

Study: Using a diabetes medication after testing positive for SARS-CoV-2 reduces risk of developing long COVID by 40%

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Taking a two-week course of metformin, a safe and affordable diabetes medication after testing positive for SARS-CoV-2 leads to 40% fewer long COVID diagnoses over the following 10 months, compared to individuals taking a placebo, finds a new study published in *The Lancet Infectious Diseases* journal.

The long-term symptoms some people experience after SARS-CoV-2 infection, known as long COVID, are an emerging chronic illness potentially affecting millions of people around the world. Currently there are no proven treatments or ways to prevent long COVID, other than reducing the risk of infection in the first place.

This is the first phase 3 randomized controlled trial of a treatment for patients in the community that shows a medication can reduce the risk of long COVID when taken after testing positive for SARS-CoV-2.

"Long COVID is a significant public health emergency that may have lasting physical health, mental health, and economic impacts, especially in socioeconomically marginalized groups. There is an urgent need to find potential treatments and ways to prevent this disease. Our study showed that [metformin](#), a medication that is safe, low-cost, and widely available, substantially reduces the risk of being diagnosed with long COVID if taken when first infected with the coronavirus. This trial does not indicate whether metformin would be effective as a treatment for those who already have long COVID," says first author Dr. Carolyn Bramante, University of Minnesota Medical School, U.S..

Participants in the trial were not hospitalized, were at a higher risk of severe COVID-19 (overweight or obesity), over the age of 30, and had tested positive for SARS-CoV-2 within the last three days but had no known previous SARS-CoV-2 infection. Trial recruitment was open from December 2020 to January 2022 with 1,126 patients given either metformin or an identical placebo pill after testing positive for SARS-

CoV-2 during that time. Participants were followed up for 10 months with data gathered by self-report questionnaire every 30 days.

Metformin prevented over 40% of cases of long COVID in the trial with 6.3% (35/564) of participants given metformin reporting a long COVID diagnosis within 10 months of follow up, compared to 10.4% (58/562) of those receiving an identical placebo.

These findings reflect previously published results from this trial which found metformin prevented over 40% of emergency department visits, hospitalizations, and deaths due to COVID within two weeks of starting the treatment, compared to a placebo.

Other arms of the trial looked at ivermectin and fluvoxamine and found that neither prevented long COVID.

"Previous studies have found that metformin stops the SARS-CoV-2 virus from replicating in the lab, which is consistent with predictions from our mathematical modeling of viral replication, so that might be what is causing the reduction in both severe COVID-19 and Long COVID diagnoses seen in this trial," says co-author David Odde, University of Minnesota biomedical engineer.

The authors acknowledge some limitations to the study, including that the trial excluded those with a BMI under 25 and those younger than 30 years, and therefore it is unknown if these findings could be generalized to those populations.

They also caution that when the long COVID assessment was added to the trial, little was known about the best assessment tool for long COVID occurrence in clinical trial participants, however they believe the use of a long COVID diagnosis from a medical provider, as well as the long duration of follow-up, would address some of the issues around the

changing nature of this disease definition.

Writing in a Linked Comment, Dr. Jeremy Faust, Harvard Medical School, U.S., who was not involved in this research, said, "If confirmed, the findings from the study by Bramante and colleagues are profound and potentially landmark [...] this is the first high-quality evidence from a randomized controlled trial to show that the incidence of long COVID can be reduced by a medical intervention, metformin—an inexpensive treatment with which clinicians have ample experience."

More information: Outpatient treatment of COVID-19 and incidence of post-COVID-19 condition over 10 months (COVID-OUT): a multicentre, randomised, quadruple-blind, parallel-group, phase 3 trial, *The Lancet Infectious Diseases* (2023). DOI: 10.1016/S1473-3099(23)00299-2 , [www.thelancet.com/journals/lan ... \(23\)00299-2/fulltext](http://www.thelancet.com/journals/lan.../23/00299-2/fulltext)

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