

REVIEW ARTICLE

Behavioral, Virologic, and Immunologic Factors Associated with the Acquisition and Severity of Mpox: A Tale of Africa and America

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Abstract

Background: Mpox (formerly monkeypox) has emerged as a critical public health issue worldwide, characterized by notable differences in acquisition and disease severity between Africa and the Americas. Understanding the interplay of behavioral, virologic, and immunologic factors is essential to addressing these disparities.

Aim: This review examines the behavioral, virologic, and immunologic determinants influencing Mpox acquisition and severity, with a focus on regional variations in Africa and the Americas.

Methodology: A narrative review was conducted using peer-reviewed articles, public health reports, and official guidelines published between 2019 and 2024. Key sources were identified via databases including PubMed, Scopus, and Google Scholar. Analysis centered on behavioral risk factors (e.g., sexual networks, wildlife exposure), virologic attributes (e.g., viral clades), and immunologic influences (e.g., vaccination status).

Results: The findings reveal distinct regional differences in Mpox transmission dynamics and outcomes. In Africa, zoonotic transmission is prominent, compounded by poor hygiene and under-resourced healthcare systems. In the Americas, outbreaks are driven predominantly by human-to-human transmission within sexual networks, particularly among men who have sex with men (MSM), and international travel. Virologically, the Central African clade demonstrates greater virulence than the West African clade, which has predominated recent global outbreaks. Immunologically, limited smallpox vaccination coverage in younger African populations has increased vulnerability, while partial cross-protection from smallpox vaccines in the Americas has mitigated disease severity to some extent.

Conclusion: Effective Mpox control necessitates region-specific public health strategies. Enhanced vaccination programs, improved healthcare infrastructure, and tailored interventions addressing behavioral and virologic drivers are critical. Global collaboration is imperative to mitigate Mpox's spread and burden while addressing socio-economic and epidemiological disparities.

Keywords: Mpox, Virologic factors, Immunologic response, Behavioral risk, Africa, America.

INTRODUCTION

Mpox, formerly referred to as monkeypox, is a zoonotic viral disease caused by the monkeypox virus (MPXV), a member of the Orthopoxvirus genus that includes the variola virus (smallpox) and vaccinia virus [1]. First identified in laboratory monkeys in 1958, human cases were reported starting in 1970, primarily in Central and West Africa [2]. Historically, Mpox was considered an endemic disease in specific African regions, causing sporadic outbreaks in rural communities, often linked to close contact with wild animals such as rodents and primates. However, recent outbreaks in non-endemic regions, including Europe and the Americas, have dramatically shifted the global public health landscape, propelling Mpox into international focus [3, 4].

Clinically, Mpox is characterized by a febrile illness, lymphadenopathy, and distinctive skin lesions resembling those of smallpox. Although the disease is generally self-limiting, clinical severity can range from mild symptoms to severe, life-threatening complications [5]. The determinants of Mpox acquisition, transmission, and severity are complex, involving behavioral, virologic, and immunologic factors. These determinants not only affect individual susceptibility but also shape broader epidemiological trends across different geographic regions.

In Africa, Mpox persists as an endemic zoonosis, with outbreaks primarily driven by zoonotic transmission from wildlife to humans. Conversely, the 2022 multi-country outbreak, especially in the Americas, was marked by sustained human-to-human transmission, often within specific social and sexual networks, such as among men who have sex with men (MSM) [6, 7]. These contrasting epidemiological patterns reflect broader disparities between Africa and the

Americas in terms of public health infrastructure, healthcare access, vaccination coverage, and social behaviors.

As of 2023, the Centers for Disease Control and Prevention (CDC) reported 99,518 global Mpox cases, underscoring the urgent need to address this evolving public health threat [9]. Understanding the behavioral, virologic, and immunologic factors that influence Mpox acquisition and severity is essential for designing effective interventions. These factors highlight the distinct challenges faced by Africa and the Americas, offering critical insights for global prevention and control strategies.

This review explores the key behavioral, virologic, and immunologic determinants of Mpox acquisition and severity, emphasizing the regional disparities between Africa and the Americas. By identifying and addressing these differences, we aim to contribute to the development of tailored and equitable public health interventions to mitigate the global impact of Mpox.

METHODOLOGY

Search and Selection Strategy

This narrative review investigates the behavioral, virologic, and immunologic factors that influence Mpox acquisition and severity in Africa and the Americas. To provide a comprehensive analysis of Mpox epidemiology in these regions, the review synthesizes data from peer-reviewed articles, public health reports, and official guidelines.

A structured literature search was conducted across multiple databases, including PubMed, Scopus, Google Scholar, and the World Health Organization (WHO) database. The search timeframe spanned from 2019 to 2024, with a particular focus on the significant outbreaks of 2022 and 2024. Search keywords included "Mpox,"

"monkeypox," "Africa," "Americas," "behavioral factors," "virologic factors," "immunologic factors," "viral clades," "vaccination," and "transmission dynamics." Gray literature from organizations such as the Centers for Disease Control and Prevention (CDC), WHO, and regional health ministries was also incorporated to ensure a thorough exploration of available evidence.

Inclusion and Exclusion Criteria

Inclusion Criteria

The inclusion criteria prioritized studies that addressed Mpox epidemiology with an emphasis on behavioral, virologic, and immunologic aspects in Africa and the Americas. Articles were included if they specifically analyzed risk factors, transmission dynamics, disease severity, and public health interventions. Only English-language studies with accessible full texts were selected.

Exclusion Criteria

Exclusion criteria ruled out articles focusing on other zoonotic diseases, studies unrelated to Africa or the Americas, and those lacking sufficient scientific rigor (e.g., anecdotal reports or opinion pieces).

Data Extraction and Analysis

Data extraction focused on key themes: behavioral risk factors (e.g., sexual networks, wildlife exposure), virologic characteristics (e.g., viral clade differences, mutation rates), and immunologic factors (e.g., vaccination coverage, immune responses). The findings were synthesized to emphasize regional variations in Mpox transmission dynamics and clinical outcomes. Thematic organization facilitated an in-depth examination of the influence of behavioral, virologic, and immunologic factors on Mpox acquisition and severity in both Africa and the Americas. This review acknowledges certain limitations. Publication bias may affect the

comprehensiveness of included studies, and data availability is uneven, particularly from low-resource settings in Africa. Additionally, emerging information from ongoing outbreaks may not be fully reflected in the analysis. Despite these challenges, this review provides valuable insights into the regional disparities and determinants of Mpox epidemiology.

Ethical Considerations

As this review exclusively utilized publicly available literature, ethical approval was not required. All included studies and data sources were appropriately cited to ensure academic integrity and transparency.

RESULTS AND DISCUSSION

Understanding Mpox Virus

The Mpox virus, a member of the **Orthopoxvirus** genus, shares its lineage with the variola (smallpox) and vaccinia viruses. This enveloped, double-stranded DNA virus exhibits a complex structure, comprising a central core, an outer envelope, and surface projections that facilitate host cell entry. Its genome, spanning approximately 190–200 kilobase pairs, encodes multiple proteins essential for viral replication and pathogenesis [10, 11]. While the Mpox virus shares significant genetic homology with other orthopoxviruses, distinct differences influence its clinical presentation and epidemiology.

The World Health Organization (WHO) has classified Mpox into two primary clades: **clade 1** and **clade 2**. These clades, representing phylogenetically distinct groups, vary in their geographic distribution, virulence, and transmission dynamics. The global Mpox outbreaks of 2022 and 2023 were primarily driven by clade 2, while clade 1 continues to circulate predominantly in Central Africa. Recently, cases linked to

travel in Africa have been identified in Sweden, Thailand, and Pakistan, highlighting the interconnected nature of Mpox epidemiology [12].

Central African Clade

The Central African clade (clade 1), endemic to regions such as the Congo Basin, is notable for its high virulence. It often causes severe disease characterized by extensive skin lesions and higher mortality rates compared to clade 2. Although zoonotic transmission—via contact with infected

animals or their bodily fluids—remains the primary mode of spread, human-to-human transmission can occur through close physical contact. While clade 1 has played a limited role in recent global outbreaks, it poses a substantial public health challenge in endemic regions due to its severity. Addressing these challenges requires enhanced surveillance, robust public health interventions, and improved healthcare infrastructure in affected areas [13].

Table 1: Characteristics of the two primary clades of Mpox virus

Aspect	Central African Clade	West African Clade
Prevalence	Predominant in Central Africa (e.g., Congo Basin)	Predominant in West Africa; recent outbreaks in the Americas
Geographic Distribution	Mainly Central Africa (e.g., Democratic Republic of Congo)	West Africa (e.g., Nigeria); increasingly observed in the Americas
Infectivity	Higher infectivity in endemic regions; more efficient human-to-human transmission in close-contact settings	Lower infectivity compared to Central African clade; less efficient human-to-human transmission
Disease Severity	Associated with more severe disease and higher case fatality rates	Generally causes milder disease; lower case fatality rates compared to the Central African clade
Symptoms	Severe symptoms including high fever, extensive skin lesions, and higher rates of complications	Milder symptoms with fewer complications; less extensive skin involvement
Mortality Rate	Higher mortality rate, particularly in resource-limited settings	Lower mortality rate; generally better outcomes due to milder disease
Transmission Dynamics	Often involves zoonotic transmission with higher risk in rural areas where contact with wildlife is common	Transmission is often related to close human-to-human contact, with less zoonotic involvement compared to Central African clade
Recent Outbreaks	Rarely reported outside endemic regions; less frequent global outbreaks	Recent global outbreaks, including in the Americas, highlighting its spread beyond endemic areas

[13, 14]

2. West African Clade

The West African clade of the Mpox virus, endemic to countries such as Nigeria, Ghana, and Cameroon, has been implicated in several recent outbreaks outside Africa. Compared to the Central African clade, the West African clade is associated with milder

disease, characterized by fewer complications and lower mortality rates. While zoonotic transmission remains the primary mode of spread, this clade has demonstrated a higher capacity for human-to-human transmission, particularly in densely populated regions [14].

The global Mpox outbreaks of 2022 and the resurgence in 2024 were predominantly driven by the West African clade. The 2022 outbreak showcased the clade's ability to spread rapidly across continents, including North America and Europe, via human-to-human transmission. Similarly, the 2024 resurgence involved ongoing transmission in previously affected areas alongside the emergence of new cases globally [15].

The relatively mild disease course associated with the West African clade has informed public health responses, prioritizing containment measures and vaccination campaigns over emergency treatments. This approach underscores the importance of sustained vigilance, enhanced epidemiological surveillance, and targeted vaccination strategies to effectively control Mpox outbreaks and mitigate their global impact [16].

Mpox in Africa

Mpox, first identified in 1958 in laboratory

monkeys, derives its name from this origin, though its primary reservoirs are rodents. The first human case was reported in 1970 in the Democratic Republic of the Congo (DRC). Since then, Mpox has been endemic in several African nations, including the DRC, Nigeria, Cameroon, and the Central African Republic (CAR), predominantly in rural, forested areas [1, 2]. In Africa, two distinct clades of the virus are recognized: the **Central African (Congo Basin) clade** and the **West African clade**. The Central African clade, primarily found in the DRC and neighboring countries, is associated with higher transmissibility and more severe disease, with a case-fatality rate reaching up to 10%. In contrast, the West African clade, predominant in Nigeria and surrounding nations, causes milder disease with a case-fatality rate below 4% [17, 18]. Figure 1 is a map of Africa showing Mpox cases on the continent between January and June, 2024 [19].

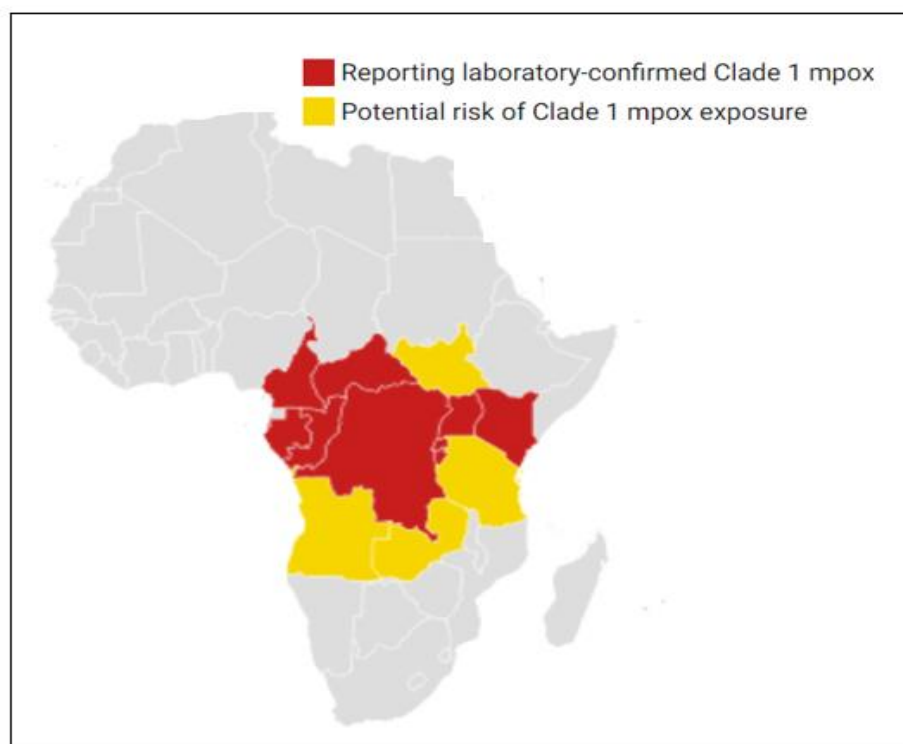


Figure 1: Mpox cases in Africa between January and June, 2024 [19]

Emergence of Clade Ib

A new variant, **clade Ib**, identified within the Central African clade, has exacerbated the ongoing Mpox crisis in Africa. This variant is suspected to exhibit greater virulence. Since early 2023, the DRC has reported over **22,000 cases and more than 1,200 deaths**, predominantly linked to clade Ib [1, 2, 5]. The outbreak has expanded to neighboring countries, including Burundi, Kenya, and Rwanda, highlighting the virus's capability for cross-border transmission and environmental adaptation. Cases have been increasingly reported in urban centers, reflecting the virus's capacity to spread across diverse demographics and geographical settings [19].

Regional and Global Distribution

While clade Ib dominates in Africa, **clade II** remains globally significant. In early 2024, the United States reported over 1,000 cases of clade II, reflecting its global epidemiological relevance [20]. The DRC continues to bear the brunt of Mpox in Africa, with **1,754 confirmed cases reported between January and June 2024**—part of an estimated **2,000 cases continent-wide** during this period [4, 14]. The Africa CDC estimates a total of **17,541 cases**, 96% of which occurred in the DRC [21]. Notably, the virus's eastward spread into regions such as Kenya and Rwanda marks a critical development, emphasizing the need for vigilant monitoring and containment efforts in densely populated and mobile populations.

Factors Contributing to Persistent Spread in Africa

1) Animal-Human Interface

Mpox remains primarily zoonotic, with humans acquiring the virus through contact with infected animals such as rodents and primates. Practices such as hunting and bushmeat consumption heighten exposure

risks, particularly in rural areas.

2) Limited Vaccination Coverage

After the eradication of smallpox in 1980, vaccination campaigns that provided cross-protection against Mpox ceased. This has resulted in waning immunity among populations born post-eradication, creating a growing pool of susceptible individuals [22, 23].

3) Healthcare Infrastructure Constraints

Inadequate healthcare infrastructure in many African regions hampers early detection, case isolation, and containment efforts. This has allowed localized outbreaks to escalate, especially when cases reach urban centers where larger outbreaks can occur.

4) Overlapping Health Crises

The persistence of Mpox in Africa is often overshadowed by competing public health emergencies such as malaria, cholera, and Ebola. This overlap frequently delays comprehensive Mpox responses. However, the resurgence of cases, particularly in Nigeria since 2017, has re-focused attention on the disease, underscoring the need for tailored public health interventions [17]. The increasing prevalence and virulence of Mpox in Africa, particularly with the emergence of clade Ib, underscore the urgency of strengthened surveillance, vaccination initiatives, and improved healthcare systems to mitigate the impact of this re-emerging zoonotic disease.

Mpox in the Americas:

Before 2022, Mpox cases outside Africa were sporadic and often linked to travel or animal importation. However, the epidemiological landscape changed dramatically with the global outbreak that began in early 2022. This outbreak, which included significant clusters in the Americas, marked a turning point in the virus's global

spread, affecting both North and South America, particularly the United States and Brazil [22].

Emergence of Mpox in the Americas

In May 2022, the first confirmed cases of Mpox were reported in non-endemic countries, beginning in Europe and quickly spreading to the Americas. By mid-2022, the World Health Organization (WHO) declared the multi-country outbreak a **Public Health Emergency of International Concern (PHEIC)**. The United States became the

epicenter of Mpox in the Western Hemisphere, with over **30,000 reported cases by the end of 2022**, spread across 47 states and territories (Figure 2) [24]. The outbreak was predominantly caused by **clade II**, known for human-to-human transmission, particularly through close physical or sexual contact. High-risk populations, including **gay, bisexual, and men who have sex with men (MSM)**, were disproportionately affected in the U.S. [25].

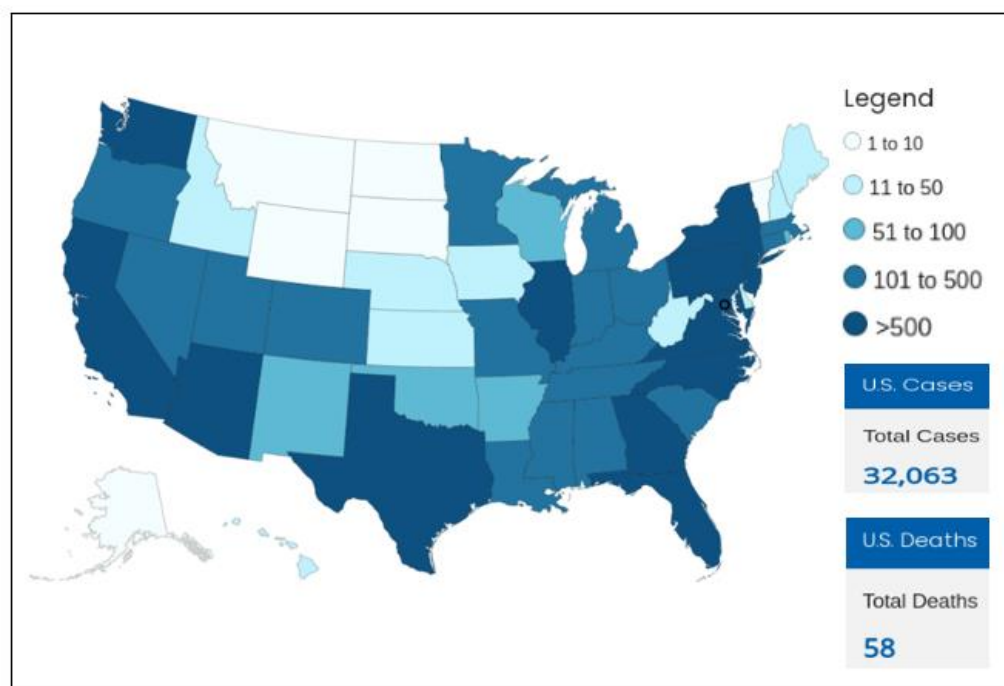


Figure 2: Mpox cases in the United States by the end of 2022 [25].

Between January and June 2024, a resurgence of Mpox cases in the United States resulted in **1,900 confirmed clade II cases**, primarily among unvaccinated high-risk individuals [26]. Ongoing surveillance, including wastewater monitoring, detected viral DNA at three sites in California and Illinois, though detection rates remained low. These findings suggest minimal community spread, with Mpox transmission largely confined to localized outbreaks among high-

risk populations. Importantly, all cases reported in the U.S. have been linked to clade II, with no detections of the more severe clade I strain, which remains endemic to the Democratic Republic of the Congo (DRC) and neighboring African countries [27]. The U.S. Centers for Disease Control and Prevention (CDC) currently assesses the risk of clade I Mpox in the U.S. as "very low," given existing containment measures and limited geographical overlap [12, 26].

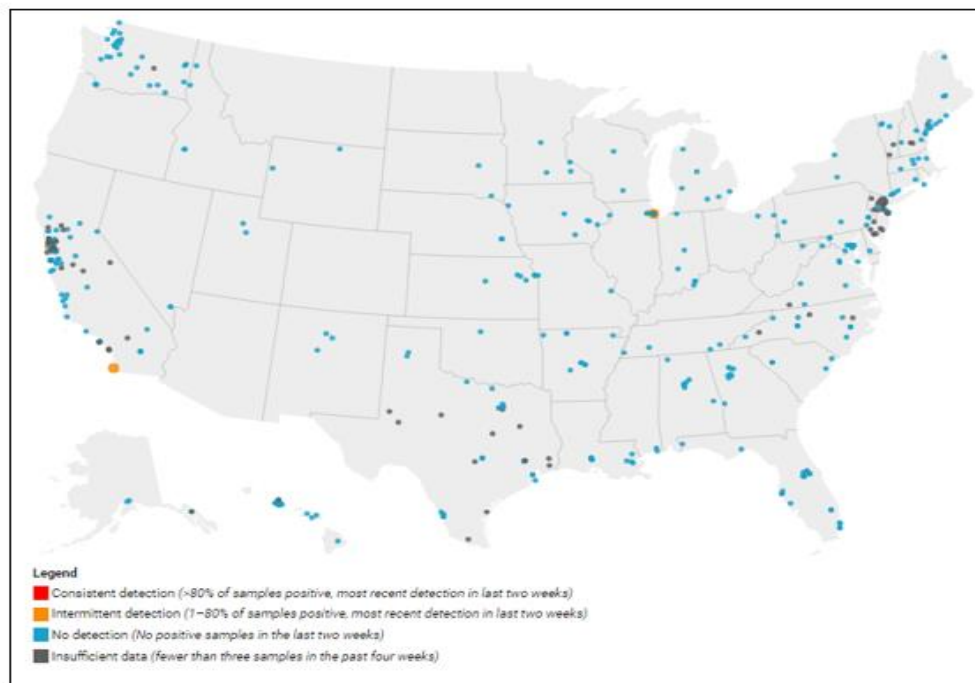


Figure 3: The map of the United States showing Mpox virus detection in wastewater between July 10 and August 6, 2024 [27].

South America also experienced a significant Mpox outbreak, with **Brazil** emerging as the hardest-hit country. Dense urban environments, delayed vaccine rollouts, and healthcare disparities contributed to the rapid spread of the virus. Brazilian health authorities partnered with international organizations to mitigate the outbreak, but certain regions faced prolonged transmission compared to North America. Countries such as **Mexico and Peru** also reported substantial Mpox cases during the 2022 outbreak, albeit on a smaller scale. However, disparities in healthcare access and public health interventions posed challenges to containment efforts across the region [29].

Factors Driving the Outbreak in the Americas

The outbreak in the Americas revealed novel epidemiological dynamics that differed from the traditional zoonotic transmission observed in Africa. These patterns included:

1. Human-to-Human Transmission

Unlike the zoonotic transmission typically associated with Mpox in Africa, the Americas outbreak was primarily driven by human-to-human transmission. Close physical contact, particularly sexual contact, was a significant driver of spread. The outbreak highlighted the role of **social and sexual networks**, especially among MSM populations, in sustaining viral transmission [30].

2. Urban Transmission Dynamics

The outbreak in the Americas predominantly affected urban populations. High population density, mobility, and interconnected social networks facilitated the rapid spread of Mpox in metropolitan areas across countries such as the United States, Brazil, and Mexico. This urban transmission pattern marked a departure from the rural and forest-associated outbreaks seen in Africa.

3. Mild Clinical Presentation

While Mpox in the Americas caused

severe disease in some cases, particularly among immunocompromised individuals, the majority of cases were mild. Symptoms such as fever, rash, and lymphadenopathy often resolved without significant complications. This mild presentation, however, posed challenges for public health responses, as the disease could be misdiagnosed or mistaken for other conditions, delaying diagnosis and control efforts [31].

Public Health Interventions

The widespread use of the **JYNNEOS (MVA-BN)** smallpox vaccine played a critical role in controlling the outbreak in the Americas. Targeted vaccination campaigns focused on high-risk populations, such as MSM and healthcare workers, curbed transmission and reduced case numbers by late 2022 [28]. Despite this progress, gaps in vaccine access and coverage—especially in regions like Brazil and parts of South America—underscored the need for equitable global distribution of vaccines and public health resources. The Mpox outbreak in the Americas highlighted the virus's potential for rapid global dissemination and revealed key epidemiological patterns distinct from traditional African outbreaks. Enhanced public health measures, including targeted vaccination and surveillance, were instrumental in mitigating the outbreak's impact. However, the disparities in healthcare access across the Americas emphasize the importance of robust and equitable public health systems to prevent future outbreaks.

Behavioral factors associated with acquisition and severity of Mpox

Behavioral factors significantly influence the acquisition and severity of Mpox, shaping its transmission patterns and clinical outcomes in different regions. The global epidemiology of Mpox reveals stark contrasts

between endemic regions, such as Africa, and areas experiencing recent outbreaks, notably the Americas. These behavioral factors are intertwined with disparities in healthcare access, cultural norms, societal behaviors, and population dynamics. A comparative analysis of these regions underscores the critical role of behavioral patterns in Mpox epidemiology.

Close Physical Contact and High-Risk Behaviors

Close physical contact is a well-established transmission route for Mpox. However, the nature of such contact differs between Africa and the Americas. In recent outbreaks in the Americas, intimate skin-to-skin contact during sexual activity has been a predominant driver of transmission, particularly among men who have sex with men (MSM). The clustering of cases within sexual networks highlights the amplifying role of such high-risk behaviors in viral spread [31]. Evidence suggests that viral DNA is present in bodily fluids such as semen, blood, and respiratory secretions, indicating that sexual contact plays a significant role in transmission. Skin-to-skin interactions, particularly during sexual activity, likely facilitate the direct inoculation of the virus, as lesions have been frequently reported in genital, rectal, and oropharyngeal areas before becoming widespread [32, 33].

Public health responses in the Americas have faced the dual challenge of addressing high-risk behaviors while avoiding stigmatization of MSM communities. Labeling Mpox as solely a sexually transmitted infection (STI) risks alienating affected populations and perpetuating harmful stereotypes. High-risk behaviors, including multiple sexual partners and attendance at group gatherings, have been linked to the rapid spread of Mpox in these

communities, necessitating nuanced health messaging [34].

In Africa, close physical contact is more commonly observed in non-sexual contexts, such as within households. Family members, especially caregivers, are at heightened risk of contracting Mpox due to prolonged exposure while tending to infected individuals. Limited access to personal protective equipment (PPE) in resource-poor settings exacerbates this risk. Unlike the Americas, sexual transmission is less commonly reported, and Mpox transmission is often associated with caregiving roles and close-knit family interactions [35].

Cultural and Traditional Practices

Cultural and traditional practices significantly influence Mpox transmission dynamics. In many parts of Africa, traditional funeral practices involve direct contact with deceased individuals, including washing and handling bodies, which can expose family members to infectious materials. These rituals, deeply embedded in cultural norms, complicate public health efforts to limit Mpox transmission during funerals and communal gatherings [36].

Additionally, subsistence hunting and the consumption of bushmeat are common in many African communities, creating another pathway for Mpox transmission. Handling and preparing bushmeat, including infected rodents and primates, can directly expose individuals to the virus. Bushmeat practices are not merely cultural but also an economic necessity, posing challenges for public health interventions aimed at mitigating zoonotic risks without threatening livelihoods.

In contrast, Mpox-related human-animal interactions in the Americas are less linked to subsistence but instead stem from the exotic pet trade and international travel. For instance, imported exotic animals, such as

rodents, have been implicated as potential reservoirs for Mpox. While zoonotic transmission is not a primary driver of recent outbreaks in the Americas, the potential remains, particularly in areas with lax wildlife trade regulations [37].

Healthcare-Seeking Behavior

Access to healthcare profoundly affects the transmission and severity of Mpox. In developed regions of the Americas, robust healthcare systems facilitate early diagnosis, treatment, and containment. Diagnostic tools, vaccines like JYNNEOS (MVA-BN), and antiviral therapies are readily available, enabling prompt interventions that mitigate disease severity and curtail outbreaks.

In contrast, limited healthcare access in many parts of Africa presents significant barriers to Mpox control. Geographical and infrastructural challenges, coupled with insufficient healthcare resources, often result in delayed diagnosis and treatment. These delays can lead to increased household transmission, more severe clinical outcomes, and unchecked spread within communities. Moreover, the absence of widespread access to vaccines and antiviral treatments exacerbates these challenges, leaving many cases undiagnosed and untreated [38].

Stigmatization and Delayed Diagnosis

Stigma surrounding Mpox poses a significant barrier to timely healthcare-seeking behavior in both Africa and the Americas. In the Americas, the association of Mpox with sexual transmission and MSM communities has heightened fears of stigmatization. This has led some individuals to delay seeking medical care, increasing the risk of further transmission. Public health campaigns must strike a delicate balance: raising awareness without reinforcing stigmatizing narratives that deter vulnerable populations from accessing care.

In Africa, stigma is often rooted in misinformation and cultural beliefs. In rural areas, Mpox symptoms may be misattributed to supernatural causes or other illnesses, delaying diagnosis and treatment. Low health literacy further compounds the issue, as communities may lack basic knowledge about Mpox transmission and prevention. Fear of ostracism can deter individuals from seeking medical attention, perpetuating the cycle of delayed diagnosis and viral spread [39].

Population Density and Mobility

Population density and mobility significantly influence Mpox transmission dynamics in both regions. Urbanization in Africa has led to the growth of densely populated informal settlements where poor sanitation, overcrowding, and inadequate healthcare access facilitate viral spread. In such settings, isolating infected individuals becomes challenging, increasing the likelihood of widespread transmission.

In the Americas, high mobility and international travel played a pivotal role in the 2022 global Mpox outbreak. Dense metropolitan areas, combined with frequent cross-border movement, enabled the rapid dissemination of the virus. The interplay of high population density and mobility underscores the importance of targeted interventions to curb Mpox transmission in urban and interconnected regions [40].

Public Awareness and Education

Public awareness and education are critical in shaping responses to Mpox. In Africa, low awareness levels and widespread misinformation hinder preventive efforts. Public health campaigns, where present, are often ineffective or underfunded, leaving communities uninformed about Mpox risks and transmission. This lack of knowledge perpetuates risky behaviors and undermines

containment efforts.

Conversely, in the Americas, public health campaigns have successfully raised awareness, contributing to early detection and improved outbreak management. However, heightened awareness has sometimes led to panic and stigmatization, particularly among populations perceived to be at higher risk. Balancing accurate information with efforts to reduce stigma remains a key challenge for public health authorities [41].

Virologic factors associated with acquisition and severity of Mpox

The virologic factors associated with the acquisition and severity of Mpox vary significantly across regions, influenced by viral strain variability, mutations, and environmental conditions. In Africa, where Mpox has been endemic for decades, these factors have shaped the disease's epidemiology, often resulting in severe clinical outcomes. Conversely, recent outbreaks in the Americas and other non-endemic regions have been characterized by distinct virologic dynamics, including strain differences and evolutionary adaptations that have facilitated human-to-human transmission.

Viral Strain Variability

Viral strain variability is one of the most critical virologic factors influencing Mpox acquisition and severity. Mpox is divided into two primary clades with distinct geographical distributions, transmission dynamics, and clinical outcomes: the Central African (Congo Basin) clade and the West African clade [1, 31].

Central African Clade

The Central African (Congo Basin) clade, circulating in countries like the Democratic Republic of the Congo (DRC), is associated with more severe disease outcomes and

higher case fatality rates. This clade is responsible for many endemic cases in Africa and poses significant public health challenges due to its potential for severe illness, particularly in resource-limited settings. Patients infected with this clade frequently exhibit pronounced febrile illness, widespread rash, and complications such as encephalitis and secondary bacterial infections. The case fatality rate for the Central African clade can reach up to 10%, especially in regions with limited healthcare infrastructure and access to supportive care.

The greater severity of the Central African clade is likely influenced by both viral and host factors. This strain exhibits higher transmissibility and pathogenicity, but coexisting conditions in endemic regions exacerbate its impact. High rates of co-infections with diseases like HIV, malaria, or tuberculosis compromise the immune system, leading to elevated viral loads and severe disease progression. Furthermore, the lack of widespread vaccination coverage and limited healthcare services in many African regions delays early detection and treatment, increasing the likelihood of severe outcomes and mortality.

West African Clade

The West African clade, responsible for recent outbreaks in developed regions such as the Americas, typically results in milder disease with lower mortality rates. The case fatality rate for this clade is around 1%, and most patients experience self-limiting illness characterized by fever, rash, and lymphadenopathy. Severe cases and complications are less frequent compared to the Central African clade.

Despite its milder presentation, the West African clade has demonstrated an ability to spread rapidly, particularly in densely populated, non-endemic settings. For

instance, the 2022 outbreaks in the Americas highlighted its efficient human-to-human transmission, especially within sexual networks involving men who have sex with men (MSM). Although the clinical outcomes in these outbreaks were less severe, the rapid dissemination underscores the need for continuous monitoring of viral evolution and transmission patterns. Robust healthcare systems in developed regions, coupled with vaccination programs providing cross-protection through the smallpox vaccine, have mitigated severe cases. However, the challenges posed by rapid spread in these regions emphasize the importance of understanding the virologic factors underpinning transmission [42].

Mutation and Adaptation

Mutation and adaptation of the Mpox virus are crucial virologic factors that influence its acquisition and severity. Like other viruses, Mpox possesses the potential to evolve, and mutations in its genome may enhance its adaptability to new hosts, environments, and transmission routes. Historically, Mpox outbreaks outside Africa were sporadic and largely attributed to zoonotic transmission from infected animals. However, during the 2022 outbreaks in the Americas and Europe, the virus exhibited an unusual capacity for sustained human-to-human transmission, often within social and sexual networks. Researchers speculate that mutations in the viral genome may have facilitated this shift, enabling the virus to spread more effectively between humans. Changes in viral surface proteins, which enhance binding to human cells, have been suggested as potential drivers of increased transmissibility. Furthermore, mutations affecting the virus's ability to evade host immune responses could play a role in sustaining human-to-human transmission,

particularly among immunocompromised individuals. While Mpox is not as transmissible as respiratory viruses like SARS-CoV-2, the potential for viral adaptation necessitates continued genomic surveillance. The rapid spread of Mpox in developed regions highlights the importance of understanding how mutations influence its transmissibility and virulence. Research into viral evolution and genomic changes is essential for designing effective public health responses and vaccines [43].

Viral Load and Infectivity

Viral load—the quantity of virus present in an infected individual—is another critical factor influencing the severity of Mpox and its transmission potential. Individuals with higher viral loads, particularly in their skin lesions, are more likely to experience severe disease and are more infectious to others.

Higher Viral Loads and Severe Disease

In severe Mpox cases, individuals often exhibit significantly higher viral loads, which correlate with extensive and prolonged viral shedding. This prolonged shedding increases the duration during which an infected person can transmit the virus, raising the risk of spread within close-contact settings. In Africa, where intra-household transmission is common, high viral loads in symptomatic individuals frequently lead to family-wide outbreaks. Co-infections with HIV—prevalent in many African regions—further compound this issue. Immunocompromised individuals, such as those living with HIV, often have reduced immune responses, allowing for greater viral replication and elevated viral loads. This dynamic not only worsens clinical outcomes but also enhances the likelihood of further transmission within resource-limited settings.

Lower Viral Loads in Developed Regions

In contrast, most Mpox cases in developed regions like the Americas have been reported

among otherwise healthy individuals, who typically exhibit lower viral loads. While this correlates with milder disease presentations, severe cases with high viral loads have still been observed in individuals with underlying health conditions or compromised immunity. These individuals are more likely to experience prolonged viral shedding, increasing the risk of secondary transmission within close-contact networks, such as sexual partners or household members [44].

Stability and Environmental Transmission

The stability of the Mpox virus under different environmental conditions significantly influences its transmission dynamics. The virus is relatively hardy and can survive on surfaces for extended periods, particularly in cool, dry environments. This stability increases the risk of transmission through fomites, such as clothing, bedding, or shared household items, especially in densely populated areas.

Environmental Stability in Endemic Regions

In Africa, environmental factors like heat, humidity, and rainfall patterns can influence viral survival and transmission. For instance, rural communities with limited access to clean water and sanitation may experience prolonged viral persistence on surfaces, elevating the risk of fomite-based transmission. Additionally, cultural practices such as traditional funeral rites—which often involve direct contact with the deceased—can increase exposure to the virus. These environmental and cultural factors underscore the need for targeted public health interventions in endemic regions.

Environmental Stability in Non-Endemic Regions

In the Americas, the virus's environmental stability has contributed to its spread in urban environments where individuals live or work

in close proximity. Shared living spaces, such as shelters, dormitories, and healthcare facilities, are particularly vulnerable to environmental transmission. Contaminated surfaces and objects frequently touched by multiple people, such as doorknobs and communal equipment, can facilitate viral spread. These settings require rigorous infection control measures, including disinfection protocols and public awareness campaigns, to mitigate transmission risks [45].

Implications for Public Health

Understanding the virologic factors influencing Mpox acquisition and severity is critical for tailoring public health strategies. The variability between the Central African and West African clades highlights the need for region-specific interventions. Genomic surveillance and research into viral mutations are essential for anticipating and mitigating the virus's evolutionary adaptations. Additionally, addressing factors like viral load and environmental stability through improved healthcare access and infection control measures can significantly reduce transmission and severity.

Immunologic factors associated with Mpox severity

Immunologic factors significantly influence the severity and outcomes of Mpox infections, with notable differences observed between populations in Africa and the Americas. These differences stem from variations in pre-existing immunity, co-infections such as HIV, and the body's innate and adaptive immune responses. Additionally, genetic predispositions and comorbidities, including malnutrition, further shape the immunologic landscape. This section examines the major immunologic factors associated with Mpox severity and highlights regional disparities that elucidate why certain populations are

more vulnerable to severe disease outcomes.

Pre-existing Immunity

Pre-existing immunity, largely determined by prior smallpox vaccination, is a key determinant of Mpox severity. Smallpox vaccination, administered extensively before smallpox eradication in 1980, offers partial cross-protection against Mpox due to the immunologic similarities between the two Orthopoxviruses.

In developed regions such as the Americas and Europe, older adults who received the smallpox vaccine decades ago retain some residual immunity to Mpox. Studies have shown that this immunity reduces disease severity, resulting in milder symptoms, faster recovery, and lower mortality rates compared to unvaccinated individuals. Despite the waning of vaccine-induced immunity over time, these benefits are still observed. However, younger populations born after 1980 lack this protection, as routine smallpox vaccination ceased following the disease's eradication. This has left these individuals more susceptible to Mpox, contributing to widespread transmission and severe cases during recent outbreaks in the Americas, particularly among unvaccinated younger adults [46].

In Africa, where Mpox has been endemic for decades, the landscape of pre-existing immunity differs markedly. Smallpox vaccination campaigns in many African countries were less extensive or unevenly distributed compared to developed regions, leaving a larger proportion of the population vulnerable to Mpox infection. Generational waning of vaccine-derived immunity further exacerbates susceptibility, particularly among younger individuals in endemic areas. The lack of comprehensive vaccination coverage, coupled with limited healthcare infrastructure, poses significant challenges

for controlling Mpox outbreaks. This gap in immunity leaves populations in these regions more vulnerable to severe Mpox, particularly in Central and West Africa where the virus circulates regularly. The absence of robust vaccination campaigns in underdeveloped areas continues to hinder efforts to curb ongoing and future outbreaks effectively.

HIV Co-infection and Immunosuppression

HIV co-infection is a critical immunologic factor that exacerbates the severity of Mpox, particularly in Africa where HIV prevalence is high [47]. The interaction between HIV and Mpox significantly complicates the immune response, resulting in worse disease outcomes for co-infected individuals.

In Africa, Mpox infections are often more severe in individuals with HIV, especially those with poorly controlled HIV or who lack access to antiretroviral therapy (ART). Immunosuppression caused by HIV undermines the body's ability to mount an effective defense against Mpox, leading to prolonged illness, severe symptoms, and increased risk of complications, including secondary infections and death. HIV-positive individuals are more likely to have higher viral loads of Mpox, enabling prolonged viral shedding and greater infectiousness. This unchecked viral replication facilitates extensive viral dissemination within the body, manifesting in severe clinical presentations such as widespread skin lesions, pneumonia, and encephalitis. In resource-limited settings where access to ART is constrained, the combination of Mpox and HIV significantly raises the case fatality rate among co-infected individuals [48].

Conversely, in developed regions like the Americas, HIV-positive individuals with access to ART typically experience better outcomes when infected with Mpox. ART

restores immune function, enabling the body to better control Mpox infection. As a result, HIV-positive individuals in these settings are less likely to experience severe outcomes, though they may still face higher risks compared to HIV-negative individuals. While HIV co-infection remains a risk factor for severe Mpox in developed regions, widespread access to ART has mitigated its impact. This underscores the importance of ensuring HIV treatment accessibility to reduce the severity of Mpox in HIV-positive populations globally [49, 50].

Innate and Adaptive Immune Responses

The interplay between the innate and adaptive immune systems is pivotal in determining Mpox severity. Severe cases are often characterized by dysregulated immune responses, including an overproduction of inflammatory cytokines, referred to as a "cytokine storm." This hyperinflammatory state can lead to tissue damage, multi-organ failure, and death, particularly in individuals with compromised immune systems.

During severe Mpox infections, excessive cytokine production—such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α)—can drive systemic inflammation, damaging vital organs like the lungs and liver. This dysregulated response is more commonly observed in individuals with weakened immunity, including those with HIV or malnutrition, both of which are prevalent in Africa. Malnutrition exacerbates immune dysfunction by impairing the production of immune cells and proteins necessary to combat the virus effectively. Additionally, co-infections with endemic diseases such as malaria or tuberculosis further compromise the immune system's ability to respond adequately to Mpox [38].

In contrast, individuals in developed regions generally benefit from better

nutritional status and fewer comorbidities that impair immune function. Consequently, the immune response to Mpox in these populations is often more controlled, reducing the likelihood of severe inflammatory reactions. However, individuals with pre-existing inflammatory or autoimmune conditions may experience exacerbated immune responses, leading to complications. The availability of immunomodulatory treatments in developed regions, such as corticosteroids or biologics, plays a crucial role in managing these severe cases. For example, interventions targeting cytokine storms can prevent organ damage and improve outcomes. Unfortunately, such treatments are often unavailable in resource-limited settings, contributing to higher mortality rates in severe Mpox cases in Africa.

Genetic Susceptibility

Emerging evidence suggests that genetic factors may influence an individual’s susceptibility to severe Mpox infection. Polymorphisms in genes associated with immune response pathways, particularly those

involved in antiviral defenses, may predispose certain individuals to worse outcomes. Genetic variability affects how the immune system detects and responds to Mpox. For instance, differences in the production of interferons—key molecules in antiviral immunity—can impact the body’s ability to control viral replication. Reduced interferon responses may allow the virus to replicate more efficiently, leading to more severe disease. Additionally, variations in the expression of viral entry receptors on host cells may influence susceptibility to infection. Some populations may carry genetic variants that render them more vulnerable to Mpox, although the specific genes involved remain an area of active research [40, 42]. Understanding these genetic factors is crucial for identifying at-risk groups and developing targeted interventions. For instance, genomic studies could inform vaccine strategies or therapeutic development aimed at enhancing antiviral immunity in genetically susceptible populations.

Table 2: Summary of Factors associated with the acquisition and severity of Mpox in Africa and the Americas

Factor	Category	Africa	Americas
Behavioral	Human-Animal Interaction	Subsistence hunting and reliance on bushmeat are prevalent, increasing direct contact with infected wildlife.	The pet trade involving exotic animals and international travel are primary exposure routes. These factors introduce the virus into new areas through less. Mode of transmission largely associated with networks of men who have sex with men (MSM)
	Healthcare Access and Practices	Limited healthcare access results in delayed diagnosis and treatment, exacerbating outbreaks	Advanced healthcare systems enable quick identification and containment, though they face challenges with imported cases and ensuring access to remote areas.
	Public Awareness and Education	Misinformation and lower literacy rates hinder effective dissemination of preventive information	Higher awareness and education levels facilitate early reporting, though they may also lead to panic and misinformation spread through social media.

Factor	Category	Africa	Americas
Virologic	Virus Strain Variability	The presence of more virulent strains like the Congo Basin strain leads to higher morbidity and mortality.	Encounter primarily with the West African strain, which is less virulent, but still poses significant health risks due to lack of immunity.
	Mutation and Adaptation	Mutations may arise due to close human-animal interactions and environmental pressures.	The potential for mutations that enhance human-to-human transmission poses a significant threat in urban settings.
	Environmental Stability	The virus's resilience in diverse climates can complicate containment efforts.	Environmental controls and infrastructure help reduce transmission, though imported cases can introduce new challenges.
Immunology	Pre-existing Immunity	Lower rates of historical smallpox vaccination reduce cross-protection	Previous vaccination programs provide some immunity, though waning over generations reduces effectiveness.
	Host Immune Response:	Nutritional deficiencies and genetic factors may compromise immune responses, increasing severity.	Generally better nutritional status and healthcare access support more robust immune responses, though lifestyle diseases can still impact outcomes.
	Comorbidities:	Higher prevalence of HIV and malnutrition exacerbates disease severity.	Chronic conditions like diabetes and obesity can affect immune function, but effective management mitigates some risks.

[6, 20]

Disparities in Mpox Outcomes

Mpox outcomes differ markedly between Africa and the Americas due to a range of interconnected factors, including mortality rates, healthcare infrastructure, access to medical care, vaccination coverage, and socioeconomic conditions. These disparities are a result of stark contrasts in how the disease is managed, how it spreads, and how public health systems respond to it. The epidemiology of the virus plays a crucial role in shaping these outcomes, with the Central African clade, which is more virulent, being endemic to Africa, and the West African clade, which causes milder disease, responsible for recent outbreaks in developed countries [7, 39].

1. Mortality Rates

One of the most striking disparities in Mpox outcomes between Africa and the Americas is the difference in mortality rates. Mortality from Mpox is significantly higher in underdeveloped

regions, particularly in Central Africa, where the more virulent Central African clade predominates. In these regions, the combination of viral virulence, underlying comorbidities, and insufficient healthcare resources creates a "perfect storm" that leads to higher mortality. The Central African clade has historically been associated with more severe disease and higher case fatality rates. In Central Africa, mortality rates can reach as high as 10%, largely driven by the aggressive nature of the viral strain and the lack of sufficient medical resources for treating severe cases. In contrast, the West African clade tends to cause milder illness with a much lower mortality rate, typically less than 1%.

In Africa, this disparity is exacerbated by high rates of co-infections, such as HIV, which compromise immune function, making it more difficult for individuals to recover from Mpox. Additionally, several other factors contribute to the elevated mortality

rates in Africa. Limited access to healthcare, delays in medical interventions, and insufficient diagnostic capabilities increase the likelihood of severe disease outcomes. The burden of other comorbidities, such as malnutrition, tuberculosis, and malaria, weakens patients, rendering them more vulnerable to complications and death [3].

In contrast, the Americas, particularly developed countries, experience significantly lower mortality rates during Mpox outbreaks. Most cases in these regions have been linked to the less virulent West African clade, which generally results in milder disease presentations. A major factor in the lower mortality rate in the Americas is the robust healthcare infrastructure, which enables early diagnosis and timely interventions. Developed countries like the United States have extensive medical resources, including early diagnosis, supportive treatments, and better management of complications, which prevent fatalities. Furthermore, these regions are equipped with more effective public health measures, including isolation protocols and the use of vaccines to control outbreaks, all of which help reduce mortality. While Mpox can still be severe in immunocompromised individuals or those with underlying health conditions, the mortality rate in these regions remains considerably lower than in Central Africa, where healthcare resources are more constrained [21].

2. Healthcare Infrastructure

The disparity in healthcare infrastructure between developed and underdeveloped countries is a key determinant of Mpox outcomes. Effective diagnosis, treatment, and management of Mpox cases depend heavily on healthcare resources, which vary significantly between Africa and the Americas. In many African regions, especially those where Mpox is endemic, healthcare

infrastructure is inadequate to effectively manage the disease. Limited access to diagnostic tools, a shortage of personal protective equipment (PPE), and insufficient isolation facilities to prevent the spread of the virus contribute to poor outcomes. Without reliable diagnostic capabilities, Mpox cases often go undetected until they reach advanced stages, delaying treatment and increasing the risk of severe disease. Moreover, healthcare workers in these areas frequently lack access to vaccines, such as the modified vaccinia Ankara-Bavarian Nordic (MVA-BN) vaccine, which can help reduce the spread and severity of the disease. In regions with endemic Mpox, healthcare systems are often overwhelmed during outbreaks, further compromising the ability to provide quality care. The presence of other major diseases, such as malaria, HIV, and tuberculosis, further strains limited healthcare resources, leaving Mpox patients with insufficient care [8].

In contrast, healthcare systems in developed regions of the Americas are better equipped to handle emerging infectious diseases like Mpox. Diagnostic tools, such as polymerase chain reaction (PCR) tests, allow for rapid identification of Mpox cases, enabling early intervention and better management of the disease. Early diagnosis is critical in preventing severe disease outcomes and limiting transmission. In addition to diagnostic capabilities, healthcare facilities in the Americas have access to vaccines and antiviral treatments that significantly reduce the severity of Mpox infections. For example, the MVA-BN vaccine, initially developed for smallpox, has been deployed during recent outbreaks to vaccinate high-risk populations. The availability of antiviral treatments and supportive care further contributes to reduced mortality rates, as patients can receive timely

care and treatment. Furthermore, robust public health networks in the Americas facilitate swift outbreak control through contact tracing, quarantine measures, and public health campaigns, which collectively help prevent widespread transmission and ensure better outcomes for patients [40].

3. Access to Vaccines and Preventive Measures

Access to vaccines and preventive measures is another critical factor in the differing Mpox outcomes between Africa and the Americas. The availability and efficient distribution of vaccines play a crucial role in controlling the spread of the virus and reducing the severity of infections. In Africa, however, vaccine availability remains a major challenge. The smallpox vaccine, which offers cross-protection against Mpox, is not widely accessible in many parts of the continent. Where Mpox is endemic, vaccination campaigns are often hindered by logistical obstacles, such as insufficient vaccine supplies, weak distribution networks, and political or economic instability. These barriers make it difficult to conduct widespread vaccination programs that could limit the transmission of the virus. Additionally, African countries may struggle to identify and vaccinate high-risk populations, such as healthcare workers, individuals in close contact with infected animals, and those living in endemic areas. As a result, these populations remain vulnerable to infection, increasing the risk of severe outbreaks and higher mortality rates [28].

In contrast, developed countries in the Americas have far greater access to vaccines and the infrastructure necessary for efficient distribution. The MVA-BN vaccine has been used effectively in recent outbreaks to immunize individuals at high risk, including healthcare workers, men who have sex with men (MSM), and those in close contact with

confirmed cases. This proactive vaccination strategy has been pivotal in reducing the severity of Mpox cases and limiting transmission. Public health campaigns in the Americas also focus on educating the public about preventive measures, such as avoiding close contact with infected individuals and practicing good hygiene. These combined efforts, alongside the availability of vaccines, have helped control Mpox outbreaks and reduce the burden of the disease on at-risk populations [45].

4. Socioeconomic and Environmental Factors

Socioeconomic and environmental factors contribute to the disparity in Mpox outcomes between Africa and the Americas. In underdeveloped regions of Africa, poverty, malnutrition, and inadequate living conditions create an environment where Mpox is more likely to spread, and individuals are more susceptible to severe disease. Many African populations live in overcrowded conditions with limited access to clean water and sanitation, increasing the risk of Mpox transmission, especially in areas where the virus is endemic. Informal settlements, where healthcare services are minimal, provide ideal conditions for the virus to spread unchecked. Malnutrition further weakens the immune system, making individuals more vulnerable to severe disease. Additionally, in rural areas, where people rely on subsistence hunting and bushmeat consumption, close contact with animals increases the risk of zoonotic transmission of Mpox. These conditions make controlling outbreaks difficult due to limited healthcare resources and infrastructure [3].

In contrast, populations in developed regions of the Americas benefit from higher living standards, including better housing, clean water, and sanitation, which reduce the risk of Mpox transmission and support better

overall health. These conditions help mitigate the severity of disease outcomes. Additionally, public health systems in the Americas are able to implement comprehensive educational campaigns to inform the public about Mpox, its modes of transmission, and preventive measures. These efforts help reduce transmission and ensure that at-risk populations understand how to protect themselves [44].

Strategies for Mpox Control in Africa and the Americas

The Mpox outbreaks in Africa and the Americas, most notably the 2022 global outbreak and the resurgence in 2024, underscore the pressing need for a comprehensive, coordinated global response. Although Mpox has long been endemic in parts

of Africa, particularly in Central and West Africa, its recent spread to other regions has highlighted the virus's potential to create significant public health challenges worldwide. Given this, effective Mpox control necessitates a multifaceted approach that addresses both immediate and long-term challenges across diverse geographical and socioeconomic contexts. Key strategies for controlling Mpox in both Africa and the Americas include strengthening surveillance, ensuring equitable vaccine distribution, enhancing public health education, and implementing broader interventions, such as bolstering healthcare infrastructure, addressing social determinants of health, promoting research and innovation, and enhancing international cooperation (Figure 4).



Figure 4: Strategies for Mpox control

1. Strengthening Surveillance

Strengthening global surveillance systems is crucial for controlling Mpox, particularly in regions where zoonotic transmission of the virus is common, such as Central and West

Africa. Enhanced surveillance allows for the early detection of cases, which is vital for preventing larger outbreaks. In Africa, where Mpox remains endemic, surveillance efforts must be paired with improved diagnostic

capabilities. Many African nations lack sufficient laboratory infrastructure to quickly and accurately identify Mpox cases. Expanding access to polymerase chain reaction (PCR) testing, considered the gold standard for Mpox diagnosis, is essential. Additionally, investments in mobile laboratories and rapid diagnostic kits capable of being deployed in remote or resource-limited settings are crucial.

In the Americas, surveillance systems are generally more advanced but must still adapt to the evolving epidemiology of Mpox. Recent outbreaks in developed countries have often been linked to specific high-risk populations, such as men who have sex with men (MSM). Surveillance strategies should therefore include routine screening of these communities and other vulnerable groups to ensure early detection and prompt intervention. Moreover, robust contact tracing systems are critical for rapidly identifying and isolating new cases, thus limiting further transmission. At the global level, real-time data sharing is essential for coordinated response efforts. International health organizations like the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) should facilitate the timely exchange of epidemiological data between nations. Collaborative research and reporting mechanisms can also help track viral mutations, identify emerging hotspots, and inform targeted interventions.

2. Improving Vaccine Equity

Ensuring equitable access to vaccines is a critical component of Mpox control, especially considering the stark contrast in vaccine availability between the Americas and Africa. While vaccines such as the Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) vaccine have been crucial in

controlling outbreaks in developed countries, African nations—where Mpox is endemic—continue to face significant barriers in accessing these life-saving interventions. Efforts must be made to ensure that vaccines are not only available during outbreaks in high-income countries but also incorporated into routine preventive strategies in endemic regions. Global health organizations, governments, and vaccine manufacturers must collaborate to create a global stockpile of Mpox vaccines, prioritizing their distribution to regions most affected by the virus. This should also include funding mechanisms that subsidize vaccine costs for low-income countries.

In Africa, vaccination campaigns face numerous logistical challenges, including the need for cold chain storage and transportation difficulties. Strengthening supply chains and improving vaccine delivery systems are essential to ensure that vaccines reach remote or underserved areas. Collaborating with local healthcare workers, community leaders, and non-governmental organizations (NGOs) can facilitate vaccine rollout and increase public trust in vaccination efforts. In the Americas, vaccination campaigns should focus on high-risk populations, such as healthcare workers, immunocompromised individuals, and sexual networks at higher risk for transmission. Additionally, vaccine distribution strategies must be equitable, ensuring that marginalized communities, including racial minorities and those in low-income neighborhoods, have equal access to vaccines.

3. Public Health Education

Effective public health education is fundamental to reducing the transmission of Mpox. Awareness campaigns should be culturally sensitive and tailored to specific high-risk populations, addressing local beliefs, practices, and misinformation. In

Africa, public health education should emphasize the zoonotic nature of Mpox and the importance of minimizing exposure to potential animal reservoirs, such as primates and rodents. Public health authorities should engage with local communities to promote the safe handling of bushmeat and provide alternatives where possible. Educational materials should also highlight the importance of seeking early medical care and recognizing symptoms, as delays in treatment can lead to more severe disease outcomes. Moreover, efforts should be made to counter misconceptions about Mpox that could contribute to stigma and discourage individuals from seeking care. For example, public health campaigns should aim to dismantle any associations between Mpox and witchcraft or supernatural causes, which may still persist in rural areas.

In the Americas, public health education should focus on raising awareness among populations most at risk, particularly MSM communities and individuals with compromised immune systems. Campaigns should provide clear information on how the virus is transmitted, including through close contact and sexual activity. Social media platforms and digital tools can be effectively leveraged to disseminate accurate information and combat misinformation, especially in urban centers where transmission may be most pronounced. Across both regions, public health campaigns must actively work to reduce the stigma surrounding Mpox, especially within sexual minority groups. The fear of judgment or discrimination can deter individuals from seeking care or disclosing symptoms, thus contributing to the spread of the virus. Community outreach programs, in collaboration with civil society organizations, should emphasize the

importance of compassion, confidentiality, and early intervention.

4. Strengthening Healthcare Infrastructure

The disparities in healthcare infrastructure between Africa and the Americas necessitate targeted investments in healthcare systems, particularly in low-resource settings. Strengthening healthcare capacity is critical for managing not only Mpox but also other infectious diseases that may exacerbate its severity. In Africa, healthcare systems face numerous challenges, including inadequate diagnostic capacity, limited access to personal protective equipment (PPE), and a shortage of trained healthcare workers. Investments in healthcare infrastructure should prioritize the establishment of specialized infectious disease units, improved hospital facilities, and the training of healthcare personnel in Mpox case management. Increasing the supply of PPE and ensuring that healthcare workers have access to vaccines are also essential to preventing transmission in healthcare settings.

In the Americas, healthcare systems are generally more robust but should continue to focus on providing supportive care for individuals affected by Mpox, especially those with underlying health conditions or immunocompromising conditions such as HIV. Integrating Mpox management into existing public health frameworks for other infectious diseases (e.g., HIV, tuberculosis) could streamline care and improve overall outcomes.

5. Addressing Social Determinants of Health

Mpox control strategies must also account for the broader social determinants of health that influence the spread of the virus. In Africa, poverty, malnutrition, and inadequate housing increase the risk of Mpox transmission, particularly in regions where

environmental conditions are conducive to zoonotic transmission and human-to-human spread. In such areas, poverty alleviation programs and efforts to improve access to clean water, sanitation, and nutrition should be integral to Mpox control strategies. Strengthening social safety nets and increasing access to healthcare can mitigate the compounding effects of poverty on disease outcomes.

In the Americas, racial and socioeconomic disparities influence Mpox outcomes. Marginalized communities often have limited access to healthcare and preventive measures, which leads to worse disease outcomes. Policymakers must prioritize healthcare equity by ensuring that Mpox-related resources are distributed fairly across all communities, regardless of their socioeconomic status.

6. Promoting Research and Innovation

Research and innovation play a pivotal role in enhancing Mpox control strategies. Further studies are needed to understand the virus's transmission dynamics, host immune responses, and potential for viral mutations. The development of new vaccines and treatments will also be critical for preventing future outbreaks. Governments and international organizations should fund research initiatives focused on Mpox, particularly in endemic regions. This should include epidemiological studies to examine the zoonotic reservoirs of the virus and clinical trials for novel vaccines and antiviral treatments. Additionally, research into genetic susceptibility and immune responses may provide valuable insights into why some individuals experience more severe disease than others. Innovations in diagnostic tools are also needed to make Mpox detection faster, more accurate, and accessible in low-resource settings. Portable diagnostic kits,

telemedicine services, and mobile health units could help bring Mpox testing and treatment to remote areas where healthcare infrastructure is limited.

7. Enhancing International Cooperation

Finally, global cooperation is essential for Mpox control. The virus knows no borders, and its control will require coordinated efforts between governments, international organizations, and non-governmental entities. Organizations such as the WHO, the CDC, and the African Union should continue to lead global health partnerships aimed at Mpox control. These partnerships can facilitate the sharing of resources, expertise, and data across borders, ensuring that all countries—regardless of income—are equipped to manage Mpox outbreaks. Given that Mpox can spread through international travel and trade, countries should enhance their cross-border surveillance and public health collaborations. This includes sharing information on cases, coordinating vaccine distribution efforts, and implementing international travel protocols when necessary.

CONCLUSION

Mpox remains a significant global health threat, with various factors influencing its transmission and severity across different regions. Behavioral factors, such as close contact and healthcare access, as well as virological aspects like viral clade variability and mutations, play a major role in shaping the disease's spread and impact. Immunological factors, including pre-existing immunity and co-infections like HIV, further influence disease outcomes. The disparities between Africa and the Americas highlight the need for region-specific public health strategies. In Africa, strengthening healthcare infrastructure, improving vaccine access, and addressing co-morbidities are

essential, while in the Americas, efforts must focus on reducing stigma and mitigating behavioral risks. Effective Mpox control requires a coordinated global response, with enhanced surveillance, equitable vaccine distribution, and robust public health education. International collaboration, investment in healthcare systems, and targeted interventions for high-risk groups are vital to reduce the impact of future outbreaks. Addressing these multifaceted factors will help lessen the global burden of Mpox and prevent future public health crises.

List of Abbreviations

ART - Antiretroviral Therapy
 AU - African Union
 CAR - Central African Republic
 CDC - Centers for Disease Control and Prevention
 DNA - Deoxyribonucleic Acid
 DRC - Democratic Republic of the Congo
 HIV - Human Immunodeficiency Virus
 IL-6 - Interleukin-6
 Mpox - Monkeypox
 MPXV - Monkeypox Virus

MSM - Men who have Sex with Men
 MVA-BN - Modified Vaccinia Ankara-Bavarian Nordic
 PCR - Polymerase Chain Reaction
 PHEIC - Public Health Emergency of International Concern
 PPE - Personal Protective Equipment
 SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2
 TNF- α - Tumor Necrosis Factor-alpha
 UC - University of California
 WHO - World Health Organization

Consent

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الجدري المائي، العوامل الفيروسية، الاستجابة المناعية، المخاطر السلوكية، أفريقيا، أمريكا

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الملخص

ال خلفية والاهداف: ظهر الجدري القردي (المعروف سابقاً باسم جدري القرد) (كمشكلة صحية عامة بالغة الأهمية في جميع أنحاء العالم، ويتميز باختلافات ملحوظة في اكتساب المرض وشدة بين أفريقيا والأمريكتين. إن فهم التفاعل بين العوامل السلوكية والفيروسية والمناعية أمر ضروري لمعالجة هذه التفاوتات ويفحص هذا الاستعراض العوامل السلوكية والفيروسية والمناعية التي تؤثر على اكتساب الجدري القردي وشدة، مع التركيز على الاختلافات الإقليمية في أفريقيا والأمريكتين.

منهجية الدراسة: أجريت مراجعة سردية باستخدام مقالات تمت مراجعتها من قبل الأقران وتقارير الصحة العامة والمبادئ التوجيهية الرسمية المنشورة بين عامي 2019 و 2024. تم تحديد المصادر الرئيسية من خلال قواعد البيانات بما في ذلك PubMed و Scopus و Google Scholar. وركز التحليل على عوامل الخطر السلوكية (على سبيل المثال، الشكايات الجنسية، والتعرض للحياة البرية)، والسمات الفيروسية (على سبيل المثال، المجموعات الفيروسية)، والتأثيرات المناعية (على سبيل المثال، حالة التطعيم).

النتائج: تكشف النتائج عن اختلافات إقليمية مميزة في ديناميكيات انتقال الجدري المائي ونتائجه. ففي أفريقيا، ينتشر انتقال العدوى من الحيوان إلى الإنسان، ويتفاقم بسبب سوء النظافة ونقص الموارد في أنظمة الرعاية الصحية. وفي الأمريكتين، تتجم الأوبئة في المقام الأول عن انتقال العدوى من إنسان إلى إنسان داخل الشبكات الجنسية، وخاصة بين الرجال الذين يمارسون الجنس مع الرجال، والسفر الدولي. ومن الناحية الفيروسية، تظهر سلالة أفريقيا الوسطى ضراوة أكبر من سلالة غرب أفريقيا، التي سادت الأوبئة العالمية الأخيرة. ومن الناحية المناعية، أدى التغطية المحدودة لتطعيم الجدري بين السكان الأفارقة الأصغر سناً إلى زيادة الضعف، في حين خففت الحماية المتبادلة الجزئية من لقاحات الجدري في الأمريكتين من شدة المرض إلى حد ما.

الاستنتاجات: إن السيطرة الفعالة على الجدري المائي تتطلب استراتيجيات الصحة العامة الخاصة بالمنطقة. وتعتبر برامج التطعيم المحسنة، والبنية الأساسية المحسنة للرعاية الصحية، والتدخلات المصممة خصيصاً لمعالجة العوامل السلوكية والفيروسية أمراً بالغ الأهمية. والتعاون العالمي ضروري للتخفيف من انتشار الجدري المائي وأعبائه مع معالجة التفاوتات الاجتماعية والاقتصادية والوبائية.

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