How Well Do Mpox Vaccines Work?

The Jynneos monkeypox vaccine is highly effective, but two doses are needed for optimal protection.

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New clusters of mpox (formerly known as monkeypox) cases have been reported as summer arrives, leading health officials to reemphasize that gay and bisexual men, transgender people and others in their sexual networks should get vaccinated—or receive their second shot if they've had only one.

"Without renewed prevention efforts, especially vaccination, we are definitely at risk of a resurgence—in fact, a substantial risk of resurgence—of mpox," Demetre Daskalakis, MD, MPH, the White House national mpox response deputy coordinator, said during a May 18 media briefing.

Mpox cases have declined dramatically since the outbreak peaked late last summer, likely due to a combination of behavior change, vaccination and natural immunity after infection. In late April, the Centers for Disease Control and Prevention (CDC) reported the first week with zero new cases. To date, the CDC has identified 30,422 mpox cases in the United States and more than 87,500 cases worldwide.

But cases have started to rise in recent months. As previously reported, French health officials identified a cluster of 17 mpox cases in the Centre-Val de Loire region in March, but this was not followed by a further rise in April, suggesting that the outbreak is contained. In Chicago, the health department has identified 31 cases since late April—averaging about seven cases per week—but only one case was reported for the week ending May 27. And in the United Kingdom, 20 cases have been reported this year, half of them in London in May.

Across these clusters, most cases continue to occur among gay, bisexual and other men who have sex with men. A majority of the new cases were among people who had been fully or partially vaccinated, raising questions about how well mpox vaccines work and for how long.

Mpox Vaccine Effectiveness

Mpox is related to smallpox, and vaccines developed to prevent smallpox also protect against mpox. The Bavarian Nordic MVA-BN vaccine, branded as Jynneos in the United States and Imvanex in Europe, was widely deployed during the 2022 outbreak, first as a subcutaneous injection and later—in an effort to stretch the limited supply—as an intradermal injection using one

fifth of the original dose. Both administration methods require two shots given about four weeks apart.

It was previously assumed that Jynneos and older smallpox vaccines protect against mpox based on animal studies and laboratory analysis of antibody levels. But now, a growing body of evidence shows how well they work in the real world.

At this year's Conference on Retroviruses and Opportunistic Infections (CROI), researchers reported that first-, second- and third-generation smallpox vaccines provide protection against mpox infection. Among participants in the French DoxyVAC trial, which evaluated doxycycline post-exposure prophylaxis and a vaccine to prevent gonorrhea, a single Jynneos dose was found to be 99% effective.

Another study presented at CROI—a retrospective analysis of U.S. military personnel who had received older vaccines to prevent smallpox—found that the first-generation Dryvax vaccine was 66% effective at preventing mpox infection, while the second-generation ACAM2000 vaccine was 72% effective. Neither of these replication-competent live virus vaccines were used in last year's mpox vaccine campaign. Jynneos contains a weakened vaccinia virus that can't replicate, so it's safe for people living with HIV and immunocompromised people.

In an analysis published in The Lancet Infectious Diseases, Marta Bertran, of the U.K. Health Security Agency, and colleagues assessed the effectiveness of a first Jynneos dose for preventing mpox in at-risk men who have sex with men. This study included 363 men who developed mpox symptoms between July 4 and October 9, 2022. Of these, 323 were unvaccinated, 32 cases occurred within 13 days after vaccination—when immunity would still be incomplete—and just eight occurred two weeks or more after the first dose. The estimated vaccine effectiveness at 14 days was 78%, leading the study authors to conclude that a single dose was "highly protective."

But other studies have not seen such high vaccine effectiveness, especially after only one dose.

In a study described in Morbidity and Mortality Weekly Report, researchers with the CDC and several city and state health departments conducted a case-control comparison of sexually active gay and bi men and transgender individuals in 12 jurisdictions. Between August 19, 2022, and March 31, 2023, a total of 309 people with confirmed or probable mpox were matched to 608 people seen at sexual health and HIV clinics who did not have a mpox diagnosis. Mpox exposure, diagnosis, vaccination status and the presence of HIV and other immunocompromising conditions were self-reported.

People with mpox were more likely to be Black or Latino, more likely to be living with HIV or other immunocompromising conditions, more likely to report homelessness and transactional sex and more likely to have had recent close contact with person known to have mpox. Nearly a quarter of study participants (23%) were fully vaccinated with two Jynneos doses, 32% were partially vaccinated with a single dose and 45% were unvaccinated.

After adjusting for age, race/ethnicity, immunocompromised status and close contacts, vaccine effectiveness was 75% for one dose and 86% for two doses. According to the CDC, the vaccine provided “substantial” and “comparable” protection regardless of administration method or immunocompromised status.

However, there were some notable differences. Vaccine effectiveness was 89% for people who received two subcutaneous doses, 80% for those who got two intradermal doses and 87% for those who received one of each. While vaccine effectiveness was 72% with one dose and 88% with two doses for people with a healthy immune system, this fell to 51% and 70%, respectively, for immunocompromised people. Although these estimates did not differ statistically, the study authors acknowledged that immunocompromised people might have “a less robust response” to the vaccine.

In a second study described in the same edition, Eli Rosenberg, PhD, of the New York State Department of Health, and colleagues compared 252 men diagnosed with mpox in New York state, excluding New York City, between July 24 and October 31, 2022, and 255 gay men and transgender people who were diagnosed with rectal gonorrhea or primary syphilis but not mpox. This method better controls for confounding factors because both groups were at risk for sexually transmitted infections (STIs) and sought testing. Other studies that include people at lower risk for mpox could inflate estimates of vaccine effectiveness.

Of the 252 men with mpox, 10 had received a single Jynneos dose less than two weeks prior to diagnosis, 10 had received one dose at least 14 days prior and only two were fully vaccinated. Among the 255 people in the control group, 23 had received one dose and 19 had received two doses 14 days or more prior to their mpox or STI diagnosis. The adjusted vaccine effectiveness was 68% for one dose and 89% for two doses. No effectiveness was observed if the single dose was administered less than 13 days prior to diagnosis.

In a third study, published in The New England Journal of Medicine, Nicholas Deputy, PhD, of the CDC’s Mpox Emergency Response Team, and colleagues conducted a case-control comparison using data from Cosmos, a nationwide electronic health records database. Of note, a large proportion of the study population was immunocompromised.

The 2,193 case patients had a recorded mpox diagnosis code or a positive mpox or orthopox virus lab test between August 15 and November 19, 2022. The 8,319 control participants were newly diagnosed with HIV or had a new or refill pre-exposure prophylaxis (PrEP) prescription. Of these, 25 case patients and 335 control participants had received two Jynneos doses while 146 and 1,000, respectively, had gotten a single dose.

Here, the estimated adjusted vaccine effectiveness was 36% with one dose and 66% with two doses—substantially lower than the level seen in the previous two studies. However, among people who were not immunocompromised, vaccine effectiveness rose to 41% with one dose and 76% with two doses. People who previously received the ACAM2000 vaccine had greater protection.

The variability in these effectiveness estimates is attributable to different populations, different data sources and varying degrees of self-selection bias. But the estimates are generally within one anothers' confidence intervals, meaning they are statistically similar.

"What we take away from these three studies is that the vaccine effectiveness is substantial and that two doses [are] definitely better than one," Christopher Braden, MD, the CDC's mpox response incident manager, said during the media briefing. "Being vaccinated will help decrease the spread of mpox in populations. It will help individuals prevent the acquisition of mpox, and it will help individuals avoid severe disease or even death."

Considering when these studies were conducted, they cannot say much about the duration of vaccine-induced immunity. Thus it is not clear whether the people who became infected after vaccination in the recent clusters never achieved full protection or if protection waned over time. Alternative explanations might include mpox virus mutations or improper vaccine administration.

Experts Urge Vaccination

Health officials and advocates stress the importance of getting both Jynneos vaccine doses. Even people who previously had mpox are advised to get vaccinated, as there have been several reported cases of reinfection. The vaccine supply is currently ample, and most health departments are now offering subcutaneous rather than intradermal administration.

But to date, mpox vaccine uptake leaves much to be desired. Although 1.2 million doses have been administered in the United States, only 23% of people at risk are fully vaccinated, and just 37% have received one dose, according to the CDC. White men are more likely to be vaccinated than Black and Latino men, and some groups still have low vaccination rates, including people living outside urban centers and those with limited access to health care.

While vaccination does not offer complete protection against infection or reinfection, it is likely to prevent severe illness. All cases in the recent Chicago cluster were mild, and no one required treatment. Plus, the more people who are vaccinated, the less mpox will circulate within communities.

"Vaccination makes getting and spreading mpox less likely and may decrease the chances of severe illness, hospitalization and death," Daskalakis said during the briefing. "Though no vaccine is perfect, even imperfect immunity in many people means a lot of immunity in the population, and the result is that we are less likely to have outbreaks."

Full vaccination is especially important for people with advanced HIV, who are more likely to develop severe mpox illness. Of the 42 people who have died of mpox in the United States, most were Black gay men with AIDS. Along with vaccination, starting and staying on antiretroviral treatment can reduce the risk for serious mpox complications.

It is not yet clear whether mpox vaccine boosters could increase or extend the duration of

protection. While further studies are underway to answer this question, health officials do not recommend booster shots at this time, nor do they advise that people who received intradermal vaccines get subcutaneous doses.

“If you didn’t get your first dose, get it. And if you didn’t get your second dose, get that. Seek health care and get tested if you have a rash, even if you’ve been previously vaccinated or had mpox,” Daskalakis said. “We need to be ready to use all the tools in the mpox prevention toolkit, including vaccines, testing and information so that people can make informed decisions about their sex lives to halt the spread and protect their health and the health of the community.”

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