

Paternal metformin use associated with major birth defects if used during period of sperm development

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A large cohort study found that babies born to men who took metformin during the period of sperm development were at increased risk for birth

defects, specifically genital defects in boys. These findings suggest that men with diabetes who are taking metformin should talk to their doctors about whether they should switch to another treatment when trying to conceive a child. However, because diabetes control also affects sperm quality, discontinuing metformin treatment could also affect birth outcomes. The findings are published in *Annals of Internal Medicine*.

Diabetes increasingly occurs in people of reproductive age, compromises sperm quality, and is associated with impaired male fertility. Some [diabetes drugs](#) may also affect male reproductive health.

Researchers from the University of Southern Denmark and Stanford University studied data from nation-wide national registries of births, patients, and prescriptions to evaluate whether the risk for [birth defects](#) varied among offspring born to men treated with insulin, metformin, or sulfonylureas prior to conception. Babies were considered exposed to a diabetes drug if their father filled at least 1 prescription during the 3 months when the fertilizing sperm were developing. The researchers compared birth defects in the babies across diabetes drugs, different times of taking the drug relative to development of fertilizing sperm, and with unexposed siblings of the babies. Babies whose fathers took insulin had no increased risk for a birth defect compared with the general group. Babies whose fathers took metformin had an increased risk for birth defects. There were too few babies whose fathers took sulfonylureas to determine risks for birth defects with any certainty. Taking metformin before or after sperm development did not increase the risk for birth defects. Unexposed siblings were also not at increased risk. According to the authors, the size of the diabetes pandemic suggests that treatment of prospective fathers with diabetes, including pharmacologic management and counseling on diet, [physical exercise](#), and [weight loss](#), should be subject to further study.

An editorial from Germaine M. Buck Louis, Ph.D., MS at George

Mason University emphasizes the importance of corroborating the findings, given the prevalence of metformin use as first-line therapy for type 2 [diabetes](#). The author also calls for guidance from clinicians to help couples planning pregnancy weigh the risks and benefits of paternal metformin use relative to other medications.

More information: Study:

<https://www.acpjournals.org/doi/10.7326/M21-4389>

Editorial: <https://www.acpjournals.org/doi/10.7326/M22-0770>

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