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Mini-Review

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A mini-review of Mpox management in low- and middle-income countries: A systems-based approach integrating CDC emerging infectious disease modelling and genomic surveillance

¹Dolapo, D., ²Abanida, E. A., and ^{*3}Adegboro, B.¹Department of Community Health, College of Health Sciences, Nile University of Nigeria, Abuja, Nigeria²Plot D-1A, Kaduna Court, Gaduwa Estate, Abuja, Nigeria³Department of Medical Microbiology and Immunology, College of Health Sciences, Nile University of Nigeria, Abuja, Nigeria*Correspondence to: boazadegboro@gmail.com; boaz.adegboro@nileuniversity.edu.ng

Abstract:

Mpox, previously known as monkeypox, is a viral illness caused by the monkeypox virus (MPXV), a species of the Poxviridae family, and genus Orthopoxvirus. The resurgence of Mpox, particularly in low- and middle-income countries (LMICs), underscores the need for a comprehensive systems-level analysis. The Centre for Disease Control and Prevention (CDC)'s Emerging Infectious Diseases (EID) modelling framework, combined with genomic surveillance, offers a robust approach to understanding and mitigating such outbreaks. Integrating these methods can enhance outbreak prediction, surveillance, and response strategies, particularly in resource-constrained settings. This review aims to identify systemic vulnerabilities and health systems gaps in control of Mpox in LMICs, opportunities for modelling Mpox within the CDC EID framework, and the role of genomic epidemiology in Mpox surveillance, especially in combination with the EID framework. We used a narrative review and followed a structured method designed to capture the range of interventions on EID modelling and genomic surveillance related to Mpox. Previous modelling results indicated that close-contact transmission within and between households were unlikely to result in a large number of Mpox clade I cases. Studies that modelled the impact of vaccination and sexual behaviour adaptations on Mpox cases found that initial decline in cases were likely caused by behavioural adaptation, but vaccination averted more cases overall and was key to hastening outbreak control. Studies revealed that the geographical pattern of Mpox reported in the Nigeria outbreak suggested a possible new and widespread zoonotic reservoir, but the animal reservoir remains unknown. Integrating genomic data into Mpox surveillance can facilitate early detection, identification of animal reservoir and inform targeted interventions. This review found that CDC successfully leveraged a SARS-CoV-2 wastewater surveillance system for Mpox and concluded that integrating the CDC's EID modelling and genomic surveillance can significantly enhance Mpox management in LMICs.

Keywords: Mpox, Emerging Infection, Modelling, Genomic Surveillance, Zoonotic outbreaks.

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Synthèse des mesures de prise en charge de la variole du singe dans les pays à revenu faible et intermédiaire: Une approche systémique intégrant la modélisation des maladies infectieuses émergentes et la surveillance génomique du CDC

¹Dolapo, D., ²Abanida, E. A., et ^{*3}Adegboro, B.¹Département de Santé Communautaire, Faculté des Sciences de la Santé, Université du Nil du Nigéria, Abuja, Nigéria²Plot D-1A, Kaduna Court, Gaduwa Estate, Abuja, Nigéria³Département de Microbiologie Médicale et d'Immunologie, Faculté des Sciences de la Santé, Université du Nil du Nigéria, Abuja, Nigéria*Correspondance à: boazadegboro@gmail.com; boaz.adegboro@nileuniversity.edu.ng

Résumé:

La variole du singe, également appelée Mpox, est une maladie virale causée par le virus de la variole du singe (MPXV), une espèce de la famille des Poxviridae et du genre Orthopoxvirus. La résurgence de la variole, notamment dans les pays à revenu faible et intermédiaire (PRFI), souligne la nécessité d'une analyse systémique globale. Le cadre de modélisation des maladies infectieuses émergentes (MIE) des Centres pour le contrôle et la prévention des maladies (CDC), associé à la surveillance génomique, offre une approche robuste pour comprendre et atténuer ces épidémies. L'intégration de ces méthodes peut améliorer la prévision, la surveillance et les stratégies de riposte aux épidémies, en particulier dans les contextes aux ressources limitées. Cette revue vise à identifier les vulnérabilités systémiques et les lacunes des systèmes de santé dans la lutte contre la variole dans les PRFI, les possibilités de modélisation de la variole dans le cadre des MIE des CDC, et le rôle de l'épidémiologie génomique dans la surveillance de la variole, notamment en combinaison avec ce cadre. Nous avons utilisé une revue narrative et suivi une méthode structurée conçue pour recenser l'ensemble des interventions en matière de modélisation des MIE et de surveillance génomique liées à la variole. Les résultats de modélisations antérieures indiquaient que la transmission par contact étroit au sein des ménages et entre eux était peu susceptible d'entraîner un grand nombre de cas de variole de clade I. Des études modélisant l'impact de la vaccination et des adaptations des comportements sexuels sur les cas de variole ont montré que la baisse initiale du nombre de cas était probablement due à l'adaptation comportementale, mais que la vaccination a permis d'éviter un plus grand nombre de cas et a joué un rôle clé dans l'accélération du contrôle de l'épidémie. Des études ont révélé que la répartition géographique de la variole observée lors de l'épidémie au Nigéria suggérait l'existence possible d'un nouveau réservoir zoonotique étendu, mais l'animal réservoir demeure inconnu. L'intégration des données génomiques à la surveillance de la variole peut faciliter la détection précoce, l'identification du réservoir animal et orienter les interventions ciblées. Cette analyse a montré que les CDC ont exploité avec succès un système de surveillance des eaux usées pour le SARS-CoV-2 afin de détecter la variole et a conclu que l'intégration de la modélisation des maladies infectieuses émergentes (MIE) des CDC et de la surveillance génomique peut améliorer considérablement la gestion de la variole dans les pays à revenu faible et intermédiaire.

Mots-clés: Variole, infection émergente, modélisation, surveillance génomique, épidémies zoonotiques.

Introduction:

Mpox, previously known as monkeypox, is a viral illness caused by the monkeypox virus (MPXV), a species of the Poxviridae family, and genus Orthopoxvirus (same genus as the variola virus that causes smallpox and the vaccinia virus that causes cowpox) (1,2). While related to smallpox, Mpox presents with less severe symptoms and is not as easily transmissible. The virus was first identified in monkeys in 1958, leading to its original name. The first human case was recorded in 1970 in the Democratic Republic of the Congo (DRC). The virus has two main clades; Clade I and Clade II. Clade I is historically found in Central Africa and is associated with more severe disease and higher fatality rates than Clade II. Clade II, prevalent in West Africa, was responsible for the global outbreak that began in 2022. Since October, 2023, a large-scale Mpox outbreak has emerged in DRC, and in March, 2024, the first individuals with Mpox were reported outside the endemic areas of the country (3,4).

The recent global resurgence of Mpox underscores the need for robust public health responses and improved surveillance. Studies have shown that MPXV is mutating at an exceptional rate for a DNA virus and its global spread is concerning, making genomic surveillance a necessity (5). Genomic surveillance, which involves analyzing the virus's genetic material, is crucial for tracking its evolution and spread, enabling researchers to identify changes and

assess potential public health implications.

The 2024 Mpox outbreak in Africa prompted swift action, with the Africa Centres for Disease Control and Prevention (Africa CDC) and the World Health Organization (WHO) declaring it a public health emergency of continental security and international concern on August 13 and 14, 2024, respectively. Weak health systems, limited surveillance and diagnostic capabilities, and lack of access to vaccines have hindered control efforts, allowing the outbreak to persist. The situation is further complicated by the emergence of new cases in non-endemic countries, including Kenya, Morocco, Rwanda, and Uganda, as well as shifting transmission patterns (6).

The resurgence of Mpox, particularly in low-and-middle-income countries (LMICs) underscores the need for a comprehensive systems-level analysis. The Centres for Disease Control and Prevention's (CDC) Emerging Infectious Diseases (EID) modelling framework, combined with genomic surveillance, offers a robust approach to understanding and mitigating such outbreaks. Integrating these methods can enhance outbreak prediction, surveillance, and response strategies, particularly in resource-constrained settings (5,7–10). Therefore, this review aims to identify systemic vulnerabilities and health systems gaps in control of Mpox in LMICs, opportunities for modelling Mpox within the CDC EID framework, and the role of genomic epidemiology in Mpox surveillance, especially in combination with the EID framework.

Methodology:

A narrative review approach was employed to synthesize evidence from diverse sources on EID modelling framework and genomic surveillance for Mpox. The review followed a structured method designed to capture the range of interventions on emerging infectious disease modelling and genomic surveillance related to Mpox. Databases searched included PubMed, Lancet, ScienceDirect, Web of Science, Google Scholar and Scopus.

Search terms were formulated using Boolean operators to combine keywords. Only English-language studies were included, and there were no restrictions on publication date. Over 20 studies were reviewed following abstract/title and full text review, with evidence drawn across countries such as DRC, Burundi, Rwanda, Uganda, Kenya, Nigeria, China and the United States.

Mpox in LMICs: Systemic vulnerabilities and health systems gaps:

The LMICs face multifaceted challenges in managing Mpox outbreaks, including socio-economic disparities, limited healthcare infrastructure, and political instability. Humanitarian crises and conflict settings further exacerbate these vulnerabilities, hindering effective disease surveillance and response. Other public health challenges include vaccine inequity, surveillance

limitations, and stigma-related barriers to disease reporting and control as highlighted in Table 1 (6,11–14). Tackling these complex challenges demands a unified global effort that combines fair vaccine distribution, enhanced surveillance, stigma-free health education, and coordinated outbreak response strategies (15,16).

Modelling Mpox within the CDC EID framework:

The CDC's EID modelling framework provides tools to simulate disease transmission dynamics and assess intervention strategies. Applying this to Mpox involves understanding outbreak patterns, identifying surveillance triggers, and incorporating a 'One Health' perspective that considers human-animal-environment interactions (Fig 1). The epidemiological model framework for mpox has been established over the past few decades, and many models that capture human-human, and animal-human interactions have been explored (17).

Previous modelling results indicated that close-contact transmission within and between households were unlikely to result in a large number of Mox clade I cases. Household transmission clusters would most likely involve 10 or fewer Mpox clade I cases, with minimal spread between households (18,19). This has an implication on the relative importance of human-human transmission vis-à-vis animal-human transmission in the outbreak of Mpox.

Table 1: Health systems and other challenges faced by low-and-middle-income countries in controlling Mpox

Category	Challenges
Health systems	Fatigue in healthcare systems Inadequate resources Differential availability of vaccines and drugs Lack of adequate laboratory infrastructure and healthcare workers Weak disease surveillance systems Delayed response mechanisms Inadequate knowledge about mpox among health care workers
Political	Political instability and crisis Funding for WHO & member states, particularly for extensive needs in Africa
Sociocultural	Ethnic considerations Stigmatization
Socioeconomic	Low educational attainment Low-income households and size of households
Humanitarian crisis related	Mobility corridors Sites for displaced people Other mobile populations Cross-border communities
Miscellaneous	Nonspecific clinical features Diagnostic challenges Lack of knowledge about mpox among community members

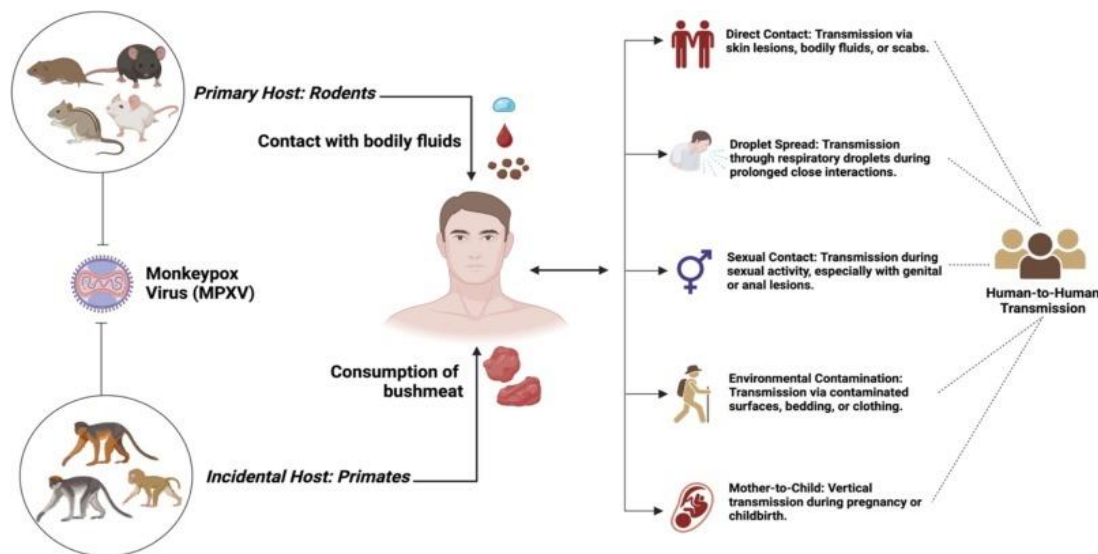


Fig 1: Interactions among human, animal reservoirs and environmental factors in Mpox transmission [Source: Verma et al.. (23)]

In addition, studies that modelled the impact of vaccination and sexual behaviour adaptations on Mpox cases in the USA during the 2022 outbreak found that initial declines in cases were likely caused by behavioural adaptation, but vaccination averted more cases overall and was key to hastening outbreak (20,21). A similar study in DRC informed the most efficient use of vaccines (22). These findings reinforce the role of modelling in identifying the most effective and also the most efficient interventions in the control of EIDs.

Role of genomic epidemiology in Mpox surveillance:

Genomic surveillance enables the identification of viral lineages, transmission chains, and mutation patterns. In LMICs, efforts like Nigeria's genomic sequencing initiatives have been pivotal in tracking diseases such as polio and Lassa fever. Studies revealed that the geographical pattern or Mpox reported in the Nigeria outbreak suggested a possible new and widespread zoonotic reservoir, but the animal reservoir remains unknown (24). Integrating genomic data into Mpox surveillance can facilitate early detection, identification of animal reservoir and inform targeted interventions. Furthermore, this is consistent with the 'One Health' approach which seeks to achieve a delicate balance between human, animal, and ecosystem health, acknowledging the intricate connections between the three domains.

Adopting a 'One Health' framework for disease surveillance, control, and prevention fosters a coordinated effort that brings together data from human, animal, and environmental health sectors, including pathogen genomics. This approach enables a comprehensive understanding of health outcomes and informs effective and efficient strategies for disease mitigation and prevention (25). This review found that CDC successfully leveraged a SARS-CoV-2 wastewater surveillance system for Mpox (26). Fig 2 is a flowchart depicting the integration of genomic data into surveillance systems.

Operationalizing a systems-based response:

Implementing a systems-based approach entails: (i) Community-based surveillance and mHealth tools: Leveraging mobile technology and community health workers to enhance real-time data collection and reporting(28); (ii) Workforce training and task-shifting: Empowering local healthcare providers through training and delegation of responsibilities to optimize response efforts (29); (iii) Data systems integration: Developing platforms that consolidate genomic and syndromic data for comprehensive analysis (25); and (iv) Cold chain and mobile labs: Innovations like mobile suitcase laboratories have been deployed in regions like the Democratic Republic of Congo (DRC) to facilitate rapid diagnostics (4).

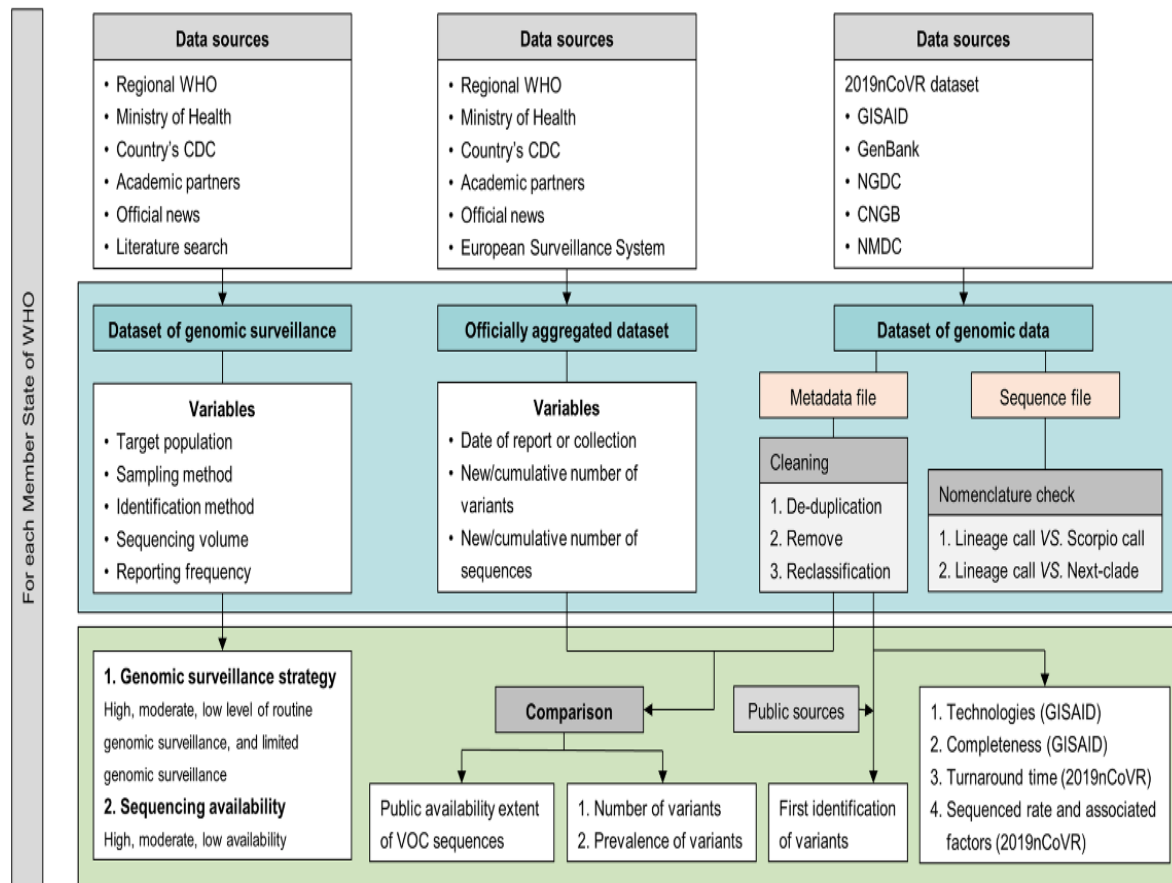


Fig 2: Flowchart depicting the integration of genomic data into surveillance systems [Source: Chen et al., (27)]

Recommendations for policy and practice:

These include investing in sequencing infrastructure and data governance to enhance local capacities for genomic analysis and establish protocols for data sharing and privacy; (ii) Embedding EID modelling into national preparedness plans with utilization of modelling tools to inform policy decisions and allocate resources effectively; (iii) Building regional data-sharing hubs and cross-border protocols to foster collaboration among neighboring countries to monitor and respond to outbreaks collectively; and (iv) Donor alignment and sustainability strategy with coordination of international funding to support long-term surveillance and response initiatives.

Conclusion:

Adopting a systems thinking approach that integrates CDC's EID modelling and genomic surveillance can significantly enhance Mpox management in LMICs. Such a multidisciplinary

strategy addresses the complexities of zoonotic outbreaks and strengthens global health security.

Contributions of authors:

AB conceptualized the project, performed literature search and reviewed the manuscript; AEA wrote the first draft and did literature search; DD did literature search and combined the searches of all the authors.

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AI use disclosure:

An initial outline of the introduction was generated with AI, after which the different sections of the review were beefed up independent of AI.

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