MONTHLY SCIENTIFIC REVIEW ON MPOX OUTBREAK

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Editors : Emeline Simon, Nathan Claveau, Eric Rosenthal, Diana Molino, Mario Delgado-Ortega, Erica Telford, Meena Murmu, Sandrine Halfen, France Lert, Yoann Allier, Armelle Pasquet and Eric D'Ortenzio

ANRS *Emerging Infectious Diseases* - Paris, France
https://anrs.fr/en/emergence-units/cellule-emergence-mpox-drc-2023/

General informations

This section presents a detailed timeline of the outbreak, with significant events related to its progression, current status and case reports.
The content of this document are subject to change as the health situation evolves. All informations comes from a valid and credible source.

Since January 2023, a nationwide resurgence of MPXV infections has been experienced in Democratic Republic of the Congo (DRC), along with an expansion to new geographical areas that were previously unaffected (including urban areas such as Kinshasa, the capital home to 17 million inhabitants).

On 21 November 2023, the Ministry of Health of DRC informed the World Health Organization (WHO) of five confirmed cases of Monkeypox viruses (MPXV) among locals - four men and one woman - who had engaged sexual relations with a Belgian resident exhibiting genital and anal lesions. The National Institute for Biomedical Research (NIBR) shortly confirmed that the Monkeypox strains identified belong to phylogenetic clade 1. **This is the first documented instance of sexual transmission of clade 1 Monkeypox viruses.**

On 17 March 2024, the Health authorities in DRC reported **14,626 suspected cases** and **654 deaths** throughout the entire year of 2023, **result**ing in a case-fatality rate (CFR) of 4.5% and constituting the highest annual incidence ever recorded in DRC. The provinces who reported the highest number of suspected cases are Equateur (North-West), Maindombe (West), Sankuru (Central) and Tshopo (North-Central). This upsurge appears to be unrelated to the multi-country outbreak of Monkeypox caused by clade II viruses declared in May 2022, as **only clade 1 viruses are currently circulating in DRC**. These numbers are likely underestimated due to limited availability and access to healthcare facilities and financial constraints in seeking medical attention. **Children under the age of 15** constituted the most affected group, accounting for **65% of mpox reported cases** and **75% of fatalities**. Disease contraction and spreading was frequently occuring during playtime interactions. As of April 2023, only 34 cases have been reported among sex workers in the DRC, leaving the full extent of clade 1 MPXV sexual transmission yet to be determined.

As of 30 June 2024, a total of **8,057 suspected cases** of mpox, **1,135 confirmed cases** and **419 associated deaths** (CFR 4.6%) has been recorded in the DRC according to the latest Africa CDC Surveillance Report. Children account for two thirds of the reported mpox cases.

Sources :
Mpox (monkeypox) - Democratic Republic of the Congo | Disease Outbreak News. World Health Organization. 23 November 2023.
Mpox - Democratic Republic of the Congo | Disease Outbreak News. World Health Organization. 14 June 2024.
Weekly Event Based Surveillance Report | Africa CDC. 22 June 2024.

Fact sheets

This section provides a short overview of of the epidemiology, virology, clinical features and risk assessment related with the disease.
The content of this document are subject to change as the health situation evolves. All informations comes from a valid and credible source.

Mpox is a **sylvatic zoonosis** with incidental human infections that usually occur sporadically in forested parts of Central and West Africa, where it is considered endemic. It is caused by the monkeypox virus, belonging to the *Poxviridae* family and Orthopoxvirus genus, similarly to variola virus (the causative agent of smallpox). The animal reservoir remains unknown, although is likely to be among rodents.

There are two known clades of MPXV : clade I (previously referred to as Congo Basin) and clade II (formerly West African clade). Clade II is further subdivided into two distinct subclades IIa and IIb. Clade I MPXV infections are at greater risk of severe disease, with an estimated **case fatality rate (CFR)** of 10-15%, whereas clade II MPXV generally causes milder symptoms and lower viremia levels. During the clade IIb 2022 multi-country outbreak, the CFR was approximately 0.03%.

The virus is **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 MPXV occasionnally occured among family relatives through respiratory droplets, direct contact with body fluids or skin abrasions or through contamined objects and household linen. However, the spread of the multi-country outbreak of clade IIb MPXV in 2022 was mainly driven by transmission via **sexual contacts**, changing the paradigm in the way MPXV can be transmitted. Since 2023, human cases of sexual transmission of clade 1 MPXV are being documented. Rural areas, where the animal reservoir may resides, are at higher risk of zoonotic transmission of MPXV. Small households or communities who are in close contact with infected animals are at higher risk of infection. High risk populations also include sex workers, gay, bisexual, or other men who have sex with men (MSM) with multiple sexual partners; or 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**. 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. 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 or individuals with advanced HIV infection. Monkeypox during pregnancy may lead to complications, such as congenital mpox or stillbirth.

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.

WHO assesses the risk posed by the outbreak as **high** at the international level. WHO evaluated a significant risk of further mpox spread to **neighbouring countries** (Central African Republic, Angola, Zambia, Tanzania, Burundi, Rwanda, Uganda and South Sudan) or to those sharing a high cultural identity with DRC.

Source : Mpox (monkeypox) | Fact Sheets. World Health Organization. 18 April 2023.

Diagnosis and care

This section offers a short overview of currently available countermeasures and recommendations for diagnosis, prevention and care.
The content of this document are subject to change as the health situation evolves. All informations comes from a valid and credible source.

Real-time PCR is the gold standard technique for **MPXV diagnosis** but its implementation requires dedicated research infrastructure and trained health personnel. **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 clinical efficacy 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, originally developed to treat smallpox, have been approved by FDA as a compassionate use for the treatment of mpox in U.S. and EU/EEA countries. Several clinical studies (UNITY, EPOXI, PALM007) are underway to evaluate the clinical efficacy of tecovirimat in treating 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®). 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 programmes. 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. 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.

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. 18 April 2023.

Scientific articles

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

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

Formulation of next-generation polyvalent vaccine candidates against three important poxviruses by targeting DNA-dependent RNA polymerase using an integrated immunoinformatics and molecular modeling approach. Kumar A., Dutt M., Dehury B., Sganzerla Martinez G., Singh K. P. and Kelvin D.J.

Published in *J Infect Public Health* on 1 July 2024
https://doi.org/10.1016/j.jiph.2024.102470

The aim of the study was formulating multi-epitope vaccines against three evolutionary closed poxviruses i.e., Mpox virus (MPXV), variola virus (VARV), and volepox virus (VPXV), using an integrated immunoinformatics and molecular modeling approach. DNA-dependent RNA polymerase (DdRp), a potential vaccine target of poxviruses, was used to determine immunodominant B and T-cell epitopes followed by interactions analysis with Toll-like receptor 2 at the atomic level. Three multi-epitope vaccine constructs, namely DdRp_MPXV (V1), DdRp_VARV (V2), and DdRp_VPXV (V3) were designed. These vaccine constructs were found to be antigenic, non-allergenic, non-toxic, and soluble with desired physicochemical properties. Protein-protein docking and interaction profiling analysis depicts a strong binding pattern between the targeted immune receptor TLR2 and the structural models of the designed vaccine constructs. State-of-the-art all-atoms molecular dynamics simulations revealed highly stable interactions of vaccine constructs with TLR2 at the atomic level. The immune simulation analysis suggested that designed vaccine constructs have the potential to induce protective immunity against targeted poxviruses. These results encourage further experimental characterisation of these next-generation polyvalent vaccines.

Potential determinants of the decline in mpox cases in Belgium: a behavioral, epidemiological and seroprevalence study. De Vos E., Van Gestel L., Brosius I., Kenyon C., Vuylsteke B., De Baetselier I., et al.

Published in *Int J Infect Dis* on 26 June 2024
https://doi.org/10.1016/j.ijid.2024.107132

This paper aimed at explaining the waning of the mpox epidemic in Belgium in 2022. The mpox outbreak reached its peak at the end of July 2022, before the start of vaccination on August 8. The study used a variety of surveillance systems carried out by the Institute of Tropical Medicine (Antwerp): mpox patients registry and information of their sexual behavior; database on PrEP users which document sexual behavior and STI testing every 3 to 6 months to assess possible changes in sexual behavior across the outbreak period and serological surveillance based on a 4 point survey among PrEP users to assess immunity. Compared to earlier cases, later mpox cases were less likely to belong to the sexual network's central group. Among HIV-PrEP users there were no notable changes in sexual behavior. Reports on sexual behavior showed no changes accross the period among PreP users considered et the most at risk group. Anti-orthopoxvirus seroprevalence did not notably increase before the start of national vaccination campaigns. The observed changes in group immunity and behavior in the population at greater risk of exposure to mpox seem unable to explain the waning of the mpox epidemic. A change in the profile of mpox patients might have contributed to the decline in cases.

Molecular epidemiology of recurrent zoonotic transmission of mpox virus in West Africa. Delia Doreen Djuicy D., Omah I. F., Parker E., Tomkins-Tich C.H., Otieno J.R., Yifomnjou O.M.H, Essengue L.L.M., Ayinla A.O., Sijuwola A.E., Njouom R., Happi C.T., et al.

Pre-print posted in *MedxRiv* on 19 June 2024
https://doi.org/10.1101/2024.06.18.24309115

In 2022, Cameroon saw a significant rise in mpox cases, with no evidence of sustained human-to-human transmission. The cause of this increase is unclear, potentially stemming from introductions from the ongoing human B.1 outbreak in Nigeria or driven by zoonotic spillover events. This study examined MPXV transmission dynamics in the border regions encompassing the Cameroonian Highlands and Guinean Lower Forest, which extend into southern Nigeria. These forest ecosystems provide suitable ecological conditions for animal reservoirs that may move across borders. Agricultural activities, subsistence hunting, wild game consumption, and human settlements in forested areas due to internal displacement heighten exposure at the human-animal interface and the risk of zoonotic transmission. The authors identified two distinct zoonotic lineages that circulate across the Nigeria-Cameroon border, including the closest outgroup to the human epidemic circulating since october 2013. They estimated that the precursor lineage circulated in an animal population for more than 45 years, which is likely where clade IIb originated. All human samples from these border regions resulted from zoonotic infections or secondary transmission of the novel clade IIb.1.

Genomic epidemiology uncovers the timing and origin of the emergence of mpox in humans.

Parker E., F. Omah I.F., Varill P., Magee A., Opeyemi Ayinla A.O., Sijuwola A.E., Ahmed M.I., Happi C.T., et al.

Pre-print posted in *MedxRiv* on 19 June 2024
https://doi.org/10.1101/2024.06.18.24309104

Five years before the 2022-2023 global mpox outbreak, Nigeria reported its first cases in nearly 40 years, with the ongoing outbreak driven by sustained human-to-human transmission. Consensus evidence indicates that MPXV clade IIb has transitioned from a zoonotic disease to one sustained by human-to-human transmission in a subpopulation in Nigeria for nearly a decade, but with questions left regarding its emergence. This study identified the closest zoonotic outgroup in southern Nigeria, using 112 MPXV genomes collected from 2021-2023. The human-transmitting lineage emerged around July 2014, circulating unnoticed until September 2017, with Rivers State as the epidemic's origin and a key source of viral export. Furthermore, the study revealed APOBEC3 activity significantly increased MPXV's evolutionary rate during human transmission. This research highlights MPXV's establishment in West Africa prior to the global outbreak and underscores the need for better pathogen surveillance and response.

No evidence of Monkeypox virus (MPXV) circulation in putative animal reservoirs in Gabon wildlife.

N'dilimabaka N., Mougnoko L. S. M., Mangombi-Pambou J. B., Mavoungou D. S. K., Koumba L. B., Moukouama S. K., Koumba I. P. K., Fenollar F., Mbala-Kingebeni P., Maganga G. D., Lekana-Douki S. E. and Lekana-Douki J. B.

Published in *Int J Infect Dis* on 13 June 2024
https://doi.org/10.1016/j.ijid.2024.107106

This study aimed to identify potential MPXV reservoirs in Gabonese wildlife to prevent future outbreaks. DNA was extracted from the livers and spleens of 2,549 animals, including bats, bushmeats, rodents, and shrews, collected between 2012 and 2021. Real-time and conventional PCR targeting orthopoxvirus genes revealed no MPXV DNA, despite the presence of potential host species like *Critcetomys*, *Crocidura*, *Praomys*, and *Atherurus africanus*. The absence of MPXV could be due to the low number of certain species sampled, the acute nature of Mpox infection, the absence of *Funisciurus anerythrus*, or sampling outside the ecological niche of the virus. Longitudinal studies in Gabon, focusing on the ecological niches of *F. anerythrus* and MPXV, are recommended for better understanding MPXV circulation.

Sustained Human Outbreak of a New MPXV Clade I Lineage in the Eastern Democratic Republic of the Congo.

Hasivirwe Vakaniaki E., Kacita C., Kinganda-Lusamaki E., O'Toole A., Wawina-Bokalanga T., Mukadi-Bamuleka D., Amuri-Aziza A., Malyamungu-Bubala N., Mweshi-Kumbana F., Mbala-Kingebeni P., et al.

Published in *Nat Medicine* on 13 June 2024
https://doi.org/10.1038/s41591-024-03130-3

This short communication describes the results of an investigation into Kamituga, a densely populated area in Eastern DRC, where a sexual transmission-driven mpox outbreak has emerged since September 2023. Among 241 suspected cases, 108 were confirmed MPXV-positive through PCR testing, with a majority being female and a median age of 22 years, differing from other endemic regions where mpox primarily affects children. A notable 28.7% of confirmed cases involved professional sex workers, and 85% of patients exhibited genital lesions. Genomic analysis identified a distinct lineage of MPXV (clade Ib) unique to Kamituga, characterized by APOBEC3-type mutations, a hallmark of MPXV human-to-human transmission. Historical sequences collected from 2011 and 2012 suggest this lineage pre-existed in a a local, non-human animal reservoir. Additionally, isolates from other provinces showed a low proportion of APOBEC3-type mutations and no connection to the Kamituga mpox outbreak, indicating that most cases elsewhere resulted from independent spillover events. Although there is no current evidence of wider dissemination of the outbreak, the Kamituga situation mirrors the 2017-2018 clade IIb MPXV outbreak in Nigeria, necessitating urgent action from both endemic countries and the international community to prevent regional and global spread of clade Ib MPXV, particularly among vulnerable populations.

Immune responses associated with mpox viral clearance in men with and without HIV in Spain: a multisite, observational, prospective cohort study.

Moraes-Cardoso I., Benet S., Carabelli J., Perez-Zsolt D., Mendoza A., Rivero A., Alemany A., Descalzo V., Alarcón-Soto Y., Grifoni A., Sette A., Moltó J., Marc A., Marks M., Mitjà O., Brander C., Paredes R., Izquierdo-Useros N., Carrillo J., Suñer C., Olvera A., and Mothe B.

Published in *Lancet Microbe* on 7 June 2024
https://doi.org/10.1016/s2666-5247(24)00074-0

Since the global mpox outbreak began in May 2022, over 90,000 cases have been reported across 110 countries, with a notable impact on people with HIV. This study, part of the MoViE cohort in Spain, compared mpox immune responses up to 6 months post-diagnosis in participants with and without HIV, and assessed their effect on disease severity and viral clearance. Conducted in Barcelona sex clinics, it involved 33 participants, including 14 with HIV. Participants with and without HIV had similar disease severity and viral clearance times. Early humoral responses, with high concentrations of IgG and IgA, were linked to milder disease and quicker viral clearance. Although antibody levels declined faster in participants with HIV, T-cell responses remained stable up to 182 days post-diagnosis. Robust B-cell and T-cell responses facilitated local viral clearance and reduced disease severity, suggesting antibodies help early viral control, while sustained T-cell responses help in preventing severe reinfection.

Longitudinal viral shedding and antibody response characteristics of men with acute infection of monkeypox virus: a prospective cohort study.

Yang, Y., Niu, S., Shen, C. et al.

Published in *Nat Commun* on 27 May 2024
https://doi.org/10.1038/s41467-024-48754-8

In this prospective cohort study, the authors systematically analyzed the longitudinal positivity rate of MPXV DNA from 993 samples collected from various body sites (skin lesions, rectum, saliva, oropharynx) and 1,633 environmental fomite swabs. These samples were obtained from 77 acute MPXV infections (including 42 HIV co-infections), collected every two to three days over a period of five months. The results showed a 100% positivity rate of MPXV DNA in skin lesions, followed by the rectum (88.16%), saliva (83.78%), and oropharynx (78.95%). The positivity rate for oropharynx samples decreased rapidly after 7 days post symptom onset, while the rectum and saliva maintained positivity rates similar to skin lesions. Additionally, 52.66% of environmental fomite swabs were positive for MPXV DNA, with the highest positivity rate (69.89%) observed in air-conditioning air outlets. Most indexes were similar between HIV and non-HIV participants, though HIV infection and rectitis were associated with higher viral loads in the rectum. These findings enhance our understanding of optimal sample selection for accurate laboratory diagnosis at different stages of infection.

Factors potentially contributing to the decline of the mpox outbreak in the Netherlands, 2022 and 2023.

Haverkate M.R., Willemstein I. JM., van Ewijk C. E., Adam P. CG., Lanooji S. J., et al.

Published in *Eurosurveillance* on 23 May 2024
https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2024.29.21.2300608

This study in The Netherlands aimed to assess the contribution of sexual behaviour change and vaccination to the decline of mpox outbreak among male at birth having sex with men (GBMSM), from the start of primary preventive vaccination (PPV) (July 25- 11 August 2022) to 31 December 31 2023. The study used several sources of data (register of mpox cases, register of individuals who accepted to report vaccination, data collected among PrEP users). Among 28 570 consultations of PrEP users at SHC in 2022, when comparing behaviour over months, no trend was found in sexual behaviour, including STI. Neither behaviour change, nor vaccination which took place after the peak of the outbreak were found to explain the decline of the outbreak. The authors hypothesised that infection-induced immunity in the groups at highest risk is an important factor explaining the fast decline of the mpox outbreak.

Incubation Period and Serial Interval of Mpox in 2022 Global Outbreak Compared with Historical Estimates. Ponce, L., Linton, N. M., Toh, W., Cheng, H., Thompson, R. N., Akhmetzhanov, A. R, Dushoff, J., and al.

Published in *Emerging Infectious Diseases* on 22 May 2024
https://wwwnc.cdc.gov/eid/article/30/6/23-1095_article

This study analyzes the transmission dynamics of mpox by comparing recent and historical epidemiological data. The global outbreak of mpox in 2022 shows increased transmissibility, primarily driven by sexually associated transmission. The comparaison between recent and historical data shows that the incubation period for mpox in 2022 was similar to historical estimates, averaging 8.1 days for the 2022 outbreak and 8.2 days historically. The serial interval (the time between successive cases in a chain of transmission) was shorter in the 2022 outbreak (8.7 days) compared to historical data (14.2 days). This shortening of the serial interval may be due to enhanced public health interventions or changes in transmission modes. The study highlights the need for continuous monitoring of temporal changes in disease transmission and the importance of tailored public health measures to control future outbreaks. The findings underscore the role of proactive vaccination campaigns and behavioral changes in reducing transmission.

Global Transboundary Transmission Path and Risk of Mpox Revealed with Least Cost Path Model. Gao S., Zeng Z., Xin Q., Yang M., Feng X., Liu X., Kan W., Chen F., Chen Y. and Chen Z.

Published in *Int J Infect Dis* on 20 May 2024
https://doi.org/10.1016/j.ijid.2024.107101

This research aimed to understand how Mpox spreads in 2023 across regions and assess the risk of transmission. A total of 72,874 cases of Mpox in 109 countries were collected to illustrate the global distribution of Mpox cases. After filtering, 770 location points were obtained with a minimum distance of 10 km between each other. The data reveal that Mpox cases are predominantly concentrated in the Americas and Europe, with the United States reporting the highest number of cases (27,096), followed by Brazil (8,521), Spain (7,239), France (4,064), the United Kingdom (3,654), and Germany (3,651).The Least Cost Path model used in this research incorporated various factors such as ecological niche modeling, MaxEnt, and risk analysis to predict potential transmission routes. The study found significant transmission pathways that could facilitate the spread of Mpox, especially through travel networks. By identifying these paths, the research provides crucial insights for implementing effective prevention and control measures. This approach highlights the importance of considering multiple variables in understanding disease transmission and offers a comprehensive framework for assessing the risk of infectious diseases on a global scale.

Serological Evidence of Mpox Virus Infection During Peak Mpox Transmission in New York City, July to August 2022. Pathela P., Townsend M. B., Kopping E. J., Tang J., Navarra T., Priyamvada L., Carson W. C., Panayampalli S. S., Fowler R. C., Kyaw N., Hughes S. and Jamison K.

Published in *J Infect Dis* on 13 May 2024
https://doi.org/10.1093/infdis/jiae181

To assess asymptomatic Mpox infection in New York city at time of Mpox outbreak peak in July-August, 2022, a seroprevalence survey was carried among asymptomatic patients with no history of smallpox or Mpox vaccination nor mpox-like symptoms. Patients attending 2 express testing clinics in Sexual Health Clinic and who were undergoing phlebotomy as part of their current testing visit were taken an additionnal blood sample and were asked to complete a survey about demographics, history of mpox-related symptoms, mpox vaccination, number and genders of sexual partners, sexual contacts since April 2022. Sera were tested to detect anti-OPVX IgM and IgG antibodies. Among 419 eligible individuals, 281 were cis-men (166 reported sex with men), 109 were cis-women and 28 trangenders. Seroprevalence was 6.4% (95%IC 4.1-8.8) with little or no variation across subgroups or sexual contacts characteristics. The results suggest not to rely only on testing patients with lesions to monitor future Mpox outbreaks and to undergo serological surveillance to measure mild or subclinical infections.

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

Technological landscape

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

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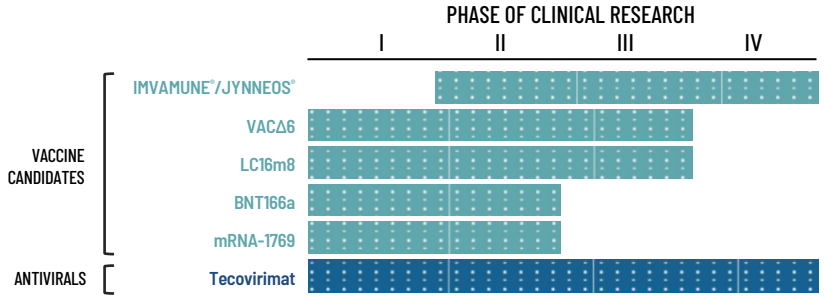
VACCINES	**IMVAMUNE®/JYNNEOS® IMVANEX®**	Viral attenuated, non-replicating vector (MVA-BN strain)	Phase 4	Third-generation smallpox vaccine authorised in EU/EEA countries, U.S. and Canada for protection against MPXV in adults. Case-control studies estimated the vaccine effectiveness at 66-86% in high-risk cohorts, with favorable safety profile and mild side effects. Limited data on use in children.
	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.
	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 2/3/4	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. A Swiss-Brazilian collaborative phase III study (UNITY) is currently underway to assess its efficacy in adults and adolescents. In RDC, a phase II randomized study (PALM007) to treat adults and children with MPXV is ongoing, with complection expected by September 2024. A EU-funded phase IV clinical trial (EPOXI) is expected to start at the end of 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.
	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.

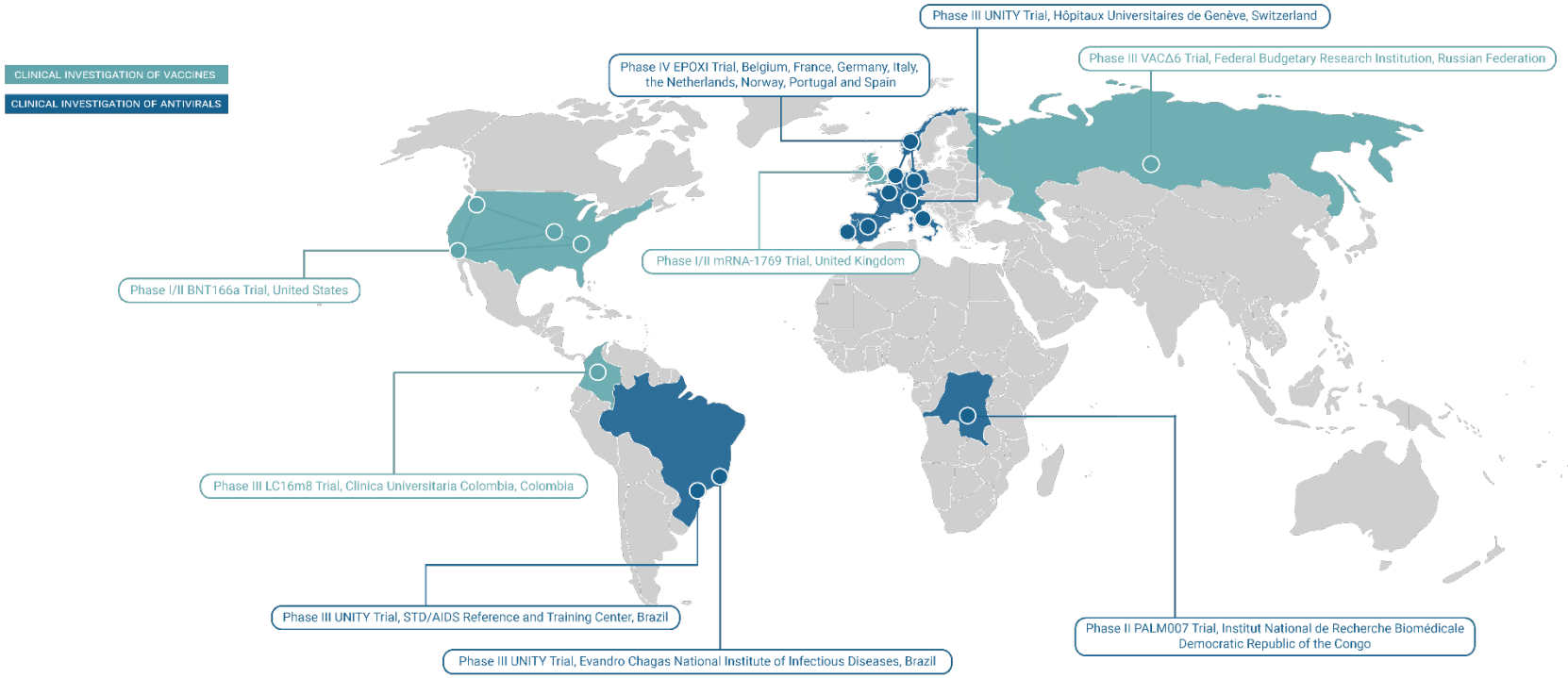
Source : Clinical Trials | National Institute of Health.

Ongoing clinical studies and sites of investigation

5 vaccines in clinical trials

1 antiviral in clinical trial





Relevant news

This section presents official reports from health agencies, manufacturers and press releases with reliable sources.
The content of this document are subject to change as the health situation evolves. All informations comes from a valid and credible source.

Mpox – Democratic Republic of the Congo.

Published by WHO on 14 June 2024
https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON522

On 1 June 2024, North Kivu Province confirmed its first case of mpox in a 19-year-old woman, expanding the affected provinces in DRC to 23 out of the 26. She had recently traveled from South Kivu, where MPXV clade I have been spreading through sexual contacts among sex workers and other groups with multiple partners. Unlike other endemic regions where mpox primarily affects children, South Kivu's outbreak predominantly affects individuals over 15. A novel variant of clade I MPXV with APOBEC3-type mutations was identified in South Kivu, suggesting adaptation of the virus to humans. Its transmissibility and severity compared to other clade I strains circulating in the country are unknown. Despite efforts to expand surveillance and testing capacity through the introduction of field-based PCR diagnostics in some provinces, national testing rates remain low at 18% , indicating potential underreporting. Other publicly available sequences from DRC show no evidence of APOBEC3-type mutations. Given the continuing high incidence, geographic expansion to previously unaffected areas, sustained community transmission, and the emergence of a novel strain of clade I MPXV, WHO assesses the risk associated with mpox in the DRC as remaining high.

Bavarian Nordic and CEPI partner to advance Mpox vaccination in Africa.

Published by CEPI on 30 May 2024
https://cepi.net/bavarian-nordic-and-cepi-partner-advance-mpox-vaccination-africa

Bavarian Nordic A/S and the CEPI have partnered to develop access of mpox vaccine for children in Africa. CEPI has awarded USD 6.5 million to support a Phase 2 clinical study evaluating the safety and effectiveness of the MVA-BN® vaccine in children aged 2 to less than 12 years compared to adults aged 18-50 years. The trial, sponsored by Bavarian Nordic, plans to enroll approximately 460 healthy individuals in endemic African regions. Results from the study could support regulatory approvals for the vaccine's use in children, providing crucial data for mpox vaccine strategies. The partnership aims to ensure equitable access to the vaccine for vulnerable populations, particularly children disproportionately affected by mpox.

Monkeypox Virus Infections After 2 Preexposure Doses of JYNNEOS Vaccine.

Published by CDC on 23 May 2024
https://www.cdc.gov/mmwr/volumes/73/wr/mm7320a3.htm

Public perception of recent increase in MPXV infections among fully vaccinated individuals receiving Bavarian Nordic's Jynneos vaccine has raised worries regarding the efficacy of the 2-dose regimen. However, a recent report by CDC confirms that two doses of Jynneos offer almost complete protection against mpox. Analyzing health records from May 2022 to May 2024, a study found that 75% of 32,819 mpox cases were in unvaccinated individuals, while only 0.8% occurred in fully vaccinated people. Despite concerns that mpox cases are rising among the vaccinated, the study revealed a persistent immunologic response in those who completed the vaccination series, resulting in a low overall infection rate of 0.1%.

U.S. Preparedness and Response to Increasing Clade I Mpox Cases in the Democratic Republic of the Congo.

Published by CDC on 16 May 2024
https://www.cdc.gov/mmwr/volumes/73/wr/mm7319a3.htm

The CDC issued a Health Alert on December 7, 2023, advising U.S. clinicians to consider clade I MPXV infection in patients with mpox symptoms who have recently been in the DRC. Despite no reported cases of clade I mpox in the U.S., the CDC warns that sexual transmission in the DRC poses a potential risk if the outbreak is not contained. The CDC has updated mpox case reporting forms to include clade- specific results and published new guidelines for handling diagnostic specimens. The CDC emphasizes the importance of diagnosing and reporting clade I MPXV to limit transmission and calls for increased vaccination and surveillance support for the DRC to prevent global spread.

Lower dose of mpox vaccine is safe and generates six-week antibody response equivalent to standard regimen.

Published by NIH on 27 April 2024
https://www.nih.gov/news-events/news-releases/lower-dose-mpox-vaccine-safe-generates-six-week-antibody-response-equivalent-standard-regimen

A study reveals that an intradermal dose-sparing mpox vaccination regimen using JYNNEOS is safe and elicits an antibody response comparable to the standard regimen at six weeks post-second dose. This regimen, studied amid the 2022 U.S. outbreak, aimed to extend limited vaccine supplies. The study, sponsored by the NIAID, enrolled 225 adults aged 18 to 50, comparing standard and dose-sparing regimens. Two weeks post-second dose, participants receiving one-fifth of the standard dose showed equivalent antibody levels to the standard regimen, though lower levels were observed by day 57. Adverse events were mild and consistent across all trial arms. However, without established correlates of protection, the efficacy of dose-sparing regimens remains uncertain, though real-world data suggest similar effectiveness to the standard regimen. Ongoing research on adolescents using the standard regimen may provide further insights.

Monkeypox virus: dangerous strain gains ability to spread through sex, new data suggest.

Published by Nature on 23 April 2024
https://www.nature.com/articles/d41586-024-01167-5

A virulent strain of monkeypox, clade I, has gained the ability to spread through sexual contact, sparking concerns of a resurgence akin to the 2022 outbreak. The Democratic Republic of the Congo faces a cluster of infections, particularly affecting sex workers, exacerbated by a humanitarian crisis and limited testing capacity. Genetic analysis reveal adapative mutations, leading to the proposal of naming the active strain clade Ib. Efforts to curb the outbreak include heightened surveillance and vaccination campaigns, though challenges persist in vaccine distribution and effectiveness against clade I. Antiviral trials are ongoing, with hopes for results within a year. Rapid diagnosis equipment are being procured to aid control efforts, emphasizing the crucial role of swift action by African health officials to prevent further spread.

Communiqué: United in the Fight Against Mpox in Africa – High-Level Emergency Regional Meeting.

Published by Africa CDC on 13 April 2024
https://www.nature.com/articles/d41586-024-01167-5

Health ministers from several African countries convened in Kinshasa on April 13, 2024, expressing concern over the prolonged Mpox epidemic in Central and West Africa and its potential cross-border transmission. They highlighted challenges in accessing medical countermeasures and emphasized the need for a coordinated regional response. Commitments were made to promote a 'One Health' approach, strengthen surveillance, enhance laboratory capabilities, and facilitate cross-border cooperation. The establishment of an Africa Taskforce for Mpox Coordination was proposed to prioritize research, capacity building, and evidence-based decision-making. Collaboration with partners like Africa CDC and WHO was urged to harmonize support efforts across affected regions.

High-level emergency regional meeting : United in the fight against mpox in Africa.

Published by WHO Afro on 13 April 2024
https://www.afro.who.int/sites/default/files/Communique_ENG_HIGH-LEVEL-EMERGENCY-REGIONAL-MEETING-ON-MPOX-IN-AFRICA-_COMMUNIQUE_ENG.pdf

On April 13th, Africa CDC organized an emergency regional meeting to address the ongoing monkeypox outbreak in Central and West African nations, emphasizing the critical need for unified action. Concerns were raised regarding the shift of transmission patterns, high mortality rates, and limited access to medical countermeasures. Participants highlighted the importance of a 'One Health' approach and coordinated responses to strengthen surveillance and laboratory capabilities. Proposals were made for establishing an Africa Taskforce to facilitate regional cooperation and support among African Union Member States, including real-time data sharing and cross-border collaboration, to enhance preparedness and response efforts.

Guidelines and practical information

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

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)