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How Well Does the Monkeypox Vaccine Work?

Studies suggest that the Jynneos vaccine offers substantial protection, but more real-world research is needed.

October 20, 2022 By Liz Highleyman

The Jynneos monkeypox vaccine (sold as Imvanex in Europe and Imvamune in Canada) has now been widely rolled out in the United States and some other high-income countries. Studies to date suggest that it offers substantial protection, including one analysis that found people who received the vaccine were about 14 times less likely to develop monkeypox. But questions remain about the vaccine's effectiveness in real-world use, and experts stress that two doses are needed for optimal protection.

The ongoing monkeypox outbreak in countries outside of Africa has slowed dramatically in the United States and Europe after peaking in late summer. As of October 20, the Centers for Disease Control and Prevention (CDC) has identified 27,835 cases of monkeypox in the United States and tallied more than 75,000 confirmed cases worldwide. Five months into the outbreak, monkeypox is still primarily occurring among gay and bisexual men and transgender people, though racial and ethnic disparities are increasing.

Vaccination has likely contributed to the decline, along with behavior change and natural immunity after infection in the group at greatest risk. As of October 18, the CDC reports that more than 975,000 Jynneos doses have been administered in the United States.

Monkeypox is related to smallpox, and the same vaccines can be used for both. Jynneos (also known as MVA-BN), which contains weakened vaccinia virus, was developed by Bavarian Nordic as a safer alternative to the live-virus ACAM2000 smallpox vaccine. Because monkeypox virus has a long incubation period, vaccines can be used both as post-exposure prophylaxis (PEP) for up to two weeks after exposure and as pre-exposure prophylaxis (PrEP) for people at risk.

Jynneos was authorized as a two-dose series administered by subcutaneous injection about a month apart. In an effort to stretch the limited vaccine supply, the United States switched to an intradermal administration method that allows a single vial to be split into five doses. Regardless of how it's administered, "receiving both vaccine doses is critical to ensure durable, lasting protection," according to CDC director Rochelle Walensky, MD, MPH.

As vaccine supplies have increased, so has eligibility. The CDC now recommends the vaccine for close contacts of people known to have monkeypox and for men who have sex with men and transgender or nonbinary people who have multiple sex partners, engage in group sex, have sex at venues such as sex clubs or bathhouses or have recently been diagnosed with a sexually transmitted infection. But eligibility varies across jurisdictions. Some also include people living with HIV and those eligible for HIV PrEP, while others include anyone with sexual risk factors regardless of their sexual orientation or gender identity.

Click here to find out where to get a monkeypox vaccine: https://mpoxvaxmap.org/

I wonder what extra gay superpowers I'll get this time.????????????

First monkeypox vaccination done, one more to go.???????? pic.twitter.com/nureJ07rOb

— Chase Anderson, MD, MS (K.C. Ardem) ????????♂???????? (@ChaseTMAnderson) August 26, 2022

Monkeypox Vaccine Effectiveness

Routine smallpox vaccination was halted after the disease was eradicated in 1980, but people over age 50 or so who were previously vaccinated are thought to have some protection against monkeypox. Research in the Democratic Republic of Congo in the 1980s found that people who had received a smallpox vaccine before it was discontinued were 85% less likely to contract monkeypox. However, some cases in the current outbreak have occurred among people who were previously vaccinated.

Jynneos was tested against monkeypox in non-human primates. While it reduced the likelihood of symptomatic illness and death, it did not reliably prevent infection. Prior to this outbreak, research in humans was limited to immunogenicity studies, which look at antibody levels after vaccination. Regrettably, Jynneos was not studied in Central and West African countries where monkeypox has been endemic for decades, and people those countries still do not have access to the vaccine.

In one Phase III trial, people randomly assigned to receive Jynneos or ACAM2000 had comparable antibody responses against smallpox. It has been assumed that Jynneos will also provide similar immunity against monkeypox, but the level of antibodies needed for protection is not clear. A small study in 2015 showed that antibody responses were similar after subcutaneous or intradermal Jynneos injections. A clinical trial is now underway to compare immune responses after subcutaneous or intradermal administration using one-fifth or one-tenth of the approved dose.

To learn more about real-world effectiveness, CDC researchers looked at outcomes among U.S. men ages 18 to 49 who were eligible for monkeypox vaccination. As described in the October 7 edition of Morbidity and Mortality Weekly Report, the analysis was based on 5,402 monkeypox cases that occurred between July 31 and September 3, when Jynneos was widely available but most people had only received their first dose.

Preliminary results suggested that men who received a single vaccine dose at least two weeks prior were 14 times less likely to contract monkeypox than eligible men who were not vaccinated. However, this analysis was based on limited data and did not control for confounding factors. For example, men who were early vaccine adopters might also have changed their sexual behavior.

“This early finding suggests that a single dose of Jynneos vaccine provides some protection against monkeypox infection,” the study authors wrote. “The degree and durability of such protection is unknown, and it is recommended that people who are eligible for monkeypox vaccination receive the complete two-dose series.”

A smaller Israeli study, published as a preprint, looked at outcomes among 1,970 vaccine-eligible members of a large health care system. Of these, 873 received one dose of Jynneos between July 31 and August 18. Three vaccinated and 15 unvaccinated people contracted monkeypox during the study period, which works out to a vaccine effectiveness estimate of 79%. “Our results suggest that a single dose of [Jynneos] is associated with a significantly lower risk for monkeypox virus infection in high-risk individuals,” the researchers concluded.

But some experts think it’s premature to say the vaccine provides such a high level of protection—especially after only one dose—and other recent reports suggest that caution is warranted.

A French study, also published as a preprint, looked at post-exposure ring vaccination of people who had close contact with a person known to have monkeypox. The analysis included 276 individuals, mostly gay men, who received a single Jynneos dose between May 27 and July 13, with a median delay of 11 days after exposure. Of these, 12 (4%) contracted monkeypox, but none had a severe case. Ten of the 12 developed monkeypox within five days after vaccination—before the vaccine fully took effect—but two had breakthrough infections at 22 and 25 days post-vaccination. Ring vaccination “was well tolerated and effective against monkeypox but did not completely prevent breakthrough infections,” the researchers wrote.

Aniruddha Hazra, MD, and colleagues from Howard Brown Health in Chicago analyzed monkeypox cases after a single dose of Jynneos. The study, published in JAMA, included 7,339 people who receiving their first vaccine dose between June 28 and September 9. Of this group, 90 tested positive. Most of these cases (77%) occurred during the first week (37 cases) or second week (32 cases) after vaccination. But eight people tested positive more than a month after their first dose, including two who did so three weeks or more after their second dose. The good news is that all but one had mild illness with fewer than 10 lesions.

In another study published as a preprint, Luca Zaeck, PhD, of Erasmus University Medical Centre in Rotterdam, and colleagues compared antibody responses in people who received Jynneos, those who received an older smallpox vaccine and those who tested positive for monkeypox. They found that Jynneos recipients had low levels of monkeypox neutralizing antibodies than the other two groups. People who received just one dose "hardly developed antibody responses" at four and eight week post-vaccination. Antibody levels remained relatively low even after the second dose, but a third dose boosted their levels.

In contrast, researchers at Bavarian Nordic reported in another preprint that single and double subcutaneous doses of Jynneos induced durable neutralizing antibody responses comparable to those seen with older smallpox vaccines. Antibody levels remained high for at least six months but then returned to pre-vaccine levels by two years. However, this does not mean immunity was lost, as B-cells and T-cells provide longer-lasting protection. This study also found that people who previously received an older smallpox vaccine saw a large and rapid increase in antibodies after a Jynneos booster. This was also seen when people who received one or two initial doses of Jynneos were given a booster two years later, suggesting the booster activates memory B-cells.

Several questions about the vaccine remain to be answered. It is not known how long vaccine protection will last, though vaccination or prior monkeypox infection are thought to confer long-term immunity. Historically, monkeypox was typically transmitted via contact with animals or household contact; it is not known how well the vaccine protects against sexual transmission of the virus. One study found that HIV-positive people with an adequate CD4 count respond well to Jynneos, but little is known about responses in those with more advanced immune suppression.

Walensky told reporters that preliminary data from the CDC analysis "provide us with a level of cautious optimism that the vaccine is working as intended." But given the mixed evidence to date, experts caution that people who receive the Jynneos vaccine may still be at risk for monkeypox, and more research is needed before relying on vaccination alone to curb the outbreak. While Jynneos certainly provides some immunity, it does not prevent infection entirely, especially after just one dose.

"It is absolutely critical that public health officials work on messaging this uncertainty to people being vaccinated," Jay Varma, MD, of the Cornell Center for Pandemic Prevention and Response, told MedPage Today. Both Walensky and Hazra said that continued risk reduction is important,

especially between the first and second doses and for two weeks after vaccination.

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