

# From Endemic to a Global Concern Once Again: A Review of Evolving Monkeypox Dynamics

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## ABSTRACT

The World Health Organization (WHO) declared the ongoing Mpox (formerly known as Monkeypox) outbreak a Public Health Emergency of International Concern (PHEIC) on 14th August 2024, this being the second time, with Mpox previously being declared a PHEIC during the 2022-2023 outbreak. Mpox is a zoonotic orthopoxvirus with a similar clinical presentation to smallpox but a notably lower mortality rate. Before the 2022 outbreak, Mpox was a rare and neglected disease, which has now drawn global attention once the cases started emerging in countries outside Africa. The WHO has stressed the importance of a coordinated response on the international front to control and contain the Mpox outbreaks in the DRC and neighboring countries in Africa. Through this narrative review, the authors aim to consolidate evidence on the Mpox virus, characteristics of its infection, treatment and prevention strategies, a review of past and current Mpox outbreaks, challenges in containing the spread of the epidemic including access to vaccines in low-income nations and vulnerable populations, and any relevant learnings from the COVID-19 pandemic that could be implemented.

**Keywords:** Monkey Pox. Mpox, Outbreak, Transmission, Endemic, Virus, Infection.

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## INTRODUCTION

The World Health Organization (WHO) declared the ongoing Mpox (formerly known as the Monkeypox virus) outbreak a Public Health Emergency of International Concern (PHEIC) on 14th August 2024, this being the second time, with Mpox previously being declared a PHEIC during the 2022-2023 outbreak<sup>1,2</sup>. Mpox was a rare and neglected disease before the 2022 outbreak. Since the beginning of 2022, the WHO has reported 99,176 Mpox cases and 208 deaths across 116 countries<sup>3</sup>. The 2022 outbreak

primarily affected non-endemic countries, with over 90% of cases identified among Men who have sex with men (MSM)<sup>4</sup>. In 2024, Mpox has again drawn global attention, with the Democratic Republic of the Congo (DRC) at the center of a new outbreak, marked by the emergence of the Clade 1b strain and a rapid spread across countries outside Africa. In 2025, DRC continues to be the most affected country, experiencing an outbreak involving both Clade 1a and Clade 1b MPXV strains<sup>5</sup>. A narrative review was conducted to synthesize evidence on

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the Mpox virus, characteristics of its infection, treatment and prevention strategies, a review of past and current Mpox outbreaks, challenges in containing the spread of the epidemic, including access to vaccines in low-income nations, the way forward, and any learnings from the COVID-19 pandemic that can potentially be implemented.

## DISCUSSION

Clinical Overview and Treatment of the Mpox Virus and Its Infection Mpox is a double-stranded DNA virus belonging to the Orthopoxvirus genus of the poxviridae family<sup>6</sup>. It can be divided into 2 genetic Clades: Clade 1 being more prevalent in Central Africa with greater mortality rates, and Clade 2 being more prevalent in West Africa with a lesser mortality rate.<sup>6</sup> Given the intracytoplasmic nature of replication, Mpox evades host cell immunity via multiple immunomodulatory mechanisms<sup>7</sup>.

Apart from the well-documented animal-to-human transmission, Mpox transmission via

human-to-human contact can spread via multiple sources of transmission due to the presence of Mpox in most of the body fluids, ranging from semen to respiratory droplets, including transmission via sexual intercourse<sup>8,9,10</sup>. With an incubation period of 7-17 days, Mpox typically presents with fever, malaise, sore throat, headaches, and a centrifugal, umbilicated rash accompanied by lymphadenopathy<sup>11</sup>.

As is the case with most viruses, supportive management is the mainstay of treatment. There is currently no approved therapeutic drug for Mpox. However, antiviral drugs such as Oral Tecovirimat (TPOXX), cidofovir, and brincidofovir, which are US Food and Drug Administration (FDA)-approved drugs for smallpox, are currently the subject of clinical trials for the treatment of Mpox<sup>12, 13</sup>. Hence, much of the current focus is towards vaccination with the administration of JYNNEOS and ACAM2000 vaccines, which have been previously used against smallpox, are FDA-approved for use against Mpox<sup>14</sup>.

**Table 1: Timeline of the Mpox Occurrence 1958-2024**

Year	Events
1958	Mpox was detected in a colony of research monkeys, with the original host unknown.
1970	The first human infection was detected in DRC, which was a 9-month-old in Basankusu County. This area had a high monkey population, but no sick monkeys were identified.
1980	Smallpox, caused by the Variola virus, was eradicated. Both Variola and Monkeypox Viruses are orthopoxvirus genus. One major difference between these viruses is their host.
2003	The first case was detected outside of Africa- due to the introduction from prairie dogs, which were infected by imported small mammals from Ghana. 47 cases were detected in the US.
2017	Nigeria had an outbreak of the clade 2 virus. Cases surged among children and young adults, with 198 suspected cases. The animal host and nature of spread are not well classified.
2022	Clade 2 infection spread around the globe. Clade 2 is less severe than Clade 1. Clade 2 is still circulating globally today.
2023	Clade 1 spread across Africa, and in 2024, both the WHO and the African CDC reported a Global Emergency over the outbreak as cases of Clade 1 continued to rise.
2024	An imported case of Clade 1 was detected in Sweden. This is the first time Clade 1 was seen outside of Africa- and has not spread. It was determined to be Clade 1b.

Adapted from: Bacterial and Viral Bioinformatics Resource Center (BV-BRC) <https://www.bv-brc.org/><sup>22</sup>

## Previous Outbreaks and Current Outbreaks of the Mpox Virus

The first case of Mpox infection was reported in 1970 in the DRC in a male child who was not vaccinated for smallpox<sup>15</sup>. Between 1981 and 2017, Clade 1 of the Mpox virus caused several outbreaks in the DRC, with fatality rates of 1-12%. After 1970, Mpox has occurred sporadically in Central and East Africa (Clade I) and West Africa (Clade II)<sup>16</sup>. In 2003, an outbreak in the United States of America (USA), known as the "2003 Midwest Mpox outbreak," was linked to the importation of wild animals (Clade II)<sup>17</sup>. Between 2003 and 2022, non-endemic regions in Europe, North America, and Asia reported a few travel-related cases.<sup>18,19,20</sup> In May 2022, an outbreak emerged and spread rapidly across Europe, the Americas, and eventually all six WHO regions, with 110 countries reporting around 87,000 cases and 112 deaths. This was followed by the WHO declaring Mpox as PHEIC on July 23, 2022, which ended in May 2023<sup>21</sup>. Since 2023, sporadic cases of Mpox infections have continued to be reported. The timeline of Mpox occurrence is as shown in **Table 1**.

In 2024, the DRC emerged as the epicenter of a new outbreak, reporting the prevalence of the Clade 1b strain. On August 14, 2024, the WHO declared Mpox a PHEIC, following a further declaration by the Africa CDC on August 13, 2024, designating it as a Public Health Emergency of Continental Security (PHECS)<sup>23</sup>. On August 16, 2024, the Africa CDC reported 18,737 Mpox cases (3,101 confirmed and 15,636 suspected) across 12 African countries since the beginning of the year, resulting in 541 deaths<sup>24</sup>. Around 95% (17,794) of the reported cases and 99% (535) of the deaths in 2024 were reported from the DRC, primarily due to the more severe and transmissible Clade 1b strain<sup>24</sup>.

So far in this outbreak, eleven countries outside Africa had reported Mpox cases<sup>5</sup>. Within Africa, 20 countries had reported cases since January 2024. As of January 2025, there have been a total of 14,700 cases of Mpox in Africa, including 66 deaths. Unlike the 2022 Mpox outbreak, the ongoing 2024 outbreak involving the Clade I strain has a higher mortality rate, but there is limited evidence to support this claim<sup>25</sup>. Moreover, unlike Clade II, which was predominantly seen in MSM, this current strain has affected a broader demographic of heterosexual men, women, and even children<sup>25</sup>. In the DRC, which remains the most affected country by Mpox, children under 15 years old account for 66% of the cases and more than 82% of the deaths<sup>26</sup>. Evidence shows that the smallpox vaccine is 80.7% effective in preventing human Mpox, and the immunity provided by prior smallpox vaccination is long-lasting<sup>27</sup>. However, low immunity to the disease and the prevalence of malnutrition could increase the risk of infection, especially among children<sup>28</sup>. Displaced people in refugee camps in eastern DRC are also at a higher risk, potentially due to overcrowding and inadequate sanitation, and also healthcare workers, especially in areas with limited access to personal protective equipment<sup>29</sup>.

### Travel-Associated Mpox and Its Implications for Pakistan

Imported travel-related cases of Mpox have been detected in eleven countries outside of Africa, including Sweden, Thailand, India, Germany, the United Kingdom of Great Britain and Northern Ireland, the United States of America, Canada, Pakistan, Belgium, China, and France<sup>5</sup>. Secondary transmission from these cases has been reported in six of these countries<sup>5</sup>. The recent spread of travel-associated Mpox serves as an important reminder for countries to tailor their prevention and containment strategies for Mpox according to the geographic source of cases to effectively break the chain of transmission. This also underscores an important public health concern given the high volume of labor migration between Countries like Pakistan and the Gulf states. Pakistan is one of the largest contributors of labor to the Gulf Cooperation Council (GCC) countries, with millions of Pakistani workers residing in countries such as Saudi Arabia, the United Arab Emirates, and Qatar, which is important for the backbone of Pakistan's economy<sup>30</sup>. The first case of Mpox in Pakistan was reported in a traveler returning from Saudi Arabia in April 2023. Since then, a total of eleven cases and one death have been reported, with the most recent case being documented in September 2024<sup>31</sup>. Although no new cases of Mpox have been reported in Pakistan since September 2024, the recent emergence of 5 cases of a new mutated strain of Mpox in China in January 2025 reiterates the need for strengthening surveillance systems in Pakistan, especially at airports, which serve as a breeding ground for emerging communicable diseases<sup>32,33</sup>. These include mandatory testing before flight, mandatory health screenings at the airports, as well as imposing travel restrictions on suspected cases to contain the spread of the virus.

### Lessons from the COVID-19 Pandemic and Potential Challenges to Contain the Mpox Outbreak

The COVID-19 pandemic revealed vulnerabilities in healthcare systems worldwide and the imperative need to improve epidemic and pandemic preparedness, lessons that are highly pertinent to the current Mpox situation. While HICs demonstrated effective containment strategies owing to their well-established healthcare infrastructure, LMICs such as Pakistan faced several challenges in containing the COVID-19 pandemic (Table 2)<sup>34</sup>. Moreover, the stigma surrounding Mpox due to its association with MSM shares several parallels with the AIDS crisis of the 1980s-90s in the United States, the effects of which are felt to date. Both health crises were met with delayed action by government and public health officials, reflecting deep-rooted inequities in access to healthcare even in HICs. Thus, the aftermath of COVID-19 and the ongoing stigma surrounding Mpox highlight the need for collaboration among government, healthcare professionals, and high-risk groups, including the LGBTQ+ community, to ensure that vulnerable groups are prioritized and that culturally sensitive prevention strategies remain central to public health efforts.

This may be particularly challenging in many Asian and Middle-Eastern countries where LGBTQ+ communities have been historically marginalized, and matters of their healthcare become a concern for their safety. A cross-sectional study conducted from 2019 to 2021 in Pakistan to explore the quality of life of transgender

individuals and MSM living with HIV found that most participants reported being treated worse than their cisgender counterparts at healthcare centers. Among them, 20 % reported being denied hospital admission due to discrimination based on their gender identity (**Table 2**)<sup>35</sup>. Similarly, beyond the challenges in access to healthcare, an in-person audit study from Pakistan where transgender actors and cisgender male actors were recruited and visited private clinics found no overtly discriminating practices, suggesting that the difference in treatment may stem from unfamiliarity with gender-sensitive care as healthcare providers receive no formal training in it in Pakistan<sup>35</sup>.

**Table 2: Challenges in Containing Mpox Outbreaks**

Challenges	Description
Healthcare infrastructure <sup>34</sup>	LMICs (e.g., Pakistan) face limited healthcare capacity
Discrimination and Stigma <sup>35</sup>	Association with MSM communities effectively limits public health response
The High-risk behavior and Chemsex <sup>36,37,38</sup>	MSM populations exhibit a higher transmission risk
Vaccine Hesitancy <sup>39,40</sup>	Resistance due to anti-vaccine movements
Limited vaccine access <sup>41, 42</sup>	High rates of inequitable distribution in Africa

**Abbreviations:** LMICs: Low- and middle-income countries; MSM: Men who have sex with men.

Furthermore, the use of psychoactive and disinhibiting recreational drugs during sex commonly known as chemsex has seen a rise in popularity during the last decade, with a higher prevalence seen in the MSM population (**Table 2**)<sup>36</sup>. Chemsex has been associated with an increased risk of high-risk sexual behaviors such as condom-less sex, multiple sex partners, and a higher risk of STI transmission, all of which could potentially increase the risk of Mpox transmission. A prevalence of 20% of chemsex use was seen among 528 Mpox cases across 16 countries between April-June 2022<sup>37,38</sup>.

Unlike the COVID-19 pandemic, where the initial lack of a vaccine hampered early response, the current Mpox situation benefits from the availability of an FDA-approved vaccine previously used for smallpox. The CDC guidelines recommend the JYNNEOS vaccine for Mpox, which requires two doses administered four weeks apart<sup>14</sup>. However, having a vaccine on its own is insufficient; effective distribution and administration are crucial. This is challenging in the case of Mpox due to the growing anti-vaccine movements, as seen during COVID-19, where vaccine hesitancy among the public became an important obstacle in achieving herd immunity (**Table 2**)<sup>39</sup>. Vaccine hesitancy continues to be a challenge for Mpox too, as demonstrated by a cross-sectional study in China, which found that the rate of Mpox vaccination hesitancy among MSM was 5.59%, with lower odds of vaccine hesitancy seen among people with higher knowledge about Mpox<sup>40</sup>.

The WHO had emphasized that containment of the Mpox outbreaks in DRC and neighboring countries in Africa is still a possibility, but requires a coordinated response on the international front, such that resources can be mobilized effectively to ensure equitable access to the vaccine (**Table 2**)<sup>41, 42</sup>. Based on learnings from previous outbreaks and pandemics, it is important to prioritize rapid identification and isolation of cases, targeted vaccination of high-risk groups and contacts, mass-level promotion of prevention strategies, and enhancing public communication to build trust and compliance towards prevention measures, including the vaccines.

**CONCLUSION**

The Mpox virus, with its evolving epidemiology and transmission pattern, is no longer a rare, self-limiting disease restricted to endemic regions of the World. The 2024 Mpox outbreak has once again caused global alarm, therefore, taking the learnings from previous outbreaks, having an enhanced surveillance system, timely investigation of cases and contacts, and wide access to treatment and prevention modalities to populations including those highly marginalized, are crucial in taking off pressure from the already strained public health infrastructure globally to contain the spread of this outbreak.

**LIST OF ABBREVIATIONS**

**WHO:** World Health Organization  
**PHEIC:** Public Health Emergency of International Concern  
**MSM:** Men who have sex with men  
**DRC:** Democratic Republic of the Congo  
**TPOXX:** Tecovirimat  
**BV-BRC:** Bacterial and Viral Bioinformatics Resource Center  
**PHECS:** Public Health Emergency of Continental Security  
**GCC:** Gulf Cooperation Council

**CONFLICT OF INTEREST**

None

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OI was involved in the study concept/ design. OI, MAQ, AA, MAQ, and SFM were involved in data collection, data analysis/ interpretation, and writing of the paper. MAQ and SFM were involved in the critical revision of the article.

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