Summary: Mpox Scenario-Based Human Health Risk Assessment for the United States as of 4 June 2024

Currently, the Center for Outbreak Response Innovation (CORI) judges the ongoing sporadic mpox infections in humans in the United States to be in Scenario 1, *meaning the virus circulating in the United States is the same clade (clade IIb) that expanded globally in 2022. Case reports are not higher than the baseline of the past 6 months.*

This judgment is based on available data from ongoing mpox case reporting to the US Centers for Disease Control and Prevention (CDC) and wastewater surveillance. However, increases in cases or clusters of cases during the summer or introduction of the more deadly clade I into the US from other countries with ongoing outbreaks may increase the health risk posed to specific populations, as described in the scenario-based risk assessment below.

See the detailed risk assessment beginning on the next page for further information.

Scenario-Based Human Health Risk Assessment for the US

	Risk to MSM community	Risk to sex workers	Risk to healthcare workers	Risk to general public
Scenario 1 – Baseline (clade IIb continued transmission)	Low-Moderate	Low-Moderate	Low	Low

Our **confidence** in these risk scores is high.

To minimize the sporadic transmission of clade IIb clade in the US, CDC and WHO recommend the following:

- All individuals with an increased risk of infection should receive 2 doses of JYNNEOS vaccine.[1]
- Clinicians should consider mpox when lesions consistent with mpox are observed in a patient, even if an alternate etiology (eg, herpes simplex virus, syphilis) is considered more likely.[2]
- Healthcare professionals should wear all recommended personal protective equipment (PPE) when completing mpox testing.[3]

Mpox Scenario-Based Human Health Risk Assessment for the United States

Center for Outbreak Response Innovation (CORI)

Updated as of June 1, 2024

In 2022, the epidemiology of mpox (formerly known as monkeypox) in the United States shifted dramatically. The virus, previously endemic in south-central Africa, found a foothold in the sexual networks of gay, bisexual, and other men who have sex with men (MSM community) in the United States as well as in Europe. The initial epidemic in the US grew to more than 30,000 reported cases and 58 deaths, with ongoing sporadic cases and clusters.[4]

The change in epidemiology and rapid spread of the virus in 2022 required urgent public health action. Public health officials and community-based organizations mounted a response that included health education, awareness raising, testing, treatment, and vaccination with a vaccine that was originally designed to protect against smallpox but is also effective against mpox.[5] By mid-summer, the public health response began to slow transmission. Vaccination campaigns and targeted interventions reduced the number of new weekly cases significantly. However, cases continue to occur among individuals at increased risk of infection, particularly those who have not been vaccinated or have received only 1 dose of vaccine.[4]

The mpox virus responsible for the 2022 global epidemic is the subtype clade IIb. Although clade IIb virus is capable of transmission via respiratory droplets, short-range aerosols, or contact with contaminated objects (fomite transmission), the majority of cases from the global epidemic were acquired through close, extended physical contact, particularly intimate or sexual contact.[5] The recorded number of mpox cases was relatively stable in the US from July 2023 to January 2024, with some clusters of ongoing transmission. To date, all mpox cases reported within the US are of the clade IIb subtype.[4] In 2024, clustered outbreaks of mpox clade IIb remain a concern in the US, especially as summer festivals, celebrations, and other events that bring people together from across the country and globe occur. High levels of immunity from prior infections and vaccination help mitigate the risk of large outbreaks. Individuals at highest risk for clade IIb infection are gay, bisexual, and other men who have sex with men; people with multiple sex partners; sex workers; and healthcare workers caring for infected patients.

Mpox Scenario-Based Human Health

In addition to the clade IIb global epidemic, an ongoing clade I mpox outbreak in the Democratic Republic of Congo (DRC), declared a national epidemic in December 2022, has raised concerns. The DRC outbreak is the largest surge in mpox cases the country has ever recorded.[6] Unlike with the clade IIb epidemic in the US in 2022–2023, and the sporadic cases of clade IIb that continue to be reported primarily among the MSM community, the ongoing clade I outbreak in the DRC has mostly affected children, with 67% of cases and 78% of deaths among children aged 15 and younger.[7] The DRC outbreak is also widespread, affecting 25 of the country's 26 provinces, including the capital city of Kinshasa. Since January 1, 2023, DRC has reported more than 20,000 suspected cases and more than 1,000 deaths.[6] Experts suspect that multiple factors are driving the DRC outbreak, including zoonotic, household, and sexual contacts, based on its extent, demographic characteristics, and genetic diversity of cases.[7]

The risks to human health from both clade I and clade II mpox are complex and may change rapidly. Risk assessment can be very helpful in times of significant uncertainty because it enables structured consideration of complex scenarios, likelihoods, and consequences to inform decisions around policy and operational action, as well as implementation of protective measures and future planning for worst-case scenarios. It is important not to wait for perfect information to estimate potential risk, because decisions must be made even in the absence of plentiful data. Therefore, the Center for Outbreak Response Innovation (CORI) conducted a scenario-based risk assessment to consider human health risks both now and in potential future scenarios.

CORI has identified 4 key scenarios that may shape the risk of mpox in the US for the upcoming year. Scenarios 1 and 2 assess the impact of clade IIb, currently present in the US. Scenarios A and B evaluate potential outbreaks of clade I, which would be a novel occurrence in the US. **It is important to note that scenarios involving clade IIb and clade I could occur simultaneously.** For example, if Scenario 2 and Scenario B occurred at the same time, public health and medical staff would face increased pressure and resource constraints, and the overall health risks to different populations might rise.

Features that would characterize each scenario include:

- **Scenario 1 – Baseline (clade IIb):** Cases of clade IIb have been stable for the last 6 months in the US with sporadic reports of ongoing clusters. This scenario examines the risk to various populations in the US should this continue.

- **Scenario 2 – Summer surge (clade IIb):** Clade IIb cases have historically surged during summer months due to increased social interactions associated with festivals and other gatherings. This scenario determines the risk to various populations in the US if a surge occurs in the next 3–4 months.
- **Scenario A – Outbreak in DRC spreads to US (clade I):** The ongoing mpox clade I outbreak in the DRC is distinctly different in transmission risks and affected populations compared to the clade IIb outbreak in the US. There are opportunities for this outbreak to spread outside of DRC, to neighboring countries and other regions of the world. If clade I cases are reported in the US, the risks to various populations in the US would change. This scenario examines the health risks among various US populations should there be sporadic imported clade I cases.
- **Scenario B – Clade I clusters or outbreak in US (clade I):** Imported clade I cases could lead to autochthonous transmission in the US, potentially resulting in small clusters or ongoing outbreaks of a clade I. This scenario examines the risks to various US populations if clade I transmission occurred within the US and if the epidemiological characteristics happening in the DRC remain similar.

  Please note: *We are evaluating the risks to human health should each scenario occur,* ***not*** *the relative risk of any one scenario occurring. This risk assessment will be updated regularly.*

Currently, CORI judges that the ongoing sporadic mpox infections in humans in the United States is in Scenario 1*, meaning the virus currently circulating in the United States is the same clade (clade IIb) that expanded globally in 2022 and case reports are not higher than the baseline of the past 6 months.*

This judgment is based on available data from ongoing mpox case reporting to CDC[4] and wastewater surveillance.[7] As of May 25, 2024, the CDC has reported no significant change in mpox case counts nationally and the reported cases continue to be predominately among individuals within the MSM community and who are unvaccinated or under vaccinated, indicating that the outbreak epidemiology has remained consistent.[7,4,8] CDC also reports that, to date, all patients with confirmed mpox who undergo clade testing have tested positive for clade IIb.[7,4] In late 2023, CDC enhanced wastewater surveillance for clades I and IIb, increasing testing locations to a total of 186 sites across 32 jurisdictions. As of May 25, 2024, all mpox virus detected through wastewater sampling has only been clade IIb.[7]

Notably, increases in cases or clusters of cases during the summer months, or the importation of mpox clade I into the US may increase the health risk posed to certain populations, as described in the scenario-based risk assessments below.

Mpox Human Health Risk Assessment Scenario Table for the US Population

Table 1. Clade IIb

	Risk Score (this is risk level to human health NOT of scenario occurring**)**			
	Risk to MSM community	**Risk to sex workers**	**Risk to healthcare workers**	**Risk to general public**
Scenario 1 – Baseline	Low-Moderate	Low-Moderate	Low	Low
Scenario 2 – Summer surge	Moderate	Moderate	Low	Low

Table 2. Clade I

	Risk Score (this is risk level to human health NOT of scenario occurring**)**				
	Risk to MSM community	**Risk to sex workers**	**Risk to healthcare workers**	**Risk to children**	**Risk to general public**
Scenario A – Sporadic imported clade I cases to US	Low-Moderate	Low-Moderate	Low	Low	Low
Scenario B – Clade I clusters or outbreak in US	Moderate-High	Moderate-High	Low-Moderate	Moderate	Low-Moderate

Methods: The purpose of this document is to consider possible future developments in this outbreak and describe corresponding risks to human populations should a given scenario occur. In Scenarios 1 and 2 (clade IIb), we consider the risk to 4 distinct populations: the

community of men who have sex with men (MSM), sex workers, healthcare workers, and the public. In Scenarios A and B (clade I), we consider those 4 populations as well as children, as this population has been disproportionately affected by clade I in previous outbreaks as well as in the current DRC outbreak.

In determining the risks to the health of each population, we considered several factors such as primary transmission pathways, current morbidity and mortality, and the primary demographics and geographies currently affected. We also assessed the extent of the current outbreak to determine if cases are sporadic, in clusters, or if there is low or high ongoing community transmission. Other factors considered include events that could increase human-to-human transmission (eg, mass gatherings, seasonal trends, school terms, etc.); the availability and effectiveness of treatments and vaccines; nonpharmaceutical measures to lower the risk of human-to-human transmission, such as personal protective equipment for healthcare workers; the potential impact of animal reservoirs; and ongoing public health preparedness and response operations to address outbreaks.

Appendix: Additional Details on Process and Recommendations

Scenario 1: Baseline

Summary

- Viral group: clade IIb
- Current primary population impacted: MSM community

In this scenario, we considered the risk to human health if there is no change in the current epidemiology of mpox in the US. This involves only sporadic cases of only clade IIb mpox primarily affecting gay, bisexual, and other men who have sex with men (MSM community), particularly those who have not been previously infected, are not vaccinated, or are under vaccinated. This baseline scenario anticipates a continuation of this transmission level and disease severity, and no change in the demographic characteristics of individuals for whom mpox cases are reported.

For this scenario, we determined the health risk **in the United States** to the **MSM community** is **low-moderate**, the health risk to the **sex worker community** is **low-moderate**, the health risk to **healthcare workers** is **low**, and the health risk to the **general public** is **low**.

Our **confidence** in these risk scores is **high** given the current level of information for each of these factors, our understanding of transmission dynamics, and the availability of treatment resources.

To minimize the sporadic transmission of mpox clade IIb in the US, the CDC and WHO recommend the following:

- All high-risk individuals should receive 2 doses of JYNNEOS vaccine.[1,9]
- Individuals can reduce their risk by talking with sexual partners about mpox and practicing safer sex and good hygiene.
- Those at increased risk are encouraged to check for symptoms such as a rash with blisters on any part of the body (often starting around the mouth, anus, or genitals), inflammation and pain in the rectum, swollen lymph nodes, and/or fever.
- Those with any mpox symptoms should seek medical advice from a healthcare professional. They should also get tested, take a break from sex, ask close contacts

and sexual partners if they have similar symptoms, and avoid close physical contact.

- Clinicians should consider mpox when lesions consistent with mpox are observed in a patient, even if an alternate etiology (eg, herpes simplex virus, syphilis) is considered more likely.[2] Clinicians and other healthcare professionals should also wear all recommended personal protective equipment (PPE) when completing mpox testing.[3]
- People who have been in contact with someone with mpox infection should seek medical advice even if they do not have symptoms. They may be eligible for vaccination, which can reduce the risk of infection and developing severe disease.[10]

Scenario 2: Summer Surge

Summary

- Viral group: clade IIb
- Projected primary population impacted: MSM community

The US experienced increased mpox activity in the summers of 2022 and 2023. This is due to a variety of reasons, including increased social interactions associated with festivals and other mass gatherings.[9] This scenario anticipates an increase in mpox transmission, with similar severity of disease as in the previous summer surges. Increased levels of immunity due to prior infection or vaccination among the MSM community will likely reduce the level of transmission below what has been observed in past summers.

For this scenario, we determined the health risk **in the United States** to the **MSM community** is **moderate**, the health risk to the **sex workers** is **moderate**, the health risk to **healthcare workers** is **low**, and the health risk to the **general public** is **low.**

Our **confidence** in these risk scores is **high** given the current level of information for each of these factors; historical knowledge from the 2022 US mpox outbreak, including our understanding of the transmission dynamics; and the availability of vaccination and treatment resources.

To minimize the potential for a summer surge in transmission of clade IIb mpox in the US, the CDC and WHO recommend:

- Mass and large gathering event planning and preparedness activities should foster community-based actions aimed at spreading precise and practical public health advice with a non-discrimination approach across different media and incorporate educational and awareness-raising initiatives related to mpox and other diseases of concern.[11]
- All high-risk individuals should receive 2 doses of JYNNEOS vaccine.[1,9]
- Individuals can reduce their risk by talking with sexual partners about mpox and practicing safer sex and good hygiene.[9]
- Those at increased risk are encouraged to check for symptoms such as a rash with blisters on any part of the body (often starting around the mouth, anus, or genitals), inflammation and pain in the rectum, swollen lymph nodes, and/or fever.
- Those with any mpox symptoms should seek medical advice from a healthcare professional. They should also get tested, take a break from sex, ask close contacts and sexual partners if they have similar symptoms, and avoid close physical contact.
- Clinicians should consider mpox when lesions consistent with mpox are observed in a patient, even if an alternate etiology (eg, herpes simplex virus, syphilis) is considered more likely.[2] Clinicians and other healthcare professionals should also wear all recommended personal protective equipment (PPE) when completing mpox testing.[3]
- People who have been in contact with someone with mpox infection should seek medical advice even if they do not have symptoms. They may be eligible for vaccination, which can reduce the risk of infection and developing severe disease.[10]

Clade IIb Mpox Human Health Risk Assessment Scenario Table for the US Population

	Risk Score (this is risk level to human health NOT of scenario occurring**)**			
	Risk to MSM community	**Risk to sex workers**	**Risk to healthcare workers**	**Risk to general public**
Scenario 1 – Baseline	Low-Moderate	Low-Moderate	Low	Low

Scenario 2 – Summer surge	Moderate	Moderate	Low	Low

Scenario A: Sporadic Imported Clade I Cases

Summary

- Viral group: clade I
- Current primary populations impacted: children and sex workers in the Democratic Republic of Congo (DRC)

Unlike clade IIb, which predominantly impacts MSM, clade I mpox now shows a distinct epidemiological pattern. Clade I patients usually present with a more pronounced, diffuse rash, and the virus is more transmissible than clade IIb.[12] Infections with clade I mpox are also more severe and more deadly than infections with clade IIb. The case fatality ratio (CFR) for clade I mpox ranges from 1.4% to more than 10%, whereas the CFR for clade II is between 0.1% and 3.6%.[5,13,14] Historically, clade I has disproportionately impacted children—both in incidence and severity—a dynamic that remains consistent in the current clade I DRC outbreak. The exact animal reservoirs and routes of transmission placing the most affected populations at risk for clade I mpox currently remain unclear, although it is expected that many routes (zoonotic, household exposure, and sexual transmission) are the key drivers.[6]

The Democratic Republic of Congo (DRC) declared mpox a national epidemic in December 2022 due to rising numbers of cases and deaths. Most cases have been reported in children aged 15 years and younger. The CFR is significantly higher among children than among adults, particularly infants younger than 1 year. Epidemiologists have also documented heterosexual transmission in the DRC epidemic, particularly in sex workers [7, 12], constituting another epidemiological difference compared to the global clade II epidemic.

For this scenario, we determined the health risk **in the United States** to the **MSM community** is **low-moderate**, the health risk to **sex workers** is **low-moderate**, the health risk to **healthcare workers** is **low**, the health risk **to children** is **low**, and the health risk to the **general public** is **low.**

Our **confidence** in these risk scores is **moderate** given the current level of information for each of these factors.

To minimize the risk of additional clade I mpox outbreaks, the CDC and WHO recommend:

- Continuing efforts to enhance case detection and surveillance in the DRC and neighboring countries.[5,15]
- Continuing distribution of sample collection and transport kits to reference hospitals and logistical support for collecting, transporting, and examining samples from suspected cases in Kenge, Kinshasa, and other affected areas.[15]
- Continuing provision of funding, personnel support, and technical assistance to the DRC.[5]
- Clinicians and public health practitioners in the US and globally should be alert for possible cases in travelers from DRC and request clade-specific testing.[5]

Scenario B: Clade I Clusters or Outbreak in US

Summary

- Viral group: clade I
- Projected primary populations impacted: MSM community, sex workers, children

While there have not been any documented cases of clade I within the US thus far, introduction and transmission of clade I in the US would be novel and could result in a larger outbreak affecting different vulnerable groups than the previous (and current) mpox clade IIb global outbreak. This could significantly change the risk levels should such a scenario occur in the US. Although clade I and clade IIb are genetically similar enough that vaccines and treatments are expected to be effective, it is not well understood how prior infection with clade IIb or vaccination might protect from infection with or complications from clade I.[16,17] While there is a relatively low likelihood of this scenario occurring because of the clade I epidemic's current geography, the potential health consequences for a broader range of populations, including children, warrant additional preparedness efforts. Surveillance and reporting must increase, both in the DRC and the US.

The drivers and modes of transmission of clade I mpox are still not well understood, making it challenging to predict the potential trajectory of a US epidemic scenario. Based on existing

knowledge of the current clade I outbreak in the DRC, we know the most at-risk populations include the MSM community, sex workers, and children. If the US experienced a clade I outbreak, we believe those in the MSM community and sex workers who engage in higher risk sexual conduct and close contact would be more likely to be infected. These populations might also experience more severe disease. We expect a lower likelihood of children becoming infected with mpox clade I in the US because the main risk factors for transmission to children in the DRC are reported to be exposure to 1) animal reservoirs, 2) higher numbers of household occupants, and 3) limited resources for sanitation and hygiene, factors that are not expected to be as relevant in the US. Although the risk of transmission to US. children is expected to be lower in the event of a clade I outbreak than in the current DRC epidemic, the consequences would be similarly high due to the increased morbidity and mortality rates among children aged 15 and younger with suspected clade I clade I mpox in the DRC.[7] Therefore, the health risk level for children would also increase, as seen in the below table.

For this scenario, we determined the health risk **in the United States** to the **MSM community** is **moderate-high**, the health risk to **sex workers** is **moderate-high**, the health risk to **healthcare workers** is **low-moderate**, the health risk **to children** is **moderate**, and the health risk to the **general public** is **low-moderate.**

Our **confidence** in these risk scores is **low**.

To minimize risk of a clade I mpox outbreak in the US, the CDC and WHO recommend:

- All high-risk individuals should receive 2 doses of JYNNEOS vaccine.[1,9]
- US clinicians and public health practitioners should be alert for possible cases in travelers from DRC and request clade-specific testing.[5]

Risk Assessment

Mpox Scenario-Based Human Health

Clade I Mpox Human Health Risk Assessment Scenario Table for the US Population

	Risk Score (**this is risk level to human health NOT of scenario occurring**)				
	Risk to MSM community	**Risk to sex workers**	**Risk to healthcare workers**	**Risk to children**	**Risk to general public**
Scenario A – Sporadic imported clade I cases	Low-Moderate	Low-Moderate	Low	Low	Low
Scenario B – Clade I clusters or outbreak in US	Moderate-High	Moderate-High	Low-Moderate	Moderate	Low-Moderate

References

1. US Centers for Disease Control and Prevention. Mpox Vaccine Recommendations. Updated April 22, 2024. Accessed June 1, 2024. https://www.cdc.gov/poxvirus/mpox/vaccines/vaccine-recommendations.html
2. US Centers for Disease Control and Prevention. Information For Healthcare Professionals | Mpox. Updated April 22, 2024. Accessed June 1, 2024. https://www.cdc.gov/poxvirus/mpox/clinicians/index.html
3. US Centers for Disease Control and Prevention. Infection Control: Healthcare Settings | Mpox. Updated April 5, 2024. Accessed June 1, 2024. https://www.cdc.gov/poxvirus/mpox/clinicians/infection-control-healthcare.html
4. US Centers for Disease Control and Prevention. Ongoing 2022 Global Outbreak Cases and Data | Mpox. Updated March 5, 2024. Accessed June 1, 2024. https://www.cdc.gov/poxvirus/mpox/response/2022/index.html
5. McQuiston JH, Braden CR, Bowen MD, et al. The CDC Domestic Mpox Response — United States, 2022–2023. *MMWR Morb Mortal Wkly Rep*. 2023;72:547-552. doi:10.15585/mmwr.mm7220a2
6. US Centers for Disease Control and Prevention. 2023 Outbreak in Democratic Republic of the Congo. Updated May 30, 2024. Accessed June 1, 2024. https://www.cdc.gov/poxvirus/mpox/outbreak/2023-drc.html
7. McQuiston JH, Luce R, Kazadi DM, et al. U.S. Preparedness and Response to Increasing Clade I Mpox Cases in the Democratic Republic of the Congo — United States, 2024. *MMWR Morb Mortal Wkly Rep*. 2024;73:435-440. doi:10.15585/mmwr.mm7319a3
8. US Centers for Disease Control and Prevention. Nationally Notifiable Infectious Diseases and Conditions, United States: Weekly Tables. Weekly cases* of notifiable diseases, United States, US Territories, and Non-US Residents week ending May 25, 2024 (Week 15). Accessed June 1, 2024. https://wonder.cdc.gov/nndss/static/2024/21/2024-21-table968.html
9. European Centre for Disease Prevention and Control. Mpox infographics: staying prepared for the summer season. Published June 1, 2023. Accessed June 1, 2024. https://www.ecdc.europa.eu/en/news-events/mpox-infographics-staying-prepared-summer-season
10. US Centers for Disease Control and Prevention. Vaccination | Mpox. Updated April 22, 2024. Accessed June 1, 2024. https://www.cdc.gov/poxvirus/mpox/interim-considerations/overview.html
11. World Health Organization. Holding mass and large gathering events during the multi-country mpox outbreak in the WHO European Region: lessons identified for future mass gathering preparedness: meeting report, 22 February 2023. Published May 4, 2023. Accessed June 1, 2024. https://www.who.int/europe/publications/i/item/WHO-EURO-2023-7420-47186-69127

12.Kibungu EM, Vakaniaki EH, Kinganda-Lusamaki E, et al. Clade I–Associated Mpox Cases Associated with Sexual Contact, the Democratic Republic of the Congo. Emerg Infect Dis. 2024;30(1):172-176. doi:10.3201/eid3001.231164
13.Pittman PR, Martin JW, Kingebeni PM, et al. Clinical characterization and placental pathology of mpox infection in hospitalized patients in the Democratic Republic of the Congo. PLoS Negl Trop Dis. 2023;17(4):e0010384. doi:10.1371/journal.pntd.0010384
14.Bunge EM, Hoet B, Chen L, et al. The changing epidemiology of human monkeypox—A potential threat? A systematic review. PLoS Negl Trop Dis. 2022;16(2):e0010141. doi:10.1371/journal.pntd.0010141
15.World Health Organization. Mpox (monkeypox) - Democratic Republic of the Congo. Published November 23, 2023. Accessed June 1, 2024. https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON493
16.Ghazy RM, Elrewany E, Gebreal A, et al. Systematic Review on the Efficacy, Effectiveness, Safety, and Immunogenicity of Monkeypox Vaccine. *Vaccines*. 2023;11(11):1708. doi:10.3390/vaccines11111708
17.World Health Organization. Department of Immunizations, Vaccines, and Biologicals (IBV). SAGE Meeting Slide Decks. Published March 2024. Accessed June 1, 2024. https://terrance.who.int/mediacentre/data/immunization/SAGE_Slidedeck_March_2024.pdf

