CDC Urges Mpox Vaccination as Deadlier Strain Spreads in Africa

The Jynneos vaccine provides ongoing protection despite waning antibody levels, including for people with HIV.

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Mpox (formerly monkeypox) cases have risen in the United States this year, though they remain far below the level seen at the peak of the outbreak in the summer of 2022. But a growing outbreak of a more deadly mpox strain in the Democratic Republic of the Congo (DRC) raises concerns about wider international spread.

The global mpox outbreak that started in May 2022 declined dramatically by the end of that year, but the virus is still circulating at a low level. As of early March, the Centers for Disease Control and Prevention (CDC) had identified more than 32,000 cases in the United States, resulting in 58 deaths. The World Health Organization (WHO) has tallied nearly 96,000 cases worldwide.

With Pride celebrations and summer travel coming up, the CDC is urging people at risk, including sexually active gay and bisexual men and people living with HIV, to receive two doses of the Jynneos (MVA-BN) vaccine. To date, however, only a quarter of eligible individuals are fully vaccinated with two doses.

Mpox in the DRC

Prior to the global outbreak, mpox was known as an uncommon disease in western and central Africa, where it largely affected children. It was typically linked to contact with wild animals, and it was not thought to spread easily between people. Mpox virus has two types, Clade I and Clade II, the former of which has historically had a higher fatality rate.

In contrast, a 2017 Clade II mpox outbreak in Nigeria mostly affected men, and sexual transmission appeared to play a key role. Likewise, the 2022 global Clade II outbreak was mainly driven by sex between men, though mpox can also spread via other types of close physical contact. This outbreak mostly involved gay and bisexual men and others in their sexual networks; about half were living with HIV. The outbreak has had a low fatality rate overall, but mpox is deadlier for people with advanced HIV.

Clade I mpox has long been endemic in the DRC, but cases began to rise last year. Between January 2023 and April 2024, there were 19,919 suspected cases and 975 deaths, for a case

fatality rate of 4.9%, according to the CDC. However, due to widespread poverty, lack of health infrastructure and ongoing armed conflict, most suspected cases have not been laboratory confirmed and are not included in official global case counts. On the other hand, given limited testing, many more people might have had asymptomatic or mild mpox that was never diagnosed, which could mean the real infection fatality rate is much lower.

The DRC appears to actually be experiencing concurrent mpox outbreaks. In some parts of the country, around two thirds of suspected cases and most deaths have been among children. In keeping with historical patterns, this is likely due to multiple separate exposures to infected animals and subsequent chains of household transmission.

At the same time, some cities and towns are seeing cases mostly among adults, apparently driven by sexual transmission—the first time Clade I mpox has been confirmed to spread in this manner. A man suspected of being the first in a cluster of cases in Kwango Province, not far from the capital Kinshasa, visited underground clubs frequented by men who have sex with men and reported several sexual contacts with both men and women.

Across the country, an outbreak in Kamituga, a mining town in South Kivu Province near the border with Rwanda and Burundi, appears to be largely attributable to heterosexual contact. This Clade I outbreak, comprising about equal numbers of men and women, was described in three recent preprints and a report in The Lancet Infectious Diseases. Interviews with people hospitalized with mpox revealed that many were sex workers. Genomic analysis found a distinct lineage of Clade Ib mpox that appears to spread from person to person more efficiently.

Jean Jacques Muyembe Tamfum, PhD, of the DRC's National Institute of Biomedical Research, and colleagues suggested that heterosexual transmission could be driving this outbreak. Patients in Kamituga generally have less severe mpox lesions, and the death rate is lower compared with historical Clade I cases. But the high prevalence of mpox among women raises concerns about mother-to-child transmission and adverse pregnancy outcomes, as four of eight pregnant women with mpox had miscarriages.

"These new features of sexual transmission now raise additional concerns over the continuing rapid expansion of the outbreak in the country in a nationally and internationally mobile key population," according to the WHO. "The risk of mpox further spreading to neighboring countries and worldwide appears to be significant." Already, the similarly named Republic of Congo, which borders the DRC to the west, is starting to see an uptick in cases.

Likening the situation in Kamituga to the 2017 Clade II outbreak in Nigeria, Placide Mbala-Kingebeni, MD, also of the National Institute of Biomedical Research, and colleagues wrote, "Given the recent history of mpox outbreaks in DRC, we advocate for swift action by endemic countries and the international community to avert another global mpox outbreak."

Mpox Risk in the U.S.

Last December, the CDC issued a health advisory alerting clinicians and health departments to be

on the lookout for Clade I mpox among travelers who have been to the DRC. The agency described U.S. preparedness and response to the DRC outbreak in the May 16 Morbidity and Mortality Weekly Report. If a case is suspected, clinicians should request clade-specific testing. Standard tests can detect both mpox clades but usually can't distinguish one from the other.

To date, no cases of Clade I mpox have been detected in the United States or in any other countries outside of the endemic areas in Africa. The CDC and other laboratories have tested around 1,200 mpox specimens, an airport surveillance program tested samples from volunteer travelers and health officials analyzed wastewater from 186 U.S. sites. All were negative for Clade I mpox.

In a May 10 rapid risk assessment, the CDC deemed the risk posed by the DRC outbreak to be "very low" for the general population and "low to moderate" for gay and bisexual men and those in their sexual networks. The potential for sustained heterosexual transmission of Clade I mpox is "likely to be low," based on the lack of widespread transmission in heterosexual networks during the global Clade II outbreak. Although mpox is commonly reported among children in the DRC, widespread transmission among kids in the United States is considered much less likely. Reasons include the absence of animal reservoirs, smaller household sizes and better access to health care and sanitation resources.

Low-level transmission of Clade II mpox continues to occur across the United States, according to the May 23 Morbidity and Mortality Weekly Report. A total of 1,802 confirmed or probable cases were reported to the CDC between October 2023 and the end of April 2024. There were about 60 cases reported per week nationwide during this period, down from a high of around 3,000 cases in July 2022. The steep decline has been attributed to a combination of natural immunity after infection, vaccination and sexual behavior change.

While this is good news, cases have risen in 2024 compared with 2023. Nearly 750 cases have been reported so far this year, more than double the number at the same time last year. Nearly all regions have reported more cases this year, albeit with substantial local variation. New York City, for example, has seen 191 cases while San Francisco has identified nine cases in 2024.

The epidemiology of Clade II mpox in the U.S. has not changed much. It continues to mainly affect gay and bisexual men, who accounted for more than 90% of cases between October 2023 and April 2024. About one third (32%) of these cases were among Latinos, 32% among white people and 25% among Black people. Of those with a known status, 48% were living with HIV. While only 10% required hospitalization, 68% of those hospitalized were HIV positive. Five people with mpox have died since October 2023, for a case fatality rate of 0.3%.

Mpox Vaccination Urged

The CDC now recommends routine vaccination for people at risk for mpox, whether or not an outbreak is underway. This includes sexually active gay and bisexual men, transgender and gender-diverse individuals, people in their sexual networks regardless of sex or gender identity and people living with HIV or on HIV pre-exposure prophylaxis (PrEP). As of April, the vaccine is

commercially available through clinics and pharmacies, but some public health sites are still offering it for free.

However, just 39% of eligible individuals have received one dose of the Jynneos vaccine, and only 25% have received both doses. This varies widely by jurisdiction, but only Washington, DC, has more than half of the eligible population fully vaccinated.

Most of the recent mpox cases involved people who are not fully vaccinated, according to a third Morbidity and Mortality Weekly Report. Of the 32,819 confirmed or probable cases reported between May 2022 and May 2024, three quarters were unvaccinated while just 271 (0.8%) were fully vaccinated. Among people who received two doses, the risk of mpox infection is estimated at around 0.1%. And among those with breakthrough infections, fully vaccinated people had milder illness, were less likely to be hospitalized and none died.

When the Jynneos vaccine was in short supply, the Food and Drug Administration authorized an intradermal injection method that allows a single vial to be split into five doses. A study presented at the European Society of Clinical Microbiology and Infectious Diseases Global Congress (ESCMID Global) in April found that this dose-sparing method and standard subcutaneous injections generate equivalent antibody responses two weeks after the second dose. Two weeks later, however, people who received the smaller intradermal dose had lower antibody levels.

A study published in The New England Journal of Medicine in December also found no significant difference in the strength of immune responses between intradermal and subcutaneous administration, but here, too, antibody levels waned over time. The researchers also saw no difference in the magnitude of immune responses between HIV-negative people and HIV-positive people with a CD4 count above 200. Another study in the Journal of Medical Virology found that the intradermal vaccination method actually appeared more effective for people with well-controlled HIV, promoting greater T-cell functionality against poxviruses.

Two other studies presented at ESCMID Global, conducted in the Netherlands and in Sweden, found that people who received two doses of the Jynneos vaccine saw their antibodies fall to low levels within months. However, those who had previously received a smallpox vaccine as children—which was discontinued in the United States in 1972—maintained high antibody levels. Both research teams suggested that the nonreplicating Jynneos MVA-BN vaccine might not generate as strong a response as the replication-competent vaccinia smallpox vaccine.

“The results presented here indicate that long-term protective immunity might need a booster dose for its maintenance,” said Klara Sondén, MD, PhD, of the Public Health Agency of Sweden. But the Dutch researchers weren’t so sure. “Regarding the potential necessity for a booster, it is premature to draw such conclusions,” they suggested. “It is unclear how waning antibody levels relate to protection. Immunity also involves other elements, such as T-cell responses. Comprehensive clinical monitoring over time, which connects infection rates with antibody levels, is required to make informed decisions about booster vaccination protocols.”

While further study of mpox vaccine effectiveness is warranted, the real-world CDC findings suggest that immunity is not waning. Although antibody levels may decline, this is not the only marker of protection. “The role of innate and cell-mediated immunity in preventing [mpox] infections is not known, and the robustness of memory or recall response after an exposure might be more important determinants of disease outcome,” the CDC authors wrote.

Mpox vaccine guidelines state that either the subcutaneous or intradermal administration method may be used, but the CDC prefers the former if Jynneos supply is adequate. People who previously received intradermal doses do not need to be revaccinated using the subcutaneous method. Although four weeks is the recommended interval between shots, people who previously received one dose—no matter how long ago—do not need to restart the series. At this time, additional booster doses are not recommended. People who have already had mpox do not need to be vaccinated. Studies indicate that Jynneos is effective against both Clade I and Clade II mpox. The same is true for the antiviral drug TPOXX (tecovirimat).

Infectious diseases don’t remain confined to one country, and the DRC outbreak underscores the need to make mpox vaccines and treatment available worldwide. While Jynneos has been widely deployed in the United States and other high-income countries, it is still not readily available in Africa. The CDC is working with health officials in the DRC to track and respond to the ongoing outbreak. “Collaboration among global health partners is now urgently needed to assist DRC in procuring and delivering sufficient vaccine where it is most needed,” Jennifer McQuiston, DVM, of the CDC’s National Center for Emerging and Zoonotic Infectious Diseases, and colleagues wrote.

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