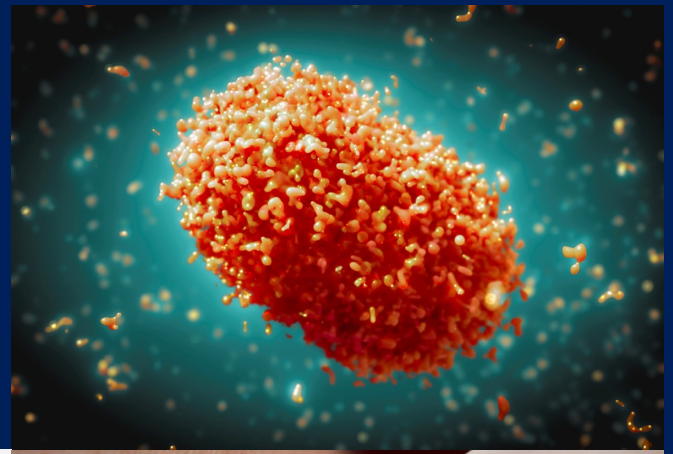
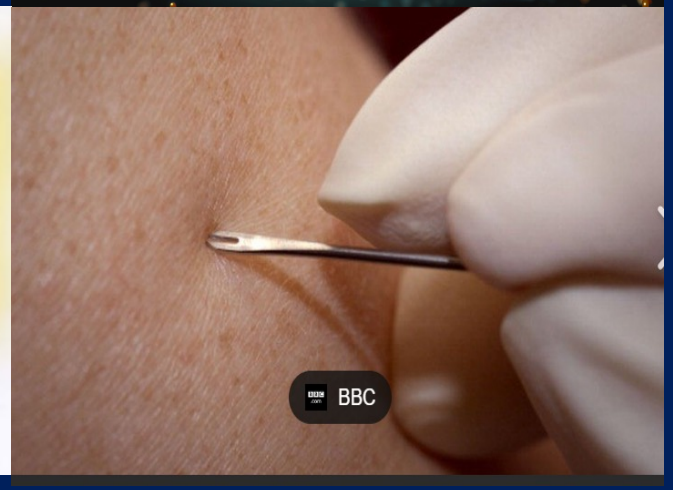
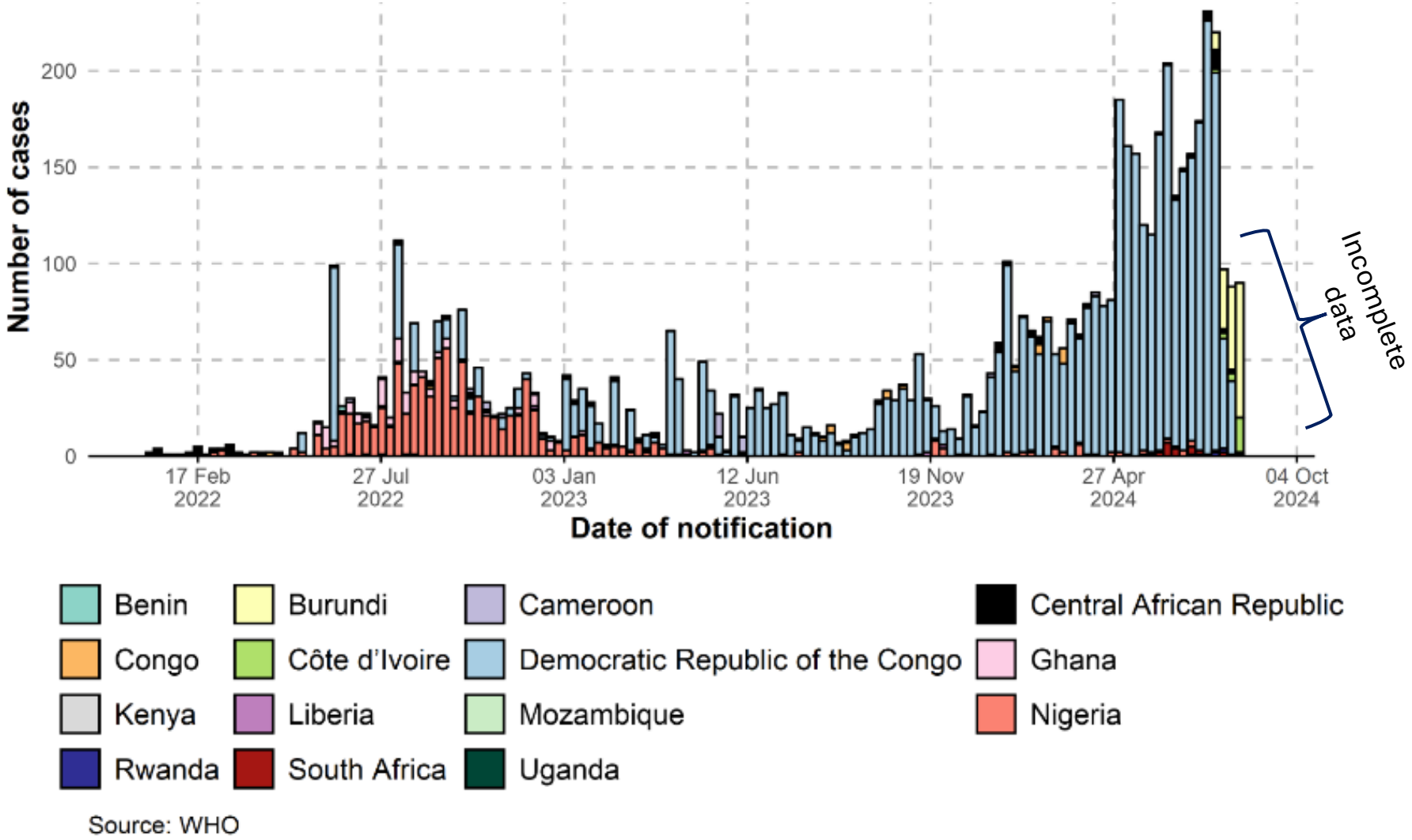
Status of mpox outbreaking the African Region and use of mpox vaccines





WHO African region epi curve, confirmed cases as of 25 Aug



Source: WHO

Total confirmed cases as of 25 August 2024 since 2022

7 658

Total confirmed deaths as of 25 August 2024 since 2022

54 (CFR = 0.7%)

Total confirmed cases and deaths from 01 Jan - 25 Aug 2024
Cases = 5281
Deaths: 32 (CFR = 0.6%)

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African countries actively affected as of 25 August 2024

Newly affected or re-affected countries in July / August 2024

- Burundi
- Rwanda
- Uganda
- Kenya
- Cote d'Ivoire
- Liberia
- Gabon
- Republic of Congo
- Nigeria
- Central Africa Republic
- South Africa

Suspected cases are being investigated in other countries.

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Newly affected countries with Clade 1b

- **Emerged in 2023** and has been spreading through sustained human-to-human transmission in eastern DRC since September 2023, in absence of zoonotic exposure.
- Detected **in six other countries: Burundi, Rwanda, Kenya, Uganda, Sweden,** and **Thailand**.
- Current estimated **Case Fatality Ratio is 0.7%** in **DRC***.
- **All mpox types of transmission still continue to occur**, but sexual contact has amplified the transmission quickly in certain networks and areas.
- **Drivers of transmission: human-to-human close contact**, including sexual contact, as well as other mpox modes of transmission.
- No deaths have been reported so far outside of DRC

Country	# confirmed cases	Distribution
Burundi	231	Dispersed in the country
Rwanda	4	3 in capital; 1 in border district
Uganda	4	Multiple districts
Kenya	2	PoE with Tanzania
Sweden	1	Travel history to Africa
Thailand	1	Travel history to Africa

**Available data from South Kivu for Epi Weeks 1-34*

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Complexities in understanding mpox transmission

- **Unknown** animal **reservoir**
- **Unclear** contribution of **zoonotic and human-to-human transmission** in African setting
- Different **distribution** of **MPXV clades** and **subclades**
- **Low sequencing** available in the African Region to monitor emerging strains
- Unclear human-to-human **transmission dynamics** in different settings
- **Different** age groups and **demographics** are affected in different geographical areas making the **comparison** of severity and outcomes **complex to interpret**
- **Multiple concurrent outbreaks**, with different characteristics are ongoing in endemic and newly affected provinces of the **DRC**
- Affected areas in the eastern part are also affected by **conflict and insecurity** which **hinder surveillance and response** activities

Standing recommendations

Standing recommendations for mpox issued by the Director-General of the World Health Organization in accordance with the International Health Regulations (2005) (IHR)

21 August 2023

"States Parties are recommended to develop and implement national mpox plans that build on WHO strategic and technical guidance, outlining critical actions to sustain control of mpox and achieve elimination of human-to-human transmission in all contexts through coordinated and integrated policies, programmes and services."

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Vaccines and other countermeasures are included, importantly, the DG's standing recommendations on mpox

States Parties are recommended to

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

B. Strengthen and sustain testing and surveillance capacity and ensure that new cases of mp…

C. Protect communities through communication and engagement; continu… …on.

D. Invest in research to better understand mpox disease… …proved vaccines, tests, and treatments.

E. Provide travelers with i… …fore, during and after travel and refrain from implementing travel-related h… …sting for travelers.

F. Deliver o… …tients, integrated within HIV and STI programmes, with access to treatments and measures to protect hea… …givers.

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

Extended to August 2025

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Vaccines & immunization are a critical component of the overall strategic framework for mpox control

Components

C1 | Emergency coordination
Strengthen emergency operations and coordination between Member States and stakeholders for public health response appropriate for the local context and integrated with key health services

C2 | Collaborative surveillance
Monitor and share information to improve collective understanding of how an outbreak is evolving, identify specific risk, and inform response measures

C3 | Community protection
Raise awareness and empower communities to adopt protective measures.

C4 | Clinical care
Provide safe and quality clinical care for individuals and prevent infections in health and community settings

C5 | Countermeasures
Improve access to effective diagnostics, vaccines and therapeutics for mpox

C6 | Research
Drive the cross-cutting research agenda in all areas

Objectives

1. Achieve control of mpox outbreaks with focus on groups at risk in each context
2. Advance mpox research and access to countermeasures
3. Minimize zoonotic transmission of monkeypox virus

Goal

Stop mpox

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Vaccine products are currently licensed across various countries for use against mpox, but are not *prequalified*

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	Canada, EU, UK: 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	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), Australia, Singapore	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

Additional details not currently available / under ascertainment

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Mpox vaccines in the African Region

- Vaccines currently not prequalified or have emergency use listing (EUL)
- WHO DG triggered the process for EUL for mpox vaccines, which will accelerate vaccine access in the African Region
- EUL also enables partners including Gavi and UNICEF to procure vaccines for distribution

R&D: evidence gaps remain on the use of mpox vaccines

Category	Evidence gap	Note
Safety	Safety during pregnancy and breastfeeding	No data
	Surveillance and monitoring of serious adverse events, including in subpopulations	No safety signals to date
	Safety in immunocompromised persons, including advanced HIV, persons with autoimmune disease	HIV not a contra-indication
	Further safety profile in persons below the age of 18 years, including in young children	LC16 licensed for children; MVA-BN-filo approved for children; MVA-BN study 12-18 years underway
Immunogenicity & effectiveness	Immunogenicity and VE in persons below the age of 18 years, including in young children	Studies proposed, RCT needed
	Vaccine effectiveness over time, need for booster	13 observational studies show 82% for 2 doses (MVA)
	Correlates of initial protection and correlates of durability of protection	Smallpox immunity gap globally
	Assessment and reporting of breakthrough infections	Expected for VE of 82%
Epidemiology	Evidence on risk factors for mpox exposure, especially in LMICs	Need to strengthen surveillance, descriptive epi
	Evidence on severity of disease, including in children, especially in LMICs	Need case-based surveillance, clinical characterization, causes of death
	Evidence on modes on transmission in LMICs, including in children	Multi-disciplinary, One Health approach
	Seroprevalence studies	Needed to assess background risk
	Duration of protection following natural exposure	Occasional re-infection documented

Studies are on-going to close these evidence gaps

Study	Location(s)	Sponsor	Product	Description
Cluster-randomization phase 3 vaccination trial to evaluate the efficacy and safety of the LC16	DRC	INRB / MSPHP (DRC); MHLW (Japan)	LC16	Open-label phase III vaccine trial to test the efficacy and safety of the LC16 vaccine in population and region where mpox occurs
SMART (Smallpox vaccine for Mpox for Post-Exposure Prophylaxis: A Cluster Randomized Controlled Trial)	Nigeria (DRC, Uganda)	McMaster University (Canada)	MVA-BN	A pragmatic, adaptive, multi-site, double-blind, cluster-randomized trial where households with one or more persons confirmed to have mpox (index) will be randomized to smallpox vaccine or control.
Non-inferiority study of MVA in children from 2 to less than 12 years of age compared to adults	TBD	Bavarian Nordic	MVA-BN	Open-label, comparative, multi-center immunogenicity and safety study in children compared to adults
Randomized controlled trial to assess the efficacy of LC16 in population HIV+, PrEP, MSM	Colombia	KM Biologics	LC16	Parallel open-label sequential randomized controlled trial
REMAIN Prospective cohort (18 years and older)	Multi-sites	Fundación FLS de Lucha Contra el Sida	MVA-BN	Observational trial to assess effectiveness of MVA-BN in Spain and Latin American countries
A two-staged phase 2 randomized, open-label trial	USA	NIAID	MVA-BN	Comparison of the immunogenicity and safety of MVA-BN in adolescents aged 12-17 years to adults aged 18-50 years
SEMVac Safety and effectiveness MVA-BN in at risk population	Germany	TBD	MVA-BN	Multicenter prospective cohort study in adults at risk

Several pathways exist for regulatory assessment of available vaccine products

#	Pathway	First steps	Benefits	Considerations
1	**WHO Emergency Use Listing/ Prequalification Procedure**	• DG decision required to allow opening of Expression of Interest (EoI) • WHO would then open EoI	• Unlocks UNICEF / Gavi procurement & support • Single entry to all Member States	• Requires specific emergency context • Indemnification and liability issues must be addressed
2	**Use under RCTs / research protocols (randomization non deployment)**	• NRA / Ethics Committees approve an mpox study protocol	• Quicker access • Opportunity to close clinical data / evidence gaps in target groups (e.g. children)	• Requires political decisions based on public health needs
3	**Stringent Regulatory Authority (SRA)-facilitated National Regulatory Authority (NRA) review**	• Country must request support from SRA • SRA shares assessment reports and /or engages in joint review with NRA	• Enables access to currently indicated age groups for possible outside of the clinical trials	• Requires safety monitoring outside of controlled clinical trial • More difficult to collect clinical data to close data gaps • Must be done for each country

NOT EXHAUSTIVE

Countries can access available mpox products through several mechanisms

#	Mechanism	Flow	Description
1	**Direct procurement**	Manufacturer to country	Countries that have the requisite policy, regulatory and financial capacity procure vaccines directly from manufacturers
2	**Pooled procurement**	Manufacturer to 3rd party to country	Global / regional initiatives to aggregate demand across countries for combined procurement from manufacturers (ex. PAHO Revolving Fund, HERA)
3	**Coordinated donations**	Country (or manufacturer) to 3rd party to country	Global / regional initiatives to accept donations from countries / partners / manufacturer for subsequent redistribution
4	**Bilateral donations**	Country to country	Countries with supply to spare donate doses (and materials) to requesting countries

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What should countries who want to use mpox vaccines do next?

- Discuss with **national immunization technical advisory groups (NITAGs)**

- Begin **regulatory approval*** for bringing new vaccines in country
  - National regulatory authority
  - Ethics review committee

- Consider research protocols as way to incorporate vaccination into the response and close key knowledge gaps

*The African Vaccine Regulatory Forum (AVAREF) platform in WHO AFRO is being used to facilitate the authorization of vaccines

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THANK YOU

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