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An Emerging Global Threat After The COVID-19 Pandemic: Monkeypox Similarities and Differences

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Abstract

During the post COVID-19 pandemic, monkeypox (mpox) has returned and become a significant concern for health. The epicenter of clade I mpox is within the Democratic Republic of Congo (DRC) where two subclade consists of Ia and Ib are now in circulation and maintain their transmission from human to human. As of late 2024, worldwide mpox cases had surpassed 100,000 across 127 nations, with the World Health Organization reporting over 260 fatalities. CDC recently reported that the spread of clade I is no longer limited to Africa, highlighting its growing potential to become a pandemic. The World Health Organization (WHO) declared the disease an international public health emergency on August 14, 2024. This undoubtedly raises the question of whether global outbreaks of mpox represent the onset of another full-blown pandemic. Although Monkeypox can lead to other public health issues (especially in areas where it is not usually endemic), it is unlikely to become a pandemic on the same scale as COVID-19. Moreover, it is more containable due to vaccine availability, its transmission dynamics, and lessons learned from COVID-19. Nonetheless, it is still important to remain vigilant to prevent outbreaks from spreading, particularly in vulnerable populations and regions with limited healthcare resources.

Keywords: COVID-19, viral infection, monkeypox, pandemic, vaccines

Introduction

Monkeypox virus (MPXV) causes the zoonotic viral infection human monkeypox (MPX). As an orthopoxvirus, it is closely related to the agent of smallpox, variola virus (Gong et al. 2022; Shchelkunova and Shchelkunov 2022). Generally, MPXV causes a self-limiting illness lasting 2 to 4 weeks, and the fatality rate ranges from 1% to 11% and depends on the host's immune system, healthcare access, and viral clade (Martínez-Fernández et al. 2023).

In 2022, clade IIb mpox emerged throughout the world with over 117,000 confirmed cases and 260 deaths being reported in 127 countries, with the majority of them that never had any contact with the disease (Centers for Disease Control and Prevention (CDC) 2025; World Health Organization (WHO) 2025). As per WHO updates (2024), several suspected and confirmed mpox cases have been documented in Central and Eastern Africa, mostly in the Democratic Republic of Congo and adjacent nations, with ongoing inquiries into clade I transmission (Centers for Disease

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Control and Prevention 2025; World Health Organization 2025). By the end of 2024, there will be low-level circulation of clade II mpox in the United States, with fewer than 200 cases per month. It is worth noting that most cases occur among unvaccinated or partially vaccinated individuals with JYNNEOS (Centers for Disease Control and Prevention 2025). There are ongoing outbreaks of clade II that occur simultaneously with clade 1 transmission worldwide. This demonstrates the criticality of the mpox epidemiology evolution and its prominent role in public health.

There are particular challenges related to the re-emergence of monkeypox in both endemic and non-endemic regions. It continues to spread globally post COVID-19 pandemic, and this puts pressure upon the already strained healthcare systems, which also reveal the weaknesses in terms of preparation in the world. Such combinations raise important questions about whether mpox will continue its role as an endemic with occasional increases or whether it has the potential to become a pandemic-level emergency.

The aim of this review, which is to investigate the parallels and distinctions between COVID-19 and mpox in terms of their origins and evolution, clinical challenges, transmissions methods, in addition to accessibility to treatments and vaccines. Through investigating these dimensions, the review attempts to capture important lessons to improve preparations in the future against emerging and re-emerging threats from viruses.

Origins

The new coronavirus, SARS-CoV-2, which first appeared in Wuhan, China, in late 2019, causes COVID-19. It is thought that the virus has zoonotic origins; it may have originated in bats and passed through an intermediate host before infecting humans (Ye et al. 2020). The virus spread quickly around the world, partly because it could persistently infect even asymptomatic people through respiratory droplets and aerosols.

By contrast, the monkeypox virus, which is a member of the Orthopoxvirus genus, causes monkeypox (Karagoz et al. 2023). In 1958, the virus was first identified in research monkeys (hence the name). However, it is predominantly found in rodents (Karagoz et al. 2023). In 1970, the Democratic Republic of Congo reported the first-ever human case of the virus. It is spread to humans through close contact with infected animals or from other humans through respiratory droplets, contaminated materials, and bodily fluids. Monkeypox did not spread as fast or widely as COVID-19 in the early stages (Bryer et al. 2022).

Structure and genome

The monkeypox virus (MPXV) is a large, double-stranded DNA orthopoxvirus. Its major clades are Clade I (Central Africa) and Clade II (IIa/IIb) (West Africa). The recent global outbreak is mainly caused by the Clade IIb lineage B.1, which stems from Nigerian outbreaks between 2017 and 2018 (Centers for Disease Control and Prevention 2025; World Health Organization 2025).

Compared to SARS-CoV-2, MPXV has a significantly different structure. SARS-CoV-2 is an enclosed single-stranded RNA virus, much like all coronaviruses. It is round, tiny (about 100 nm in diameter), and coated with a porcupine-like sheath of spike (S) proteins (Wang et al. 2020). Angiotensin-converting enzyme 2 (ACE2) enables S proteins to bind to host cells. This protein is ubiquitously expressed in organs throughout the human body, ultimately leading to infection (Ni et al. 2020; Zhang et al. 2021).

On the other hand, MPXV is a large virus, measuring 220–450 nm. It is also enveloped and belongs to the Poxviridiae family (Verma and Gangwar 2024). Its double-stranded DNA genome is contained in a core composed of enzymes that play a critical role in facilitating replication and immune evasion (Verma and Gangwar 2024). The virus that causes monkeypox belongs to the Orthopoxvirus genus within the Poxviridae family. Only four pathogens (i.e., the vaccinia virus, monkeypox virus, cowpox virus, and the extinct variola virus, the causative agent of smallpox) have supposedly infected humans within the Orthopoxvirus genus (Elsayed et al. 2022; Kumar et al. 2022).

As with SARS-CoV-2, the surface proteins of MPXV enable the virus to enter host cells (Realegeno et al. 2017). Nonetheless, poxviruses use 11-12 transmembrane proteins rather than a single protein to bind to host cells. In turn, this likely causes glycosaminoglycans or laminin on the cell surface to bind to one another (Duchoslav and Boura 2023).

Evolution and variants

The evolutionary implications of the discrepancies between the genomes of SARS-CoV-2 and MPXV are significant. RNA viruses can replicate haphazardly, as seen with SARS-CoV-2. Replication errors are neither detectable nor correctable by RNA polymerase, which replicates the viral genome (Pachetti et al. 2020). In contrast to other RNA viruses, Coronaviruses possess an enzyme (exoribonuclease) that has some proofreading capabilities (Wright et al. 2022). This does not completely prevent mutations in SARS-CoV-2, although it can slow the process down (Khailany et al. 2020). Random mutations consequently emerge and can replicate rapidly if they promote viral fitness (Chen et al. 2020). This was evident throughout the COVID-19 outbreak. The SARS-CoV-2 Delta strain has dominated the pandemic scene in 2021. At the start of 2022, Omicron (a strain that is highly contagious) became the dominant variant, and now, all currently circulating variants are related to Omicron (Kannan et al. 2021; Fernandes et al. 2022). The high transmissibility of Omicron is thought to be associated with a series of S protein mutations that enable binding to ACE2 and help the virus evade host antibodies (Vitiello et al. 2022).

RNA viruses mutate more freely and quickly than DNA viruses such as MPXV. Compared to RNA viral replication, DNA polymerase and other enzymes involved in DNA viral replication are more suited for mistake correction and proofreading (Domingo et al. 2021). On average, Poxviruses mutate once or twice a year. By contrast, the MPXV strain that spread in 2022 mutated 50 times, which is far more than the strains identified in 2018-2019 (Desingu et al. 2022; Yu et al. 2023). The mutations indicated that the virus was spreading between humans in Europe and Africa for many years prior to the 2022–2023 surge in cases (Chakraborty et al. 2022). This is different from the mutation patterns that are evident in SARS-CoV-2, which are significantly associated with replication errors that may become fixed in certain populations.

The double-stranded DNA virus monkeypox consists of two genetic clades: the Central African (Congo Basin) clade and the West African clade (Kugelman et al. 2014; Altindis et al. 2022). These two clades occur together only in one country, Cameroon, and are geographically divided (Nakazawa et al. 2015). Outbreaks of the West African clade have been reported in several neighboring countries, including Liberia, Nigeria, Sierra Leone, and the Ivory Coast. It has also been imported into the USA from Ghana (Forni et al. 2023). Meanwhile, the Central African clade has been identified primarily in Cameroon, Gabon, the Republic of Congo, Sudan, the Central African Republic, and the Democratic Republic of Congo (Velavan and Meyer 2022; Forni et al. 2023). It is important to note that these two clades differ substantially, not just in terms of geographical differences, but also in epidemiologic and clinical characteristics. The Central African clade is endemic in the Democratic Republic of Congo, with over 2,200 cases reported each year. Thus, it appears to be more prevalent than the West African clade (Forni et al. 2023). Moreover, the Central African strain is likely related to more severe disease and higher transmissibility than the West African clade, the latter of which tends to have a lower case fatality rate (CFR) of < 1%, and there have never been any reported cases of human-to-human transmission (Forni et al. 2023).

On the other hand, the Congo Basin clade may have a CFR of up to 11%, and reports have documented up to 6 consecutive human-to-human transmissions. By comparison, a comprehensive study found a substantial difference in CFR between the West African clade (4.0%; 95% CI: 1.9%–6.9%) and the Central African clade (11.0%; 95% CI: 8.7%–13.7%) (Bunge et al. 2022).

The first genomic sequence of a case recently found in Portugal was reported by Isidro et al. (2022). For phylogenomic characterization and quick reconstruction, the scientists employed shotgun metagenomics. Based on preliminary genetic evidence, the 2022 monkeypox virus is most closely related to the viruses that moved from Nigeria to the UK, Israel, and Singapore between 2018 and 2020. It is thought to belong to the West African clade (Caria et al. 2022; Isidro et al. 2022).

Transmission

The respiratory virus SARS-CoV-2 can linger in the air for minutes or even hours. It is transmitted through virus-laden aerosols, which are tiny droplets produced during breathing (Ranga 2021). An infection can spread to other people if they inhale these aerosols. SARS-CoV-2 is particularly difficult to contain because it spreads quickly through the air; one infected person can infect many others simply by breathing. Furthermore, even if a person has no symptoms, they can still transmit COVID-19 (Cevik et al. 2020; Patel et al. 2020).

MPXV is not a respiratory virus, even though it can still be transmitted through saliva and respiratory secretions (Venkatesan 2022). However, it is predominantly spread through direct contact with the rash, scabs, or bodily fluids of an infected individual. Alternatively, it can be spread congenitally or by using objects/touching surfaces used by an infected person. Nonetheless, the risk of contracting the disease by bumping into someone or trying on clothes at a store is relatively low.

Extended contact with clothing that had already been handled by a person with prolonged contact with mpox sores would be required to cause infection (Kaler et al. 2022). Thus, the disease is more likely to be contracted by living with an individual diagnosed with it, where contact tends to be more regular and prolonged. Furthermore, sexual contact can promote the transmission of the virus. In fact, this played a significant role in the spread of the virus during the 2022-2023 outbreak and continues to be a primary transmission route in affected African countries (Sah et al. 2022; Venkatesan 2022). As MPXV is primarily spread through close, prolonged contact, its transmissibility is much lower than that of COVID-19.

Mpox global spread and mutation risk

Since 22nd May 2022, transmissions between individuals have spread beyond Central and West Africa. The initial outbreak was related to Clade IIb (B.1 lineage), which has spread across the Middle East, Asia, Europe, and America. Despite Clade I mpox cases being predominantly confined to Central Africa, increasing genetic diversity and heightened mobility raise concerns about potential dissemination. Ongoing genomic and epidemiological monitoring is thus important (Centers for Disease Control and Prevention 2025; World Health Organization 2025)

Genomic surveillance reveals that the Clade IIb B.1 lineage has accumulated an unusually high number of APOBEC3-associated mutations despite the slow mutation rate of orthopoxviruses (Edet et al. 2023). This aligns with human-to-human transmission. Recent analyses have revealed enrichment of APOBEC3 signatures in 2022–2025 sequences and documented co-circulating sublineages within B.1 (Otieno et al. 2025).

In terms of Clade I (Ib), CDC has revealed low overall diversity but clear APOBEC3-signature changes in addition to ~1.1-kb deletion, meaning the loss of complement-control protein gene (Jakobsdottir et al. 2022). This is clade Ia—molecular indication of adaption when it is transmitted between humans (Jakobsdottir et al. 2022). In 2025, WHO reported the rapid expansion of Clade Ib within East and Central Africa (World Health Organization 2025).

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Genetic variability and its implications for evolution, transmission, and control

Despite slower evolution in DNA viruses than in RNA viruses, MPXV has demonstrated accelerated microevolution during sustained human-to-human transmission. Analysis of genome isolates conducted between 2022 and 2025 has revealed the significant strength of the APOBEC3-mediated mutational signature (GA→AA, TC→TT), demonstrating that it is capable of host-driven editing during replication in humans (Delamonica et al. 2023). The mutations have generated dozens of single-nucleotide polymorphisms within lineage B.1, consistent with the hypothesis of continuous adaptation to human hosts. The few pieces of evidence pertaining to intra-host diversity and co-infection (≈4–6%) have supported the notion of a continuous evolutionary process (Delamonica et al. 2023; O'Toole et al. 2023).

The distribution and transmissibility are dependent on clade-specific variability (Okwor et al. 2023). Clade I and its Ib sublineage have reemerged in Central and Eastern Africa, despite Clade IIB being the predominant strain in global outbreaks, with greater spread and alleged higher transmission efficiency between humans compared with historical trends (Okwor et al. 2023; Satheshkumar et al. 2025). The diversification of this clade suggests the potential for distinct epidemiological trajectories.

From an immunological perspective, most antigenic regions targeted by smallpox vaccines remain highly conserved. JYNNEOS (MVA-BN) has demonstrated its efficacy in protection, with two doses providing 66% to 86% protection against symptomatic infection (Sultana

et al. 2024; Taha et al. 2024). Breakthrough infections remain especially common among partially vaccinated individuals, driven by vaccine escape resulting from genetic drift that has not been determined (Papukashvili et al. 2022).

Antiviral resistance is the immediate challenge. The prominent treatment, tecovirimat, targets the F13L gene product (VP37), which is critical for viral egress. Immunocompromised patients receiving long-term therapy have revealed resistance-associated mutations in VP37 (e.g., E353K and related substitutions), which confer decreased susceptibility (Smith et al. 2023; Chenchula et al. 2025). This highlights the need for routine resistance genotyping to address persistent and severe cases, in conjunction with the development of other therapies.

In comparison, SARS-CoV-2 exhibits rapid antigenic evolution due to its vulnerability to RNA-dependent RNA polymerase errors, short generation times, and a large global host population. Since the end of 2022, Omicron and its sublineages have led the evolutionary process (Telenti et al. 2022).

There is a noticeable increase of BA.2.86 ("Pirola") that contains more than 30 spike mutations in comparison to its precursor of BA.2 (Esmaeilzadeh et al. 2024). JN.1, which is its descendant, has received a further L455S receptor-binding domain (RBD) substitution. It maintains infectivity while enhancing immune escape (Lu et al. 2024). Through early 2025, the dominant strains worldwide are JN.1 and its derivatives (e.g., KP.2) (Feng et al. 2025). Practical studies have shown that these mutations have improved ACE2 receptor binding and resistance to neutralizing antibodies, thereby balancing transmissibility and immune evasion (Feng et al. 2025).

The epidemiological impact of this continuous genetic turnover is clear: successive replacement waves of Omicron sublineages, each an improvement over its predecessors through enhanced immune escape (Shiraz and Tripathi 2023). SARS-CoV-2 has continuously restructured its global presence, which is dissimilar to MPXV, that restricts to mainly clade-bound.

The effectiveness of vaccines was challenged but not completely disproved. The latest vaccines in 2024–2025 target JN.1/KP.2 antigens. CDC data have revealed a 33% decrease in emergency visits, while hospitalizations among older adults have decreased by 45–46% (Trilla et al. 2025). Despite the frequency of breakthrough infections, it remains protective against severe disease, and its efficacy against death has been maintained, demonstrating that spike variability has minimal impact on the preservation of T-cell-mediated immunity (Riou et al. 2021). It is a different scenario from mpox from a therapeutic standpoint. The spike drift causes a widespread spread of monoclonal antibodies; however, oral antivirals such as nirmatrelvir and ritonavir maintain their general efficacy, as evidenced by less prevalent resistant mutations at the current time (Akinosoglou et al. 2022). Despite such positive development, it is still essential to maintain continuous monitoring.

The genetic implications necessitated the development of tailored surveillance strategies. Priority should be placed on clade-aware genomic monitoring and mpox resistance testing. Meanwhile, variant tracking and vaccine antigen updating are critical for SARS-CoV-2. The two aforementioned scenarios highlight the broader principle that, despite pathogens evolving at different rates and scales, genomic surveillance must remain central to outbreak preparedness.

Symptoms and disease severity

The symptoms of COVID-19 typically appear between 2- and 14-days following exposure to SARS-CoV-2. These symptoms include fever, chills, sore throat, headache, runny or congested nose, and loss of smell or taste (Alimohamadi et al. 2020). For most people, it takes a few days to a few weeks to recover, though some experience longer-lasting symptoms (long COVID) for more than 3 months (long-lasting COVID) for more than three months. COVID-19 can also be fatal, with over 7.75 million deaths reported globally as a result of the disease since 2020. Nonetheless, there has been a decline in the death rate, which is partially due to the accessibility of treatments and vaccinations (Yong 2021). A person's age, immunization history, number of infections, the SARS-CoV-2 variant responsible for the infection, and other factors can all impact the risk of developing severe COVID-19 (Alimohamadi et al. 2020; Yong 2021).

After exposure to MPXV, it can take up to 3 weeks for mpox symptoms to emerge (McFarland et al. 2023). Although every case is different, the symptoms are often similar to those that are present in the early stages of COVID-19 (e.g., headache, fever, and chills) (Yon et al. 2023). Furthermore, mpox is clinically distinct from COVID-19 because it typically presents with a painful, itchy rash that spreads over the face, genitals, and extremities (Maronese et al. 2023).

Mpox typically subsides in 2–4 weeks, although it can be quite serious and sometimes even fatal. The type of MPXV causing the infection impacts the severity of the disease (clade I viruses (Li et al. 2023; Yon et al. 2023). The severity of the disease is also influenced by factors such as age (young children are more prone to developing severe disease), health status (e.g., people with HIV are at a greater risk of developing severe mpox), and access to medical care and vaccinations (Musuka et al. 2024).

Diagnosis

There are now quick antigen tests available, so anyone may check their own COVID-19 status. However, for COVID-19 diagnosis, nucleic acid amplification tests (NAATs)—such as polymerase chain reaction (PCR) assays—are generally more sensitive. These tests can be performed at point-of-care settings, such as pharmacies, or in labs. To identify SARS-CoV-2 RNA, the assays isolate and amplify the viral RNA from patient samples. Other NAATs may be used at home (Yüce et al. 2021).

Testing using nucleic acid amplification can be specific for either monkeypox virus or orthopoxviruses. NAAT, using real-time or traditional PCR, is necessary for the definitive diagnosis of monkeypox virus infection (Altindis et al. 2022). It is recommended that skin lesions be employed as clinical samples for laboratory testing. This involves providing swabs of the lesion's surface or exudate, roofs from many lesions, or lesion crusts (Jain et al. 2024). Paired acute and convalescent samples are needed for serological testing for IgG, which is usually detectable 8 days after symptom onset. IgM antibodies for monkeypox virus usually become detectable 5 days after symptoms first appear. Nonetheless, it is important that a monkeypox diagnosis not be based solely on the presence of antibodies in serum or plasma (Stefano et al. 2023).

Prevention and treatment

When the COVID-19 disease first emerged, no vaccines were available. This was because the virus was new and only discovered in late 2019. However, several vaccines have now been approved for use in the USA. The COVID-19 vaccine, approved by the U.S. Food and Drug Administration (FDA), protects individuals against severe disease and hospitalization. It can be administered to people aged six months and over (Wang et al. 2021). Several antivirals (e.g., Paxlovid) have also been developed to treat COVID-19, although they can only be effective if administered within 5 days of symptom onset (Hashemian et al. 2023).

In the early months of 2020, when COVID-19 initially appeared, there were no vaccines available. However, this is not the case with mpox, as vaccinations are already available. The most popular vaccine is live attenuated and sold under the trademark JYNNEOS. In addition to preventing mpox in people aged 18 and over, JYNNEOS was developed to prevent smallpox (Behera et al. 2023). The manufacturer of JYNNEOS, Bavarian Nordic, is presently examining the vaccine's safety and effectiveness for use in children and adolescents (2–12 years old) (12–17 years old) (Poland et al. 2022).

Individuals who have previously been vaccinated against smallpox may have some protection against monkeypox (Simpson et al. 2020). Nonetheless, as the original smallpox vaccines no longer exist, it is unlikely that individuals aged < 40–50 years will have been vaccinated. In 2019, JYNNEOSTM (also known as IMVAMUNE, IMVANEX, and MVA-BN) was approved by the US FDA for use in adults aged ≥ 18 years with a high risk of severe smallpox or monkeypox. Furthermore, this vaccine has also been approved for use in Europe to protect against smallpox. It has also been used in the United Kingdom on an off-label basis against monkeypox. Another vaccine used to prevent smallpox is ACAM2000®, which was licensed by the FDA in August 2007 and can be used to prevent smallpox in individuals at high risk of infection. The Centers for Disease Control and Prevention have emergency access to investigational new drugs. They also permit ACAM2000® to be used to protect individuals against non-variola Orthopoxvirus infections (including monkeypox).

Treatment and outcomes

At present, no highly effective treatments have been developed for SARS-CoV-2. However, some drug classes used include antiviral agents, anti-inflammatory agents, plasma, low-molecular-weight heparins, and hyperimmune immunoglobulins. Clinical researchers are testing several potential treatments based on the pathological features and different clinical stages of COVID-19. Antiviral agents have been shown to pre-

vent disease progression in the early stages of SARS-CoV-2, and immunomodulatory agents combined with antivirals may lead to better clinical outcomes in patients with severe COVID-19.

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Although monkeypox tends to be a self-limiting disease, some individuals have a higher risk of developing more serious illness or even dying from the disease. Such individuals include newborns, children, and those with underlying immune deficiencies (Hasan and Saeed 2022; Singhal et al. 2022; Zardi and Chello 2022).

Severe monkeypox can lead to a number of complications, including skin infections, pneumonia, altered sensorium, and eye infections (which can ultimately cause vision loss). A systematic review performed before the current outbreak revealed an overall CFR of approximately 8.7%. Nonetheless, the findings also revealed that CFR differed across regions, ranging from 0 to 11%. It is possible, however, that this figure is overestimated due to the limited surveillance in endemic countries. Only one death was reported in the most recent outbreak, and this occurred in Nigeria during the second quarter of 2022. Meanwhile, the estimated CFR was approximately 0.03% (1/3413).

Global impact and public health responses

COVID-19 has had a significant impact around the world. In fact, the impacts have been unprecedented in modern history. Millions of people have died as a result of the pandemic, healthcare systems have been overwhelmed, and many countries have experienced rapid economic downturns. Many countries were unprepared for the scale of the virus and its rapid transmission, which resulted in protracted lockdowns, travel restrictions, and interruptions to daily life. The development of variations such as Delta and Omicron made it much more difficult to control the pandemic, despite the record-breaking speed at which vaccinations were produced.

The response to COVID-19 has involved a combination of public health measures, including widespread testing, contact tracing, quarantine, social distancing, and eventually, mass vaccination campaigns. Even though COVID-19 vaccines were developed and administered on an unprecedented scale, the global response has been largely unequal, and significant disparities have been seen in vaccine access between high and low-income countries.

On the other hand, monkeypox outbreaks have generally been more regionally contained, despite alarming rises in cases in areas where the virus had not previously been endemic. Monkeypox has not disrupted the world as much as COVID-19, even though it is dangerous, especially in immunocompromised individuals. The spread of monkeypox has been slowed down in part by the limited human-to-human transmission of the virus and the availability of smallpox vaccination, which provides some protection against the disease.

Most public health responses to monkeypox concentrate on containing the virus and providing vaccinations in affected regions. Although no specific treatments have been developed for monkeypox, it is possible to treat the disease with antiviral drugs developed for smallpox. Examples of public health efforts include educating at-risk populations, increasing surveillance, and administering vaccines to control outbreaks.

Furthermore, the outbreak of COVID-19 highlighted that pandemics are both biomedical matter and psychosocial crises. The psychological toll occurs from various and related factors such as fear of transmission, uncertainty, misinformation and the social consequences of infection status (Bhola et al. 2022; Aljaberi et al. 2023). The aforementioned factors influence the public's response towards containment strategies including vaccination, quarantine and isolation.

There is insufficient understanding, clinical results, and widespread fear and anxiety as a result of mortality reports during the initial period of the COVID-19 pandemic. Such responses are also common with mpox within regions with little exposure to this disease. Individuals were very worried about severe illness or death in addition to graphical display of pustular rashes, which has further increased the public's distress (Jesse and Obohwemu 2024; Liu et al. 2025). The uncertainty contributed to helplessness, which resulted in anxiety

disorders, depression and even few reported cases of individuals exhibiting symptoms related post-traumatic stress.

COVID-19 pandemic has highlighted the adverse impact of "infodemic". This means the rate of misinformation being spread is higher than factual information (Caceres et al. 2022). Panics ensued as a result of false narratives related to transmission, origins or vaccine safety. It resulted in individuals rebelling against public health guidance and distrustful of institutions (Caceres et al. 2022; Vasconcellos-Silva and Castiel 2020). Mpox has experienced similar challenges especially when connecting the disease to particular social or sexual group of individuals (Smith et al. 2024). This misrepresents the risks perception in addition to individuals being less likely to get medical attention.

Stigma is present in both of the aforementioned diseases, which worsen the negative psychological consequences. Individuals diagnosed with COVID-19 and healthcare workers have to avoid social interaction (Bagcchi 2020). Mpox on the other end experience stigma based on individuals' sexual orientation within certain communities, which exhibit similar stigma of HIV/AIDS. Such stigma exacerbate isolation, encourages secrecy in addition to resistance towards vaccination and testing (Orsini et al. 2024). It also results in psychological harm in the long term, which increases the stigma experienced by vulnerable populations.

Fear, stigma and misinformation have a direct adverse impact upon compliance with critical public health measures (Wasim et al. 2023). During COVID-19, distrust and psychological exhaustion, also known as pandemic fatigue result to individuals against quarantine or vaccination campaigns (Islam et al. 2021). Mpox exhibits parallel challenge in terms of individuals may refuse to quarantine and/or they may not vaccinate themselves due to stigma (Nerlich and Jaspal 2025). Therefore, mental health burden becomes an epidemiological driver, which plays a role in the spread and control of the disease.

The comparison of the two pandemics has revealed that mental health must be integrated into outbreak response planning. There is an equal significance in diagnostic testing and vaccination campaigns along with clear communication, community engagement and prior distribution of information that is accurate as well as psychosocial support. Messaging and protecting vulnerable group would decrease the level of stigma, which is critical to ensure more intervention compliance by individuals.

Conclusion

Mpox emergence post COVID-19 pandemic highlights the continuous challenges faced by the health systems in the world to address emerging and re-emerging infectious diseases. Despite mpox distinct clinical presentation in comparison to other pustular skin disorders, the outbreaks have demonstrated that physicians from a wide range of disciplines such as primary care, sexual health, dermatology and emergency medicine need to constantly remain attentive towards diagnosis and managing cases. Disregarding the awareness may results to delayed diagnosis and increased transmission.

Essentially, the various experiences of mpox and COVID-19 have highlighted the critical role of preparedness. The exponential spread of COVID-19 was the result of initial poor immunity coupled with its airborne transmission and emergence of variance that are highly transmissible. In comparison, despite the in-depth understanding of its characteristics and lower transmissibility, it remains a prominent pathogen in specific regions such as Africa. This is due to limited healthcare resources and access to vaccine. Such variance in global response indicates an imbalanced equality in the health care preparation. Higher income countries have a higher responds rate to address outbreaks by deploying vaccines quickly. Meanwhile, lower income countries are met with challenges and burdens.

The mpox outbreak reveals that despite its transmissibility does not reach pandemic level, it could still potentially have an adverse impact upon health, social and economy if ignored. Biomedical solutions are needed to contain the spread. This necessitates equitable vaccine distribution, strong diagnosis capability, detecting case in a rapid manner and efficient communication within the community in order to fight against misinformation and any stigmas. Complacency must be eliminated within the global health systems. COVID-19 has taught us the critical nature of early intervention, streamlined communications and international co-operations, all of which must be taken into consideration when developing strategies related to outbreak preparation.

The conclusion is that priorities must be placed on mpox rather than treating it as a second or localized priority. It is a test for the world to be able to respond to its outbreak by drawing the difficult COVID-19 lessons. The development of equitable, responsive public

health infrastructure and resilience are critical, and these are not limited to mpox but also other outbreak that is deemed inevitable.

From a significant standpoint, the threat by COVID-19 and mpox should not be regarded as equal. The world was not prepared for the transmissibility of COVID-19 and its mortality rate has made its pandemic to become historical case. Meanwhile, mpox limited its transmission between humans and majority of its transmission is confined into specific regions and risk groups. However, the resurgence of clade I within Africa and continuous transmission of clade II within non-endemic countries highlight the risk of underestimating the capability of zoonotic pathogens that circumvent diagnosis, vaccination and the resilience of the health system.

There are two essential conclusions that can be drawn from the aforementioned differences. Firstly, despite mpox does not have the capability to result in COVID-19 pandemic equivalent threat, international attention is still necessary to avoid entrenched transmission in the wider population. The second is the lessons that were drawn from the COVID-19 pandemic pertaining to the importance of preparation such as genomic surveillance, early case detection, equitable distribution of vaccines as well as investment into the health system capacity. Negate of such preparation increases the risk of mpox evolution into a more serious strain that may result in significant challenge to public health.

To summarize, despite mpox is not classified as the equivalent of COVID-19 in terms of threat level, it remains essential to be prepared globally. The comparison of the two pathogens has revealed the current progress while vulnerabilities are still present. Improving preparation will limit the spread of mpox as well as develop the collective capacity to address any future threats from the emergence of infectious disease, which is inevitable. Future research must emphasize improved genomic surveillance of mpox variants, comprehensive investigations of zoonotic reservoirs and transmission mechanisms, and assessments of vaccine immunogenicity and cross-protection against new clades. Table I represents comparative difference between COVID-19 and mpox.

Table I
Comparative table between COVID-19 and Mpox.

Feature	**COVID-19 (SARS-CoV-2)**	**Mpox (Monkeypox virus, MPXV)**
Causative agent	Novel coronavirus (SARS-CoV-2), Coronaviridae family. Single-stranded RNA virus, enveloped, novel coronavirus (SARS-CoV-2)	Monkeypox virus (MPXV) (Orthopoxvirus genus, Poxviridae family) Double-stranded DNA virus
First identification	China's Wuhan (December 2019)	Central and West Africa (Democratic Republic of Congo, 1970, first human case)
Transmission	Aerosols, respiratory droplets, intimate touch, infected surfaces, and seldom via fomites	bodily fluids, breathing droplets from extended contact, infected items, close skin-to-skin contact, and zoonotic overflow from wild animals
Incubation period	2–14 days (median 5 days)	5–21 days (median 7–14 days) (median 7–14 days) 5–21 days
Clinical presentation	Fever, cough, sore throat, dyspnea, loss of taste or smell, and exhaustion can all lead to pneumonia, acute respiratory distress syndrome, and multi-organ failure.	Headache, fever, lymphadenopathy (a crucial distinguishing factor), and rash that develops from macules to papules to vesicles to pustules to scabs
Complications	Myocarditis, ARDS, thromboembolism, and extended COVID syndromes around 0.5–2% overall (greater in older, immunocompromised, and unvaccinated individuals)	Sepsis, encephalitis, bronchopneumonia, secondary bacterial infection, and corneal infection (visual impairment)
Case fatality rate (CFR)	~0.5–2% overall (higher in elderly, immunocompromised, unvaccinated)	Clade I (Congo Basin) is more severe than Clade II (West African); historically, 1–11%
Global impact	WHO declared a public health emergency of international concern in January 2020, with over 770 million confirmed illnesses and over 7 million fatalities worldwide.	A public health emergency of international concern was declared in July 2022; since then, over 110 nations have been impacted, with thousands of cases beyond endemic areas. Since 2022

Variants/Clades and its Transmissibility impact	Omicron, Delta, Gamma, Beta, and Alpha (with sublineages) The variant waves cycle rapidly throughout the world with a lineage dominance by JN.1 between 2024 and 2025 Specific variants have risen within immune escape or transmissibility, which resulting in replacement waves.	Many sublineages of Clades I (Congo Basin, greater virulence) and II (West Africa, lesser severity) have been identified. The global trend is Clade IIb while Clade I.Ib is limited to Central and East Africa. It is being exported due to individual travels to other countries. Average transmissions between humans. The change in the genetics do not produce explosiveness that is similar to COVID-18.
Vaccines	Many (inactivated vaccinations, viral vectors, and mRNA) extensively used	Cross-protection is offered by smallpox vaccinations (JYNNEOS/Imvamune, ACAM2000); ring vaccination techniques are employed.
Treatment	Antivirals (molnupiravir, nirmatrelvir-ritonavir, and Remdesivir) and supportive care	For severe instances, supportive care and antivirals (tecovirimat, brincidofovir, and cidofovir)
Prevention and control	Lockdowns, mask use, mass vaccination, testing, tracking, and cleanliness	Public awareness, targeted immunization, contact tracking, infection prevention, and case isolation
Long-term concerns	Immunoevasive variations emerging, vaccine reluctance, and prolonged COVID	Stigma, possible endemicity outside of Africa, and restricted access to vaccines in low-income areas
Vaccine escape	There is a marked immune escape during infection level. The updated vaccine of JN.1/KP.2 remains effective against severe disease	Insufficient evidence pointing towards antigenic escape with JYNNEOS remains protective. The protection is higher if 2 doses are administered.

Availability of data and materials

The datasets used and/or analyzed during the study are available from the corresponding author on reasonable request

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Authors' contributions

H.Al-Momani, A.A, H.A – resources, conceptualization, original draft writing. H. Al-Momani, D.A, I.O,A.I.K,H.T and A.M.Z – review and editing.

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The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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