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ASEAN BIODIASPORA VIRTUAL CENTER

MPOX

FOCUS REPORT

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EDITORIAL ADDRESS
ASEAN Biodiaspora Virtual Center, 2/F Ministry of Health, Jl. H.R. Rasuna Said, Blok X5, Kav. 4-9, Jakarta Selatan,, Jakarta, Indonesia
E-mail: support@biodiaspora.org

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MPOX FOCUS REPORT

Introduction

Mpox, once mainly affecting animals in Africa, has emerged as a global concern (Otu et al., 2022). Mpox was used to known as monkeypox because it was first found in monkeys in 1958, the virus then jumped to humans in 1970 (Cabanillas et al., 2023; Carrubba et al., 2023). Because of the change of transmission nature and emerging global pandemics, WHO changed the name into mpox (CDC US, 2022; WHO, 2022a).

While originally thought to only jump from animals to humans, mpox has surprised us recently by proving it can spread easily between people. This close contact transmission can happen through various ways, including touching infected skin sores, sharing bodily fluids, breathing in close proximity to someone who's sick, or using contaminated objects (Bížová et al., 2022).

Nowadays, faster travel and trade have led to outbreaks worldwide, including a major one in 2022 (Bunge et al., 2022; Costello et al., 2022; Meo et al., 2023). Though no longer a global health emergency, mpox is still rising in some Asian regions due to its evolution and movement of people (Nuzzo et al., 2022; Sabeena, 2023; WHO, 2023a). This previously overlooked disease now demands renewed attention.

The disease is caused by the monkeypox virus (MPXV), a double-stranded DNA virus and a member of the Orthopoxvirus genus within the Poxviridae family. Being a close relative of the eradicated smallpox virus, MPXV shares some similarities with the virus that caused smallpox, eradicated in 1980 (Jezek et al., 1987; Yang, 2022).

People vaccinated against smallpox before 1980, when the vaccination program ended, were five times less likely to get mpox than those unvaccinated. This data, gathered in the Democratic Republic of Congo from 2005 to 2007, suggests that the old-school smallpox vaccines offered an impressive 80.7% protection against mpox (Rimoin et al., 2010). Further studies in the same country (1981-1986) backed this up, showing that a specific vaccine called Dryvax was 85% effective against this disease originating from animals (Ježek et al., 1988).

This review explores mpox, covering how it spreads, how it works in the body, its genetic makeup, and potential treatments studied over time. It also offers insights for preventing future outbreaks, drawing lessons from past efforts.

Method

This report explores the landscape of mpox disease in the ASEAN region, investigating factors such as its prevalence, disease burden, preventive measures, and updates on treatment. Utilizing databases such as PubMed, Embase, and Scopus, the analysis incorporates real-time information gathered from official reports and news articles detailing cases of mpox. The report constructs a coherent narrative that reveals trends, patterns, and existing challenges in the ongoing efforts to combat mpox in the ASEAN region, providing a thorough understanding of the disease and associated strategies.

Mpox Case Definition and Diagnosis

1. New Confirmed Case

Table 1. Case definition for new case (WHO, 2023b)

Suspect Case	Probable Case	Confirmed Case
A person who is a contact of a probable or confirmed mpox case in the 21 days before the onset of signs or symptoms, and who presents with any of the following: acute onset of fever (>38.5°C) headache, myalgia (muscle pain/body aches) back pain profound weakness fatigue A person presenting since 01 January 2022 with an unexplained acute skin rash, mucosal lesions orlymphadenopathy (swollen lymph nodes). And for which the following common causes of acute rash or skin lesions do not fully explain the clinical picture: varicella zoster, herpes zoster,	A person presenting with an unexplained acute skin rash, mucosal lesions, or lymphadenopathy (swollen lymph nodes). **AND** One or more of the following: has an epidemiological link[1] to a probable or confirmed case of mpox in the 21 days before symptom onset. Identifies as gay, bisexual, or other man who has sex with men. has had multiple and/or casual sexual partners in the 21 days before symptom onset. has detectable levels of anti-orthopoxvirus (OPXV) IgM antibody[2] (during the period of 4 to 56 days after rash onset); or a four-fold rise in IgG antibody titer based on acute (up to day 5-7) and convalescent (day 21 onwards) samples; in the	A person with laboratory confirmed mpox virus infection by detection of unique sequences of viral DNA by real-time polymerase chain reaction (PCR)3 and/or sequencing.

measles, herpes simplex, bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, molluscum contagiosum, allergic reaction (e.g., to plants); and any other locally relevant common causes of papular or vesicular rash.	absence of a recent smallpox/mpox vaccination or other known exposure to OPXV. has a positive test result for orthopoxviral infection (e.g., OPXV-specific PCR without MPXV-specific PCR or sequencing)[3]	

Discarded Cases

A suspected or probable case for which laboratory testing of lesion fluid, skin specimens or crusts by PCR and/or sequencing is negative for MPXV. Conversely, a retrospectively detected probable case for which lesion testing can no longer be adequately performed (i.e., after the crusts fall off) and no other specimen is found PCR-positive, would remain classified as a probable case. A suspected or probable case should not be discarded based on a negative result from an oropharyngeal, anal, or rectal swab.

2. Reinfection Case

Mpox reinfection occurs when a person who was classified as a confirmed or probable mpox case, has a recurrence of mpox symptoms after complete resolution of the initial confirmed or probable MPXV infection.

Table 2. Case definition for reinfection case (CDC US, 2023)

Suspected Reinfection	Probable Reinfection	Confirmed Reinfection
A case that fits the clinical description of mpox reinfection and meets any of the following criteria: • New rash*, **OR** • Meets one of the epidemiologic criteria and has a high clinical suspicion for mpox.	A case that meets the criteria for a suspect mpox reinfection case **AND** demonstrates one of the following from a patient specimen: • Orthopoxvirus or MPXV DNA by polymerase chain reaction of a clinical specimen **OR** • Orthopoxvirus using immunohistochemical or electron microscopy testing methods **OR** • Demonstrable increase in anti-Orthopoxvirus IgG antibodies in paired serum samples collected within 3 days of symptom onset and 7-14 days after symptom onset, for patients with no prior mpox/smallpox vaccination or vaccinated ≥180 days prior to symptom onset	A case that meets criteria for a probable mpox reinfection case **AND** has significant single nucleotide polymorphisms (SNPs) or genetic variation between MPXV genetic sequences‡ from clinical specimens obtained from two or more episodes of MPXV infection separated by complete resolution of symptoms within the same individual.

3. **Considerations for Mpox Reinfection**

    - Persistent mpox virus infection is defined as mpox virus infection without clinical improvement or resolution of symptoms.
    - Relapsed mpox virus infection is defined as mpox virus infection that has improved, but not completely resolved, followed by clinical worsening or new mpox symptoms.
    - Patients with severe immunodeficiency such as in people living with HIV with CD4 counts <200 can be at risk for persistent and/or relapsed mpox virus infections.
    - Patients may develop symptoms caused by other infections during mpox virus infection or after their initial infection resolves.

4. **Diagnosis**

    Identifying mpox is challenging due to its similarity to other infections and conditions. It's crucial to differentiate it from other sexually transmissible infections like chickenpox, measles, bacterial skin infections, scabies, herpes, syphilis, and medication-associated allergies. Testing is crucial for early treatment and preventing further spread. The preferred laboratory test for mpox is polymerase chain reaction (PCR), which can be taken directly from the rash or collected on oropharyngeal, anal, or rectal swabs. Blood testing is not recommended, and antibody detection methods may not be effective as they do not differentiate between different orthopoxviruses.

Mpox Disease Transmission

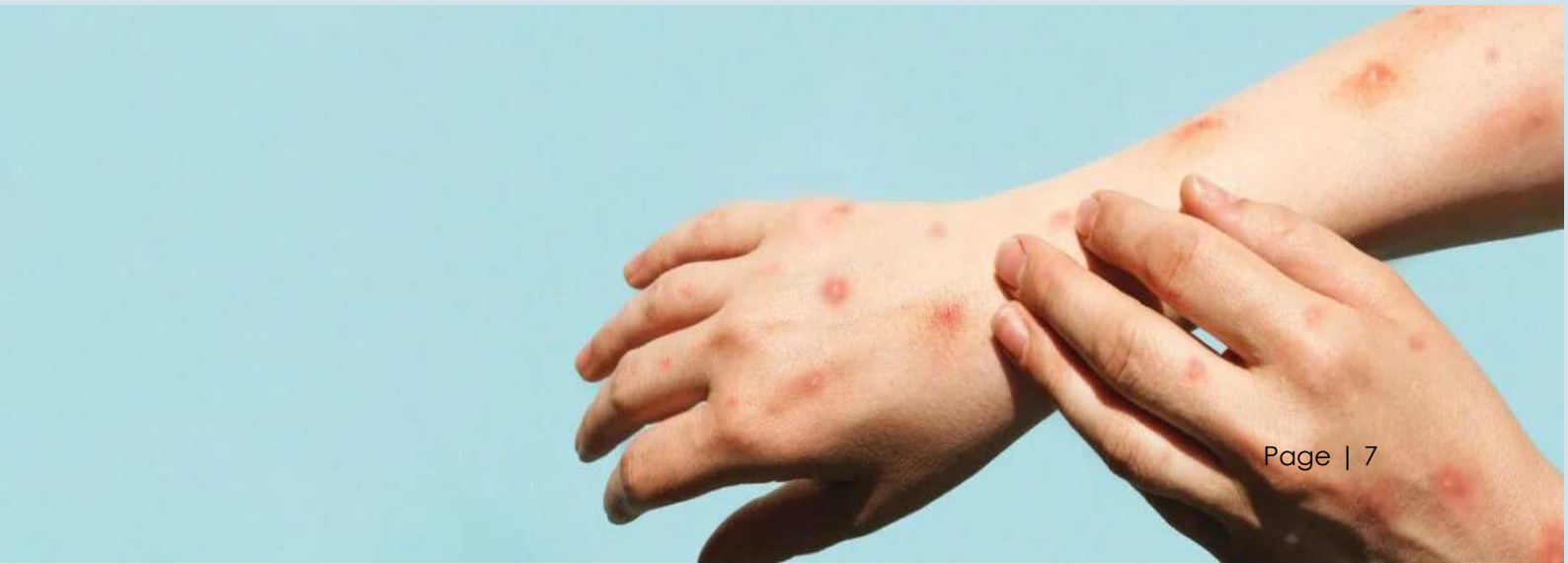
Mpox is a virus that spreads through close contact with infected individuals, including face-to-face, skin-to-skin, mouth-to-mouth, or mouth-to-skin contact. The global outbreak began in 2022 and mostly spreads through sexual contact. Infected individuals are considered infectious until their lesions have healed, which usually takes 2 to 4 weeks. The virus can persist on clothing, bedding, towels, objects, electronics, and surfaces touched by the infected person. Those who touch these items may become infected, especially if they have cuts or abrasions or touch their eyes, nose, mouth, or other mucous membranes without washing their hands. The virus can also spread during pregnancy, during or after birth, or from a parent to an infant or child during close contact. There is limited information on whether the virus can be caught from infected individuals before symptoms or after their lesions have healed. Live mpox virus has been isolated from semen, but it is not yet known if infection can spread through semen, vaginal fluids, amniotic fluids, breast milk, or blood.

Table 3. Mpox disease transmission from animal to human and vice-versa

From animals to humans	From humans to animals
Mpox can spread to people through physical contact with infected animals, such as monkeys and tree squirrels, or through eating infected meat. To reduce the risk of catching the virus, avoid unprotected contact with wild animals, especially those that are sick or dead. In countries carrying the virus, thoroughly cook any food containing animal parts or meat before consumption.	Several reports of the mpox virus being identified in pet dogs have been confirmed, but it's unclear if these are true infections or if the detection was due to surface contamination. As many animals are susceptible, there's a risk of the virus spreading from humans to animals. People with confirmed or suspected mpox should avoid close contact with pets, livestock, and wildlife.

Population at Risk of Mpox

Individuals who have close contact with someone with mpox, including sexual contact, are at risk of contracting the virus. This includes face-to-face, skin-to-skin, mouth-to-mouth, and mouth-to-skin contact. Additionally, contact with clothing, bedding, towels, objects, and electronics touched by someone with mpox is also risky. To reduce the risk of infection, those living with someone with mpox should take steps to prevent infection. A person diagnosed with mpox should be assessed by a healthcare provider to determine if isolation can be safely managed at home. Health workers should follow infection prevention and control measures to protect themselves while caring for patients with mpox.



Case Management

1) Treatment for Mpox

Research on smallpox therapeutics has led to the development of products that may also be useful for treating mpox. For example, in January 2022, the European Medicines Agency approved tecovirimat, an antiviral developed for smallpox, for mpox treatment under exceptional circumstances. However, experience with these therapeutics in mpox outbreaks is growing, and their use is usually accompanied by clinical trials or expanded access protocols (WHO, 2023c).

The limited availability of antiviral medications for the treatment of monkeypox (MPX) necessitates careful consideration of their use, particularly for individuals at risk of severe disease or those presenting with severe MPX. The World Health Organization (WHO) has established a standardized case record form on their Clinical Platform to aid Member States in collecting and analyzing data to enhance understanding of clinical characterization and therapeutic responses (WHO, 2022b)

Table 4. Summary of antiviral treatment for Mpox

Aspects	Tecovirimat	Brincidofovir	Cidofovir	NIOCH-14
License	EMA, FDA, Health Canada	EMA, FDA	FDA	Not specified
Antiviral Activity	Orthopoxvirus including Mpox virus	Double-stranded DNA viruses, including poxviruses	Mpox virus	Orthopoxvirus
Mechanism of Action	Inhibits viral envelope formation by targeting p37	Suppresses polymerase-mediated DNA synthesis	Inhibits Mpox virus replication via DNA polymerase	Comparable activity to tecovirimat, targets orthopoxviruses
Formulations	Oral, intravenous	Oral	Intravenous	Not specified

Reported Side Effects	Headache, nausea, abdominal pain, vomiting	Elevated hepatic transaminases, diarrhea, nausea, vomiting, abdominal pain	Renal toxicity	Not specified
Pregnancy Considerations	Information not provided	Not recommended during pregnancy	Information not provided	Information not provided
Clinical Efficacy Data	Demonstrated efficacy against orthopoxviruses	Limited patient data, clinical efficacy uncertain	Intravenous cidofovir used in cytomegalovirus treatment	Limited patient data, clinical efficacy uncertain

2) Prevention

a. Behavioral Prevention

Table 5. Prevention can be taken when someone has not or has been infected with mpox.

Protect yourself	Protect Others If You Are Recovering From Mpox At Home
• If someone you know is diagnosed with or has suspected mpox, avoid close contact with them, including sexual contact. • Know the symptoms and check yourself regularly. • If you have symptoms, seek health advice and self-isolate while you wait to get tested. • Get vaccinated if it is available to you.	• Isolate in a separate room. • Use a separate bathroom, or clean and disinfect (with household disinfectant) after each use. • Clean hands frequently using soap and water or an alcohol-based hand sanitizer. • Clean and disinfect frequently touched surfaces and objects. • Avoid sweeping and vacuuming.

• Clean and disinfect environments that could have been contaminated with the virus from someone who is infectious. • Stay informed about mpox in your area. • Have open, non-judgmental conversations with people you come into close contact with (especially sexual contact) about any symptoms you or they may have	• Use separate dishes, cups, bedding, towels, and electronics. • Do your own laundry. Put everything in a plastic bag before carrying it to the washing machine. Use soap and water > 60 degrees. • Open windows

b. Vaccination

Three vaccines against mpox have been developed over the years, including non-replicating vaccines (MVA-BN), minimally replicating vaccines (LC16), and replicating vaccinia-based vaccines (ACAM2000). These vaccines are approved for preventing mpox, but only for individuals at risk, such as those in close contact with someone with mpox or in a high-risk group. Mass vaccination is not currently recommended. If you are at high risk of mpox exposure due to an ongoing outbreak, consult your healthcare provider about available vaccine options. The WHO recommends vaccinations for those in close contact with someone with mpox or in a high-risk group. Vaccines are a crucial tool in protecting communities against mpox and should be used in combination with other public health and social measures. Vaccines provide protection against infection and severe disease, but it takes several weeks for immunity to develop. Initial vaccine effectiveness studies show promising results, but further research will provide more information on their effectiveness in different settings.

(i) Primary preventive (pre-exposure) vaccination (PPV)

Primary preventive (pre-exposure) vaccination (PPV) is recommended for groups at high risk for exposure to monkeypox in the current multi-country outbreak.

Persons at the highest risk of exposure in the current multi-country outbreak are gay, bisexual, or other men who have sex with men (MSM) with multiple sexual partners. Others at risk may include individuals with multiple casual sexual partners; sex workers; health

workers at risk of repeated exposure; laboratory personnel working with orthopoxviruses; clinical laboratory and health care personnel performing diagnostic testing for monkeypox; and outbreak response team members (as designated by national public health authorities). The level of risk of infection may vary between the groups and could be used by countries for prioritization in case of limited vaccine supply.

For groups at risk of developing more severe disease if they are infected with monkeypox virus, including children, pregnant women and immunocompromised persons, vaccination against monkeypox as a PPV measure is not recommended because of their higher risk of severe disease. If, however, they are at high risk of exposure, persons in these groups should be prioritized for PPV.

Specific considerations apply as to vaccine choice for special population groups at high risk of severe disease.

(ii) Post-exposure preventive vaccination (PEPV)

Post-exposure preventive vaccination (PEPV) is recommended for contacts of cases, ideally within four days of first exposure (and up to 14 days in the absence of symptoms).

Children, pregnant women, and immunocompromised persons may be at risk of developing more severe disease when infected with monkeypox virus. In case of limited vaccine supply, these populations, if exposed, should be offered vaccination in a priority.

Specific considerations apply as to vaccine choice for special population groups at high risk of severe disease.

(iii) Choice of vaccine

For healthy adults, non-replicating vaccine (MVA-BN), minimally replicating vaccines (LC16) or replicating vaccinia-based vaccines (ACAM2000) are appropriate for use.

MVA-BN is administered as a 2-dose subcutaneous injection (0.5ml dose) given at least 4 weeks apart. LC16 and ACAM2000 are both administered as a single dose using the scarification method with a bifurcated needle.

For individuals for whom replicating (such as ACAM2000) or minimally replicating (LC16) vaccine is contraindicated (i.e. severe immune deficiency), the non-replicating (MVA-BN) should be used; likewise

for individuals for whom there are warnings or precautions because of e.g. immunosuppression therapies or atopic dermatitis, the non-replicating (MVA-BN) vaccines should be used.

Vaccine recipients must be informed that the level and duration of protection is currently unknown, and that it takes approximately 2 weeks from time of finalizing a complete series (2 doses) of vaccination with MVA-BN for peak immunity to develop. For the minimally and non-replicating vaccines peak immunity is expected to occur 4 weeks after vaccination (1 dose).

Mpox Epidemiology

1. Global Epidemiology

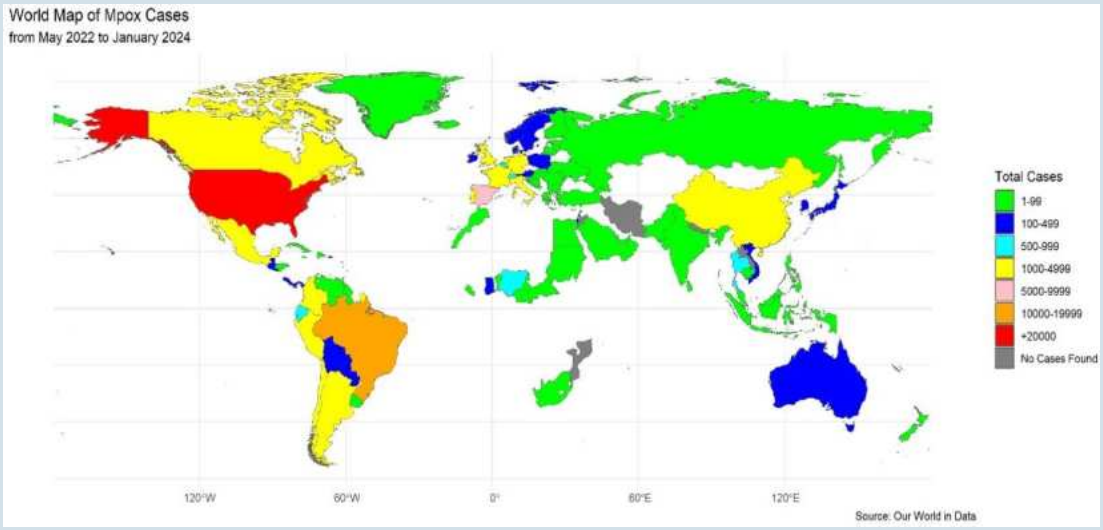


Figure 1. Distribution of Mpox Cases in The World

As we can see from the map above, the largest number of cases comes from The United States of America which has had more than 20,000 cases since May 2022. The second largest contributor on mpox cases in the world is Brazil which has around 10,000 to 19,999 cases since the disease first detected.

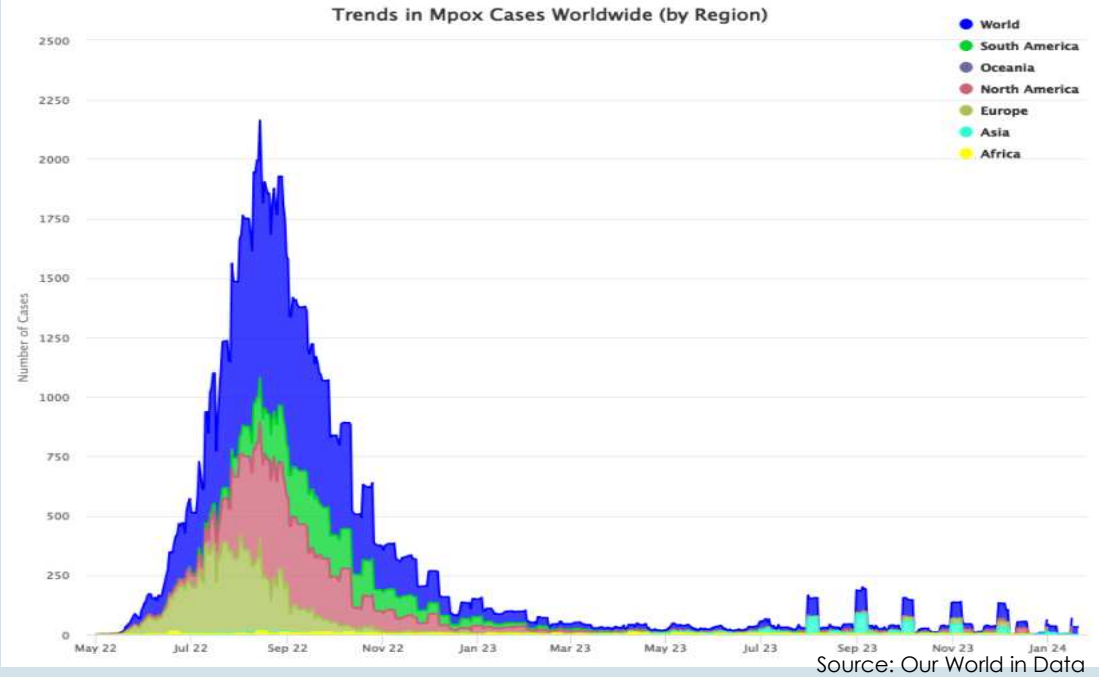
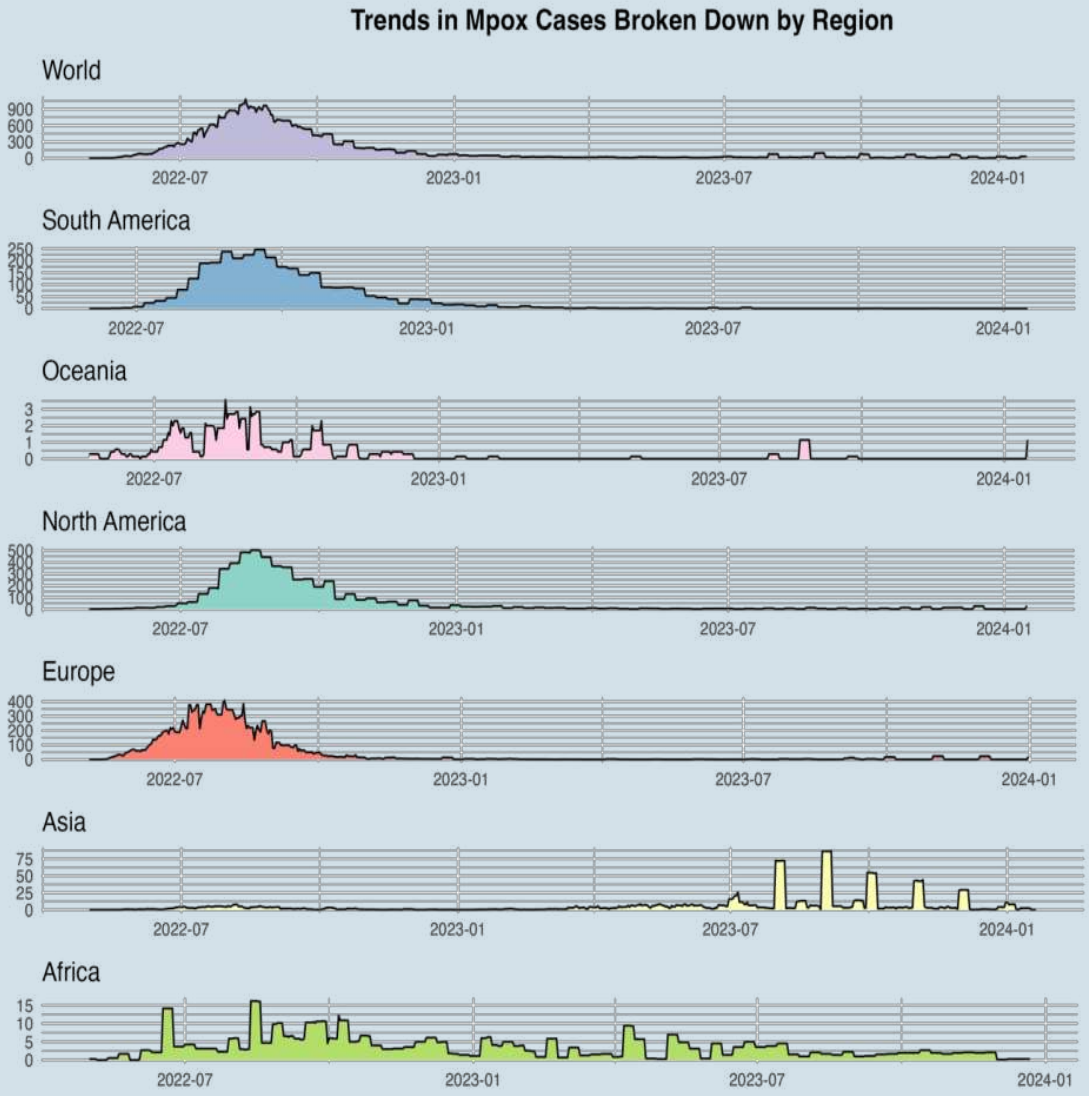


Figure 2. Trend of Mpox Cases in The World by WHO Region

From the total cases represented in the world as it is depicted from the figures above, North America had the highest contribution on Mpox cases. The trend was followed by South America Region. The mpox cases reached a peak in September 2022. After November 2022, the cases across the globe started to decrease gradually.



Source: Our World in Data

Figure 3. The Mpox cases breakdown by region

As the graphs broken down into each region, it is clearly seen that the trends in the region were quite varied. At the beginning of the Mpox outbreak, only few cases were seen in the Asian Region. Meanwhile, the cases were already quite high in some regions such as North America, South America and Europe. These three regions reported hundred cases in just several months when the outbreak occurred.

Altough the Asian region had only few cases since the beginning of the disease outbreak, the data showed that the region later impacted by the outbreak started in the begining of July 2023. Since then, the cases in the region were fluctuated every weeks up until January 2024.

Compared to other regions, the data of African region reveals that the cases of mpox in the region differ in term of the trends. The cases in this region exist since the beginning of the outbreak yet it has small number of

cases compared to the others. However, Oceanian region was the least contributors for the mpox cases according to the Figure 3.

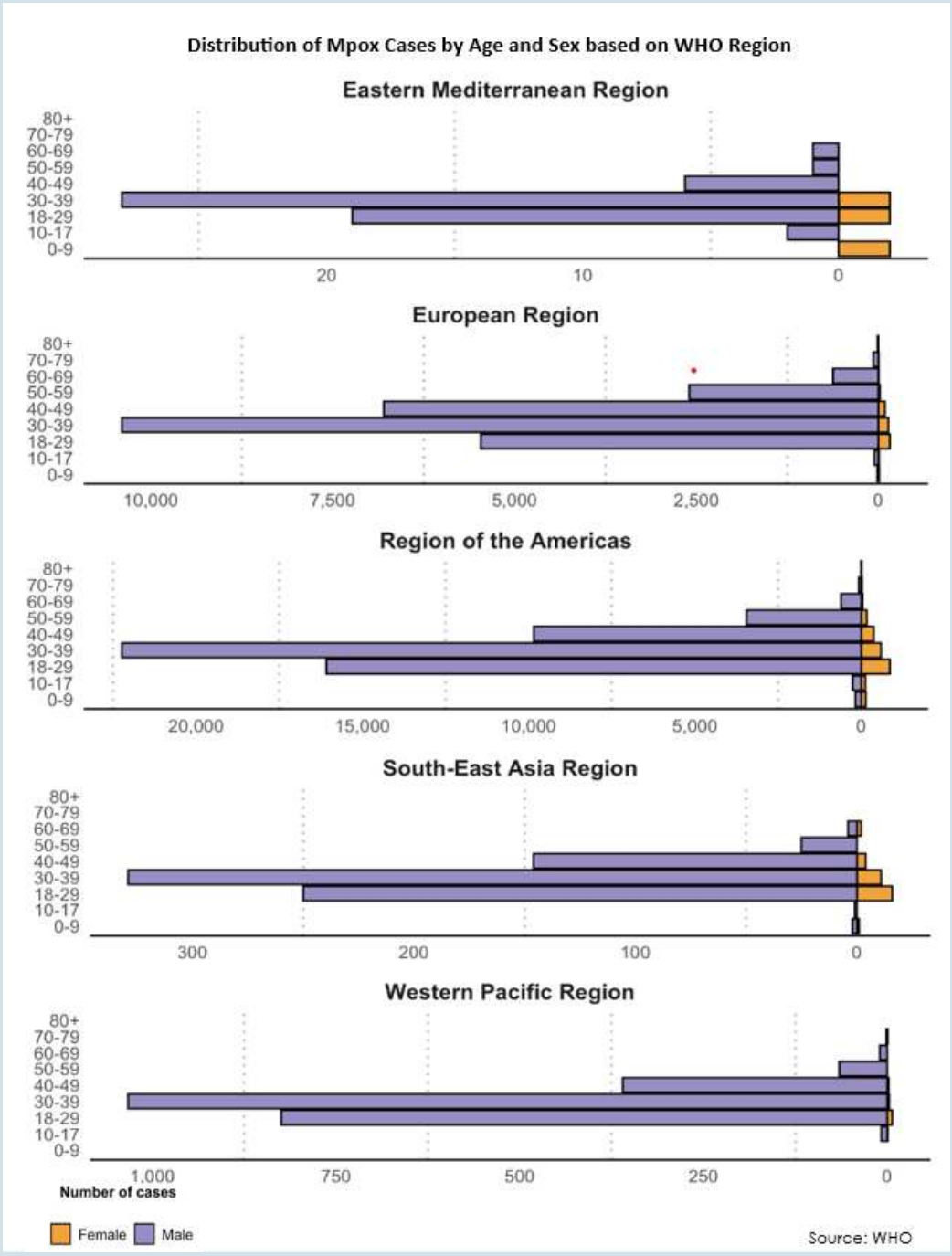


Figure 4. The Distribution of Mpox cases by Age and Sex based on WHO Region

Based on the Figure 4, the cases of mpox in each region mostly infected males with the age of range 30-39. For female, the cases mostly occurred to those who have the age ranges from 18 to 29 years old. The least number of cases in every region in the world were contributed to the group of females and males with age ranges from zero to nine years old.

2. Regional Epidemiology

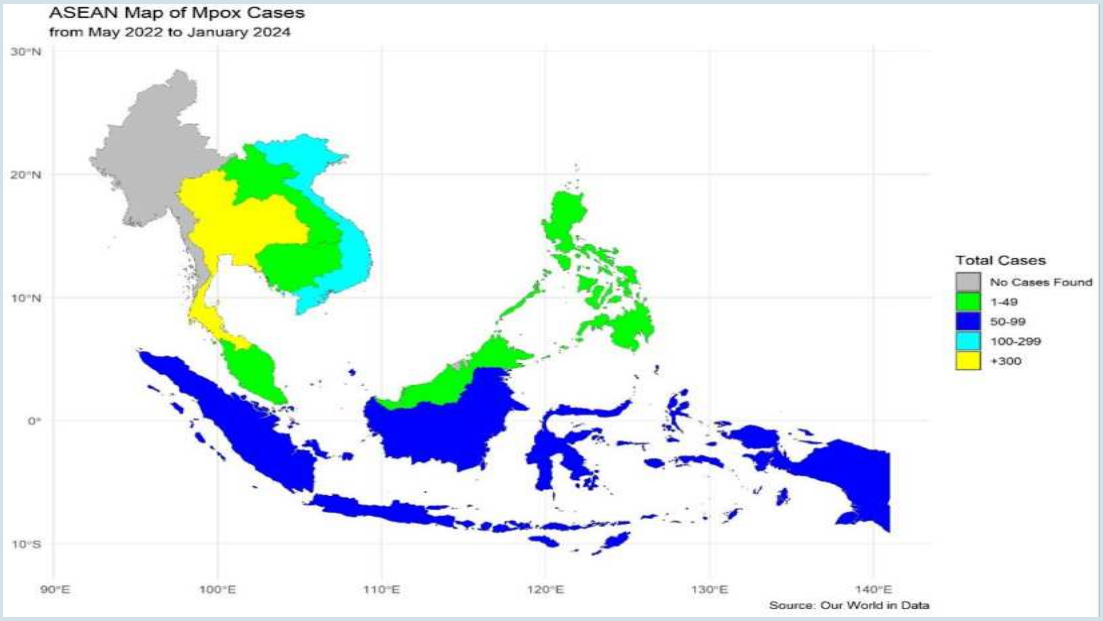


Figure 5. The Distribution of Mpox Cases in the Asean Region

The map above shows that the largest number of cases in the ASEAN region were found in Thailand. This trend is followed by Vietnam as the country that contributes the second largest number of mpox cases in the region. Meanwhile, the least number of mpox cases were found in Lao PDR. Among the AMS, there are two countries that have no mpox cases until now: Myanmar and Brunei Darussalam.

The breakdown cases by the AMS in the following Figure 6 shows that the average number of cases in the region were different between the states. Singapore was higher than the other countries at the beginning of the outbreak. The Philippines showed the similar feature near the end of 2022. Meanwhile, Thailand, Vietnam, and Indonesia experienced the same trend in the late of 2023.

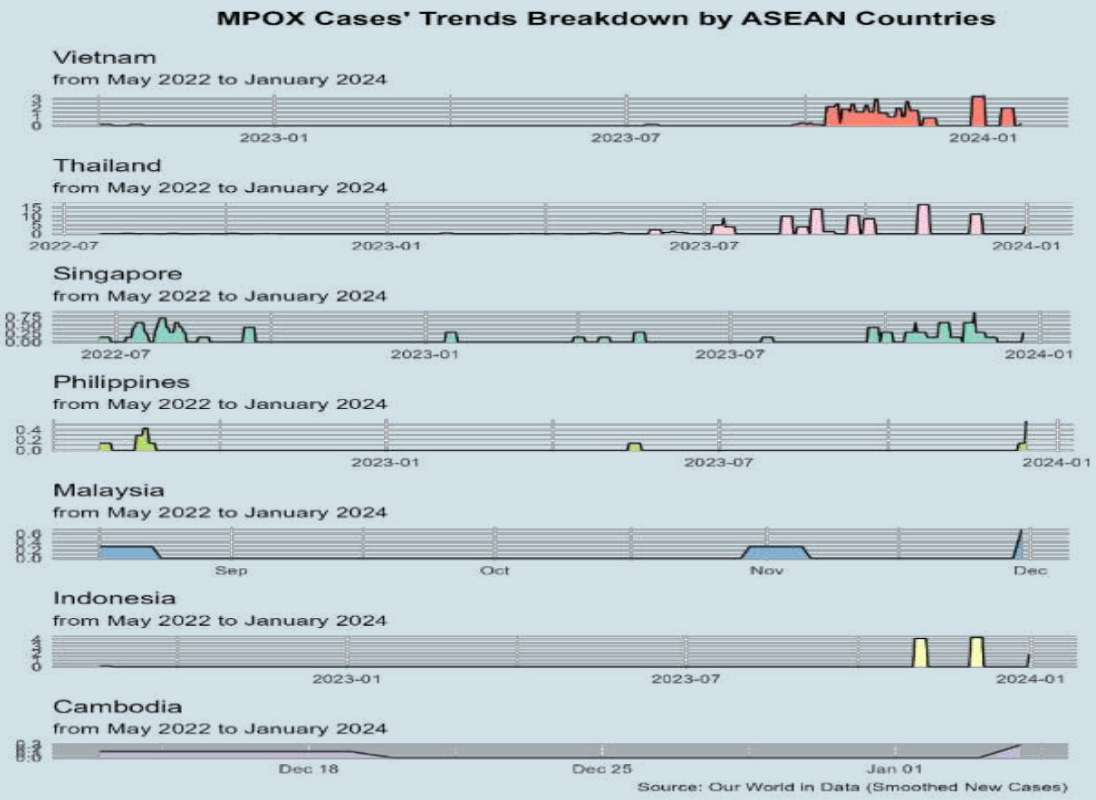


Figure 6. The Trends of Mpox Case in The ASEAN Region

Policy and Recommendation

WHO Response to Mpox Outbreak

WHO and its collaborators persist in offering assistance to nations through five interconnected core elements (5Cs) focusing on preparedness, readiness, and response (WHO, 2023d). Essential actions and mechanisms of WHO support encompass various activities within each core component, including, but not restricted to, the following

Table 6. WHO Response to Mpox Outbreak

Emergency Coordination	• Providing emergency response support at global, regional and country levels through technical guidance, surge support and mobilization of resources • Supporting national authorities with establishing or enhancing coordination mechanisms and public health capacities at national and sub-national levels employing a One Health approach
Collaborative Surveillance	• Supporting national authorities to ensure surveillance, epidemiological investigation and contact tracing which is inclusive of affected communities, animal contacts, and leverages approaches and lessons learned from the COVID-19 pandemic. • Supporting the genomic sequencing of the monkeypox virus found in the current outbreak and scale-up of testing across all six WHO regions, providing diagnostic capacity and trainings, and ensuring centralised procurement and shipment of diagnostic kits
Community Protection	• Working closely with affected communities to develop risk communication and community engagement (RCCE) strategies for preventive, risk-reduction, and other social measures. Ensuring evidence-based information for prevention efforts, enhanced case identification, contact tracing, testing and treatment. • Utilizing the WHO Information Network for Epidemics (EPI-WIN) for working with global communities of practice to inform stakeholders and the general population, providing real-time intelligence on challenges and best practices in monkeypox prevention, testing and treatment

Safe and Scalable Care	• Supporting coordination and effective implementation of case/clinical management for monkeypox and regularly monitoring health service availability and capacity, particularly for primary care, sexual health services, and appropriate intensive care support where needed • Supporting countries to implement appropriate IPC measures to mitigate and control transmission of the disease in health care and community settings and providing capacity-building for countries through the development and delivery of training to health workers
Countermeasures and Research	• Working with scientists, partners, and manufacturers of medical countermeasures (MCM) to assess global supply and demand and encourage scaling up of vaccine production and supporting equitable access. • Supporting countries with MCM rollout through guidance, training and capacity-building measures, procurement of vaccines and therapeutics; working with countries to support integration of vaccines and therapeutics research with ongoing public health response

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