

82810\_Auto\_Edited.docx

**Name of Journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 82810

**Manuscript Type:** MINIREVIEWS

**Inequity in the global distribution of mpox vaccines**

Distribution of mpox vaccines

Marcos Roberto Tovani-Palone, Neel Doshi, Paolo Pedersini

## **Abstract**

Monkeypox (mpox) is a public health emergency of international concern that emerged in mid-2022 that has spread to 110 countries. The clinical findings of the disease vary according to the seriousness of the cases, and although its case fatality risk has not been high, a significant percentage of patients require hospitalization. In this context, local initiatives have been taken to extend the limited supply of mpox vaccines during the early outbreak period; however, such measures have not been sufficient to contain the spread of cases and ensure equity in the global distribution of the vaccines. As a result, endemic regions of low-income countries continue to have insufficient access to mpox vaccines. Despite this, there is little discussion in the literature about the difficulties in achieving adequate vaccination coverage rates for the target audience of mpox, considering the global scope of the disease. In this article, we briefly discuss general aspects of the disease, including its surveillance, the current global context of mpox vaccination, issues on global allocation of health resources, and propose related recommendations.

**Key Words: Monkeypox; Smallpox Vaccine; Health Inequities; Vaccination coverage; Vaccination hesitancy; Healthcare financing.**

Tovani-Palone MR, Doshi N, Pedersini P. Inequity in the global distribution of mpox vaccines. *World J Clin Cases* 2023; In press

**Core Tip:** The development and implementation of new global public health policies, to ensure in the short term greater equity in global health financing, may lead to positive impacts in the global distribution of mpox vaccines, while providing more safe and adequate management of both this outbreak and future pandemics.

## **INTRODUCTION**

### **Introduction**

Along with the ongoing coronavirus disease 2019 (COVID-19) pandemic, a recent public health threat has put the world on high alert, the global outbreak of monkeypox (mpox). According to World Health Organization (WHO) data, confirmed disease cases exceeded 86,000 in April 2023, with more than 110 deaths spread to 110 countries. Based on the WHO regions, the Americas and the European regions are the most affected, accounting for more than 90% of all cases. Furthermore, as an endemic disease in West and Central Africa, mpox is also expected to require more attention by governments and health authorities and special care in the current period <sup>[1]</sup>.

In an attempt to gain greater support, sufficient vaccine production, more equitable access by the population, and the implementation of medical countermeasures for coordinated global action to combat the spread of cases of the disease, the World Health Organization declared mpox a public health emergency of international concern (PHEIC) in July 2022 <sup>[2,3]</sup>. In light of this, local initiatives have been taken to extend the limited supply of vaccines during the early outbreak period. In this context, although dose-saving approaches have been implemented in some countries, such as the United States, this type of measure has not been sufficient to contain the spread of the disease <sup>[4]</sup> and ensure equity in the global distribution of vaccines. As a result, African countries in special have been having insufficient access to mpox vaccines [5,6].

Although the number of cases reported globally peaked in August 2022 [7], an uneven distribution of health resources, negating any equitable prospects, could threaten different regions of the world with significant limitations of such resources. Despite this, there is little discussion in the literature about the difficulties in achieving adequate vaccination coverage rates for the target audience of mpox, considering its global scope. Here, we briefly discuss general aspects of the disease, including its surveillance, the current global context of vaccination, issues on global allocation of health resources, and propose related recommendations.

## **Etiology and spread of mpox**

Mpox is a zoonotic viral infection caused by the mpox virus (MPXV) whose affected patients present with different symptoms and complications, which can lead to death in severe cases. Characteristically a rash similar to that of smallpox may be observed [5]. On the other hand, its transmission and case fatality rates have been substantially lower when compared to smallpox infection [1]. MPXV corresponds to an orthopoxvirus with a double-stranded deoxyribonucleic acid (DNA) virus, belonging to the same genus as the variola, vaccinia, and cowpox viruses [5]. During the outbreak in 2022, a new lineage and also sub-lineages of the virus were identified. In this context, the lineage B.1, classified as clade IIb for its close relationship to clade II, has been predominant in the worldwide spread of mpox [8,9]. Although this suggests that the current outbreak has a major infection source [9], knowing how such variants may affect transmissibility, virulence and human adaptation remains a challenge.

## **Transmission routes, diagnosis and clinical course of mpox**

Among the transmission routes of mpox, the most common include skin-to-skin and sexual contacts [2]. Similar to coronavirus disease 2019 (COVID-19), its diagnosis is mainly made by polymerase chain reaction (PCR), using lesion swabs or body fluids [5,10]. Different studies report incubation periods for mpox virus ranging from 7 to 10 days, with the majority of affected patients having systemic disease, of which approximately 40% progress to complications. Although related mortality rates are less than 1%, about 1 to 13% of cases may require hospitalization, which is expected to burden health systems significantly [5,11]. Figure 1 illustrates a proposed general mechanism for the transmission cycle and clinical manifestations of mpox in humans.

Figure 1. Basic mechanism related to mpox in humans.

LS: lymphatic system.

Source: Adapted from [2,5,11].

### Surveillance, case investigation and contact tracing

According to the latest WHO recommendations published in 2022, the following actions of response to the multi-country outbreak of mpox should be prioritized and implemented: providing accurate information to people who may be at increased risk of simianpox virus infection, ensuring access to pre- and post-exposure mpox vaccination for at-risk populations, preventing the spread of the virus, as well as protecting vulnerable individuals and frontline healthcare workers. In this context, it is imminent that doctors working in private or public settings and hospital surveillance services <sup>1</sup> report suspected cases immediately to local and national public health authorities and, as soon as possible to the WHO. In suspected cases of the disease, the <sup>5</sup> case investigation should consist of a clinical examination of the patient in a well-ventilated room, using appropriate personal protective equipment. Patients should be questioned about possible sources of exposure and safe specimen collection should be obtained and forwarded to laboratories [7].

<sup>1</sup> As soon as a suspected case is identified, identification and tracing of all possible <sup>1</sup> contacts should be initiated. Contacts of probable and confirmed cases must be monitored or self-monitored daily for any signs or symptoms for a period of 21 days from the last contact with confirmed cases or contaminated materials during the infectious period. However, in the absence of symptoms, quarantine or exclusion from work is not required during the contact monitoring period, which differs from the recommendations for surveillance of COVID-19. During the monitoring, contacts without symptoms <sup>3</sup> are encouraged to practice hand hygiene and respiratory etiquette and avoid contact with children, immunocompromised people, or pregnant women.

Known contacts are also advised to avoid sexual contact with others during the monitoring period. This is because the evidence on the possible transmission of MPXV before the onset of symptoms continues to be reviewed. Therefore, regardless of whether or not symptoms are present, this recommendation is strongly encouraged to be followed. It is also worth noting that non-essential travel is discouraged [7].

### **Current context of mpox vaccination**

In the current context of the global mpox outbreak, the non-replicating modified vaccinia Ankara (MVA) has been one of the most used for both post-exposure prophylaxis and pre-exposure prophylaxis for people at high risk for mpox. Such a vaccine is commonly administered subcutaneously in two doses, with a 4-week interval between doses. However, given the shortage of vaccine supplies, different countries have authorized the intradermal administration of a single dose for adults. Thus, the extent of vaccine coverage for larger populations could be expected. In this case, only one-fifth of the volume of the subcutaneous route is needed [5]. Recent research conducted by Bertran *et al* demonstrated that a single dose of the attenuated MVA-Bavaria Nordic smallpox vaccine is highly protective against symptomatic mpox disease, making it a useful tool for controlling outbreaks of the disease when rapid protection is required [12]. Moreover, using the intradermal route may increase immunogenicity and induce similar antibody responses to the subcutaneous route [5].

The main target audience for mpox vaccination in newly affected countries has been homosexual, bisexual, and others who are at the highest risk of contracting mpox. Health professionals and people who have had contact with infected people have also been included due to the possibility of medium and high risks of exposure to infection. However, despite worldwide concern about mpox vaccination for vulnerable populations, appropriate access to antiviral treatment and vaccines remain an obstacle to be overcome by different endemic countries [5,6]. Even with strong recommendations

<sup>1</sup> from GAVI, the Vaccine Alliance, the Global Fund to Fight AIDS, Tuberculosis and Malaria, for the need to increase the coverage of mpox vaccines on a global scale, their administration has been made available especially to populations in North America and Europe, with a strong limitation of supplies to low-income countries [5].

<sup>2</sup> Although the outbreak has subsided in countries such as the United Kingdom and the United States due to the deployment of vaccines and therapies, in addition to changes in awareness and social behavior, the same has not been confirmed for countries in West and Central Africa. According to the only announcement made in 2022 by the African Centers for Disease Control and Prevention, the African Union should receive by then a donation of only 50,000 doses from South Korea. If, on the one hand, these vaccines may be the first on the continent not designated for research purposes, on the other hand, such amount is too small for the target public of mpox vaccination campaigns across the continent [6]. In addition to the shortage of vaccines, a delay in African countries' access to tecovirimat, an antiviral authorized for emergency use in the treatment of severe mpox [13], has been reported [6]. It is evident therefore that Africa still lacks adequate access to vaccination and antiviral treatment [5,6], which is essential for patients with severe manifestations and people at risk of serious disease [5].

This is not much unlike what happened during the COVID-19 pandemic, when the African continent, in particular, received low and late numbers of COVID-19 vaccines [14], in addition to having faced a possible underreporting of cases [15]. The existence of inequity in the global distribution of mpox vaccines and possible underreporting [6], together with the increase in vaccine hesitancy since the beginning of the pandemic [16] and the resurgence of other previously eradicated infectious diseases [17,18], should call for swift and urgent action. Although mass vaccination of the population is neither required nor recommended for mpox, efforts to contain this global outbreak must be mainly focused on ensuring equitable vaccine distribution, with a concern also aimed at



low- and middle-income countries. In light of this, other urgent measures must be taken, including massive global support to enable affected countries to respond equitably and effectively to the outbreak, including increased funding for mpox screening centers. This action is expected to strengthen the disease surveillance and contribute towards access to adequate treatment and preventive health services. Moreover, controlling the spread of mpox through broad and efficient measures involving a variety of specific measures (Table 1) is also essential.

Table 1. Other key points to contain the spread of mpox.

1. Massive fight against misinformation
2. Strong information campaign strategy
3. Support from global health agencies
4. Effective collaboration with local laboratories, hospitals and Universities
5. Commitment of Ministries of Health of affected countries and partners
6. Implementing genome surveillance
7. Standardized and robust pharmacovigilance
8. Collaborative efficacy studies of vaccines with standardized protocols and data collection tools

Source: Adapted from [2,4,9].

### **Importance of global allocation of health resources amidst the mpox outbreak**

A further important point in this connection is the lack of equity in the global allocation of health resources, which may prevent implementing many relevant actions in low and middle-income countries. The conclusions of the study by Micah *et al* demonstrate that, on the one hand, global health expenditures continue to grow, while, on the other hand, it remains unequally distributed around the world [19].

As a result of this problem, a much worse situation for mpox may be expected in several countries beyond what has been reported, especially in low-income countries. This is due to the potential for underreporting of cases, which may be related, among other factors, to the occurrence of the disease in rural areas [20] in addition to the scarcity of health resources. This context, added to the persistent weaknesses of many health systems, should generate additional limitations, strongly impacting the capacity of surveillance systems and the implementation of effective vaccination programs. In order to improve this situation, a more planned allocation of financial resources to implement new <sup>6</sup> interventive measures and surveillance programs, especially using cheap and quick strategies such as wastewater monitoring the DNA of MPXV [9], may be required.

As mentioned earlier, it is also true that <sup>2</sup> contrary to what has happened in developed regions of the world, adequate supplies of vaccines and treatments against mpox have not materialized in Africa. Likewise, the knowledge gained about the virus has done little to change the course of the outbreak on the continent. Therefore, if, on the one hand, there has been an increase in world attention focused on MPXV in the context of the current outbreak, the resulting benefits have been restricted, at first, only to developed countries. Not unlike that, most research on this topic has been published by researchers based in high-income countries [6], which, importantly, implies the need for more investments and better targeted funding towards robust and globalized scientific advances aimed at the proper management of the disease and the control of its spread.

Furthermore, even though many uncertainties remain about proven therapies and comparative data on safety and efficacy related to the treatment of affected individuals, this should be yet another viable opportunity for financing the development of predesigned adaptive trial protocols, which may enable faster discovery of effective drugs against viruses with pandemic potential [21].

## **CONCLUSION**

### **Final consideration**

In light of the current situation, the WHO, together with other international alliances, could play a key role in the development and implementation of global public health policies to ensure, in the short term, greater equity in global health funding, which should positively impact the global distribution of mpox vaccines as well as provide more appropriate management of this outbreak and future pandemics. Only after building better health systems will it be possible to control this and other imminent global emergencies satisfactorily and move closer to meeting the related Sustainable Development Goals <sup>[22]</sup>.

## **ACKNOWLEDGEMENTS**

We thank the Italian Ministry of Health-Ricerca Corrente 2023 and Saveetha Institute of Medical and Technical Sciences for supporting this study.

# 9%

SIMILARITY INDEX

### PRIMARY SOURCES

- |          |                                                                                                                                                                                                                                                                          |                      |
|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|
| <b>1</b> | <a href="https://reliefweb.int">reliefweb.int</a><br><small>Internet</small>                                                                                                                                                                                             | 75 words — <b>3%</b> |
| <hr/>    |                                                                                                                                                                                                                                                                          |                      |
| <b>2</b> | Max Kozlov. "WHO may soon end mpox emergency — but outbreaks rage in Africa", Nature, 2023<br><small>Crossref</small>                                                                                                                                                    | 45 words — <b>2%</b> |
| <hr/>    |                                                                                                                                                                                                                                                                          |                      |
| <b>3</b> | <a href="https://www.mdpi.com">www.mdpi.com</a><br><small>Internet</small>                                                                                                                                                                                               | 34 words — <b>1%</b> |
| <hr/>    |                                                                                                                                                                                                                                                                          |                      |
| <b>4</b> | Oriol Mitjà, Dimie Ogoina, Boghuma K Titanji, Cristina Galvan, Jean-Jacques Muyembe, Michael Marks, Chloe M Orkin. "Monkeypox", The Lancet, 2023<br><small>Crossref</small>                                                                                              | 29 words — <b>1%</b> |
| <hr/>    |                                                                                                                                                                                                                                                                          |                      |
| <b>5</b> | <a href="https://www.iss.it">www.iss.it</a><br><small>Internet</small>                                                                                                                                                                                                   | 20 words — <b>1%</b> |
| <hr/>    |                                                                                                                                                                                                                                                                          |                      |
| <b>6</b> | <a href="https://www.ncbi.nlm.nih.gov">www.ncbi.nlm.nih.gov</a><br><small>Internet</small>                                                                                                                                                                               | 19 words — <b>1%</b> |
| <hr/>    |                                                                                                                                                                                                                                                                          |                      |
| <b>7</b> | Zhe Zhou, Mengqiao Li, Yuxin Zhang, Lingchen Kong et al. "Fe-Fe Double-Atom Catalysts for Murine Coronavirus Disinfection: Nonradical Activation of Peroxides and Mechanisms of Virus Inactivation", Environmental Science & Technology, 2023<br><small>Crossref</small> | 17 words — <b>1%</b> |

---

EXCLUDE QUOTES	ON	EXCLUDE SOURCES	< 12 WORDS
EXCLUDE BIBLIOGRAPHY	ON	EXCLUDE MATCHES	< 12 WORDS