

Context

- On 14 August 2024, the WHO declared mpox a Public Health Emergency of International Concern due to the rapid spread of subclade Ib in the Democratic Republic of the Congo (DRC) and five neighbouring countries that had not previously been affected by mpox.
- The mpox Global Strategic Preparedness and Response Plan (September 2024–February 2025) highlighted the urgent need for proactive measures and research to address critical knowledge gaps.
- We had previously maintained [a living evidence profile \(LEP\) of the best-available evidence related to the mpox outbreak](#) with 11 versions produced between May 2022 and October 2022 (at which time no further updates were deemed necessary).
- Version 12 was published in [August 2024](#), which was requested to solely focus on published evidence syntheses and single studies about clade I (including Ia and Ib) given the global spread.
- Version 13 bridged the previous versions from 2022 with the latest developments related to the mpox outbreak in 2024, where we identified a total of 172 evidence documents: 140 evidence syntheses related to mpox published between 2019 to 5 November 2024, 31 new single studies on clade I (including Ia and Ib) that were published since version 12, and one set of slides from a global conference.
- In this final update of the LEP, we include and summarize 20 new evidence documents (13 highly relevant evidence syntheses and seven new single studies) published between 6 November 2024 to 3 February 2025.

Best-available evidence related to the mpox outbreak

27 February 2025

[MHF product code: LEP 6.14]

Box 1: Evidence and other types of information

+ Global evidence drawn upon



Evidence syntheses selected based on relevance, quality, and recency of search

+ Forms of domestic evidence used (🇨🇦 = Canadian)



Evaluation



Data analytics

* Additional notable features

Prepared in three business days using an 'all hands on deck' approach

Question

- What is the best-available evidence related to the mpox outbreak?

High-level summary of key findings

- This LEP includes evidence documents from the previous version, giving a total count of 192 evidence documents (153 evidence syntheses, 38 single studies, and one set of slides from a global conference).

- Our findings focus on new insights from the newly identified 20 evidence documents (13 highly relevant evidence syntheses and seven single studies) related to mpox.
- Generally, the new evidence documents align with the previous findings on the biology and epidemiology of mpox.
- Specifically, there continues to be insights on the genomics and transmission about clade I.
- Further, we identified some evidence on the hospitalization risk for people living with HIV in North America or Europe.
- There continues to be limited information about effective prevention and control strategies, diagnosis, prognosis, and treatment that differentiated the impacts based on clades and subclades.
- There is a lack of evidence on the long-term health impacts of mpox infections and the socio-economic consequences of outbreaks in affected communities.

Framework to organize what we looked for

- Biology
 - Clade I
 - Subclade Ia
 - Subclade Ib
 - Clade II
 - Subclade IIa
 - Subclade IIb
- Epidemiology
 - Transmissibility
 - Geographic spread
 - Protective immunity
- High-risk populations
 - 2SLGBTQI+
 - Children
 - Pregnant people
 - People who are immunocompromised
 - Healthcare workers
 - Other
- Prevention and control

Box 1: Approach and supporting materials

At the beginning of each living evidence profile and throughout its development, we engage a subject matter expert and citizen partners, who help us to scope the question and ensure relevant context is taken into account in the summary of the evidence.

We identified evidence addressing the question by searching PubMed. Updated searches were conducted on 4 September 2024, 1 October 2024, 5 November 2024, 22 January 2025, and 3 February 2025 to identify any evidence syntheses about mpox, as well as any single studies focused on clade I since the last version. The search strategies used are included in Appendix 1. In contrast to synthesis methods that provide an in-depth understanding of the evidence, this profile focuses on providing an overview and key insights from relevant documents.

We appraised the methodological quality of evidence syntheses that were deemed to be highly relevant using the first version of the [AMSTAR](#) tool. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality, medium-quality evidence syntheses are those with scores between four and seven, and low-quality evidence syntheses are those with scores less than four. The AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to evidence syntheses pertaining to delivery, financial or governance arrangements within health systems or implementation strategies.

Note that the timing, frequency, and scope of future updates of this LEP will be determined in collaboration with the requestor.

A separate appendix document includes:

- 1) methodological details (Appendix 1)
- 2) overview of the included evidence syntheses and single studies (Appendix 2a-c)
- 3) Key findings from the high-quality evidence syntheses and new single studies (Appendix 3)
- 4) details about each identified high-quality synthesis (Appendix 4)
- 5) details about each identified single study (Appendix 5)
- 6) categorization of the medium and low-quality syntheses (Appendices 6, 7)
- 7) documents that were excluded in the final stages of review (Appendix 8)

This update to the living evidence profile was prepared in the equivalent of three day of a 'full court press' by all involved staff.

- Information and education (e.g., including risk communication)
- Non-pharmaceutical measures to prevent infection
- Non-pharmaceutical measures to control the spread of infections
- Pharmaceutical measures used as part of public health strategies
- Strategies grounded in behavioural science
- Surveillance and reporting
- Diagnosis
- Clinical presentation
 - Symptom onset and duration
 - Complications
 - Variability in clinical presentation
- Prognosis (e.g., clinical severity, including morbidity and mortality)
- Treatment

What we found

We identified 20 new evidence documents (13 evidence syntheses and seven single studies) on mpox that were published since our last update (6 November 2024 to 3 February 2025). This LEP also includes evidence documents from the previous version, giving a total count of 192 evidence documents (153 evidence syntheses, 38 single studies, and one set of slides from a global conference).(1-192)

We describe the findings from all 20 evidence documents as they were all deemed to be highly relevant to the research question. Details of each identified evidence synthesis and single study are available in Appendices 4 and 5.

Coverage by and gaps in existing evidence syntheses and domestic evidence

The evidence syntheses and single studies continue to provide historical and recent insights of mpox in terms of biology, epidemiology, high-risk populations, prevention and control, diagnosis, clinical presentation, and treatment. Generally, the new evidence documents align with the previous findings on the biology and epidemiology of mpox. The majority of the evidence syntheses were either medium or low quality (based on the AMSTAR tool). There continues to be insights on genomics and transmission about clade I. Further, we identified some evidence on the hospitalization risk for people living with HIV in North America or Europe, but there was substantial heterogeneity in the results. We did not identify any new relevant information about the prognosis of mpox.

There are still gaps in the evidence on mpox. There is limited information about prevention and control, diagnosis, prognosis, and treatment that differentiates the impacts based on clades and subclades. Finally, there continues to be a lack of evidence on the long-term health impacts of mpox infections and the socio-economic consequences of outbreaks in affected communities.

Key findings from included high-quality evidence syntheses and single studies

Biology

Emerging research has highlighted the recent gaps in understanding the biology of mpox and its subclades. A scoping review (pre-print) focusing on clades I and II identified a lack of knowledge related to how the virus alters the host's physiology and biochemistry.(8)

Clade I

Clade I monkeypox virus, historically prevalent in Central Africa, exhibits distinct biological characteristics that set it apart from other clades.(124) Genomic analysis has revealed that clade I possesses certain genes, such as a homolog of the vaccinia virus complement control protein, which are absent in the West African clade (clade II). This may contribute to its potential for increased virulence, however there is still uncertainty.(8)

A new study from 2025 described the detection of clade Ib variant in China for the first time. The phylogenetic analysis revealed that it was related to sequences from African countries (Burundi, DRC, Kenya, and Uganda), United Kingdom, Sweden, United States, and Thailand.(184) The authors concluded that there is a need for strengthening contact tracing and management in Guangzhou (where the case of clade Ib appeared in China). A 2024 global analysis of 10,670 sequences collected from 65 countries (including Canada) revealed that most of the genetic data originated from outbreaks between 2022 and 2024.(121)

Biologically, the incubation period of mpox can vary between clades. Comprehensive analyses of the 2022 global outbreak and historical data estimated a pooled mean incubation period of 8.1 days (95% CI: 7.0–9.2 days) across all clades. Clade I infections were characterized by a mean of 7.3 days (95% CI: 5.0–10.2 days), whereas clade II infections showed a mean of 8.9 days (95% CI: 6.6–11.7 days). However, these differences were not statistically clear and could be due to sampling variability.(128;187) Similarly, one study in an evidence synthesis from the UK Health Security Agency indicated that the incubation period of clade I was estimated to be a median of seven days. However, the estimate included both suspected and confirmed cases, where the clade for some of these cases was unknown.(173)

DNA extracted from a single lesion is sufficient to conduct complete genome sequencing of the monkeypox virus strain, allowing for accurate determination of the virus's genetic lineage and potential geographic origin.(51) This genetic analysis capability enhances our understanding of the virus's biology.

Epidemiology

Unspecified clade

The identified evidence syntheses and single studies describe historical and recent transmission patterns and potential reservoirs for mpox. An evidence synthesis (including three Canadian studies) reported a shift in mpox transmission patterns from pre- to post-2022.(59) The authors reported that prior to 2022, most of the reported cases were caused by animal-to-human transmission, but almost all reported cases since 2022 had a history of human contact, particularly sexual transmission. Another evidence synthesis reported that the 2022 mpox outbreak also saw higher average ages and comorbidity rates than previous years, emphasizing the need for global cooperation to address the spread and impact.(40) Another evidence synthesis published in the Lancet described how clades I and II have distinct transmission patterns and clinical characteristics, which are likely influenced by route of exposure, infectious dose, and host immune response.(176) Finally, a study reported that the 2023 mpox outbreak in Katako-Kombe, DRC, found an attack rate of 2.15 per 1,000 population, a case fatality rate (CFR) of 4.6%, and a reproduction rate (R0) of 1.29, indicating sustained human-to-human transmission. The authors indicated that early medical intervention led to a 100% survival rate, while delayed care increased fatalities with higher rates of complications.(186)

In terms of reservoirs, three evidence syntheses indicated that skin lesions have high viral loads, which could contribute to high infectivity and drive rapid transmission, especially during direct skin-to-skin contact through close physical proximity.(132;133;192)

Clade I

Clade I monkeypox virus has historically been known for its circulation in southern, forested regions of African countries in the Congo basin, primarily the DRC and Cameroon.(155) The geographic spread of clade I appears to be expanding, with travel-related infections originating largely in Ghana, Côte d'Ivoire, the DRC, and spreading to other countries. Historically, clade I transmission has been primarily zoonotic, with high exposure to rodents (91%) and non-human

primates (77%).(36;37) However, recent evidence indicates evolving transmission patterns.(74) A cluster of clade I mpox infections in March 2023 in the DRC was reported to be transmitted through sexual contact, a route previously associated only with clade II.(74) Another evidence synthesis reported that there have been significant impacts in rural areas in the DRC. The authors indicated that controlling the epidemic in these areas has been challenging due to resource limitations.(177)

Subclade Ia and Ib

Genomic studies provided insights into the recent evolution and spread of mpox clades Ia and Ib. Regarding subclade Ia, a study reported that multiple strains of mpox have circulated in the Republic of the Congo during the 2024 outbreak after analysing samples collected from Brazzaville, Point-Noire, Likouala, Cuvette-Centrale, and Plateaux, which were likely introduced through both cross-border human-to-human transmission and direct zoonotic events. The study also indicated that there is evidence of local spread in previously unaffected areas.(171)

For subclade Ib, three studies from the DRC added insights to understanding transmission modes and disease severity. For example, clade Ib been linked to sustained human-to-human transmission, including but not limited to sexual transmission.(19;76;162) One of the studies also reported that in addition to subclade Ib being present in the DRC, there appears to be patterns associated with subclade Ia, which suggests multiple zoonotic introductions.(76) These new findings align with studies previously reported (142;152) as well as with two published evidence syntheses on human-to-human transmission patterns.(59;175) Similarly, a recent 2025 prospective cohort study published in the Lancet indicated that the clade Ib outbreak in Kivu, DRC, was mostly spread through close contact, which was found among adults, children, and pregnant women. Almost half of the confirmed cases were reported to be female.(188)

Clade II

A global genomic analysis reported that clade IIb appears to have shown more cases of human-to-human transmission across different geographical regions spread than clade I.(121) Clade IIb may have faster transmission dynamics compared to clade I and subclade Ib.(104)

High-risk populations

Unspecified clade

Since 2022, most of the mpox outbreaks have primarily affected MSM.(4;59;95) There have also been reported and confirmed cases of mpox among people living with HIV, women, and children. For example, a medium-quality evidence synthesis from 2025 reported that people living with HIV have a statistically significant increased risk of hospitalization from mpox with a pooled risk ratio of 1.57 (95% CI: 1.18–2.08). Most of the studies reported in this evidence synthesis were conducted in North America or Europe. However, the authors indicated that there was substantial heterogeneity in the meta-analysis and that the pooled estimate of risk should be interpreted with caution. Specifically, the pooled estimate of risk may not accurately reflect specific subgroups or regions. The authors concluded that there needs to be targeted prevention, early diagnosis, and improved clinical management strategies for people living with HIV.(180)

Growing concerns have emerged regarding the impact of mpox among women and children in endemic regions.(140) In pregnant people, moderate to severe monkeypox virus infections have been associated with high rates of miscarriage, intrauterine fetal death, and perinatal loss, highlighting the need for maternal and fetal monitoring according to the seven reported cases in the synthesis.(28) Among the cases, two were reported to have suspected vertical transmission where one of the fetuses showed hydrops (i.e., severe swelling in the body). However, the authors indicated that the risk of congenital mpox has not been established. As reported in the previous LEP, outbreaks in Central African Republic have occurred since 2018, which primarily affected forested regions and younger populations, with children under 16 being particularly vulnerable.(16) Similarly, in the DRC, 60% of cases were found in children under 14 years of age.(37)

Subclade Ia and Ib

Subclade Ia appears to primarily affect children under the age of 15, who make up more than 90% of cases.(152) Specific to the subclade Ib findings in the DRC, most cases appear to be mainly in adults (85%). Of these cases, 52% are female, and 15% are children under 15. The HIV co-infection rate among those with known status was 7%, though it is important to note that the baseline HIV prevalence in the studied population is not specified in the available data, nor is the number of people with viral suppression from treatment as compared to no treatment.(152)

Prevention and control

Unspecified clade

The use of vaccines was predominately described in the available research evidence for the prevention and control of mpox. A recent study from 2025 reported that there is potential for the use of peptide-based vaccines, which could improve accessibility in regions lacking cold-chain infrastructure.(189) An evidence synthesis (literature last searched in 2022) noted the use of smallpox vaccine (MVA-BN vaccine), vaccinia immunoglobulin, and antiviral medicines can be used to prevent spreading of mpox (all clades).(8) The synthesis also notes that some existing antiviral medicines used to treat orthopox virus infection may be used alone or in combination with vaccines to treat mpox. These include tecovirimat and brincidofovir, which have been used in the U.K. to reduce viral titres in patients with mpox (clade not specified). In addition, the synthesis highlights the importance of personal protective equipment, including masks, goggles, gloves, or specific impervious long-sleeved gowns in clinical settings.(8) Another evidence synthesis reported that there is limited evidence on the effectiveness of contact-tracing, sexual behaviour modification and asymptomatic testing to prevent the transmission of mpox.(123) For example, the utility of asymptomatic testing was limited, however there may be some utility to raise awareness and increase case finding during an outbreak. The authors of two evidence syntheses indicated that examples of strategies include the combination of educational campaigns, vaccination of high-risk populations, non-pharmaceutical measures (e.g., handwashing), supportive care, and use of antivirals for specific circumstances.(183;191)

There are variations in vaccine acceptance across different regions of the world. An evidence synthesis reported higher prevalence of mpox vaccination acceptance in Asian and African countries compared to North America and Europe among healthcare workers.(108) Another evidence synthesis reported a higher acceptance in European countries compared to Asian countries. The sub-analysis of the study revealed that vaccine acceptance was highest among the LGBTI communities, followed by healthcare workers and the general population.(161) Similarly, an evidence synthesis by the UK Health Security Agency reported that people in the community of gay, bisexual and men who have sex with men (gbMSM) from the United States and the Netherlands were willing to receive a vaccination. Additionally, this population group were also likely to reduce their number of sexual partners and encounters if recommended by their healthcare providers.(174)

Clade II

A 2024 systematic review reported that the MVA-BN vaccine is highly effective in preventing mpox clade IIb, with vaccine effectiveness (VE) estimated at 76% for one dose (95% CI: 64–88%) from 12 studies, and 82% (95% CI: 72–92%) for two doses from six studies. Additionally, the vaccine prevented hospitalization with an effectiveness of 67% (95% CI: 55–78%), Post-exposure prophylaxis (PEP) shows limited effectiveness at 20% (95% CI: 24–65%) from seven studies, which was influenced by timing and exposure conditions.(126)

Diagnosis

There appear to be efforts to improve the diagnosis of mpox, including the development and availability of diagnostic kits. Historically, a scoping review from 2022 (pre-print) found that there was a lack of mpox virus-specific rapid diagnostic kits, but rather the available kits at that time were adapted from other viruses such as smallpox or other orthopox viruses.(8) Since then, a recent 2024 survey indicated that European Centres in the European Union have showed a high capability for confirming cases by PCR and to identify clades and/or subclades.(82). Further, two single

studies and an evidence synthesis indicated that PCR has been proven to be an accurate tool for detecting and differentiating mpox clades.(142;178;185)

Clinical presentation

Unspecified clade

Symptoms of mpox have become more varied over time between 1970 to 2023, although the prevalence of lesions and rashes remain consistent.(151) According to the findings presented at an international conference convened on 29 and 30 August 2024 by the World Health Organization,(152) the face is the primary rash site in 82% of cases, often with a centrifugal distribution and over 100 lesions in 51% of cases. High rates of lymphadenopathy (80%, mainly submaxillary and cervical) and febrile prodrome (80%) are common. Further, an evidence synthesis reported that oral lesions were found to be among the first clinical signs of mpox, and ulcers on the dorsal surface of the tongue and lips were the most commonly affected areas.(12) Another evidence synthesis described the clinical presentation of mpox as including a prodromal period with fever, headache, night sweats, myalgia, coryzal illness (i.e., common cold), and peripheral lymphadenopathy, and after one to two days, the presentation of lesions in the mucosal surfaces and skin.(8)

A recent evidence synthesis from 2025 described atypical manifestations of mpox. The authors indicated that a high degree of diagnostic suspicion (e.g., when individuals present with cutaneous lesions) and familiarity with atypical clinical presentations are crucial for identifying any suspected cases of mpox.(181) Two evidence syntheses reported that the mpox virus can lead to eye-related symptoms and complications such as conjunctivitis, eyelid lesions, and in some severe cases, corneal opacity that can cause blindness. These symptoms were found to be more common in Africa compared to other regions, highlighting the need for healthcare workers in endemic regions to prioritize early detection and treatment.(49;136) Other reported symptoms in both clades include otolaryngologic (i.e., headache, sore throat, cough, cervical lymphadenopathy) and neurological and psychiatric presentations (i.e., encephalitis, confusion, seizures) symptoms.(11;143)

Prognosis

Historically, an evidence synthesis reported that the 2022 mpox outbreak was spreading quickly with 35% of cases resulting in hospitalization and 5% fatality rate of both clades.(15) Recent surveillance data from a WHO conference presentation describes global mortality rates between 5–10% for clade Ia, 0.7% for clade Ib, 0% for clade IIa, and 3–5% for clade IIb.(152)

Clade I

Related to high-risk populations, an evidence synthesis reported that pediatric case fatality rate reached 11% (95% CI: 4–20) according to a pooled analysis of studies spanning from 1972 to 2023 in 16 countries. Higher fatality rates were observed in clade I compared to clade IIa and IIb in endemic regions.(137) One medium quality evidence synthesis reporting on historic data (between 1970 and 2014) noted that the median age for mpox infection in the DRC was under 16.(15) A single study of clade I infections (from 2001 until 2021) in the Central African Republic similarly found particularly high rates of case fatality among children and those in close contact with wildlife.(16)

Treatment

In the context of mpox, an evidence synthesis with 18 uncontrolled studies reported that individuals were treated with tecovirimat (n= 61), cidofovir (n= 7), and brincidofovir (n= 3), where 83% individuals reported to have complete resolution of symptoms. (145) Additionally, an evidence synthesis on the effectiveness of tecovirimat (published 21 December 2024) reported that tecovirimat was linked to faster lesion healing, symptom relief, and reduced viral shedding in some mpox patients (i.e., those with mild to moderate illness), but its effectiveness in severe cases (i.e., those requiring hospitalization) and its role in complete viral clearance remain unclear due to limited data and study

design limitations.(190) A randomized, placebo-controlled clinical trial (RCT) called PLATINUM-CAN is being conducted in Canada to assess tecovirimat in MPXV infection. It is a sister study to the PLATINUM-UK at Oxford University, where they aim to combine the results of both clinical trials.

A Cochrane review of therapeutics for treating mpox found no evidence from RCTs regarding the efficacy and safety of treatments. However, tecovirimat appears to not cause serious safety concerns (based on very low-certainty evidence), while brincidofovir may cause liver injury.(47) A recent high-quality evidence synthesis produced in 2022 noted that recovery can be supported by antiviral medications such as tecovirimat and brincidofovir, rehydration therapy and nutritional supports.(8) A recent single study reported on the use of oral tecovirimat (600 mg twice daily) for treating patients with mpox and reported that by day 14 most individuals had been discharged and were confirmed negative using real-time PCR detecting viral DNA from blood samples or lesion swabs. The study reported that the median time from the initiation of treatment until the absence of active lesions was five days.(107)

Next steps based on the identified evidence

We identified several knowledge gaps that were highlighted in the evidence that we included in this rapid evidence profile that could be explored to improve our understanding and management of mpox outbreaks. Generally, the gaps remain largely unchanged since the last LEP. Specifically, there needs to be a continued focus on generating high-quality evidence syntheses and studies that specify and study the impact of the clades and subclades, particularly on the biology, impact on high-risk populations, effective prevention and control strategies such as information, education, and non-pharmaceutical measures, and prognosis for both general and high-risk populations. Moreover, while equity was considered as part of the methodological process of reviewing included evidence in this LEP, there is a need for more comprehensive analysis in any future and more in-depth evidence syntheses.

Some specific areas for important next steps identified from the literature include the need to:

- continue supporting the early detection of and timely response to outbreaks (clade I and clade II), including using standardized reporting protocols, leveraging genomic surveillance to track the evolution and transmission dynamics of the virus, and strengthen surveillance systems
 - continue to leverage genomic surveillance to track the evolution of the virus
 - implement more active epidemiologic surveillance to better understand the true incidence of mpox
- generate evidence related to potential treatments (e.g., randomized controlled trials), investigating the long-term health outcomes for survivors of mpox infections, studying the socio-economic impacts of mpox outbreaks on affected communities, examining how environmental factors that influence mpox transmission and persistence (e.g., describing a One Health approach, virus survival on environmental conditions, investigating the roles of fomites or through air transmission), and exploring effective non-pharmaceutical measures and education (including the use of behavioural science)
- determine any differentiating diagnosis and prognosis of the mpox clades and subclades.

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