# Data supporting CDC recommendations that mpox vaccine booster doses are not needed at this time September 13, 2024

### **Background**

CDC recommends vaccination with two doses of JYNNEOS for people in the U.S. at risk of *Monkeypox virus* (MPXV) infection, regardless of clade. If you are a gay, bisexual, or other man who has sex with men, or if you're transgender, gender non-binary, or gender-diverse AND have other <u>sexual risk factors</u>, you should get two doses of the JYNNEOS vaccine. People can find out if they are eligible and where to receive JYNNEOS vaccine at cdc.gov/mpox.

JYNNEOS vaccine may also be offered as post-exposure prophylaxis to those individuals (if not already vaccinated) exposed to a person diagnosed with either clade I or clade II MPXV<sup>1</sup>.

MPXV has two distinct genetic types, clade I (with subclades Ia and Ib) and clade II (with subclades IIa and IIb), which are endemic to Central and West Africa, respectively. Clade II is responsible for the ongoing global mpox outbreak that began in 2022, is predominantly transmitted through intimate and sexual contact, and has disproportionately affected gay, bisexual, and other men who have sex with men (MSM). Clade I MPXV, currently causing outbreaks in the Democratic Republic of the Congo (DRC) and spreading to neighboring countries in Eastern and Central Africa, has historically caused a higher proportion of severe infections than clade II MPXV.

Both clade Ia and clade Ib MPXV are circulating in DRC. Clade Ib MPXV cases predominate in the eastern part of DRC and epidemiologic data at this time indicate that while patients of any age may have been exposed via contact with infected wildlife or through close personal contact in households, adult cases are frequently associated with sexual contact with someone who has mpox. Unlike cases that predominate in males during the ongoing global clade IIb outbreak, an equal number of clade Ib cases have been reported in men and women.

Neither clade Ia nor clade Ib MPXV has been reported in the United States, and the <u>risk to the general</u> population in the United States is considered low at this time.

Given these outbreaks and the World Health Organization's declaration of a <u>Public Health Emergency of International Concern</u> in August 2024, interest in mpox vaccination and questions about vaccine boosters have arisen. In this document, the Centers for Disease Control and Prevention (CDC) seeks to explain the reasoning behind vaccine recommendations, including reasons why booster doses are not recommended at this time.

<sup>&</sup>lt;sup>1</sup>CDC web pages: Exposure Risk Assessment for Community Contacts; Infection Control: Healthcare Settings

# Two doses of JYNNEOS vaccine are effective at preventing most MPXV infections.

JYNNEOS vaccine is licensed for prevention of smallpox and both clades of MPXV infection in adults. CDC recommends vaccination with two doses of JYNNEOS for people in the United States at risk of mpox.

Two doses of JYNNEOS vaccine can prevent MPXV infection and reduce the severity of mpox symptoms in people who have been vaccinated. Data from a multijurisdictional study in the U.S. demonstrated significant JYNNEOS vaccine effectiveness against mpox:

- 75% for one dose and
- 86% after two doses<sup>2</sup>

In addition, a recent study from the United Kingdom Health Security Agency<sup>3</sup> estimated the effectiveness of the two-dose primary series of JYNNEOS at 80% for cases diagnosed in 2023.

No vaccine is 100% effective, but there are very few reports to CDC of mpox after vaccination with two doses of JYNNEOS vaccine. Data collected from May 2022-May 2024<sup>4</sup> during the clade IIb mpox outbreak in the United States show that infections after the two dose JYNNEOS vaccine series were rare. These infections:

- Were observed in <1% of people vaccinated with two doses of JYNNEOS vaccine (271 cases), which is consistent with the expected high degree of effectiveness after two doses
- Occurred at disparate time intervals after vaccination with no pattern that can be attributed to waning immunity
- Were associated with less severe infections when they occurred.

# Why CDC does not recommend booster doses for the general population vaccinated during the ongoing clade IIb mpox outbreak.

Unpublished data from a CDC study<sup>5</sup> in the Democratic Republic of the Congo that began in 2017 with 1,600 healthcare personnel receiving two doses of JYNNEOS demonstrated only <u>one</u> reported laboratory-confirmed infection in this region of high clade I mpox transmission. This study indicated that a booster dose five years after receiving the JYNNEOS primary series leads to a rapid and robust antibody response irrespective of circulating antibody levels at the time of booster dose. These results suggest that

<sup>&</sup>lt;sup>2</sup> Estimated Effectiveness of JYNNEOS Vaccine in Preventing Mpox: A Multijurisdictional Case-Control Study — United States, August 19, 2022–March 31, 2023 | MMWR (cdc.gov)

<sup>&</sup>lt;sup>3</sup> Early Release - Mpox Epidemiology and Vaccine Effectiveness, England, 2023 - Volume 30, Number 10—October 2024 - Emerging Infectious Diseases journal - CDC

<sup>&</sup>lt;sup>4</sup> Monkeypox Virus Infections After 2 Preexposure Doses of JYNNEOS Vaccine — United States, May 2022–May 2024 | MMWR (cdc.gov)

<sup>&</sup>lt;sup>5</sup> Study Details | JYNNEOS Smallpox Vaccine in Adult Healthcare Personnel at Risk for Mpox in the Democratic Republic of the Congo | ClinicalTrials.gov

immunity does not wane for at least five years; a seven-year time point is currently being evaluated. Serologic studies<sup>6</sup> have shown antibody titers decrease a few months after vaccination. However, it is not known if a specific antibody titer is required to provide protection. Further, the levels of circulating titers are not the only marker of protection. Cell-mediated immunity and innate immunity are important components of the immune response and do not corelate with level of antibody titer. Thus, the clinical significance of decreasing titers is unknown.

Additionally, the recent United Kingdom study<sup>7</sup> that estimated JYNNEOS effectiveness at 80% following the 2-dose primary series of JYNNEOS looked at cases that occurred from January 1 to December 31, 2023. As most people in this study received JYNNEOS from July 2022-March 2023, these findings further support the durability of JYNNEOS protection.

Based on currently available data from the unpublished CDC study, protection after the two doses JYNNEOS vaccine series does not wane for at least five years. Thus, booster doses are not recommended for anyone in the general population who was vaccinated during the ongoing clade II mpox outbreak in the United States that began in 2022.

Why does CDC recommend booster doses for certain healthcare providers and laboratorians with potential exposure to high levels of monkeypox virus?

Booster doses have always been recommended for certain laboratory workers at risk for *orthopoxvirus* infection due to their increased occupational risk. MPXV research laboratorians and certain clinical laboratorians (i.e., those performing *orthopoxvirus* and MPXV diagnostic testing) may work with high concentrations of virus (i.e., 100-1000 times higher than concentrations encountered from an mpox lesion) and occasionally experience needlestick accidents and other unusual virus exposures. For these reasons, booster doses are recommended every two years to maintain high levels of protection.

#### Additional information

## CDC recommendations on boosters may differ from those of some other countries.

Another country recently<sup>8</sup> recommended a booster dose for people vaccinated two or more years ago, given studies showing a reduction in neutralizing antibodies in the two years following a two-dose primary vaccination. Although neutralizing antibody titers are known to decrease 6 months following the two-dose primary series, there is no established correlate of protection. This also does not consider that well-mediated immunity and innate immunity are important components of the immune response and

<sup>&</sup>lt;sup>6</sup> Serological responses to the MVA-based JYNNEOS monkeypox vaccine in a cohort of participants from the Democratic Republic of Congo - PMC (nih.gov)

<sup>&</sup>lt;sup>7</sup> Early Release - Mpox Epidemiology and Vaccine Effectiveness, England, 2023 - Volume 30, Number 10—October 2024 - Emerging Infectious Diseases journal - CDC

<sup>&</sup>lt;sup>8</sup> Haute Autorité de Santé - Opinion No. 2024.0058/AC/SESPEV of 29 August 2024 of the College of the Haute Autorité de Santé on the vaccination strategy against mpox (has-sante.fr)

don't corelate with antibody titer levels. As noted above, CDC studies in DRC have shown a robust antibody response following booster doses up to five years following the primary vaccine series. This suggests that there would be a robust immune response from exposure to MPXV in a person vaccinated within the last five years. Therefore, at this time CDC does not recommend booster doses for those vaccinated during the ongoing clade IIb mpox outbreak, which began in 2022.

# CDC vaccination recommendations for immunocompromised individuals may differ from those recommended by other countries.

Another country has recommended two doses plus a third dose at least 28 days after the second dose for immunocompromised individuals<sup>9</sup>. There are data to support additional doses for immunocompromised individuals for some vaccine-preventable diseases. However, there are limited data to support this practice for JYNNEOS vaccine given the newness of its wide use. JYNNEOS has been studied as a 2-dose, double dose, and 3-dose series in patients with HIV, including those with low (<200 cells/mm³) CD4 counts¹0. There was no significant difference in seroconversion rates with the addition of the third dose or by doubling the dose, with similar seroconversion rates across groups. Additional doses were discussed in the June 2023 meeting of the U.S. Advisory Committee on Immunization Practices (ACIP), and the ACIP did not believe the available data supported an additional dose in people who are immunocompromised. Therefore, CDC does not recommend additional doses of vaccine for that population.

## Why you don't need to be vaccinated if you have recovered from mpox

Recovery from MPXV infection (regardless of clade) likely confers protection from either clade of mpox. It is possible for individuals who have recovered from mpox to experience a reinfection, but reinfections are very rare. Reinfection has occurred in less than 0.001% of people in the United States who previously had mpox.<sup>11</sup> In these rare instances, the second infection was generally milder than the initial infection. Because of this, people who have recovered from mpox are not recommended to receive JYNNEOS vaccine doses at this time.

<sup>&</sup>lt;sup>9</sup> Haute Autorité de Santé - Opinion No. 2024.0058/AC/SESPEV of 29 August 2024 of the College of the Haute Autorité de Santé on the vaccination strategy against mpox (has-sante.fr)

<sup>&</sup>lt;sup>10</sup> A randomized phase II trial to compare safety and immunogenicity of the MVA-BN smallpox vaccine at various doses in adults with a history of AIDS - PubMed (nih.gov)

<sup>11</sup> Monkeypox Virus Infections After 2 Preexposure Doses of JYNNEOS Vaccine — United States, May 2022–May 2024 | MMWR (cdc.gov)