

# Diabetes drug may decrease COVID-19 death risk in women

A recent study found an association between metformin and a significantly reduced mortality risk in women with type 2 diabetes or obesity who were hospitalized with COVID-19.

People with [certain medical conditions](#), including obesity and type 2 diabetes, have an increased risk of severe COVID-19, and may require hospitalization, intensive care, or mechanical ventilation. The risk of death from the illness is also higher for these groups.

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[Visceral fat](#) accumulating around organs may lead to insulin resistance, increasing the risk of developing type 2 diabetes. Meanwhile, visceral fat cells secrete inflammatory substances, such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- $\alpha$ ), and D-dimer, which may be associated with severe COVID-19.

People with type 2 diabetes also have increased levels of TNF- $\alpha$ , which contributes to insulin resistance. In addition, the anti-inflammatory cytokine IL-10 is present in lower levels in people with obesity and type 2 diabetes.

# Anti-inflammatory effects

Metformin, a safe, effective, relatively inexpensive drug, elevates anti-inflammatory IL-10 levels while decreasing the inflammatory markers TNF- $\alpha$  and IL-6 in people with or without diabetes.

Due to metformin's anti-inflammatory effects and early reports of decreased COVID-19 mortality rates in people taking the drug, researchers at the University of Minnesota Medical School, in Minneapolis, and UnitedHealth Group (UHG), in Miami, FL, decided to investigate whether metformin decreased COVID-19 death risk — and whether any reduction would be sex-specific.

They refer, in their study paper, to previous findings that metformin reduced inflammation to a greater extent in women than in men.

**“While effective therapies to mitigate the harm of the SARS-CoV-2 virus are being developed, it is important that we also look to and evaluate commonly used medications with good safety profiles for their potential to combat the virus,” stated Dr. Deneen Vojta, co-senior study author and executive vice president of research and development at UHG.**

The researchers conducted a retrospective analysis of claims data from January 1 through June 7, 2020, from UHG's Clinical Discovery Claims Database. This contains enrollment records, medical claims, laboratory results, and pharmacy claims for individuals of diverse ages, races, and ethnicities who had been admitted to hospitals with COVID-19 throughout the 50 states.

People included in the study were 18 years or older, had a diagnosis of obesity or type 2 diabetes, and had at least 6 months of continuous enrollment in UHG during 2019. Each had also been admitted to a hospital for COVID-19.

In total, the study analyzed the claims data of 6,256 individuals, with 3,923 in the non-metformin group and 2,333 in the metformin group.

In the non-metformin group, the average age was 76 years, approximately 55% were female, and 95% had type 2 diabetes. In the metformin group, the average age was 73 years, approximately 48% were female, and 99% had type 2 diabetes.

**In all, 20.2% of those in the non-metformin group died of COVID-19 during hospitalization, compared with 16.9% of the metformin group.**

The study did not show that metformin use significantly decreased COVID-19-related mortality in the overall group of men and women. However, the subgroup analysis of data by sex demonstrated a significant association between metformin use and decreased mortality in women.

**Among people with type 2 diabetes or obesity, the study found a 21–24% reduction in mortality among women who had filled a metformin prescription before hospitalization, compared with women who had not.**

There are certain limitations to the study. For instance, retrospective analyses are often affected by biases and unmeasured confounders. Also, claims data do not provide information about adherence to metformin treatment, account for patients who paid cash for metformin, or differentiate among people with different classes of obesity.

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# Wide-reaching consequences

In the U.S., more than 42% of women have obesity, and [16.2 million](#) women have diabetes. The use of a medication that is relatively inexpensive, is readily available, and has a good safety profile might significantly reduce COVID-19-related mortality in this at-risk population.

“Observational studies like this cannot be conclusive but contribute to growing bodies of evidence. Seeing a bigger association with protection in women over men may point toward inflammation reduction as a key way that metformin reduces risk from COVID-19.”

– Principal investigator Dr. Carolyn Bramante

Dr. Bramante and Dr. Christopher Tignanelli, a co-senior author of the study, plan to conduct a multi-site, prospective, randomized pilot study with Dr. Ken Cohen, executive director of clinical research at UHG Research and Development, to understand how metformin may decrease mortality, plus the optimal duration and timing of the treatment.

This upcoming study may provide the data needed to discern the true impact of metformin on COVID-19-related mortality.

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