

Can this diabetes drug really slow aging, curb weight gain, reduce dementia? What's behind the metformin craze?

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Is an ancient compound the new "wonder drug"?

Metformin, a common medication to control diabetes, has become the



controversial darling of tech's health-conscious digerati who are enticed by preliminary research suggesting it might help promote longevity, reduce dementia and prevent a whole host of other conditions—including, most recently, long COVID.

With origins that date back to Medieval Europe, metformin has been used for decades as a powerful tool to lower blood sugar in people with diabetes. In those patients, it also offers cardiovascular benefits and weight loss.

Now, it is increasingly popular for use in conditions that have nothing to do with diabetes. Intrigued by early studies and promotion on TikTok, Instagram and health-focused blogs, Americans are seeking "off-label" prescriptions for metformin, using a drug for a different condition or at a different dosage than what is FDA-approved

But experts urge caution, saying the data isn't sufficient to start recommending daily doses.

According to UC San Francisco infectious disease expert Dr. Peter Chin-Hong, "I'd be very wary about using metformin off-label at this point," citing lack of extensive research. "The evidence has to be really strong," he said, "if you take a drug for a particular indication in which there's not a lot of good data."

"Certainly, a lot of young healthy people are looking into taking it with hopes of kind of optimizing their health and 'biohacking' to improve their longevity down the line," said Stanford University endocrinologist Dr. Marilyn Tan. While it's unlikely to do harm, Tan said, "there's also no proven benefit from any randomized controlled trial in terms of antiaging effects. . . . It's not FDA-approved for any of these other indications."



Metformin, or dimethylbiguanide, traces its history back to a traditional herbal medicine in Europe called Galega officinalis, or goat's rue. While it can cause side effects in people with kidney problems, it improves blood-sugar control by improving <u>insulin sensitivity</u>, reducing the amount of sugar released by the liver into the blood and increasing glucose absorption.

It is now the fourth most widely prescribed medication in the nation. About 20 million Americans were prescribed the drug in 2020.

What is tantalizing are preliminary findings—based on animal studies and imperfect clinical trials that have not been reproduced—that hint that the drug may help slow aging and increase life expectancy. While the underlying mechanism remains unclear, it may create cellular changes that improve the body's responsiveness to insulin and boost blood vessel health.

Its reputation has grown with a recent barrage of social media attention, including a viral posting by Silicon Valley-based internet entrepreneur and "biohacker" Serge Fague, who described taking two grams of the medication every day.

"Have you heard about metformin?" asked one Twitter influencer. The New York City-based longevity company NOVOS, which has enlisted Harvard's Dr. George Church and other highly esteemed scientists to its advisory board, posted on Instagram: "Metformin: The secret to antiaging?"

Publicity was further boosted last week, when a University of Minnesota team reported that about 6% of metformin patients infected with the SARS CoV-2 virus went on to experience long COVID, compared to 11% of those who were not on the drug. The study is not yet peer-reviewed.



But there is a better drug—the FDA-authorized virus-killing Paxlovid—to reduce the risk of long COVID, said Chin-Hong. "Metformin doesn't make sense, from an infectious disease perspective, to work against long COVID," he said. "It's not a card-carrying antiviral."

Off-label prescribing is legal and common. An estimated 20% of all prescriptions in the U.S. are for off-label use, according to the Agency for Healthcare Research and Quality. Beta-blockers, for instance, are approved to reduce risk of high blood pressure and heart problems but are used off-label to treat anxiety.

But off-label prescriptions may put people at risk of receiving ineffective or even harmful treatment if there is a lack of scientific evidence, said Chin-Hong.

"In tech circles, people use a lot of things off-label—for example, for weight loss," said Chin-Hong. "It's promoted by celebrities on TikTok. But it's always a dangerous enterprise to use something off-label."

Doctors have long prescribed metformin off-label for these conditions:

- Menstrual irregularities in women with polycystic ovary syndrome. In the 1990s, metformin was shown to lower testosterone levels in women with this common hormonal disorder, suggesting that it might help. But at present, there is no clear evidence to support broad metformin use in those patients, according to a 2017 University of Chicago analysis.
- Gestational diabetes mellitus. Metformin is an effective and safe alternative to insulin for women who develop glucose intolerance during pregnancy. It also controls maternal weight gain and reduces the risk of gestational hypertension, according to a 2016 database review by physicians at Peking University First



Hospital.

- Prevention or delayed diabetes. Two decades of evidence support the use of metformin to prevent or delay Type 2 diabetes among higher-risk patients or people with elevated <u>blood sugar</u>, a condition called "prediabetes," concluded a 2018 evaluation of 40 studies by a team at the Los Angeles-based Veterans Administration.
- Weight gain from antipsychotic medicines. Certain patients, especially those who are young and healthy, are less likely to gain weight if they take metformin soon after taking medication for schizophrenia and other psychiatric disorders, according to a 2017 review of published studies by a team at UCLA Medical Center. But it doesn't help after weight gain already has occurred.

Other studies looked at the potential of metformin to:

- Reduce the risk of dementia or stroke. A 2016 analysis by Australian scientists found that cognitive impairment was significantly less common in diabetics who received metformin. In a 2013 study in Taiwan, the drug also offered diabetic patients some protection against stroke. But its use by people without diabetes for the prevention of dementia or stroke was not supported by either of those studies.
- Slow aging. A 2021 analysis of results from several large studies by a team in Canada and Qatar indicates that metformin may induce anti-aging changes in diabetics. It improved the health of diabetic patients in the study while they were alive, although the effect was modest. However it remains controversial as to whether metformin is protective in people who are metabolically normal, the team found.

"There's a lot of interest in it, and additional studies are warranted to see if there are more benefits," said Tan. "But no studies have conclusively



shown a clinically significant benefit for any of those conditions."

"It's a great diabetes drug," she said.

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