

How Alarming is Monkeypox threat perception?

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As the world finally emerges from the grip of COVID-19, a new threat looms: Mpox (formerly known as Monkeypox). In August 2024, the World Health Organisation (WHO) declared Mpox a global health emergency due to the rising cases of the new strain, clade I Mpox in Africa and Sweden, underscoring the urgent need for coordinated global action to monitor and contain the virus. As of September 2024, 2082 confirmed Mpox cases were reported globally, marking the highest number of monthly cases globally since November 2022. Nearly 400 cases have been reported in Asia Pacific this year. How are Asia Pacific countries stepping up surveillance measures and preparing their healthcare systems to combat Mpox? And just how significant is the threat posed by this outbreak? Let's explore.



Two years after the World Health Organization (WHO) declared a global health emergency over an Mpox outbreak, a deadlier strain, clade 1b, emerged in the Democratic Republic of the Congo (DRC) in September 2023. This came just months after the WHO had ended the 2022 global health emergency in May 2023. By August 2024, the new outbreak, largely concentrated in the DRC and its African neighbours, was declared a Public Health Emergency of International Concern (PHEIC), sparking concerns of a wider spread similar to the 2022 outbreak, which affected 122 countries.

There are two clades of Mpox: clade I and clade II. Endemic to Central Africa, clade 1 is the most deadly, causing a severe illness and – in past outbreaks – killing up to 10 per cent of those who become unwell. Clade II, on the other hand, which had spread globally in 2022, has a survival rate of over 99.9 per cent and is endemic to West Africa. Five countries in Africa (Burundi, DRC, Kenya, Rwanda and Uganda) and three countries outside of Africa (Sweden, Thailand, India) have reported clade 1b monkeypox virus (MPXV) as of September 22, 2024.

Since the beginning of Mpox monitoring in 2022 and up to August 2024, over 106,310 confirmed cases of Mpox due to MPXV clade I and clade II, including over 234 deaths, were reported by more than 123 countries globally, according to WHO.

The Asia-Pacific region has also reported a few cases of Mpox, with Australia being the worst affected. In 2024, Australia recorded 257 confirmed cases, with the majority concentrated in Victoria (114 cases) and New South Wales (102 cases). Other affected regions include Queensland (24 cases), the Australian Capital Territory (12 cases), South Australia (4 cases), and the Northern Territory (1 case).

Singapore too has recorded 14 cases, Vietnam has documented 49 cases, while the Philippines has seen 18 cases. In Indonesia, 88 Mpox cases were confirmed, South Korea 11 cases. Elsewhere in the region, Malaysia, Thailand and India each reported one case.

Asia Responds

The WHO's designation of Mpox as a public health emergency underscores the urgency of addressing the disease's potential for rapid spread, particularly in populations with low immunity due to the end of smallpox vaccination programmes. The emergence of Mpox cases in non-endemic regions has raised concerns about public health preparedness. The Asian countries have responded to the WHO's announcement by introducing various measures, such as enhancing surveillance and public health education, to monitor potential cases and prevent outbreaks.

In response to the Mpox threat, Singapore has announced a series of measures following the WHO declaration of Mpox as a global public health emergency in August. Singapore's comprehensive response plan includes vaccinating two high-risk groups, implementing temperature screenings at select locations, and establishing protocols for handling suspected and confirmed cases. As part of a coordinated, whole-of-government effort, the Ministry of Health (MoH) has enhanced public health preparedness to address a potential Mpox clade I outbreak.

All healthcare practitioners and institutions have been instructed to remain vigilant in detecting and reporting Mpox cases, especially those suspected to be clade I infections. Suspected cases will be promptly transferred to hospitals for further evaluation and treatment if needed. Upon confirmation of a clade I case, the Ministry of Health will initiate immediate contact tracing, and close contacts will be quarantined in a government-designated facility for 21 days, consistent with the observed incubation period in Africa. To strengthen containment efforts, Singapore has also tightened border controls and begun screening incoming passengers at airports for early detection of Mpox cases.

China too has announced strengthened surveillance at ports of entry in response to the Mpox outbreak. Travellers arriving from regions with confirmed Mpox cases who show symptoms such as fever, headache, back pain, or rashes must declare their condition to customs. In addition, aircraft, vessels, and cargo arriving from affected areas will undergo sanitation procedures. These measures, which took effect from August 2024, will be enforced for the next six months to monitor people and goods entering the country for Mpox.

South Korea's Korea Disease Control and Prevention Agency (KDCA) stated that the Mpox situation remains manageable under current protocols. However, South Korean authorities have decided to ramp up quarantine and surveillance measures.

India has been taking proactive measures against Mpox. The country has implemented a comprehensive strategy involving expert consultations, enhanced surveillance, laboratory preparedness, and awareness campaigns. While remaining vigilant, Indian health authorities have assessed a low risk of a large-scale outbreak, demonstrating a balanced approach to public health management in the face of emerging infectious diseases.

Australia has implemented a response plan for Mpox that involves surveillance, contact tracing, and vaccinations for high-risk groups. A vaccination programme for Mpox was initiated in Australia in August 2022. By the end of 2022, 30,346 people received 1 dose of JYNNEOS, with another 16,954 people completing a course of Mpox vaccination (2 doses) in that year. In 2024, there has been a resurgence of clade II cases in Australia. Most cases have been acquired in Australia and a small number have been in people who were fully vaccinated.

The Australian Technical Advisory Group On Immunisation (ATAGI) recommendations for Mpox vaccination have been updated in August 2024 to remove the age restriction; people of all ages who are at risk of exposure to Mpox are recommended to receive the Mpox vaccination. The ATAGI noted that it is monitoring the evolving Mpox epidemiology in Australia and other affected regions. Vaccine recommendations will continue to be reviewed and updated if required.

Indonesia is reactivating the COVID-era health tracking system, previously known as PeduliLindungi. This initiative is part of the government's preventive measures against Mpox. Countries such as Vietnam and Malaysia have strengthened the monitoring and detection of suspected cases at border checkpoints and within public and private healthcare establishments.

Preparedness

Regarding Mpox prevention, vaccinations are the most effective strategy. The WHO has advocated for targeted vaccinations of high-risk populations rather than mass immunisation. Currently, the WHO recommends the use of Bavarian Nordic's MVA-BN vaccine and Japan-based KM Biologics' LC16 vaccine, the latter being the only Mpox vaccine licensed for children. If these vaccines are unavailable, the WHO suggests using Emergent BioSolutions' ACAM2000 vaccine, which recently received approval from the US Food and Drug Administration (FDA) for a supplemental Biologics License Application (sBLA). This approval allows ACAM2000 to be administered to individuals considered at high risk for Mpox infection. Bavarian Nordic's MVA-BN vaccine is also approved by Singapore and Australia.

Unlike the COVID-19, big pharma isn't rushing to develop treatments for Mpox. The effort is largely being led by smaller biotech companies.

US-based NanoViricides Inc highlighted the need for new treatments to manage the recurring Mpox, since there is a short supply of the limited vaccines that are available, which are developed as smallpox vaccines. Following the WHO's PHEIC announcement, the company considered that its novel investigational antiviral NV-387 is eligible for evaluation for Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI), as a treatment for the virus. The experimental drug has completed a phase I study. Promising animal studies of NV-387 have shown that the drug was as effective as the current approved drug tecovirimat when emulating the direct skin infection by the virus. This is notable because direct skin infection is thought to be the major mode of transmission of the virus in the current epidemic of Mpox clade 1 and clade 1b.

Another promising vaccine candidate for Mpox, TNX-801, developed by Tonix Pharmaceuticals, has similarities to the original smallpox vaccine. This drug was the only vaccine to successfully eliminate a contagious viral pathogen, according to Tonix. In contrast to mRNA vaccines, TNX-801 is designed to elicit a robust T-cell response, "facilitating long-term immunity and potentially eliminating the need for repeated boosters. For example, pre-clinical data shows that the drug significantly reduced viral shedding, suggesting that it can block forward transmission. On August 26, 2024, Tonix announced a collaboration with Bilthoven Biologicals (Bbio) to develop GMP manufacturing processes for its Mpox vaccine. Bbio is part of the world's largest vaccine manufacturer, the Cyrus Poonawalla Group, which also includes the Serum Institute of India.

"The streamlined regulatory processes established during the COVID-19 pandemic, such as the US FDA's Emergency Use Authorizations (EUAs), have set a precedent for fast-tracking vaccines and treatments for emerging diseases. These also allow trials to start faster without compromising safety. Additionally, streamlined processes are now aiding Mpox treatment trials, expediting approval timelines while ensuring rigorous review standards are taken into action. This has equipped Tonix to engage with regulatory bodies efficiently, ensuring that TNX-801 is evaluated swiftly," said **Dr Seth Lederman, Co-Founder, CEO and Chairman of Tonix Pharmaceuticals**.

Another American biotech GeoVax Inc has the cGMP Master Seed Virus for GEO-MVA (GeoVax-Modified Vaccinia Ankara) and is exploring options to accelerate production of the MVA-vaccine (against Mpox and Smallpox) through cGMP clinical grade production.

In Asia, both China and India are actively developing Mpox vaccines. The Serum Institute of India is working on its own vaccine, while China has approved its first Mpox vaccine for clinical trials, which began on September 9, 2024. The vaccine, developed by the Shanghai Institute of Biological Products—a subsidiary of the state-owned pharmaceutical giant Sinopharm—has shown promising results in early studies, indicating effective immunity against the highly infectious virus. Sinopharm is also known for creating China's first COVID-19 vaccine in 2020.

Currently, the only antiviral agent approved for Mpox treatment is tecovirimat (TPOXX), which has been authorised by regulators in the UK and European Union for Mpox and other orthopoxviruses. Originally developed for smallpox, tecovirimat has been repurposed for Mpox treatment.

"Ongoing trials throughout the world are working to demonstrate the benefit of treating Mpox patients with tecovirimat. One of the biggest challenges is that, similar to antiviral therapies for flu and COVID-19, treatment likely needs to be initiated soon after infection to reduce pain, rash, and other complications of Mpox infection. In many parts of the Democratic Republic of Congo (DRC) and other African countries experiencing outbreaks, patients often do not seek care until they have been sick for many days, limiting the potential benefit of antiviral treatment. In those situations, optimising other forms of clinical care, such as good wound cleaning and antibiotics for skin infections, is paramount," said **Dr Jay Varma, Former Executive Vice President and Chief Medical Officer, SIGA Technologies**. Tecovirimat recently missed critical clinical endpoints on a major clinical trial addressing it as a therapy against Mpox.

Much of the research on Mpox is focused on developing preventive vaccines, with comparatively less emphasis on therapies and diagnostics. "Progress on developing and approving new Mpox diagnostics and therapies has been limited. The primary

focus has been on getting existing vaccines approved by WHO and affected countries, as well as addressing research gaps related to vaccines, such as efficacy of those for use in individuals under 18 years of age and the development of new vaccines including using new vaccine platforms. WHO is currently reviewing six Mpox diagnostic products. On the contrary, there is already a WHO-prequalified vaccine for Mpox prevention,” said **Javier Guzman, Director of Global Health Policy and Senior Policy Fellow at the Center for Global Development**

Despite the availability of diagnostics and treatments, the irony is that they remain inaccessible to the African populations most affected by this disease. Similar to the COVID-19, developed nations have begun hoarding vaccines. The Africa Centres for Disease Control and Prevention (Africa CDC) reported that its request for \$245 million (£187 million) to address the outbreak is only 10 per cent funded. Although Mpox was first identified in humans in the DRC in 1970, African nations vulnerable to its spread are still dependent on vaccine donations from the stockpiles of wealthier countries. Not only are vaccines scarce, but people in these nations also lack sufficient diagnostic kits to identify the disease. According to FIND, an organisation specialising in the development of new diagnostics, only 16 per cent of suspected cases in the DRC are undergoing testing. It is a stark reminder of the inequities in global health access.

“Similar to what happened during the peak of COVID-19, the biggest challenge for healthcare providers in the DRC and other low-income settings is access to supplies and equipment to collect, transport, and diagnose Mpox. There needs to be a greater global effort to manufacture and distribute these, as well as to support validation and supply of fully-automated diagnostic assays. An important area of research is developing rapid diagnostic tests that can be used at the point-of-care, such as those that detect viral antigens,” said Dr Jay Varma.

How big of a threat is it?

There are two clades (groups) of Mpox: clade I (prevalent in central Africa) and clade II (prevalent in west Africa). Just 1 day after WHO's second declaration, the first case of Mpox was reported from Sweden and Thailand. This is the first time an Mpox case of clade I was reported outside Africa (clade Ib). Considering that the estimated case fatality of clade I is higher (10 per cent) than clade II (1–3 per cent), there could be a major risk to global health.

Some experts in India have criticised the WHO's declaration for potentially inciting unnecessary panic and emphasised the importance of raising awareness among high-risk groups, including individuals living with HIV. Given that the monkeypox virus is closely related to the smallpox virus, these experts believe that individuals over 44 who received the first-generation smallpox vaccine during early vaccination campaigns may have some immunity to Mpox. Several studies suggest that the cellular and humoral immunity provided by first-generation smallpox vaccines is long-lasting.

However, there are experts who are of the opinion that it's better to be prepared. “The WHO declared Mpox as a Global Health Threat in August 2024, recognising the migration of the virus throughout Africa, expanding to Europe and North America and Asia. The current strain (clade) is more virulent than that of the 2022 outbreak and is more casually transmitted, with approximately 70 per cent of reported cases in Africa occurring among children. Mpox is a global threat that knows no boundaries, no race, no creed. Now is the time to apply everything we learnt from the COVID-19 to monkeypox, by trying to get ahead of this virus, before it reaches the other territories it has not touched yet, but in a most likely scenario will in a matter of time,” said **David Dodd, CEO, GeoVax Inc.**

Also, as the old adage goes, viruses know no boundaries. The past 20 years—in which there have been global outbreaks of SARS, influenza H1N1, Ebola, MERS, COVID-19, and Mpox—shows that an outbreak anywhere can lead to outbreaks everywhere. Therefore, it is important that all countries and people working in health-related fields prepare for Mpox.

“The current global outbreak has shown the potential for global transmission, especially in non-endemic countries. Its spread through close contact poses risks, in particular vulnerable populations,” said Dr Lederman.

“The 2022 emergency was declared because Mpox had spread from Nigeria to all continents. This was the first time the virus had spread to so many regions and caused numerous illnesses. The 2024 emergency was declared due to a severe, uncontrolled outbreak in the Democratic Republic of the Congo caused by a potentially more dangerous strain of Mpox. This strain has now spread to several neighbouring countries in Africa, as well as one in Sweden and another in Thailand,” said Dr Jay Varma.

He added, “When a new strain or variant of a virus emerges, we focus on two major questions/areas of concern. First, does it spread more easily from one person to another? Second, does it make people sicker? Regarding transmission, we do not believe that clade I spreads more easily than clade II. However, the situation is complicated by the detection of a new variant (clade 1b) in the DRC. This variant was first identified in men visiting female sex workers, and researchers are concerned it may spread more easily through heterosexual sex, although this has not been confirmed. In terms of severity, we have long

known that clade I causes more severe rashes and higher death rates than clade II. The current DRC outbreak has a death rate of around 3.7 per cent for clade I infections, compared to less than 1 per cent for clade II infections globally. This aligns with laboratory studies indicating that clade I is more severe than clade II.”

The risk of Mpox spreading further is a real and present threat. Although the risk is low to medium, it could be higher if community transmission occurs in multiple countries. Swift action can make a critical difference in controlling the outbreak.

While it is essential for other countries to have strategies and action plans in place, it is absolutely crucial to address the epicentre of the current outbreak—Africa—through equitable vaccine distribution. Ten million doses are needed for the entire continent. Without these vaccines, Mpox will continue to spread.

“This outbreak involves a new, more lethal strain of the Mpox virus that spreads more efficiently from person to person. Unlike the 2022 outbreak, this strain is not restricted to a specific group and is rapidly spreading beyond the Democratic Republic of Congo to other African countries and even outside of the continent. Despite this, and the fact that vaccines and diagnostic tests are available, demand still exceeds supply, and current donations are insufficient. A total of 3.6 million vaccine doses have been pledged (620K of the Bavarian Nordic vaccine and 3 million of the LC16 vaccine), but this falls short. Fractional dosing could be a potential solution to address the shortage, but African countries are hesitant due to indemnification and liability issues,” said Guzman.

The vaccines have not arrived yet, and addressing this is crucial for tackling broader health inequalities.

While it's good for other countries to be prepared, it is of utmost importance that the African region is prioritised for response efforts. Because no one is safe till everyone is safe.

Ayesha Siddiqui