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INTERSECTING PANDEMICS: ANALYZING THE RELATIONSHIP BETWEEN MPOX AND COVID-19

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Abstract

The re-emergence of the mpox (formerly known as monkey pox) virus following the COVID-19 pandemic poses significant challenges to global public health. This review examines the epidemiological trends of mpox, highlighting a marked increase in post-COVID-19 cases. Key issues, including stigma, misinformation, and public awareness, hinder effective control measures, as affected populations may be reluctant to seek testing and treatment. Access to healthcare remains a critical concern, particularly in resource-limited settings, where inadequate infrastructure complicates outbreak response and surveillance efforts.

Advancements in diagnostic technologies and vaccination campaigns, initially developed in response to COVID-19, have proven instrumental in addressing the mpox outbreak. Polymerase chain reaction remains the gold standard for accurate diagnosis, while innovations in point-of-care testing and genomic sequencing offer opportunities for enhanced surveillance and response. Vaccination strategies, including the use of JYNNEOS and ACAM2000 vaccines, have shown promise, yet challenges persist, including public hesitancy, misinformation, and logistical barriers to equitable distribution, particularly in resource-limited settings.

Vaccination plays a pivotal role in managing mpox outbreaks; however, challenges related to vaccine distribution and public hesitancy must be addressed to ensure effective coverage. The review also explores advancements in diagnostic methods developed after COVID-19, emphasizing their importance for timely case identification. It acknowledges persistent barriers to accurate reporting and highlights the necessity of ongoing research to improve mpox preparedness and response, as well as to enhance health infrastructure and international collaboration strategies. Recommendations include increasing public awareness, engaging communities in vaccination efforts, and fostering global partnerships to combat the spread of mpox and other infectious diseases.

Keywords: *mpox, COVID-19, infectious diseases, epidemiology, vaccination, diagnostics, global health, surveillance systems, public health response, stigma, misinformation, outbreak management, pandemic preparedness, healthcare infrastructure.*

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Introduction

Monkeypox (Mpox) Virus: Mpox has historically been limited to endemic regions in Africa, but in recent years, there have been increasing reports of cases in non-endemic countries. This shift in geographical distribution has raised concerns about the potential for more widespread transmission and the global risk associated with zoonotic infections. The largest outbreak outside Africa occurred in 2003 in the United States, linked to the importation of infected animals. More recently, there was a significant outbreak in 2022, with cases reported in several countries across Europe, North America, and other regions. Immunocompromised individuals are at a higher risk of mpox virus (MPXV) infection and are more likely to develop severe disease. This underscores the critical role of immune competence in controlling and clearing MPXV infections. Previous studies, including our own, have highlighted similarities between MPXV and other Poxviridae family viruses in their impact on the immune system [*Saghazadeh A, Rezaei N, 2023*].

Monkeypox Virus History and Previous Outbreaks: Mpox is a viral zoonotic disease caused by the mpox virus. Mpox virus and variola virus belong to the same family, and variola virus is responsible for causing smallpox. The mpox disease was first identified in 1958 when two outbreaks occurred in colonies of monkeys kept for research purposes, hence the name “monkey pox”. The first human case was reported in the Democratic Republic of Congo in 1970. Since then, sporadic outbreaks have been reported primarily in Central and West African countries, particularly in regions with close interactions between humans and wildlife [*Billioux B J et al., 2022*].

Structure and Characteristics of the Mpox Virus: The mpox virus is an enveloped, double-stranded DNA virus that belongs to the Orthopoxvirus genus within the Poxviridae family, mpox diagram shown in fig. 1 flow diagram with image of mpox. It shares structural similarities with other orthopoxviruses, including the variola virus, which causes smallpox, and the vaccinia virus, which is used in the smallpox vaccine. The virus has a complex structure with a brick-shaped appearance, and its genome encodes multiple proteins responsible for viral replication, host immune evasion, and pathogenicity. Due to its genetic similarity to the variola virus, the smallpox vaccine has shown some efficacy against mpox [*Rabaan A A et al., 2023*].

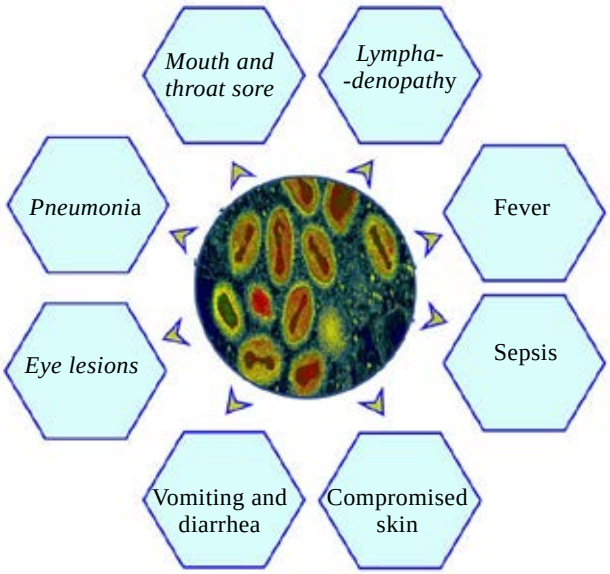

Figure 1. *Multi-organ system involvement of mpox with diagram of mpox* [*Rabaan A A et al., 2023*]

Transmission Modes and Incubation Period: Mpox is primarily a zoonotic disease, meaning it is transmitted from animals to humans. The virus can spread through direct contact with the blood, bodily fluids, or skin lesions of infected animals. Human-to-human transmission can occur through respiratory droplets, close physical contact, or contact with contaminated objects, such as bedding or clothes. Fig. 2 illustrates the mechanisms used by the pathogenic virus to infect and incubate. The incubation period for Mpox typically ranges from 5 to 21 days, with symptoms appearing on average within 6 to 13 days after exposure [*Zinnah M A et al., 2024*].

Comparison of Mpox Virus with Other Orthopox viruses (e.g., Smallpox): Mpox and smallpox share many clinical features, including fever, headache, muscle aches, and a characteristic rash. However, Mpox is generally less severe than smallpox, with a lower mortality rate. Smallpox had a case fatality rate of approximately 30%, while Mpox has a reported case fatality rate ranging from 1% to 10%, depending on the virus strain and the availability of medical care. Unlike smallpox, which was eradicated globally in 1980 through vaccination, Mpox continues to persist in certain regions, primarily due to its zoonotic nature and the lack of widespread vaccination efforts [*Bhardwaj P et al., 2024*].

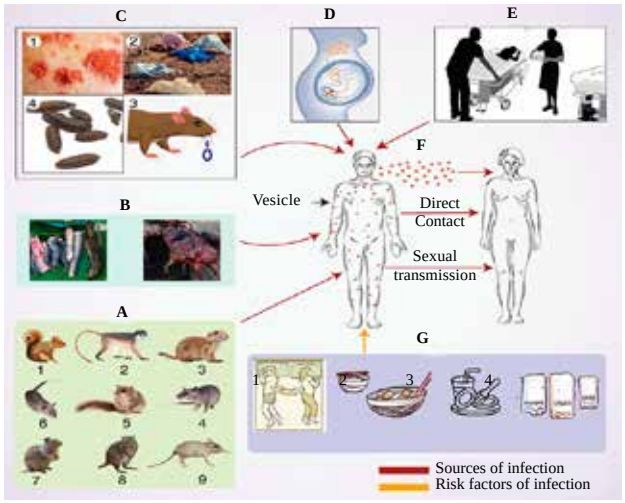

FIGURE 2. *Spread of mpox. (A) Schematic diagram illustrating various modes of mpox transmission. Numbers represent different animal species: 1. rope squirrel, 2. sooty mangabey, 3. prairie dog, 4. gambian pouched rat, 5. African dormice rodent, 6. African giant pouched rat, 7. sun squirrel, 8. rufous-nosed rat, 9. elephant shrew. (B) Bush meat as a source of infection. (C) Transmission through 1. skin crusts, 2. materials used by infected individuals, 3. contaminated saliva, and 4. fecal matter. (D) Transmission via the placenta. (E) Infections acquired in healthcare settings. (F) Spread through respiratory droplets and direct physical contact. (G) Shared usage of contaminated items: 1. beds, 2. food, 3. drinking glasses and utensils, and 4. towels [Zinnah M A et al., 2024].*

Outbreaks and Geographical Distribution: Mpox was first identified in humans in the Democratic Republic of Congo in 1970, during a period when global efforts to eradicate smallpox were at their peak. Since then, the disease has been primarily reported in Central and West African countries, including the Democratic Republic of Congo, Nigeria, and Cameroon. The virus is thought to be maintained in nature through a reservoir host, with rodents being the most likely candidates. Human infections have typically occurred in areas where close contact between humans and wildlife is common, particularly through hunting and handling infected animals.

The most significant outbreak outside Africa occurred in the United States in 2003, resulting from the importation of infected rodents from Ghana. This incident highlighted the potential for mpox to spread beyond endemic regions, especially through the global trade of exotic animals. The recent outbreak in 2022 demonstrated a shift in the epidemiology of mpox. Figure 3 illustrates the top 10 most affected nations globally, where The United States of America (n = 29,860), Brazil (n = 10,709), Spain (n = 7518), France (n = 4114), Colombia (n = 4066), the United Kingdom (n = 3735), Peru (n = 3723), Mexico (n = 3696), Germany (n = 3690), and Canada (n = 1460). The epidemiology of mpox shows widespread transmission in non-endemic countries, suggesting changes in the virus's transmission dynamics or increased human susceptibility.

BRIEF OVERVIEW OF COVID-19

The COVID-19 pandemic and Its Impact on Global Health: The COVID-19 pandemic, caused by the SARS-CoV-2 virus, emerged in late 2019 and rapidly escalated into a global health crisis. By March 2020 [*Sargsyan K M et al., 2021*], the World Health Organization (WHO) declared COVID-19 as a pandemic, resulting in unprecedented social, economic, and healthcare disruptions worldwide [*Sharma A et al., 2020*]. Over the course of the pandemic, more than 700 million cases and over 6 million deaths were reported globally, affecting nearly every aspect of life, including healthcare infrastructure, economies, and daily routines. Healthcare systems across the world were overwhelmed, with a significant shift in resources toward controlling COVID-19, which led to the neglect of routine healthcare services, including the surveillance of other infectious diseases [*Filip R et al., 2022*]. As shown in the Figure 4 flow diagram, the pathogen responsible for COVID-19, known as the SARS-CoV-2 virus, employs diverse adap-

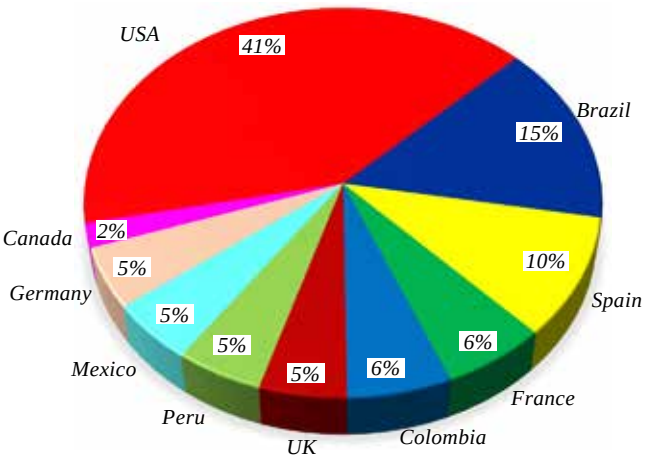

FIGURE 3. *Top 10 most affected nationic worldwide [Srivastava S et al., 2023].*

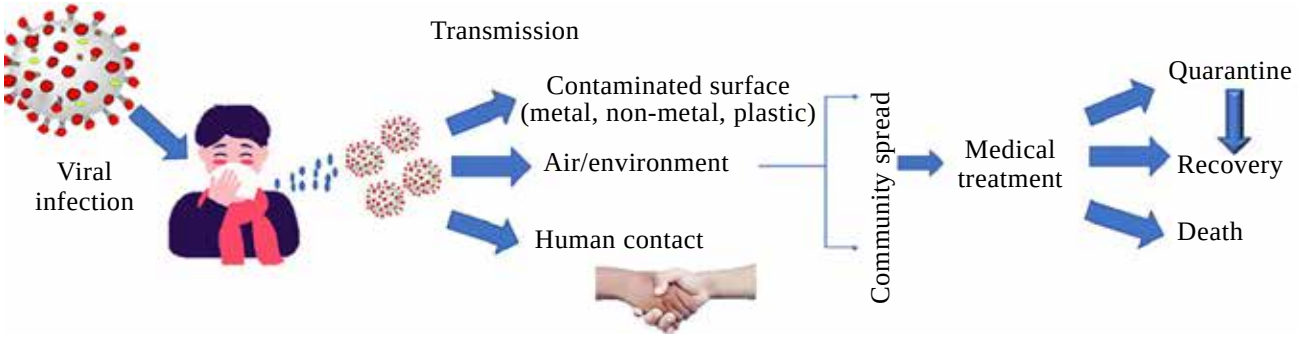

Figure 4. A short Covid-19 transmission information flowchart [Sharma et al. 2020].

tation mechanisms to spread among humans and within communities. Figure 5 illustrates a schematic representation of the changes in genesis and transmission of the severe acute respiratory syndrome coronavirus-2.

The COVID-19 pandemic also led to a rise in health disparities, with vulnerable populations experiencing greater challenges in accessing healthcare and preventive measures. Anthroponotic diseases such as Severe Acute Respiratory Syndrome (SARS-CoV-2) and Middle East Respiratory Syndrome (MERS-CoV) have inflicted severe harm on human health, resulting in significant mortality. Both coronavirus infections were widespread, often reaching epidemic proportions. However, numerous shortcomings in the classifications of these infections negatively affected the understanding and elucidation of the complex pathological disorders that develop in the host organism during the infectious process caused by these coronaviruses [*Zilfyan A V et al., 2021*]. Furthermore, it triggered widespread behavioral changes, including mask wearing, hand hygiene, and social distancing, which helped reduce the transmission of many infectious diseases [*Sabahgoulian C B et al., 2021*]. However, it also disrupted regular immunization programs, disease surveillance systems, and global health security, setting the stage for the emergence and re-emergence of other infectious diseases, including the mpox virus.

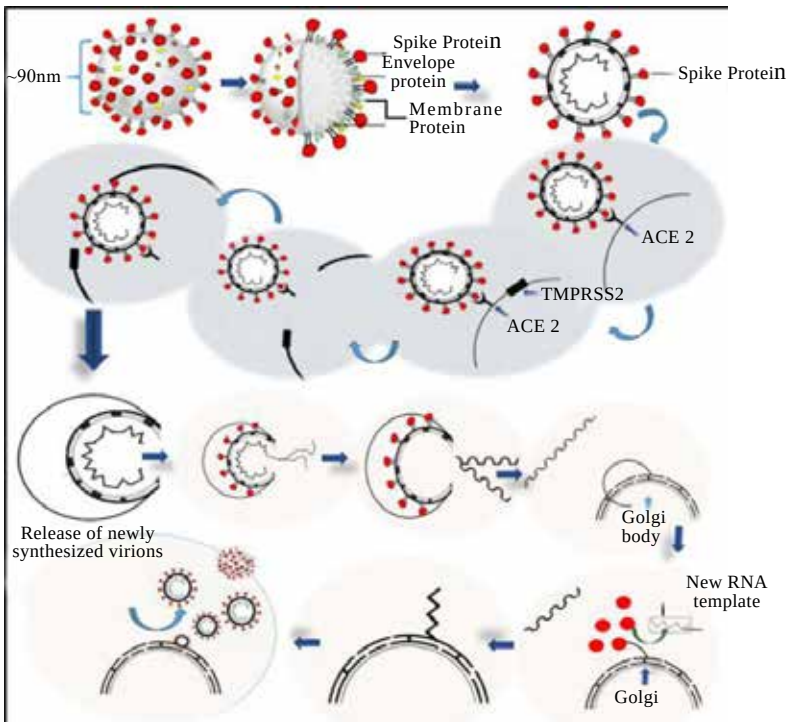

Figure 5. Schematic representation of the genesis and transmission of severe acute

Global Epidemiological Trends Post-COVID-19

Analysis of Mpox Cases Reported After the COVID-19 Pandemic: The COVID-19 pandemic altered the global landscape of infectious disease surveillance and response, leading to notable changes in the epidemiology of other diseases, including mpox. Prior to the COVID-19 pandemic, mpox was primarily confined to Central and West African nations, where sporadic outbreaks would occur periodically, especially in rural areas with close human-animal interactions. However, in 2022, a substantial rise in cases was observed globally, marking one of the largest and most widespread mpox outbreaks recorded outside of Africa [*Srivastava S et al., 2023*]. According to the World Health Organization (WHO), over 87,000 confirmed cases of mpox were reported across more than 110 countries

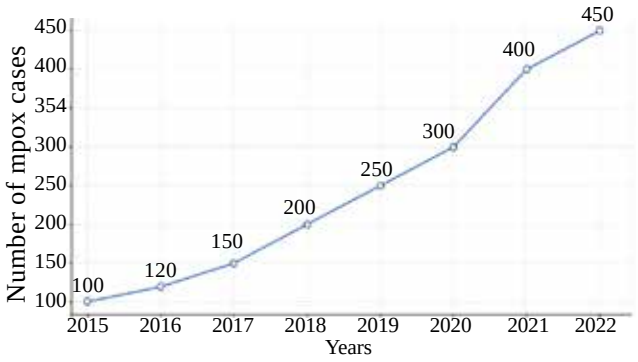

Figure 6. *Trends Analysis of Mpox Cases (Pre and Post Covid-19)*

in 2022, predominantly affecting regions that had not previously reported significant mpox activity. Figure 6 illustrates the Trends Analysis of mpox Cases Pre & Post Covid-19. This sudden surge was characterized by clusters of infections in Europe, North America, and parts of Asia. Unlike earlier outbreaks, which often involved zoonotic transmission from animals to humans, the 2022 outbreak was largely driven by human-to-human transmission, suggesting a shift in the virus's transmission dynamics [*Srivastava S et al., 2023*].

Geographical Spread and Variations in Outbreak Patterns: The geographical distribution of mpox cases during the 2022 outbreak represented a significant deviation from historical patterns. Traditionally, the disease was endemic in regions such as the Democratic Republic of Congo, Nigeria, and Cameroon, with cases rarely spilling over into non-endemic countries. However, during the recent outbreak, countries like the United Kingdom, Spain, Portugal, the United States, and Brazil reported substantial numbers of mpox cases for the first time. In the United States alone, over 30,000 cases were confirmed, highlighting a dramatic expansion of the virus's geographical footprint.

The variations in outbreak patterns across different regions can be attributed to several factors, including differences in public health infrastructure, varying levels of disease awareness, and local practices related to hygiene and sexual behavior. While some regions saw a rapid rise in cases followed by a quick decline due to aggressive public health interventions, others struggled with prolonged outbreaks due to delays in implementing effective control measures.

Factors Contributing to the Re-Emergence of Mpox: Several factors contributed to the re-emergence of mpox in the post-COVID-19 era, including:

- Impact of the COVID-19 Pandemic on Surveillance Systems: The pandemic diverted significant resources and attention away from routine disease surveillance, which may have allowed mpox outbreaks to grow unnoticed. Additionally, the global focus on COVID-19 resulted in reduced funding and staffing for the monitoring of other infectious diseases, weakening early detection efforts for mpox cases [*Zinnah M A et al., 2024*].
- Behavioral Changes and Social Practices: The easing of COVID-19 restrictions in 2022 led to increased international travel, mass gatherings, and social events, creating opportunities for the rapid spread of infectious diseases, including mpox. The 2022 outbreak was notably associated with transmission within certain social networks, particularly among men who have sex with men (MSM), where close physical contact facilitated the spread of the virus. This pattern underscores the need for targeted health education and intervention within affected communities [*Mohamed Abdoul-Latif F et al., 2024*].
- Globalization and Animal Trade: The global trade of animals, particularly exotic pets, has historically been a risk factor for the introduction of zoonotic diseases like mpox into new regions. Although this was not the primary driver of the 2022 outbreak, the historical U.S. outbreak in 2003 was directly linked to the importation of infected animals from West Africa, illustrating how the movement of wildlife can play a role in the spread of zoonotic diseases [*Suraka B et al., 2024*].
- Reduction in Smallpox Immunity: The discontinuation of routine smallpox vaccination after its eradication in 1980 has led to a decline in cross-immunity against other orthopoxviruses, including mpox. Older populations who received the smallpox vaccine continue to have some degree of protection, but younger, unvaccinated individuals are more susceptible to infection. This waning immunity in the general population has been identified as a key factor in the resurgence of mpox cases globally [*Van Dijck C et al. 2023*].

Effects on Disease Surveillance and Control Mechanisms

COVID-19 severely affected global disease surveillance and control mechanisms, revealing both strengths and weaknesses. On the one hand, the pandemic led to a surge in the development and deployment of innovative digital health tools, such as contact tracing apps, telemedicine platforms, and real-time data-sharing systems, which enhanced the ability of health authorities to track and respond to the virus. These advancements demonstrated the potential for technology to revolutionize disease surveillance and response in the future [*Lundberg A L et al., 2024*].

On the other hand, the focus on COVID-19 led to significant lapses in the surveillance of other infectious diseases. For instance, routine reporting of diseases like tuberculosis, HIV, and malaria decreased significantly in 2020 and 2021, as resources were diverted to fight the pandemic. The reduced surveillance capabilities made it difficult to monitor the emergence of new infections or the resurgence of existing ones, such as mpox. The delay in detecting and responding to the mpox outbreak in 2022 is partly attributed to these weakened surveillance systems, which struggled to pivot quickly after being focused on COVID-19 for so long [*Harada N M et al., 2024*].

The pandemic also affected laboratory networks worldwide. Many laboratories that previously conducted testing for a range of infectious diseases were repurposed to handle the high volume of COVID-19 tests, leading to a backlog in diagnostic services for other conditions. This repurposing meant that early warning signs of emerging outbreaks, such as mpox, might have been missed, as fewer resources were available for laboratory-based surveillance of other pathogens [*Badar N et al., 2024*].

Lessons Learned from COVID-19 and Their Application in Controlling Mpox Outbreaks

The COVID-19 pandemic provided numerous lessons that have proven useful in controlling the recent mpox outbreaks, highlighting the need for adaptable, resilient, and integrated public health systems. Key lessons include:

- Importance of Rapid Response and Early Detection: One of the critical lessons from COVID-19 was the need for rapid identification of cases and swift response to outbreaks. Countries that acted quickly in implementing testing, contact tracing, and isolation measures were generally more successful in controlling the spread of the virus. In the case of mpox, early detection through vigilant surveillance and rapid response teams enabled countries to contain local outbreaks more effectively. For example, the use of targeted testing and contact tracing in high-risk communities helped limit the spread of mpox in countries like the United States and the United Kingdom during the 2022 outbreak [*Branda F et al., 2024]*.
- Data Sharing and International Collaboration: The global nature of the COVID-19 pandemic emphasized the importance of data sharing and international collaboration in managing infectious diseases. Initiatives like the World Health Organization's COVID-19 dashboard, which provided real-time data on cases and deaths worldwide, played a crucial role in understanding the spread of the virus and coordinating international efforts. Similar approaches have been applied to mpox, where real-time data-sharing networks helped track the spread of the virus and inform public health responses. Enhanced communication between health agencies across borders has been critical in managing mpox outbreaks, enabling faster information exchange and more coordinated action [*Gashema P et al., 2024*].
- Strengthening Health Infrastructure and Workforce: The strain experienced by healthcare systems during the COVID-19 pandemic underscored the need for resilient health infrastructure and a well-prepared workforce. Investments in healthcare infrastructure, such as expanding laboratory capacities, improving hospital facilities, and ensuring the availability of essential medical supplies, have been essential in managing subsequent health crises, including the mpox outbreak. Training healthcare workers to handle a range of infectious diseases, beyond just COVID-19, has also been critical in ensuring a more robust response to new outbreaks. This approach has helped countries avoid the pitfalls of narrow focus and prepare for a range of health threats [*Adamu A A et al., 2024*].
- Vaccine Development and Deployment: The suc-

cess of the COVID-19 vaccination campaigns demonstrated the potential of rapid vaccine development and deployment. The use of mRNA technology, for instance, allowed for the swift production of effective COVID-19 vaccines, which played a pivotal role in controlling the pandemic. Similarly, the lessons learned from the COVID-19 vaccine rollout have informed strategies for distributing vaccines to control mpox, particularly among high-risk populations. The existing smallpox vaccine, which offers protection against Mpox, has been used in targeted immunization campaigns to curb the spread of the virus [*Zhang W et al., 2024*].

- Public Health Communication and Education: Clear, consistent, and transparent communication was vital during the COVID-19 pandemic to address public fears, combat misinformation, and encourage adherence to public health measures. Countries that communicated effectively with their populations were more successful in implementing health protocols. This lesson has been critical in managing mpox outbreaks, as public health agencies have focused on educating communities about transmission risks, symptoms, and preventive measures. Effective communication strategies have been particularly important in addressing stigma associated with mpox, ensuring that affected populations are not marginalized [*Adamu A A et al., 2024*].

Complications and Risk Factors for Severe Illness

Although mpox is generally a self-limiting disease, complications can arise, especially in individuals with weakened immune systems, young children, and pregnant women. Severe complications include secondary bacterial infections, pneumonia, sepsis, encephalitis, and corneal infection, which can lead to vision loss. According to studies conducted during previous outbreaks in Africa, the case fatality rate of mpox ranges from 1% to 10%, with higher rates observed in children and immunocompromised individuals [*Amer F et al., 2023*].

√ Immunosuppression: People with conditions that weaken the immune system (e.g., HIV/AIDS, cancer, organ transplant recipients) are at a higher risk of severe disease.

√ Age: Young children, especially those under 8 years old, are more susceptible to severe forms of the disease.

√ Pregnancy: Pregnant women are at increased risk of complications, and there is a possibility of vertical transmission, which can lead to adverse outcomes for the fetus.

Diagnostic Approaches and Challenges

Current Diagnostic Methods for Mpox: The primary diagnostic approach for mpox involves laboratory confirmation through polymerase chain reaction (PCR) testing of swabs taken from skin lesions. Polymerase chain reaction is considered the gold standard for diagnosing mpox due to its high sensitivity and specificity. Samples can also be taken from blood, throat swabs, and other body fluids, but the viral load in these specimens may be lower than in lesions, which can affect the accuracy of the test [*Asif S et al., 2024*].

In addition to polymerase chain reaction, serological tests that detect antibodies against the mpox virus can be used to confirm past infections, although they are less effective for diagnosing active cases. table 1 shows the Comparison of Diagnostic Methods. The vital culture, although less commonly used, can also help in isolating the virus, but this method is time-consuming and requires specialized laboratory facilities.

Innovations and Advancements in Diagnostic Techniques Post-COVID-19: The COVID-19 pandemic led to significant advancements in diagnostic technologies, many of which have been

Table 1.

Diagnostic Methods Comparison for Mpox

	Method		
	polymerase chain reaction	Serology	Point-of-Care Tests
Type	Molecular test	Antibody detection	Rapid diagnostic kits
Sensitivity	High	Variable	Medium
Specificity	High	Variable	Medium
Time to Result	4-6 hours	1-2 days	15-30 min
Use Case	Confirmatory diagnosis	Past infection detection	Field settings, quick screening

Table 2.

Summary of Mpox Antiviral Treatments and Supportive Care

Treatment	Mechanism of Action	Administration Route	Common Side Effects	Recommendations for High-Risk Groups
Tecovirimat	Inhibits viral envelope protein	Oral	Headache, nausea	Recommended
Cidofovir	Inhibits viral DNA polymerase	Intravenous	Nephrotoxicity	Limited
Brincidofovir	Lipid-conjugated derivative, improved safety	Oral	Nausea, diarrhea	Limited, requires more studies
Supportive Care	Symptom management, hydration	Various	N/A	Recommended

applied to improve the diagnosis of other infectious diseases, including mpox. Innovations such as point-of-care (POC) testing, rapid antigen tests, and high-throughput sequencing have been explored to enhance the speed and accuracy of mpox diagnostics.

- Point-of-Care (POC) Testing: The development of portable, rapid diagnostic tests that can be used at the point of care has been one of the major advancements spurred by the COVID-19 pandemic [*Nagri S K et al., 2021*]. These tests provide results within minutes and can be particularly useful in remote settings where laboratory facilities are limited. Efforts are underway to develop POC tests for mpox that can quickly identify the presence of the virus using samples from skin lesions [*Tran N K et al., 2023*].
- Next-Generation Sequencing (NGS): NGS technology, which gained widespread use during the COVID-19 pandemic for tracking SARS-CoV-2 variants, has been employed to analyze the genetic makeup of the mpox virus. This approach not only helps in diagnosing mpox but also in understanding the genetic variations and potential mutations in the virus, which can inform public health strategies and vaccine development [*Zowawi H M et al., 2021*].
- Digital Health Platforms and Artificial Intelligence: The use of digital health platforms to integrate diagnostic data, track outbreaks, and monitor patient outcomes has become more prevalent. Artificial intelligence (AI) tools are also being developed to analyze images of skin lesions, aiding in the differential diagnosis of Mpox and other similar conditions. These technologies hold promise for streamlining the diagnostic process and enabling faster. In addition, more accurate identification of cases [*Dabla P K et al., 2021*].

Treatment Options and Management Strategies

Available Antiviral Treatments and Supportive Care

While no treatments are specifically approved by the FDA for mpox, several antiviral medications used for other orthopoxviruses have been used for patients with severe mpox infections. The treatment of mpox primarily focuses on supportive care, as there is no specific antiviral approved solely for mpox as shown in table 2. Supportive care includes managing symptoms, maintaining adequate hydration, and preventing secondary bacterial infections. However, antiviral agents that were developed for smallpox have shown efficacy against mpox and are often used in clinical settings. fig. 7 illustrates the comparison between mpox treatment side effects and administration routes, especially for severe cases [*Khan I et al., 2024*].

- Tecovirimat (ST-246): Tecovirimat is the first antiviral drug specifically approved by the U.S. Food and Drug Administration (FDA) for the treatment of smallpox, but it has been used under expanded access protocols to treat mpox. It works by inhibiting the viral envelope protein, preventing the virus from spreading to other cells. Tecovirimat has demonstrated safety and efficacy in animal models

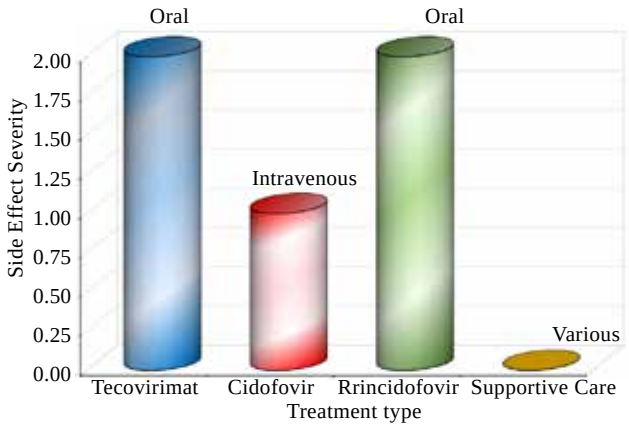

Figure 7. *Comparison between Mpox treatment side effects and administration routes.*

and compassionate use cases during recent mpox outbreaks. While more clinical trials are needed, it is currently recommended for patients at higher risk of severe disease, such as those with immunocompromising conditions, pregnant women, and children [*Titanji B K et al., 2024*].

- Cidofovir and Brincidofovir: Both are antiviral agents with activity against orthopoxviruses. Cidofovir is an intravenous drug originally used to treat cytomegalovirus (CMV) infections, and it has shown in vitro efficacy against mpox. However, its use is limited due to nephrotoxicity. Brincidofovir, a lipid-conjugated derivative of cidofovir, has a better safety profile and can be administered orally, making it a more convenient option. Clinical experience with brincidofovir for mpox remains limited, and further studies are needed to establish its effectiveness [*Titanji B K et al., 2024*].
- Supportive Care: Supportive care is essential for managing mpox symptoms. This includes pain management, treating skin lesions to prevent secondary bacterial infections, and maintaining fluid and electrolyte balance. Patients with mild cases can often recover at home with proper isolation and symptom management, while those with severe cases may require hospitalization.

Vaccine Development and Use in Controlling Mpox Outbreaks

The success of smallpox eradication demonstrated the effectiveness of vaccination in controlling Orthopoxvirus infections. The smallpox vaccine has historically provided cross-protection against mpox due to the similarity between the viruses. Following the cessation of routine smallpox vaccination after its eradication, population immunity to orthopoxviruses, including mpox, declined as vaccine shown in Table 3, contributing to the emergence of new cases in the subsequent years [*Wang X et al., 2024*].

- **JYNNEOS (MVA-BN):** JYNNEOS is a third-generation, non-replicating vaccine that has been approved for the prevention of both smallpox and mpox. It is a safer alternative to older vaccines like ACAM2000, as it can be used in immunocompromised individuals and has a more favorable safety profile. During the 2022 mpox outbreak, JYNNEOS was used in targeted vaccination campaigns to curb the spread, especially among high-risk groups, including healthcare workers, men who have sex with men (MSM), and individuals with known exposure to confirmed mpox cases [*Wang X et al., 2024*].
- **ACAM2000:** ACAM2000 is a live, replicating virus vaccine derived from the original smallpox vaccine. Although effective, it carries a higher risk of adverse effects, particularly in immunocompromised individuals, pregnant women, and those with certain skin conditions. Its use is therefore limited to situations where JYNNEOS is not available, and it is contraindicated in people with certain health conditions [*Wang X et al., 2024*].
- **Ring Vaccination Strategy:** The ring vaccination strategy, which was successful in eradicating smallpox, involves vaccinating the close contacts of confirmed cases to form a protective "ring" around the infected individual, thereby preventing the spread of the virus. This method has been employed during recent mpox outbreaks to control transmission, focusing on known contacts and high-risk populations [*Kretzschmar M et al., 2004*].

Public Health Preparedness and Future Outbreak Prevention

Lessons from COVID-19: Strengthening Health Infrastructure and Surveillance: The COVID-19 pandemic exposed significant gaps in global health infrastructure, prompting widespread improvements. These lessons are critical for enhancing preparedness for future outbreaks of mpox and other emerging infections. Key lessons include [*Lal A et al., 2022*].

Table 3.

Vaccine Options for Mpox Prevention

Vaccine Name	Type	Administration Route	Efficacy	Safety Profile	Target Groups
JYNNEOS	Non-replicating vaccine	Subcutaneous	High	Safe for immunocompromised	Healthcare workers, high-risk populations
ACAM2000	Live, replicating virus	Subcutaneous	High	Riskier, contraindicated in some cases	General population in high-risk regions

- **Enhanced Surveillance Systems:** Building robust, real-time surveillance systems that can quickly detect and report cases of emerging infections is essential. During COVID-19, countries developed digital tools for case tracking and data sharing, which have been adapted for monitoring mpox outbreaks. Early detection systems can facilitate rapid responses, helping to contain the spread before outbreaks become widespread [*Bashier H et al., 2021*].
- **Healthcare Infrastructure Investment:** Strengthening healthcare infrastructure by increasing laboratory capacity, expanding healthcare workforce training, and ensuring the availability of essential supplies is critical. Investments made during the COVID-19 pandemic have been repurposed for managing mpox, highlighting the benefits of having flexible, well-equipped healthcare systems [*Bedi J S et al., 2021*].
- **Public Health Workforce Training:** Training healthcare workers to identify and manage emerging infections, including mpox, is essential for a rapid and effective response. During the COVID-19 pandemic, many countries invested in workforce training, which has improved the management of subsequent outbreaks like mpox [*Mahmood S et al., 2020*].

Importance of Global Collaboration and Information Sharing: The interconnected nature of global health means that infectious disease outbreaks cannot be managed in isolation. Collaboration between countries, international organizations, and research institutions is crucial for sharing information, resources, and best practices. The COVID-19 pandemic underscored the need for global cooperation, and similar strategies are being applied to control mpox. Initiatives like the World Health Organization's International Health Regulations (IHR) facilitate information sharing and ensure coordinated responses to infectious disease threats [*Branda F et al., 2024*].

Global collaborations also extend to vaccine development, where joint efforts can accelerate the production and distribution of vaccines, ensuring that countries with fewer resources have access to these critical tools. Partnerships between governments, non-governmental organizations, and the private sector have been instrumental in addressing the recent mpox outbreaks and will be vital for preventing future ones [*Torales J et al., 2024*].

Challenges in Controlling Mpox Spread

Issues Related to Stigma, Misinformation, and Public Awareness

Controlling the spread of mpox faces significant challenges rooted in stigma and misinformation. The perception of mpox as a disease primarily affecting certain populations, particularly men who have sex with men (MSM), has led to social stigma [*Budhwani H et al., 2024*]. This stigma not only affects individuals' willingness to seek treatment or testing but also hampers public health campaigns aimed at raising awareness about the disease. Misinformation regarding the transmission and severity of mpox can lead to fear and discrimination, further isolating affected individuals and undermining public health efforts [*Copen C E et al., 2023*].

To address these issues, public health authorities must prioritize education campaigns that provide accurate information about mpox transmission, symptoms, and treatment options. Utilizing trusted community leaders and leveraging social media platforms can help dispel myths and encourage positive health-seeking behaviors. Moreover, integrating comprehensive sexual health education into public health strategies can promote understanding and reduce stigma associated with mpox and other sexually transmitted infections [*Edinger A et al., 2023*].

Access to Healthcare in Resource-Limited Settings: Access to healthcare is another critical challenge in controlling mpox spread, particularly in resource-limited settings. Many affected regions lack the necessary infrastructure to support effective surveillance, diagnosis, and treatment. For example, limited laboratory capacity hinders timely diagnostic testing, leading to delays in identification and response to outbreaks. Inadequate healthcare facilities may also struggle to manage patients with severe illness, increasing the risk of mortality and further transmission [*Nka A D et al., 2024*].

Efforts to improve access to healthcare must focus on strengthening local health systems. This includes investing in laboratory capacities, training healthcare workers, and ensuring the availability of necessary treatments and vaccines. Additionally, partnerships between governments, internation-

al organizations, and non-governmental organizations can facilitate resource allocation and provide technical assistance to improve healthcare delivery in underserved areas [*Chen F et al., 2024*].

Overcoming Challenges in Vaccination and Outbreak Response: Vaccination is a cornerstone of public health strategy for controlling mpox outbreaks. However, ensuring equitable access to vaccines and effective outbreak response remains a challenge. In some cases, vaccine distribution may be hampered by logistical challenges, particularly in rural or remote areas where healthcare infrastructure is limited. Furthermore, vaccine hesitancy fueled by misinformation or distrust in health authorities can hinder uptake, leaving communities vulnerable to outbreaks [*Aspinall R et al., 2007*].

To overcome these challenges, tailored vaccination campaigns that consider local contexts and community needs are essential. Engaging community leaders and providing clear, transparent information about the safety and efficacy of vaccines can help build trust and increase acceptance. Additionally, implementing a robust monitoring and evaluation framework to assess vaccination efforts and outbreak response can inform adaptive strategies and improve effectiveness in controlling mpox [*Coustasse A et al., 2021*].

Conclusion

The re-emergence of mpox in the post-COVID-19 era underscores the persistent threat of zoonotic diseases and the complex interplay of global health challenges. The increased prevalence of mpox cases, driven by disrupted surveillance systems, behavioral changes, and waning immunity, highlights the need for strengthened public health infrastructure and comprehensive outbreak response strategies. Advances in diagnostics and vaccination technologies provide valuable tools for managing the disease, but issues such as stigma, misinformation, and inequitable healthcare access, particularly in resource-limited settings, hinder their effectiveness.

Addressing these challenges requires a multifaceted approach, including robust international collaboration, community engagement, and sustained investments in health systems. Lessons learned from the COVID-19 pandemic, such as the importance of early detection, rapid response, and effective communication, must be applied to enhance mpox preparedness and response. By fostering global partnerships, improving access to vaccines and treatments, and prioritizing public awareness, we can not only control the spread of mpox but also build resilient systems capable of addressing future infectious disease threats.

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