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 9 Compilation of risk of bias

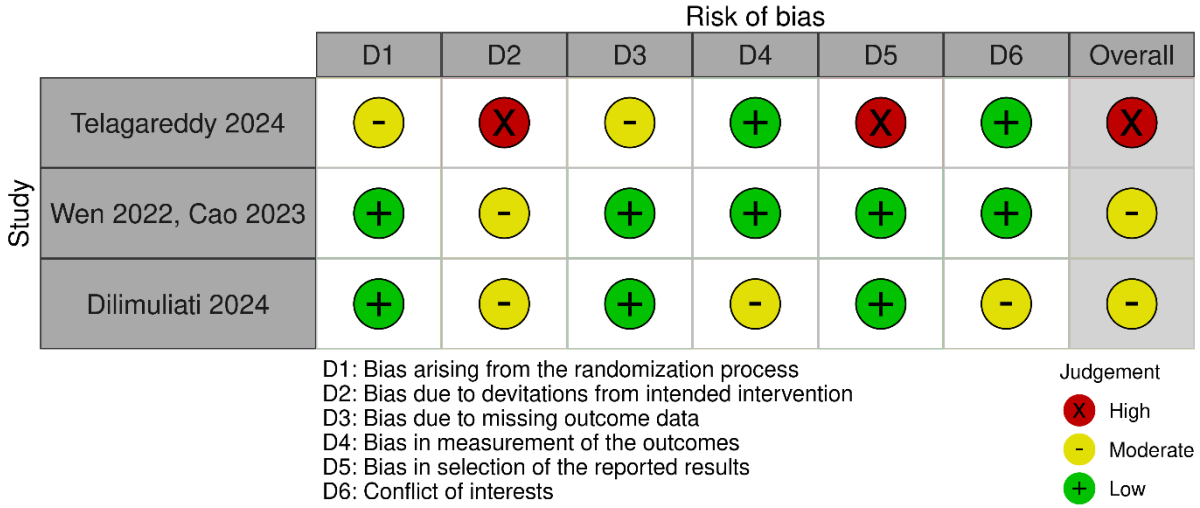
Table of contents

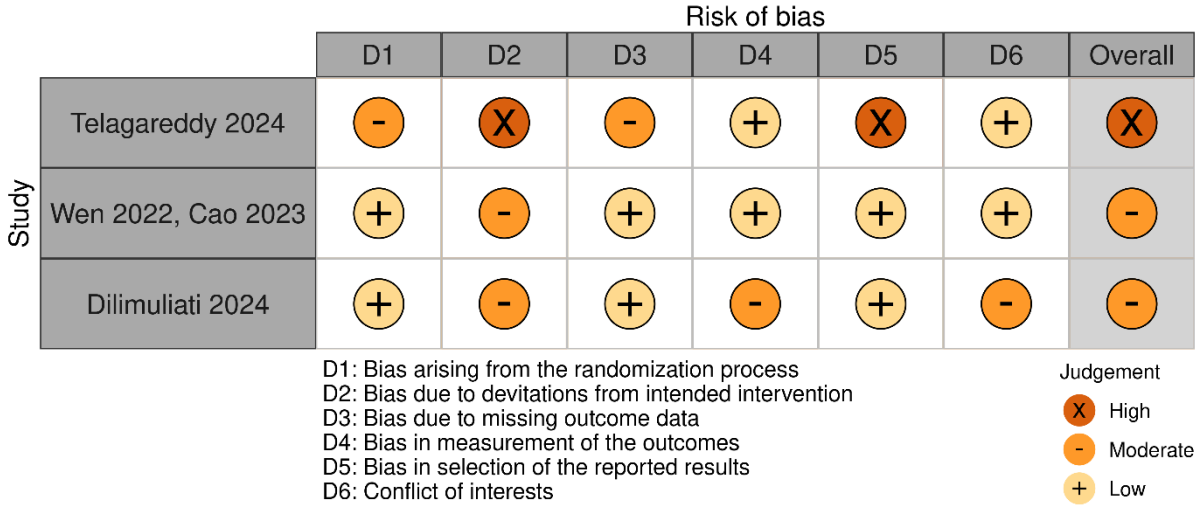
Studies with low, moderate or high risk of bias have been included in the report. Studies with unacceptably high risk of bias have been excluded (Appendix 3).

1 Traffic light graphs

Metformin

Studies: [1-4]

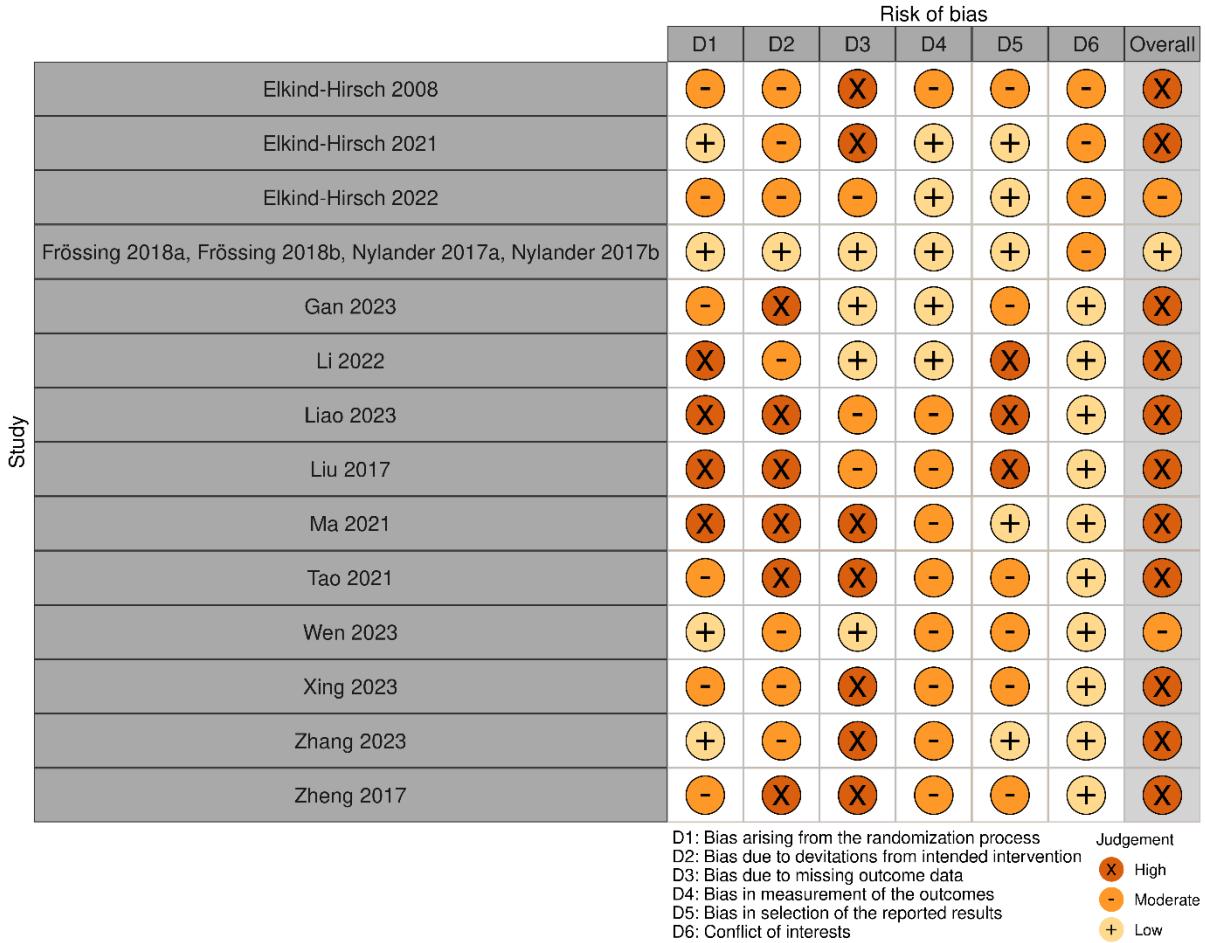




GLP-1 analogues

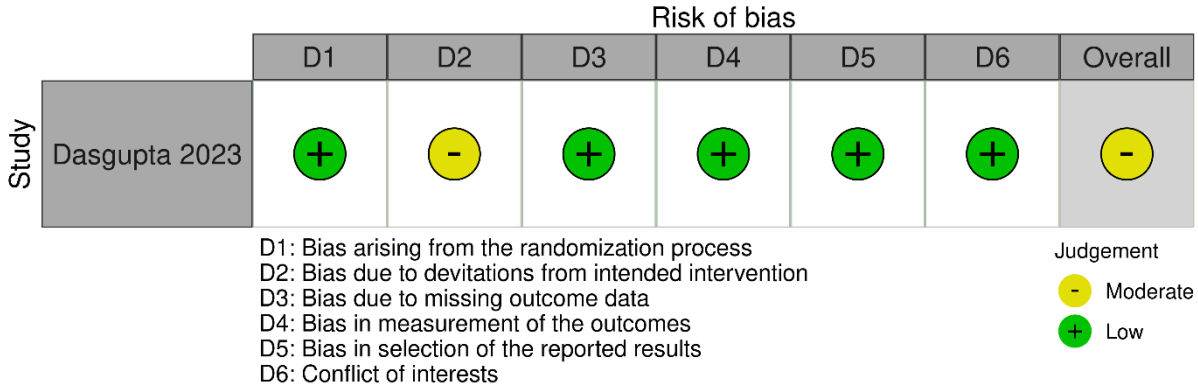
Studies: [5-20]

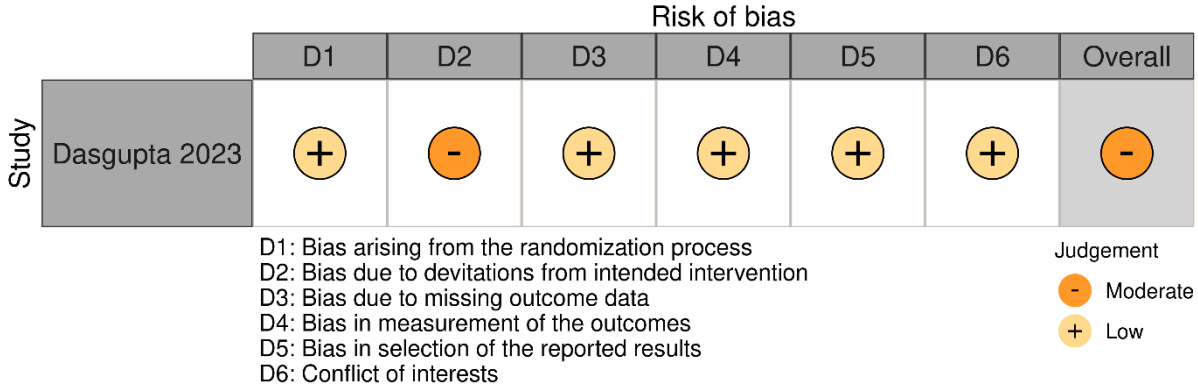

Risk of bias
D1
D2
D3
D4
D5
D6
Overall
Study
Elkind-Hirsch 2008
Elkind-Hirsch 2021
Elkind-Hirsch 2022
Frössing 2018a, Frössing 2018b, Nylander 2017a, Nylander 2017b
Gan 2023
Li 2022
Liao 2023
Liu 2017
Ma 2021
Tao 2021
Wen 2023
Xing 2023
Zhang 2023
Zheng 2017
D1: Bias arising from the randomization process
D2: Bias due to devitations from intended intervention
D3: Bias due to missing outcome data
D4: Bias in measurement of the outcomes
D5: Bias in selection of the reported results
D6: Conflict of interests
Judgement
High
Moderate
Low



Combined contraceptive pills

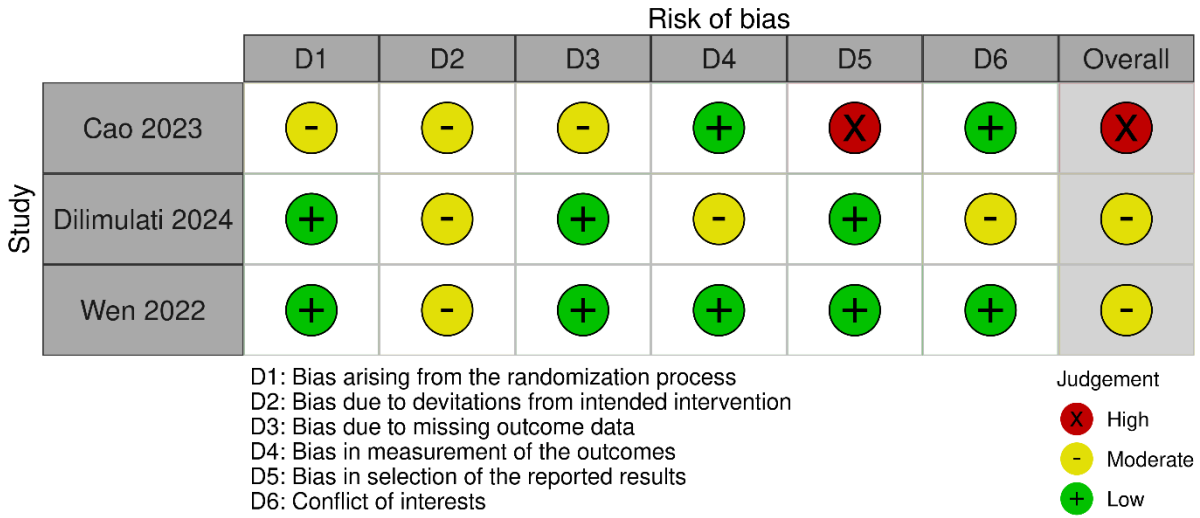
Study: [21]

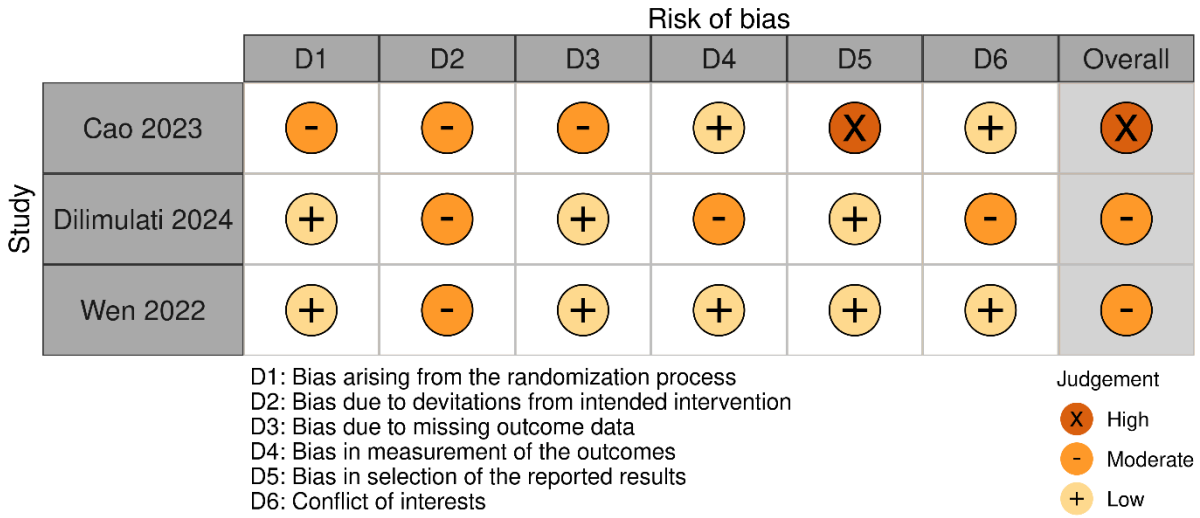




2 Traffic light graph for RCTs with other interventions

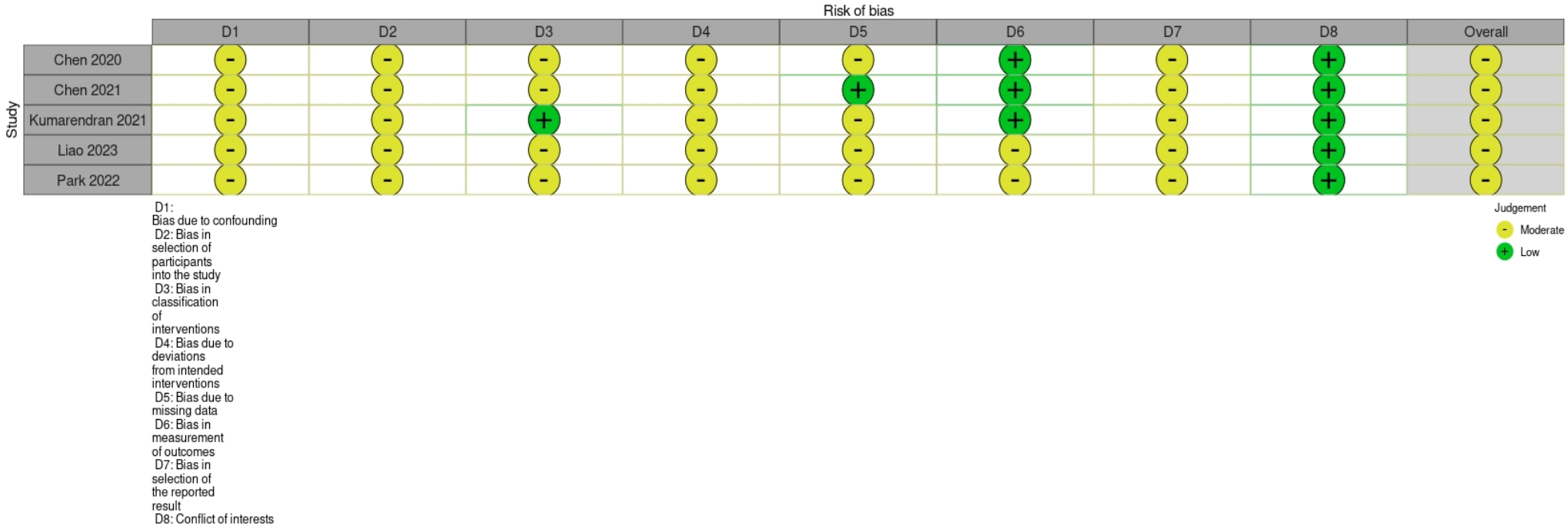
Studies: [1] [2] [4]

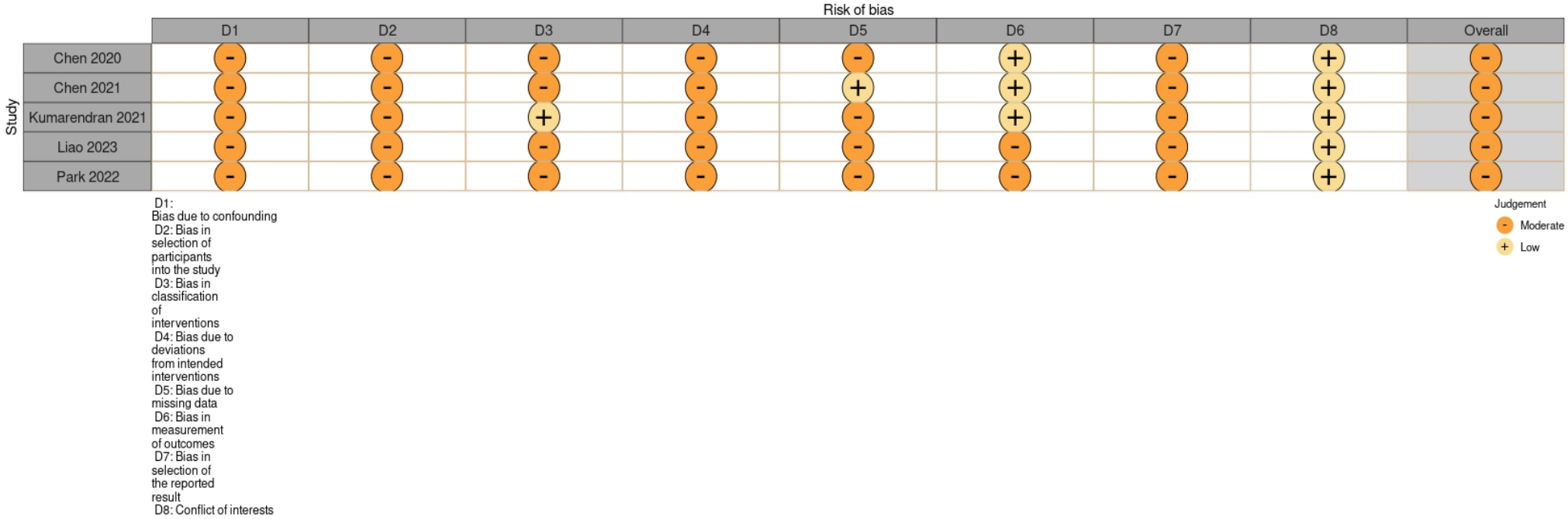

Risk of bias
D1
D2
D3
D4
D5
D6
Overall
Study
Cao 2023
Dilimulati 2024
Wen 2022
D1: Bias arising from the randomization process
D2: Bias due to devitations from intended intervention
D3: Bias due to missing outcome data
D4: Bias in measurement of the outcomes
D5: Bias in selection of the reported results
D6: Conflict of interests
Judgement
High
Moderate
Low


Risk of bias
D1
D2
D3
D4
D5
D6
Overall
Study
Cao 2023
Dilimulati 2024
Wen 2022
D1: Bias arising from the randomization process
D2: Bias due to devitations from intended intervention
D3: Bias due to missing outcome data
D4: Bias in measurement of the outcomes
D5: Bias in selection of the reported results
D6: Conflict of interests
Judgement
High
Moderate
Low

3 Traffic light graph for non-randomised studies

Studies: [22] [23] [24] [12] [25].





Visualisations made using Robvis [26].

4 References

1. Cao J, Nie G, Dai Z, Shan D, Wei Z. Comparative effects of acupuncture and metformin on insulin sensitivity in overweight/obese and lean women with polycystic ovary syndrome and insulin resistance: a post hoc analysis of a randomized trial. Front Med (Lausanne). 2023;10:1232127. Available from: https://doi.org/10.3389/fmed.2023.1232127
2. Dilimulati D, Shao X, Wang L, Cai M, Zhang Y, Lu J, et al. Efficacy of WeChat-Based Digital Intervention Versus Metformin in Women With Polycystic Ovary Syndrome: Randomized Controlled Trial. J Med Internet Res. 2024;26:e55883. Available from: https://doi.org/10.2196/55883
3. Telagareddy R, Kumar PR, Pattanaik SR, Dash DK, Patro D, Sahoo BK, et al. Serum Irisin in Polycystic Ovary Syndrome and its Alteration with Metformin Intervention. Indian J Endocrinol Metab. 2024;28(1):91-7. Available from: https://doi.org/10.4103/ijem.ijem_379_23
4. Wen Q, Hu M, Lai M, Li J, Hu Z, Quan K, et al. Effect of acupuncture and metformin on insulin sensitivity in women with polycystic ovary syndrome and insulin resistance: a three-armed randomized controlled trial. Hum Reprod. 2022;37(3):542-52. Available from: https://doi.org/10.1093/humrep/deab272
5. Elkind-Hirsch K, Marrioneaux O, Bhushan M, Vernor D, Bhushan R. Comparison of single and combined treatment with exenatide and metformin on menstrual cyclicity in overweight women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2008;93(7):2670-8. Available from: https://doi.org/10.1210/jc.2008-0115
6. Elkind-Hirsch KE, Chappell N, Seidemann E, Storment J, Bellanger D. Exenatide, Dapagliflozin, or Phentermine/Topiramate Differentially Affect Metabolic Profiles in Polycystic Ovary Syndrome. J Clin Endocrinol Metab. 2021;106(10):3019-33. Available from: https://doi.org/10.1210/clinem/dgab408
7. Elkind-Hirsch KE, Chappell N, Shaler D, Storment J, Bellanger D. Liraglutide 3 mg on weight, body composition, and hormonal and metabolic parameters in women with obesity and polycystic ovary syndrome: a randomized placebo-controlled-phase 3 study. Fertil Steril. 2022;118(2):371-81. Available from: https://doi.org/10.1016/j.fertnstert.2022.04.027
8. Frøssing S, Nylander M, Chabanova E, Frystyk J, Holst JJ, Kistorp C, et al. Effect of liraglutide on ectopic fat in polycystic ovary syndrome: A randomized clinical trial. Diabetes Obes Metab. 2018;20(1):215-8. Available from: https://doi.org/10.1111/dom.13053
9. Frøssing S, Nylander M, Kistorp C, Skouby SO, Faber J. Effect of liraglutide on atrial natriuretic peptide, adrenomedullin, and copeptin in PCOS. Endocr Connect. 2018;7(1):115-23. Available from: https://doi.org/10.1530/ec-17-0327

10. Gan J, Chen J, Ma RL, Deng Y, Ding XS, Zhu SY, et al. Metagenomics study on taxonomic and functional change of gut microbiota in patients with obesity with PCOS treated with exenatide combination with metformin or metformin alone. Gynecol Endocrinol. 2023;39(1):2219342. Available from: https://doi.org/10.1080/09513590.2023.2219342

11. Li R, Mai T, Zheng S, Zhang Y. Effect of metformin and exenatide on pregnancy rate and pregnancy outcomes in overweight or obese infertility PCOS women: long-term follow-up of an RCT. Arch Gynecol Obstet. 2022;306(5):1711-21. Available from: https://doi.org/10.1007/s00404-022-06700-3

12. Liao CC, Chien CH, Yu TS, Li JM. Integrated Chinese and Western Medicine for Coronary Heart Disease Prevention in Polycystic Ovary Syndrome: A 19-Year Nationwide Cohort Study. J Multidiscip Healthc. 2023;16:3959-73. Available from: https://doi.org/10.2147/jmdh.S442816

13. Ma RL, Deng Y, Wang YF, Zhu SY, Ding XS, Sun AJ. Short-term combined treatment with exenatide and metformin for overweight/obese women with polycystic ovary syndrome. Chin Med J (Engl). 2021;134(23):2882-9. Available from: https://doi.org/10.1097/cm9.0000000000001712

14. Nylander M, Frøssing S, Clausen HV, Kistorp C, Faber J, Skouby SO. Effects of liraglutide on ovarian dysfunction in polycystic ovary syndrome: a randomized clinical trial. Reprod Biomed Online. 2017;35(1):121-7. Available from: https://doi.org/10.1016/j.rbmo.2017.03.023

15. Nylander M, Frøssing S, Kistorp C, Faber J, Skouby SO. Liraglutide in polycystic ovary syndrome: a randomized trial, investigating effects on thrombogenic potential. Endocr Connect. 2017;6(2):89-99. Available from: https://doi.org/10.1530/ec-16-0113

16. Tao T, Zhang Y, Zhu YC, Fu JR, Wang YY, Cai J, et al. Exenatide, Metformin, or Both for Prediabetes in PCOS: A Randomized, Open-label, Parallel-group Controlled Study. J Clin Endocrinol Metab. 2021;106(3):e1420-e32. Available from: https://doi.org/10.1210/clinem/dgaa692

17. Wen Q, Fang S, Liang Y, Tian Y, Chen Y, Yuan J, et al. Short-term effect of beinaglutide combined with metformin versus metformin alone on weight loss and metabolic profiles in obese patients with polycystic ovary syndrome: a pilot randomized trial. Front Endocrinol (Lausanne). 2023;14:1156521. Available from: https://doi.org/10.3389/fendo.2023.1156521

18. Xing C, Zhao H, Zhang J, He B. Effect of metformin versus metformin plus liraglutide on gonadal and metabolic profiles in overweight patients with polycystic ovary syndrome. Front Endocrinol (Lausanne). 2022;13:945609. Available from: https://doi.org/10.3389/fendo.2022.945609

19. Zhang Y, Qu Z, Lu T, Shao X, Cai M, Dilimulati D, et al. Effects of a Dulaglutide plus Calorie-Restricted Diet versus a Calorie-Restricted Diet on Visceral Fat and Metabolic Profiles in Women with Polycystic Ovary Syndrome: A Randomized Controlled Trial. Nutrients. 2023;15(3). Available from: https://doi.org/10.3390/nu15030556

20. Zheng S, Zhang Y, Long T, Lu J, Liu X, Yan J, et al. Short term monotherapy with exenatide is superior to metformin in weight loss, improving insulin resistance and inflammation in Chinese overweight/obese PCOS women. Obesity Medicine. 2017;7. Available from: https://doi.org/10.1016/j.obmed.2017.06.003

21. Dasgupta S, Mondal J, Goswami B, Dasgupta J. Randomized control trial to compare effects of ultra-low dose (Ethinylestradiol 20 µg or 15 µg) with low dose (Ethinylestradiol 30 µg) hormonal pills on lipid discordance in non-obese PCOS women. Obstet Gynecol Sci. 2023;66(6):572-83. Available from: https://doi.org/10.5468/ogs.23142

22. Chen SF, Yang YC, Hsu CY, Shen YC. Risk of bipolar disorder in patients with polycystic ovary syndrome: A nationwide population-based cohort study. J Affect Disord. 2020;263:458-62. Available from: https://doi.org/10.1016/j.jad.2019.12.007

23. Chen SF, Yang YC, Hsu CY, Shen YC. Risk of schizophrenia in patients with polycystic ovary syndrome: a nationwide population-based cohort study from Taiwan. J Psychosom Obstet Gynaecol. 2021;42(4):272-8. Available from: https://doi.org/10.1080/0167482x.2020.1735342

24. Kumarendran B, O'Reilly MW, Subramanian A, Šumilo D, Toulis K, Gokhale KM, et al. Polycystic Ovary Syndrome, Combined Oral Contraceptives, and the Risk of Dysglycemia: A Population-Based Cohort Study With a Nested Pharmacoepidemiological Case-Control Study. Diabetes Care. 2021;44(12):2758-66. Available from: https://doi.org/10.2337/dc21-0437

25. Park B, Lee H, Park S, Lee ES, Lee JJ, Lee Y, et al. Trend changes and factor analysis of endometrial hyperplasia in patients with polycystic ovarian syndrome based on the Korean National Health Insurance Database. BMC Womens Health. 2022;22(1):439. Available from: https://doi.org/10.1186/s12905-022-02015-2

26. McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. Research Synthesis Methods. 2020;n/a(n/a). Available from: https://doi.org/10.1002/jrsm.1411