People With Substance Use Disorders May be at Higher Risk for SARS-CoV-2 Breakthrough Infections

Co-occurring health disorders appear to contribute to increased risk, NIH study suggests.

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An analysis of electronic health records of nearly 580,000 fully vaccinated people in the United States found that the risk of SARS-CoV-2 breakthrough infection among vaccinated patients with substance use disorders was low overall, but higher than the risk among vaccinated people without substance use disorders. The study was published [October 5] in World Psychiatry and led by researchers at the National Institute on Drug Abuse (NIDA), part of the National Institutes of Health, and Case Western Reserve University in Cleveland, Ohio.

The study also found that co-occurring health conditions and adverse socioeconomic determinants of health, which are more common in people with substance use disorders, appear to be largely responsible for the increased risk of SARS-CoV-2 breakthrough infections. People with substance use disorders — such as alcohol, cannabis, cocaine, opioid, and tobacco use disorders — also had elevated rates of severe outcomes, including hospitalization and death, following breakthrough infections.

“First and foremost, vaccination is highly effective for people with substance use disorders, and the overall risk of COVID-19 among vaccinated people with substance use disorders is very low.” said NIDA Director Nora D. Volkow, MD, and one of the lead authors on the study. "We must continue to encourage and facilitate COVID-19 vaccination among people with substance use disorders, while also acknowledging that even after vaccination, this group is at an increased risk and should continue to take protective measures against COVID-19.”

Analyses conducted in the early stages of the pandemic found that people with substance use disorders were at increased risk of SARS-CoV-2 infection, and were more likely to have severe disease requiring hospitalization or resulting in death. This was particularly true for Black people with a substance use disorder. Since then, vaccines became widely available for people ages 12 and older that greatly reduce the risk of COVID-19 and severe disease.

However, clinical trials evaluating the effectiveness of these vaccines did not specifically include people with substance use disorders. Because many people with substance use disorders are

immunocompromised due to drug use and co-occurring diseases, researchers hypothesized that this population might be at increased risk of breakthrough infections after getting vaccinated.

To investigate these questions, researchers analyzed electronic health records from nearly 580,000 people in the United States with and without substance use disorders who were fully vaccinated against COVID-19 between December 1, 2020, and August 14, 2021, and who had not been infected with SARS-CoV-2 before the vaccination. The status of infection was based on the ICD-10 diagnosis code of COVID-19 or lab-test confirmed presence of SARS-CoV-2 and related RNA.

They determined the proportion of people in each group who contracted SARS-CoV-2 at least 14 days after their final vaccination. This analysis was repeated after matching patients with and without substance use disorders for demographic characteristics; socioeconomic factors that influence health, such as housing or employment instability; and lifetime physical illnesses, such as high blood pressure, heart disease, obesity, or diabetes. The team also examined if fully vaccinated people with breakthrough infections had a different risk for hospitalization and death compared with matched people without breakthrough infections.

The researchers found that the risk of breakthrough infections was significantly higher in people with substance use disorders than in those without: 7% of vaccinated people with substance use disorders had a breakthrough infection during the study, compared with 3.6% of vaccinated people without substance use disorders. The risk of breakthrough infection varied slightly among people with different substance use disorders, ranging from 6.8% for people with tobacco use disorder to 7.8% for those with cannabis use disorder.

The study suggests that the increased risk of breakthrough infections in people with substance use disorders was primarily due to co-occurring diseases and adverse socioeconomic characteristics. When these factors were controlled for, people with most substance use disorders no longer had elevated rates of breakthrough infections. The only exception were people with cannabis use disorder, who still were 55% more likely to experience breakthrough infections as people without substance use disorders, even though patients with cannabis use disorder tended to be younger and had fewer co-occurring health conditions than those with other substance use disorders. The authors hypothesized that factors such as adverse effects of cannabis on lung and immune function may have contributed to the higher risk for breakthrough infection in this group.

In addition, breakthrough infections were found to greatly increase the risk of severe outcomes, including hospitalization and death, regardless of the presence of substance use disorders. Among the people with substance use disorders, 22.5% of those with a breakthrough infection required hospitalization, and 1.7% died during the study period, compared with 1.6% and 0.5%, respectively, among people with substance use disorders but no breakthrough infection. Additionally, the risk of severe outcomes after breakthrough infection was higher in patients with substance use disorders than in those without substance use disorders.

“From previous studies, we knew that people with substance use disorders may be particularly vulnerable to COVID-19 and severe related outcomes. These results emphasize that, while the

vaccine is essential and effective, some of these same risk factors still apply to breakthrough infections," said Rong Xu, Ph.D., professor in the Center for Artificial Intelligence in Drug Discovery at Case Western Reserve University. "It is important to continuously evaluate the effectiveness of COVID-19 vaccines and the long-term effects of COVID-19, especially among people with substance use disorders."

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