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, Mathilde Certoux, Armelle Pasquet and Eric D'Ortenzio

ANRS Emerging Infectious Diseases - Paris, France
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INDEX

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 **96,000 cases** and **184 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 I 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 30 July 2024, there have been **13,791 suspected cases** and **450 deaths** (CFR: 3.3%), 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 **68% of mpox reported cases** and **85% of fatalities**. Disease contraction and spreading are likely attributable to zoonotic transmission and interactions during playtime.

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 tranmission 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 Ib)**, 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 I 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.

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.

Between 25th July and 2nd of August 2024, human mpox infections were reported for the first time in **Rwanda**, **Burundi**, **Kenya** and **Uganda**, 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, though sequencing results from Burundi are still pending. In response to this alarming developments, the WHO announced on 7th August that an Emergency Committee under the International Health Regulations (IHR) will be convened in the coming days to determine if these mpox outbreaks warrant designation as PHEIC. Concurrently, 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 I, including the novel variant, 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 II 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. Outbreak Report, 30 July 2024: Mpox Situation in Africa | Africa CDC. 30 July 2024.
iv. Multi-country outbreak of mpox, External situation report#34. World Health Organization. 28 June 2024.
v. DR Congo grants emergency use for 2 mpox vaccines | News Brief. CIDRAP. 27 June 2024.
vi. WHO Director-General's opening remarks at the media briefing– 7 August 2024. World Health Organization.
vii. Risk to EU/EEA from variant mpox virus 'very low' | News. ECDC. 29 July 2024.

Timeline of events

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

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.

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.

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 its first mpox case 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): Kenya (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 Ia 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.

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 Ib variant.

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

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 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.

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

Events linked with clade IIb lineage B.1 MPXV outbreaks - Global

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 **rare sylvatic zoonosis** with incidental human infections occurring sporadically in rural communities adjacent to or within tropical forests 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), cowpox virus and vaccinia virus. The animal reservoir remains unknown, although 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 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 through respiratory droplets, direct contact with body fluids or skin abrasions or through contamined objects and household linen, although it is usually limited to household members. However, the spread of the global outbreak of clade IIb MPXV in 2022 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. 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. As of 2022, 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.

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.

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.

Multi-omics characterization of the monkeypox virus infection. Huang, Y., Bergant, V., Grass, V. et al.

Published in *Nat Commun* on 8 August 2024
https://doi.org/10.1038/

In this study, the authors conducted an in-depth multi-omics analysis, examining the transcriptome, proteome, and phosphoproteome of MPXV-infected primary human fibroblasts to explore virus-host interactions. Beyond the expected disruptions in immune-related pathways, they identified significant regulation of the HIPPO and TGF-β pathways. These findings reveal dynamic phosphorylation events in both host and viral proteins, with MAPKs emerging as key regulators of these processes. Notably, dynamic phosphorylation of the viral protein H5, which modulates its binding to dsDNA has been observed. This extensive dataset uncovers critical signaling events and pathways disrupted by MPXV, broadening our understanding of poxvirus biology. Through integrated pathway analysis and drug-target prediction, the authors identified potential therapeutic targets, inhibitors targeting MTOR, CHUK/IKBKB, and splicing factor kinases with potent antiviral effects against both MPXV and VACV.

An mpox quadrivalent mRNA vaccine protects mice from lethal vaccinia virus challenge. Li E., Gong Q., Zhang J., Guo G., Xie W., Chen D., Shen Y., Hong D., Li Z., Wang Q., Wang C., Wang Y., Chiu S.

Published in *Antiviral Res* on 31 July 2024
https://doi.org/10.1016/j.antiviral.2024.105974

In this study, authors developed a multivalent mRNA vaccine candidate, MPXV-1103, which expresses the full-length B6, A35, A29 and M1 proteins with three flexible linkers (G4S1)3 in a single sequence. Compared with the monovalent MPXV mRNA vaccine candidates or the quadrivalent mRNA vaccine from mixtures of the four monovalent MPXV mRNA vaccines, MPXV-1103 elicits a robust humoral response and an MPXV-specific T-cell response and protects mice from lethal vaccinia virus (VACV) challenge, with no live virus detected in the nasal or lungs even at dosages as low as 1 μg. Furthermore, analysis of complete blood counts and photomicrographs of tissue from the main organs of mice vaccinated with MPXV-1103 at doses of 5 μg and 20 μg revealed that two doses of MPXV-1103 did not cause any observable pathological changes in the mice. These results suggest that MPXV-1103 is a promising vaccine candidate for defending against MPXV infection.

Estimating the relative importance of epidemiological and behavioural parameters for epidemic mpox transmission: a modelling study. Chaturvedi, M., Rodiah, I., Kretzschmar, M. et al.

Published in *BMC Medicine* on 18 July 2024
https://doi.org/10.1186/s12916-024-03515-8

The modeling study (compartmental, stochastic, discrete-time model) attempted to capture the importance of variation of the parameters of sexual and non sexual transmission of mpox and of the effectiveness of non-medical interventions to describe the spread of the epidemic in the whole general population. The study considered various contexts of transmission: transmission in the MSM population, transmission to children and between children in kindergarten and transmission within medical care and studied the impact of immunity resulting from previous smallpox vaccination and of contact tracing. Sensitivity analyses were carried out showing the need to better ascertain the epidemiological and intervention parameters.

Africa should research the long-term sequelae of mpox. Komakech A., Ngongheh Ajong B., Kalala D., Nora Efire N., Kacita C., Hasivirwe Vakaniaki E., Izudi J., Liesenborghs L., and Ndembi N.

Published in *Lancet Glob Health* on 17 July 2024
https://doi.org/10.1093/cid/ciae https://doi.org/10.1016/S2214-109X(24)00288-2

Mpox, initially declared a global health emergency by WHO in July 2022 due to its rapid spread outside Africa, saw a decline in cases by May 2023, leading to the lifting of the emergency status. Despite this, mpox remains a critical issue in Africa, where it was first identified in 1970. While response efforts have focused on immediate containment, the long-term sequelae of mpox,

particularly in Africa, are underexplored. Emerging evidence suggests that these sequelae, including skin scarring, alopecia, blindness, and other systemic complications, may be severe, especially with the more virulent clade I virus prevalent in Central Africa. There is an urgent need for comprehensive research on these long-term effects to inform care strategies. Research priorities should include longitudinal studies to document sequelae, investigation of common symptoms, and person-centered qualitative research. Multisectoral collaboration and strong advocacy are essential to support this research, which will be crucial for improving public health outcomes in Africa.

A Second Mpox Outbreak in Brazil: A Call for Action to Guarantee Equity in Access to Health Innovations. Telford E., D'Ortenzio E., and Yazdanpanah Y.

Published in *Clin Infect Dis* on 16 July 2024
https://doi.org/10.1093/cid/ciae292

In this editorial, associated to an article describing the second wave of mpox in Brazil from da Silva et al., authors analyse the reasons for the mpos resurgence, identify research topics to focus on to tackles the mpox epidemics, and call for equity in access to health innovations. In particular, it is suggested approaches on which research should focus include surveillance for early case detection and genomic surveillance, immunity and vaccination, and robust evaluation of potential treatment through randomised clinical trials. It is essential that these tools are made equitably accessible by all countries, and in particular in those that are mostly affected by mpox and do not have access to treatments or vaccines.

Exploring the Resurgence of a Neglected Disease: Lessons From the 2023–2024 Mpox Outbreak in Rio de Janeiro, Brazil. Secco Torres Silva M., Coutinho C., Silva Torres T., Avelar Magalhães M., Yanavich C., Echeverría-Guevara A., Oliveira Bastos M., Silva Martins P., Braga Mesquita M., and al.

Published in *Clin Infect Dis* on 16 July 2024
https://doi.org/10.1093/cid/ciae290

The article discusses the resurgence of mpox (monkeypox) in Rio de Janeiro, Brazil, following a significant global outbreak in 2022 that saw cases decline by 90% by 2023. Despite this decline, a new outbreak emerged in Rio in late 2023, underscoring the need for continuous surveillance and equitable health measures. The study compares the characteristics of mpox cases from the initial outbreak (June 2022 - May 2023) to the recent one (September 2023 - January 2024), noting a higher prevalence among men who have sex with men, individuals with HIV, and those using PrEP. The findings highlight the critical need for sustained mpox vaccination and prevention strategies, particularly in vulnerable populations and regions with limited healthcare access.

The Fading of the Mpox Outbreak Among Men Who Have Sex With Men: A Mathematical Modelling Study. Xiridou M., Miura F., Adam P., Op de Coul E., de Wit J., and Jacco Wallinga J.

Published in *J Inf Dis* on 15 July 2024
https://doi.org/10.1093/infdis/jiad414

The study aims to assess the factors contributing to the fading of the 2022 Mpox outbreak before the introduction of pre-exposure vaccination in the Netherlands. In the Netherlands the peak of the outbreak was reached during the second week of July 2022. To explain the observed course of the epidemics (daily Mpox confirmed cases) in a 200 000 estimated MSM population, the modelling is based of various parameters : detailed parameters of sexual behavior in the MSM populations classified in 4 groups (very high, fairly high, fairly low and low sexual activity) including adaptation behavior, previous vaccination for older generations and post exposure vaccination among Mpox contacts, duration of infectiousness among cases, rates of transmission. The model showed a fairly high concentration of the epidemic in the very high sexual activity group, the decline of the epidemic was somewhat accelerated by behavioral adaptation but was attributed mostly to the immunity acquired among the most sexually active. Without vaccination, the outbreak could have waned by November 2022. The model showed that a ater import of new cases of unvaccinated men would lead to a small number of cases.

Escalating mpox epidemic in DR Congo. Boisson-Walsh A.

Published in *The Lancet* on 9 July 2024
https://doi.org/10.1016/s1473-3099(24)00446-8

DRC is facing a severe mpox outbreak, with cases tripling early this year compared to 2023. The outbreak involves a novel subclade Ib, which have been initially reported in sex workers in Kamituga, South Kivu and has rapidly spread due to high transmissibility through sexual contacts. According to scientists, the epidemic is spreading rapidly due to the movement of sex workers visiting mining towns for work and to cross-border mining and commercial ventures, posing a risk to nearby countries such as Burundi,

Tanzania and Rwanda. This variant's atypical transmission pattern complicates efforts to control the epidemic and has significant implications for public health, particularly for women at reproductive age. Despite coordinated efforts by DR Congo's health authorities and international partners, the response remains limited, with no approved vaccines or medicines for at-risk populations despite urgent measures promised during the Africa CDC and WHO conference settled in April 2024.

Global prevalence and correlates of mpox vaccine acceptance and uptake: a systematic review and meta-analysis. K., Isma'il Tsiga-Ahmed, F., Musa, M.S. et al.

Published in *Commun Med* on 9 July 2024
https://doi.org/10.1038/s43856-024-00564-1

The article provides a comprehensive systematic review and meta-analysis focusing on the global acceptance and uptake of the monkeypox (mpox) vaccine. After screening 2,531 studies, the researchers included 61 studies that involved a total of 263,857 participants from 87 countries. The analysis revealed a global vaccine acceptance rate of 59.7%, indicating that a little over half of the population is willing to receive the mpox vaccine. However, the actual uptake rate is significantly lower, at 30.9%, suggesting that many individuals who express willingness do not follow through with vaccination. Acceptance rates vary considerably across different regions and populations. Notably, LGBTQI+ communities and individuals living with HIV show higher acceptance rates compared to other groups, likely due to their heightened awareness and perceived risk. The study underscores a significant gap between vaccine intent and actual uptake, which could be attributed to various factors such as vaccine accessibility, misinformation, or distrust in health systems. This gap emphasizes the need for targeted public health interventions that address these barriers, aiming to boost both vaccine confidence and accessibility, particularly in vulnerable populations.

African mpox surges show lack of vaccine access. Adepoju P.

Published in *The Lancet* on 6 July 2024
https://doi.org/10.1016/s0140-6736(24)01393-x

As of July 2024, two independent mpox outbreaks have been occurring in Africa : in South Africa, who battles an outbreak among MSM, driven by sxual intercourse and skin-to-skin contact, similar to the global outbreak in 2022 ; and in DRC, where a more extensive outbreak is affecting thousands of children and adults, with a new variant detected in the eastern region of South Kivu, distinct from the strains observed in the rest of the country and showing sustained human-to-human transmission. Scientists attribute the outbreaks to decreasing herd immunity due to the cessation of smallpox vaccination and are urging international support for funding and vaccine provision. Authorities in DRC approved two mpox vaccines in late June 2024. Progress were also made in mpox screening and contact tracing but are still far from optimal diagnostic capabilities.

The 2023 – 2024 multi-source mpox outbreaks of Clade I MPXV in sub-Saharan Africa: Alarm bell for Africa and the World. Cevik M., Tomori O., Mbala P., Scagliarini A., Petersen E., Low N., Heymann ., Shan Lee S., and Blumberg L.

Published in *Int J Inf Dis* on 1 July 2024
https://doi.org/10.1016/j.ijid.2024.107159

The article discusses the 2023–2024 outbreaks of Clade I mpox (formerly known as monkeypox) in sub-Saharan Africa, particularly in the Democratic Republic of Congo (DRC). Unlike previous outbreaks caused by Clade IIb, which primarily affected men who have sex with men (MSM), the Clade I outbreaks are marked by severe symptoms and higher mortality rates, especially among children. The article notes that Clade I has been spreading in new regions and is now transmitted through sexual contact, with significant cases reported among sex workers. The DRC has seen a dramatic rise in suspected cases, with children under 15 years being the most affected group. The situation is further complicated by limited healthcare resources and ongoing armed conflicts, which hamper surveillance and response efforts. The authors call for urgent action, including enhanced surveillance, vaccination, and a coordinated regional response to prevent the spread of the virus to neighboring countries and beyond.

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

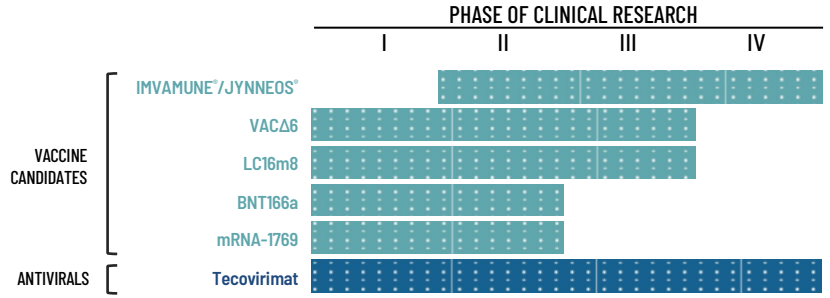
This section outlines the current pipeline of drug development, clinical trials and technologies aimed at preventing and treating the disease.

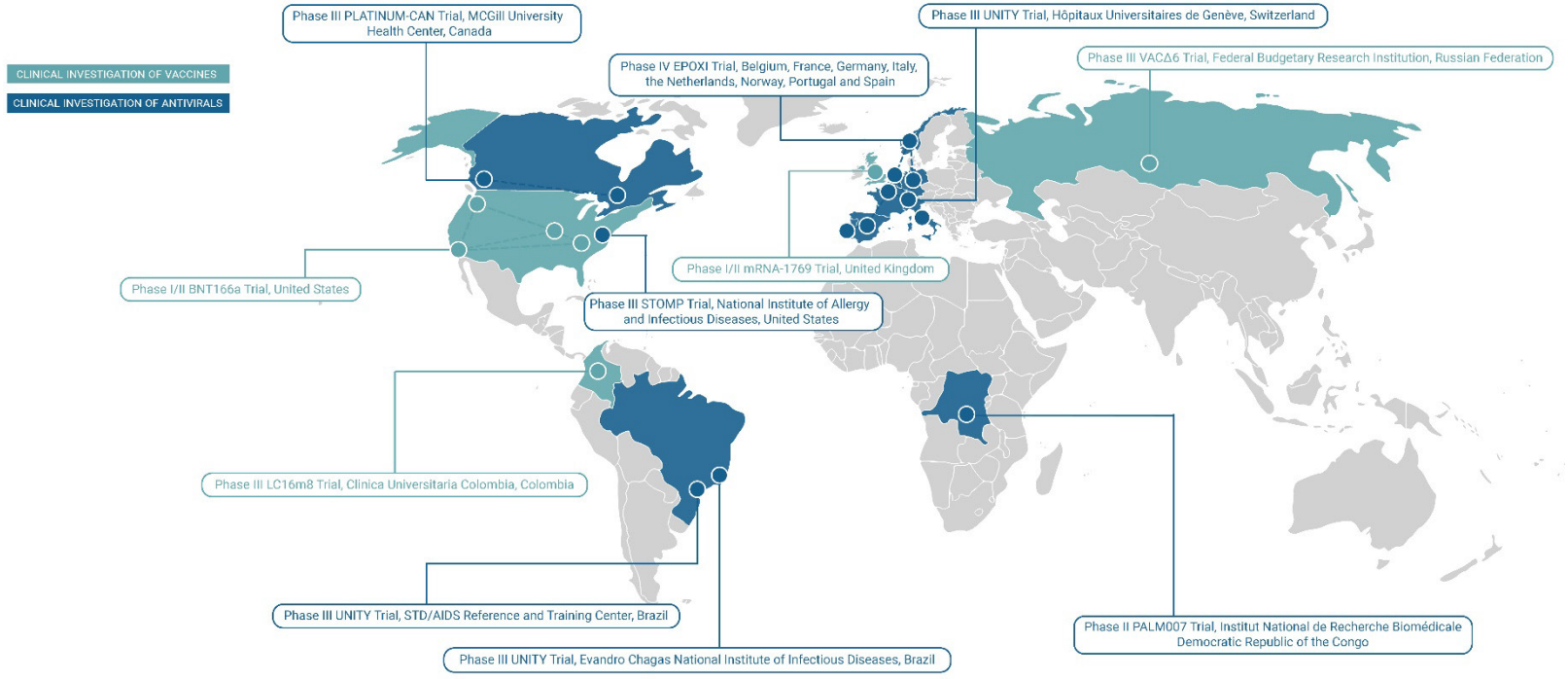
VACCINES	**IMVAMUNE®/JYNNEOS® IMVANEX®**	Viral attenuated, non-replicating vector (MVA-BN strain)	Phase 3/4	Third-generation smallpox vaccine authorised in EU/EEA countries, U.S. and Canada for protection against MPXV in adults. Case-control studies estimated the vaccine effectiveness at 66-86% in high-risk cohorts, with favorable safety profile and mild side effects. Limited data on use in children. 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 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

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





Relevant news

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

Deadlier strain of mpox spreads to multiple African countries. Cohen J.

Published in *Science* on 9 August 2024
https://www.science.org/content/article/deadlier-strain-mpox-spreads-more-african-countries

A severe mpox outbreak in the Democratic Republic of the Congo (DRC), marked by nearly 14,000 cases and 450 deaths, is the first to show sexual transmission among adults, raising concerns of further spread beyond its borders. This outbreak has already expanded to some neighboring countries, with sequencing confirming the presence of the recently identified clade Ib variant in Uganda and Kenya, which has emerged and spread in the eastern part of DRC during the past several months. The WHO is concerned that this outbreak could be the precursor to a new mpox epidemic across the continent, and is considering declaring a Public Health Emergency of International Concern (PHEIC). WHO, Africa CDC, and other partners are calling for increased funding for diagnostics, therapeutics, and vaccines to combat the outbreak. Africa CDC has allocated $10.4 million to strengthen surveillance and vaccine access across the continent. Meanwhile, the DRC has approved two mpox vaccines and received 50,000 doses from the United States, which have yet to be administered to high-risk populations.

WHO to convene emergency committee to weigh mpox spread in Africa.

Published by CIDRAP on 7 August 2024
https://www.cidrap.umn.edu/mpox/who-convene-emergency-committee-weigh-mpox-spread-africa

The Head of the World Health Organization announced plans to convene an emergency committee to assess the escalating mpox situation in Africa, where a novel clade has spread beyond the DRC to other nations. This clade, associated with more severe disease, has recently been confirmed in Kenya, Rwanda, and Uganda, with suspected cases in Burundi. Meanwhile, clade 1a, endemic in parts of Africa, is driving outbreaks in the DRC, Central African Republic, and Republic of Congo. The global clade 2 strain, responsible for the 2022 global outbreak, is causing cases in Cameroon, Ivory Coast, Liberia, Nigeria, and South Africa. The WHO has already drafted a regional response plan requiring $15 million and allocated an initial $1 million from its emergency fund. Additionally, the WHO has initiated the process for emergency use of two smallpox vaccines, already approved and recommended in some affected regions, such as DRC and Nigeria. The emergency committee will determine if the situation meets the criteria for a Public Health Emergency of International Concern (PHEIC).

New clinical trial will assess if mpox vaccination works after virus exposure.

Published by CEPI on 28 July 2024
https://cepi.net/new-clinical-trial-will-assess-if-mpox-vaccination-works-after-virus-exposure

A new clinical trial, named SMART trial, is set to launch in the DRC and other African countries to assess whether the MVA-BN vaccine can protect individuals after exposure to MPXV viruses. Funded by CEPI and the Canadian Institutes of Health Research, the trial will involve over 1,500 participants in the DRC, Uganda, and Nigeria, focusing on households with laboratory-confirmed mpox cases. The study aims to determine if post-exposure vaccination can reduce the risk of secondary infections or lessen the severity of the disease. The study is due to launch next month in the DRC, enrolling participants from Kamituga, South Kivu province, a region which has recently reported mpox cases. The trial is the first of its kind to evaluate post-exposure vaccination for mpox, with the potential to guide public health responses and improve preparedness in Africa. The WHO and Africa CDC emphasize the importance of this trial in controlling the spread of mpox and enhancing response efforts across the continent.

Mpox - South Africa.

Published by WHO on 9 July 2024
https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON525

South Africa reported 20 confirmed mpox cases, including three deaths (CFR: 15%), between May 8 and July 2, 2024, marking the first mpox cases in the country since 2022. The cases occurred in three of the nine provinces : Gauteng, Western Cape, and KwaZulu-Natal. The affected individuals are men aged between 17 and 43 years, with many identifying as MSM and reported sexual contacts as type of exposure. Notably, 15 of the cases are living with unmanaged or newly diagnosed HIV infection and avanced HIV disease. All cases were symptomatic, with extensive skin lesions and 18 required hospitalization. None of the confirmed cases reported a history of international travel and none reported attending high-risk social gatherings. The high

prevalence of HIV among the patients and the absence of international travel history suggest sustained community transmission, with confirmed cases likely representing only a fraction of the actual number. While the risk to the general population is low, the risk to MSM and sex workers remains moderate. The situation underscores the continued global threat of the clade IIb mpox outbreak and the potential for cross-border spread.

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.

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)