

PARSEMUS FOUNDATION

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Metformin drastically reduces COVID hospitalization, study shows

Widely available drug reduced emergency room visits, hospitalization, and death by COVID-19 by more than half if started within 4 days of symptoms

San Francisco, CA August 18, 2022 — The widely available diabetes drug metformin reduced serious outcomes by more than half if started within 4 days of COVID symptoms in a large randomized, double blind controlled trial, the University of Minnesota announced today. The results were published Aug. 18 in the New England Journal of Medicine.

The study was primarily funded by three philanthropic foundations: Parsemus Foundation, Rainwater Charitable Foundation, and Fast Grants.

"This was really intriguing to us early on when we learned that people who take metformin were catching COVID less and being hospitalized less," said Elaine Lissner, founder and trustee of small California nonprofit Parsemus Foundation, which works on low-cost solutions neglected by the pharmaceutical industry. "But you don't know whether it's just coincidence until you start at the beginning, with a rigorous randomized trial."

"When we learned that researchers at the University of Minnesota were already trying to raise funds to test it, we jumped at the opportunity."

A little-known past

Metformin, also known as Glucophage, has an added benefit: a little-known past in the 1950s as an anti-viral called "Fluamine." In more recent research, it also seems to affect mTOR inflammation pathways. Since COVID involves viral inflammation, lead researcher Dr. Carolyn Bramante and team thought the combination of anti-inflammatory plus antiviral action was intriguing enough to put to the test.

The study almost didn't happen, though. At the time, most government and pharmaceutical funds were going to vaccine research, or the search for profitable new drugs.

"We took a chance and gave what we could, enough to get the first few study sites started and generate preliminary data to strengthen the case for other funders," said Linda Brent, executive director of the Parsemus Foundation. "But the study never would have made it if it weren't for the dedicated larger funders who believed in it right away and came on board with critical support."

Three medications studied

For added rigor, the large University of Minnesota study compared three medications that were considered promising at the time—fluvoxamine, an antidepressant that had shown strong results in previous studies; ivermectin, the object of much interest and passion; and metformin — and provided valuable answers, even about the drugs that were not the clear winner.

"You can argue about details, but in the end, this was kind of 'three strikes and you're out' for ivermectin," said Lissner. "But ivermectin deserved this kind of careful study, head-to-head with other medications, to finally get solid answers. You have to give everything a fair test."

"And I think a lot of us were pretty disappointed that the fluvoxamine results were not conclusive. We did learn that the dose the study used, which was a third to half as much as used in previous studies in an attempt to avoid side effects, was not enough to make a significant difference. I don't think the door is closed on fluvoxamine at higher doses, though."

"But in the end," added Lissner, "you have to accept what the science tells you, no matter which you were rooting for. And it's probably better this way. Metformin is an incredibly common drug, taken by millions of people all over the world. There's no stigma like with an antidepressant, and it's a lot easier to take than the other two."

In 2019, metformin was the fourth-most commonly prescribed medication in the United States, with more than 85 million prescriptions written for over 17 million patients. FDA guidelines indicate that it should not be taken by people with advanced kidney disease, and should be taken with food, or in extended-release formulation, to avoid stomach upset. Side effects are minor and include loose stools. Metformin is also considered safe for use in pregnant women.

The study included 1323 participants most at risk of serious outcomes—adults over 30 and with BMI over 25 kg/m2—to get lifesaving results more quickly. Future studies could include lower-risk participants. However, studies of metformin for other indications, such as the national TAME trial by the American Federation for Aging Research, remain unfunded.

"I think there are lessons for all of us in making sure our global clinical trial systems are more robust and ready to jump in on globally critical studies like this in the future," emphasized Lissner. "It shouldn't be little foundations like us funding studies of global importance. In the meantime, I hope all the hard work and late nights pay off, and clinicians around the world take notice: metformin, an exceedingly inexpensive drug they prescribe every day, if given to high-risk people with COVID right away, can reduce serious outcomes by more than half."

Details about the study results were published online August 18 in <u>the New England Journal of Medicine</u> and can be found in <u>the University of Minnesota's COVID-OUT study press release</u>.

About the Parsemus Foundation (San Francisco): The Parsemus Foundation works to create meaningful improvements in human and animal health and welfare by advancing innovative and neglected medical research. The foundation's focus is on supporting proof-of-concept studies and then pursuing press coverage of the results, so that the advances change treatment practice rather than disappearing into the scientific literature. As a small, agile nonprofit organization, the Parsemus Foundation was able to pivot from its regularly funded programs to a new focus on COVID-19 treatment during the pandemic. More information on the Parsemus Foundation and the work presented here can be found at:

https://www.parsemus.org/humanhealth/covid-19/