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PCOS

# Metformin risk for offspring

Women with polycystic ovary syndrome (PCOS) are often prescribed metformin during pregnancy to reduce the risk of PCOS-associated complications; however, the long-term effects for the offspring are largely unknown. A recently published follow-up study of two randomized controlled trials (RCTs) suggests that in utero exposure to metformin increases the risk of overweight in early childhood.

The Norwegian study included data on 182 children who had been born to mothers involved in the Pilot and PregMet RCTs. "Metformin passes the placenta, and the foetus is thus exposed to the drug," explains author Liv Guro Engen Hanem. "The follow-up was conducted to investigate possible effects of intrauterine metformin exposure on offspring health." During the RCTs, the mothers received metformin at 1,700 mg or 2,000 mg, or a placebo, daily. For the follow-up, the researchers collected data from the offspring health records regarding height, weight, BMI and head circumference up to the age of 4 years.

The researchers found that from 6 months old, metformin-exposed children had increased weight and BMI, which persisted to the age of 4 years. Furthermore, more children in the metformin group than in the placebo group had overweight at 4 years. "Metformin is known to ameliorate insulin resistance and hyperandrogenism in non-pregnant women with PCOS," explains Hanem. "Our findings were surprising, as we expected these effects also in pregnancy, and thus a positive impact on the intrauterine environment and offspring health."

The researchers, led by Eszter Vanky, have now conducted a follow-up of the offspring to the age of 8 years, including physical and cognitive examinations, as well as information of previous illnesses. "We suggest that intervention studies with metformin in pregnancy should follow up the long-term health of offspring," concludes Hanem.

*Claire Greenhill*

**ORIGINAL ARTICLE** Hanem, L. G. E. et al. Metformin use in PCOS pregnancies increases the risk of offspring overweight at 4 years of age; follow-up of two RCTs. *J. Clin. Endocrinol. Metab.* https://doi.org/10.1210/jc.2017-02419 (2018)