Mpox and the path to elimination

5th WAIDID conference, Milan, Italy

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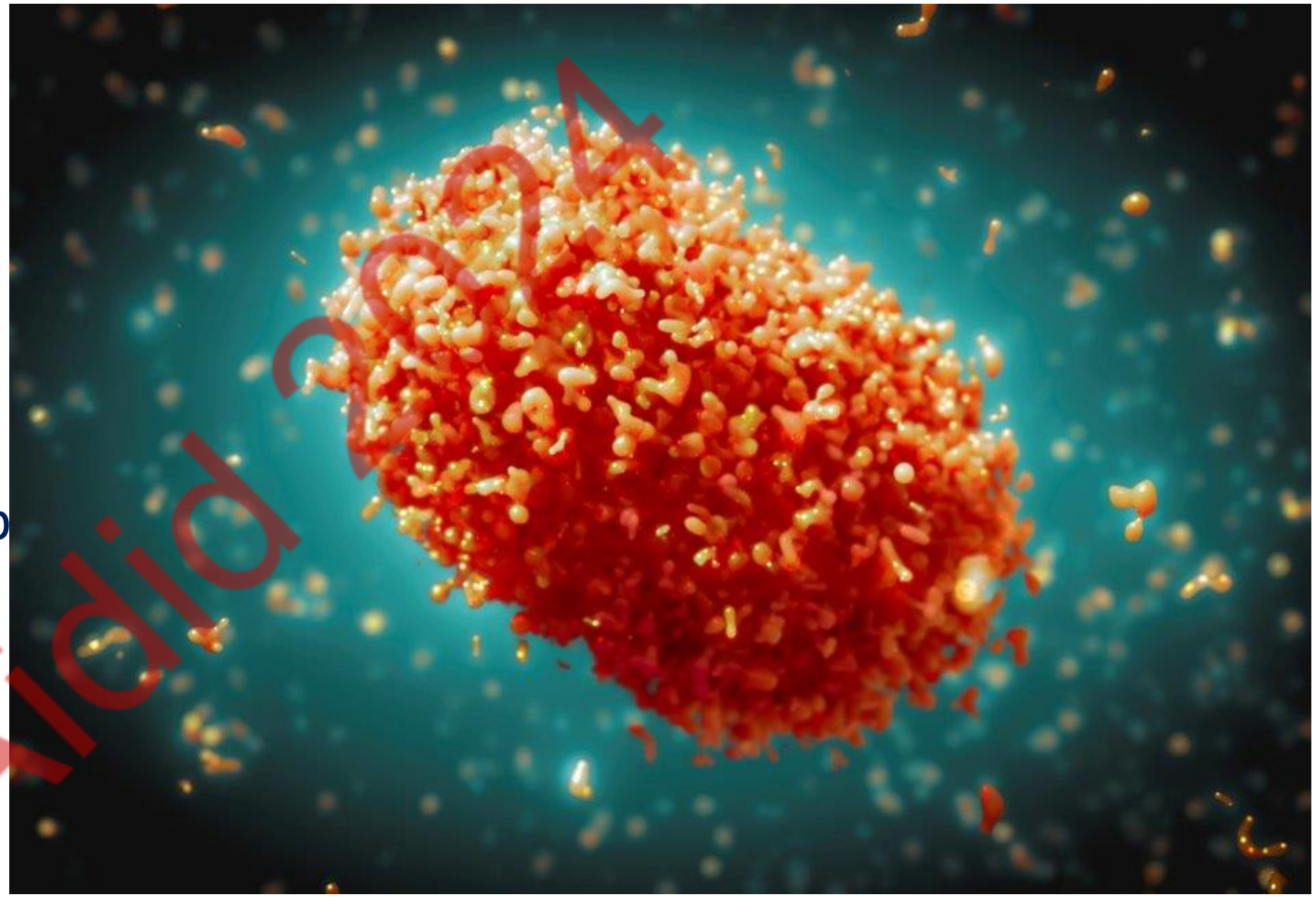
Technical lead for poxvirus diseases
Health Emergencies Programme

30 November 2024

World Health Organization

Content

- Mpox and the monkeypox virus (MPXV)
- Global epidemiological update
- WHO response
- Strategic framework and next step



Monkeypox virus, illustration. Credit: MAURIZIO DE ANGELIS/SCIENCE PHOTO LIBRARY

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Overview of the current situation and evolution of outbreak

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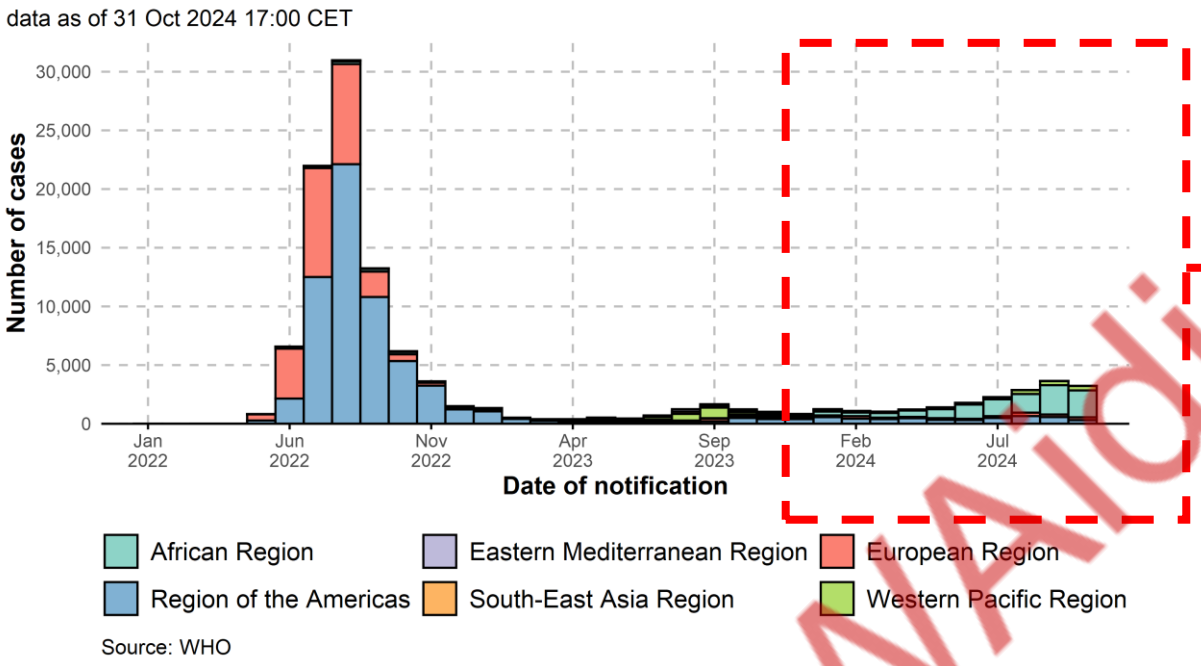
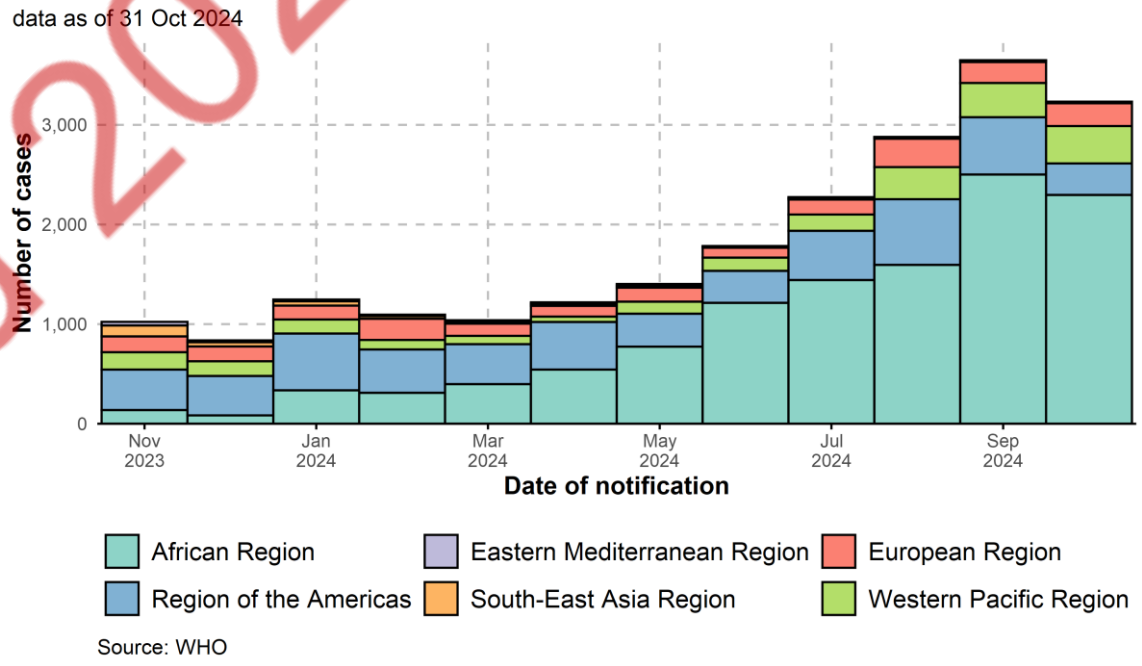
Confirmed mpox cases by month and WHO Region

01 Jan 2022 – 31 November 2024

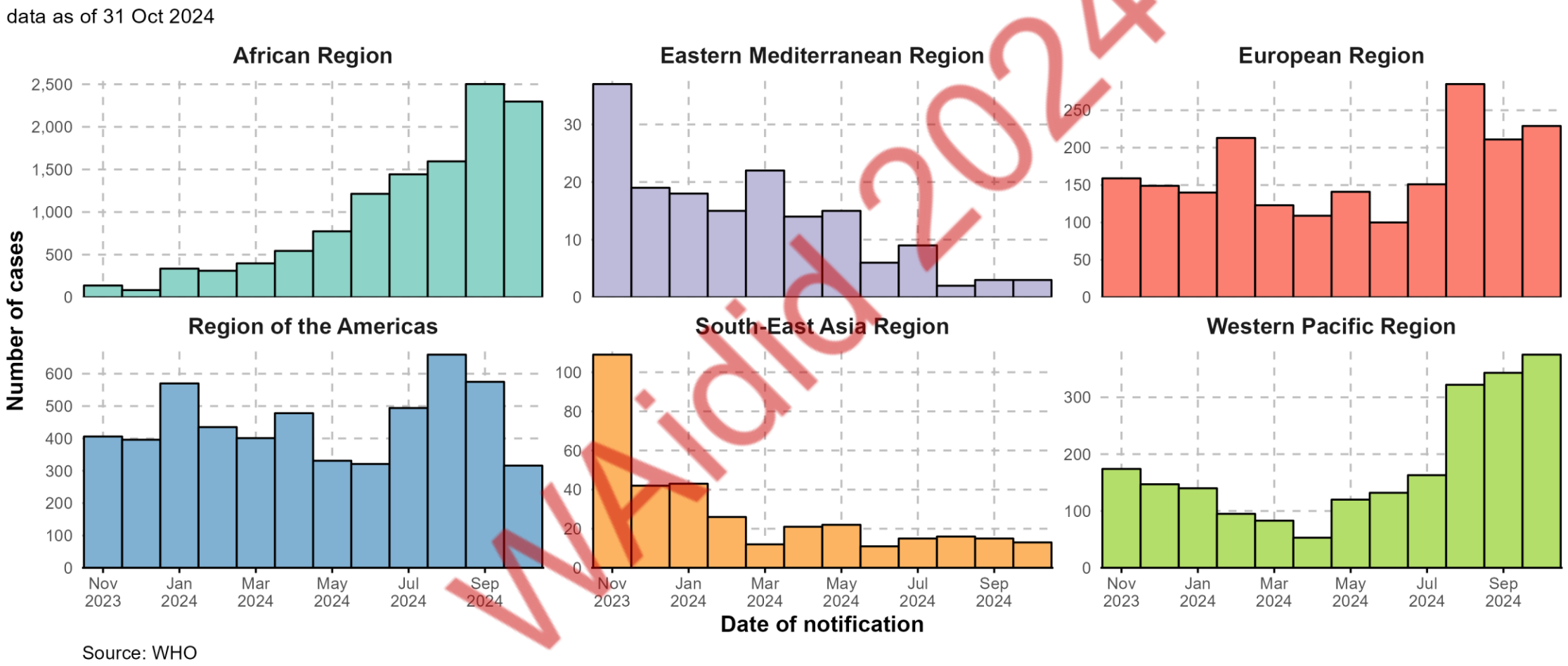


01 November 2023 – 31 October 2024



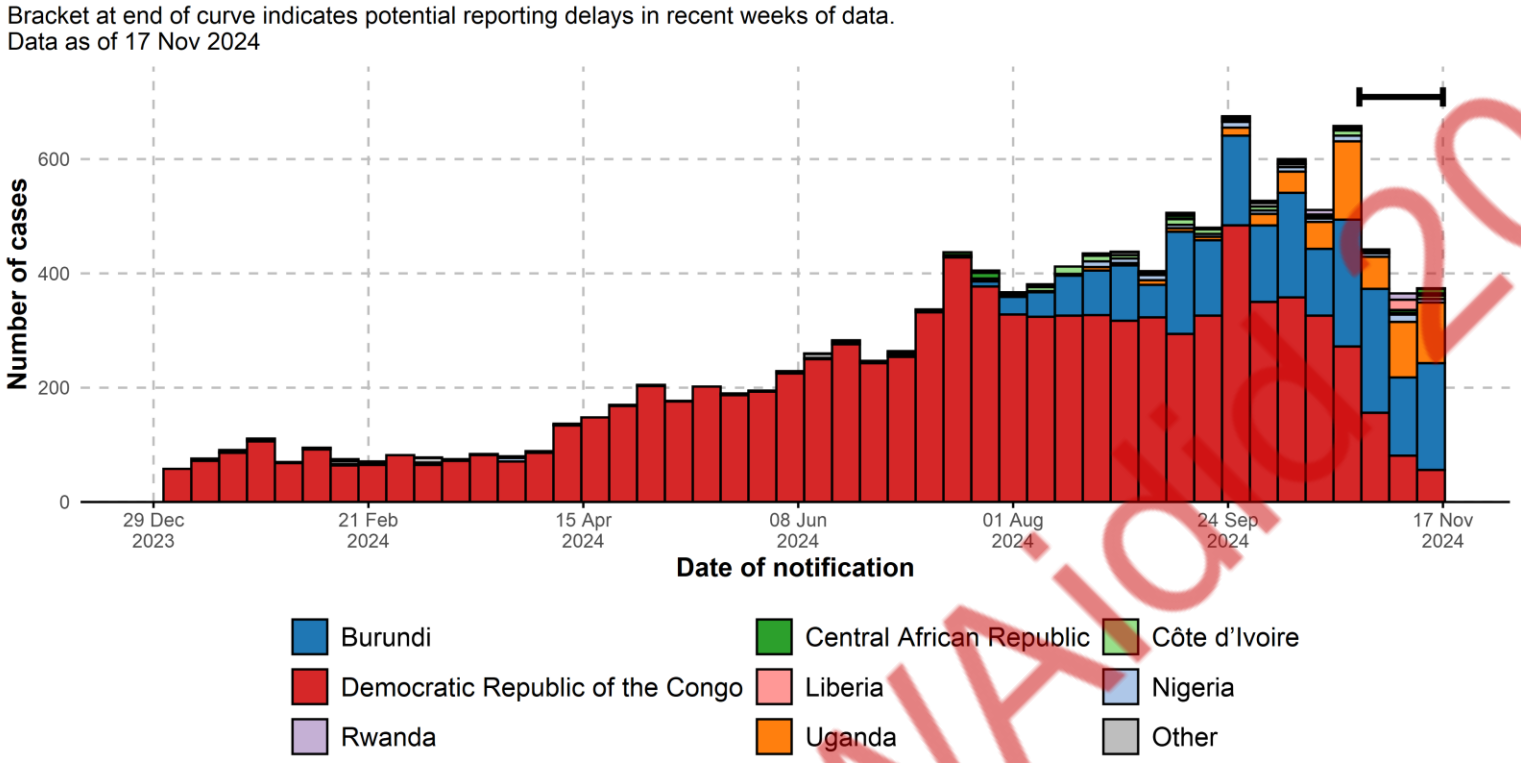
Epidemic curve by region

November 2023 to October 2024 – Note different y-axis scales



Epidemic curve of *confirmed* mpox cases in Africa

01 January – 17 November 2024



Source: WHO

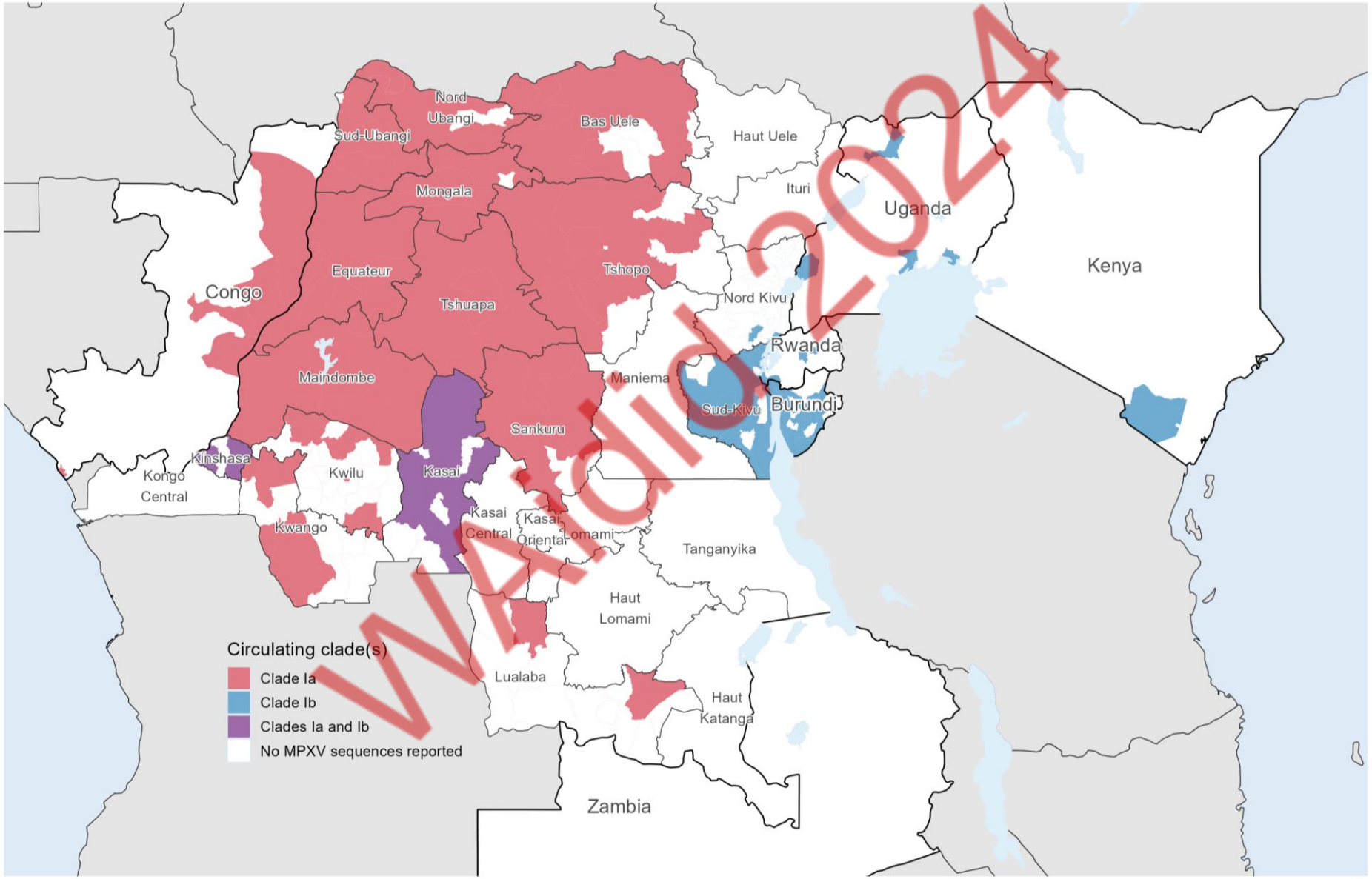
Total lab confirmed cases in 2024

12 596

Total lab confirmed deaths in 2024

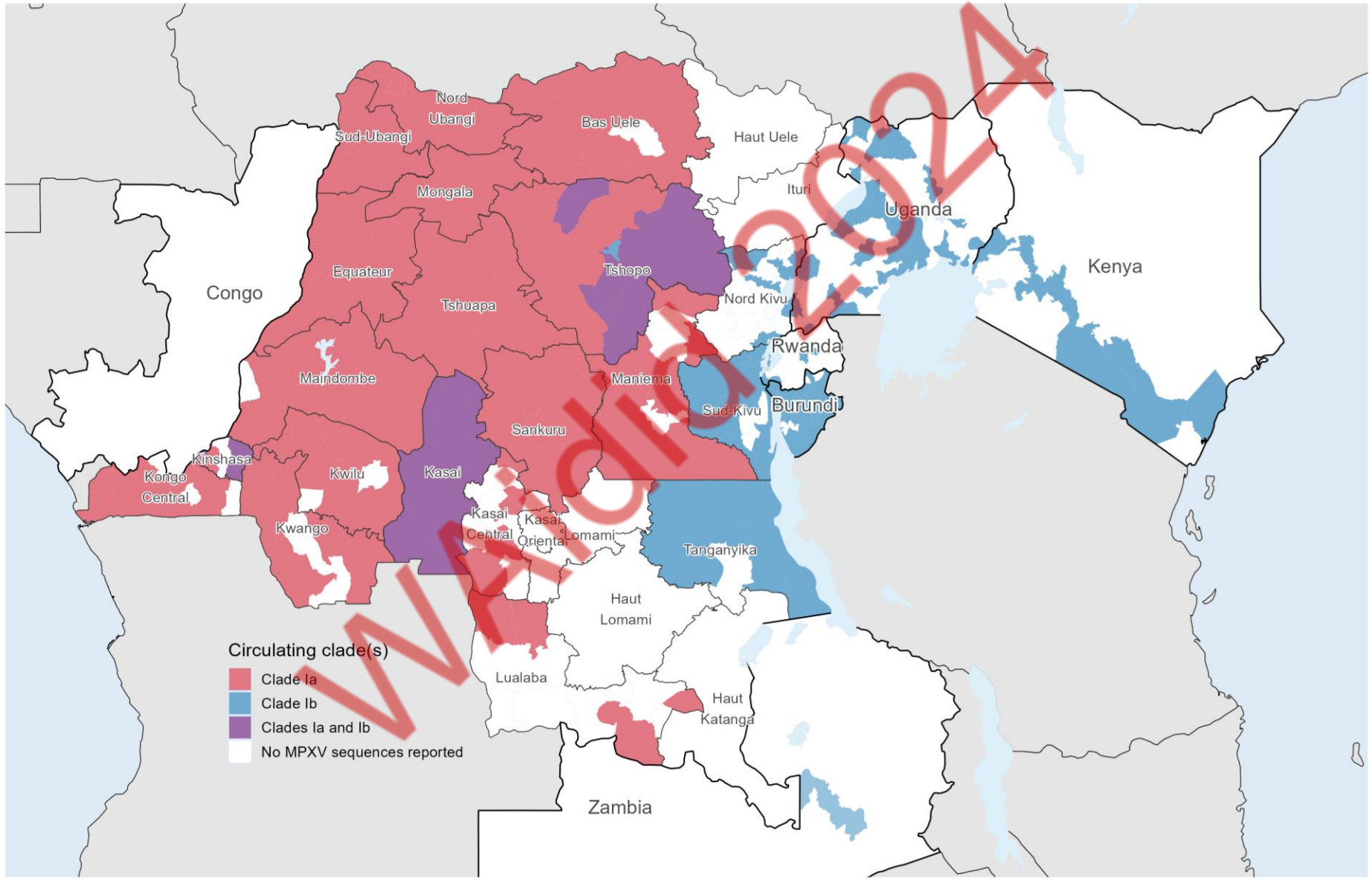
54

Clade distribution in the Democratic Republic of the Congo and neighbouring countries: **1 January – 17 August 2024**



Source: MPXV genome sequences and metadata accessible via INRB, Genbank, and GISAID

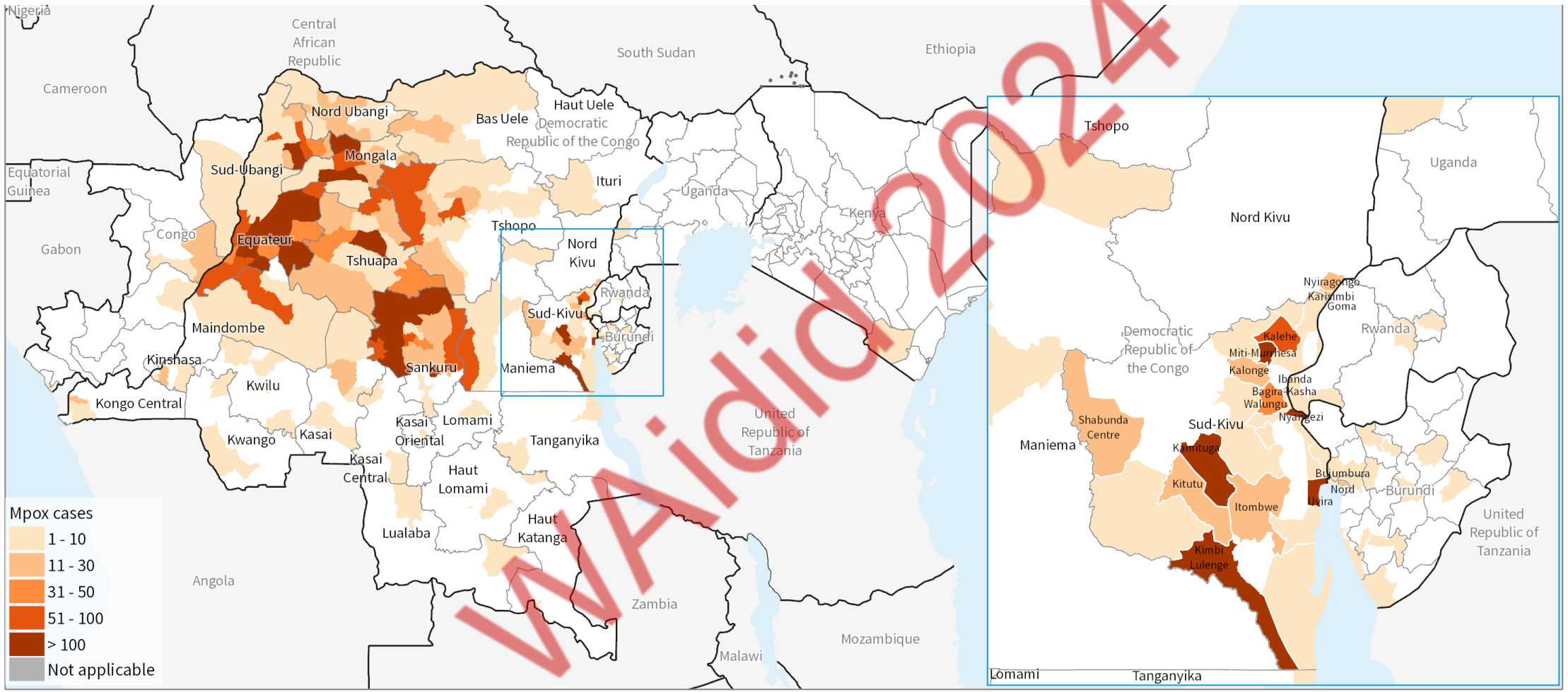
Clade distribution in the Democratic Republic of the Congo and neighbouring countries: **18 August – 10 November 2**024



Source: MPXV genome sequences and metadata accessible via INRB, Genbank, and GISAID

Mpox cases in the Democratic Republic of the Congo, Burundi, Rwanda, Uganda, Kenya, Congo: **May – July 2024**

Note: syndromic cases for DRC, confirmed cases for Burundi, Uganda, Kenya



The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme
Map Date: 21 November 2024

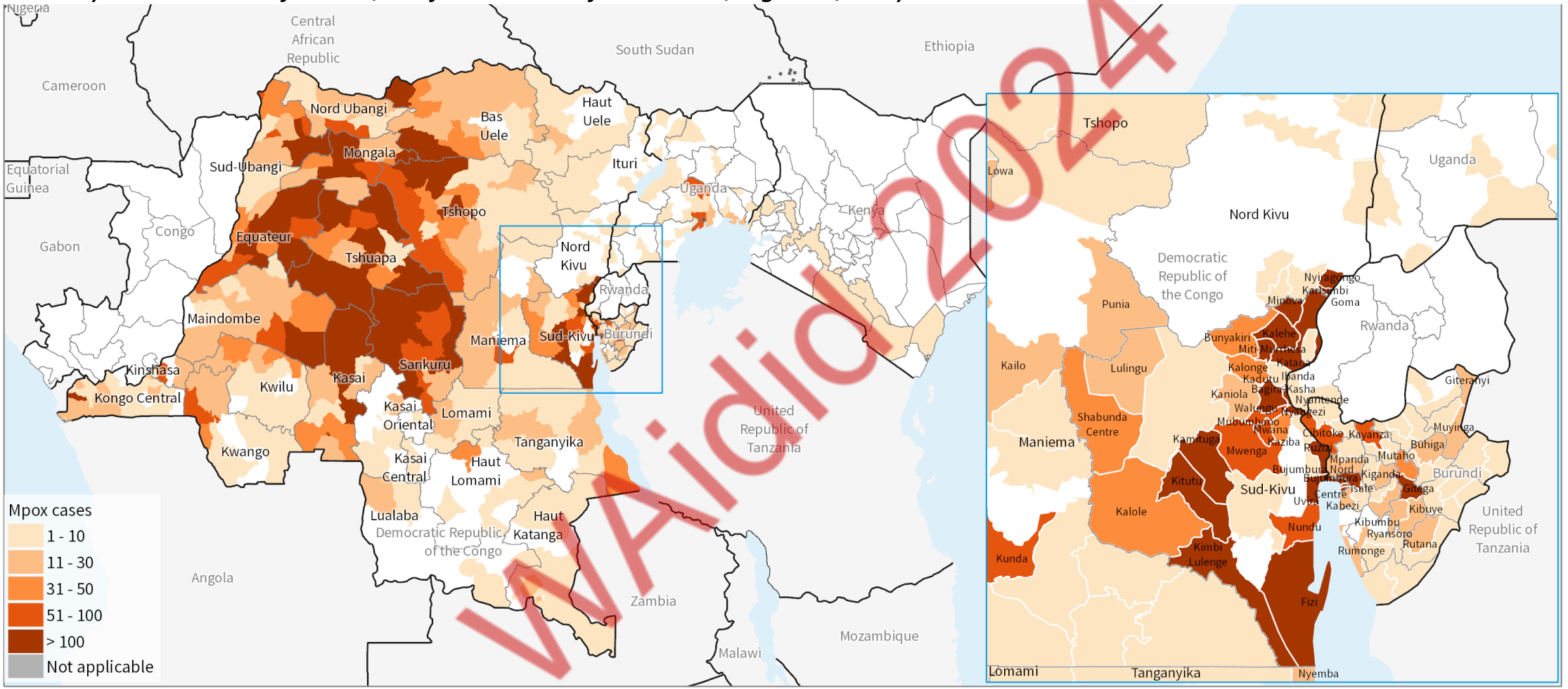
0 250 Km

* The reporting period differ by country: Burundi (11/18/2024), Congo (7/18/2024), Democratic Republic of the Congo (11/10/2024), Kenya (11/10/2024), Rwanda (10/20/2024), Uganda (11/18/2024).
** Data are primarily for confirmed cases only except for the Democratic Republic of the Congo, which includes both suspected and confirmed cases.

World Health Organization

Mpox cases in the Democratic Republic of the Congo, Burundi, Rwanda, Uganda, Kenya, Congo: **August – October 2024**

Note: syndromic cases for DRC, confirmed cases for Burundi, Uganda, Kenya



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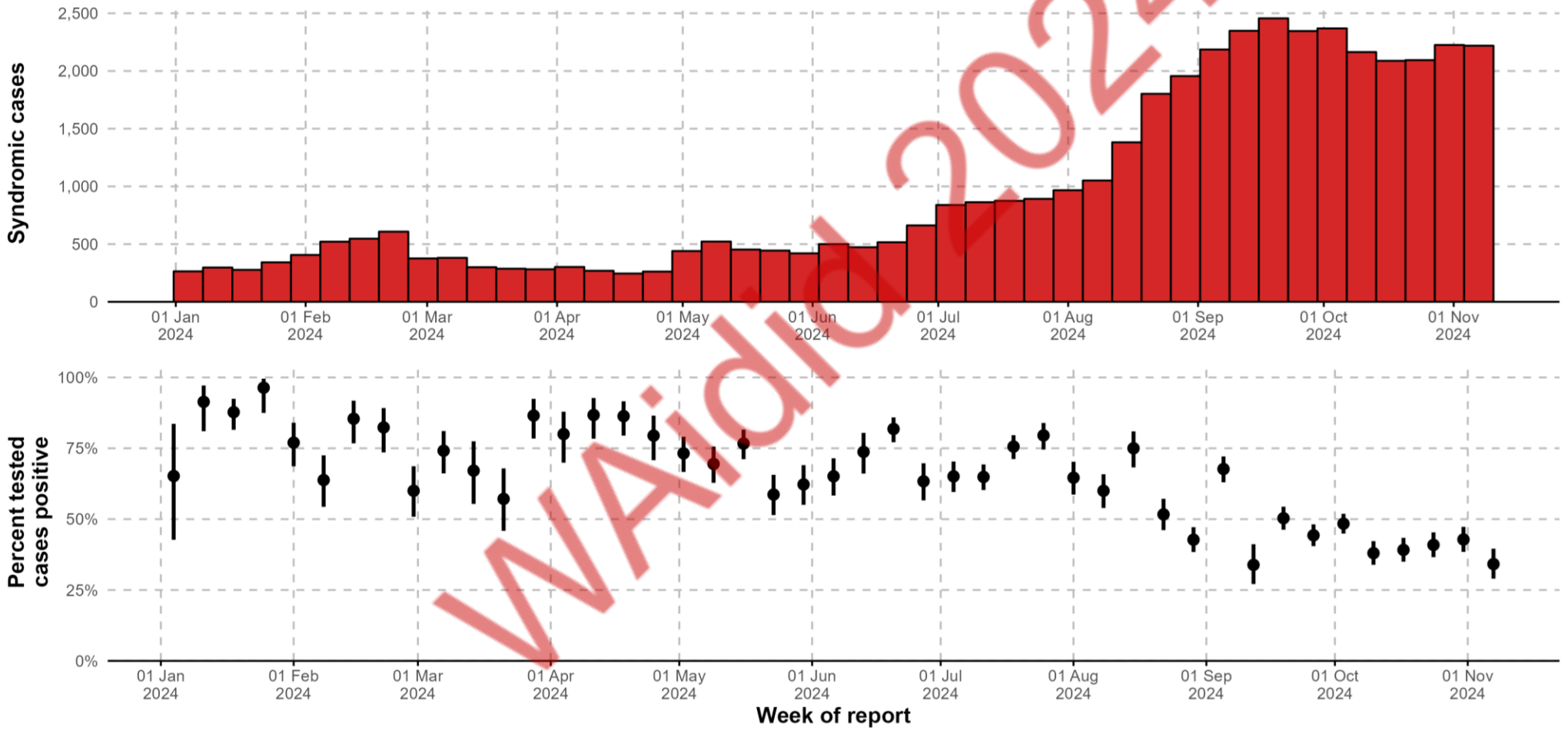
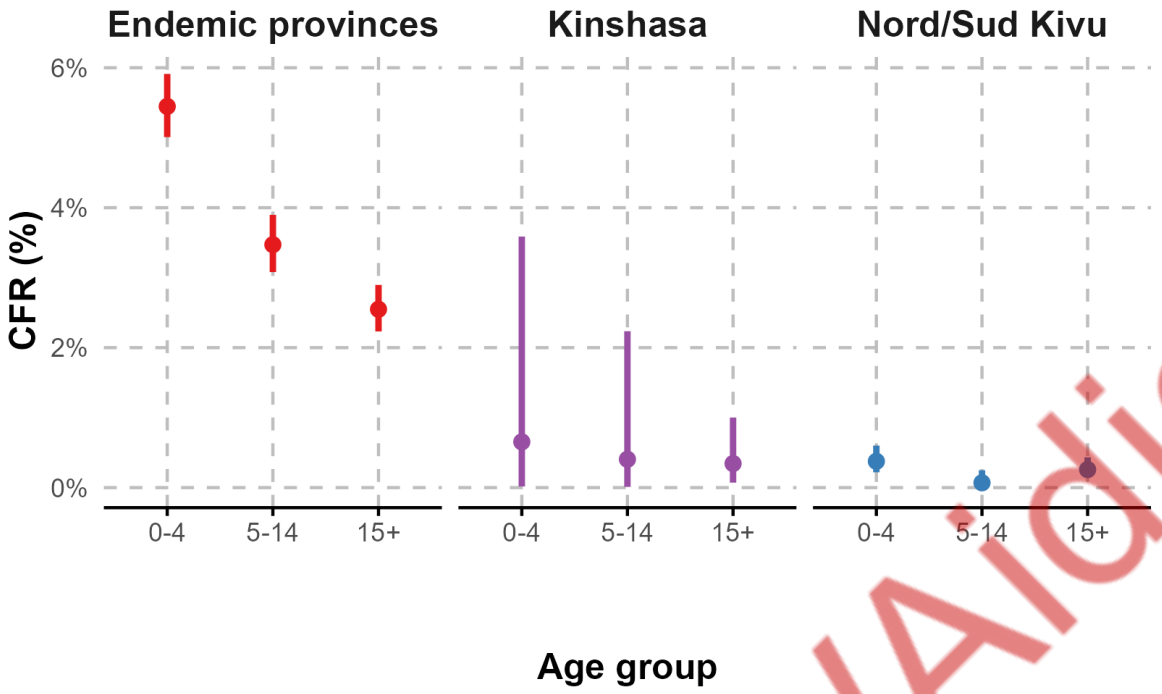
DRC: Epidemic curve (all cases, syndromic)

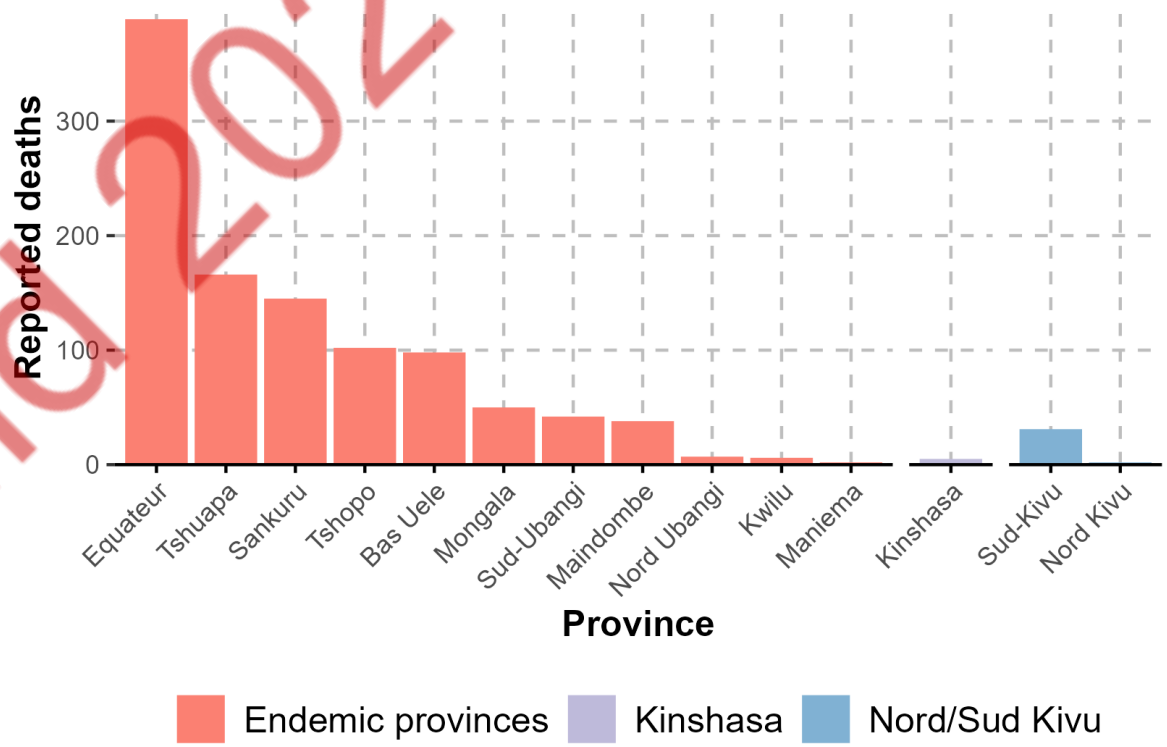
Data as of 10 November 2024



DRC: Mortality, from syndromic reporting (all cases)

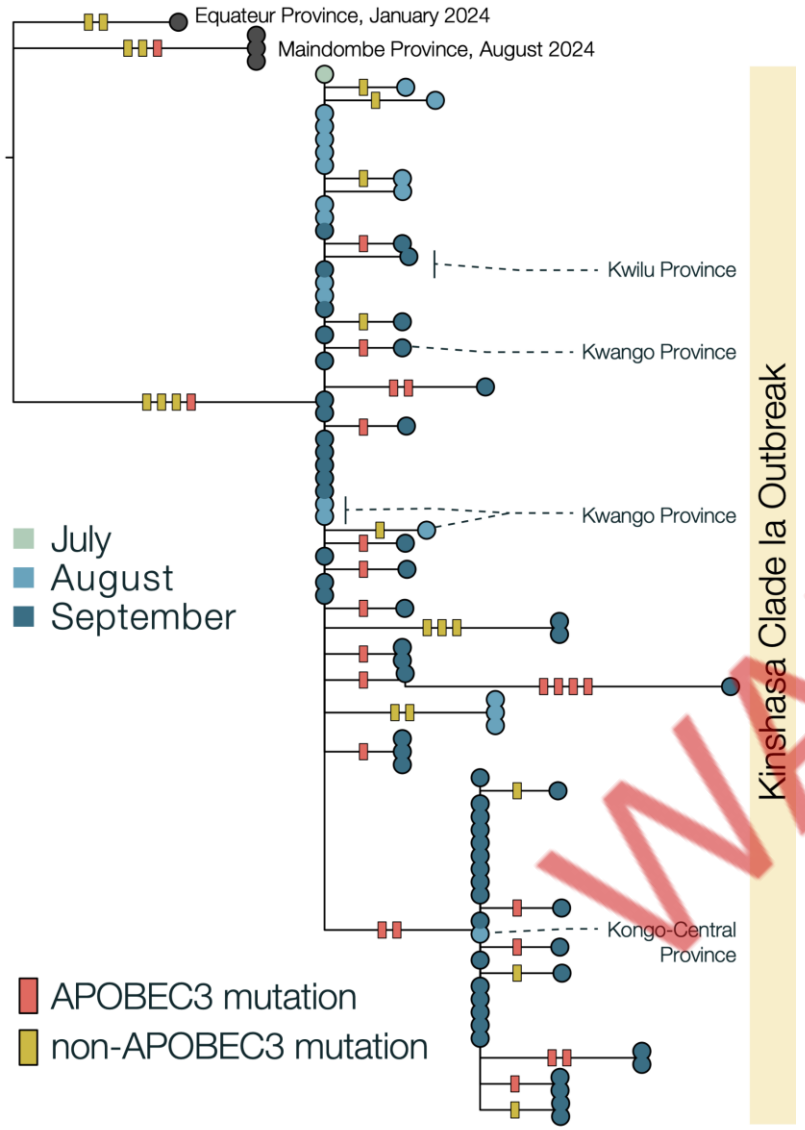
Data as of 10 November 2024





Endemic provinces: 26829 cases, 1045 deaths
Nord/Sud Kivu: 12859 cases, 33 deaths
Kinshasa: 1273 cases, 5 deaths

Kinshasa: Emergence of a clade Ia outbreak associated with sustained human-to-human transmission



Most clade Ia cases have been associated with **zoonotic transmission**

An outbreak of clade Ia associated with **sustained human-to-human transmission** is now occurring in Kinshasa

This outbreak has also been detected in Kwilu, Kwango and Kongo-Central provinces

The outbreak shows an **APOBEC3-like mutational signature**, similar to clade Ib

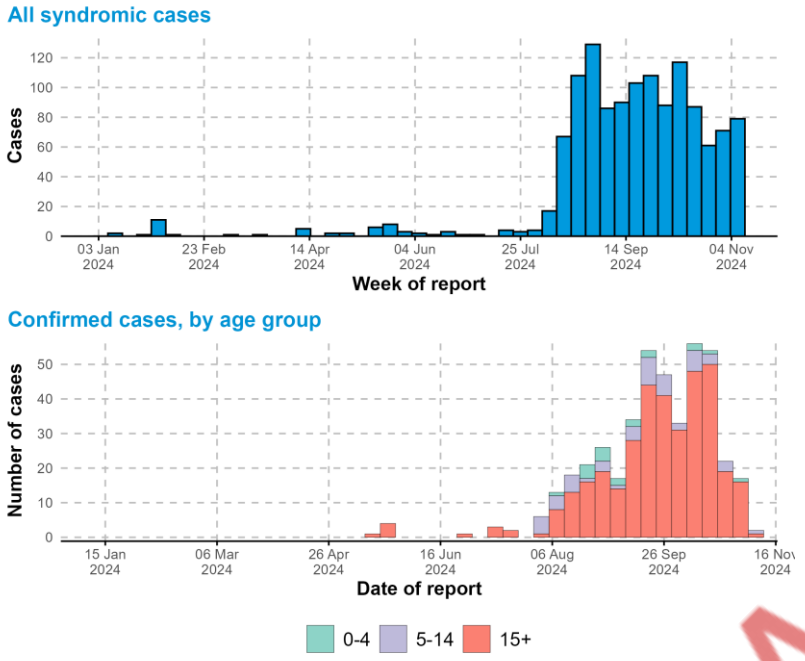
Transmission routes from one person to another unknown

There are now outbreaks of mpox due to **clade IIa MPXV** in West Africa (Liberia, Côte d'Ivoire) not seen before

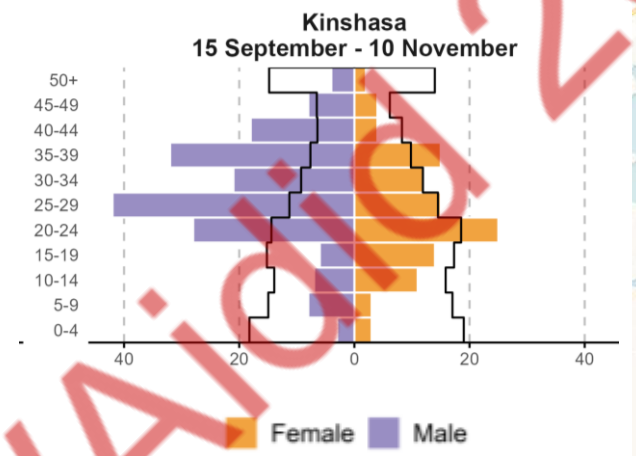
DRC, Kinshasa: time, person, place

Data as of 10 November 2024

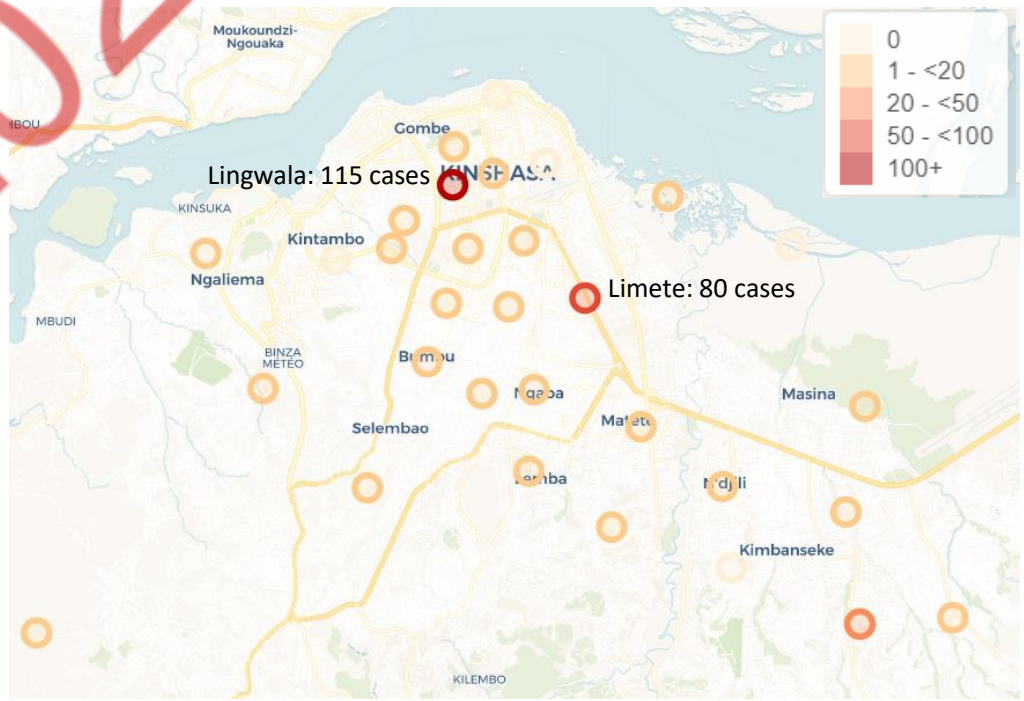
Cases over time



Age & sex : 15 Sept – 10



Geographic distribution (HZ): all cases last

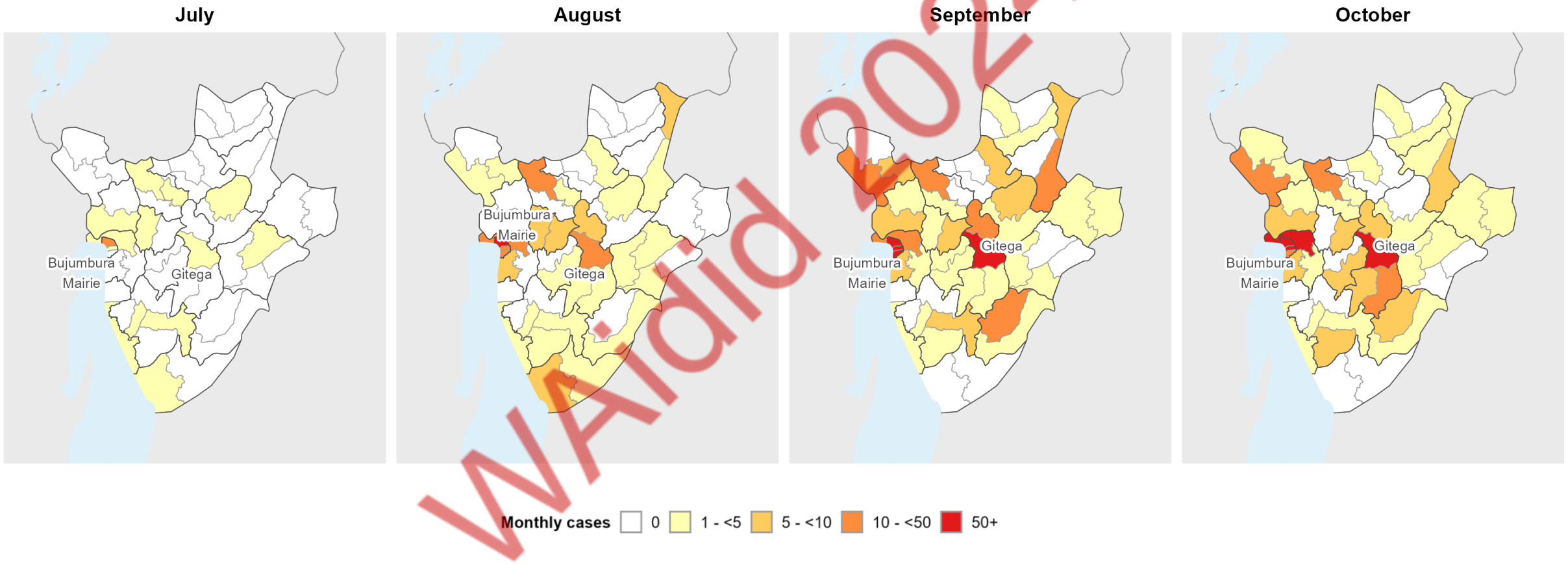


Burundi: geographical trends

Data as of 10 November

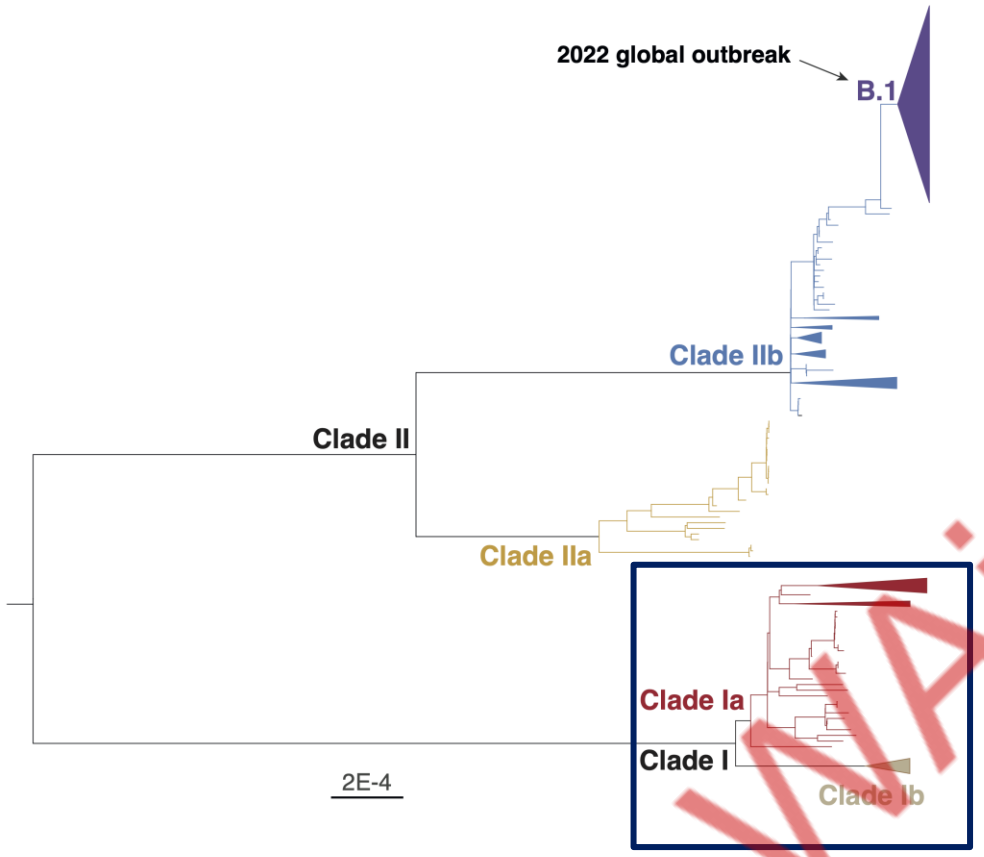
Burundi: confirmed mpox cases by month

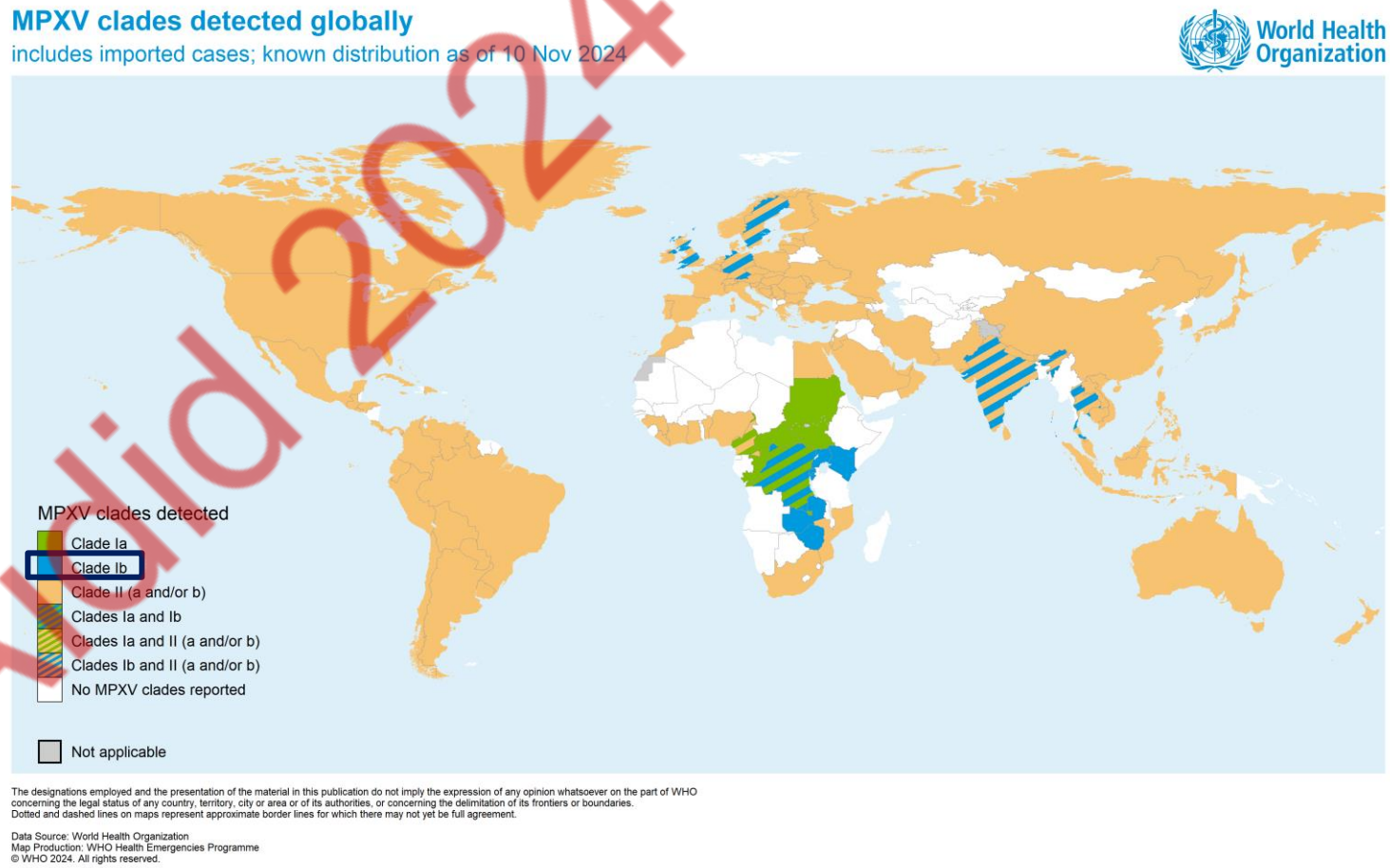
as of 10 November 2024



Monkeypox virus (MPXV) clades detected globally

January 2022 – October 2024





The proportion of samples sequenced is still low and the information available might not be fully representative of the clade distribution; on 15 November 2024, the United States of America also notified WHO of a first case of mpox due to clade Ib MPXV ; on 22 November, Canada notified a case of mpox due to clade Ib; on 28 November, the UK reported a second importation

Countries who have reported mpox due to clade Ib MPXV

01 July – 28 November 2024

Country	Confirmed cases	Confirmed deaths	Origin / travel
Burundi	2,003	1	DRC, cross-border, 24 July 2024
Uganda	521	1	DRC, cross-border, 24 July 2024
Rwanda	37	0	DRC, cross-border, 24 July 2024
Kenya	17	1	Uganda, Tanzania, 25 July 2024
Sweden	1	0	East Africa
Thailand	1	0	RDC
India	1	0	**UAE**
Germany	1	0	Rwanda
Zimbabwe	1	0	**Tanzania**
Zambia	1	0	Zambia
United Kingdom	5	0	East Africa, 2 importations, 3 contacts
USA	1	0	East Africa
Canada	1	0	East Africa

Rapid risk assessment: summary table

Data as of 10 November

Risks groups*	Overall Public Health Risk	Risk of national and international spread	Confidence in the available information
Clade Ib **Mostly affecting non-endemic areas for mpox in the Democratic Republic of the Congo and neighbouring countries,** where mpox is spreading through human-to-human close contact, including sexual contact. International spread is predominantly linked to sexual contact	**High**	**High**	**Moderate**
Clade Ia **Mostly affecting mpox-endemic areas in the Democratic Republic of the Congo,** with sporadic cases reported from other Central and East African countries, where mpox is linked to zoonotic spillover events as well as human-to-human transmission, mainly through close physical contact, including sexual contact	**High**	**Moderate****	**Moderate**
Clade II MPXV (historically endemic areas) **Nigeria and countries of West and Central Africa where mpox is endemic**, affecting children and adults, and is linked to zoonotic spillover events as well as human-to-human transmission, mainly through close physical contact, including sexual contact	**Moderate**	**Moderate**	**Moderate**
Clade IIb MPXV **Global risk**, where outbreaks predominantly affect adult men who have sex with men and spread predominantly through sexual contact	**Moderate**	**Moderate**	**Moderate**

**All mpox outbreaks must be considered in their local context for in-depth understanding of epidemiology, modes of transmission, risk factors for severe disease, viral origins and evolution, and relevance of strategies and countermeasures for prevention and control.*

*** This group represents a very broad geographical area, with countries and regions that have very diverse health systems and response capacities, and, in selected countries or regional blocs in this group, the risk may vary and/or be assessed as low.*

A Public health emergency of international concern (IHR, 2005)

- Declared
  - 23 July 2022
- Lifted
  - 14 May 2023
- Declared
  - 14 August 2024
- Maintained
  - 22 November 2024

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WHO Response Plan

- WHO Response
- Global SPRP & Continental Plan
- Funding Appeal
- Underpinned by Strategic Framework (2024-2027)

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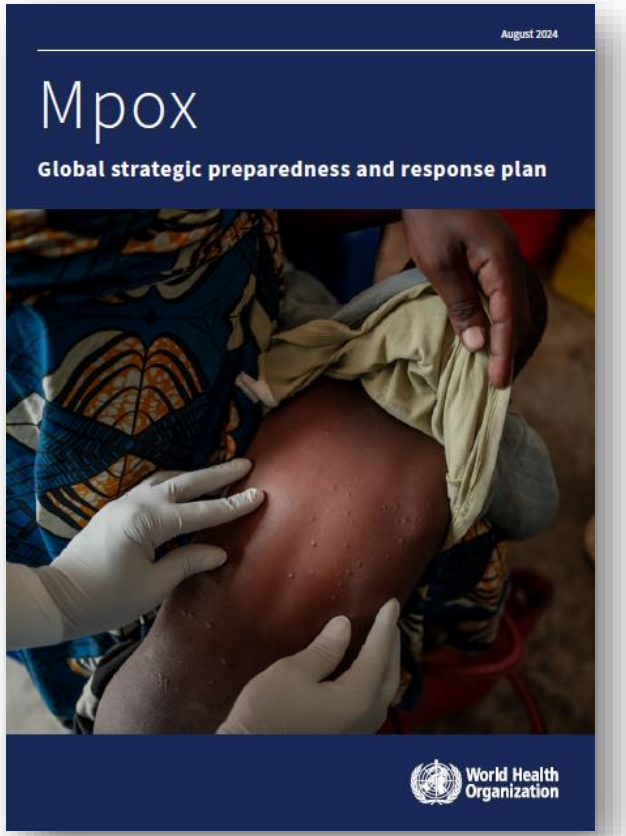
Mpox Comprehensive Strategic Preparedness & Response Plan



RESPONSE STRATEGY	OBJECTIVES	GOAL
C1 | Strengthened collaborative surveillance and detection Monitor and share information to improve collective understanding of how an outbreak is evolving, identify specific risk and inform response measures	Rapidly Detect And Control Outbreaks	Stop Outbreaks of Mpox Transmission
C2 | Enhanced community protection Raise awareness and empower communities to adopt protective measures		
C3 | Safe and scalable care Provide safe and quality clinical care for individuals and prevent infections in health settings	Advance Mpox Research & Access to Countermeasures	
C4 | Equitable access to medical countermeasures Ensure equitable access to effective diagnostics, vaccines and therapeutics for mpox response measures		
C5 | Emergency coordination Strengthen coordination between Member States and partners for public health response appropriate for the local context and risk	Minimize Animal to Human Transmission	

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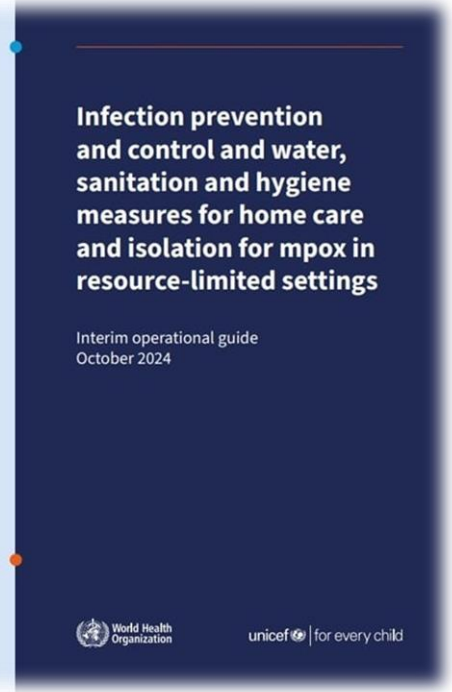
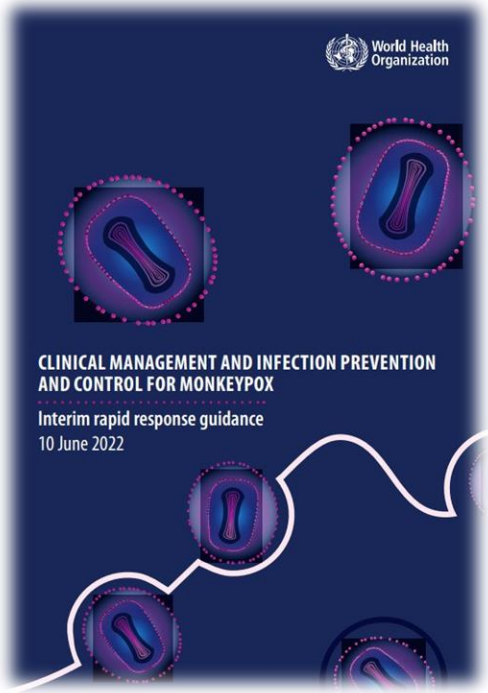
Clinical care





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Severe disease and complications

Skin exfoliation	*- May develop in patients with heavy rash burden, leading to dehydration and protein loss* *- Minimize fluid loss, promote skin healing, ensure hydration and nutrition* *- Bedside or surgical debridement as needed, skin grafting in severe cases*
Necrotizing soft tissue infection	*- Suspect in patient with edema, crepitus, malodorous discharge, pain out of proportion to appearance of infection* *- Can be caused by monkeypox virus and/or bacterial pathogens*
Ocular lesions	*- Patients may have non-specific ocular symptoms (e.g conjunctivitis)* *- Ophthalmologist evaluation and good eye care* *- May consider trifluridine drops if available*
Encephalitis	*- Consider lumbar puncture for cerebrospinal fluid evaluation* *- Monitor neurological status and control seizures with anti-epileptics* *- Treat co-infections with antibiotics and/or antivirals as indicated*

Other complications include balanitis, vaginal lesions, myocarditis, pneumonitis, bacterial co-infection, sepsis and shock

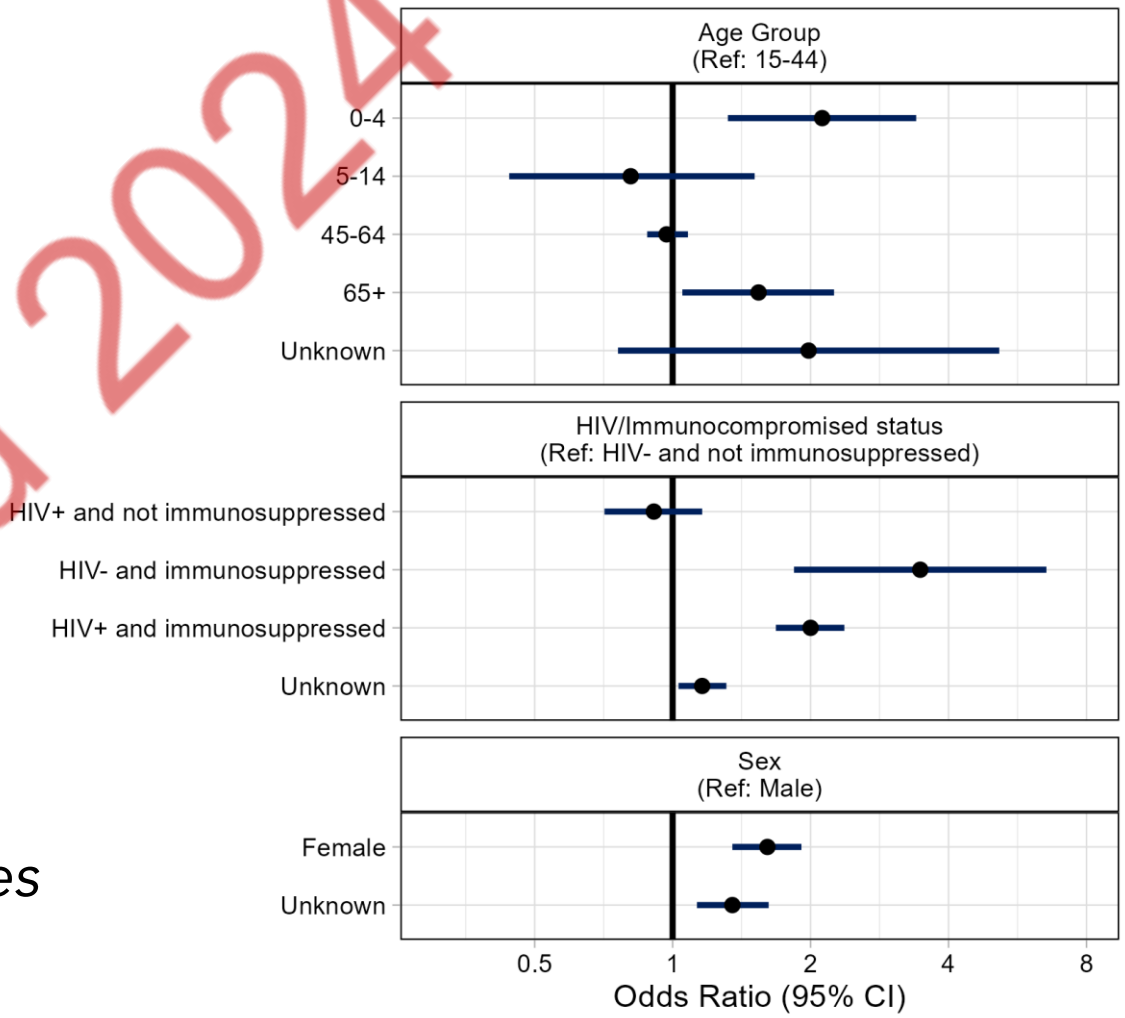
Role of HIV in mpox outcomes

WHO global data

- *Risk factor analysis shows an **increased odds of hospitalization** for:*
  - ***Children** < 5 years old*
  - ***Elderly** > 65 years old*
  - ***Female sex***
  - ***Immunocompromised**, due to HIV or other immunocompromising conditions*

- ***Risk for death** (data not shown) higher odds for:*
  - ***Immunocompromised** cases, due to HIV or other immunocompromising conditions*

- ***HIV infection** alone, treated, controlled does not lead to higher risk of mpox complications*



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Henry Laurenson-Schafer, Nikola Sklenovská, Ana Hoxha, Steven M Kerr, Patricia Ndumbi, Julia Fitzner, et al. Description of the first global outbreak of mpox: an analysis of global surveillance data. Lancet Glob Health. 2023 Jul;11(7):e1012-e1023. doi: 10.1016/S2214-109X(23)00198-5.

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Intersection between HIV & mpox

What we know

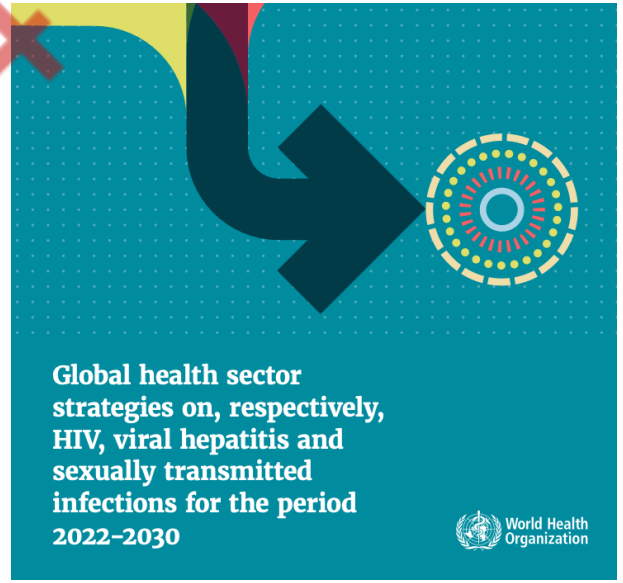
- *Both mpox and HIV can be transmitted in sexual networks*
- *Among IIb outbreak cases with known HIV status, ~ **50%** are living with HIV*
- *Immunesuppression from uncontrolled HIV infection or other conditions is a risk factor for severe or fatal disease; **same pattern is beginning to appear for clade Ib***

Clinical and public health implications

- *Strong HIV prevention and care are central pillars of mpox outbreak preparedness and response*
- *Eliminating stigma and discrimination supports equal access to services*
- *Person-centred delivery of mpox control interventions in sexual health services (including HIV programmes) can improve outcomes and efficiency*

What we don't know – research priorities for HIV-mpox

- *Therapeutics RCTs are still underway*
- *Role of HIV immune reconstitution inflammatory syndrome (IRIS)*
- *Relationship between HIV infection and mpox immune response [antibodies/cell mediated immunity]*
- *Interactions between antiretrovirals and mpox antivirals/therapeutics*



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Key messsages

Unusual skin or mucosal lesions should be assessed for mpox by a healthcare provider

Persons with mpox should be treated symptomatically with optimal supportive care to alleviate symptoms and prevent complications; ALL cases must be reported to your public health authority

Persons with HIV and severe immunosuppression with mpox are at risk of death

Persons with mpox should be screened for HIV and other STI's to allow for diagnosis and treatment

If person with mpox has complications or severe disease consider antivirals (still under study)

mpox prevention

Vaccine

Prevents infection and complications of mpox

Education

Helps people make informed decisions about their sex lives and how to protect themselves and others

Testing

Allows for public health action, supportive care and access to therapeutics.

Mpox outbreak situation

Today

MPXV outbreaks continue, clade IIb, clade Ib, now clades Ia and IIa

PHEIC Aug 2024

May 2022

MPXV clade IIb outbreaks spread around globe

PHEIC July 2022

2017

MPXV clade IIb outbreak in Nigeria

1980s

Mpox re-emerges in Africa

The public needs access to reliable vaccines to prevent serious mpox disease and death

WHO Strategic Advisory Group of Experts on Immunization (SAGE) recommends

Pre-exposure vaccination for people at high risk of exposure

Post-exposure vaccination

Using third-generation vaccines known as MVA-BN or LC16m8*

*Note: 2nd generation vaccines such as ACAM-2000, although not having an mpox indication, are also recommended by WHO SAGE with risk-benefit assessment where non- or minimally-replicating vaccines not available

Vaccine products licensed for use against mpox or authorized for emergency use

Product	Description	Dosing	Administration / presentation	Where licensed	Indicated age group
MVA-BN	Non-replicating vaccinia-based vaccine, 3rd generation	Two doses four weeks apart	• Needle and syringe (subcutaneous or intradermal administration) • Liquid frozen or freeze-dried	Canada, EU, USA, UK, Switzerland, Nigeria	CA, EU, UK, CH: 18+ US: 18+ <18 under EUA
LC16	Minimally replicating vaccinia-based vaccine, 3rd generation	Single dose regimen	• Bifurcated needle, percutaneous route/administration • Freeze-dried Multidose vials	Japan, DRC	All ages, no limitations
ACAM2000	Replicating vaccinia-based vaccine, 2nd generation	Single dose regimen	• Bifurcated needle, percutaneous route/administration • Freeze-dried Multidose vials	USA (Emergency investigational new drug)	US: 16+
OrthopoxVac	Non-replicating, vaccinia-based vaccine, 4th generation	Single dose regimen	• Needle and syringe (intradermal administration) • Freeze-dried	Russian Federation	18 to 60 years
CJ-50300	Live replicating, 2nd generation	Single dose regimen	• Bifurcated needle • Freeze-dried, multidose vials	Republic of Korea (Emergency Use Authorization)	20 to 60 years

Not currently in use for mpox prevention and response

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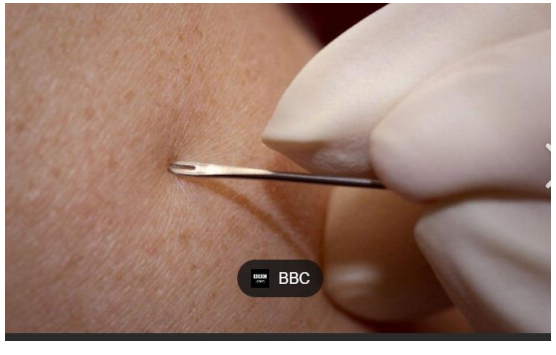


Mpox vaccine options

Globally, three vaccines have been granted mpox indications (regardless of viral clade)

MVA-BN

- Regulatory authority approvals: Imvanex (EU, UK), Imvamune (Canada), or Jynneos (Switzerland, USA) in adults + DRC, Nigeria, Rwanda…
- WHO prequalified October 2024

Manufactured by BAVARIAN NORDIC A/S Kvistgård, Denmark

LC16m8

- Stringent regulatory authority approval: Japan for children and adults
- WHO emergency use listing November 2024

ACAM-2000

- Also approved for mpox prevention in adults

Manufactured by kmb KM Biologics Co., Ltd. Kumamoto, Kyushu, Japan

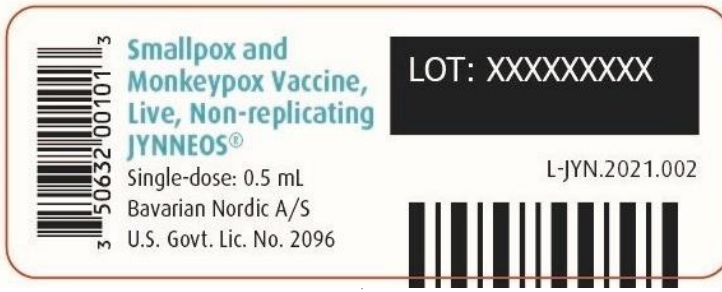
Modified Vaccinia Ankara (MVA or MVA-BN) (1/3)

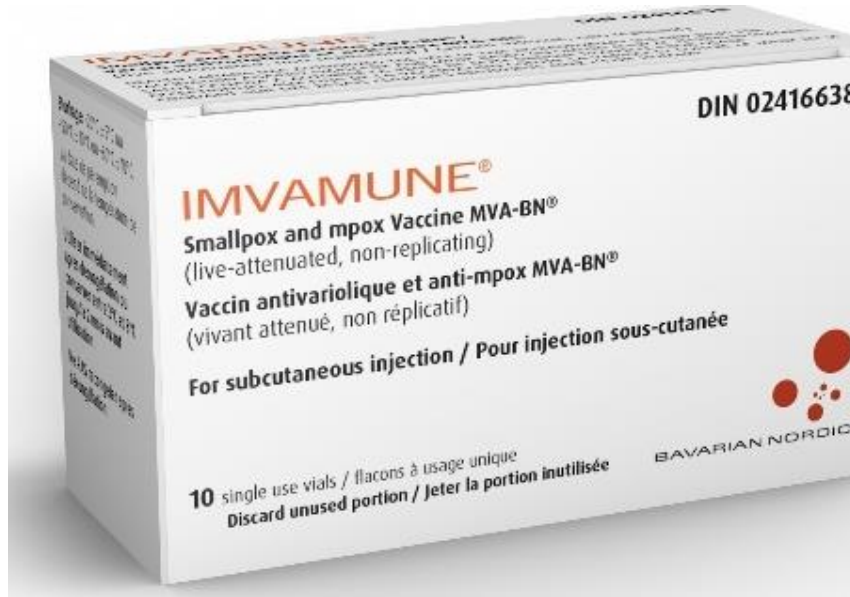
Product development at Bavarian State Vaccine Institute in Munich in **1970s** yielding *Modifiziertes Vakziniavirus Ankara*, or modified vaccinia Ankara (MVA)

MVA-BN traces its heritage to the **1950s** at the Turkish Vaccine Institute in Ankara

In **1998**, one vial of MVA transferred to Bavarian Nordic A/S, developed into product known as MVA-BN

Prevention of mpox infection in adults added as indication: 2019 to 2024





Modified Vaccinia Ankara (MVA-BN) (2/3)

Safety

- MVA virus cannot replicate in human cells
- MVA-BN cannot induce cutaneous “take” reaction
- Common injection-site reactions:
  Pain, redness, swelling, induration, itching
- Common systemic events:
  Muscle pain, headache, fatigue, nausea, chills

No significant safety signals detected

- After ~2 million doses administered globally
  - Including hundreds of children
  - Including thousands living with HIV
- After vaccination of
  - People with atopic dermatitis
  - People with weakened immune systems
- With vaccination during pregnancy

Modified Vaccinia Ankara (MVA-BN) (3/3)

Programmatic Considerations

- Administer two doses of MVA-BN 28 days apart
- Begin post-exposure preventive vaccination (PEPV) as soon as possible after exposure
- Reduced-dose intradermal administration
  - Requires specific training
  - As safe and as immunogenic as subcutaneous
- Packaged in single-dose vials
- Cold-chain requirements [−80°C 9 years, −50°C 5 years, −20°C 3 years; after thawing, store at 2°C–8°C for up to 2 months (EU label) and 4 weeks (US label)]

WHO/SAGE Recommendations

MVA-BN suitable for:

- People at risk for repeated exposure to mpox
- Close contacts of people with mpox
- Children – off-label use
  - Note, used *via* emergency provisions in many countries
- Pregnant women
- People with proliferative skin disease
- People with weakened immune systems

LC16m8 or LC16 (1/3)

Origins

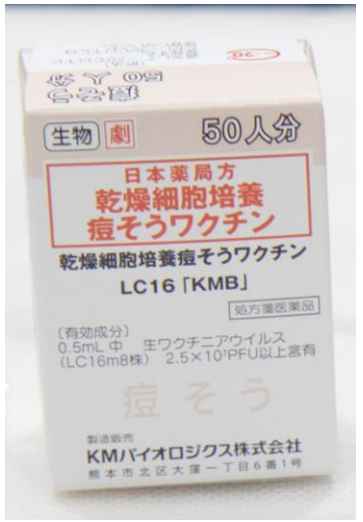
LC16m8 is attenuated, replicating vaccinia virus strain developed in early **1970s**. Initially produced by Chiba Serum Institute near Tokyo

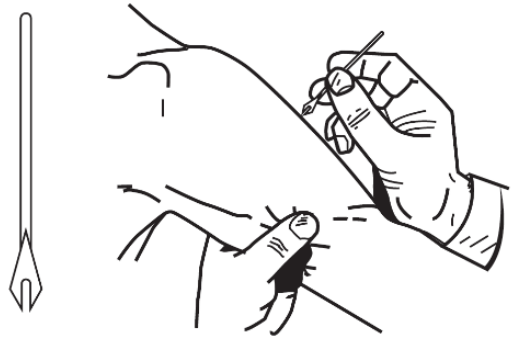
Transferred to Chemo-Sero-Therapeutic Research Institute (Kaketsuken) as of **2002**

Prevention of mpox infection added as an indication in July **2022**

Today

KM Biologics manufactures finished product called LC16 “KMB” Given by inoculation (scarification) with bifurcated needle





LC16m8 has lower neurovirulence and replication competence than traditional vaccinia strains

LC16m8 or LC16 (2/3)

Safety

- Multiple studies among tens of thousands of human volunteers given LC16m8: LC16m8 is well-tolerated
- 1974-75: **10,578** Japanese children (most <4 y) closely followed after LC16m8
- Common site reactions: Tenderness, fever, fatigue, rash, redness, itching, autoinoculation
- Other adverse events: Swollen lymph nodes, febrile seizures, anaphylaxis
- Researchers attributed no severe adverse events to vaccination
- LC16m8 is suitable for children at risk of exposure to MPXV virus
- Containing a minimally replicating virus, LC16m8 is unsuitable for people who are immune suppressed, have proliferative skin diseases, or are pregnant

LC16m8 or LC16 (3/3)

Programmatic Considerations

- One dose by inoculation (scarification) with 15 punctures of a bifurcated needle
- Begin post-exposure preventive vaccination (PEPV) as soon as possible after exposure
- Scarification and related infection-control procedures require specific training
- Packaged in multi-dose vials (up to 250 doses per vial)
- Freeze-dried (lyophilized) product
- Cold-chain requirements non-reconstituted product (<−20°C 10 years)*

*Note: Japanese MHLW have indicated that under emergency use, data support stability for up to 24 hours at 37°C after reconstitution. Further, after aseptic dispensing, the vaccine retains potency at 4°C for up to one month. MHLW have further confirmed stability prior to reconstitution at 5°C 2 years, 37°C 4 weeks

WHO/SAGE Recommendations

- LC16m8 suitable for:
  - People at risk for repeated exposure to mpox
  - Close contacts of people with mpox
  - Approved for use in children
  - Immune-competent people (may include persons living with HIV if treated and controlled)

Vaccine allocation

September 2024

AfricaCDC

p of October Vaccine Allocation Ro und, 899,000 doses of MVA-BN vaccin

Country	Recommended allocation	Conditional allocation	Total doses	Comments on Conditionalities
Central African Republic	12.300		12.300	
Democratic Republic of the Congo	548.100	217.100	765.200	*Expanded use to 12-17 yrs*
Kenya	10.700		10.700	
Rwanda	38.600		38.600	
Uganda	10.000		10.000	
Côte d'Ivoire	11.300		11.300	
Liberia	10.800		10.800	
Nigeria	11.600	18.500	30.100	*Experience once vx starts*
South Africa		10.000	10.000	*Confirm vx, inter-action review*
Totals	**653.400**	**245.600**	**899.000**	

- Allocation quantities do not meet the full needs of countries
- Deliveries are commencing this week

November allocation round: 975,700 doses for delivery from December

Way forward

- **Addressing acute needs of public health emergency while reaching Long-term goals:**
  - ✓ While controlling the upsurge, support future national programmes (including surveillance , research, medical countermeasures…)
- **Monitoring and Evaluation to guide response activities:**
  - ✓ Conduct operational reviews to readjust responses
- **Urgent Call to Action:**
  - ✓ Raise awareness of all clinicians
  - ✓ Improve notification of cases to better understand the epidemiology
  - ✓ Mobilization of additional financial resources
  - ✓ Further research on prevention, treatment and response
  - ✓ Further vaccines donation and allocation

World Health Organization

Strategic framework for enhancing prevention and control of mpox

Goal

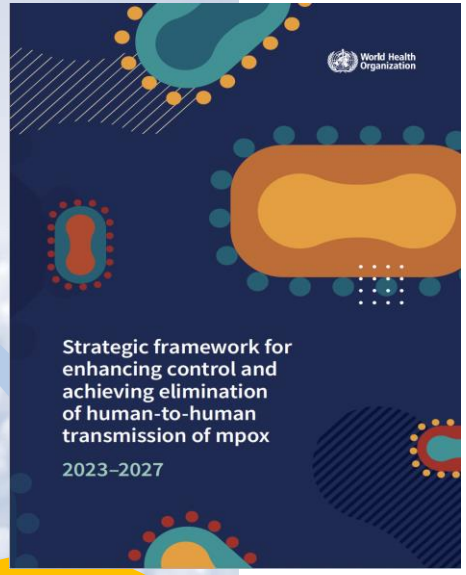
Achieve and sustain elimination of human-to-human transmission of mpox

Objectives

Achieve control of mpox outbreaks in every context

Advance mpox research and access to countermeasures

Minimize zoonotic transmission of mpox



Key consideration

Goal and objectives apply for all countries and contexts for all modes of transmission

Strategic framework for enhancing prevention and control of mpox- 2024-2027 (who.int)

Strategic framework for enhancing prevention and control of human-to-human mpox transmission : approaches and guiding principles

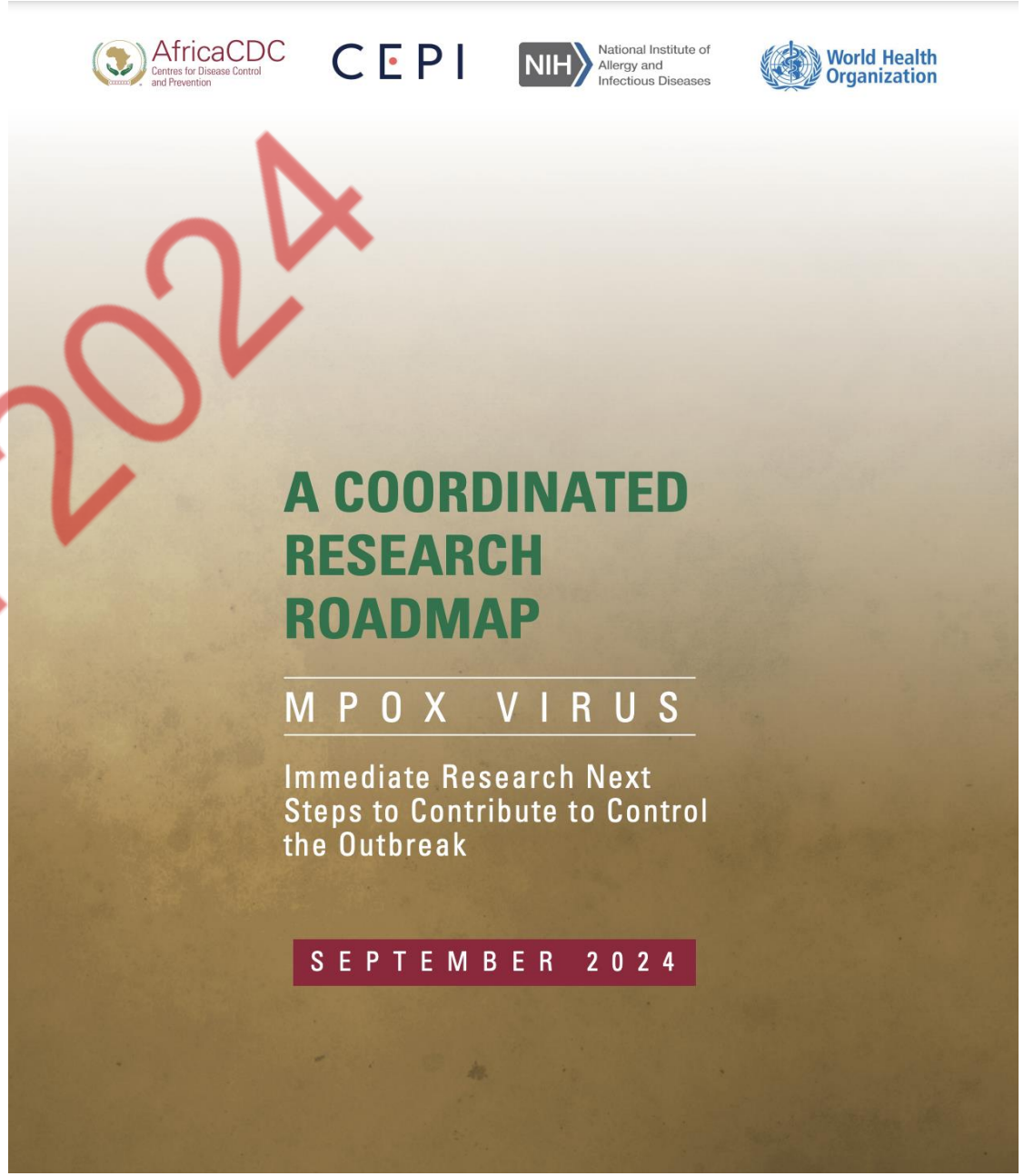
- **Communicate – Collaborate - Integrate**

Approach	*Guiding Principles*
Know your epidemic	*Community leadership*
Know your risks	*Equity and human rights*
Know your community	*Context-specific collaboration and integration*
Know your needs	*Commitment to continuous learning*
Take action	

WHO Operational Response

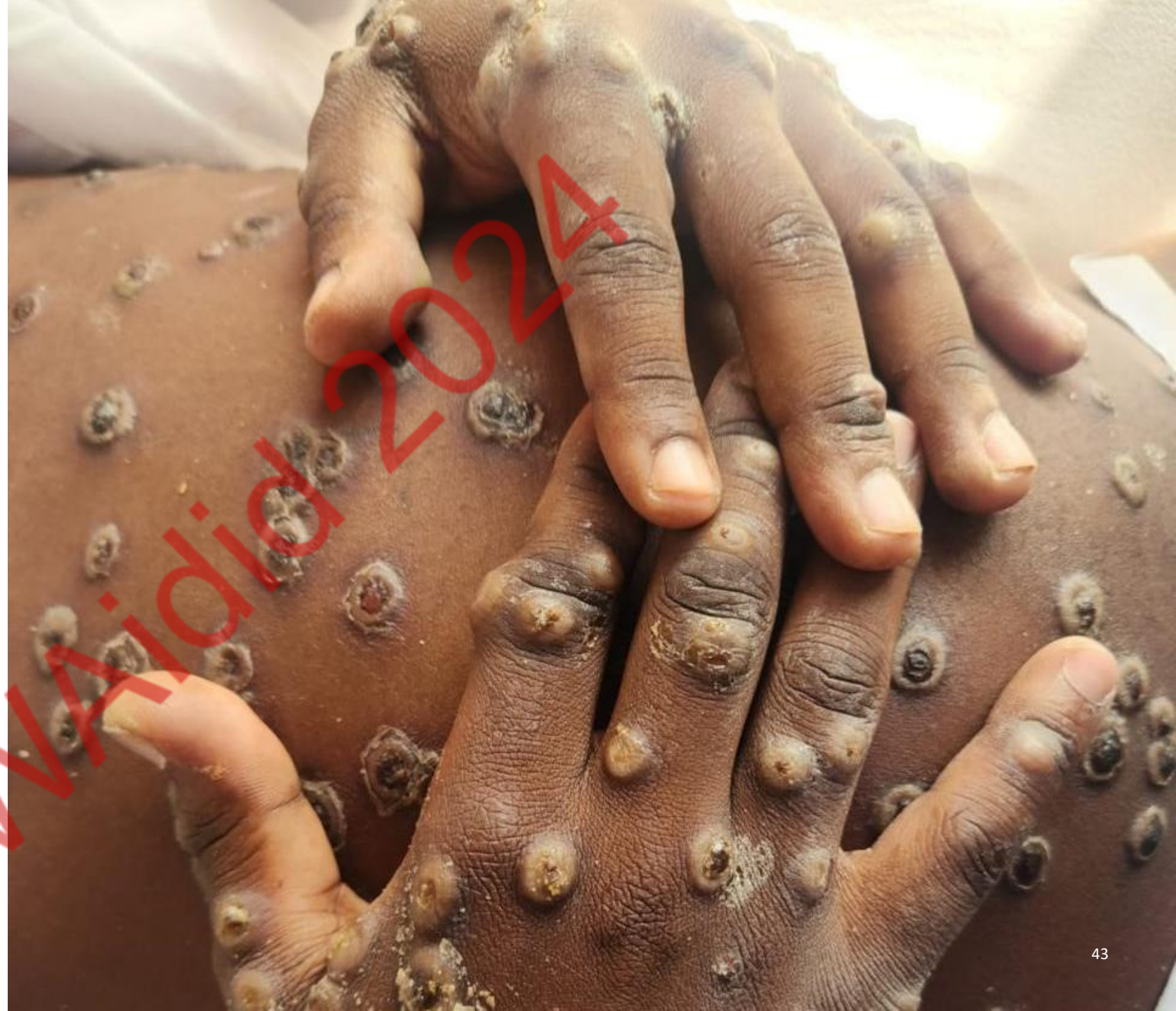
World Health Organization

More research is needed



World Health Organization

Questions & Discussions



World Health Organization

Therapeutics

Tecovirimat

- inhibits viral envelope formation of MPXV by targeting the viral protein p37
- licensed by the European Medicines Agency (EMA) for the treatment of smallpox, mpox, cowpox and complications from immunization with vaccinia and by the United States Food and Drug Administration (FDA) and Health Canada for smallpox

Brincidofovir

- inhibits replication of MPXV by inhibiting polymerase-mediated synthesis of DNA
- licensed by the EMA and FDA for treatment of smallpox

NIOCH-14

- analogue of tecovirimat with comparable activity against orthopoxviruses, approved by the Russian Ministry of Health

Cidofovir

- approved by FDA for treatment of CMV but inhibits replication of MPXV by inhibiting DNA polymerase

Vaccinia immune globulin

- composed of antibodies from individuals inoculated with the smallpox vaccine

Preferable to use antivirals under randomized clinical trials (RCTs) and when not possible, may be used under compassionate use or expanded access protocols