

Risk of Breakthrough COVID-19 Infections and Disease in Vaccinated People with HIV

In the clinical trials that led to the approval of effective COVID-19 vaccines, there were relatively few participants with HIV (in some cases, they were only included after activists protested their exclusion). But since COVID-19 vaccines became available, multiple studies have demonstrated that these vaccines are also highly effective in people with HIV.

In general, people with HIV whose viral load is suppressed by antiretroviral therapy (ART) have a similar response to COVID-19 vaccines as their HIV-negative counterparts. After vaccination, both antibody and T cell responses against the SARS-CoV-2 virus are generated at equivalent levels.

The exceptions are the relatively small proportion of people with HIV whose CD4 T cell counts remain below the normal range (e.g., <200) despite ART, and those with detectable HIV viral loads who are not receiving HIV treatment. In these groups, immune responses induced by COVID-19 vaccination have been reported to be lower, on average.

Two recent studies have assessed the risk of breakthrough COVID-19 infection and severe illness in large numbers of vaccinated people with HIV. The term “breakthrough” refers to the SARS-CoV-2 virus breaking through the immune defenses created by vaccination. Importantly, the immune defenses can still greatly limit the damage caused by the virus, which is why vaccination is associated with a massively reduced risk of severe illness and death from COVID-19.

The first study reviewed the health records of 33,029 people with HIV and 80,965 people without HIV to assess the frequency of breakthrough infections, which were defined based on laboratory evidence of SARS-CoV-2 infection or a COVID-19 diagnosis after full vaccination.¹

In the overall population, the number of people experiencing breakthrough infections during the nine months after vaccination was low (approximately 3.8%).

However, when the records of people with and without HIV were compared, the proportion of people with HIV with breakthrough infections was found to be higher: 4.4% compared with 3.5% in the HIV-negative group. This equates to an approximately 28% higher risk of breakthrough COVID-19 infection during the nine months after vaccination.

People with CD4 counts above 500 had an approximately 34% lower risk of breakthrough infection compared to people with counts less than 200. Perhaps surprisingly, people with unsuppressed viral load at the time of full vaccination were not found to be at a statistically high risk of breakthrough infection; however, they represented a small proportion of the population analyzed (<10%) and no information is provided about their levels of viral load.

The same group of researchers conducted a second study, which assessed the risk of severe COVID-19 illness among fully vaccinated people with HIV.² Severe COVID-19 illness was defined as hospitalization within 28 days after a breakthrough SARS-CoV-2 infection, with COVID-19 the primary or secondary diagnosis.

The study compared outcomes among 1,241 people with HIV and 2,408 people without HIV who had breakthrough COVID-19 infections after full vaccination. Overall, the proportion of people who experienced severe illness was low and the difference between the groups was not significant: 7.3% of people with HIV and 6.7% of those without.

Notably, the risk of severe illness was 59% higher among people with HIV whose CD4 T cell counts were below 350 compared with people without HIV. Additional factors associated with a higher rate of severe illness in people with HIV included female sex, being older, and having a cancer diagnosis. Previous COVID-19 was associated with a lower risk.

Of the people who required hospitalization, 10% required mechanical ventilation and 8% died, but HIV status did not influence the risk of these outcomes.

The authors of these two studies point out that the U.S. Centers for Disease Control (CDC) currently recommends additional COVID-19 vaccine doses only for people with “advanced and untreated HIV” (advanced defined as a CD4 T cell count <200).³ In their first paper in the scientific journal *JAMA Network Open* they write:

“Our findings indicate all PWH may benefit from being included in this recommendation, as the risk of breakthrough was higher in PWH than PWOH [people without HIV] regardless of CD4 count (reflecting advanced disease) or HIV viral suppression (reflecting treatment).”

In their second paper, also published by *JAMA Network Open*, they add:

“In addition to PWH with severe immune suppression, PWH with moderate immune suppression may benefit from being included in the CDC’s recommendations for those with advanced and untreated HIV. Clinicians should continue to promote risk-reduction measures among PWH. The potentially increased risk of severe COVID-19 breakthrough illness in PWH with moderate and severe immune suppression merits ongoing surveillance to inform vaccine recommendations as the pandemic persists, immunity to primary vaccine series and booster doses wane, and new variants emerge.”

The latest CDC COVID-19 vaccination recommendations for immunocompromised people, including those with advanced and untreated HIV, are for an additional COVID-19 primary immunization for recipients of the Pfizer/BioNTech, Moderna, or Johnson & Johnson vaccines followed by boosters with the new bivalent vaccines that include proteins from the Omicron SARS-CoV-2 variant (see box).

WHAT ARE BIVALENT COVID-19 VACCINES?

Bivalent means the vaccines include two components derived from the virus SARS-CoV-2. One component is the outer spike protein from the original SARS-CoV-2, which started the COVID-19 pandemic. The second component is the same protein from the Omicron variant of SARS-CoV-2, which emerged much more recently. As viruses replicate, they mutate, and mutations can change the protein structure of the virus in ways that lessen the efficacy of vaccine-induced immune responses. The bivalent vaccines aim to create or boost immune responses to both old and new SARS-CoV-2 variants. Bivalent vaccines are now available in the U.S. from two manufacturers, Moderna and Pfizer/BioNTech.

These new study results may suggest that the current CDC COVID-19 vaccination recommendations for immunocompromised people should be modified to include either everyone with HIV or those with HIV and moderate immune suppression (CD4 T cell counts <350). However, the CDC Advisory Committee on Immunization Practices (ACIP) is not currently considering changes to the recommendations.

At a minimum, the new findings indicate that people with HIV should discuss the best approach to COVID-19 vaccination for their individual circumstances with their providers and be diligent about receiving COVID-19 vaccine boosters when eligible.

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¹ Coburn SB, Humes E, Lang R, et al. Analysis of postvaccination breakthrough COVID-19 infections among adults with HIV in the United States. *JAMA Netw Open*. 2022 Jun 1;5(6):e2215934.

² Lang R, Humes E, Coburn SB, et al. Analysis of severe illness after postvaccination COVID-19 breakthrough among adults with and without HIV in the US. *JAMA Netw Open*. 2022 Oct 13;5(10):e2236397.

³ Centers for Disease Control and Prevention (U.S.). COVID-19 vaccines for moderately to severely immunocompromised people. Updated Nov 3, 2022. <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html>