Mpox in Africa: Evolving Epidemiology and Urgent Priorities for Action.

Nachega outlines the emergency of Mpox, from zoonosis to human transmission. He highlights the gaps in surveillance, diagnosis, and treatment and gives policy and Public Health recommendations.

Introduction

Since the eradication of smallpox in 1980, mpox (formerly monkeypox) has emerged as the most serious orthopoxvirus threat to human health. Caused by the monkeypox virus (MPXV), the disease is characterized by fever, lymphadenopathy, a vesiculopapular rash, and a high risk of bacterial superinfection. Two genetically distinct viral clades—Clade I, which predominates in Central Africa, and Clade II, seen mostly in West Africa—differ in clinical severity. Clade I carries a case fatality ratio (CFR) of up to 10%, while Clade II is associated with CFRs of less than 3% [1].

For over four decades, mpox outbreaks in Africa were mostly zoonotic, with limited human-to-human transmission. However, this changed dramatically in 2022 when Clade IIb (lineage B.1) caused a global outbreak involving more than 95,000 confirmed cases across 117 countries [1,2,3]. This event exposed the epidemic potential of MPXV and highlighted critical gaps in global preparedness and response.

While the Clade IIb epidemic has subsided in most non-endemic settings, Clade I outbreaks have intensified in Africa, especially in the Democratic Republic of Congo (DRC), which reported a record 14,753 suspected cases in 2023 [1]. This surge is a warning sign that mpox remains a growing public health threat on the continent and demands urgent attention from health authorities, policy makers, and researchers alike.

From Zoonosis to Human Transmission: A Shifting Paradigm

Historically, Clade I MPXV transmission was primarily zoonotic, occurring through contact with wild animals such as rodents and non-human primates. Human cases were usually limited to forested areas, with only sporadic secondary transmission [1]. That began to change with the 2017 Clade II outbreak in Nigeria, which was the first to show sustained human-to-human transmission, including through suspected sexual contact [2].

Jean B. Nachega, MD, PhD, MPH, FAAS[1,2,3],Departments of Epidemiology, Infectious Diseases and Microbiology, University of Pittsburgh School of Public Health, Pittsburgh, PA, USA[1]; Departments of Epidemiology and International Health, Johns Hopkins School of Public Health Baltimore, MD, USA[2]; and [3]Department of Medicine, Stellenbosch University Faculty of Medicine and Health Sciences, Cape Town, South Africa

Genomic analyses of the 2022 global outbreak virus (Clade IIb B.1) revealed a striking pattern of APOBEC3-driven mutations, indicating sustained human adaptation and non-canonical evolution over time[4,5]. These findings suggest that Clade IIb may have been circulating silently among humans since at least 2015. The epidemic demonstrated how human-to-human transmission, particularly in networks of men who have sex with men (MSM), can fuel widespread outbreaks across continents.

As global attention centered on Clade IIb, Clade I infections surged in remote and conflict-affected areas of Central Africa. The DRC has consistently reported the highest number of mpox cases globally, but the recent upsurge signals a shift from zoonotic spillover to increasingly efficient person-to-person spread, particularly in household and community settings [1].

Emergence of Clade Ib in Eastern DRC and Beyond

In October 2023, an outbreak of mpox was reported for the first time in Kamituga Health Zone, a densely populated mining town in South Kivu Province. Epidemiological investigations led by Katoto et al. [6] revealed a pattern of transmission centered around high-risk populations such as sex workers and miners, with strong evidence of human-to-human spread, including sexual transmission.

Sequencing efforts by Masirika and colleagues [7] identified a novel Clade I sub-lineage among infected individuals, genetically distinct from previously circulating Clade I strains. Further analysis by Vakaniaki et al.[8] confirmed that this lineage—provisionally named Clade Ib—showed APOBEC3-linked mutations, consistent with efficient human adaptation. These findings mirror the evolutionary criteria used to define Clades IIa and IIb [4]. The emergence of Clade Ib marks a critical development, potentially representing a transitional form of MPXV that combines the high virulence of Clade I with increased transmissibility among humans. Its spread beyond the Eastern DRC—the epicenter of the epidemic—to neighboring countries and beyond, along with the re-emergence of Clade IIb outbreaks in Nigeria and South Africa, led to the WHO's 2024 declaration of a Public Health Emergency of International Concern. This underscores the urgent need to strengthen prevention, treatment, and research efforts (Figure 1).

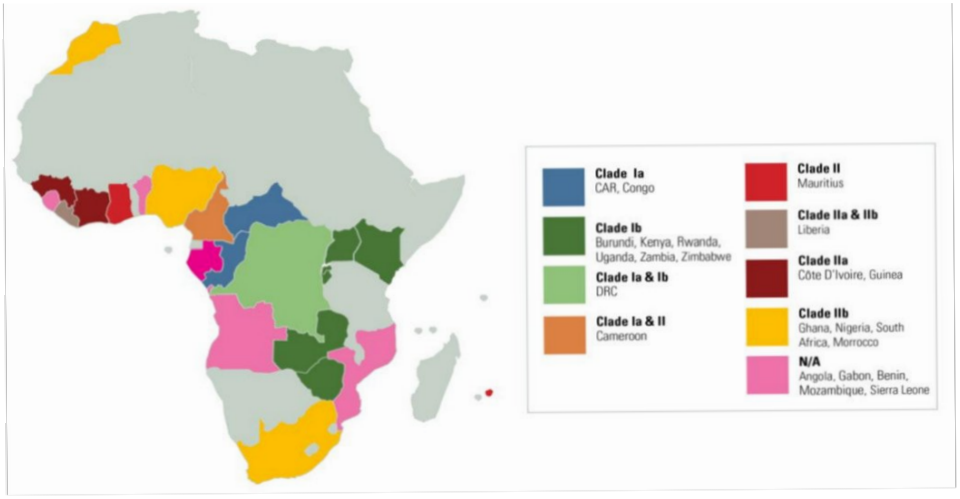


Figure 1: Geographic expansions of mpox in African countries as of February 2025. Source: Africa CDC

A Disproportionate Burden on Children—and Emerging Threats in Adults

Despite increasing recognition of sexual and close-contact transmission among adults, particularly MSM and sex workers, children continue to bear the brunt of mpox cases and deaths in Africa [1]. This is likely due to a combination of biological, social, and healthcare access vulnerabilities. Pediatric cases often present with more severe disease and are less likely to receive timely care.

Whittles et al. [9] recently modeled age-specific CFRs and found that the risk of death from Clade I mpox sharply declines with age. This pattern may reflect partial immunity in older individuals due to past smallpox vaccination campaigns. However, children born after 1980 have no such protection, and vaccination coverage remains virtually nonexistent in endemic areas.

Co-infections—especially with HIV—are another emerging concern. During the 2022 Clade IIb outbreak, individuals with advanced HIV disease were at significantly increased risk for severe mpox and death [1]. With high HIV prevalence in parts of Central and Eastern Africa, there is a critical need to understand the interaction between immunosuppression and Clade Ib infections.

Gaps in Surveillance, Diagnosis, and Treatment

Africa's response to mpox is hampered by major deficiencies in diagnostics, surveillance, and clinical care. Access to confirmatory testing is extremely limited, often requiring transport of samples to central laboratories with turnaround times of several days to weeks[1]. While the GeneXpert platform has been adapted for MPXV detection, its deployment remains sparse and inconsistent.

Surveillance efforts rely heavily on syndromic case definitions that are difficult to distinguish from other common febrile rash illnesses, including chickenpox and bacterial skin infections. Under-reporting and misclassification are likely, especially in rural and insecure regions. The lack of systematic community-level surveillance further obscures the true scale of transmission [1].

There are also limited treatment options. Although tecovirimat (TPOXX) is approved for compassionate use in severe mpox cases in some countries, recent trial data have questioned its effectiveness, particularly against Clade I MPXV. Results from the STOMP trial in the United States and the PALM007 trial in the Democratic Republic of the Congo found that tecovirimat did not significantly reduce the time to lesion resolution in patients infected with Clade Ia MPXV. However, no major safety concerns were reported [10]. These findings underscore the urgent need to develop alternative therapeutics and to evaluate treatments specifically targeting Clade I and emerging lineages such as Clade Ib.

Vaccines, including MVA-BN (JYNNEOS), have been used for post-exposure prophylaxis in high-income countries but remain largely inaccessible in endemic regions. With limited vaccines and effective antivirals, African countries are left to manage outbreaks with limited tools

Research and Response: Building Momentum through MpoxReC

To address these gaps, the Mpox Research Consortium (MpoxReC) was established in 2023, bringing together African and global partners to strengthen evidence-based responses to mpox. The consortium includes researchers, clinicians, virologists, and public health leaders with deep expertise in outbreak response and genomic surveillance [1].

One of MpoxReC's flagship projects is a prospective cohort study in South Kivu Province, Eastern DRC. This study will follow patients infected with Clade Ib over a two-year period to assess transmission dynamics, disease progression, and outcomes, including among children, MSM, and persons living with HIV. The study also incorporates genomic sequencing to monitor viral evolution and identify emerging variants.

MpoxReC is working closely with Africa CDC and national health authorities to expand laboratory



Mpox patient - istock, courtesy of Mustafa Kaya

capacity, deploy point-of-care diagnostics, and train local surveillance teams. These investments are critical not only for mpox, but also for broader pandemic preparedness efforts in the region.

Policy and Public Health Recommendations

Given the rapidly changing mpox landscape in Africa, the following strategic priorities are recommended for national governments and regional stakeholders:

1. Strengthen Surveillance Systems

Mpox should be designated a notifiable disease in all African Union member states. Integrated Disease Surveillance and Response (IDSR) platforms must be expanded to include real-time reporting and laboratory confirmation of mpox cases.

2. Expand Diagnostic Access

Decentralize MPXV testing through the roll-out of rapid molecular platforms such as GeneXpert. Build capacity in regional labs and ensure cold-chain logistics for sample transport.

3. Targeted Vaccination Strategies

Prioritize vaccine access for high-risk groups, including health workers, contacts of confirmed cases, and vulnerable populations in outbreak zones. Leverage global procurement mechanisms to secure MVA-BN supply.

4. Integrate Mpox and HIV Services

Screen for mpox in HIV clinics and vice versa. Offer mpox education and contact tracing in sexual health services and expand syndromic management protocols to include mpox indicators.

5. Invest in African-led Research

Fund longitudinal studies, social science research, and clinical trials in endemic regions. Support consortia like MpoxReC to foster local innovation and sustainable response capacity.

Conclusion

Mpox in Africa is no longer a sporadic zoonosis. The rise of Clade Ib in Eastern DRC signals a new phase of the epidemic—one that combines high virulence with growing potential for sustained human transmission. Without urgent action, this could evolve into a broader regional health crisis.

Strengthening surveillance, diagnostics, and vaccine access—while investing in African research networks—is essential to reverse current trends. With coordinated leadership and global solidarity, we can contain the threat of mpox and build more resilient health systems for the future.

References:

1. Ndembi N, et al. Evolving Epidemiology of Mpox in Africa in 2024. N Engl J Med. 2025.
2. Ogoina D, et al. The 2017 Human Monkeypox Outbreak in Nigeria. PLoS One. 2019.
3. World Health Organization. Mpox Global Situation Update. 2024.
4. Isidro J, et al. Phylogenomic Characterization of MPXV. Nat Med. 2022.
5. O'Toole Á, et al. APOBEC3 Editing in MPXV. Science. 2023.
6. Katoto PDM, et al. Shifting Transmission in South Kivu. Lancet Infect Dis. 2024.
7. Masirika LM, et al. Novel Clade I Sub-lineage in Kamituga. Eurosurveillance. 2024.
8. Vakaniaki EH, et al. Sustained Human Transmission of Clade Ib. Nat Med. 2024.
9. Whittles LK, et al. Age Patterns of Clade I Severity. medRxiv. 2024.