

# What can research evidence tell us about Monkeypox Outbreak?

## A Rapid Evidence Review

[Aug 02, 2022]



### Key Findings

Monkeypox (MPX) has a similar virus family and symptoms with that of smallpox.

- ❖ The symptoms of monkeypox include fever, headache, muscle aches, backache, swollen lymph nodes, chills, exhaustion, rash that occurs on the face, within the mouth, hands, feet, chest, genitals, or anus.
- ❖ Males make up more than half of monkeypox cases in most outbreaks.
- ❖ According to WHO report many of the cases that have been reported in this outbreak have been identified among men who have sex with men.
- ❖ According to the WHO, the current case fatality rate (CFR) for monkeypox is 3–6% and all deaths were among unvaccinated against smallpox.
- ❖ Avoiding coming into close, skin-to-skin contact with the monkeypox infected individual, washing hands frequently or use an alcohol-based hand sanitizer, not handling or touching the bedding, towels, or clothing of a sick person, avoiding contact with rodents, primates and other animals, having safer sex etc were methods identified for prevention of monkeypox.
- ❖ There are no treatments specifically for monkeypox virus infections. However, antiviral drug (Tecorivimat) and vaccines developed to protect against smallpox may be used to prevent and treat monkeypox virus infections.

### What is Rapid evidence Review?

Rapid evidence review addresses the needs of policymakers and managers for research evidence that has been appraised and contextualized to a specific context in a matter of hours or days. This rapid evidence review goes beyond research evidence and integrates multiple types and levels of evidence

### For whom is this Rapid Evidence Review for?

This document was created in response to the current situation of monkeypox outbreak. It aims to provide the best available evidence to inform the Ethiopian public health emergency response.

### + Included:

- **Key findings** from the available studies and guidelines

### ✗ Not included:

- Recommendations
- Detailed descriptions



## Introduction

Monkeypox is a viral zoonotic disease (a virus that spreads from animals to people) which has similar symptoms with that of smallpox. However it is milder, rarely fatal and less contagious than smallpox. Monkeypox is caused by monkeypox virus, which belongs to the orthopoxvirus genus in the family Poxviridae. There are two distinct genetic clades of monkeypox virus: the Central African (Congo Basin) clade and the West African clade. The Congo basin clade has historically caused more severe diseases and was thought to be more transmissible (Radonić et al., 2014; CDC, 2022d; WHO, 2022a).

### Why monkeypox become important currently?

Although, monkeypox cases were common or endemic in African countries, recently cases have been documented in non-endemic nations since the beginning of May 2022. The currently laboratory confirmed cases were mainly from European region (86%) and region of the America (11%). The majority of confirmed cases were with travel histories to Europe and North America (WHO, 2022d).

### Global trends of Monkeypox

As of August 02, 2022, a total 25,391 confirmed cases of monkeypox and 10 deaths (six from endemic and four from outside of endemic countries) has been reported globally. Almost all (98.7%) of these cases were from 76 countries that have not historically reported monkeypox cases (CDC, 2022a; WHO, 2022d). This is the first time in history where cases and continuous chains of transmission have been documented in countries which do not have direct or indirect epidemiological links with Central or West African regions (WHO, 2022a). Cases of monkeypox have been reported from seven endemic and three non-endemic African countries since the start of 2022. Sudan, a country bordering Ethiopia, has reported the first case of monkeypox virus on July 31<sup>st</sup>, 2022 (CDC, 2022). See the map in figure 1 that shows the global monkeypox outbreak.

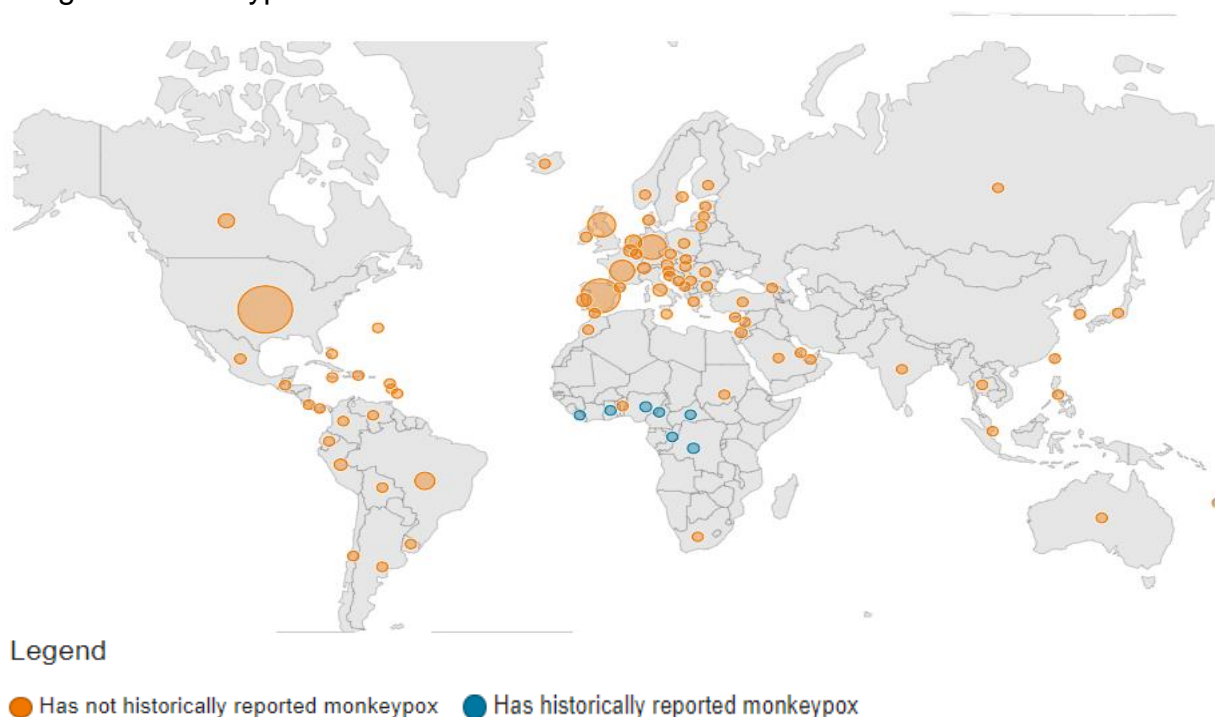


Fig 1: Monkeypox outbreak global map as of Aug 02, 2022 (CDC, 2022).

More recently, there has been a continuous increase in the number of monkeypox cases globally. As a result, as of July 23, 2022 monkeypox outbreak was declared as a Public Health Emergency International Concern (PHEIC) by WHO (WHO, 2022<sup>e</sup>) which clearly depicts the global concern to the disease and the threat that the disease is posing worldwide. Figure 2 below shows the global trend of monkeypox cases based on the date of notification by region.

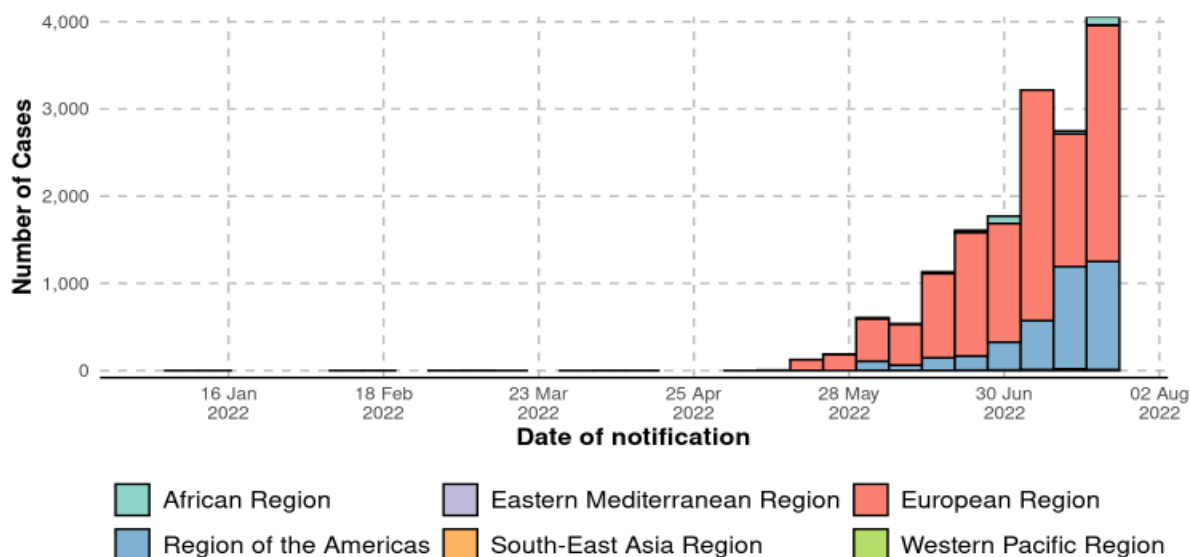


Fig 2: Global trend of Monkeypox outbreak as of July 22, 2022 (WHO, 2022).

## Aim of the review

The aim of this review is to summarize the best available evidence on monkeypox virus concerning cases definition, mode of transmission, risk factors, pathophysiology and clinical manifestation, screening and diagnosis, case fatality, case management, prevention and control and prognosis of monkeypox virus. The current situation of monkeypox outbreak in Ethiopia and the country's preparedness and response is also included in this review.

## Sign and Symptoms of Monkeypox

The pathogenesis, sign and symptom of monkeypox are similar to those of smallpox. The symptoms of monkeypox are fever, headache, muscle aches, backache, and swollen lymph nodes. Other symptoms like chills, exhaustion, rash that occurs on the face, within the mouth, and other regions of the body, such as the hands, feet, chest, genitals, or anus, and can resemble pimples or blisters. Before entirely healing, the rash passes through several stages. This procedure can take several weeks to complete. A rash may appear first, followed by subsequent symptoms in some cases. Some people merely get a rash. Monkeypox differs from smallpox in that it causes lymphadenopathy. This usually happens with the commencement of a fever, 1–2 days before the development of the rash, or very rarely with the onset of the rash. Lymph nodes in the neck (submandibular and cervical), armpits (axillary), and groin (inguinal) can expand on both sides of the body or just one (CDC, 2022; WHO, 2022).

## Mode of transmission

Direct animal to human transmission can occur as a result of direct contact with blood, body fluids, cutaneous or mucosal lesions of infected animals. Transmission can occur when eating uncooked meat and other animal product of infected animals (WHO, 2022b).

Close contact with respiratory secretions, skin sore of an infected person or recently contaminated object can cause human-to-human transmission. Prolonged period of face to face contact is required for transmission through respiratory droplet particles. Mother to fetus transmission can also happen through placenta which can result in congenital monkeypox. Close contact between mother and newborn is also a favourable condition for monkeypox transmission from mother to child (WHO, 2022b).

Findings from systematic review also reported the following issues on monkeypox transmission. A 1980s study involving 338 monkeypox cases in the Democratic Republic of Congo (DRC) found that animal sources were suspected in 72.5 % (245/338) of cases, while human sources were suspected in the remaining 27.5 %. Contrary to this, only 22% of 419 cases in the 1990s from the same country were animal sources while 78% were human sources (Bunge *et al.*, 2022).

## Risk Factors for Monkeypox

Human-to-human transmission was linked to risk behaviors such as sharing a room or bed, living in the same house, and drinking or eating from the same dish. Animal-to-human transmission risk is reportedly enhanced by sleeping outside or on the ground, living near or visiting the forest, regular exposure to sick animals or cleaning their cages/bedding (Beer and Bhargavi Rao, 2019; Bunge *et al.*, 2022).

According to WHO report many of the cases that have been reported in this outbreak have been identified among men who have sex with men. Given that the virus is currently moving from person to person in these social networks, men who have sex with men may currently be at higher risk of being exposed if they have close contact with someone who is infectious (WHO, 2022b).

### How this evidence Review was prepared?

A rapid evidence synthesis approach adapted from the SURE Rapid Response Service was applied to search and summarize the best available evidence on different aspects of monkeypox virus. To answer the questions under review the authors of this review searched for relevant studies from databases including PubMed, the Cochrane Library, Health system evidence, Epistemonikos, Google scholar and SUPPORT summary. To include all papers published on Monkeypox virus, we searched articles using the word “monkey pox, Monkeypox, Smallpox”. Additionally, guidelines from international organizations like World Health Organizations (WHO), Centre for Disease Control and Prevention (CDC) and other research articles were also included to support the finding of the review.

All systematic reviews conducted on monkeypox virus were included for this review. The included studies were filtered for English language. The last search was made on July 26, 2022, with no date restriction. Non-transparent reviews (e.g. news, letters, editorials, reports, communications, comments, and correspondence) were excluded.

We found 6 articles through search of different data bases mentioned above. After screening for the titles and abstracts of the articles, two (Beer and Bhargavi Rao, 2019; Bunge *et al.*, 2022) of them which satisfy the inclusion criteria were included in the final review in addition to the WHO and CDC

Males account for majority of all cases in most outbreaks. Over 80% of cases in the 1970-9, 1981-6, and 1996-7 cohorts were under the age of 15 but the median age of cases is steadily increasing since the 1970s. Traders, students, artisans, healthcare professionals, farmers, hunters, and transportation workers were among the most commonly stated occupations affected by monkeypox (Beer and Bhargavi Rao, 2019; Bunge *et al.*, 2022).

Infants, young children, pregnant women, patients with complications and immune-compromised individuals were identified as a high-risk groups for death due to monkeypox (Beer and Bhargavi Rao, 2019).

People, who received a smallpox vaccination, had a lower overall attack rate (0.95/1000) than those who had not received a smallpox vaccination (3.6/1000) (Bunge *et al.*, 2022).

### **Laboratory diagnosis of Monkeypox**

Polymerase chain reaction (PCR) of skin lesion material or additional specimens, such as an oral or nasopharyngeal swab, as appropriate, is the main diagnostic procedure for diagnosing monkeypox (WHO, 2022c).

Serology test might not be accurate; hence it shouldn't be utilized as a sole diagnostic test in the first place. A case that otherwise satisfies the criterion of a suspected or probable case should not be discarded if the blood PCR test was the only test performed and it came out negative (WHO, 2022c).

### **Monkeypox Case Definitions**

According to the WHO, the case definitions for suspected and probable cases are given as follow:

#### **Suspect Case**

A person of any age presenting since 01 January 2022 with an unexplained acute rash or one or more acute skin lesions

#### **AND**

One or more of the following signs or symptoms

- Headache,
- Acute onset of fever (>38.5oC),
- Lymphadenopathy (swollen lymph nodes)
- Myalgia (muscle and body aches)
- Back pain
- Asthenia (profound weakness)

#### **AND**

For which the following common causes of acute rash or skin lesions do not fully explain the clinical picture: varicella zoster, herpes zoster, 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.

*N.B. It is not necessary to obtain negative laboratory results for listed common causes of rash illness in order to classify a case as suspected. Further, if suspicion*

*of monkeypox infection is high due to history and/or clinical presentation or possible exposure to a case, the identification of an alternate pathogen which causes rash illness should not preclude testing for MPXV, as coinfections have been identified.*

### **Probable case**

A person meeting the case definition for a suspected case

#### **AND**

One or more of the following:

- has an epidemiological link [prolonged a face-to-face exposure in close proximity, including health workers without appropriate PPE (gloves, gown, eye protection and respirator)<sup>1</sup>; direct physical contact with skin or skin lesions, including sexual contact; or contact with contaminated materials such as clothing, bedding or utensils] to a probable or confirmed case of monkeypox in the 21 days before symptom onset
- has had multiple or anonymous sexual partners in the 21 days before symptom onset
- has detectable levels of anti-orthopoxvirus (OPXV) IgM antibody b (during the period of 4 to 56 days after rash onset); or a four-fold rise in IgG antibody titre based on acute (up to day 5-7) and convalescent (day 21 onwards) samples; in the absence of a recent smallpox/monkeypox 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)

### **Prognosis**

Monkeypox is normally a self-limited disease with symptoms lasting from two to four weeks. Monkeypox typically resolves on its own without medical intervention. Monkeypox complications can include secondary infections, bronchopneumonia, sepsis, encephalitis, and corneal infections with subsequent vision loss (WHO, 2022c). According to the WHO monkeypox, the current case fatality rate (CFR) is around 3–6%. However, findings from systematic reviews reported a pooled estimate of case fatality rate of 8.7% from the previous cases. The CFR for the Central African clade (10.6%) was significantly higher than that of the West African clade (3.6 %) (Bunge *et al.*, 2022).

A review reported the secondary attack rate (SAR) for monkeypox to range between 0-11 % (Beer and Bhargavi Rao, 2019). Another report from systematic review revealed the SAR to range from 0.3–10.2% in five decades (1970s to 2010-2019) (Bunge *et al.*, 2022).

### **Prevention and Control**

#### **Prevention:**

The following measures are important in preventing the disease before it occur (CDC, 2022b):

- ❖ Avoid coming into close, skin-to-skin contact with the monkeypox rash.
  - Avoid touching the rash or sores of person who has monkeypox.

- Avoid kissing, hugging, sexual intercourse, and cuddling with someone who has monkeypox.
- Never share cup or food utensils for dining.
- ❖ Wash your hands frequently with soap and water or use an alcohol-based hand sanitizer, especially following contact with sick persons.
- ❖ Do not handle or touch the bedding, towels, or clothing of a sick person.
- ❖ Avoid coming into contact with rodents and primates, who are the main carriers of the monkeypox virus. Avoid touching bedding or other items that ill or dead animals have touched, as well as sick or dead animals.
- ❖ Monkeypox patients should stay isolated. When possible, keep them away from other family members and pets if they have an active rash or other symptoms.
- ❖ Thoroughly cook all foods containing meat or animal products.

### **Vaccination and treatment**

There are no treatments specifically for monkeypox virus infections. However, monkeypox and smallpox viruses are genetically similar, which means that antiviral drugs and vaccines developed to protect against smallpox may be used to prevent and treat monkeypox virus infections.

Although vaccination is not recommended at this stage, it might be important for the following people:

- Person who has a close contact with those who have the monkeypox
- Person who may become into contact with the virus
- Person who may be at a higher risk of contact with the virus, such as those who conduct laboratory tests to identify monkeypox

JYNNEOS (also known as Imvamune or Imvanex) and ACAM2000 are the two vaccines that have been approved by the U.S. Food and Drug Administration (FDA) for use in preventing monkeypox infection (CDC, 2022d).

After diagnosis, health professionals has to follow the health of a patient, try to alleviate symptoms, prevent dehydration, and administer antibiotics to treat any development of secondary bacterial infections. The outcome of the disease is worse for people of immune deficiencies (WHO, 2022c).

Although they haven't been researched as a monkeypox treatment, antiviral medications may be helpful (WHO, 2022c). Tecorivimat which is an antiviral drug recently got approval from the European Medicines Agency for the treatment of orthopovirus-associated infections, including monkeypox although the effectiveness and safety is not well known at this time (WHO, 2022d).

## Monkeypox situation in Ethiopia

In Ethiopia there is no confirmed or probable monkeypox case reported till August 02, 2022 (CDC, 2022a). However, there were 113 suspected cases and all tested negative to date (EPHI, 2022).

Based on the WHO advice on the urgent need to raise awareness about Monkeypox and undertake comprehensive case finding and isolation, the Ethiopia Public Health Institute (EPHI) has moved its Public Health Emergency Operation Center (PHEOC) from **WATCH MODE** to the **ALERT MODE** with the aim of:

- Strengthening active surveillance and rumour/alert investigation, and screening
- Risk communication and awareness creation
- Improvement of laboratory investigation capabilities
- Developing scenario-based planning and exercises
- guidelines and training materials development
- Conducting health workforce capacity building

Lab supplies were obtained from UK health security, orientation on sample management and onsite training on testing was given for laboratory workers and testing has started at influenza lab within EPHI. Surveillance of monkeypox has been started and virtual training was delivered and alert letter was distributed to regions. Rumour collection and verification are ongoing through the national contact centre (8335) and the regional toll-free lines and screening activities are on-going and integrated with COVID-19 and other public health emergency activities. Fact sheets, interim monkeypox surveillance guideline and preparedness and response plan was developed and distributed.

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### **Contribution of Authors**

- All authors equally contribute to the development of the review.

### **Conflict of interest**

- There is no conflict of interest to declare.

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