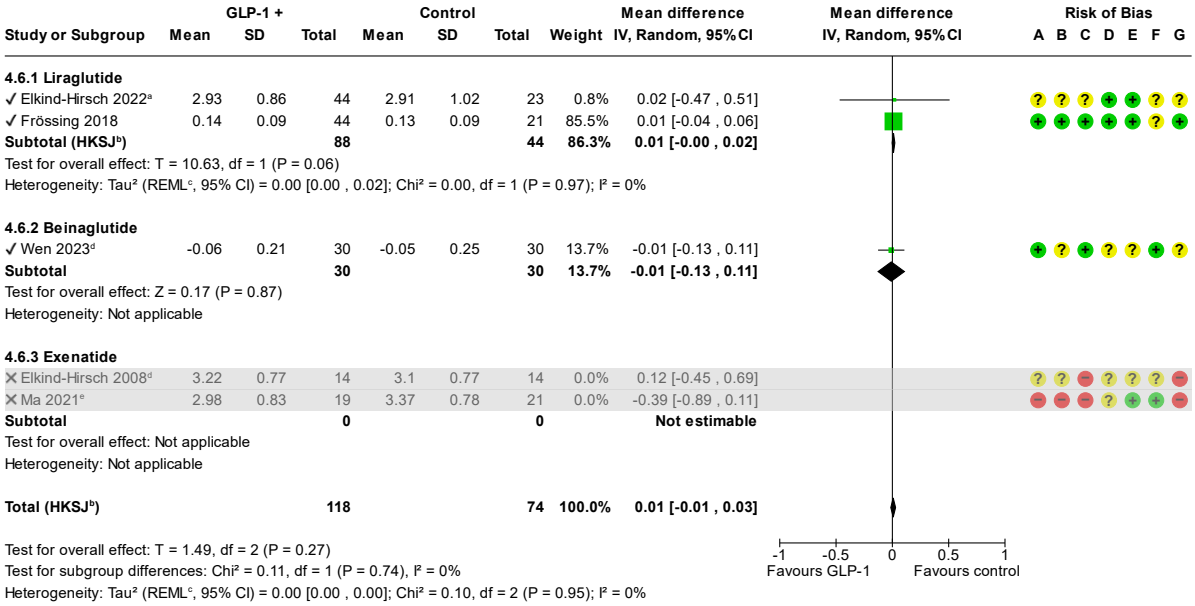
Footnotes

[a]with lifestyle intervention for both groups
[b]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[c]Tau² calculated by Restricted Maximum-Likelihood method.
[d]with metformin for both groups

Risk of bias legend

(A) Risk of bias arising from the randomization process
(B) Risk of bias due to deviations from the intended interventions
(C) Missing outcome data
(D) Risk of bias in measurement of the outcome
(E) Risk of bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

LDL (mmol/l) – without high risk of bias



Footnotes

[a]with lifestyle intervention for both groups
[b]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[c]Tau² calculated by Restricted Maximum-Likelihood method.
[d]with metformin for both groups
[e]with metformin and CPA/EE for both groups

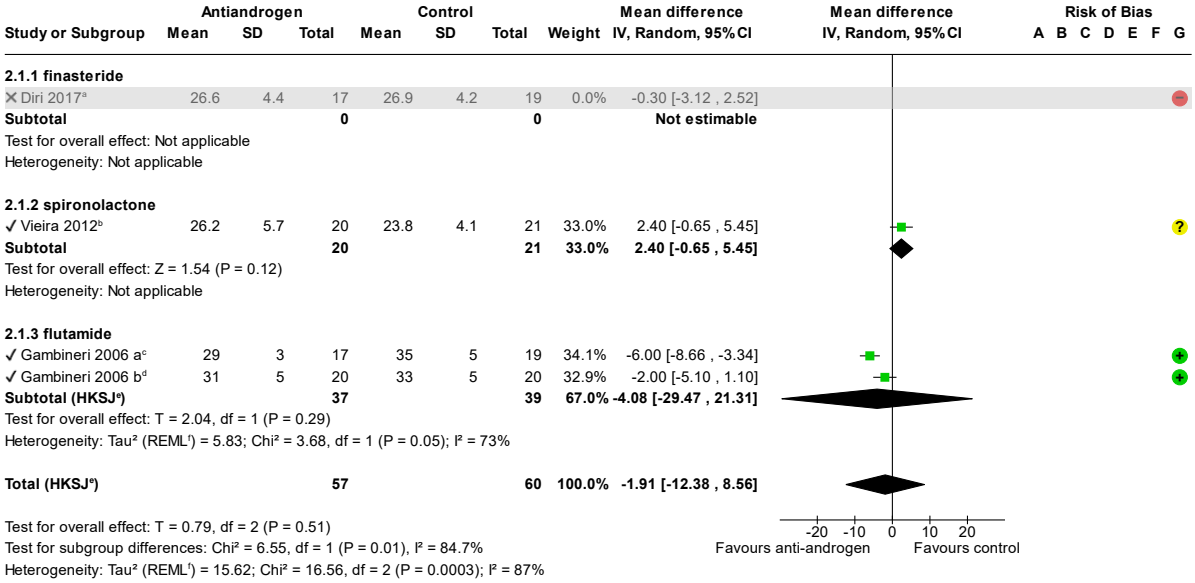
Risk of bias legend

(A) Risk of bias arising from the randomization process
(B) Risk of bias due to deviations from the intended interventions
(C) Missing outcome data
(D) Risk of bias in measurement of the outcome
(E) Risk of bias in selection of the reported result
(F) Conflict of interest
(G) Overall risk of bias

5 Long term analyses

5.1 Sensitivity analyses for antiandrogens+

BMI (kg/m²)



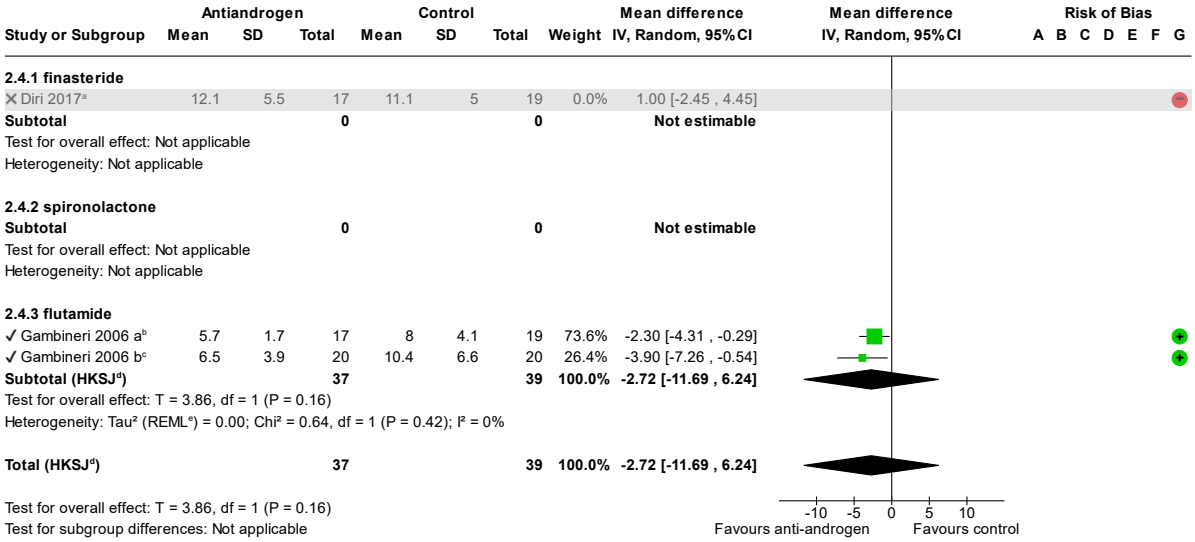
Footnotes

[a]with metformin for both groups
[b]with oral contraceptives for both groups
[c]with lifestyle intervention for both groups
[d]with metformin and lifestyle intervention for both groups
[e]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[f]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Hirsutism



Study or Subgroup	Antiandrogen Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
2.4.1 finasteride								
✕ Diri 2017[a]	12.1	5.5	17	11.1	5	19	0.0%	1.00 [-2.45 , 4.45]
Subtotal			**0**			**0**		**Not estimable**
Test for overall effect: Not applicable								
Heterogeneity: Not applicable								
2.4.2 spironolactone								
Subtotal			**0**			**0**		**Not estimable**
Test for overall effect: Not applicable								
Heterogeneity: Not applicable								
2.4.3 flutamide								
✓ Gambineri 2006 a[b]	5.7	1.7	17	8	4.1	19	73.6%	-2.30 [-4.31 , -0.29]
✓ Gambineri 2006 b[c]	6.5	3.9	20	10.4	6.6	20	26.4%	-3.90 [-7.26 , -0.54]
Subtotal (HKSJ[d])			**37**			**39**	**100.0%**	**-2.72 [-11.69 , 6.24]**
Test for overall effect: T = 3.86, df = 1 (P = 0.16)								
Heterogeneity: Tau² (REML[e]) = 0.00; Chi² = 0.64, df = 1 (P = 0.42); I² = 0%								
Total (HKSJ[d])			**37**			**39**	**100.0%**	**-2.72 [-11.69 , 6.24]**
Test for overall effect: T = 3.86, df = 1 (P = 0.16)								
Test for subgroup differences: Not applicable								
Heterogeneity: Tau² (REML[e]) = 0.00; Chi² = 0.64, df = 1 (P = 0.42); I² = 0%								

Footnotes
[a]with metformin for both groups
[b]with lifestyle intervention for both groups
[c]with metformin and lifestyle intervention for both groups
[d]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[e]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

5.2 Sensitivity analyses for metformin+

No sensitivity analyses.