WHO EPIWIN

Genomics in the mpox health emergency response

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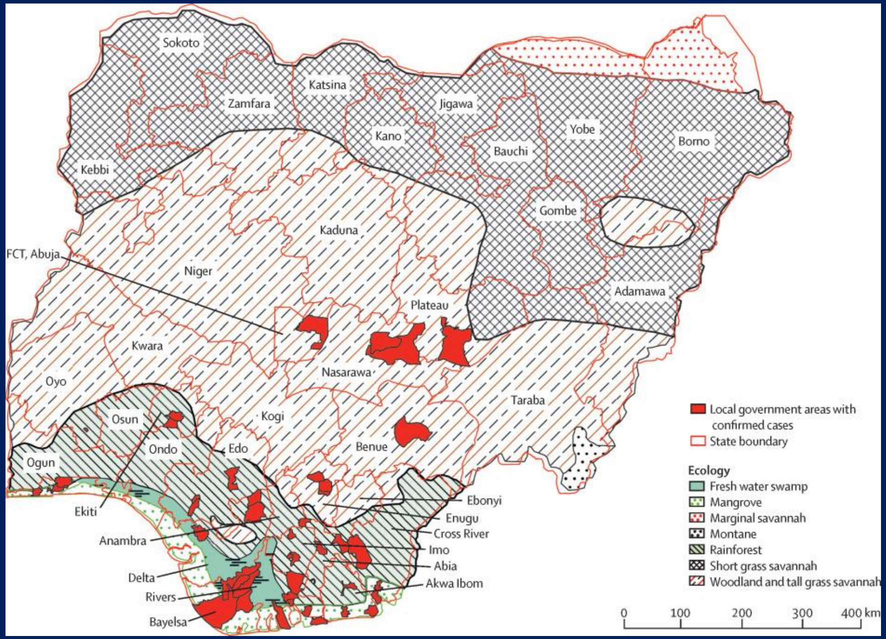
April 16th 2025

IPSN

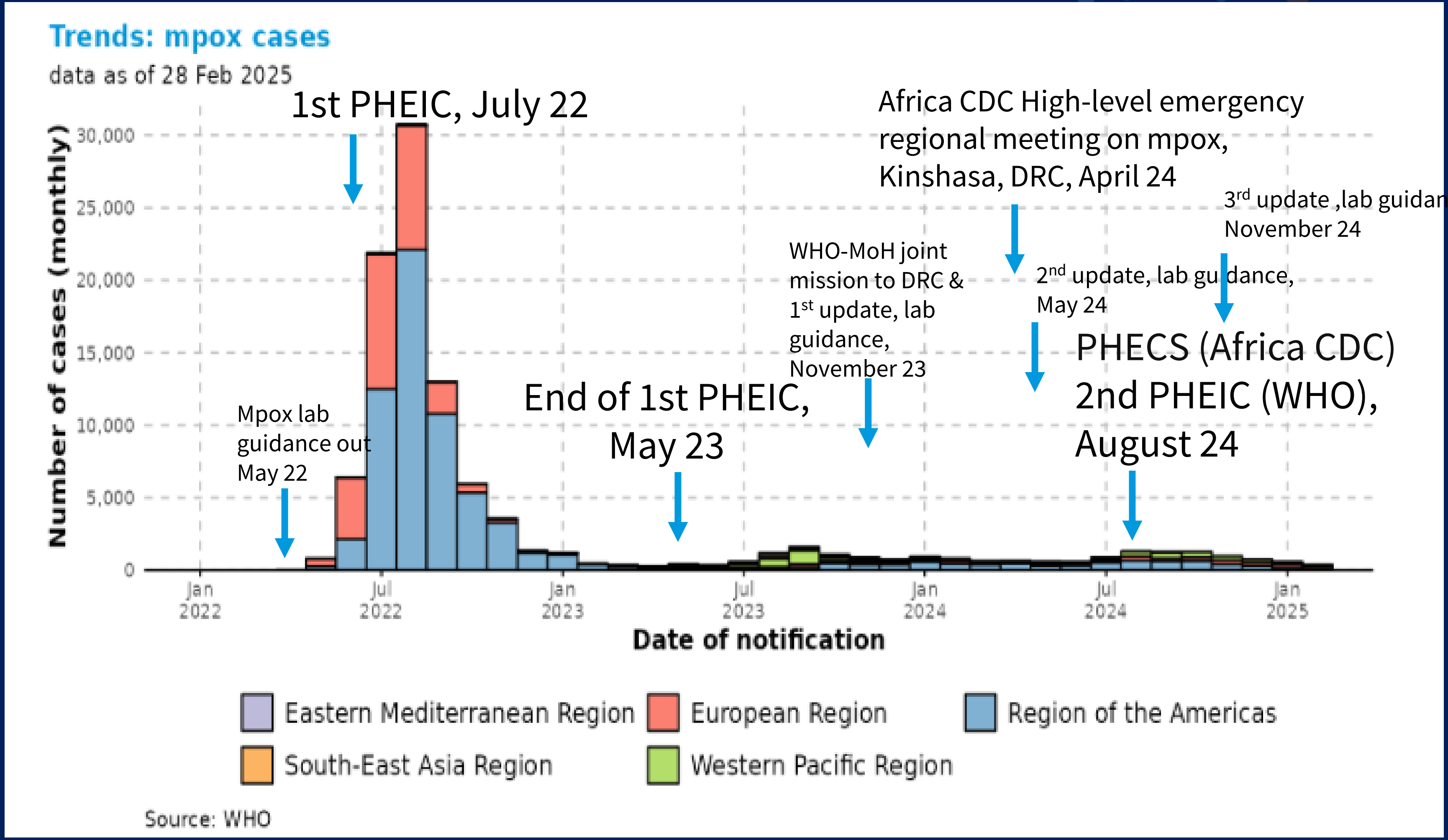
Mpox

- Mpox virus is a dsDNA virus, *orthopoxvirus* genus, *poxviridae* family
- Historically linked to zoonotic transmission; African rodents, especially squirrels, are suspected to be involved
- Endemic in Central (Clade I) and Western Africa (Clade II)
- Caused sporadic clade II cases outside of Africa in the 2000s
- Large outbreak in Nigeria in 2017-2018: genomic data suggested that there have been multiple introductions into the human population from animal reservoir, with some evidence of human-to-human transmission



Yinka-Ogunleye A et al Lancet ID 2019

Global epidemiology of mpox, 2022-ongoing


Trends: mpox cases

data as of 28 Feb 2025

Mpox lab guidance out May 22

1st PHEIC, July 22

End of 1st PHEIC, May 23

WHO-MoH joint mission to DRC & 1st update, lab guidance, November 23

Africa CDC High-level emergency regional meeting on mpox, Kinshasa, DRC, April 24

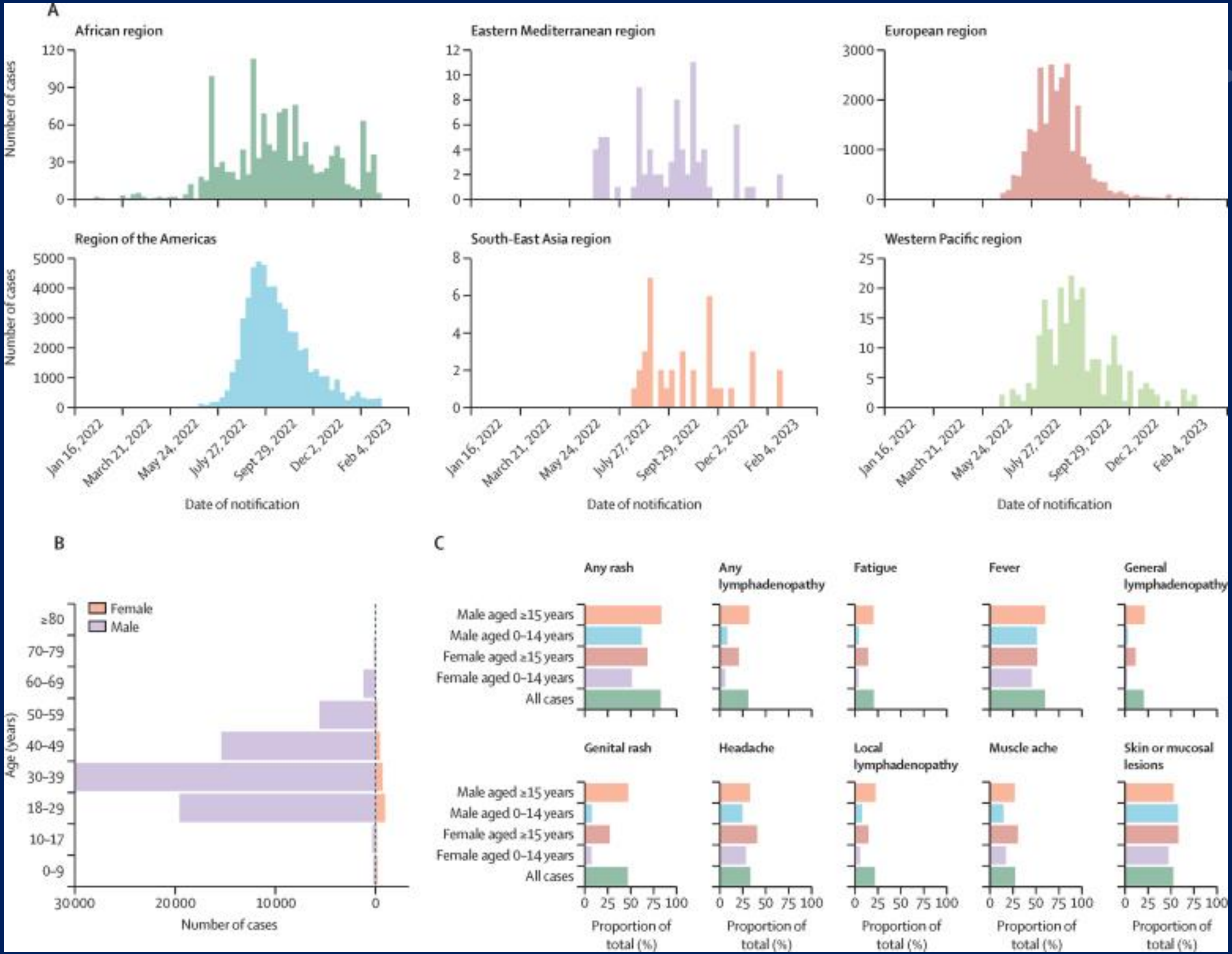
2nd update, lab guidance, May 24

PHECS (Africa CDC) 2nd PHEIC (WHO), August 24

3rd update ,lab guidance, November 24

Source: WHO

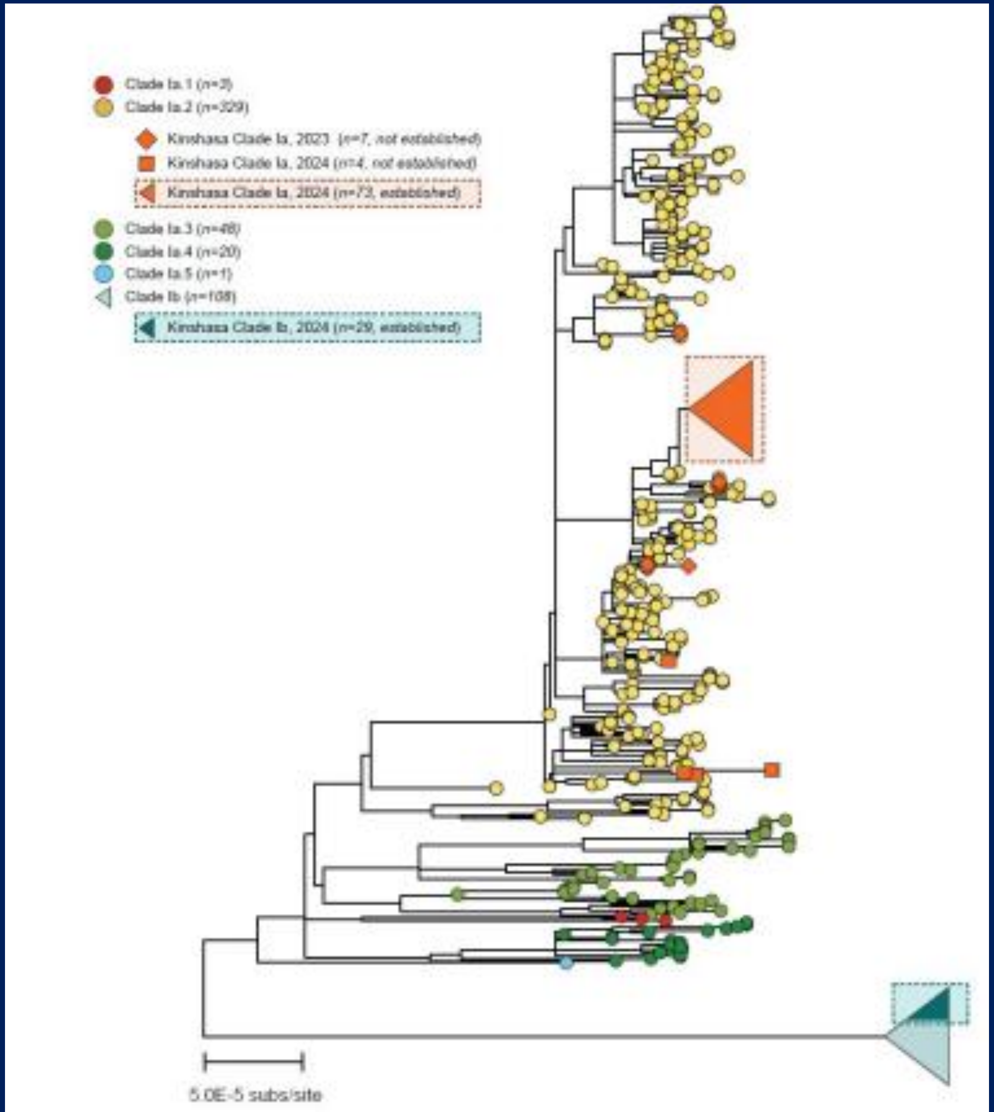
MPXV Clade IIb multi-country outbreak, 2022-2024



- WHO Global data from Jan 2022 to Jan 2023
- 96% males
- 89% self-identify as MSM
- Of those with known HIV status, almost half were HIV-positive
- Increased odds of hospitalization for those immunosuppressed either due to being HIV positive or other immunocompromising conditions
- Sexual transmission among MSM as main driver of mpox epidemiology

Laurenson-Schafer et al Lancet GH 2023

Inferring type of transmission from genetic data



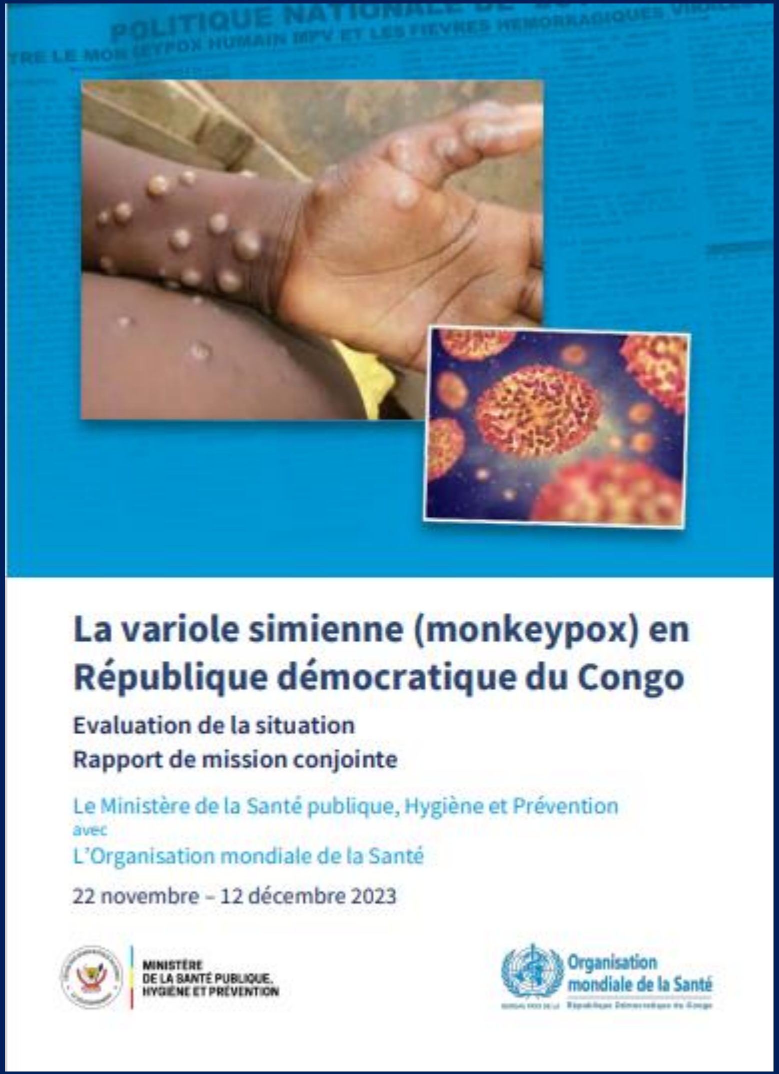
- Researchers identified specific mutations in the virus's genome that are characteristic of editing by human APOBEC3 enzymes—proteins that can induce mutations in viral DNA.

- These mutations have been accumulating since at least 2016 in Nigeria, suggesting that MPXV has been transmitting among humans for several years, rather than being solely a zoonotic infection from animal reservoirs

- This finding indicates a shift in the virus's transmission dynamics, highlighting the importance of monitoring its evolution and spread in human populations.

O’Toole et al Science 2023; Kinganda-Lusamaki et al Cell 2024; Wawina Bokalanga et al Lancet accepted

WHO-MoH Joint mission, November 2023, DRC



La variole simienne (monkeypox) en République démocratique du Congo

Evaluation de la situation
Rapport de mission conjointe

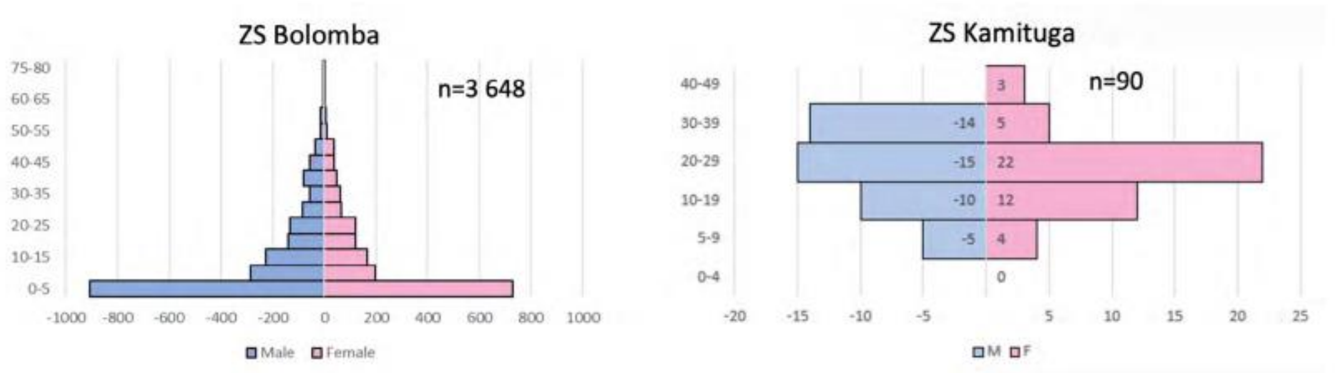
Le Ministère de la Santé publique, Hygiène et Prévention
avec
L'Organisation mondiale de la Santé

22 novembre – 12 décembre 2023

MINISTÈRE DE LA SANTÉ PUBLIQUE, HYGIÈNE ET PRÉVENTION

Organisation mondiale de la Santé

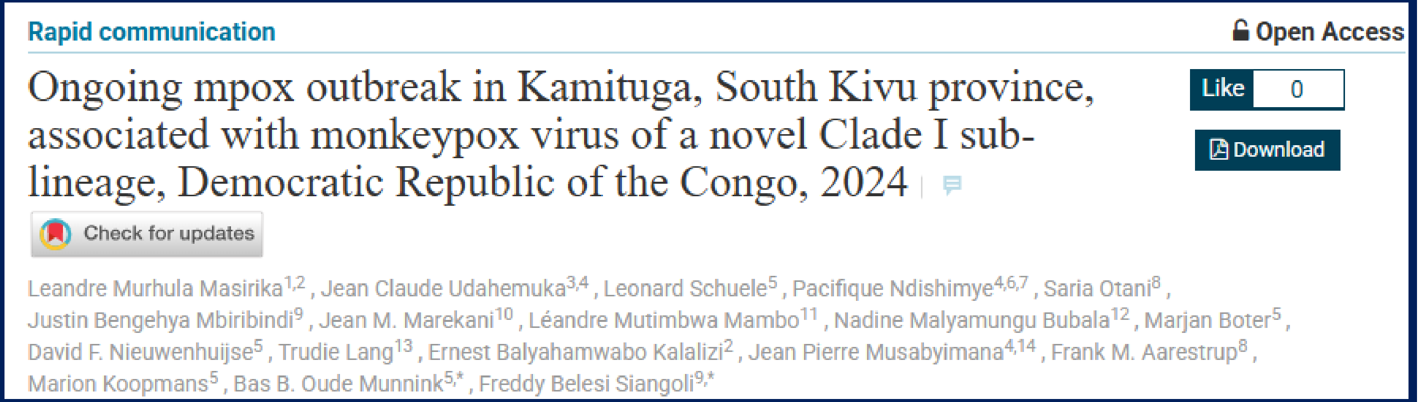
Figure 4. Répartition par âge et par sexe des cas suspects de monkeypox dans les Zones de Santé de Bolomba (Equateur) et Kamituga (Sud Kivu), Semaines épidémiologiques 1 - 48, 2023



- Another major shift in the epidemiology (this time mpox clade I) in newly affected province (South Kivu)
- Involvement of sex workers and their clients

[La variole simienne (monkeypox) en République démocratique du Congo: Évaluation de la situation Rapport de mission conjointe (22 novembre – 12 décembre 2023) - Democratic Republic of the Congo | ReliefWeb]

Genomic analysis reveals emergence of clade Ib



Rapid communication Open Access

Ongoing mpox outbreak in Kamituga, South Kivu province, associated with monkeypox virus of a novel Clade I sub-lineage, Democratic Republic of the Congo, 2024

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Leandre Murhula Masirika[1,2] , Jean Claude Udahemuka[3,4] , Leonard Schuele[5] , Pacifique Ndishimye[4,6,7] , Saria Otani[8] , Justin Bengehya Mbiribindi[9] , Jean M. Marekani[10] , Léandre Mutimbwa Mambo[11] , Nadine Malyamungu Bubala[12] , Marjan Boter[5] , David F. Nieuwenhuijse[5] , Trudie Lang[13] , Ernest Balyahamwabo Kalalizi[2] , Jean Pierre Musabyimana[4,14] , Frank M. Aarestrup[8] , Marion Koopmans[5] , Bas B. Oude Munnink[5,*] , Freddy Belesi Siangoli[9,*]

Brief Communication | Open access | Published: 13 June 2024

Sustained human outbreak of a new MPXV clade I lineage in eastern Democratic Republic of the Congo

Emmanuel Hasivirwe Vakaniaki, Cris Kacita, Eddy Kinganda-Lusamaki, Áine O'Toole, Tony Wawina-Bokalanga, Daniel Mukadi-Bamuleka, Adrienne Amuri-Aziza, Nadine Malyamungu-Bubala, Franklin Mweshi-Kumbana, Léandre Mutimbwa-Mambo, Freddy Belesi-Siangoli, Yves Mujula, Edyth Parker, Pauline-Chloé Muswamba-Kayembe, Sabin S. Nundu, Robert S. Lushima, Jean-Claude Makangara-Cigolo, Noella Mulopo-Mukanya, Elisabeth Pukuta-Simbu, Prince Akil-Bandali, Hugo Kavunga, Ombotimbe Abdramane, Isabel Brosius, Eugene Bangwen, Koen Vercauteren, Nadia A. Sam-Agudu, Edward J. Mills, Olivier Tshiani-Mbaya, Nicole A. Hoff, Anne W. Rimoin, Lisa E. Hensley, Jason Kindrachuk, Cheryl Baxter, Tulio de Oliveira, Ahidjo Ayouba, Martine Peeters, Eric Delaporte, Steve Ahuka-Mundeke, Emma L. Mohr, Nancy J. Sullivan, Jean-Jacques Muyembe-Tamfum, Jean B. Nachega ✉, Andrew Rambaut, Laurens Liesenborghs & Placide Mbala-Kingebeni ✉

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Rapid communication Open Access

Real-time PCR assay to detect the novel Clade Ib monkeypox virus, September 2023 to May 2024

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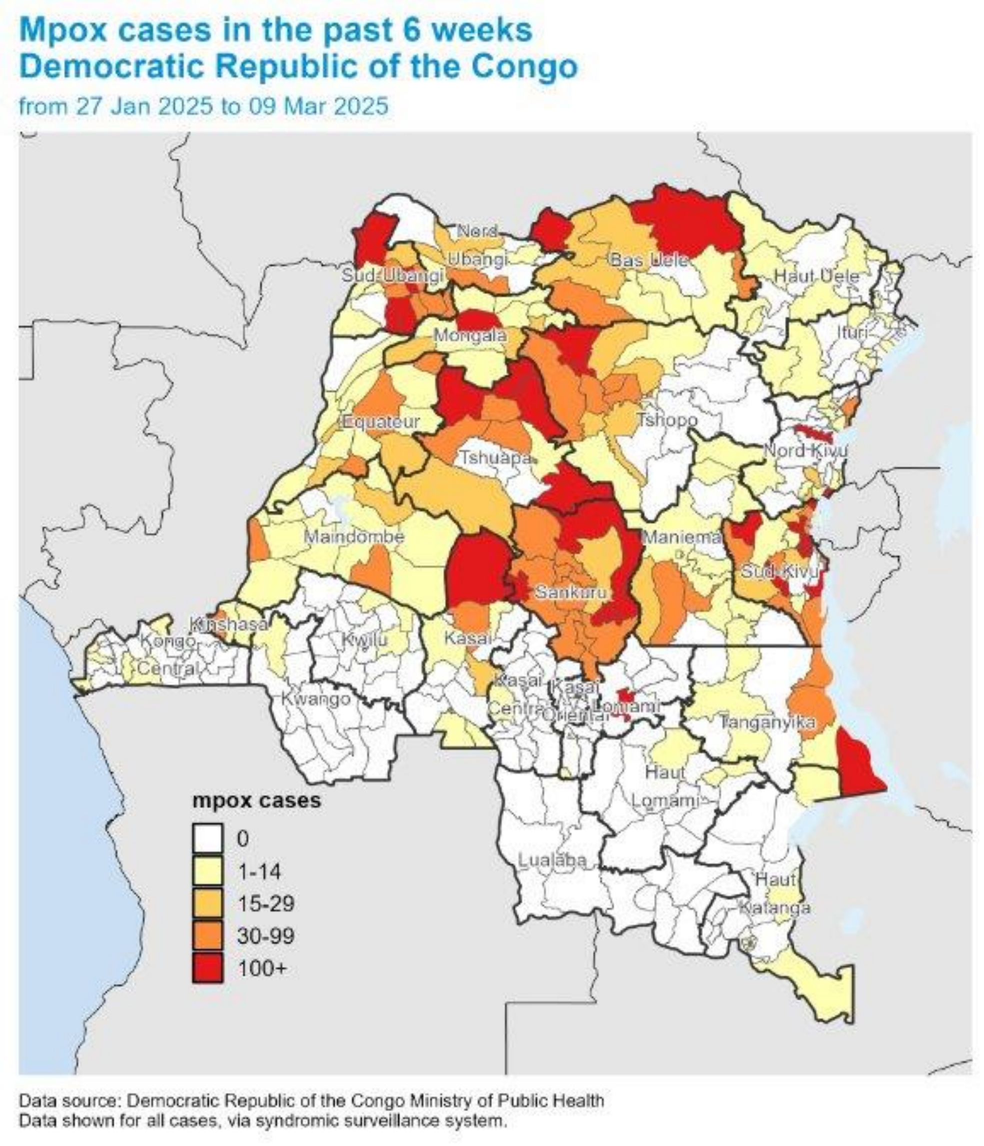
Leonard Schuele[1,*] , Leandre Murhula Masirika[2,3,4,*] , Jean Claude Udahemuka[5,6,*] , Freddy Belesi Siangoli[7] , Justin Bengehya Mbiribindi[7] , Pacifique Ndishimye[6,8] , Frank M Aarestrup[9] , Marion Koopmans[1] , Bas B Oude Munnink[1] , Richard Molenkamp[1] , GREATLIFE MPOX group[10]

- While most OPXV and MPXV PCR protocols still detected the new subclade, the most widely use clade-specific PCR (Li et al J Vir Methods 2010) failed to detect clade Ib because of a deletion in the the C3L target gene
- Updated lab guidance published shortly after report of diagnostic failure

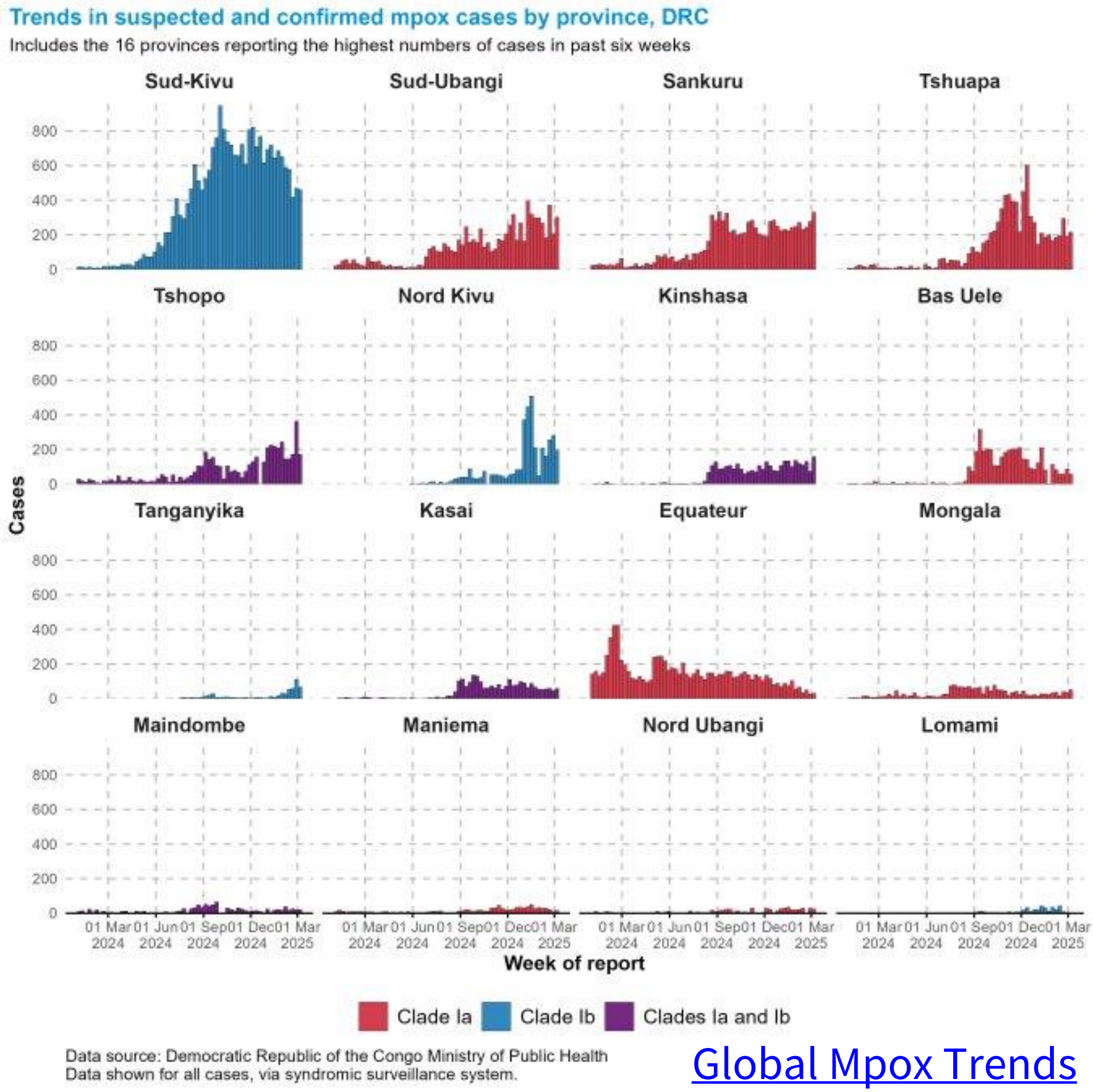
Murhula Masirika et al Eurosurveillance 2024; Vakaniaki et al Nat Med 2024

DRC: **suspected** and **confirmed** mpox cases



Mpox cases in the past 6 weeks
Democratic Republic of the Congo
from 27 Jan 2025 to 09 Mar 2025

Data source: Democratic Republic of the Congo Ministry of Public Health
Data shown for all cases, via syndromic surveillance system.



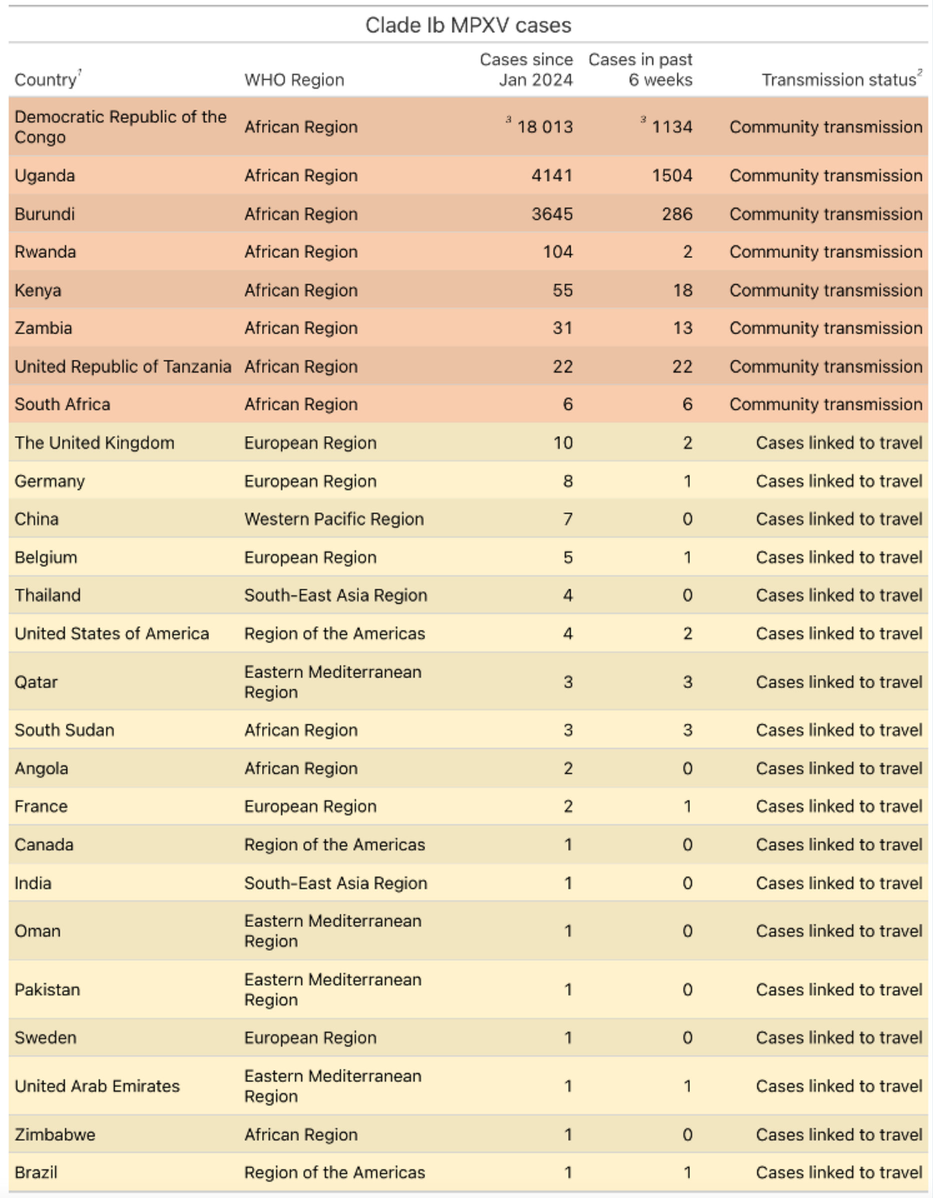
Trends in suspected and confirmed mpox cases by province, DRC
Includes the 16 provinces reporting the highest numbers of cases in past six weeks

Data source: Democratic Republic of the Congo Ministry of Public Health
Data shown for all cases, via syndromic surveillance system.

[Global Mpox Trends]

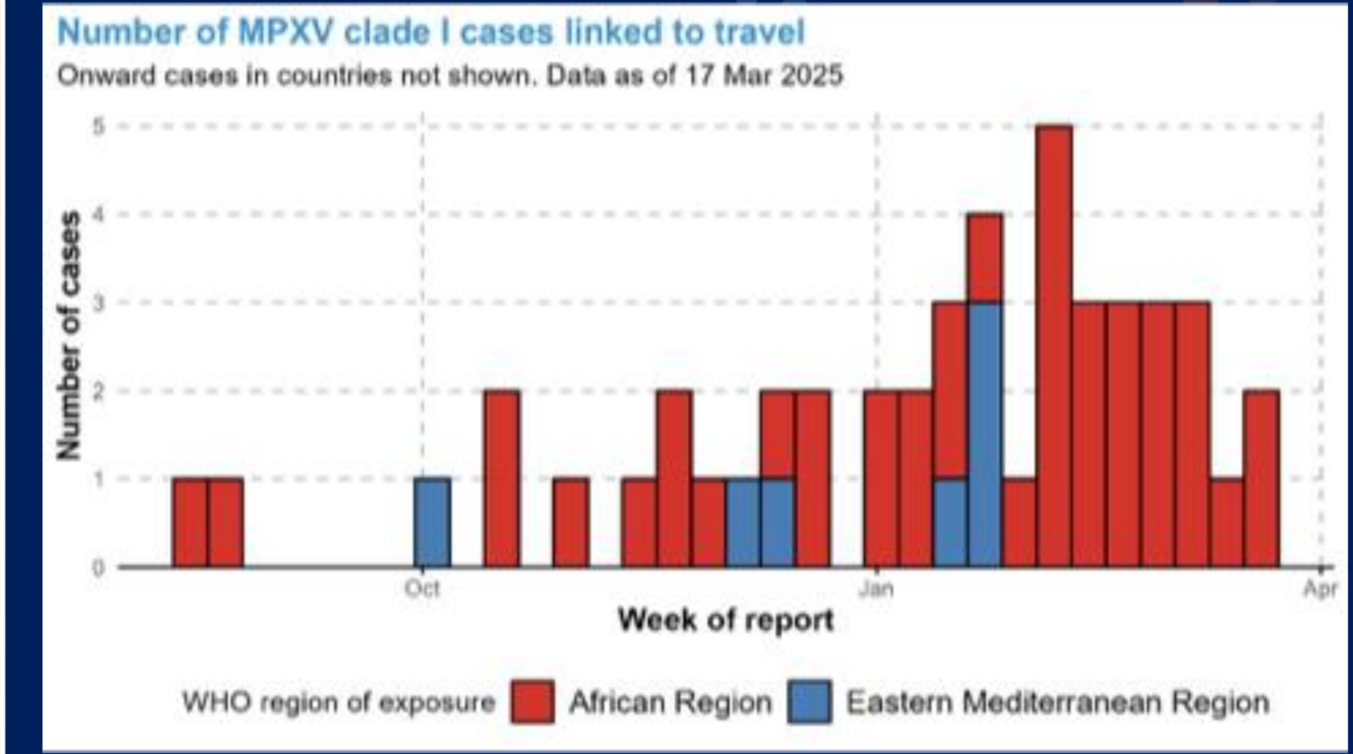
Ongoing epidemic, decreasing trends; surveillance in Sud and North Kivu compromised

Continued circulation of clade Ib MPXV



Clade Ib MPXV cases

Country[1]	WHO Region	Cases since Jan 2024	Cases in past 6 weeks	Transmission status[2]
Democratic Republic of the Congo	African Region	[3] 18 013	[3] 1134	Community transmission
Uganda	African Region	4141	1504	Community transmission
Burundi	African Region	3645	286	Community transmission
Rwanda	African Region	104	2	Community transmission
Kenya	African Region	55	18	Community transmission
Zambia	African Region	31	13	Community transmission
United Republic of Tanzania	African Region	22	22	Community transmission
South Africa	African Region	6	6	Community transmission
The United Kingdom	European Region	10	2	Cases linked to travel
Germany	European Region	8	1	Cases linked to travel
China	Western Pacific Region	7	0	Cases linked to travel
Belgium	European Region	5	1	Cases linked to travel
Thailand	South-East Asia Region	4	0	Cases linked to travel
United States of America	Region of the Americas	4	2	Cases linked to travel
Qatar	Eastern Mediterranean Region	3	3	Cases linked to travel
South Sudan	African Region	3	3	Cases linked to travel
Angola	African Region	2	0	Cases linked to travel
France	European Region	2	1	Cases linked to travel
Canada	Region of the Americas	1	0	Cases linked to travel
India	South-East Asia Region	1	0	Cases linked to travel
Oman	Eastern Mediterranean Region	1	0	Cases linked to travel
Pakistan	Eastern Mediterranean Region	1	0	Cases linked to travel
Sweden	European Region	1	0	Cases linked to travel
United Arab Emirates	Eastern Mediterranean Region	1	1	Cases linked to travel
Zimbabwe	African Region	1	0	Cases linked to travel
Brazil	Region of the Americas	1	1	Cases linked to travel



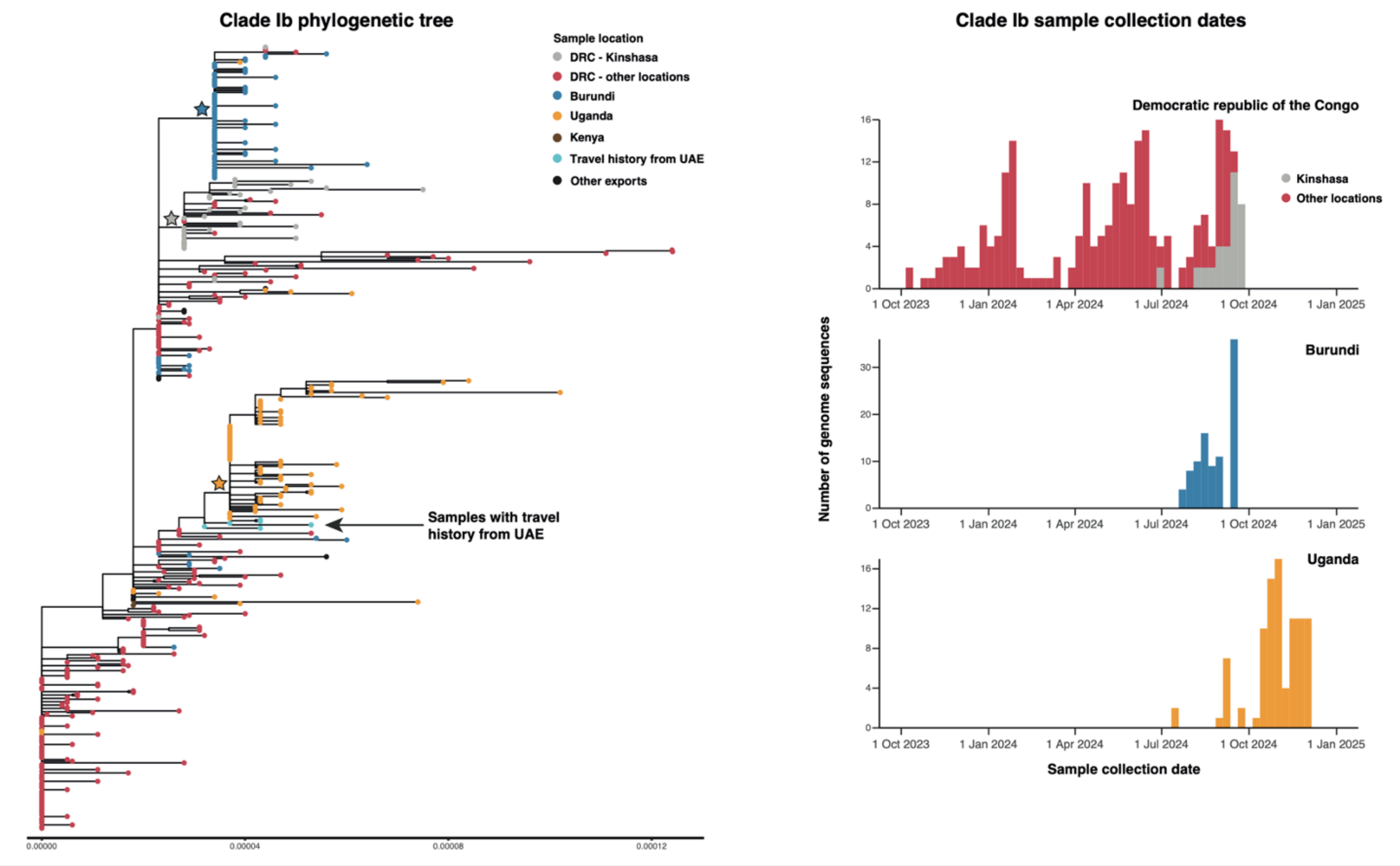
Number of MPXV clade I cases linked to travel

Onward cases in countries not shown. Data as of 17 Mar 2025

- Continuous exportation of clade Ib cases;
- 26 countries reported at least clade Ib case; 8 African countri have community transmission

[Global Mpox Trends]

Continued circulation (and exportation) of clade Ib



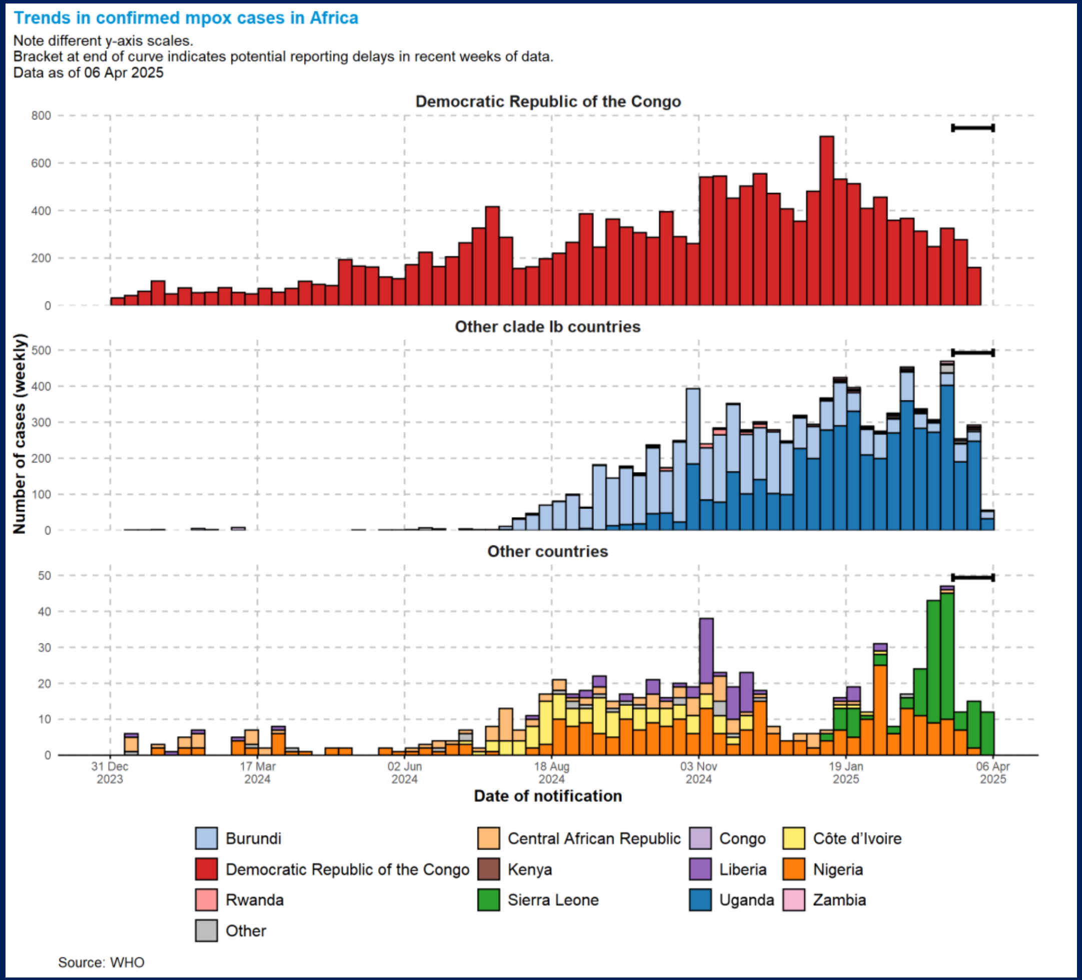
Clade Ib phylogenetic tree

Clade Ib sample collection dates

- Exportation of clade Ib includes cases with travel history to UAE which cluster with clade Ib from Uganda

Chris Ruis, WHO

Continued circulation of MPXV in Africa



Trends in confirmed mpox cases in Africa

Note different y-axis scales.
Bracket at end of curve indicates potential reporting delays in recent weeks of data.
Data as of 06 Apr 2025

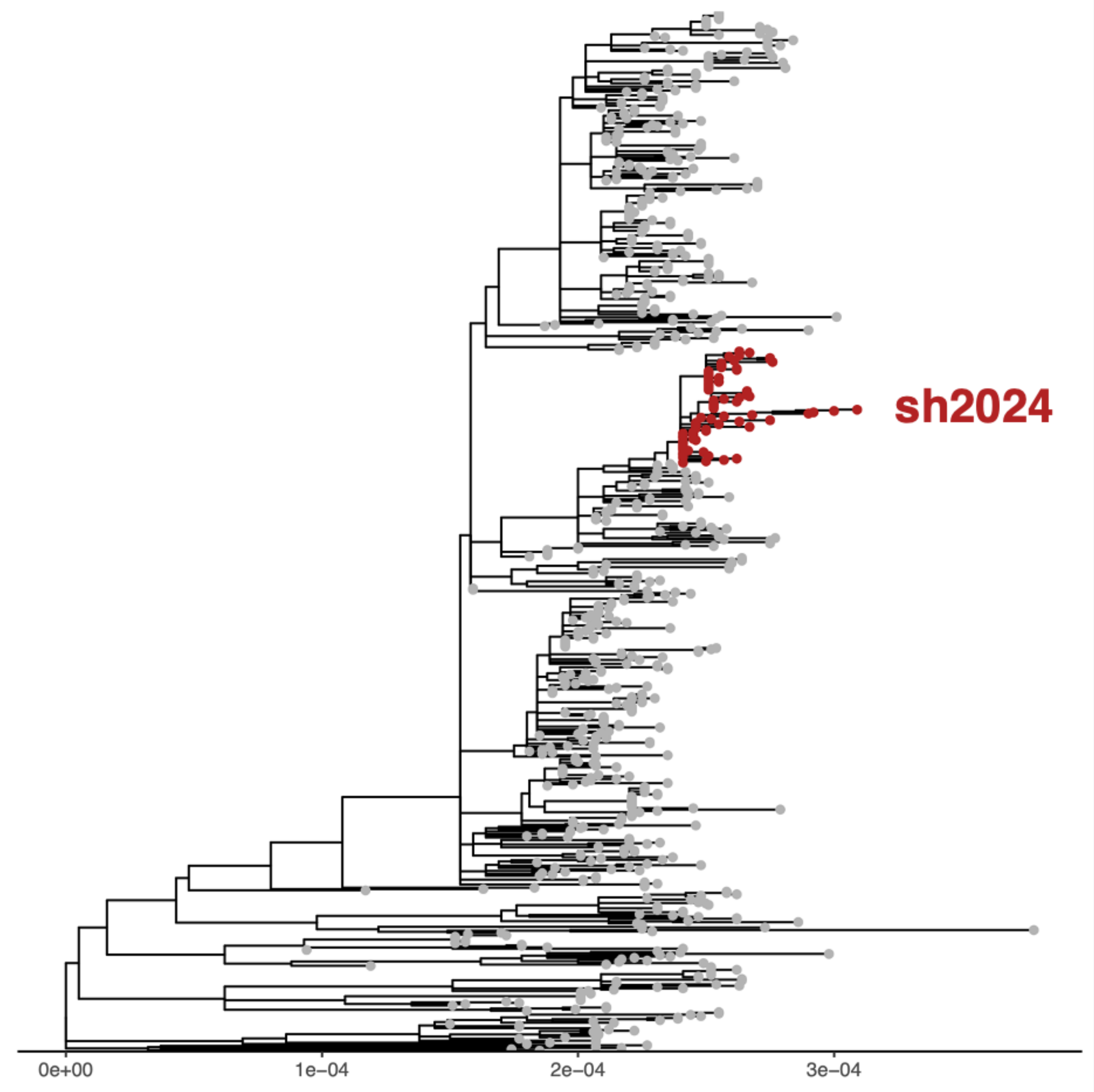
Source: WHO

- Decreasing trends in DRC and Burundi, increasing trends in Uganda, Kenya
- Substantial increase in circulation in Sierra Leone (sequencing ongoing)

Sustained human-to-human transmission within MPXV clade Ia

Ireland clade Ia case clusters within sh2024

Sequencing for recent Clade Ia case from PDR China not available yet



Chris Ruis, WHO

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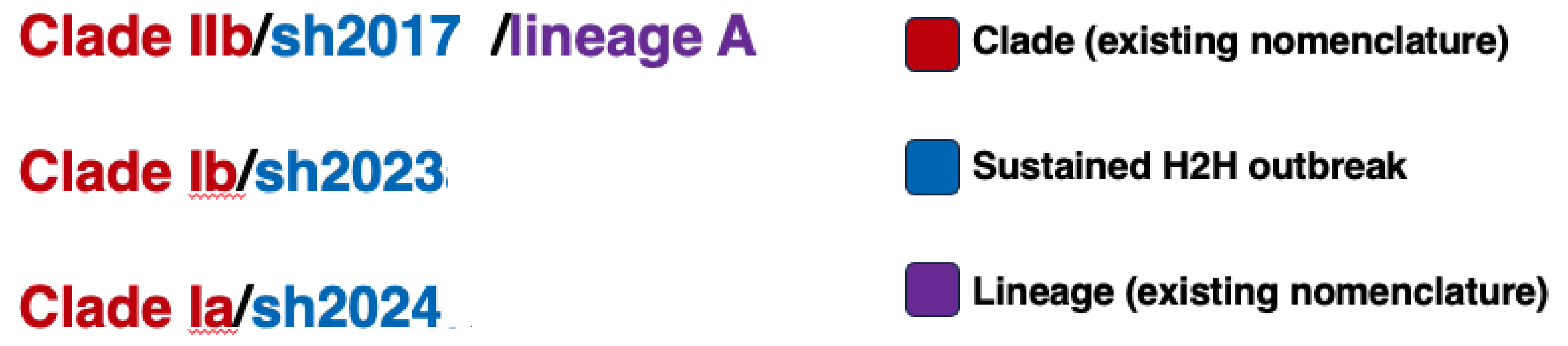
Proposed nomenclature for sustained human-to-human outbreaks of MPXV



Clade IIb/sh2017 /lineage A

Clade Ib/sh2023

Clade Ia/sh2024

🟥 Clade (existing nomenclature)

🟦 Sustained H2H outbreak

🟪 Lineage (existing nomenclature)

- Bridges the current clade and lineage systems with an additional outbreak label
- Outbreak label important for early warning of new viruses with accumating APOBEC3-like mutations

Global Mpox Trends

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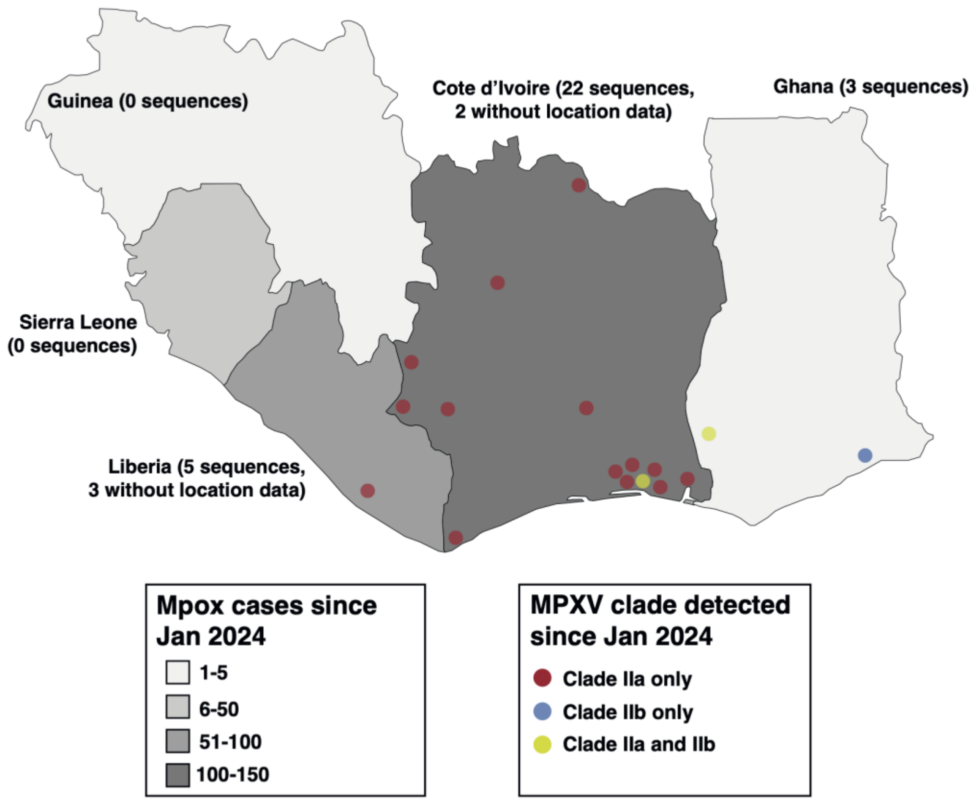
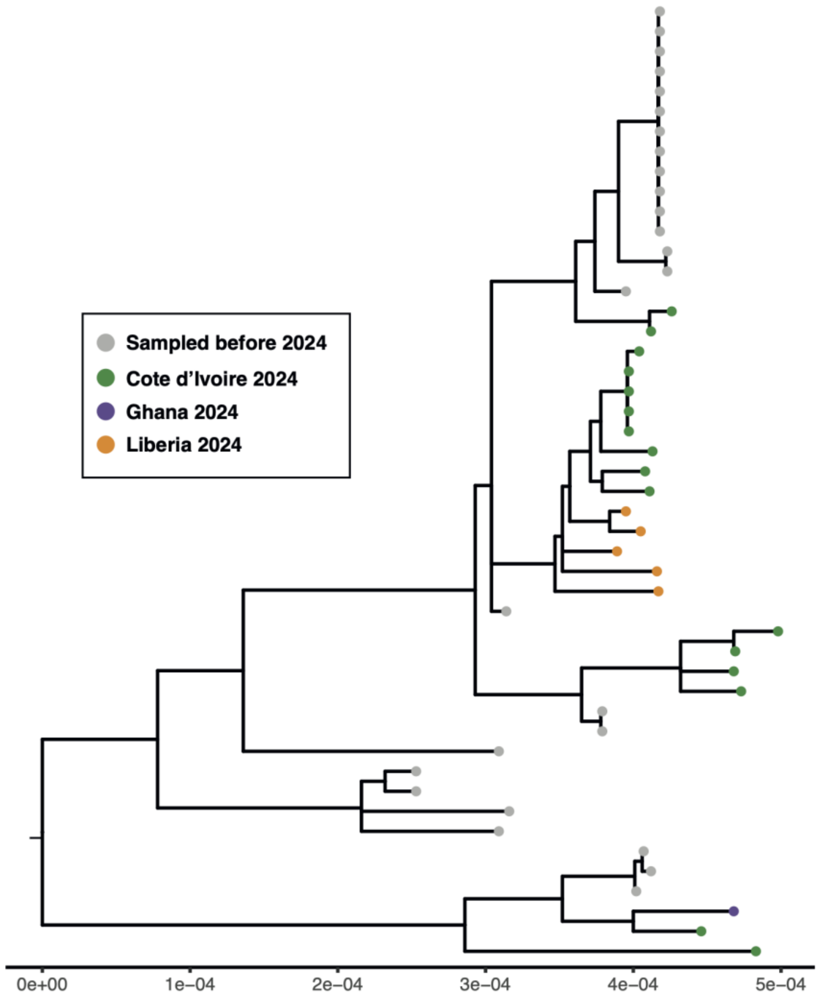
Many zoonotic spillovers of clade IIa in West Africa during 2024



Mpox cases and MPXV genome sequences in West Africa (since Jan 2024)



Clade IIa phylogenetic tree

- Clade IIa detected in Guinea, Liberia, Ghana, Cote d'Ivoire
- Ongoing sequencing in Sierra Leone
- After clade IIb, clade Ib and recently clade Ia (Kinshasa outbreak), is clade IIa going to be linked to sustained human to human transmission?

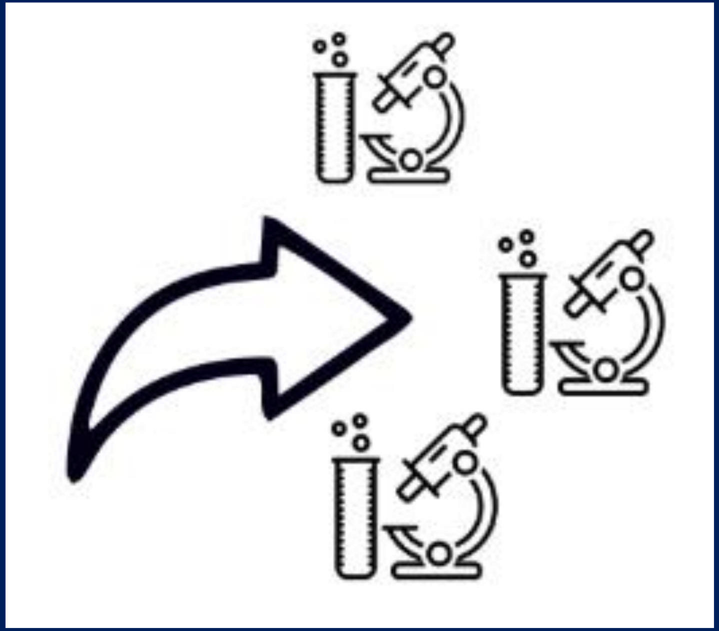
Chris Ruis, WHO

Fire-footed rope squirrels (*Funisciurus pyrropus*) are a reservoir host of monkeypox virus (*Orthopoxvirus monkeypox*)

- Study describes outbreak of MPXV in a group of wild sooty mangabeys (Cercocebus atys) in Taï National Park (Côte d'Ivoire
- The outbreak affected one third of the group between January and April 2023, killing four infants.
- Scientists analysed rodents and wildlife carcasses from the region and identified a MPXV-infected fire-footed rope squirrel (Funisciurus pyrropus), found dead 3 km from the mangabey territory.
- MPXV genomes from the squirrel and the mangabey were identical.
- Video record of consumption of the same squirrel species in 2014.
- Faecal samples from mangabeys identified two faecal samples containing the DNA of the firefooted rope squirrel, and one was MPXV positive

Fabian Lendertz et al Research Square 2025

WHO Biohub



- Triggered by concerning epidemiology in DRC, sourcing of Clade I isolate for the WHO Biohub started.
- Genomic data confirmed threat posed by clade Ib emergence to neighbouring countries in early 2024
- Clade Ia and Ib isolates or inactivated DNA shared to 40 laboratories in 18 countries for:
  - diagnostic preparedness
  - functional characterization
- One nation used it to run a national EQA that enrolled 15 laboratories
- To know more, please visit WHO BioHub

WHO Global MPXV EQA Programme

using WHO Biohub material

May 2023

WHO ships panels of its first Global MPXV EQA programme to **145** laboratories in **117** countries & territories.

December 2023

Sourcing of Clade Ia via the WHO BioHub System

April 2024

Preparation of **EQA panel** materials start using WHO Biohub clade Ia material

August 2024

Africa CDC declares **PHECS**; WHO declares **second PHEIC**

October 2024

WHO **ships panels** of second round of **MPXV EQA programme** to **180** laboratories in **126** countries & territories.

March 2025

Results released for second round of MPXV EQA panel.

Planning for new EQA ongoing

World Health Organization

Lisa Stevens, WHO

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Summary of the evaluation of the parameter “Monkeypox virus (DNA)”

Sample No.	**7418A-240924-05**	**7418A-240924-02**	**7418A-240924-01**	**7418A-240924-03**	**7418A-240924-04**
Sample properties	MPXV positive	MPXV positive (Clade Ia)	MPXV negative (OPXV positive)	MPXV positive (Clade IIb)	MPXV negative
Approx. viral load [copies/ml]	500,000	500 (close to LoD)	500,000	500,000	-
Target value for all methods	Positive	Positive	Negative	Positive	Negative
Success rate	95.9% (210 / 219)	75.8% (166 / 219)	93.6% (205 / 219)	96.3% (211 / 219)	95.9% (210 / 219)

Conclusions

- Mpox genomics allows us to infer about which viruses spread through sustained human-to-human transmission

- For mpox, 3 strains have signatures of sustained human-to-human transmission (clade IIb/sh2017; clade Ib/sh2023 and clade Ia/sh2024)

- Genomics has been instrumental for
  - early warning of new variants with potential to spread
  - diagnostic preparedness to clade Ib (supported by the WHO Biohub and WHO EQA programme)
- Coming soon: two WHO (in collaboration with IPSN) documents on genomics (one generic, one mpox-specific)

IPSN

1. Analytical considerations for genomic surveillance of MPXV

Aims of the Document

- Summarise **technical and analytical recommendations** based on evidence from literature and guided by the Community of Practice

- Serve as a **technical primer** for new groups entering the field
  - *Static document*: general recommendations
  - *GitHub repository*: dynamic resource, community-driven updates

- Identify **common and best practices** for:
  - Sample preparation
  - Genome sequencing approaches
  - Genomic analysis and downstream analysis
  - Data sharing strategies

- Promote **harmonization of protocols and workflows** to strengthen global MPXV genomic surveillance efforts

2. Attributes and principles of genomic data-sharing platforms supporting surveillance of pathogens with epidemic and pandemic potential

Aims of the Document

- Operationalize the **guiding principles for pathogen genome data-sharing**, focusing on pathogen genomic data-sharing platforms (PGDSPs).
- Describe **attributes and operational principles** of PGDSPs to support **effective, timely and equitable sharing** and access to genomic data
- Enable **data producers and users to advocate** for the implementation of the operational principles
- Assist **genomic data producers in selecting a PGDSP** for their data
- Help steer **donor investments** towards sustainable funding

Acknowledgement

- WHO
  - Mpox IMST Epi & Lab Pillars
  - IPSN team

- DRC for sharing of data and virus isolates
- Partners in the Mpox Dx consortium