

WEEKLY SCIENTIFIC REVIEW ON MPOX OUTBREAK

EDITION 13 NOVEMBER 2024 No. 39

The content of this document are subject to change as the health situation evolves. All informations comes from a valid and credible source.

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General informations

This section details the history and latest developments of the outbreak, with updates on its current status and risk assessment.

During summer 2022, an unprecedented mpox outbreak affecting multiple regions outside the African continent, with no previous history of sustained community transmission, has led to the WHO declaring a **Public Health Emergency of International Concern (PHEIC) on 23rd July 2022**. This outbreak, caused by **clade IIb MPXV strains from B.1 lineage**, resulted in nearly **109,699 cases** and **236 deaths** in more than 100 countries. The spread of this epidemic was mainly driven by local, in-country transmission via sexual contact among men who have sex with men (MSM), rather than at the animal-human interface as seen previously during zoonotic outbreaks observed in Africa. Timely and concerted public health responses from governments, international health organizations and affected communities - primarily MSM – yielded a significant decline of the disease burden throughout the following months, leading the WHO to end the mpox emergency status on 10th May 2023. While progress has been made in tackling the epidemic, human mpox cases and clusters are still being reported widely, notably in endemic countries, and concerted efforts must be pursued to ensure long-term management of the disease.

Since the beginning of 2023, the increasing frequency of outbreaks with **clade la MPXV** in African regions, particularly in the Democratic Republic of the Congo (DRC), has become a major concern. In 2023, health authorities in DRC have reported 14,626 suspected cases and 654 deaths, the **highest incidence ever recorded in the country**. This year, and as of 3 November 2024, there have been **8,882 confirmed cases** (39 501 suspected cases) and **43 confirmed deaths** (1073 suspected deaths) representing a **two-fold increase compared to the same period last year**. Additionally, case reports have been expanding into previously unaffected regions, with 25 of the 26 provincial health departments reporting active mpox circulation as the current epidemic unfolds, including three new provinces notifying cases this year. The provinces reporting the highest numbers of suspected cases are Equateur (North-West), Sud Unbangi (North-West), Sankuru (Central), Tshopo (North-Central) and South Kivu (East). **Children under the age of 15** are the most affected group, accounting for **66%**



of mpox reported cases and 82% of fatalities. Disease contraction and spreading are likely attributable to zoonotic transmission and interactions during playtime. In 2024, the number of reported cases has continued to rise in certain settings in Africa where the disease is endemic, such as the Central Africain Republic, the Republic of the Congo, Cameroon, Côte d'Ivoire, Liberia and Nigeria.

Between April and September 2023, the Ministry of Health of the DRC informed the WHO of outbreaks in previously unaffected provinces, linked to **sustained human-to-human transmission**, without suspected animal exposure. In April, a cluster of six confirmed mpox cases was reported in Kwango province among locals – five men and a woman – who had engaged in sexual relations with a Belgian resident presenting with genital and anal lesions. **This is the first formally documented sexual transmission of clade I MPXV viruses**. In August, four independent mpox clusters were recorded in Kinshasa, each originating from individuals who had been exposed in other provinces and subsequently traveled to the capital. In September, epidemiological reports from Kamituga identified a cluster of patients among adults, many of whom identified as sex workers, further supporting the shift towards sexual transmission patterns. Since then, the local outbreak of Kamituga has been expanding geographically in the rest of South Kivu province (East) and recently to neighbouring North Kivu, with 373 confirmed mpox cases as of 2 June 2024. The majority of the cases are among **persons aged over 15 years**, who have reported both sexual and non-sexual direct contacts. No evidence of zoonotic transmission have been reported in the province since the start of the outbreak.

Phylogenetic analyses revealed a **novel variant of clade I MPXV (sublineage lb)**, which is estimated to have emerged around mid-September 2023 in Kamituga, and have been responsible for the local outbreaks found in South and North Kivu via sustained human-to-human transmission. This variant exhibits **APOBEC-3 type mutations**, indicative of viral adaptation to human hosts. Although clade Ib MPXV currently accounts for a minority of reported mpox cases in the country, the rapid evolution of the outbreak in South and North Kivu, particularly among sex workers, raises significant concern about further expansion in the eastern mining provinces and other countries which share national borders or high cultural identities with DRC. The introduction of clade Ib MPXV into various and possibly intersecting sexual networks could facilitate and amplify the spread and the burden of this historically more virulent clade, although it remains unknown if this variant is more transmissible or causes more severe disease than other circulating strains. Furthermore, the potential for human-to-human transmission is enhanced in urban settings such as Kinshasa, the capital home of 17 million inhabitants, where the implementation of containment measures is more challenging.

Between 23 September and 3 November 2024, human mpox infections were reported in **Rwanda**, **Burundi** (1030 confirmed cases), Kenya and **Uganda** (324 confirmed cases), all four neighbouring countries of the DRC. Several patients had recently traveled to the DRC or other regions with suspected MPXV circulation. Sequencing confirmed the **clade 1b sublineage** in cases detected in Rwanda, Kenya, and Uganda and Burundi. Several countries — Gabon, Guinea, Ghana, Zambia and Zimbabwe — recently reported its first mpox cases, lifting the **number of affected African countries to 17**.

In August and September 2024, travelers returning from high-risk regions have been detected with clade 1b mpox in some countries outside Africa, including Sweden, Thailand, and India, marking the first documented cases of clade 1 outside the African continent.

On 14th August 2024, in response to these alarming developments, **the WHO declared a second PHEIC related to mpox outbreak**, based on the recommendations of an IHR Emergency Committee. This decision came a day after the Africa CDC had designated the escalating outbreak in DRC and in a growing number of countries in Africa as **a Public Health Emergency of Continental Security (PHECS)** on August 13, 2024. The WHO is reviewing the risk assessment for mpox for the general population and is developing a new regional response plan to support surveillance, preparedness and response efforts. This plan will be implemented in collaboration with the governments of the affected countries, the Africa CDC, NGOs, and civil society. Additionnally, in collaboration with international partners and manufacturers, the WHO has activated the emergency process to accelerate vaccine access and donations for both MVA-BN and LC16, particularly for lower-income countries that have not yet issued their own national regulatory approval for the vaccines.

The Africa CDC assesses the risk of mpox in African countries as **high** due to the higher case fatality rate on the continent, despite the disease being moderately transmissible and usually self-limiting. In the EU/EEA, the risk from clade 1, including the novel variant 1b, is considered **very low**, as there is no evidence of its circulation outside Central Africa, and current vaccines and treatments are expected to remain effective. The risk of infection from mpox clade 2b, remains low for the general population and moderate among higher risk groups such as MSM or other individuals who have multiple sexual partners.

Sources:

- i. Mpox (monkeypox) Democratic Republic of the Congo | Disease Outbreak News. World Health Organization. 23 November 2023.
- ii. Mpox Democratic Republic of the Congo | Disease Outbreak News. World Health Organization. 14 June 2024.
- iii. Mpox African Region | Disease Outbreak News. World Health Organization. 22 August 2024.
- iv. Africa CDC Epidemic Intelligence Weekly Report, 16 August 2024.
- v. Multi-country outbreak of mpox, External situation report#34. World Health Organization. 28 June 2024.
- vi. DR Congo grants emergency use for 2 mpox vaccines | News Brief. CIDRAP. 27 June 2024.
- $vii. \quad \text{WHO Director-General's opening remarks at the media briefing-} \ 7 \ \text{August 2024.} \ \text{World Health Organization.}$
- viii. Risk to EU/EEA from variant mpox virus 'very low' | News. ECDC. 29 July 2024.



Scientific articles

This section presents relevant articles published on peer-reviewed scientific journals or pre-print platforms.

Hidden in plain sight: the threat of mpox to children and adolescents. Sanchez Clemente N, Le Doare K, Mupere E, Nachega JB, Rulisa S, Titanji B.

Published in Lancet Child Adolesc Health on 29 October 2024 https://doi.org/10.1016/s2352-4642(24)00298-0

Despite evolving mpox epidemiology, with an increase in sexual transmission among adults, children and adolescents remain the most affected group. Of the 7851 individuals with mpox notified to WHO by the Democratic Republic of the Congo Ministry of Health from January to May, 2024, 5254 (70%) were younger than 15 years, including 321 people who died (83% of total fatalities due to mpox). Young children are at particular risk of severe outcomes from mpox due to malnutrition and co-infections, underscoring the urgent need for a targeted response in children. To address the crisis, the authors urgently insist on the need of a deeper understanding of transmission dynamics, including asymptomatic or presymptomatic spread, to refine vaccination strategies. They advocate for rapid vaccine deployment in Democratic Republic of the Congo and neighboring regions, paired with rigorous safety monitoring in the priority populations of children, pregnant individuals, and displaced communities.

Africa's mpox strategic preparedness and response plan: a coordinated continental effort to boost health security. Ndembi N, Ngongo N, Foláyan MO, Yameogo JM, Braka F, Gueye SA, Matshidiso M, Kaseya J.

Published Lancet Glob Health on 29 October 2024 https://doi.org/10.1016/s2214-109x(24)00464-9

In response to a significant 2024 mpox outbreak in Africa, the Africa CDC and WHO declared the outbreak a public health emergency, urging a unified continental response. The outbreak has particularly impacted children and people with HIV/AIDS, with cases spreading to non-endemic countries. A comprehensive Africa-wide Mpox Preparedness and Response Plan (CMPRP) was developed to improve containment, health system resilience, and coordinated actions across member states. The plan focuses on community engagement, expanded lab capacities, and enhanced vaccine accessibility, including local production. Funding requirements are estimated at \$599 million, with contributions needed from various global funds and organizations. Ten strategic pillars support the response, including improved surveillance, community outreach, and targeted vaccination. Despite a pledged \$1.1 billion, gaps in funding remain, particularly for case management and infection prevention. This initiative aims to curb the current outbreak while reinforcing Africa's long-term public health infrastructure.

Clade I mpox virus genomic diversity in the Democratic Republic of the Congo, 2018-2024: Predominance of zoonotic transmission. Kinganda-Lusamaki E, Amuri-Aziza A, Fernandez-Nuñez N, Makangara-Cigolo JC, Pratt C, Vakaniaki EH, Hoff NA, Luakanda-Ndelemo G, Akil-Bandali P, Nundu SS, Mulopo-Mukanya N, Ngimba M, Modadra-Madakpa B, Diavita R, Paku-Tshambu P, Pukuta-Simbu E, Merritt S, O'Toole Á, Low N, Nkuba-Ndaye A, Kavunga-Membo H, Shongo Lushima R, Liesenborghs L, Wawina-Bokalanga T, Vercauteren K, Mukadi-Bamuleka D, Subissi L, Muyembe-Tamfum JJ, Kindrachuk J, Ayouba A, Rambaut A, Delaporte E, Tessema S, D'Ortenzio E, W Rimoin A, E Hensley L, Mbala-Kingebeni P, Peeters M, Ahuka-Mundeke S.

Published *Cell* on 24 October 2024 https://doi.org/10.1016/j.cell.2024.10.017

In this study, the authors sequenced and characterized MPXV genomes from samples collected between February 2018 and March 2024 from 14/26 provinces in the Democratic Republic of the Congo (DRC). High-quality genomes were generated for 337 patients to document whether the increase in number of cases is due to zoonotic spillover events or viral evolution, with enrichment of APOBEC3 mutations linked to human adaptation. This study highlights two patterns of transmission contributing to the source of human cases. All new sequences from the eastern South Kivu province (n = 17; 4.8%) corresponded to the recently described clade lb, associated with sexual contact and sustained human-to-human transmission. By contrast, all other genomes are clade la, which exhibits high genetic diversity with low numbers of APOBEC3 mutations compared with clade lb, suggesting multiple zoonotic introductions.



Global genomic surveillance of monkeypox virus. Mukadi-Bamuleka D, Osman MM, Hussein H, Raja MA, Fotsing R, Herring BL, Keita M, Rico JM, Gresh L, Barakat A, Katawera V, Nahapetyan K, Naidoo D, Floto RA, Cunningham J, Van Kerkhove MD, Lewis R, Subissi L.

Published Nat Med on 23 October 2024 https://doi.org/10.1038/s41591-024-03370-3

In this study, the authors sequenced and characterized MPXV genomes from samples collected between February 2018 and March 2024 from 14/26 provinces in the Democratic Republic of the Congo (DRC). High-quality genomes were generated for 337 patients to document whether the increase in number of cases is due to zoonotic spillover events or viral evolution, with enrichment of APOBEC3 mutations linked to human adaptation. This study highlights two patterns of transmission contributing to the source of human cases. All new sequences from the eastern South Kivu province (n = 17; 4.8%) corresponded to the recently described clade lb, associated with sexual contact and sustained human-to-human transmission. By contrast, all other genomes are clade la, which exhibits high genetic diversity with low numbers of APOBEC3 mutations compared with clade lb, suggesting multiple zoonotic introductions.

Genetic sequencing analysis of monkeypox virus clade I in Republic of the Congo: a cross-sectional, descriptive study. Yinda CK, Koukouikila-Koussounda F, Mayengue PI, Elenga RG, Greene B, Ochwoto M, Indolo GD, Mavoungou YVT, Boussam DAE, Ampiri BRV, Mfoutou CCM, Mbouala YDK, Ntoumi F, Kankou JM, Munster VJ, Niama FR.

Published *Lancet* on 16 October 2024 https://doi.org/10.1016/s0140-6736(24)02188-3

In this study, the authors aimed to provide insights into the ongoing mpox epidemic by describing the sequencing analyses of samples obtained from individuals with mpox in Republic of the Congo and phylogenetically comparing them with those from neighboring DR Congo. 61 samples were collected from individualos with suspected mpox, 31 of which were positive for monkeypox virus and were included in the analysis. Phylogenetic analysis of sequences showed two major clusters within clade Ia. One cluster was made up of four sequences from this study clustering with two monkeypox virus sequences from the current DR Congo outbreak, three older sequences from Central African Republic sequenced between 2017 and 2018, and seven sequences from DR Congo sequenced in 2006–07 and 2022. The second cluster was made up of 16 sequences from this study clustering with sequences from the current DR Congo outbreak. In addition, sequences from Republic of the Congo show multiple phylogenetic positioning suggesting the occurrence of multiple co-circulating strains in the human population.

This section provides a digested list of new articles published since the last review. The complete repository in Excel format can be found here.



Relevant news

This section presents official reports from health agencies, manufacturers and press releases with reliable sources.

Mpox Outbreak in Uganda Situation Update - 11 November 2024.

Published by AFRO-WHO on 11 November 2024

https://www.afro.who.int/countries/uganda/publication/mpox-outbreak-uganda-situation-update-11-november-2024

It is 111 days since the start of the current mpox outbreak in Uganda. Cumulatively, 448 confirmed cases and one death have been registered in Uganda across 38 districts. Working age adults (19-49) years are the most hit at 65% of the cases. The Kampala Metropolitan Area accounts for majority of the cases (61%).

Daily briefing: Variant of mpox virus is getting better at human-to-human transmission.

Published by Nature on 31 October 2024

https://www.nature.com/articles/d41586-024-03583-z

An mpox virus variant appears to be spreading between humans in Central Africa. Plus, we delve into what makes the human brain so special.

Monkeypox virus keeps getting better at spreading among humans.

Published by Nature on 30 October 2024

https://www.nature.com/articles/d41586-024-03531-x

Analysis of a clade la strain of the virus circulating in Central Africa shows genetic mutations indicative of sustained human-to-human spread.

Mpox vaccination shortage delays Kinshasa's drive against outbreak.

Published by Reuters on 13 November 2024

Democratic Republic of Congo has been unable to launch an mpox vaccination campaign in the capital Kinshasa due to a shortage of doses, the country's response leader said, while cases countrywide continue to rise, especially among children.



Timeline of events

This section presents a detailed chronology of the outbreak, with significant events related to public health strategies.

4 confirmed cases in Britain

4 November 2024

Three cases of Clade Ib mpox have been detected in household contacts of the first case, the UK Health Security Agency (UKSHA) can confirm. This brings the total number of confirmed cases to 3

The first case had recently travelled to countries in Africa that are seeing community cases of Clade Ib mpox.

Source: Latest update on cases of Clade Ib mpox - UK Health Security Agency (UKHSA). 4 November 2024.

First Mpox Outbreak Reported in Zimbabwe

13 October 2024

Zimbabwe reported its first mpox cases, a 11-year- old child and an adult from two separate towns who recently traveled to South Africa and Tanzania, respectively. The report did not give information on clades involved.

Source: Zimbabwe Records First Mpox Cases - Ministry of Health On High Alert Amid Response Plan Roll Out. 13 October 2024.

Launch of mpox vaccination campaign I DRC

5 October 2024

Since the surveillance system was alerted, 6 suspected cases meeting the definition of mmpox cases have been notified, placed in isolation, treated and sampled. Of the 6 samples taken and sent to the National Public Health Laboratory, one tested positive for Mpox. He is a 30-year-old man who has spent the last 2 weeks in Uganda, a country currently affected by the epidemic.

Source : Ministère de la santé et des affaires sociales. 22 August 2024.

22 August 2024

First Mpox Case Reported in Gabon

Since the surveillance system was alerted, 6 suspected cases meeting the definition of mmpox cases have been notified, placed in isolation, treated and sampled. Of the 6 samples taken and sent to the National Public Health Laboratory, one tested positive for Mpox. He is a 30-year-old man who has spent the last 2 weeks in Uganda, a

country currently affected by the epidemic. Source: Ministère de la santé et des affaires sociales. 22 August 2024

First Mpox case in Mauritius

26 October 2024

Mauritius on October 26 announced its first mpox case, which involves a 49-year-old man who had traveled from Nigeria. The patient is being treated in isolation at a hospital in Port Louis.

Source: Cidrap

First Mpox Outbreak Reported in Zambia

10 October 2024

Zambia's Ministry of Health confirmed the country's first mpox case in a 32-year-old Tanzanian truck driver. The patient presented with a body rash, joint pain, sore throat, and general malaise. The report did not give information on the clade involved.

Source: Africa CDC Epidemic Intelligence Weekly Report, 12 October 2024

First case of Mpox clade lb in India

23 September 2024

A 38-year-old Indian man living in Kerala has been diagnosed with clade Ib MPXV, after travelling from the United Arab Emirates. The patient is currently hospitalized for isolation purposes. No related infections were found in the 57 contacts, including airline passengers. India is the third country outside of Africa to report the novel clade. Source: India reports first case of mpox from fast-spreading clade 1b variety

First case of Mpox clade lb in Thailand

21 August 2024

A 66-year-old European man, who arrived in Thailand last week from an undisclosed African country, has been diagnosed with clade Ib MPXV. Authorities are monitoring 43 close contacts, none of whom have shown symptoms thus far.

Source: The ministry of public health of Thailand. 21 August 2024.



First case of Mpox clade lb in Sweden

15 August 2024

A person who sought medical care in Stockholm has been diagnosed with mpox after returning from a region in Africa currently experiencing a major clade I outbreak. This marks the first detection of clade Ib mpox outside the African continent.

Source: The Public Health Agengy of Sweden,. 15 August 2024.

First Mpox Outbreak Reported in Uganda

1st August 2024

Uganda's Ministry of Health confirmed two new mpox cases in Kasese District, both imported from the DRC. The cases include a 37-year-old Ugandan woman married to a Congolese man and a 22-year-old Congolese woman, both presenting with skin rash, swollen lymph nodes, and general malaise. Source: Mpox update (29): Uganda (KS) conf. | ProMED. 4 August 2024

First Mpox Outbreak Reported in Burundi

28 July 2024

Burundi's Ministry of Public Health declared eight confirmed mpox cases, with no deaths, in Bujumbura Nord, Gitega, and Isare districts, following initial alerts and positive lab results. Patients presented with fever and rash. Sequencing to determine the viral clade are pending. This is the first cases of mpox reported in Burundi.

Source : Outbreak Report, 30 July 2024: Mpox Situation in Africa | Africa CDC. 30 July 2024.

DRC granted approval for MVA-BN and LC16 vaccines

27 June 2024

The DRC has approved the emergency use of two smallpox vaccines - MVA-BN (Bavarian Nordic, Denmark) and LC16 (KM Biologics, Japan) - to address the escalating mpox outbreak, involving a novel clade lb variant.

Source: DR Congo grants emergency use for 2 mpox vaccines | News Brief, CIDRAP, 27 June 2024.

First case of Mpox reported in the Philippines in 2024

19 August 2024

A 33-year-old Filipino man, with no history of travel outside the country, has been identified as the 10th mpox case reported since the outbreak began, with the previous case detected in December 2023.

Source: The Department of Health of the Philippines, 19 August 2024

Ivory Coast Records Four New Mpox Cases

2nd August 2024

Four new non-lethal mpox cases were confirmed in Abidjan, Ivory Coast. All new and previous patients are under treatment and showing favorable progress.

Source : Mpox update (30): Côte d'Ivoire (AB) confirmed cases. | ProMED. 7 August 2024.

First Mpox Case Reported in Kenya

31 July 2024

Kenya has confirmed a case of mpox at a Taita Taveta border point with Tanzania. The virus was detected in an individual, reportedly a long-distance truck driver, who was travelling from Uganda to Rwanda through Kenya.

Source : Mpox Update (27): Kénya (Taita Taveta) | ProMED. 2 August 2024.

First Mpox Outbreak Reported in Rwanda

25 July 2024

Rwanda's Ministry of Health reported its first mpox outbreak with two confirmed cases in Gasabo and Rusizi districts. The cases, a 33-year-old female and a 34-year-old male, had traveled to DRC and tested positive for mpox Clade la sublineage. This is the first cases of mpox reported in Rwanda.

Source : Outbreak Report, 30 July 2024: Mpox Situation in Africa | Africa CDC. 30 July 2024.



First Mpox Outbreak Reported in South Africa since 2022

May - July 2024

South Africa reported 20 confirmed mpox cases, including three deaths, across three provinces (Gauteng, KwaZulu-Natal, and Western Cape). All cases were symptomatic males aged 17 to 43, mostly self-identifying as MSM and living with advanced HIV disease. None had a history of international travel or attendance at high-risk events, and sexual contact was the reported exposure. Sequencing identified clade IIb sublineage. These are the first mpox cases in South Africa since 2022.

Source: Mpox - South Africa | Disease Outbreak News. World Health Organization. 9 July 2024.

High-level Emergency Regional Meeting on mpox in Africa

11 - 13 April 2024

Health Ministers from several Central and West African countries, along with international partners, convened in Kinshasa to address the ongoing mpox epidemic in the region. They expressed serious concern over the changing transmission dynamics, high mortality rates, and the lack of access to countermeasures. The ministers emphasized the urgent need for a coordinated regional approach, including strengthening surveillance, preparedness, and response efforts at national and cross-border levels. The meeting concluded with the creation of an Africa Taskforce for Mpox Coordination, supported by Africa CDC, WHO, and other partners, to bolster epidemic response and ensure harmonized efforts across the continent.

Source: Communiqué "United in the fight against mpox in Africa" | High-level emergency regional meeting. 13 April 2024.

WHO lifted PHEIC status for global mpox outbreak

10 May 2023

The WHO announced that the global mpox outbreak no longer constitutes a PHEIC, following the recommendation of the International Health Regulations (IHR) Emergencies Committee, in response to the significant and sustained decline in mpox cases. The Committee recommended transitioning to a long-term strategy to manage the ongoing public health risks posed by mpox.

Source: Fifth Meeting of the International Health Regulations (2005) (IHR) Emergency Committee on the Multi-Country Outbreak of mpox (monkeypox). 11 May 2023.

Mpox Outbreak in DRC: Shifting Patterns and Geographical Expansion

April – September 2023

While the DRC is experiencing his worst mpox outbreak since the beginning of the year, with thousands of cases and hundreds of deaths, three previously unaffected provinces in the southern and eastern parts of the country (Kwango, Kinshasa and South Kivu) have reported outbreaks linked with sustained human-to-human transmission for the first time, without animal exposure. Clusters of patients included adult women and men presenting with anal and genital lesions and who reported sexual contacts prior to symptoms onset. This is the first documented instances of sexual transmission of clade I MPXV viruses

Source: Mpox (monkeypox) - Democratic Republic of the Congo | Disease Outbreaks News, WHO, 23 November 2023.

WHO declared the escalating global mpox outbreak a PHEIC

23 July 2022

WHO declared a Public Health Emergency of International Concern (PHEIC) in response to the escalating mpox outbreak affecting multiple non-endemic countries, who reported for the first time sustained community transmission through sexual contacts, particularly among men who have sex with men (MSM) with multiple sexual partners.

Source: WHO Director-General's statement at the press conference following IHR Emergency Committee regarding the multi-country outbreak of monkeypox. 23 July 2022.

Events linked with clade Ia / Ib MPXV outbreaks - Africa



Fact sheets

This section provides a short overview of of the epidemiology, virology, clinical features and risk assessment related with the disease.

Mpox is a **zoonotic infectious disease** caused by the monkeypox virus (MPXV), belonging to the *Poxviridae* family and Orthopoxvirus genus, similarly to variola virus (the causative agent of smallpox), cowpox virus and vaccinia virus. The animal reservoir remains unknown, but African rodents such as tree squirrels and Gambian pouch rats (*Cricetomys gambianus*) are currently considered to be strong candidates, as they were implicated in international spread.

There are two known clades of MPXV: clade 1 (previously referred to as Congo Basin), originating from eastern regions in Central Africa, and clade 2 (formerly West African clade) prevalent in West Africa. Clades 1 and 2 are further subdivided into four distinct subclades: 1a, 1b, 2a, and 2b. Variants 1b and 2b which emerged in recent years exhibit APOBEC-3 type mutations, indicative of viral adaptation to human hosts. Clade I MPXV infections are at greater risk of severe disease, with a case fatality rate (CFR) ranging from 3 - 10%, while clade II MPXV generally causes milder symptoms, lower viremia and a reduced lethality rate of 1 - 3%. The global mpox outbreak caused by the clade IIb in 2022-2023 showed a CFR of less than 0.1%. Some factors, beyond virological aspects, such as limited access to medical care or co-existing health conditions, might confound the case fatality rates. In many African countries, a significant proportion of the population is living with untreated or undiagnosed HIV, leading to a mortality rate from mpox that is twice as high in immunocompromised individuals compared to those with healthy immune systems. The higher death rate among children under five years old may also be partly due to malnutrition and limited access to healthcare, particularly in rural regions of DRC.

Clades Ia and IIa are **transmitted from animals to humans** through contact with live and dead animals through hunting or consumption of contaminated bushmeat. Secondary **human-to-human transmission** of these clades occasionally occurs via respiratory droplets, direct close contacts with body fluids or skin abrasions, or through contamined objects and household linens, though such transmission is usually limited to household members. Clades Ib and IIb have demonstrated sustained human-to-human transmission without the need for reintroduction from animal reservoirs. Notably, the 2022-2023 global outbreak was mainly driven by local, in-country transmission through **sexual contacts** among men who have sex with men (MSM), rather than at the animal-to-human interface seen in previous zoonotic outbreaks. Populations at higher risk of zoonotic transmission include small households or communities living in rural areas adjacent to or within tropical forests of Central and West Africa, where animal reservoirs may reside. High-risk groups for community transmissions also include sex workers, gay, bisexual, MSM with multiple sexual partners, or any other individuals with multiple casual sexual partners.

The **incubation period of MPXV** ranges from 2 to 21 days, although some people may contract the infection without developing symptoms. Patients are considered infectious from the time of symptom onset until skin lesions have crusted and a fresh layer of skin has formed underneath.

The **disease** is often mild, self-limiting with symptoms usually resolving spontaneously in **two to four weeks** but may last longer in immunocompromised individuals. A febrile prodrome with fever, muscle aches, sore throat and lymphadenopathy (swollen lymph nodes) appear first and last for 1 to 4 days, followed by cutaneous and/or mucosal rash. Typically, the lesions evolve through macules, papules, vesicles and pustules, before crusting over and desquamating. Lesions can manifest in the face, trunk, limbs, palms, conjunctival, urethral, penile, vaginal, genital and ano-rectal areas. Symptoms can be mild or severe, and patients may develop single or multiple lesions which can be very itchy or painful. Infected individuals remain contagious until all sores are healed, and a new layer of skin has formed. Complications may occur, such as secondary skin infections, septicemia, encephalitis or corneal ulceration. Although rarely fatal, severe systemic forms with multi-organ involvement and higher case fatalities have been observed in vulnerable groups, such as young children, individuals with a weakened immune system or with advanced HIV infection. Contracting mpox during pregnancy may lead to complications, such as congenital mpox, stillbirth or even death of the newborn.

MPXV is classified as a **risk group 3 (RG-3) pathogen** and requires stringent containment and appropriate safety measures to minimize risk to laboratory personnel. Standard operating procedures must be ensured for specimen collection, storage, packaging and transport. All specimens collected for laboratory investigations should be regarded as potentially infectious and handled with caution. Primary preventive vaccination is recommended for health workers, including laboratory personnel at risk for repeated exposure.

Source: Mpox(monkeypox)| Fact Sheets. World Health Organization. 26 August 2024.



Diagnosis and care

This section offers a short overview of currently available countermeasures and recommendations for diagnosis, prevention and care.

Due to the range of health conditions that cause similar-appearing skin lesions, clinical differentiation of mpox is difficult without laboratory diagnosis. Detecting viral nucleic acids using **polymerase chain reaction (PCR)** is the gold standard technique for confirming **MPXV diagnosis**, but its implementation requires dedicated research infrastructure and trained health personnel. The reliability of results depends on the type of biological specimen, with optimal samples obtained directly from skin lesions — whether crusts or exudates — via swabbing. In the absence of visible epidermal wounds, testing can be conducted on mucosal specimens using oropharyngeal or rectal swabs. Blood samples are not recommended for molecular testing since detectable viremia occurs in the early clinical course of infection. In areas with active circulation of multiple orthopoxviruses, diagnostic tests for other conditions should be considered if feasible. **Point-of-care (POC)** and **antigen rapid diagnostic test (AgRDT)** are rapid, cost-effective and easily interpretable diagnostic tools for use by health workers with minimal laboratory training to conduct MPXV diagnosis effectively in the field. POC tests such as GeneXPert (Cepheid, U.S.) and Standard M10 MPX/OPX® (SD Biosensor, South Korea) show promising clinical sensitivity on lesion samples and oropharyngeal swabs for clade I MPXV diagnosis. AgRDT shows high specificity but low sensitivity and their potency for clade I MPXV screening remains to be investigated.

Therapeutic management relies mainly on supportive care, managing pain and preventing further complications. One antiviral, tecovirimat, developed in 2002 to treat smallpox, has been approved by the Food and Drug Administration (FDA) and European Medicines Agency (EMA) as a compassionate use for the treatment of mpox in U.S. and EU/EEA countries. Several clinical studies (UNITY, EPOXI, MOSA, STOMP, PALM007, PLATINUM/PLATINUM-CAN) are underway in different regions of the world to evaluate the clinical efficacy of tecovirimat in treating mpox in adults and children.

There are currently **three vaccines** approved in different jurisdictions for the prevention of mpox. These third-generation smallpox vaccines contain non-replicating or minimally-replicating strains of vaccinia virus such as MVA-BN (Bavarian Nordic, Denmark), LC16 (KMB Biologics, Japan) and OrthopoxVac (Russia). The most commonly administered vaccine has been the MVA-BN, for which a favorable safety profile with mild side effects has been documented. MVA-BN is approved by U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) for use in high-risk adult populations against mpox in U.S. (JYNNEOS®), Canada (IMVAMUNE®) and EU/EEA countries (IMVANEX®). 1st and 2nd generation smallpox vaccines widely used in the 1950-1970s, such as the replication-competent vaccines Dryvax and ACAM2000®, also provides cross-protection against mpox, although populations under the age of 40 or 50 years do not benefit from prior smallpox vaccination programs. ACAM2000® is currently approved by the FDA for emergency use in U.S., but is not authorized in EU/EEA countries owing to significant side effects. To date, vaccines have been provided to their most vulnerable populations in 83 countries. However, they are not yet widely available, particularly in countries where the disease is endemic.

On 27th June 2024, **the DRC has granted emergency use approval for two smallpox vaccines**, MVA-BN (Bavarian Nordic, Denmark) and LC16 (KMB Biologics, Japan), in response to the escalating outbreak in the country.

The WHO Strategic Advisory Group of Experts (SAGE) on Immunization **recommended vaccination for the following population groups**: residents of high-risk areas (e.g. rural communities); sex workers, gays, bisexuals, MSM or other individuals with multiple casual sexual partners; health workers repeatedly exposed to mpox (such as those performing diagnostic tests or providing care); and contacts of mpox patients, including children, household members or in congregate settings.

 $Source: Mpox (monkeypox) | \ Fact Sheets. \ World \ Health \ Organization. \ 26 \ August \ 2024.$



Technological landscape 🕵



This section outlines the current pipeline of drug development, clinical trials and technologies aimed at preventing and treating the disease.

| VACCINES | IMVAMUNE®/JYNNEOS® IMVANEX® | Viral attenuated, non- replicating vector (MVA-BN strain) | Phase 3/4 | Third-generation smallpox vaccine authorized in EU/EEA countries, U.S. and Canada for protection against MPXV in adults. Case-control studies estimated the vaccine effectiveness at 66-86% in high-risk cohorts, with favorable safety profile and mild side effects. Limited data on use in children. Have been approved for emergency use in DRC on 27 June 2024. |
|------------|---|---|----------------|---|
| | VACΔ6 (OrthoPoxVac®) | Live-cell based vaccine | Phase 3 | Licensed in the Russian Federation. Currently being evaluated for safety and protection against smallpox, mpox and other orthopoxviruses. |
| | LC16m8 | Viral attenuated, low replicating vector | Phase 3 | Authorized for active immunization against smallpox in Japan since 1975. This vaccine has been licensed by Japan to provide protection against MPXV in adults and children. Currently being evaluated for safety and protection against mpox in high-risk populations. Have been approved for emergency use in DRC on 27 June 2024. |
| | BNT166a, BNT166c | multivalent mRNA vaccine | Phase 1/2 | Developed by BioNTech. Two mRNA based-multivalent vaccines developed for active immunization against mpox. Provides protection against MPXV clade I/IIb in mice and macaques. BNT166a is currently being evaluated for safety, tolerability and immunogenicity. |
| | mRNA-1769 | mRNA vaccine | Phase 1/2 | Developed by Moderna. Currently being evaluated for safety, tolerability and immunogenicity in adults. |
| | ACAM2000® | live vaccinia virus (NYCBH strain) | Restricted use | Second-generation smallpox vaccine. Currently approved by FDA for emergency use in U.S. Not authorized in EU/EEA countries due to significant side effects. |
| | VACV Tian Tan | live vaccinia virus (Tian tan strain) | Restricted use | First-generation smallpox vaccine used routinely in China and discontinued in 1981. Half of vaccinated individuals maintain neutralized antibodies and long-lasting humoral immunity even after 40 years, which provides cross-protection against MPXV. |
| | Dryvax | live vaccinia virus (NYCBH strain) | Restricted use | First-generation smallpox vaccines which made significant contribution to smallpox eradication campaigns. Associated with serious side effects. |
| TREATMENTS | Tecovirimat (TPOXX®) | Antiviral | Phase 2/3 | The first FDA-licensed drug for the treatment of smallpox. Approved in 2022 for the treatment of mpox in U.S. and EU/EEA countries. Demonstrated therapeutic effects against mpox in animal models. Safe and well-tolerated in healthy volunteers. The MPX-RESPONSE consortium, funded by European Commission and participating countries, includes three phase III clinical trials covering different geographic regions: UNITY in Argentina, Brazil and Switzerland, launched in March 2023; EPOXI in Europe which started recruiting in August 2024; MOSA in 3 to 10 African countries and expected to launch end of October 2024. |
| | NIOCH-14 | Antiviral | Phase 1 | Analogue of tecovirimat licensed in the Russian Federation for the treatment of mpox. Has demonstrated similar effectiveness than tecovirimat in mice models. Clinical efficacy against mpox is still uncertain. |
| | Cidofovir / Brincidofovir | Antiviral | Restricted use | Approved by FDA for the treatment of smallpox. Showed <i>in vivo</i> and <i>in vitro</i> antiviral activities against several orthopoxviruses. No clear benefit in three treated mpox patients in a recent observational study. |
| | Intravenous Vaccinia Immune Globulin (VIGIV) | Human anti-vaccinia antibodies | Restricted use | Considered for emergency use in mpox patients with severe complications or unable to mount an immune response in the U.S. Data on the effectiveness of VIGIV for mpox are lacking. |

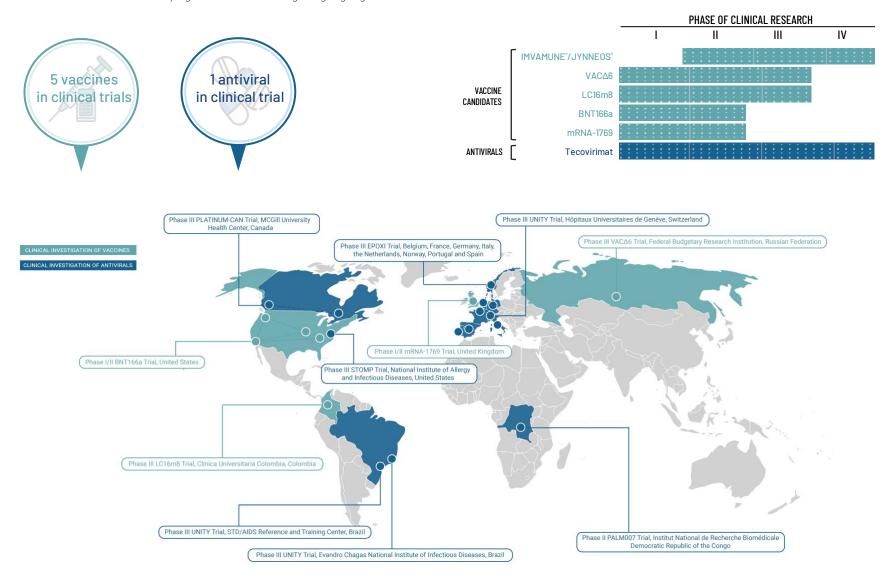
Source : Clinical Trials | National Institute of Health.



Ongoing clinical studies and sites of investigation



This section provides an overview of clinical trials in progress. Further details regarding ongoing interventional studies can be found here.





Guidelines and practical information

This section lists official manuals of recommendations for clinical practice or public health policy published by leading health organizations.

| 17 September 2024 | NIAID Research Agenda for 2024 Mpox – September 2024 | | | |
|--------------------|--|--|--|--|
| 12 September 2024 | Mpox: scenarios and technical elements of preparedness and response for clade I (UKHSA) | | | |
| August 29, 2024 | Avis du collège de la Haute Autorité de santé relatif à la stratégie de vaccination contre le mpox (HAS) | | | |
| · | Temporary recommendations issued by WHO to States Parties in relation to the public health emergency of | | | |
| August 19, 2024 | international concern associated with the upsurge of mpox (WHO) | | | |
| May 24, 2024 | Strategic framework for enhancing prevention and control of mpox - 2024-2027 (WHO) | | | |
| March 20, 2024 | Surveillance, case investigation and contact tracing for mpox (monkeypox): Interim guidance, 20 March 2024 (WHO) | | | |
| November 9, 2023 | Diagnostic testing for the monkeypox virus (MPXV): interim guidance, 9 November 2023 (WHO) | | | |
| May 13, 2023 | Infection au Monkeypox virus : procédure opérationnelle de prélèvement (COREB) | | | |
| April 27, 2023 | Infection par le Monkeypox virus : repérer et prendre en charge un patient en France (COREB) | | | |
| April 20, 2023 | Définition de cas et contacts et conduite à tenir pour la recherche des contacts (SPF) | | | |
| April 14, 2023 | Public health considerations for mpox in EU/EEA countries (ECDC) | | | |
| March 20, 2023 | Public health advice on mpox and congregate settings: settings in which people live, stay or work in proximity (WHO) | | | |
| March 9, 2023 | Public health advice for gay, bisexual and other men who have sex with men on the recent outbreak of mpox (WHO) | | | |
| December 16, 2022 | Révision du plan de lutte contre la variole (HCSP) | | | |
| November 20, 2022 | Monkeypox strategic preparedness, readiness, and response: Operational planning guidelines (WHO) | | | |
| November 16, 2022 | Vaccines and immunization for monkeypox: interim guidance (WHO) | | | |
| October 5, 2022 | Monkeypox Strategic Preparedness, Readiness, and Response Plan (WHO) | | | |
| September 30, 2022 | Public health advice for sex workers on mpox (WHO) | | | |
| September 1, 2022 | Risk communication and community engagement public health advice on understanding, preventing and addressing stigma and discrimination related to mpox (WHO) | | | |
| August 16, 2022 | Monkeypox infection prevention and control guidance for primary and acute care settings (ECDC) | | | |
| June 30, 2022 | Risk communication and community engagement approaches during the monkeypox outbreak in Europe, 2022 (ECDC/WHO) | | | |
| June 28, 2022 | Considerations for contact tracing during the monkeypox outbreak in Europe, 2022 (ECDC) | | | |
| June 10, 2022 | Clinical characterization of mpox including monitoring the use of therapeutic interventions (WHO) | | | |
| June 10, 2022 | Clinical management and infection prevention and control for monkeypox: Interim rapid response guidance (WHO) | | | |
| June 10, 2022 | Navigating monkeypox: considerations for gay and bisexual men and other men who have sex with men (ECDC) | | | |
| June 9, 2022 | Monkeypox - Aide au diagnostic dermatologique et au traitement symptomatique (COREB) | | | |
| June 09, 2022 | avis relatif à la conduite tenir pour les cas confirmés d'infection à Monkeypox virus (MPXV) à risque de forme grave et pour les personnes contacts à risque d'infection par MPXV (HCSP) | | | |
| July 09, 2022 | Mesures de prévention vis-à-vis de l'infection à Monkeypox virus (HCSP) | | | |
| May 24, 2022 | avis relatif à la conduite à tenir autour d'un cas suspect, probable ou confirmé d'infection à Monkeypox virus (HCSP) | | | |