Does viral evolution influence the public health response to mpox outbreaks?

Viral sub-species classification workshop
Bacterial and Virus - Bioinformatics Resource Center
National Institutes of Health (NIH)
National Institute of Allergy and Infectious Diseases (NIAID)

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Technical lead for orthopoxvirus diseases
Head, Smallpox Secretariat

10 April 2024
### Global mpox epidemiology - confirmed cases (most clade IIb MPXV)

#### Cumulative: 01 Jan 2022 – 29 Feb 2024

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed cases</td>
<td>94,707</td>
</tr>
<tr>
<td>Deaths</td>
<td>181</td>
</tr>
<tr>
<td>Countries reporting cases</td>
<td>117</td>
</tr>
</tbody>
</table>

#### 2024 to date: 01 – 31 Feb 2024

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed cases</td>
<td>715</td>
</tr>
<tr>
<td>Deaths</td>
<td>2</td>
</tr>
<tr>
<td>Countries reporting cases</td>
<td>29</td>
</tr>
</tbody>
</table>

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**Total mpox cases** from 1 Jan 2022, as of 29 Feb 2024

**Total mpox deaths** from 1 Jan 2022, as of 29 Feb 2024

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**Notes:** All data shown includes probable and confirmed mpox cases.
Global mpox outbreak - epidemic curve, over 2 years and last 6 months, confirmed cases

01 Jan 2022 – 29 Feb 2024

01 Sep 2023 - 29 Feb 2024

Notes: All data shown includes probable and confirmed mpox cases.
Epidemic curves by WHO region, confirmed cases

Notes: Different Y-axis scales between charts.
Global mpox deaths by region, among confirmed cases

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Mpx deaths</th>
<th>Mpx cases</th>
<th>Case fatality ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMR</td>
<td>138</td>
<td>60 887</td>
<td>0.2%</td>
</tr>
<tr>
<td>EUR</td>
<td>8</td>
<td>26 843</td>
<td>0.03%</td>
</tr>
<tr>
<td>WPR</td>
<td>18</td>
<td>2 834</td>
<td>0.6%</td>
</tr>
<tr>
<td>AFR</td>
<td>22</td>
<td>2 429</td>
<td>0.9%</td>
</tr>
<tr>
<td>SEAR</td>
<td>2</td>
<td>833</td>
<td>0.2%</td>
</tr>
<tr>
<td>EMR</td>
<td>1</td>
<td>95</td>
<td>1%</td>
</tr>
</tbody>
</table>

Although reporting of mpox deaths is not exhaustive, its variability might be due to differences in:
- Surveillance system and detection of cases
- Access and quality of health services
- Presence of comorbidities such as uncontrolled HIV
- MPXV clade I, IIa, IIb and lineage differences + gene deletions and APOBEC mutations

Notes: All data shown includes confirmed mpox deaths
Mpox in the African Region in 2022-24 – Global surveillance data

- **2,712 laboratory-confirmed cases** and **22 deaths among confirmed cases**.
- These represent **3%** of global confirmed cases and **12%** of global deaths.
- Nigeria and DRC report the most cases in the African Region.

Median age is **17 (IQR: 7 - 32)**.
Standing recommendations for mpox issued by Director-General in accordance with IHR (2005) – August 2023 – August 2024

**States Parties are recommended to:**

<table>
<thead>
<tr>
<th>A. Have <strong>national mpox plans</strong> integrated into broader health systems. Capacities that have been built in resource-limited settings and among marginalized groups should be sustained.</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. Strengthen and sustain <strong>testing and surveillance</strong> capacity and ensure that new cases of mpox are notified nationally and to WHO.</td>
</tr>
<tr>
<td>C. Protect communities through <strong>communication and engagement</strong>; continue to build trust and fight stigma and discrimination.</td>
</tr>
<tr>
<td>D. <strong>Invest in research</strong> to better understand mpox disease and transmission patterns, and to develop improved vaccines, tests, and treatments.</td>
</tr>
<tr>
<td>E. <strong>Provide travelers with information</strong> to protect themselves and others before, during and after travel and refrain from implementing travel-related health measures, including mpox screening and testing for travelers.</td>
</tr>
<tr>
<td>F. <strong>Deliver optimal clinical care</strong> for mpox patients, integrated within HIV and STI programmes, with access to treatments and measures to protect health workers and caregivers.</td>
</tr>
<tr>
<td>G. <strong>Work towards equitable access to safe, effective and quality-assured vaccines</strong>, tests and treatments for mpox.</td>
</tr>
</tbody>
</table>


Mpox in the Democratic Republic of the Congo

Provinces affected by mpox (February 2024)

Suspected (clinically compatible) cases of mpox reported (1996 to W8-2024)

2021: 2,993 cases; 81 deaths, CFR 2.7%
2022: 5,677 cases; 213 deaths, CFR 3.7%
2023: 14,626 cases; 654 deaths, CFR 4.5%
2024 (W1-W12): 4,538 cases, 296 deaths, CFR 6.5%

Source: Ministère de la santé, hygiène et prévention
Public Health Response – Joint WHO/MOH Mission

- Joint mission in Nov – Dec 2023, including full participation of national HIV/AIDS control programme.
- To assess mpox outbreak and public health response.
Mpx in the Democratic Republic of the Congo – 2022 to 2024

- **Cumulative W1 – W8 2024:**
  - 3576 suspected cases and 264 deaths reported (CFR=7.4%).

- **Epidemiological Week 8 2024:**
  - 570 suspected cases and 30 mpx deaths (5.3%)

**Source:** Ministère de la santé, hygiène et prévention

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**Mpx suspected cases W1-2022 to W8-2024.**

**Mpx deaths W1-2022 to W8-2024.**
Epidemiological situation of mpox in **Equateur Province**

**Equateur in 2024 (W1 – W8):**
- 2034 suspected cases and 208 deaths, CFR = **10.2%**.
- Accounts for 64% of cases and 84% deaths reported in DRC in 2024.
- Lotumbe Health Zone most affected, 1696 cases, 202 deaths, **CFR 11.9%**
- Annualized incidence per 100k: Equateur 444, Bolomba 335, Lotumbe 6543

**For reference**
- For smallpox prior to eradication, DRC reported in 1963
  - a peak of 5523 cases and 710 deaths (CFR 12.8%, 16% for variola major and 2.9% for variola minor).

WHO. Smallpox and its eradication. Table 18.1. https://iris.who.int/handle/10665/39485
Mpox in the Democratic Republic of the Congo – clade I confirmed/presumed

Suspected cases of mpox reported by age, sex, and health zone (2023)

- **Rising number** of cases, deaths reported
  - 12% laboratory-confirmed, >60% test+
  - co-infection 2 mpox/HIV, 1 mpox/HIV/syphilis,

- **Geographic expansion** – 23/26 provinces, Kinshasa
  - Affecting mining areas, South Kivu
  - Border countries at risk – civil unrest, population movements

- **Sexual transmission**, sex workers, key populations, households

- **Rising case fatality** ratio
Examples of mpox cases, Kamituga, SK (October 2023)
Animal to human transmission
Rapid risk assessment – Democratic Republic of the Congo
7 December 2023

<table>
<thead>
<tr>
<th>Risk question</th>
<th>Likelihood</th>
<th>Consequence</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk for human health?</td>
<td>Likely</td>
<td>Moderate</td>
<td>High</td>
</tr>
<tr>
<td>Risk of event spreading?</td>
<td>Highly likely</td>
<td>Moderate</td>
<td>High</td>
</tr>
<tr>
<td>Risk of insufficient control capacities?</td>
<td>Almost certain</td>
<td>Major</td>
<td>Very High</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Incidence - general population (cases per 100,000)</th>
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<tbody>
<tr>
<td>2022 - 2023</td>
</tr>
<tr>
<td>Global</td>
</tr>
<tr>
<td>USA</td>
</tr>
<tr>
<td>DRC</td>
</tr>
<tr>
<td>Equateur</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>14</td>
</tr>
<tr>
<td>248</td>
</tr>
</tbody>
</table>

End 2023: incidence was 1224 cases /100,000 pop in Bolomba HZ

Globally, the mpox outbreak remains a WHO grade 2 protracted emergency
MPXV Genomic epidemiology by clade

Clade I MPXV likely to be endemic in eastern Africa (confirmed in South Sudan and Sudan)

Data from GenBank and GISAID as of 16/02/2024
MPXV phylogeny prior to global outbreak – clade I

- West African clade (Iib) outbreak begins, Nigeria 2017
- Central African clade outbreaks continue sporadically in several countries
- Cameroon only country to have both clades
- Steadily growing case reports in the DRC but few are sequenced
Clades renamed
- Central African clade to clade I
- West African clade to clade II

Global IIb outbreak linked almost exclusively to sexual transmission

New outbreak in Sudan
- Clade I from 2022 Sudan close to clade I from 2005 South Sudan
MPXV Genomic epidemiology – clade I

- Divergent lineages within clade I:
  - Sequences from Sudan (2005, 2022)
  - New clade I cluster 2024 (South Kivu)
- South Kivu: Gene deletion of CDC-recommended clade I specific PCR target location leading to potential diagnostic failure if relying on clade-specific tests only.
  - In DRC, non-v variola orthopoxvirus generic PCR is followed by clade-specific PCR as needed (strategy would detect novel strain).
- Outside DRC, diagnostic algorithm review is recommended
- Mutations suggestive of APOBEC activity

Source: GenBank and GISAID as of 16/02/2024
MPXV Genomic epidemiology by clade

- Gaps in reporting of clade I sequences (in GenBank and GISAID)
- Resurgence of clade I driven by DRC

Data from GenBank and GISAID as of 16/02/2024, acknowledgement to Lorenzo Subissi and colleagues for genomic epidemiology and phylogenetic figures.
Mpox in the Democratic Republic of the Congo – in summary

2024

• Continuing rise in reported cases, deaths
  • One in five health zones already reporting >4500 cases
  • Approx 10% laboratory-confirmed, nationally >75% test+
  • mpox/HIV, mpox/HIV/syphilis: >7 cases now reported
  • Equateur – outbreak focus moving to new health zones (e.g. from Bolomba HZ to Lotumbe HZ)
  • Role of zoonotic transmission not known
  • Kamituga, South Kivu outbreak continues

• Outbreaks of mpox represent a health security risk
  • Global immunity gap since smallpox eradication and cessation of vaccination

• Continuing enhanced studies in animals (e.g. Sud Ubangi bat colony)

11-13 April 2024- Interministerial meeting on mpox in the African region, Kinshasa, DRC
Epidemiology and transmission dynamics

- Differences in disease severity and fatality, particularly in endemic areas (children most affected)
- Recognition as a sexually transmissible disease with HIV/STI co-infections in all contexts
- Enhanced human-to-human transmission (clade IIb APOBEC-related mutations also suspected for clade I)
- Impact on transmissibility and reverse impact of enhanced transmission on continuing viral evolution

Performance of diagnostics: gene deletions leading to diagnostic failure of clade I specific PCR

- Assessment and review of diagnostic protocols
- Recommendations may differ by context
- Need for sequencing for confirmation in some circumstances
- Update of WHO laboratory guidance in process
Global, regional and local outbreaks of mpox – public health implications of viral sub-species and viral evolution (1)

Performance of therapeutics
- Early evidence of resistance to antiviral agent tecovirimat seen in a few immunocompromised patients with prolonged MPXV infections; suggests combination therapy desirable

Performance of vaccines
- Vaccine effectiveness is high pre-exposure, low in post-exposure – may be linked to shorter incubation period of clade IIb
- Currently unknown if vaccinia vaccine effectiveness of 3rd generation vaccines will differ by clade
- Importance of adapting vaccination strategies and vaccines selected to local context
- New vaccine development targets conserved OPXV genes

One Health
- Continuing enhanced studies in animals (e.g. in Nigeria, DRC Sud Ubangi bat colony)
Global strategic framework for mpox (2024 – 2027)

Goal

Achieve sustained elimination of human-to-human transmission of mpox

Objectives

(1) Achieve control of mpox in every context

(2) Advance mpox research and access to countermeasures

(3) Minimize animal-human transmission

Elimination of human-to-human transmission is the absence of new cases (without defined travel history or zoonotic exposure) for \( \geq \) three months in the presence of adequate surveillance. This goal applies to all countries and contexts.
THANK YOU