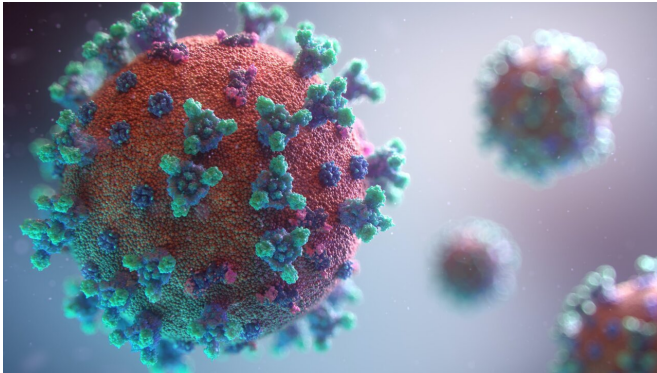


Trial suggests metformin effective at reducing odds of serious outcomes for COVID-19 patients seeking early treatment

18 August 2022, by Kat Dodge



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In work published in the *New England Journal of Medicine*, researchers—led by the University of Minnesota Medical School and School of Public Health—have found that metformin, a commonly prescribed diabetes medication lowers the odds of emergency department visits, hospitalizations, or death due to COVID-19 by over 40 percent—and over 50 percent if prescribed early in onset of symptoms. The study also found no positive effect from treatment with either ivermectin or low-dose fluvoxamine.

"We are pleased to contribute to the body of knowledge around COVID-19 therapies in general, with treatments that are widely available," said Carolyn Bramante, MD, principal investigator of the study and an assistant professor of internal medicine and pediatrics at the U of M Medical School. "Our trial suggests that [metformin](#) may reduce the likelihood of needing to go to the emergency room or be hospitalized for COVID-19."

Bramante noted that this was a secondary outcome of the trial; the primary outcome included

whether someone had low oxygen on a home oxygen monitor, and none of the medications in the trial prevented the primary outcome.

The COVID-OUT trial was the nation's first to study whether [metformin](#), a medication for type 2 diabetes; low-dose fluvoxamine, an antidepressant; and ivermectin, an antiparasitic, or their combinations could serve as possible treatments to prevent ER visits or hospitalization, as well as Long-COVID.

The [study design](#) was simple—patients were randomly assigned to receive one of the three drugs individually, placebo, or a combination of metformin and fluvoxamine or metformin and ivermectin. Although the study was placebo-controlled with exact-matching placebo pills, Dr. Bramante says 83% of volunteers received medications supported by existing data because of the six-arm design. Each participant received 2 types of pills to keep their treatment assignment masked, for 3 to 14 days of treatment. Each volunteer tracked their symptoms, and after 14 days, they completed a survey.

The 1,323 participants in the trial were limited to adults with a [body mass index](#) greater than or equal to 25 kg/m², which qualifies as overweight—for instance, someone who was at least five feet and six inches tall and weighed more than 155 pounds. To qualify for the study, volunteers enrolled within three days after receiving a positive COVID-19 test. It was among the first randomized clinical trials for COVID-19 to include pregnant women.

The study included those who were vaccinated and those who were not. This is the first published trial where the majority of participants were vaccinated.

"Although we know COVID-19 vaccines are highly

effective, we know that some new strains of the virus may evade immunity and vaccines may not be available worldwide. So we felt we should study safe, available and inexpensive outpatient treatment options as soon as possible," said Bramante. "Understanding whether outpatient treatments could ensure more people survive the illness if they contract it and have fewer long-term symptoms is an important piece of the pandemic response."

[10.1016/S2666-7568\(20\)30033-7](https://doi.org/10.1016/S2666-7568(20)30033-7)

Provided by University of Minnesota Medical School

The clinical trial launched in January 2021 after U of M Medical School researchers identified, through computer modeling and [observational studies](#), that outpatient metformin use appeared to decrease the likelihood of mortality from, or being hospitalized for COVID-19. Their research, in partnership with UnitedHealth Group, was published in the *Journal of Medical Virology* and in *The Lancet Healthy Longevity*. Test-tube studies also found that metformin inhibited the COVID-19 virus in lab settings. These findings, along with additional prospective studies supporting the use of higher-dose fluvoxamine and ivermectin, provided the evidence to include all three medications as well as combination arms.

"Observational studies and in vitro experiments cannot be conclusive but do contribute to bodies of evidence," said Bramante, who is also an internist and pediatrician with M Health Fairview. "To complete this study, we enrolled volunteers nationwide through six institutions in the U.S., including in Minneapolis."

More information: Carolyn T. Bramante et al, Randomized Trial of Metformin, Ivermectin, and Fluvoxamine for Covid-19, *New England Journal of Medicine* (2022). [DOI: 10.1056/NEJMoa2201662](https://doi.org/10.1056/NEJMoa2201662)

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