Mpox Scenario-Based Human Health

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Evolving Outbreaks Updates

The mpox virus is classified into 2 main clades, clade I and clade II, with each further subdivided into clade Ia, the newly identified clade Ib, clade IIa, and clade IIb, the clade which was responsible for the 2022 global outbreak. Since the 2022 clade IIb mpox outbreak began, there have more than 124,753 cases and more than 272 deaths reported in 128 countries, though world-wide reported data likely do not include the most recent outbreaks in the Africa region. The US has reported 34,490 mpox cases and 63 deaths as of December 31, 2024.

Multiple countries across the world have experienced increased mpox activity in July, August, and September of 2024, with new detections of clade I and IIb in at 20 countries in Africa and new cases reported in the Americas, Europe, Oceania, and Asia.

Unlike clade IIb, which is primarily limited to the MSM community, the new clade Ib mpox now shows distinct epidemiological and clinical trends. Clade I has predominantly been detected in the DRC, with positive cases in all 26 provinces, however there have been outbreaks across Africa and cases reported in Germany, the UK, India, Sweden, Pakistan, Belgium, and Thailand in 2024. On November 16, 2024, the first case of clade Ib mpox was detected in the US and the second was detected on January 14, 2025. Historically, clade I has disproportionately impacted children—both in incidence and severity—a dynamic that remains consistent in the current clade I DRC outbreak. Currently, 67% of cases and 78% of deaths from Clade I in the DRC have been among persons 15 years or younger. Clade I patients usually present with a more pronounced, diffuse rash, and the virus is more transmissible than clade IIb Infections with clade I mpox are also more severe and more deadly than infections with clade IIb. The fatality risk ranges from 1.4 to more than 10%, whereas the CFR for clade II is between 0.1% and 4% 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. whereas the CFR for clade II is between 0.1% and 4% 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.

The 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. Africa CDC reports that almost 70% of the cases in DRC are in children younger than 15 and that the caseload in this age group accounts for 85% of all deaths. Epidemiologists have also documented heterosexual transmission in the DRC epidemic, particularly involving sex workers, constituting another epidemiological difference compared to the global clade II epidemic.

**Please note:* *Detailed mpox situation updates are available on the CORI website.*

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

Appendix: Additional Details on Process and Recommendations

Scenario 1: Clade I Surge in Africa

Summary

- Viral group: clade Ib and IIb
- Projected primary population impacted: MSM community, sex workers, and children

This scenario anticipates an increase in clade I and II mpox transmission in Africa, with similar severity of disease for each respective clade, though a faster and stronger surge in the more deadly clade Ib. 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, the health risk to children is low and the health risk to the general public is low.

Our **confidence** in these risk scores is low given the current level and availability of information for each of these factors; historical knowledge from past outbreaks on transmission dynamics; the availability of vaccination and treatment resources; and the federally mandated CDC reporting freeze and recent administration changes at the federal, state, and local level. We have chosen to reduce our confidence score primarily due to our low confidence in the comprehensiveness of the surveillance measures and reporting at this time. Confidence levels in risk scores may return to high once CDC reporting resumes

Scenario 2: Sporadic Imported Clade I Cases

Summary

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

This scenario anticipates the importation of occasional clade I cases into the US, but no sustained local transmission. For this scenario, we determined the health risk in the United States to the MSM community is moderate, the health risk to sex workers is moderate, the health risk to healthcare workers is low, the health risk to children is low-moderate, and the health risk to the general public is low.

Our **confidence** in these risk scores is low given the current level and availability of information for each of these factors; historical knowledge from past outbreaks on transmission dynamics; the availability of vaccination and treatment resources; and the federally mandated CDC reporting freeze

and recent administration changes at the federal, state, and local level. We have chosen to reduce our confidence score primarily due to our low confidence in the comprehensiveness of the surveillance measures and reporting at this time. Confidence levels in risk scores may return to high once CDC reporting resumes

Scenario 3: Sustained Clade I Transmission in the US

Summary

- Viral group: clade Ib and IIb
- Projected primary populations impacted: MSM community, sex workers, children

While there have not been any documented cases of clade Ib within the US thus far, introduction of clade Ib to the US would be novel and could result in a larger outbreak affecting different vulnerable groups than those primarily impacted by clade IIb mpox virus. This could significantly change the risk levels should such a scenario occur in the US. The potential health consequences for a broader range of populations, including children, warrant additional preparedness efforts. Surveillance and reporting must increase, both across Africa and the US.

Although clade Ib 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. The antiviral drug Tecovirimat that is used to reduce symptoms and shorten the length of infection for clade IIb mpox infections, has produced no medical benefit when used in clade Ib cases.

The drivers and modes of transmission of clade Ib 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 Ia and Ib outbreak in the DRC, we know the most at-risk populations include the MSM community, sex workers, and children. If the US experienced a sustained clade Ib 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 Ib 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 Ib 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 mpox in the DRC.

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, the health risk to children is moderate-high, and the health risk to the general public is low-moderate.

Our **confidence** in these risk scores is low given the current level and availability of information for each of these factors; historical knowledge from past outbreaks on transmission dynamics; the availability of vaccination and treatment resources; and the federally mandated CDC reporting freeze and recent administration changes at the federal, state, and local level. We have chosen to reduce our confidence score primarily due to our low confidence in the comprehensiveness of the surveillance measures and reporting at this time. Confidence levels in risk scores may return to high once CDC reporting resumes

Recommendations for all scenarios to minimize risk of a clade Ib mpox outbreak in the US:

- Vaccination and other medical counter measures
  - All individuals with an increased risk of infection should receive 2 doses of JYNNEOS vaccine and 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 and other healthcare professionals should also wear all recommended personal protective equipment (PPE) when completing mpox testing.
  - 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
- Behavior-related activities
  - Individuals can reduce their risk by talking with sexual partners about mpox and practicing safer sex and good hygiene.
- Mass gatherings and other social gatherings
  - 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 nondiscrimination approach across different media and incorporate educational and awareness-raising initiatives related to mpox and other diseases of concern.
- Surveillance, case detection, and management
  - 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.

- Continuing efforts to enhance case detection and surveillance in the DRC and neighboring countries.
- 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.
- Continuing provision of funding, personnel support, and technical assistance to the DRC
- 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.

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

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 steadily growing 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**, the 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 and availability of information for each of these factors; historical knowledge from past outbreaks on transmission dynamics; the availability of vaccination and treatment resources; and the federally mandated CDC reporting freeze and recent administration changes at the federal, state, and local level. We have chosen to reduce our confidence score primarily due to our low confidence in the comprehensiveness of the surveillance measures and reporting at this time. Confidence levels in risk scores may return to high once CDC reporting resumes.

Scenario 2: Autumn Clade II Surge

Summary

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

This scenario anticipates an increase in clade IIb mpox transmission throughout the autumn months, with similar severity of disease and affected populations.

For this scenario, we determined the health risk **in the United States** to the **MSM community** is **moderate**, the health risk to **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 **low** given the current level and availability of information for each of these factors; historical knowledge from past outbreaks on transmission dynamics; the availability of vaccination and treatment resources; and the federally mandated CDC reporting freeze and recent administration changes at the federal, state, and local level. We have chosen to reduce our confidence score primarily due to our low confidence in the comprehensiveness of the surveillance measures and reporting at this time. Confidence levels in risk scores may return to high once CDC reporting resumes.

Scenario 3: Autumn Clade IIb Case Decline

Summary

- Viral group: clade IIB
- Current primary populations impacted: MSM community, sex workers

In this scenario, we consider the impacts on human health in the US if there were to be a decline of clade IIb mpox cases through the autumn months.

For this scenario, we determined the health risk **in the United States** to the **MSM community** is **moderate**, the health risk to **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 **low** given the current level and availability of information for each of these factors; historical knowledge from past outbreaks on transmission dynamics; the availability of vaccination and treatment resources; and the federally mandated CDC reporting freeze and recent administration changes at the federal, state, and local level. We have chosen to reduce our confidence score primarily due to our low confidence in the comprehensiveness of the surveillance measures and reporting at this time. Confidence levels in risk scores may return to high once CDC reporting resumes.

Recommendations for all scenarios to minimize the transmission of mpox clade IIb in the US:

- Vaccination and other medical counter measures
    - All individuals with an increased risk of infection should receive 2 doses of JYNNEOS vaccine and 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 and other healthcare professionals should also wear all recommended personal protective equipment (PPE) when completing mpox testing.
    - 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
- Behavior-related activities
    - Individuals can reduce their risk by talking with sexual partners about mpox and practicing safer sex and good hygiene.
- Mass gatherings and other social gatherings
    - 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 nondiscrimination approach across different media and incorporate educational and awareness-raising initiatives related to mpox and other diseases of concern.
- Surveillance, case detection, and management
    - 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.

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