

## Have diabetes? Quitting metformin could take toll on your brain

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Millions of people with diabetes take the drug metformin to control their blood sugar levels.



Meant to be taken for the long term, new research now suggests that stopping it early may up the risk of developing thinking and memory problems as patients age.

"We found that staying on metformin prevents or delays dementia onset, and this is very encouraging," said researcher Sarah Ackley, an epidemiologist at Boston University.

People who stopped metformin early were 21% more likely to be diagnosed with dementia when compared to folks who stayed on the drug, the study showed.

"Metformin has broad benefits, which is why it's given first in <u>diabetes</u> treatment, and it's recommended people stay on it unless it's contraindicated," Ackley said. People might stop using metformin due to side effects such as kidney problems or because they prefer to manage their <u>blood sugar</u> without medications.

For the study, researchers looked at new cases of dementia among people with type 2 diabetes, including 12,220 people who stopped taking metformin and 29,000 who stayed the course in a large database from the Kaiser Permanente Northern California health care system.

The study wasn't designed to say how, or even if, metformin may prevent age-related memory changes.

A subsequent increase in <u>blood sugar levels</u> or use of insulin after stopping metformin did not seem to play a role.

"Metformin's other effects are likely responsible, and this understanding could help the field identify effective interventions and preventive strategies in future research," said study author Scott Zimmerman, an epidemiologist at the University of California, San Francisco.



If you are taking metformin and considering stopping, talk to your doctor first, he said.

"Many factors need to be balanced for each individual, including individual dementia risk, severity of metformin side effects and what the patient wants," Zimmerman said. "The benefits of metformin beyond just preventing diabetes complications could be part of the conversation."

The findings were published Oct. 25 in the journal <u>JAMA Network</u> <u>Open</u>.

The results align with existing literature that suggests metformin lowers the risk of developing dementia, said Yuko Hara, director of Aging and Alzheimer's Prevention at the Alzheimer's Drug Discovery Foundation in New York City.

Metformin is used with diet and exercise to manage type 2 diabetes, and type 2 diabetes is a well-established risk factor for dementia, explained Hara, who was not part of the new study.

"Type 2 diabetes and Alzheimer's disease share several characteristics, including impaired glucose uptake into the brain, [and] glucose is critical for brain function," she said. In addition, the two conditions are linked to insulin resistance and higher levels of oxidative stress.

"If you have type 2 diabetes, effectively managing it with metformin or with other anti-diabetic medications plus lifestyle interventions may reduce dementia risk and protect your brain from cognitive decline," Hara noted.

It's too early to say that stopping metformin will increase the chances of developing dementia, said Dr. John Buse, director of the Diabetes Care



Center at the University of North Carolina at Chapel Hill.

There may be other factors driving the findings: There have been concerns that metformin can reduce vitamin B12 levels, and lower levels of B12 can increase risk for memory and thinking issues, said Buse, who was not involved with the study.

"Metformin stopping may be a symptom and not a cause of <u>dementia</u>," he noted.

The bottom line? "This is a brilliant idea worthy of more study, but certainly not a strong signal that stopping metformin is a bad idea," Buse said.

There are reasons to stop taking metformin, including kidney problems.

But, "if there is no good reason to stop <u>metformin</u>, clearly it is about as effective and safe a medication as exists, and one should think about continuing it," Buse added.

**More information:** Scott C. Zimmerman et al, Metformin Cessation and Dementia Incidence *JAMA Network Open* (2023) DOI: 10.1001/jamanetworkopen.2023.39723

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