# MONTHLY SCIENTIFIC REVIEW ON MPOX OUTBREAK

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https://anrs.fr/en/emergence-units/cellule-emergence-mpox-drc-2023

## Situation at a glance

- Since the beginning of 2024, the increasing frequency of outbreaks with **clade I MPXV** in the Democratic Republic of Congo (DRC) and now in non-endemic african regions has raised major public health concerns. In response to this situation, the World Health Organisation (WHO) activated the highest level of global health alert by declaring a Public Health Emergency of International Concern (PHEIC).
- By 9 December 2024, **13,257 mpox confirmed cases** and **60 deaths** had been reported in **20 African countries**, marking the highest incidence and widest geographical spread ever recorded on the continent. The DRC is the most affected country, with 9,247 cases and 43 deaths, representing a two-fold increase compared to the same period last year.
- A novel **clade I MPXV variant (sublineage 1b)** linked with sexual and non-sexual human-to-human transmission is spreading rapidly in Eastern DRC and neighboring countries such as Rwanda, Burundi, Kenya, Uganda and more recently Zambia and Zimbabwe.
- Between August and October 2024, travelers returning from high-risk regions tested positive for clade 1b in some countries outside Africa, including Sweden, Thailand, India, United Kingdom, Germany and Canada. **The risk for EU/EEA citizens** is considered **low** for the general population but **moderate** for those living or traveling to high-risk areas, or having close contact with affected communities.

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# Scientific articles

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

## Monkeypox clade IIb in France in 2023–2024. Rahia M., Fouere S., Gilbert M., Bachelard A., Taieb F., Sellem B., Herms F., Cazanave C., Valin N., Monsel G., Yazdanpanah Y., Ghosn J., Peiffer-Smadja N.

Published in *Lancet Reg Health Europe* on 1 December 2024
https://doi.org/10.1016/j.lanepe.2024.101114

This article examines Monkeypox (MPX) Clade IIb cases in France between August 2023 and July 2024. It reports 36 cases identified in 13 hospitals and clinics, primarily in Paris. Patients were mostly men (88%), with a median age of 32, and 87% were men who have sex with men (MSM). Vaccination rates were low: only 28% had received two doses of the third-generation smallpox vaccine (MVA-BN), while 58% were unvaccinated despite eligibility. Most cases did not involve travel to endemic areas, and only 22% of patients reported sexual contact with symptomatic individuals. Transmission appears to involve asymptomatic carriers, contributing to the spread within high-risk populations. Clinically, genital or anal lesions were the most common symptom, with vaccinated individuals showing fewer lesions than unvaccinated ones. Atypical presentations were rare. A third of patients were living with HIV, most with controlled infections, although some were immunocompromised due to conditions like Kaposi's sarcoma. The study highlights the role of sporadic transmission and the need for better vaccination coverage. Waning immunity in vaccinated individuals underscores the necessity of sustained public health efforts. Researchers call for further studies on MPX dynamics and vaccine efficacy to inform future outbreak management strategies.

## Breastfeeding mothers in DR Congo should have access to the mpox vaccine. Hombach J., Lewis R., van Holten J., Scott J. A., Neuzil K. M.

Published in *Lancet Global Health* on 1 December 2024
https://doi.org/10.1016/s2214-109x(24)00478-9

The WHO's 2024 position paper on smallpox and mpox vaccines initially lacked guidance for breastfeeding women, which was present in earlier 2022 interim guidance. This omission has since been corrected. WHO guidance now clarifies that breastfeeding women, while not a specific risk group, should be vaccinated if they belong to epidemiological risk groups (e.g., healthcare workers or case contacts). Non-replicating MVA-BN vaccines are recommended for lactating women, while ACAM2000 and LC16 vaccines are not advised due to safety concerns. Breastfeeding should not be discontinued post-vaccination. WHO emphasizes the importance of including lactating women in future vaccine research and thanks stakeholders for highlighting this issue, ensuring updated and consistent recommendations.

## Agile, on-demand wastewater surveillance of virus infections to support pandemic and outbreak response in Rotterdam-Rijnmond, the Netherlands, 2020 to 2022. Besijn E., Whelan J., Bijkerk P., Sips G. J., Langeveld J., Izquierdo-Lara R. W., van Baarle E., Schilperoort R., Koopmans M. P. G., de Graaf M., Medema G., Fanoy E.

Published in *Eurosurveillance* on 29 November 2024
https://doi.org/10.2807/1560-7917.es.2024.29.47.2400055

This study build on case studies carried out in 2020–2022 in a Dutch urban region to test if local community-level wastewater surveillance could provide comprehensive, real-time infectious disease transmission data upon acute demand from a public health (PH) service. Passive samplers for SARS-CoV-2 and MPXV were deployed in small wastewater catchment areas to assess this method's feasibility, utility, adaptability, strengths and limitations in informing PH actions. Results showed for example a large increase in SARS-CoV-2 RNA concentration in wastewater that was timely identified in a locality, which triggering adapted PH responses (information and testing). For MPXV, wastewater data suggested no further local transmission. The case studies suggested that on-demand wastewater surveillance using passive samplers can be a valuable and agile tool for tracking the spread of SARS-CoV-2 and MPXV at community level, and to improve PH awareness and responses. Optimal stakeholder engagement and consideration of ethical and legal issues, especially on local sewage sampling, will be essential to ensure political and social acceptance.

## Monkeypox virus isolation from longitudinal samples in 11 hospitalised patients.

Callaby H., Olvera J., Emery K., Richards K. S., Killip M., Groves N., Beadsworth M. B. J., Price D. A., Cooke G. S., Collini P., Cole J., Dunning J., Semple M. G., Baillie J. K., ISARIC4C Investigators, Rampling T., Houlihan C. F.

Published in *Lancet Infectious Diseases* on 28 November 2024
https://doi.org/10.1016/s1473-3099(24)00735-7

While diagnostic swabs' Monkeypox virus (MPXV) PCR cycle threshold (Ct) is assumed to correlate with infectiousness, the evidence is weak. Prolonged MPXV shedding is widely reported, but the duration of infectiousness remains unclear. The authors used the ISARIC WHO Clinical Characterisation Protocol UK to enroll patients admitted to UK hospitals for severe mpox. 169 samples from 11 patients were collected and inoculated into African Green Monkey Kidney cells, incubated, and monitored for cytopathic effects. Studying Ct values and duration of culture positivity (max 109 days) the authors show that immunocompromised patients can remain contagious with MPXV for extended periods, particularly through respiratory and oral routes, especially when oropharyngeal lesions are present. Infection prevention guidance should recommend close virological follow-up for these patients, who might need extended isolation.

## Exploration of drug repurposing for Mpox outbreaks targeting gene signatures and host-pathogen interactions.

Imani, S., Aminnezhad, S., Alikarami, M.

Published in *Sci Rep* on 27 November 2024
https://doi.org/10.1038/s41598-024-79897-9

In this study, the authors developed an in silico host-pathogen interaction (HPI) network and applied weighted gene co-expression network analysis (WGCNA) to explore interactions between Mpox and host proteins. Subtype-specific host-pathogen protein-protein interaction networks were constructed, and key modules from the HPI and WGCNA were integrated to identify significant host proteins. Analysis of 55 differentially expressed genes in Mpox infection revealed 11 kinases and 15 transcription factors as key regulators. They identified 16 potential drug targets, categorized into 8 proviral genes (ESR2, ERK1, ERK2, P38, JNK1, CDK4, GSK3B, STAT3) designated for inhibition, and 8 antiviral genes (IKKA, HDAC1, HIPK2, TF65, CSK21, HIPK2, ESR2, GSK3B) designated for activation. Promising FDA-approved candidates were identified, including kinase inhibitors, steroid hormone receptor agonists, STAT3 inhibitors, and notably Niclosamide.

## Crystal structure of F10 core protein from Mpox virus reveals its potential inhibitors.

Zhao R., Zhu X.-Y., Zhang J., Xie Z.-Y., Hu W.-S., Han Q.-H., Fan J.-Y., Yang Y.-N., Feng B.-Y., Cao J.-M., Zhou X., Wang D.-P.

Published in *International Journal of Biological Macromolecules* on 25 November 2024
https://doi.org/10.1016/j.ijbiomac.2024.138079

In this study, the authors determined the crystal structure of the F10 core protein at a high resolution of 1.5 Å, and identified a cavity between the F10 core protein and NPH-I through superimposition of the MPXV F10 core protein and the vaccinia virus (VACV) RNA polymerase (RNAP). The authors observed a significant structural similarity between the two proteins. They further conducted a virtual screening based on this cavity, and identified 28 compounds as potential MPXV inhibitors. This is the first study to screen for inhibitors targeting MPXV RNAP. This study may facilitate the development of novel ways for the discovery of anti-MPXV compounds against emerging pathogens.

## Evaluation of a commercial Multiplex Real-Time PCR Assay for orthopoxvirus and monkeypox virus detection, and simultaneous subclade Ib identification.

Wawina-Bokalanga T., Haesler M., Akil-Bandali P., Ola-Mpumbe R., Kinganda-Lusamaki E., Makangara-Cigolo J.-C., Pukuta-Simbu E., Cikaya-Kankolongo F., et al.

Pre-print published in *MedxRiv* on 20 November 2024
https://doi.org/10.1101/2024.11.20.24317626

In this study, authors assessed the performance of a novel GDS multiplex real-time PCR assay designed for MPXV detection and simultaneous subclade Ib identification. The test was assessed using samples from the 2024 mpox outbreak in the DRC, including skin lesion swabs and blood. Authors retrospectively analyzed 43 mpox-positive samples previously assigned as subclade Ib (WGS with Illumina or Oxford Nanopore), 67 prospective samples that tested mpox-positive (without known subclade) using a

routine PCR method, and 87 samples that tested mpox-negative. All 43 samples previously assigned to subclade Ib were confirmed, demonstrating 100% concordance with sequencing data. Among the 67 prospective mpox-positive samples, all samples tested positive for mpox, of which 8 tested subclade Ib positive, showing 100% concordance with sequencing results and real-time PCR. Among 87 samples initially tested negative for mpox, five tested positive using the new assay; this new result was validated by retesting the five samples with OPXV-specific and MPXV-generic primers/probes. In this study, the GSD real-time PCR assay proved to be highly sensitive and specific, making it suitable for use in the current mpox outbreak.

## mRNA vaccines: A promising platform for safer, more effective next-generation Orthopoxvirus immunization. Han X., Huang Q., Yan J.

Pre-print published in *Cell Host & Microbe* on 13 November 2024
https://doi.org/10.1016/j.chom.2024.10.014

The mpox virus (MPXV), a zoonotic Orthopoxvirus, continues to pose significant public health challenges, particularly following the waning immunity from discontinued smallpox vaccination. Traditional vaccines (e.g., ACAM2000, JYNNEOS) have limitations, such as adverse effects and suboptimal protection, underscoring the need for next-generation vaccines. mRNA-1769, a four-antigen mRNA vaccine, has demonstrated superior efficacy in a recent study by Mucker et al., showing significantly fewer lesions, reduced viral loads, and milder disease in nonhuman primates compared to MVA vaccines. The mRNA platform elicited robust immune responses, including enhanced antibody titers and Fc-effector functions critical for viral clearance. While promising for safety and scalability, further research is needed to assess the durability of mRNA vaccine immunity compared to live-virus vaccines. These findings highlight mRNA vaccines as pivotal tools for managing mpox and future Orthopoxvirus outbreaks.

## Diagnostic accuracy of three mpox lateral flow assays for antigen detection in the Democratic Republic of Congo and the United Kingdom. Ishara-Nshombo E., Somasundaran A., Romero-Ramirez A., Kontogianni K., Mukadi-Bamuleka D., Mukoka-Ntumba M., Muhindo-Milonde E., Mirimo-Nguee H., Parkes J., et al.

Pre-print published in *MedxRiv* on 7 November 2024
https://doi.org/10.1101/2024.11.07.24316894

In this study we assessed the diagnostic accuracy of three brands of rapid diagnostic tests for antigen detection (Ag–RDT) of MPXV: FlowFlex Monkeypox Virus Antigen Rapid Test (ACON Biotech Co., Ltd., Hangzhou, China), Ecotest Monkeypox Antigen Rapid Test (Assure Tech. Co., Ltd, Hangzhou, China), and STANDARD Q Monkeypox Ag Test (SD Biosensor, Inc. Republic of Korea). Samples used were skin lesion swabs (SS) and upper–respiratory tract swabs (URS) from 68 participants in the Democratic Republic of the Congo (DRC) and from 16 in the United Kingdom (UK). Although the specificity of the three Ag–RDT was high (100%), sensitivity was estimated as 15.79% (95% CI, 5.52–37.57%) for Flowflex and Ecotest and as 10.53% (95% CI, 2.94–31.39%) for Standard–Q using SS in the DRC. The sensitivity was estimated as 0.00% (95% CI, 0.0–20.6%) among URS in the DRC. In the UK, the sensitivity of the three Ag-RDT was 0.00% among SS (95% CI, 0.0–12.7%) and among URS (95% CI, 0.0–21.5%). The limit of detection (LOD) of all Ag–RDT was determined to be 1.0× 104 pfu/ml (1.3×105 copies/mL) using viral culture. These results show that none of the three Ag–RDT reached the target clinical sensitivity and thus authors do not recommend them as diagnostic or screening tool for suspected mpox cases.

## Addressing transnational exploitation and armed conflict in the response to mpox. Ratevosian J., Heisler M., Carpino T., McHale T., Musheku J., Beyrer C.

Published in *Lancet* on 7 November 2024
https://doi.org/10.1016/s0140-6736(24)02418-8

In this correspondence paper, the authors examined 32 MPXV Ib sequences added to the Global Initiative on Sharing All Influenza Data from Oct 13, 2023, to Aug 28, 2024. Phylogenetic analysis showed that MPXV Ib strains have diverged into four lineages and Ib sequences have evolved into 14 subgroups based on nine tandem repeat polymorphisms. This result confirms that the MPXV Ib tandem repeats are mutating more frequently than those in clade IIb (11 subgroups), which were involved in the 2022 outbreak as mentioned earlier. This study underscores that the genomes of MPXV clade Ib, which is involved in the 2024 mpox outbreak, are diverging faster than those of MPXV clade IIb, which was involved in the 2022 mpox outbreak, owing to an unusually high incidence of recombination.

## Genomic analysis confirmed the importation of first mPox Clade Ib case in Kerala, India from Dubai, UAE.

Shete A. M., Chenayil S., Sahay R. R., Sindhu C. B., Yadav S., Gawande P., Patil D. Y., Kumar A., Mohandas S., Yadav P. D.

Published in *J Infect* on 4 November 2024
https://doi.org/10.1016/j.jinf.2024.106342

In this letter to the editor, the authors reported the first confirmed case of mpox clade Ib infection with edematous penile lesions and phimosis in an apparently healthy individual, a 38-year-old male, working as fabrication shop worker in Dubai, UAE arrived India on September 13, 2024. The patient showed significant improvement after treatment and recovered completely without any complications. The detection of case with travel history from UAE, which has never reported Clade Ib infection raises the concerns of undetected Clade Ib circulation in high-risk group of individuals. The current study noted deletion in C3L target used for clade differentiating PCR recommended earlier; emphasizing the importance and need for clade specific testing and sequencing. This could have significant implications for tracking the spread and managing the Clade Ib virus in non- endemic countries.

## Mpox Vaccine Acceptance, Democratic Republic of the Congo.

Petrichko S., Kindrachuk J., Nkamba D., Halbrook M., Merritt S., Kalengi H., Kamba L., Beya M., Hoff N. A., Luhata C., Kaba D. K., Rimoin A. W.

Published in *Emerg Infect Dis* on 1 November 2024
https://doi.org/10.3201/eid3012.241226

This study assesses attitudes and vaccine acceptance by province in Democratic Repiblic of Congo (DRC), and respondents sociodemographic characteristics in the contexte of Mpox reseurgence since 2022. Despite high infection rates, vaccine access in Africa remains limited. A survey conducted in the DRC with over 5,000 participants found 61% acceptance for an Mpox vaccine, with higher acceptance among healthcare workers and in rural areas. The study highlights regional variations, noting lower acceptance in provinces like Sankuru, where Mpox awareness is minimal. The authors emphasize the need for targeted education and robust community engagement to enhance vaccine rollout and combat the disease effectively.

*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.**

## NIH Study Finds Tecovirimat Was Safe but Did Not Improve Mpox Resolution or Pain.

Published by NIH on 10 December 2024
https://www.nih.gov/news-events/news-releases/nih-study-finds-tecovirimat-was-safe-did-not-improve-mpox-resolution-or-pain

The STOMP study's interim results showed that tecovirimat (TPOXX) did not reduce lesion healing time or alleviate pain in adults with mild to moderate clade II mpox at low risk for severe disease. No safety concerns were found, but the lack of efficacy led to the discontinuation of further participant enrollment. The study found a less than 1% chance that tecovirimat would prove effective if completed. The open-label arm did not include a placebo, so tecovirimat's impact on severe cases remains unclear. These results align with previous findings and underscore the need for more research into mpox treatments.

## Mpox continues its Africa spread as clade 1b confirmed in 2 more nations.

Published by CIDRAP on 5 December 2024
https://www.cidrap.umn.edu/mpox/mpox-continues-its-africa-spread-clade-1b-confirmed-2-more-nations

Mpox outbreaks in Africa are increasing, with 36 new deaths and 2,708 new cases reported last week, raising the total to 1,200 deaths and 62,171 cases in 20 countries. Most deaths and cases are from the Democratic Republic of the Congo (DRC), the outbreak's epicenter. The virus has been identified in Zimbabwe and Zambia, with a novel clade 1b virus detected. Clade 2 mainly affects adults, while clade 1a, more common in the DRC, disproportionately impacts children. Overall, 34.2% of cases involve children under 15, and over half (54.2%) of cases affect females, with outbreaks showing regional variations.

## UK reports fifth imported mpox case.

Published by UKHSA on 29 November 2024
https://www.gov.uk/government/news/ukhsa-detects-first-case-of-clade-ib-mpox

A new case of Clade Ib mpox has been confirmed in Leeds, England, in an individual who recently returned from Uganda, where community transmission of Clade Ib is ongoing. The person is receiving care at Sheffield Teaching Hospitals NHS Foundation Trust. This is the fifth case of Clade Ib mpox in England in recent weeks, with no links to previous cases. The risk to the UK population remains low, and the UK Health Security Agency (UKHSA) is monitoring close contacts, offering testing and vaccination as needed. All prior cases have fully recovered.

## Public Health Agency of Canada confirms the first case of clade I mpox in Canada.

Published by Public Health Agency of Canada on 22 November 2024
https://www.canada.ca/en/public-health/news/2024/11/public-health-agency-of-canada-confirms-the-first-case-of-clade-i-mpox-in-canada.html

On November 22, 2024, the Public Health Agency of Canada (PHAC) confirmed the first case of clade I mpox in Manitoba. The travel-related case is linked to an ongoing outbreak in central and eastern Africa. The individual, who sought medical care upon returning, is currently isolating. A public health investigation, including contact tracing, is underway. While clade II mpox has been present in Canada since 2022, this is the first case of clade I. The risk to the general population remains low, and PHAC continues to monitor the situation.

## Second meeting of the International Health Regulations (2005) Emergency Committee regarding the upsurge of mpox 2024.

Published by WHO on 22 November 2024
https://www.who.int/news/item/28-11-2024-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-upsurge-of-mpox-2024

On November 22, 2024, the WHO's Emergency Committee met to assess the ongoing mpox upsurge, particularly cases linked to monkeypox virus clade Ib. Despite some progress in controlling the spread, the Committee noted the increasing number of cases and the operational challenges faced in responding to the outbreak. It emphasized the need for stronger national commitments and a coordinated international response. The Committee confirmed that mpox outbreak still warrant a public health emergency of international concern (PHEIC) and issued revised temporary recommendations to address the crisis.

## WHO adds LC16m8 mpox vaccine to Emergency Use Listing.

Published by WHO on 19 November 2024
https://www.who.int/news/item/19-11-2024-who-adds-lc16m8-mpox-vaccine-to-emergency-use-listing

The World Health Organization (WHO) has granted Emergency Use Listing (EUL) for the LC16m8 mpox vaccine, the second vaccine supported by WHO following the declaration of the mpox public health emergency in August 2024. This approval will improve access to vaccines in areas experiencing surging outbreaks, particularly in Africa. Japan has announced a donation of 3.05 million doses to the Democratic Republic of the Congo, the hardest-hit country. The LC16m8 vaccine, developed by KM Biologics in Japan, is recommended for individuals over one year old and is administered as a single dose using a bifurcated needle. However, minimally replicating vaccines, such as LC16m8, should not be used during pregnancy and in people who are immunocompromised. This listing is a significant step in the global effort to combat the mpox outbreak, complementing other public health measures.

## Smallpox Drug in Clinical Trials for Treating Mpox in Africa.

Published by Africa CDC on 8 November 2024
https://africacdc.org/news-item/smallpox-drug-in-clinical-trials-for-treating-mpox-in-africa/

The Africa CDC is leading a clinical trial, the MpOx Study in Africa (MOSA), to evaluate the antiviral drug brincidofovir for treating Mpox patients at risk of severe complications. Brincidofovir, currently approved for smallpox, has not yet been tested in double-blind, placebo-controlled studies for mpox. This trial, set to begin in late 2024, will be conducted in Democratic Republic of the Congo (DRC). It aims to address the urgent need for approved treatments for mpox, a disease causing significant health risks, especially among vulnerable populations such as women, children and immunocompromised patients. The study will include interim analyses, with the first one expected in early 2025.

# Timeline of events

**This section presents a detailed chronology of the latest events, related to the outbreak.**

### 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 in DRC

**5 October 2024**

The Democratic Republic of the Congo has started a mpox vaccination campaign in North Kivu, prioritizing health workers, responders, and high-risk groups. The campaign will extend to 11 affected health zones in Equateur and South Kivu. A total of 265,000 MVA-BN vaccine doses, donated by Gavi and the U.S. government, will be administered as part of a broader response including surveillance, community engagement, and case management.

Source : The Democratic Republic of the Congo kicks off mpox vaccination. 5 October 2024.

### First Mpox Case Reported in Gabon

**22 August 2024**

Since the surveillance system was alerted, 6 suspected cases meeting the definition of mpox cases have been notified, placed in isolation, treated and sampled. Of the 6 samples collected, one tested positive for Mpox. The patient was a 30-year-old man who 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.

### Four cases of Mpox clade Ib in United Kingdom

**4 November 2024**

Three household contacts have been tested positive for clade 1b after being in close contact with a British traveler recently returning from an affected African country.

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

### 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. C The report did not give information on clade involved.

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

### First case of Mpox clade Ib 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 imported clade 1b mpox case. 23 September 2024.

# 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 minimise risk to laboratory personnel. Standard operating procedures must be ensured for specimen collection, storage, packaging and transport. All speciments 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 differenciation 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.

**There is currently no treatment approved specifically for MPXV infections**. 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. On 15 August 2024, preliminary analysis of the PALM007 trial show that the tecovirimat did not reduce the duration of lesions in adults and children with mpox clade 1. However, the mortality rate among trial participants (1.7%), regardless of whether they received the drug, was significantly lower than the rate observed in the local general population (3.6% or higher). These findings emphasize the importance of access to hospital care and medical support in improving clinical outcomes for patients with mpox.

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 favourable 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®). ACAM2000® is currently approved by the FDA for emergency use in U.S., but is not authorised in EU/EEA countries owing to significant side effects. Vaccines are not 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 LC16m8 (KMB Biologics, Japan), in response to the escalating outbreak in the country. Nigeria was the second african country to authorize the use of MVA-BN on 13th August 2024. However, many other African nations impacted by the epidemic have yet to finalize ethical and regulatory approvals at the national level.

The deployment of vaccines in Africa has enabled the launch of clinical trials to assess vaccination outcomes in contexts specific to the continent and its populations. One such initiative, the SMART clinical trial, aims to determine whether **post-exposure vaccination with MVA-BN can reduce the risk of severe illness or death** in individuals who have been exposed to the virus, such as within family settings. Another trial, supported by CEPI and EDCPT3, will investigate **the safety and immunogenicity of MVA-BN in pregnant and breastfeeding women, as well as infants up to two years old**. This is the first trial targeting vulnerable populations at high risk for mpox, potentially providing crucial data to extend vaccination access to these groups, who may face serious complications but are not yet eligible for vaccination.

Source : Clinical Trials | National Institute of Health.
Source : Mpox (monkeypox) | Fact Sheets. World Health Organization. 26 August 2024.

# Technological landscape

**This section outlines the current pipeline of drug development aimed at preventing and treating the disease.**

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| VACCINES | **IMVAMUNE®/JYNNEOS® IMVANEX®** | Viral attenuated, non-replicating vector (MVA-BN strain) | Phase 3 | Third-generation smallpox vaccine authorised 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 and in Nigeria on 13 August 2024. Clinical trials assessing the safety and efficacy in different populations are due to be launched in late 2024 and early 2025. |
| | **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 authorised 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 *in vivo* and *in vitro* antiviral activities against several orthopoxviruses. No clear benefit in three treated mpox patients in a recent observational study. A clinical trial led by Africa CDC will be conducted in DRC in late 2024. |
| | **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. |

# Guidelines and practical information

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

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| 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) |
| August 19, 2024 | Temporary recommendations issued by WHO to States Parties in relation to the public health emergency of 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 themonkeypox 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) |