

4.4 Metformin and combined oral contraceptive pills

Is metformin versus the COCP with or without other agents effective for management of features of PCOS in adolescents and adults with PCOS?

Clinical need for the question

Metformin and COCP have different mechanisms of action and efficacy on various outcomes in PCOS, as a complex and heterogeneous condition. The comparative role of these agents and the role of combining these agents together and with other relevant agents remains unclear and has been prioritised.

Summary of systematic review evidence

Given the extensive studies included and the meta-analyses, further information, including detailed references and study characteristics, can be found in the technical report in [Section 4.4](#).

COCP versus metformin. Twenty-five RCTs were captured with four RCTs in adolescents. Those reporting mean $\pm$ SD were included in meta-analysis, with subgroup analysis for adults and adolescents. Overall, there were no differences between treatments regarding BMI, weight or WHR, with very low certainty of evidence. No differences were seen in the subgroups. Menstrual cycle duration became shorter with COCP treatment compared with metformin, with moderate certainty of evidence. There was no difference in hirsutism (very low certainty of evidence), but COCP treatment resulted in lower FAI, total testosterone, androstenedione and higher SHBG levels (low certainty of evidence), and lower free testosterone and DHEAs (very low certainty).

In adolescents, similar results were seen with hyperandrogenism, but with very low certainty of evidence, except for total testosterone, which was lower after COCP treatment with moderate certainty of evidence. For free testosterone, no difference was seen between treatments, with very low certainty of evidence.

In adults, there was no difference in hirsutism with a very low certainty of evidence. FAI and total testosterone levels were lower after COCP treatment with low certainty and free testosterone lower with very low certainty. SHBG levels were higher (low certainty), androstenedione lower (moderate certainty) and DHEAS lower (very low certainty) after COCP, compared with metformin.

For metabolic outcomes, insulin was lower overall (low certainty), and in adults (moderate certainty) after metformin. In adolescents there was no difference in insulin (very low certainty of evidence). HOMA-IR was lower after metformin treatment both overall and in adults, with very low and low certainty of evidence respectively. Cholesterol levels were lower after metformin both overall (very low certainty) and in subgroups (low certainty). There were no differences in LDL, HDL or triglyceride levels, except for adolescents, where lower LDL levels were seen after metformin treatment (low certainty). CRP levels were lower after metformin treatment, overall (low certainty), in adults (low certainty), and in adolescents (very low certainty). Glucose levels did not differ, overall or in the subgroups.

COCP versus COCP + metformin. Eighteen RCTs were identified all in adults. Combined therapy resulted in lower FAI (moderate certainty), higher SHBG and lower DHEAS (low certainty) and lower androstenedione (very low evidence certainty). Combined therapy also reduced insulin and HOMA-IR with very low and low certainty respectively. With moderate certainty, the effect on total testosterone did not differ between treatments. There were no differences in blood lipids, CRP or anthropometry (low or very low certainty). There was no difference in QoL. COCP + metformin seemed to be associated with more gastrointestinal side-effects.

