



The 2023 – 2024 multi-source mpox outbreaks of Clade I MPXV in sub-Saharan Africa: alarm bell for Africa and the World

Muge Cevik , Oyewale Tomori , Placide Mbala ,  
Alessandra Scagliarini , Eskild Petersen , Nicola Low ,  
David Heymann , Shui Shan Lee , Lucille Blumberg

PII: S1201-9712(24)00230-3  
DOI: <https://doi.org/10.1016/j.ijid.2024.107159>  
Reference: IJID 107159

To appear in: *International Journal of Infectious Diseases*

Please cite this article as: Muge Cevik , Oyewale Tomori , Placide Mbala , Alessandra Scagliarini , Eskild Petersen , Nicola Low , David Heymann , Shui Shan Lee , Lucille Blumberg , The 2023 – 2024 multi-source mpox outbreaks of Clade I MPXV in sub-Saharan Africa: alarm bell for Africa and the World, *International Journal of Infectious Diseases* (2024), doi: <https://doi.org/10.1016/j.ijid.2024.107159>

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2024 Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.  
This is an open access article under the CC BY-NC-ND license  
(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

## The 2023 – 2024 multi-source mpox outbreaks of Clade I MPXV in sub-Saharan Africa: alarm bell for Africa and the World

**Authors:** Muge Cevik<sup>1,2</sup>, Oyewale Tomori<sup>3</sup>, Placide Mbala<sup>4,5</sup>, Alessandra Scagliarini<sup>2,6</sup>, Eskild Petersen<sup>2,7,8</sup>, Nicola Low<sup>9</sup>, David Heymann<sup>10</sup>, Shui Shan Lee<sup>2,11</sup>, Lucille Blumberg<sup>2,12</sup>

### Affiliations:

<sup>1</sup> Division of Infection and Global Health Research, School of Medicine, University of St Andrews, St Andrews, U.K.

<sup>2</sup> International Society for Infectious Diseases

<sup>3</sup> African Centre of Excellence for Genomics of Infectious Diseases, Redeemer's University, Ede, Osun State, Nigeria

<sup>4</sup> Institut National de Recherche Biomédicale, Kinshasa, Democratic Republic of Congo

<sup>5</sup> Université de Kinshasa, Democratic Republic of Congo

<sup>6</sup> Dipartimento di Scienze Mediche e Chirurgiche, Alma Mater Studiorum Università di Bologna, Italy

<sup>7</sup> Institute for Clinical Medicine, Faculty of Health Science, University of Aarhus, Denmark

<sup>8</sup> PandemiX Center, Department of Science and Environment, Roskilde University, Denmark

<sup>9</sup> Institute of Social and Preventive Medicine, University of Bern, Bern, CH-3012, Switzerland

<sup>10</sup> Global Health Security Department, London School of Hygiene & Tropical Medicine, London, UK

<sup>11</sup> S.H. Ho Research Centre for Infectious Diseases, The Chinese University of Hong Kong

<sup>12</sup> Division of Public Health Surveillance and Response, Centre for Emerging Zoonotic and Parasitic Diseases, National Institute for Communicable Diseases a Division of the National Health Laboratory Services, Sandringham, Johannesburg, South Africa

**Correspondence:** Lucille H. Blumberg, National Institute for Communicable Diseases, Private Bag X4, Sandringham 2131, South Africa. E-mail: [lucilleb@nicd.ac.za](mailto:lucilleb@nicd.ac.za)

Human mpox (formerly monkeypox) has historically received little attention until 2022, when we saw a reemergence beyond endemic countries [1,2]. In this global outbreak, mpox caused by Clade IIb monkeypox virus (MPXV) was introduced to countries that had never experienced mpox or had collectively reported fewer than ten imported cases, with few secondary cases. This global outbreak was characterised by unique patterns of person-to-person transmission[3] sustained within sexual networks among men who have sex with men (MSM) [4]. Few clinical cases in women were reported [5]. This outbreak of Clade IIb MPXV decelerated at the beginning of 2023; [6] however, in April 2024, 27 countries still reported new cases to the World Health Organization, including the growing Clade IIb outbreak in South Africa mainly affecting MSM. Meanwhile, the increasing frequency of outbreaks with Clade I MPXV in endemic regions, especially in the Democratic Republic of Congo (DRC), has become a major source of concern.

MPXV is subdivided into two distinct clades: Clade I (formerly known as the Congo Basin or Central African clade) and Clade II (formerly known as the West African clade) [7]. Clade II is subdivided into two subclades, IIa and IIb, the latter being responsible for the 2022 – 2024 ongoing multi-country outbreak having originated in Nigeria.

The number of reported cases of mpox linked to Clade I MPXV has been progressively rising in Central Africa in all age groups, especially in infants and young children, characterised by different epidemiological patterns, with more severe clinical symptoms and higher mortality than Clade II. Notably, in 2023, the DRC reported a record number of suspected (clinically-compatible) cases, especially in provinces which have never reported mpox cases before [1], suggesting a growing outbreak and a shift towards increased human-to-human transmission. As of May 2024, 23 out of 26 provinces reported at least 1 suspected case. In 2024 alone, over 7000 suspected cases were reported with case fatality ratio of 5.3%. Children  $\leq 15$  years represent 67% of suspected cases and 84% of the deaths. According to the surveillance data, children under the age of 1 are reported to be four times more likely to die than those over the age of 15.

Based on epidemiological and genomic sequencing data, there appear to be at least two independent Clade I MPXV outbreaks ongoing in the DRC: (i) among adults, with affected women identifying as sex workers and (ii) in new provinces mostly affecting children. The transmission of Clade I through sexual contact was reported for the first time in April 2023 [8]. The first documented case of Clade I MPXV transmitted through sexual contact was confirmed in a man who had travelled between Belgium and the DRC and had sexual encounters in Kwango province (southwest) [8]. Subsequent epidemiological reports from South Kivu (east) in Kamituga health zone suggested a shift towards transmission through sexual contact between adults, with many of the women identifying as sex workers [9-12]. Phylogenetic analyses of the outbreak in Kamituga have identified a new sublineage of Clade I MPXV distinct from the strains found in established endemic areas to date [11,13]. Comparing these sequences to earlier zoonotic infections in neighbouring provinces suggests that this lineage likely pre-existed in a local, non-human animal reservoir [6,11]. While DRC has identified local transmission in urban settings related to travel and trade from endemic provinces, health areas continuously reporting mpox cases in South Kivu tend to be in poor, densely populated, mining areas with a high number of bars that are sustaining the local sex industry [10,11]. However, genomic evidence from limited sequences represents

multiple independent spillover events from reservoir hosts followed by secondary transmission, suggesting that most cases elsewhere in the country are not linked to a single human outbreak or increased transmissibility [11,13]. Cases being reported in several previously unaffected areas of DRC confirms these observations. Overall, in the DRC outbreaks, children are the most affected population with high mortality rates. This suggests that direct transmission through family and community contact remains a major route of infection. However, further genomic analysis is needed to ascertain these observations.

Without intervention, given the proximity of DRC to neighbouring countries, these outbreaks have the potential to lead to a multi-country outbreak. There are limited investigations available from the current DRC outbreaks, and published reports from Kamituga represent a minority of mpox cases reported during this surge. Nevertheless, these investigations suggest a shift in the transmission dynamics of Clade I MPXV and at-risk populations. Current outbreaks highlight the vulnerability of the global health efforts and need for rapid response in the region. Similarly important, transmission of other sexually transmitted infections particularly HIV remains a major concern. A previously undescribed severe disseminated and necrotising form of Clade II infection with multi-organ involvement including lung, and secondary bacterial infections, and death, was associated with people living with HIV who fell below CD4 threshold that defines an opportunistic illness ( $CD4 < 200 \text{ cells/mm}^3$ ) [14]. Therefore, it is imperative to understand whether the new lineage of Clade I can also present similarly. As observed during the 2022 mpox outbreaks, the sexually associated secondary attack rate of mpox may be higher than previous estimates in non-sexually-associated contexts highlighting an immediate need for control efforts to inform and protect affected communities [15].

There are important actions to consider, including enhanced surveillance to track the growth of mpox epidemics as well as control and prevention strategies, which include vaccination. Leveraging diagnostic capacities in the region is urgently needed, to understand transmission dynamics that could inform prevention strategies and particularly for diagnosis of people with symptoms to get medical care, and know for whom isolation at home or in hospital is needed. The armed conflicts in the region have adverse effects on community surveillance and reporting of cases further limiting efforts to determine the true burden of mpox. Risk management and communication is also crucial to enhance equitable access to vaccines and reduce mpox stigma.

Vaccination remains the most effective strategy, particularly given the high mortality rates seen in children. Since the beginning of the millennium, experts have warned about the effects of waning immunity, after cessation of smallpox vaccination [16]. During the global outbreak, third-generation vaccines proved to be safe and greatly effective. However, access to vaccines and especially the distribution efforts in a conflict zone remains challenging. While there are active discussions between vaccine suppliers and the DRC, there is no active immunisation campaign yet. We are aware that CEPI and Bavarian Nordic are planning vaccine trials of the MVA-BN<sup>®</sup> non-replicating vaccine among children in Africa [17]. Bavarian Nordic also announced that they have submitted an application to the US FDA for approval of a freeze-dried formulation, which will ease logistics and hopefully be stable at room temperature [18]. Therefore, an immediate plan is urgently needed for

development and deployment of a vaccination strategy, that makes sure sex workers and other vulnerable or marginalised populations at risk will be prioritised.

A high-level emergency meeting on mpox took place in Kinshasa from 11-13 April 2024. Participants acknowledged the alarming, protracted and ongoing mpox epidemics in several countries in Central and West Africa. Amidst calls to implement an urgent and coordinated response, the main outcome of the meeting was an agreement to draft a regional roadmap for addressing mpox in Africa, after more than 50 years of mpox epidemics in the region. The outcome of this high-level meeting falls far short of expectations. There are serious concerns about the changing dynamics of transmission and high mortality particularly among children, as well as the disease's effects on morbidity and the social and economic spheres. Given the possible risk of transmission to neighbouring countries and beyond, there is an urgency for action, led by African countries, governments, and scientists to address these unmet needs. Ongoing mpox outbreaks in Africa, especially affecting the vulnerable in inaccessible areas, represent an alarm bell for not only the African region but also the world especially given the newly recognised route of transmission through sexual contact amid repressive government policies and limited social acceptance of diversity of sexual orientation in some countries. In addition, given that animal-to-human transmission accounts for at least some of the Clade I infections, there is need to move from a crisis response model to a risk-based One Health approach that would improve disease control and management capacities in endemic countries and enhance prevention strategies in disease-free countries [19]. "No one is safe until everyone is safe" is a slogan we heard often during the COVID-19 pandemic, which is now also required for the growing global and regional mpox outbreaks.

### **Acknowledgements**

We thank the input provided by Dr Rosamund Lewis, World Health Organization and Prof Jean-Jacques Muyembe-Tamfum, INRB.

### **Conflict of Interest**

We declare that we have no conflicts of interest. The opinions expressed in this article are those of the authors and do not reflect the official position of any of their affiliating organisations.

### **Transparency declaration**

MC and NL received research grant from the Canadian Institutes of Health Research (CIHR) (Grant No. 202209MRR-489062-MPX-CDAA-168421). EP acknowledges financial support for the PandemiX Center, from the Danish National Research Foundation (grant No. DNRF170).

**Authors' contributions:**

LC and SH conceptualised this editorial, MC wrote the first and subsequent drafts and all authors contributed to the final version of the manuscript and approved it for publication.

**References:**

1. WHO. WHO Disease outbreak news November 2023. [Internet]. [cited 2024 Jun 1]. Available from: <https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON493>
2. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, et al. Monkeypox Virus Infection in Humans across 16 Countries — April-June 2022. *N Engl J Med* 2022;387(8):679–91. doi: 10.1056/NEJMoa2207323
3. Cevik M, Orkin C. Changing face of mpox. *Clin Microbiol Infect* 2023;29(12):1485–6. doi: 10.1016/j.cmi.2023.10.011
4. Low N, Bachmann LH, Ogoina D, McDonald R, Ipekci AM, Quilter LAS, et al. Mpox virus and transmission through sexual contact: Defining the research agenda. *PLoS Med* 2023;20(1):e1004163. doi: 10.1371/journal.pmed.1004163
5. Caria J, Pinto R, Leal E, Almeida V, Cristóvão G, Gonçalves AC, et al. Clinical and Epidemiological Features of Hospitalized and Ambulatory Patients with Human Monkeypox Infection: A Retrospective Observational Study in Portugal. *Infect Dis Rep* 2022;14(6):810–23. doi: 10.3390/idr14060083
6. WHO. 2022–24 mpox (monkeypox) outbreak: global trends. [Internet]. [cited 2024 May 30]. Available from: [https://worldhealthorg.shinyapps.io/mpx\\_global](https://worldhealthorg.shinyapps.io/mpx_global)
7. Okwor T, Mbala PK, Evans DH, Kindrachuk J. A contemporary review of clade-specific virological differences in monkeypox viruses. *Clin Microbiol Infect* 2023; 29(12):1502–1507. doi: 10.1016/j.cmi.2023.07.011
8. Kibungu EM, Vakaniaki EH, Kinganda-Lusamaki E, Kalonji-Mukendi T, Pukuta E, Hoff NA, et al. Clade I–Associated Mpox Cases Associated with Sexual Contact, the Democratic Republic of the Congo. *Emerg Infect Dis* 2024;30(1):172–176. doi: 10.3201/eid3001.231164
9. Katoto PD, Muttamba W, Bahizire E, Malembaka EB, Bosa HK, Kazadi DM, et al. Shifting transmission patterns of human mpox in South Kivu, DR Congo. *The Lancet Infectious Diseases*. 2024 Jun;24(6):e354–5. doi: 10.1016/S1473-3099(24)00287-1

10. Masirika LM, Nieuwenhuijse DF, Ndishimye P, Udahemuka JC, Steeven BK, Gisèle NB, et al. Mapping the distribution and describing the first cases from an ongoing outbreak of a New Strain of mpox in South Kivu, Eastern Democratic Republic of Congo between September 2023 to April 2024. medRxiv 24307057 [Preprint] May 10, 2024 [cited 2024 May 30]. Available from: <https://doi.org/10.1101/2024.05.10.24307057>
11. Vakaniaki EH, Kacita C, Kinganda-Lusamaki E, O'Toole Á, Wawina-Bokalanga T, Mukadi-Bamuleka D, et al. Sustained Human Outbreak of a New MPXV Clade I Lineage in the Eastern Democratic Republic of the Congo. Nat Med 2024;[ePub online Jun 13] doi: 10.1038/s41591-024-03130-3
12. Masirika LM, Udahemuka JC, Ndishimye P, Martinez GS, Kelvin P, Nadine MB, et al. Epidemiology, clinical characteristics, and transmission patterns of a novel Mpox (Monkeypox) outbreak in eastern Democratic Republic of the Congo (DRC): *an observational, cross-sectional cohort study*. medRxiv 24303395 [Pre-print] March 5 2024 [cited 2024 May 30]. Available from: <https://doi.org/10.1101/2024.03.05.24303395>
13. Masirika LM, Udahemuka JC, Schuele L, Ndishimye P, Otani S, Mbiribindi JB, et al. Ongoing mpox outbreak in Kamituga, South Kivu province, associated with monkeypox virus of a novel Clade I sub-lineage, Democratic Republic of the Congo, 2024. Euro Surveill 2024;29(11):2400106. doi: 10.2807/1560-7917.ES.2024.29.11.2400106
14. Ogoina D, Damon I, Nakoune E. Clinical review of human mpox. Clin Microbiol Infect 2023;29(12):1493-1501. doi: 10.1016/j.cmi.2023.09.004
15. Endo A, Murayama H, Abbott S, Ratnayake R, Pearson CAB, Edmunds WJ, et al. Heavy-tailed sexual contact networks and monkeypox epidemiology in the global outbreak, 2022. Science 2022;378(6615):90–4. doi: 10.1126/science.add4507
16. Desai AN, Thompson GR, Dodson D, Neumeister SM, Arutyunova AM, Trigg K, et al. Mpox Infection in Children—Infection Control Implications for Household Contacts. Open Forum Infect Dis 2023;10(2):ofad003. doi: 10.1093/ofid/ofad003.
17. Bavarian Nordic. Bavarian Nordic and CEPI partners to advance mpox vaccination in Africa [Internet]. [cited 2024 Jun 13]. Available from: <https://www.bavarian-nordic.com/investor/news/news.aspx?news=6958>.
18. Bavarian Nordic. Bavarian Nordic submits supplemental BLA (Biologics License Application) seeking U.S. FDA approval of freeze-dried formulation of smallpox and mpox vaccine. [Internet]. [cited 2024 Jun 13]. Available from: <https://www.bavarian-nordic.com/investor/news/news.aspx?news=6959>
19. De Pascali AM, Brandolini M, Peli L, Sambri V, Cricca M, Scagliarini A. Zoonotic orthopoxviruses after smallpox eradication: A shift from crisis response to a One Health approach. IJID One Health. 2024;2:100018. doi: 10.1016/j.ijidoh.2024.100018