
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)

Dr Rosamund LEWIS

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Head, Smallpox Secretariat

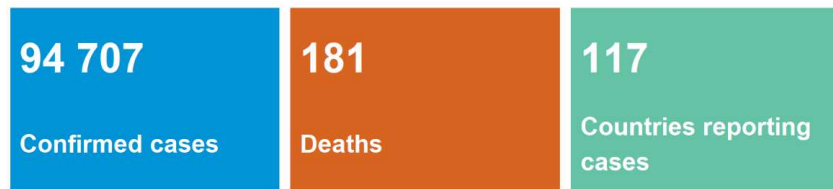
10 April 2024



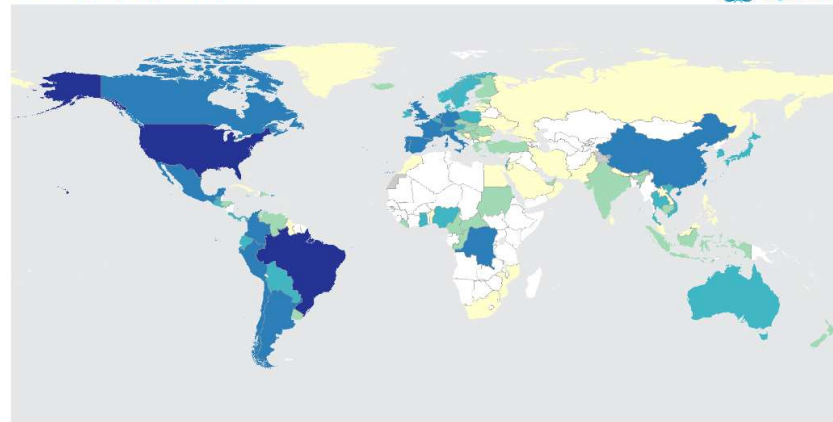
**World Health
Organization**

Global mpox epidemiology - confirmed cases (most clade IIb MPXV)

Cumulative: 01 Jan 2022 – 29 Feb 2024



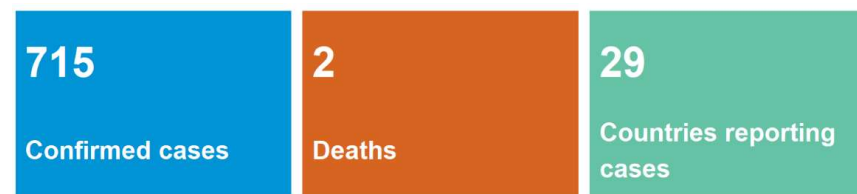
Total mpox cases
from 1 Jan 2022, as of 29 Feb 2024



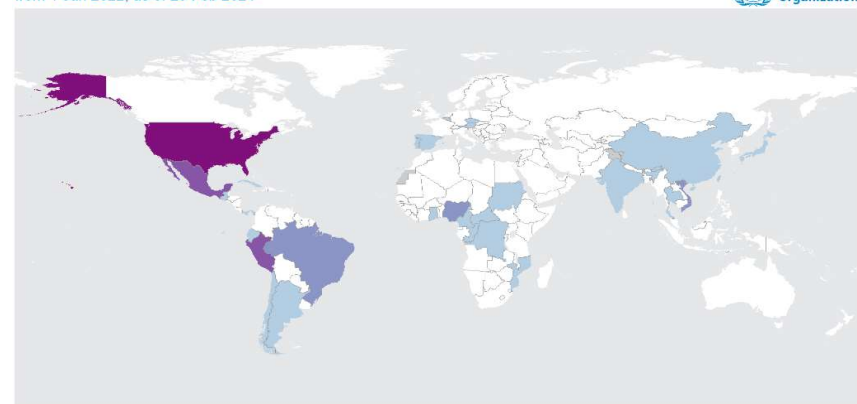
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Date: Source: World Health Organization
Map: Production: WHO Health Emergencies Programme
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2024 to date: 01 – 31 Feb 2024



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

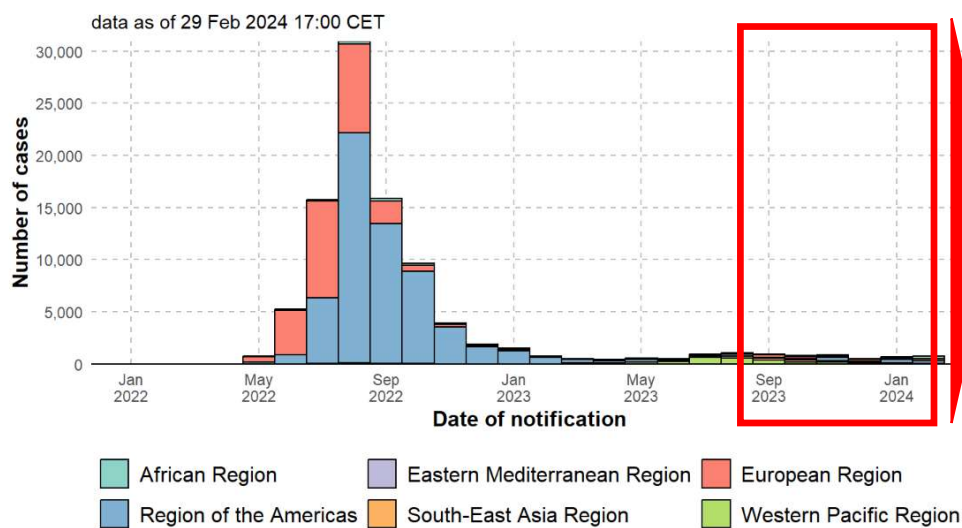


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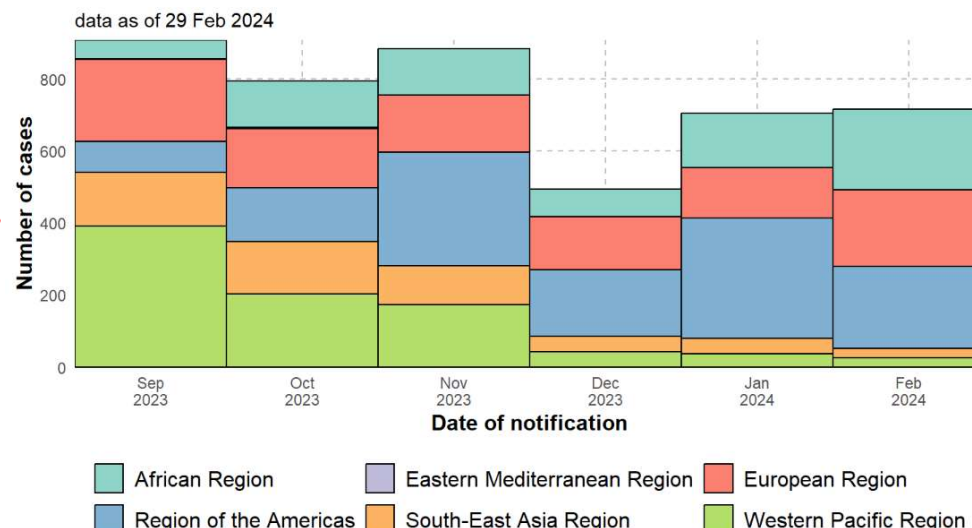
Global mpox outbreak - epidemic curve, over 2 years and last 6 months, confirmed cases

01 Jan 2022 – 29 Feb 2024



Source: WHO

01 Sep 2023 - 29 Feb 2024

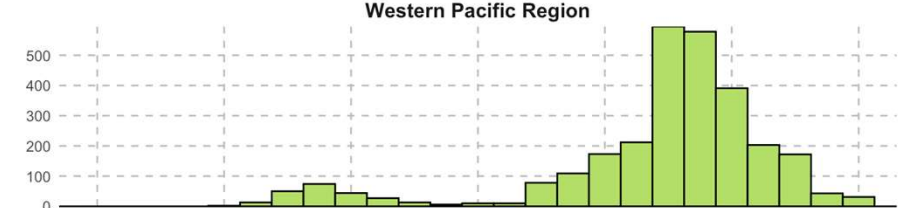
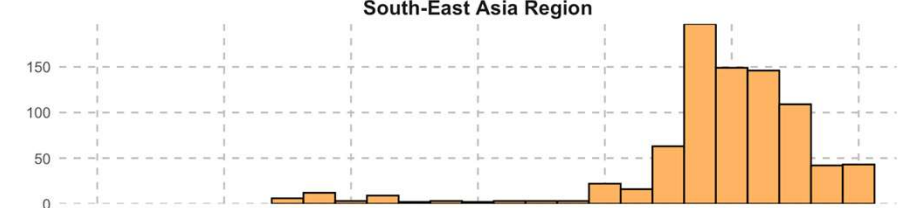
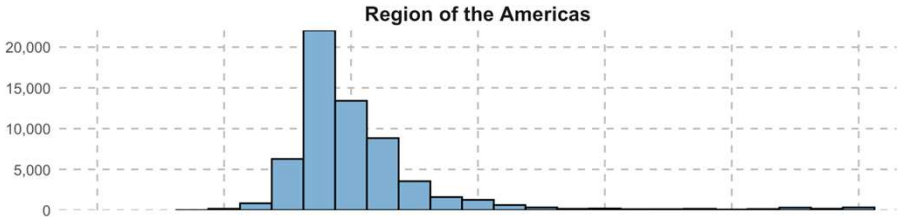
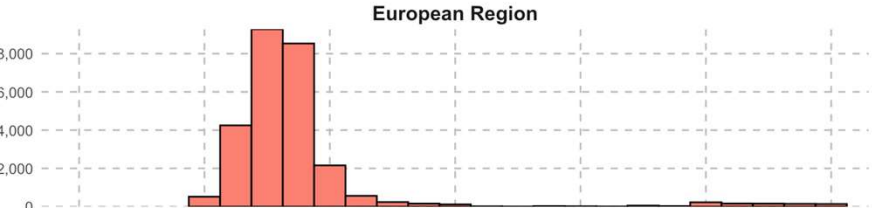
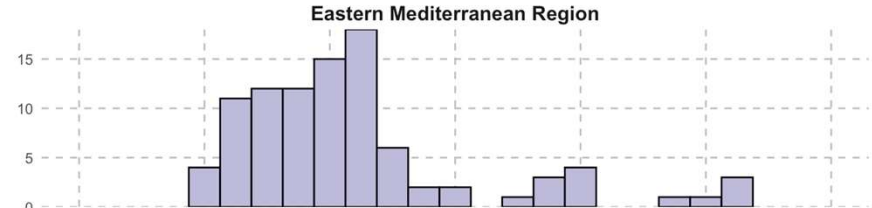
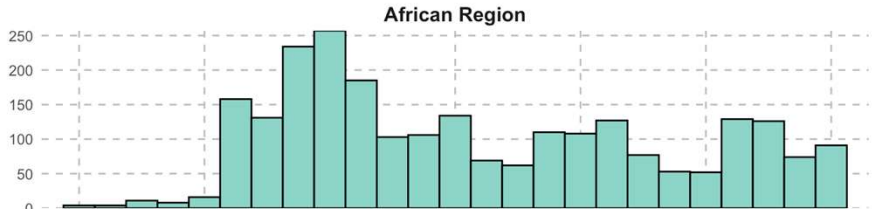


Source: WHO

Notes: All data shown includes probable and confirmed mpox cases.

Epidemic curves by WHO region, confirmed cases

data as of 31 Jan 2024 17:00 CET



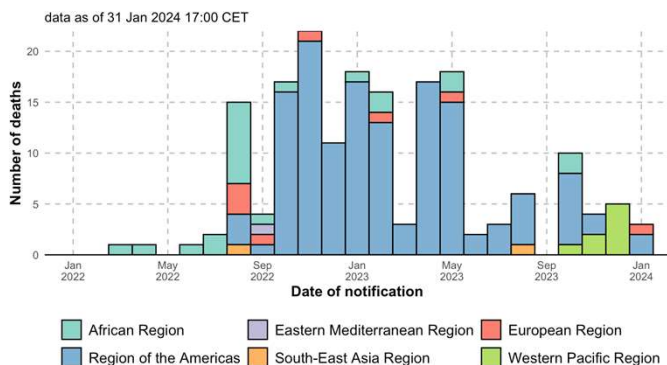
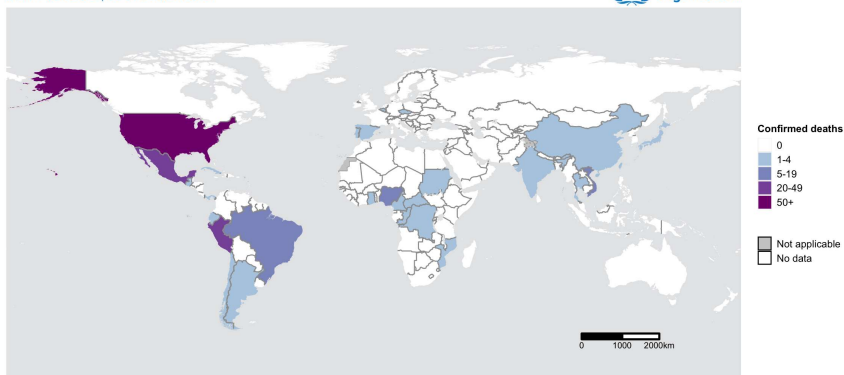
Source: WHO

Notes: Different Y-axis scales between charts.



Global mpox deaths by region, among confirmed cases

Total mpox deaths
from 1 Jan 2022, as of 31 Jan 2024



Source: WHO

Notes: All data shown includes confirmed mpox deaths

WHO region	Mpox cases	Mpox deaths	Case fatality ratio
AMR	60 887	138	0.2%
EUR	26 843	8	0.03%
WPR	2 834	18	0.6%
AFR	2 429	22	0.9%
SEAR	833	2	0.2%
EMR	95	1	1%

Although reporting of mpox deaths is not exhaustive, its variability might be due to differences in:

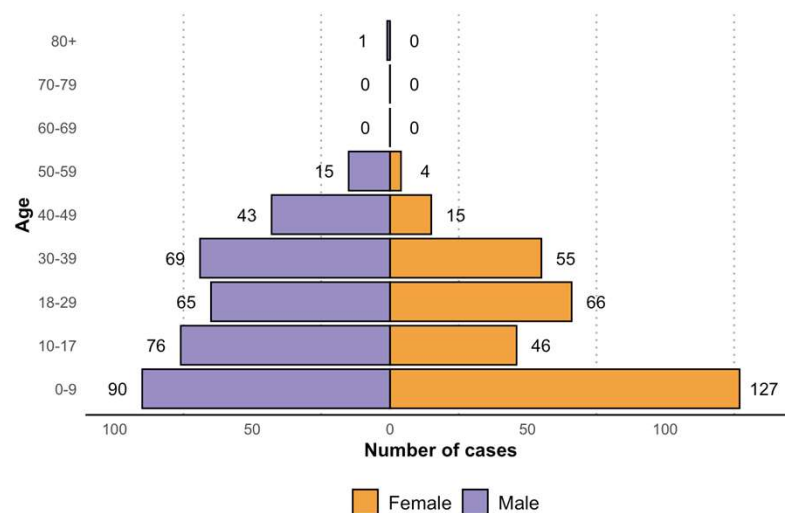
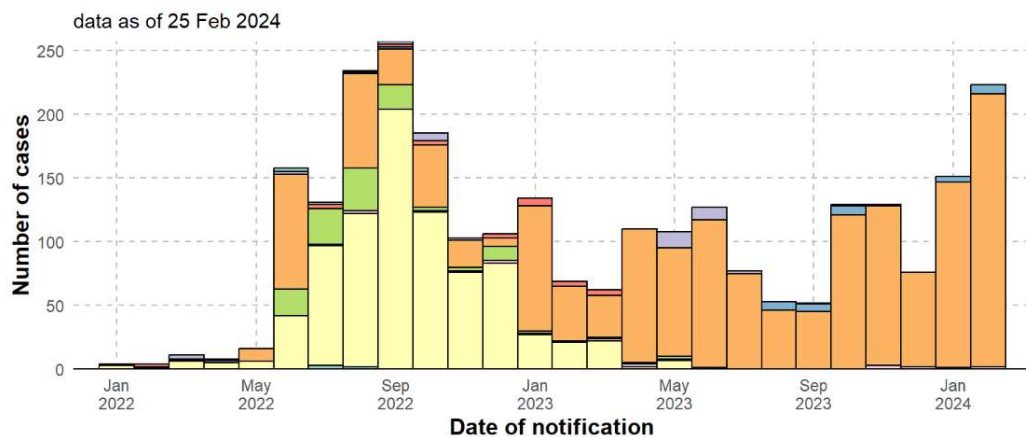
- Surveillance system and detection of cases
- Access and quality of health services
- Presence of comorbidities such as uncontrolled HIV
- **MPXV clade I, IIa, IIb and lineage differences + gene deletions and APOBEC mutations**



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)**.



Source: WHO

Source: WHO
672 cases with age-sex data

Standing recommendations for mpox issued by Director-General in accordance with IHR (2005) – August 2023 – August 2024

States Parties are recommended to:

A. Have **national mpox plans** integrated into broader health systems. Capacities that have been built in resource-limited settings and among marginalized groups should be sustained.

B. Strengthen and sustain **testing and surveillance** capacity and ensure that new cases of mpox are notified nationally and to WHO.

C. Protect communities through **communication and engagement**; continue to build trust and fight stigma and discrimination.

D. **Invest in research** to better understand mpox disease and transmission patterns, and to develop improved vaccines, tests, and treatments.

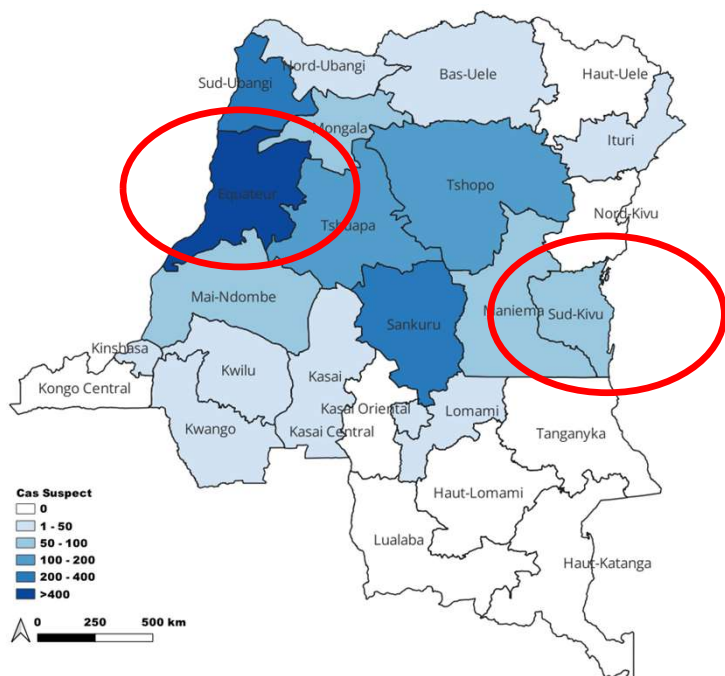
E. **Provide travelers with information** to protect themselves and others before, during and after travel and refrain from implementing travel-related health measures, including mpox screening and testing for travelers.

F. **Deliver optimal clinical care** for mpox patients, integrated within HIV and STI programmes, with access to treatments and measures to protect health workers and caregivers.

G. **Work towards equitable access to safe, effective and quality-assured vaccines, tests and treatments for mpox.**

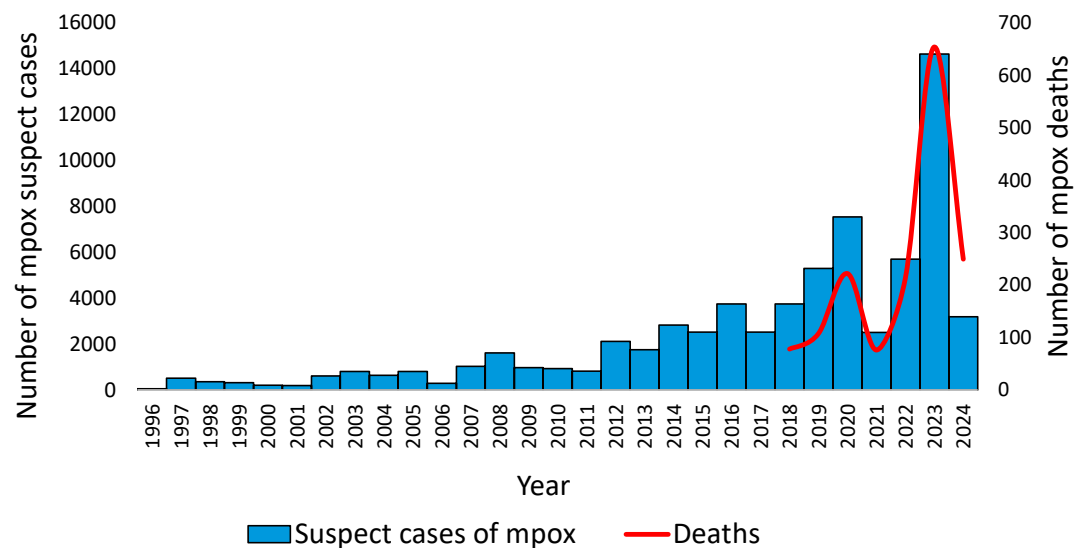
Mpox in the Democratic Republic of the Congo

Provinces affected by mpox (February 2024)



Source: Ministère de la santé, hygiène et prévention

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): 4538 cases, 296 deaths, CFR 6.5%

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.



Mpox (monkeypox)- Democratic Republic of the Congo

23 November 2023

<https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON493>

EMERGING INFECTIOUS DISEASES®

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Volume 30, Number 1—January 2024

Dispatch

Clade I-Associated Mpox Cases Associated with Sexual Contact, the Democratic Republic of the Congo



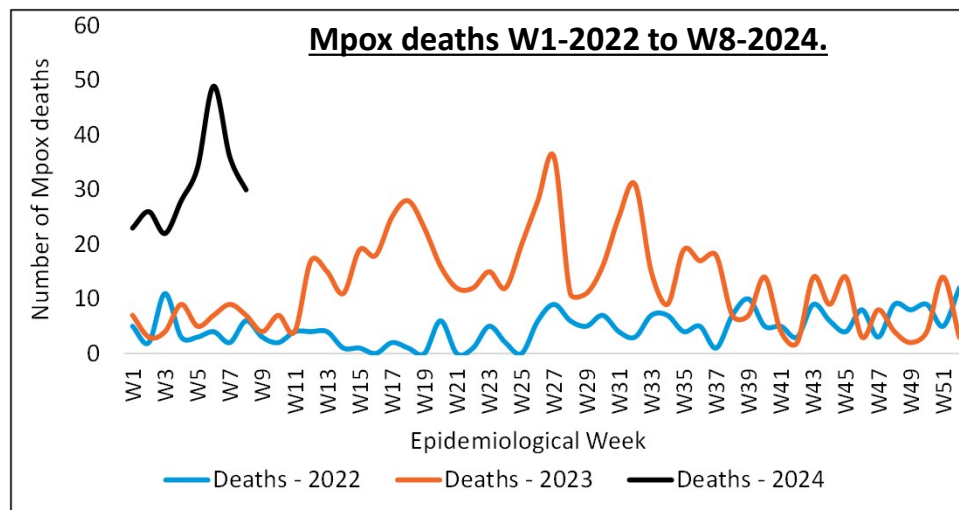
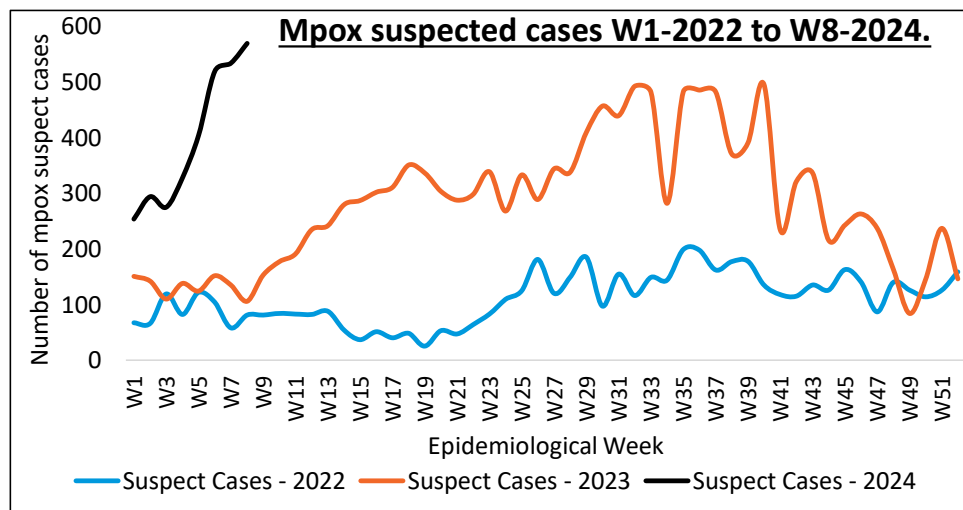
Mpox in the Democratic Republic of the Congo – 2022 to 2024

- **Cumulative W1 – W8 2024:**

- 3576 suspected cases and 264 deaths reported (CFR=7.4%).

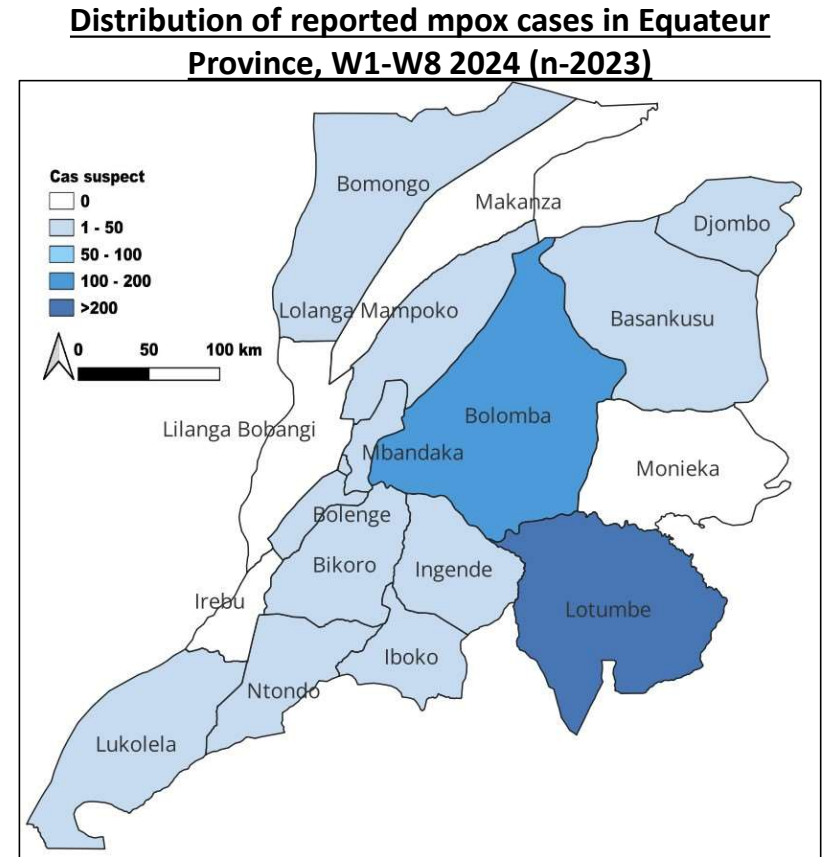
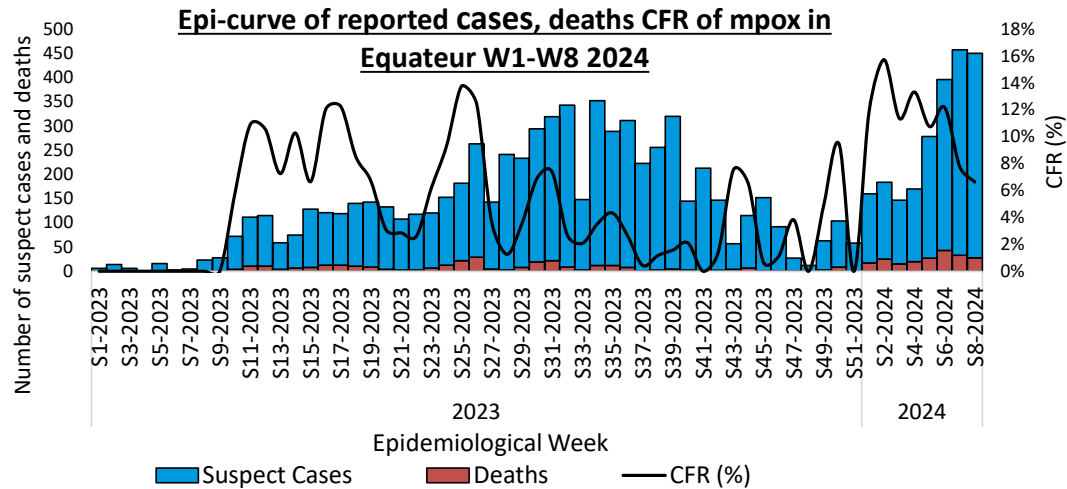
- **Epidemiological Week 8 2024:**

- 570 suspected cases and 30 mpox deaths (5.3%)



Source: Ministère de la santé, hygiène et prévention

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

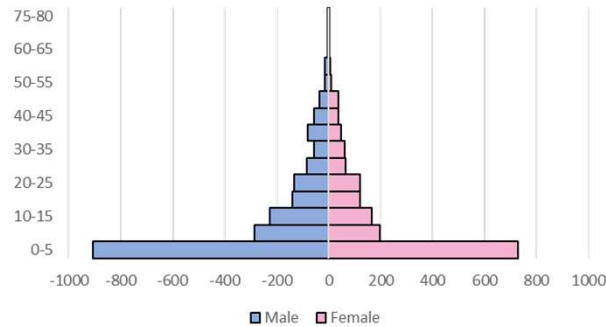
- For smallpox prior to eradication, DRC reported in 1963
 - a peak of 5523 cases and 710 deaths (CFR 12.8%, 16% for variola major and 2.9% for variola minor).

WHO. Smallpox and its eradication. Table 18.1. <https://iris.who.int/handle/10665/39485>

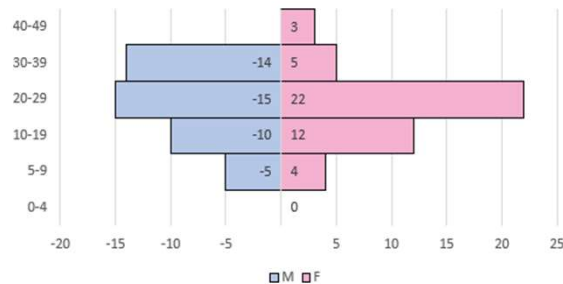
Mpox in the Democratic Republic of the Congo – clade I confirmed/presumed

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

Bolomba,
Equateur



Kamituga,
South Kivu



- **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



Public health response – Joint WHO/MOH Mission

Rapid risk assessment – Democratic Republic of the Congo

7 December 2023

Incidence - general population (cases per 100,000)			
2022 - 2023		2023	
Global	USA	DRC	Equateur
1	10	14	248

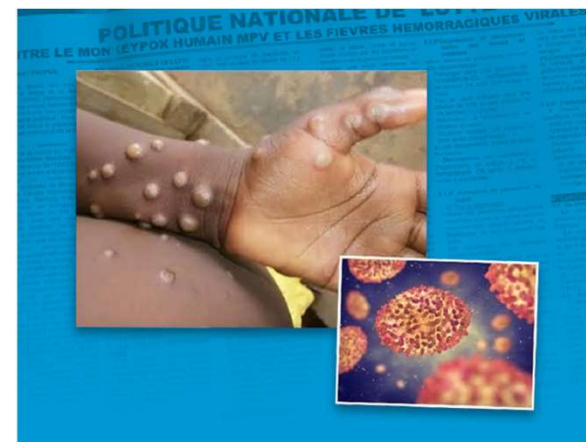
Risk question	Assessment		Risk
	Likelihood	Consequence	
Risk for human health?	Likely	Moderate	High
Risk of event spreading?	Highly likely	Moderate	High
Risk of insufficient control capacities?	Almost certain	Major	Very High

Overall risk level	Confidence in the available information
High	Moderate

[Mission Report](#)

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

Globally, the mpox outbreak remains a WHO grade 2 protracted emergency



La variole simienne (monkeypox) en République démocratique du Congo

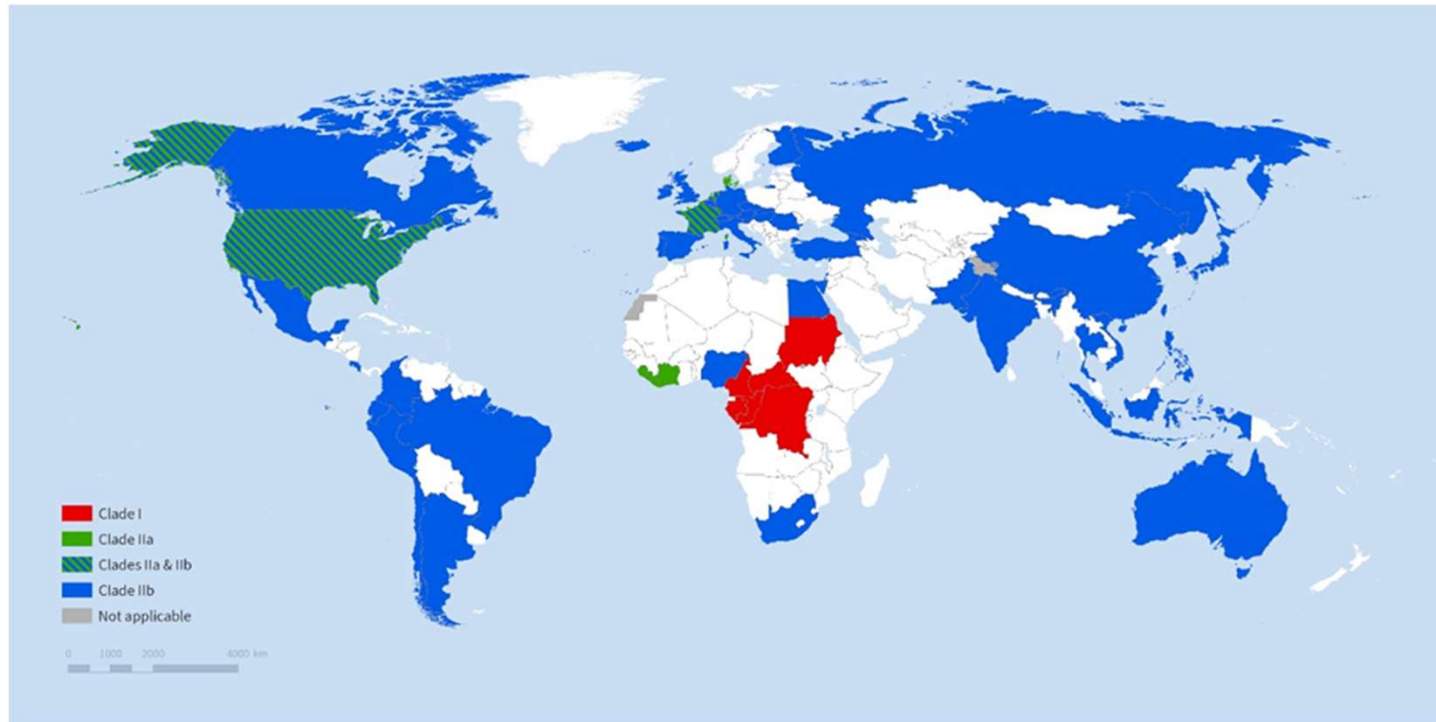
Evaluation de la situation
Rapport de mission conjointe

Le Ministère de la Santé publique, Hygiène et Prévention
avec
L'Organisation mondiale de la Santé

22 novembre – 12 décembre 2023



MPXV Genomic epidemiology by clade

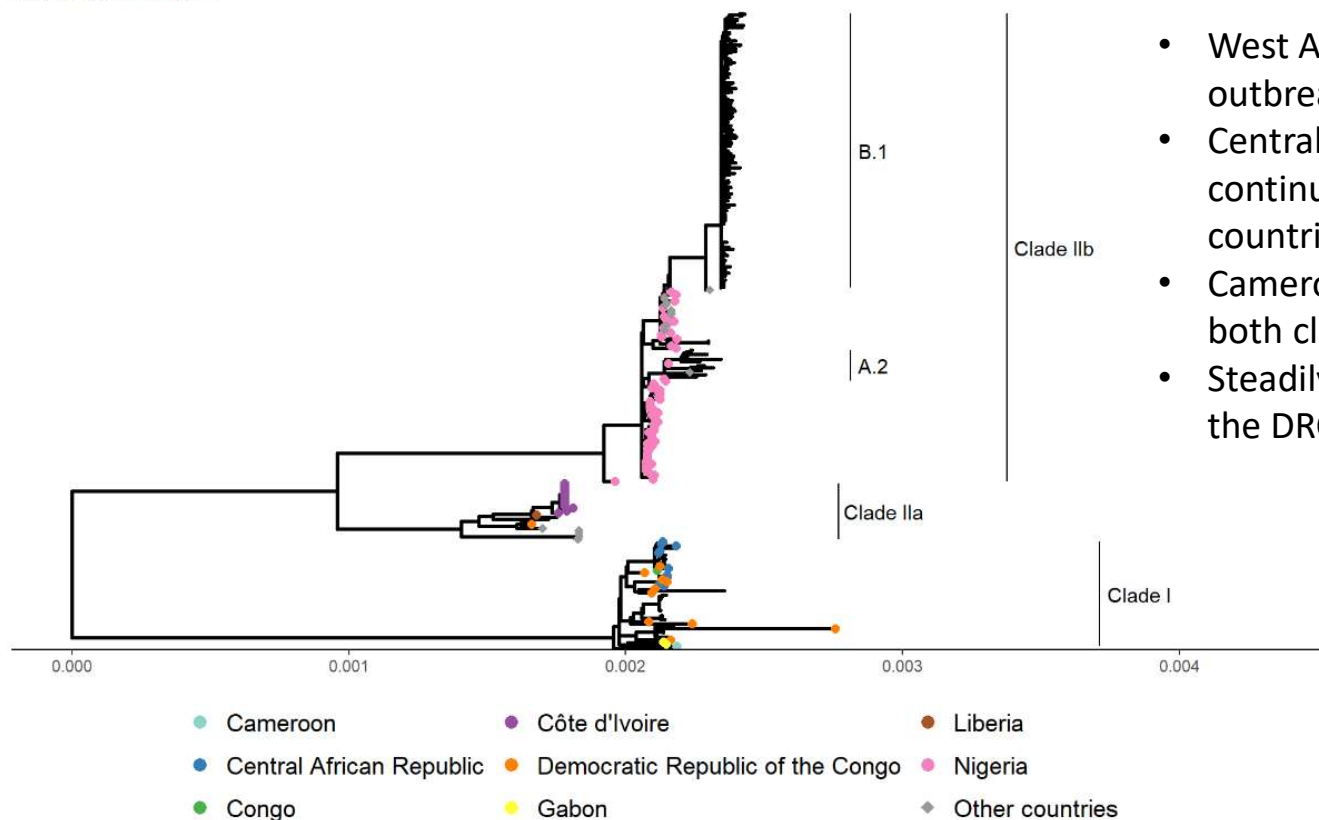


Clade I MPXV likely to be endemic in eastern Africa (confirmed in South Sudan and Sudan)

Data from GenBank and GISAID as of 16/02/2024

MPXV phylogeny prior to global outbreak – clade I

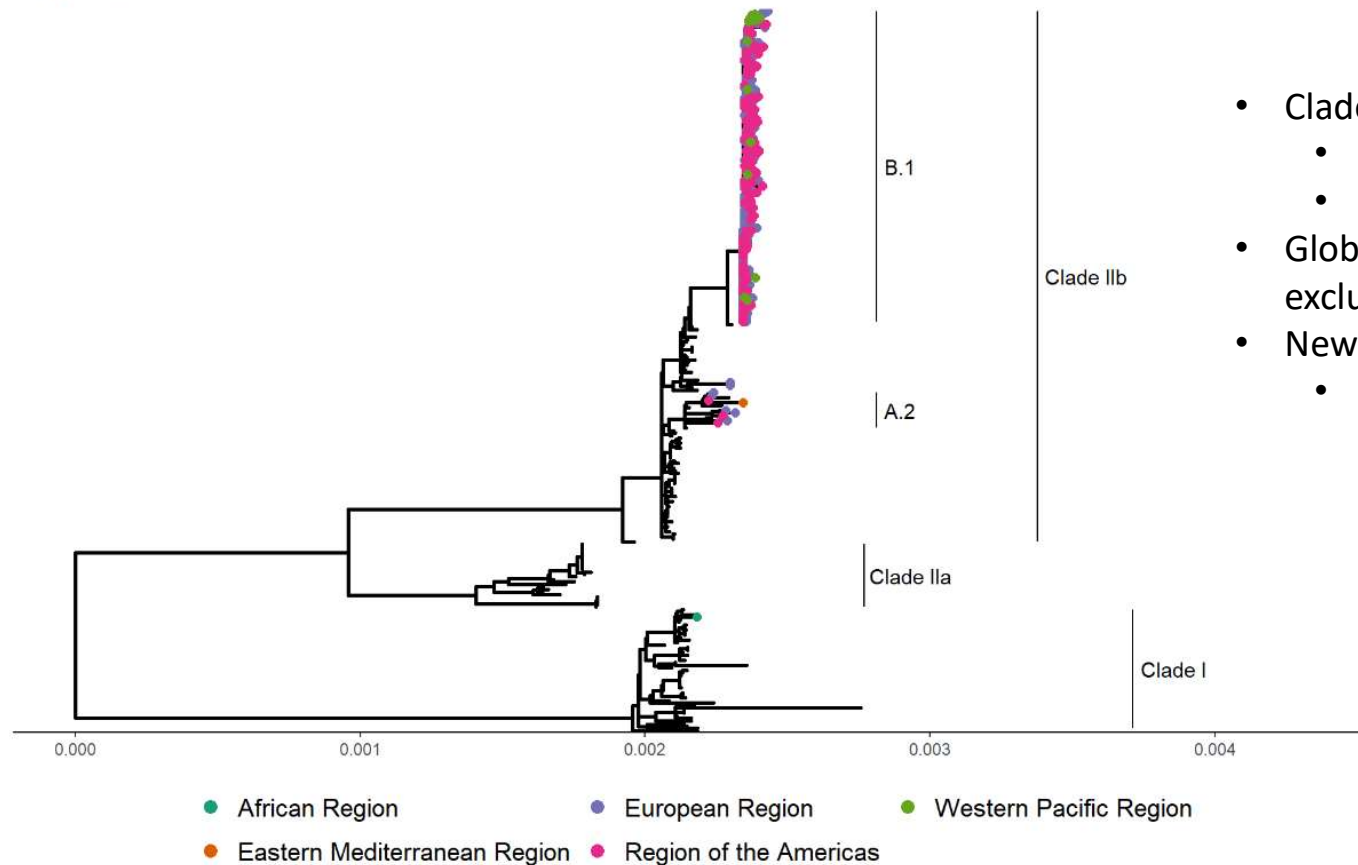
B.1 clade shown at smaller scale for visual clarity
 Ends labeled for cases before 2022, by country of origin
 Data as of 26 Jul 2023



- 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

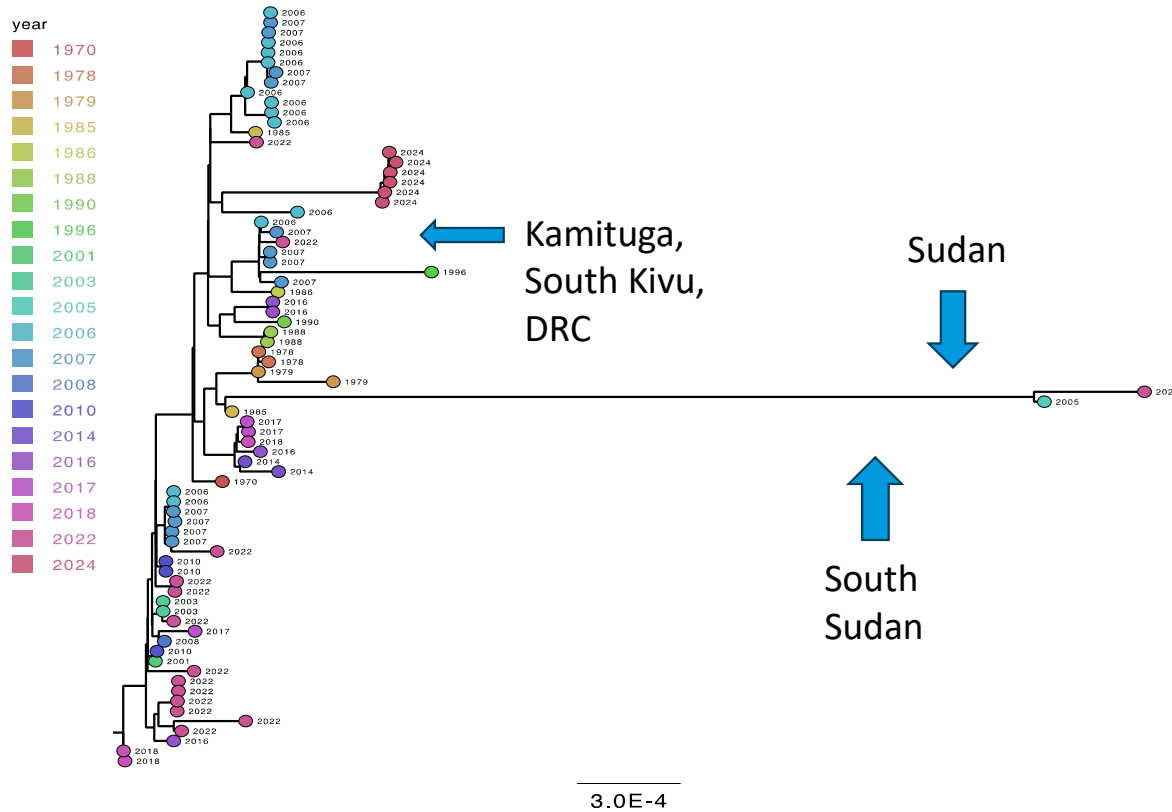
MPXV phylogeny during global outbreak – clades I, II, IIb

B.1 lineage reduced in scale for clarity
Data as of 26 Jul 2023



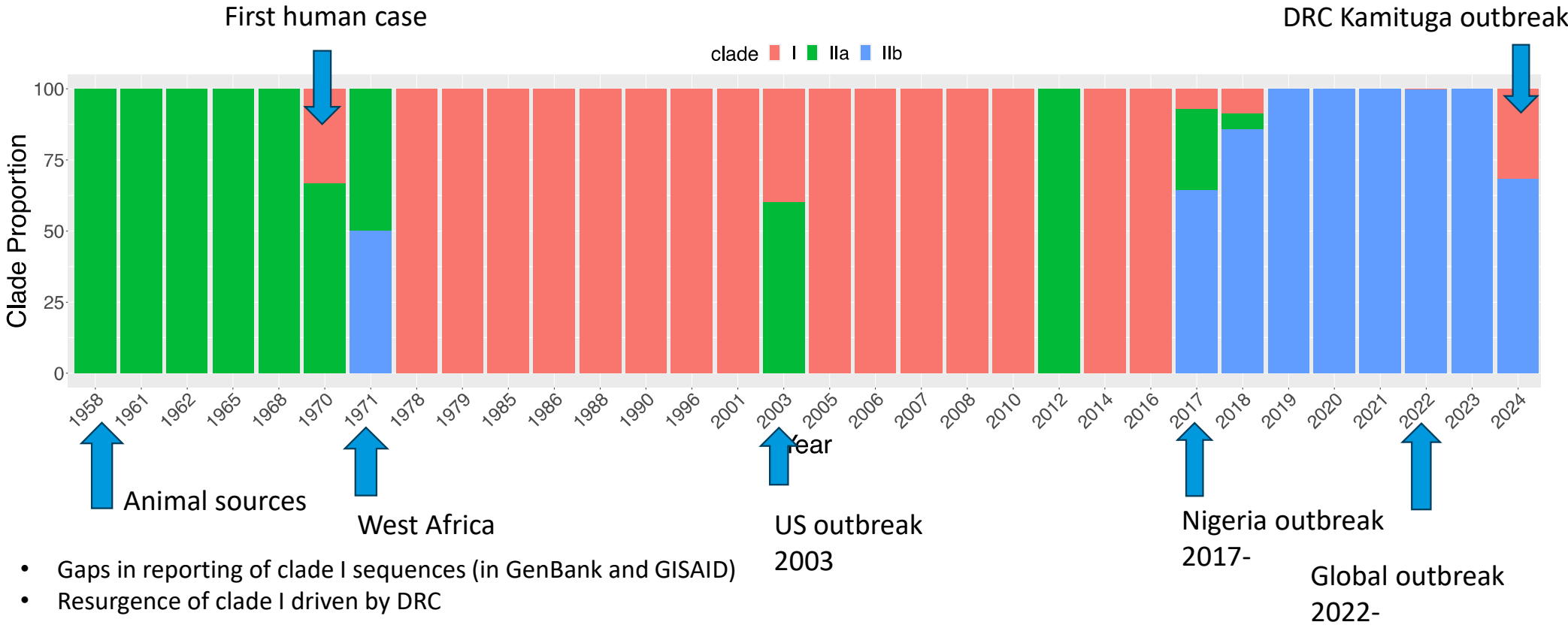
- Clades renamed
 - Central African clade to clade I
 - West African clade to clade II
- Global IIb outbreak linked almost exclusively to sexual transmission
- New outbreak in Sudan
 - Clade I from 2022 Sudan close to clade I from 2005 South Sudan

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-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

MPXV Genomic epidemiology by clade



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

20 *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



COORDINATION ET COLLABORATION
POUR UN CONTROLE ACCELERE DES
URGENTES SANITAIRES

LUTE CONTRE LE MPOX ET LE CHOLERA EN RDC

Réunion de haut niveau des partenaires

10 février 2024



Global, regional and local outbreaks of mpox – public health implications of viral sub-species and viral evolution (1)

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



[DRC Sitrep Mpxx 001-2024-FV.pdf](#)

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)



[meeting report here](#)



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