Researchers show that Paxlovid remains highly effective on omicron variants

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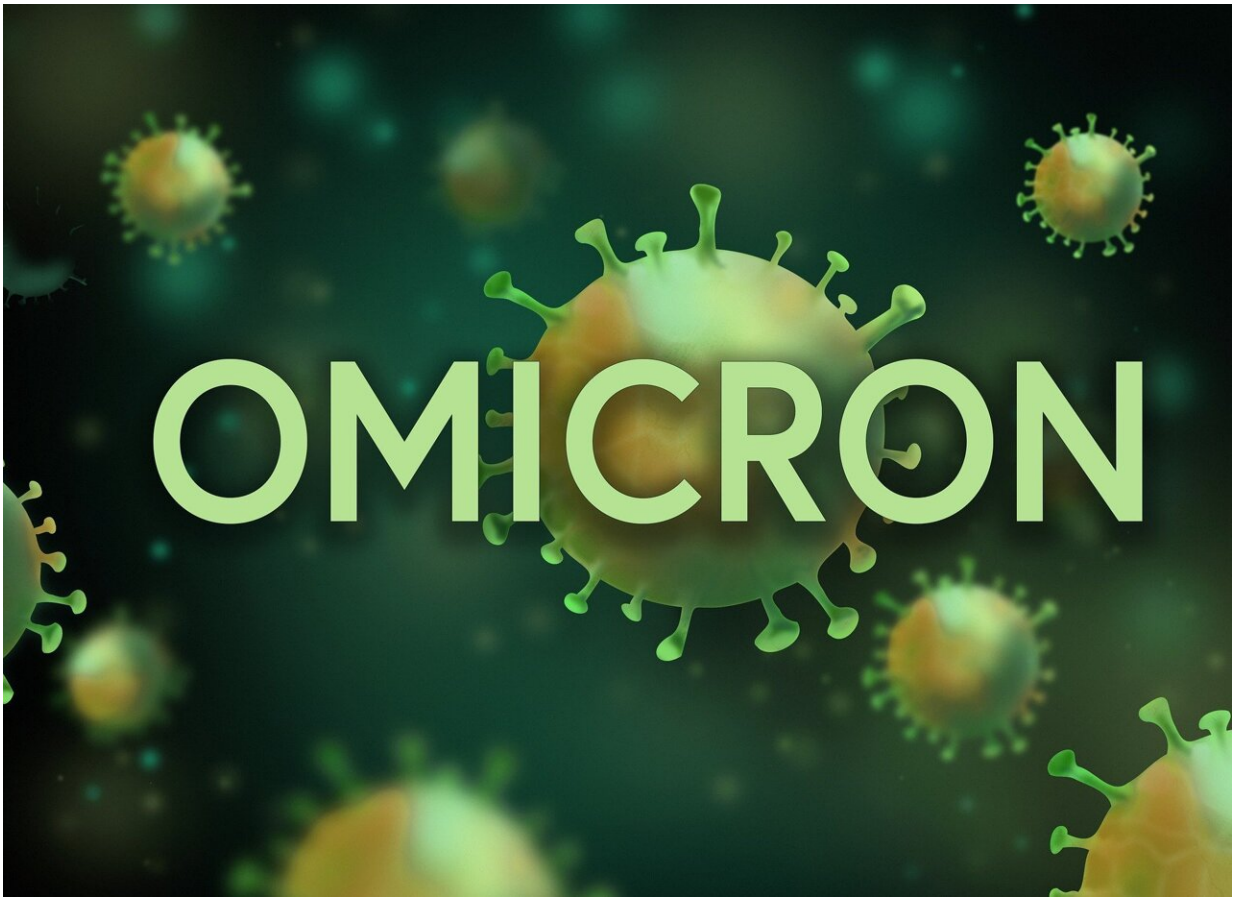

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Researchers have conducted one of the first studies to examine the effectiveness of nirmatrelvir-ritonavir (Paxlovid) in non-hospitalized

patients during an omicron period of the COVID-19 pandemic that includes BA.4 and BA.5 subvariants.

Though many Coloradans are proceeding as though the COVID-19 pandemic is over, the virus continues to circulate, evolve and have an impact—especially for older adults and those with underlying medical conditions. Furthermore, because of the evolution of variants, doctors have fewer treatment options.

"We are really struggling with maintaining effective therapeutic options for high-risk patients with COVID-19," says Adit Ginde, MD, professor of emergency medicine at the University of Colorado School of Medicine. "Particularly because the monoclonal antibody treatments we had been using and relying on for the past year-and-a-half are no longer effective against recent omicron subvariants because the virus has changed."

Ginde is also principal investigator of the Monoclonal Antibody (mAb) Colorado project of the Colorado Clinical and Translational Sciences Institute (CCTSI), supported by the National Center for Advancing Translational Sciences of the National Institutes of Health.

Right now, the only two effective antiviral treatment options are Paxlovid and Remdesivir. So, Ginde and a team of researchers swung into action to determine if Paxlovid is effective against omicron variants B.4 and B.5. Ginde is also an emergency medicine physician at the UCHealth University of Colorado Hospital.

"This study was one of the first to strongly suggest a benefit for the antiviral medication, nirmatrelvir-ritonavir, also known as Paxlovid, to prevent hospitalization and death for patients infected with recent omicron SARS-CoV-2 variants," said Neil Aggarwal, MD, MHSc, lead author of the study just published in *The Lancet Infectious Diseases* and

associate professor of medicine in the University of Colorado School of Medicine. Aggarwal is also a critical care and pulmonary physician at UCHealth University of Colorado Hospital.

The study is what is called "observational," which means researchers examined the data of patients who had one or more risk factors for severe disease, hospitalization or death—and who either did or did not receive Paxlovid. They evaluated the rate of hospitalization or death and found that the use of Paxlovid significantly reduced rates of hospitalization and death.

Ginde explained that an observational study design using real-world data is meant to imitate a clinical trial. "We used data provided to us from the UCHealth system—a statewide health system and the largest one in Colorado," Ginde said. This particular study involved 28,000 patients.

Aggarwal explained that Paxlovid was effective in preventing hospitalization among almost all important subgroups of outpatients that were assessed and who qualify for its use under the Emergency Use Authorization (EUA), including those vaccinated. "As a physician who can treat patients in the outpatient setting, I would be very comfortable using Paxlovid as a first-line treatment for adults acutely infected with COVID during the current omicron phase, vaccinated or not, provided there are no contraindications to its use," Aggarwal said.

This study is noteworthy as it is one of the first to examine the effectiveness of Paxlovid in non-hospitalized patients during an omicron period of the COVID-19 pandemic that includes BA.4/BA.5 subvariants. Beyond its effectiveness in keeping patients out of the hospital, Paxlovid was associated with lower rate of post-treatment emergency department visits, that suggests a lower likelihood of more severe rebound symptoms, although the study could not evaluate effect on milder rebound symptoms.

Real world evidence is particularly important for doctors who must make treatment recommendations for their patients. "We provide clinicians with nearly real-time data to help support decision making with robust systematic data," Ginde said. "If we can confirm benefits of a therapy, clinicians can be confident in prescribing a treatment, and patients can feel comfortable receiving treatment. If we find agents are losing effectiveness, we need to know that as well and change the treatments offered to patients."

Real world data platforms require multiple collaborations that leverage many components of an academic medical center. Researchers with expertise in informatics, biostatistics, dissemination and implementation, clinical trials and bioethics are all critical.

"It takes a while to build this capability. But once you have the infrastructure, you can use it for COVID and other conditions," Ginde said. "The FDA has also put out guidance to be able to use real world evidence for regulatory decision-making."

Ginde and his team plan to publish other real-world study results of the effectiveness of Remdesivir against omicron subvariants and an update on Paxlovid effectiveness for more recent omicron subvariants, including XBB.1.5 and BQ.1.

He said, "The laboratory data suggest that Paxlovid is still effective at neutralizing the virus in recent omicron subvariants. However, we plan to evaluate ongoing clinical effectiveness in patients through our upcoming analyses."

More information: Real-world use of nirmatrelvir-ritonavir in COVID-19 outpatients during the era of Omicron variants including BA.4/BA.5: A retrospective cohort study, *The Lancet Infectious Diseases* (2023).

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