Are People With HIV at Greater Risk for COVID-19 Breakthrough?

The good news is that only 4% of HIV-positive people experienced COVID breakthrough after vaccination.

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People living with HIV appear to be more likely to get breakthrough COVID-19 after vaccination, according to a study published in JAMA Network Open. A follow-up analysis found that people with HIV also had a substantially higher risk of severe breakthrough illness. These findings suggest that HIV-positive people might benefit from extra vaccine doses even if they are not considered moderately or severely immunocompromised.

“These findings should alert all people with HIV to their greater risk of COVID-19 breakthrough and can inform official recommendations about COVID-19 vaccination for people with HIV,” senior study author Keri Althoff, PhD, MPH, of Johns Hopkins Bloomberg School of Public Health, said in a press release.

While most people with well-controlled HIV respond well to COVID vaccines, those who are not on antiretroviral treatment and those who have a detectable viral load or a low CD4 T-cell count may not fare as well. This is another good reason to start antiretroviral therapy promptly. But even people on effective treatment may have subtle immune impairment or persistent immune activation that could affect their response to vaccines and susceptibility to SARS-CoV-2, the coronavirus that causes COVID-19.

The Centers for Disease Control and Prevention (CDC) recommends two initial doses of the Pfizer-BioNTech or Moderna vaccine or a single initial dose of the Johnson & Johnson vaccine, followed by a Pfizer-BioNTech or Moderna booster. People ages 50 and older are eligible for a second booster four months after their last shot. For moderately or severely immunocompromised people ages 12 and up, the primary series now consists of three Pfizer-BioNTech or Moderna doses or two J&J doses to be followed by two boosters. This group includes organ transplant recipients, people receiving cancer treatment and people with advanced or untreated HIV.

Althoff and coinvestigators with the Corona Infectious Virus Epidemiology Team, part of the long-running NA-ACCORD cohort study, compared breakthrough COVID-19 in people with and without HIV.

The researchers looked at electronic health records from four prospective cohorts of people receiving care at integrated health systems and academic health centers: Kaiser Permanente Mid-Atlantic States, Kaiser Permanente Northern California, the University of North Carolina Chapel Hill HIV Clinic and the U.S. Veterans Affairs Healthcare System.

HIV-positive adults who were fully vaccinated against COVID prior to June 30, 2021, were matched with three fully vaccinated HIV-negative individuals of the same age, sex, race/ethnicity and vaccination date. For this study, "fully vaccinated" was defined as two weeks after completion of the standard initial vaccine regimen, although nearly half also received a third primary dose or a booster.

The analysis included 33,029 HIV-positive and 80,965 HIV-negative participants. Most (92%) were men, 70% were age 55 or older, 41% were Black, 38% were white and 13% were Latino. More than 90% of people with HIV were on treatment with an undetectable viral load, and the median CD4 count was high (636), but a quarter had a prior AIDS diagnosis.

A quarter of participants received two doses of the Pfizer-BioNTech vaccine, 26% received three Pfizer-BioNTech shots, 22% received two Moderna doses and 20% received three Moderna shots. Only about 7% received one or two J&J doses. People with HIV were more likely to have received an additional dose and less likely to have gotten the J&J vaccine. About 6% had already had COVID before they were fully vaccinated, with a slightly higher rate in the HIV-positive group (5.7% versus 6.9%).

Follow-up continued through December 31, 2021. A breakthrough was defined as the first SARS-CoV-2 infection (confirmed by a PCR or antigen test) or COVID diagnosis after full vaccination.

The overall cumulative risk of COVID breakthrough nine months after full vaccination was low (3.8%), as seen in several other general population studies. The risk of breakthrough was greatest with the J&J vaccine (5.7%), followed by the Pfizer-BioNTech vaccine (4.4%) and the Moderna vaccine (2.8%).

But HIV-positive people had a higher breakthrough rate compared with their HIV-negative peers: 4.4% versus 3.5%, representing a 28% risk increase for people with HIV. In the HIV-positive and HIV-negative groups, the respective breakthrough rates were 55 versus 43 cases per 1,000 person-years. People with HIV also had higher breakthrough rates for each vaccine type.

Among people with HIV, younger age and a prior history of COVID-19 were associated with increased breakthrough, which might reflect greater SARS-CoV-2 exposure. Not surprisingly, people who had received an additional primary or booster dose were less likely to experience a breakthrough. Although there was no association between the likelihood of breakthrough and HIV viral load suppression, having a high CD4 count (500 or above) was associated with fewer breakthroughs.

A follow-up analysis, available as a preprint, found that among 1,241 HIV-positive and 2,408 HIV-

negative people with COVID breakthrough, the risk of severe illness (defined as hospitalization within 28 days after a breakthrough) was low and comparable in the two groups, at 6.7% and 7.3%, respectively. However, among HIV-positive people with a CD4 count below 350 (indicating moderate to severe immune suppression), the risk of severe breakthrough illness was 59% higher.

If you are interested in understanding breakthrough risk among people with versus without HIV, checkout our follow-up analysis on *severity* of breakthrough (https://t.co/ecqw1VVwLa) spearheaded by @Raynellang!

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— Sally B. Coburn, PhD (@SallyBCoburn1) June 7, 2022

“In this study, COVID-19 vaccination, especially with an additional dose, was effective against infection with SARS-CoV-2 strains circulating through December 31, 2021,” the researchers concluded. But this was before the height of the first omicron wave, which started late that year. Omicron variants are better at evading immunity from vaccination or prior infection, leading to higher breakthrough rates.

The higher risk of breakthrough COVID seen in this study led the researchers to suggest that the recommendation for an additional primary vaccine dose should be extended to all people with HIV, even if they are not moderately or severely immunocompromised.

“Policymakers who establish the guidelines should consider the benefits and risks of an additional dose of vaccine in the primary series not only for those with severe or untreated HIV but also include those with moderate immune suppression or even all persons with HIV,” said lead study author Sally Coburn, PhD, MPH.

Click here to read the study abstract.

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