

RAPID REVIEW

Brief Overview of Monkeypox Virus Subclades

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Key Findings

- There are four Monkeypox Virus (MPXV) subclades (Ia, Ib, IIa, and IIb), all of which were first identified in West or Central Africa and have varying endemic locales, affected populations, modes of transmission and severity level.
- The newly identified subclade Ib was first detected in the Democratic Republic of Congo in September 2023 and rapidly spread to nearby countries in Central and East Africa, prompting the World Health Organization (WHO) to declare a Public Health Emergency of International Concern (PHEIC) on August 14, 2024. Travel-associated cases have been detected in several countries outside Africa, including Canada.
- Subclade IIb is responsible for a large global outbreak in non-endemic regions that began in 2022 with ongoing human-to-human transmission, predominantly among adult gay, bisexual, and men who have sex with men (gbMSM).
- Subclade Ia primarily affects children under 15 years of age while the other subclades (Ib, IIb, and IIa) are associated with infection in individuals over 15 years old
- All four MPXV subclades can be transmitted through human-to-human and animal-to-human contact (zoonotic transmission). Subclades Ia, IIa, Ib, and IIb can spread through household non-sexual contact and subclades Ib and IIb can also be transmitted through direct close contact including sexual contact.
- Subclade Ia has the highest case fatality rate (CFR), ranging from 5%-10%, followed by subclade IIa (range: 1%-3%), subclade Ib (range: 0.7%-1.4%), and subclade IIb with the lowest reported CFR at 0.1%.

Introduction

Mpox is a viral disease caused by the monkeypox virus (MPXV) and belongs to the Poxviridae family, the same family as the virus that causes smallpox.¹ MPXV has two distinct clades, clade I and clade II, each further classified into two subclades (i.e., Ia, Ib, IIa and IIb) which can be classified further into various lineages and sublineages.^{1,2} Laboratory methods such as genome sequencing are used to identify different subclades of MPXV infection.^{1,2} MPXV is endemic in West and Central African countries where it primarily spreads to humans through contact with infected wild animals.¹ Transmission can also occur through direct close or sexual contact with an infected person as well as through contact with objects contaminated by an infected person (e.g., clothing, bedding).¹

Mpox may start with flu-like symptoms, such as fever, chills, headaches, muscle aches, fatigue, swollen lymph nodes and sore throat, that can present before or after rash or lesions develop.³ Mpox rash or lesions can be painful and can occur throughout the body or may be limited to specific regions such as

the main site of infection (e.g., mouth, genitals). The rash or lesions eventually evolve from flat to raised fluid-filled blisters that progress into ulcers that then scab over. In Canada, most individuals with mpox have recovered from their infection within two to four weeks with treatment typically focused on pain control, wound care, and symptom management.⁴ Young children, persons with weakened immune systems and pregnant women are at higher risk for more severe mpox that may result in hospitalization.⁴ Individuals with a partial or fully completed smallpox vaccine (which provides protection against mpox) series are less likely to become infected with MPXV and develop severe disease.⁵ Historically, clade I MPXV causes more severe mpox infection than clade II.⁶

This Rapid Review provides a high-level summary of key differences between the four MPXV subclades, including current geographic spread, routes of transmission, key populations affected, and case fatality rates. This review is important for awareness among public health practitioners and healthcare providers given ongoing local transmission of subclade IIb in Canada and the risk of transmission of subclade Ib.⁷

Background

The MPXV subclade IIb mpox outbreak that occurred in Ontario from May to December 2022 coincided with outbreaks in many non-endemic countries across the world. The global rise in mpox prompted the WHO to declare a PHEIC on July 23, 2022, which remained in place until May 10, 2023.¹ Mpox transmission during the global outbreak occurred primarily through close contact (including intimate and sexual contact) between infected individuals and predominantly among gbMSM. After sporadic detection of mpox in 2023, Ontario experienced a significant increase in cases in 2024.^{8,9} Other countries globally have also continued to report subclade IIb mpox activity due to ongoing local transmission.^{3,10,11}

In September 2023 a new MPXV subclade was detected (Ib) in the DRC.^{1,12} Rapid spread of this subclade to nearby countries in Central and East Africa prompted the WHO to declare another mpox PHEIC on August 14, 2024.^{1,12,13} Since August 2024, several countries outside of Africa have detected subclade Ib cases including Canada.¹⁴

Methods

Public Health Ontario (PHO) Library Services designed and executed searches of scientific and grey literature to identify relevant evidence on this topic.

For the indexed literature, PHO Library Services searched MEDLINE, Embase, Medrxiv and Biorxiv between September 18, 2024 and September 19, 2024. Searches were limited to primary studies, reviews and editorials published in English and included preprints; case reports and animal studies were excluded. To further to limit the number of articles to be reviewed, data were extracted from primary studies published since 2014 and from reviews published since 2020. Title and abstract screening and full text screening were done by five reviewers independently using Covidence. Any disagreements about the inclusion of an article were resolved through discussion. All included articles were extracted using a standardized template in Microsoft Excel.

The grey literature search results contained a list of targeted resources from key international public health institutes. No jurisdictional limits were applied to the search. The results were screened and eligible sources underwent data extraction using a standardized template in Microsoft Excel.

Results

The following tables highlight key differences between the MPXV subclades in terms of the populations affected, geographical location of spread, primary modes of transmission, and case fatality rate (CFR). Since MPXV subclade Ib has recently been identified, data is still emerging and results reported below may change with time. Data from endemic regions may not be generalizable to non-endemic regions due to various factors including differences in transmission patterns, access to prevention measures including vaccination, and health system differences (e.g., availability of MPXV testing, access to health services, access to treatment).

Geographical Location of Spread

Table 1 describes the geographic distribution of MPXV subclades. All MPXV subclades were first detected in either Central or West Africa.^{1,15} Since August 2024, subclade Ib has been detected in countries outside Africa including Canada.¹⁶ Subclade IIb was responsible for a large global outbreak beginning in 2022 with ongoing detection of cases in previously non-endemic regions.¹⁷

Table 1: Geographic Location of Spread

Subclade Ia	Subclade Ib	Subclade IIa	Subclade IIb
• Endemic in Central Africa • Identified in neighboring areas in Central Africa and Republic of Congo¹⁵	• First detected in Central Africa • Outbreaks in neighboring African countries • Travel-associated case(s) detected outside of Africa including Canada	• Endemic in West Africa	• Endemic in West Africa • Ongoing transmission in non-endemic countries since 2022.

Key Populations Affected

Table 2 shows that MPXV subclades can predominantly affect different age cohorts. Subclade Ia primarily affects children under 15 years, while subclade Ib and subclade IIb are associated with individuals over 15 years, including sex workers and gbMSM. Subclade IIa predominantly affects adults.¹⁸

Table 2: Age of Key Populations Affected

Subclade Ia	Subclade Ib	Subclade IIa	Subclade IIb
• Individuals less than 15 years of age	• Individuals 15 years of age and older	• Individuals 18 years of age and older	• Individuals 15 years of age and older

Primary Routes of Transmission

Table 3 shows primary human-to-human and animal-to-human transmission routes for MPXV. All subclades can spread through household non-sexual contact and through infected animal-to-human contact, predominantly from infected rodents or ingestion/handling of contaminated foods (e.g. bush meat).^{15,16,18,19} For subclades Ib and IIb, transmission can occur through direct sexual contact.^{15,16,18,19} Evidence shows that MPXV can also spread from an infected person to their fetus and through contact with contaminated surfaces, materials (e.g. clothing, towels), or objects (e.g., needles, razors).¹

Table 3: Primary Route of Transmission

	Subclade Ia	Subclade Ib	Subclade IIa	Subclade IIb
Human to Human	Household non-sexual contact	- Household non-sexual contact - Direct sexual contact	Household non-sexual contact	- Household non-sexual contact - Direct sexual contact
Animal to Human	- Contact with infected animal - Ingestion and handling of contaminated foods	- Contact with infected animal - Ingestion and handling of contaminated foods	- Contact with infected animal - Ingestion or handling of contaminated foods	- Contact with infected animal - Ingestion or handling of contaminated foods

Reported Case Fatality Rates (CFR)

Table 4 provides CFRs reported in the literature for each MPXV subclade. Subclade Ia has the highest CFR,^{15,20} followed by subclade IIa,^{15,20} subclade Ib,^{15,20,21} and subclade IIb with the lowest CFR.^{15,20,21}

Table 4: Reported Case Fatality Rates

Subclade Ia	Subclade Ib	Subclade IIa	Subclade IIb
5%-10%	0.7%-1.4%	1%-3%	0.1%

Conclusion

MPXV is a global public health concern as it is no longer confined to endemic regions in Central and West Africa due to ongoing transmission of subclade IIb globally and recent detection of subclade Ib outside of Africa. Using data from both endemic and non-endemic regions, this brief overview of MPXV subclades describes differences in key age groups affected, geographic location of current spread, primary routes of transmission, and CFR reported in the literature. Surveillance efforts that involve sequencing to identify the subclade of MPXV can help public health authorities to understand the evolving epidemiology of MPXV on both a local and global scale

References

1. Public Health Agency of Canada. Mpox (monkeypox): for health professionals [Internet]. Ottawa, ON: Government of Canada; 2024 [modified 2024 Nov 18; cited 2025 Feb 11]. Available from: <https://www.canada.ca/en/public-health/services/diseases/mpox/health-professionals.html>
2. Otieno JR, Ruis C, Onoja AB, Kuppalli K, Hoxha A, Nitsche A, et al. Global genomic surveillance of monkeypox virus. *Nat Med*. 2025;31(1):342-50. Available from: <https://doi.org/10.1038/s41591-024-03370-3>
3. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Mpox [Internet]. Toronto, ON: King's Printer for Ontario; 2024 [modified 2024 Oct 29; cited 2025 Feb 11]. Available from: <https://www.publichealthontario.ca/en/Diseases-and-Conditions/Infectious-Diseases/Vector-Borne-Zoonotic-Diseases/Mpox#:~:text=Mpox%20typically%20involves%20a%20painful,muscle%20aches%2C%20and%20sore%20throat>
4. Public Health Agency of Canada. Mpox: public health management of human cases and associated human contacts in Canada [Internet]. Ottawa, ON: Government of Canada; 2025 [modified 2025 Feb 24; cited 2025 Feb 11]. Available from: <https://www.canada.ca/en/public-health/services/diseases/mpox/health-professionals/management-cases-contacts.html>
5. Public Health Agency of Canada; National Advisory Committee on Immunization; Committee to Advise on Tropical Medicine and Travel. Canadian immunization guide [Internet]. Evergreen ed. Ottawa, ON: Government of Canada; 2014 [modified 2024 Nov 25; cited 2025 Feb 11]. Part 4, immunizing agents: smallpox and mpox vaccines. Available from: <https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-21-smallpox-vaccine.html>
6. Schnirring L. Canada confirms first imported clade 1b mpox case. CIDRAP [Internet]. 2024 Nov 25; Mpox [cited 2025 Feb 11]. Available from: <https://www.cidrap.umn.edu/mpox/canada-confirms-first-imported-clade-1b-mpox-case#:~:text=The%20Public%20Health%20Agency%20of,illness%20involving%20the%20novel%20clade.&text=The%20patient%20from%20Manitoba%20sought,shortly%20after%20returning%20from%20travel>
7. Public Health Agency of Canada. Archived: rapid risk assessment: clade 1 mpox virus outbreak in the Democratic Republic of the Congo, public health implications for Canada [Internet]. Version 1.0. Ottawa, ON: Government of Canada; 2024 [archived 2025 Jan 16; cited 2025 Feb 11]. Available from: <https://www.canada.ca/en/public-health/services/emergency-preparedness-response/rapid-risk-assessments-public-health-professionals/clade-1-mpox-virus-outbreak-democratic-republic-congo.html>
8. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Enhanced epidemiological summary: mpox in Ontario: January 1, 2023 to May 31, 2024 [Internet]. Toronto, ON: King's Printer for Ontario; 2024 [modified 2024 Jun 25; cited 2025 Feb 11]. Available from: https://www.publichealthontario.ca/-/media/Documents/M/24/mpox-ontario-epi-summary.pdf?rev=f32d51b829ec436597d70be67971743b&sc_lang=en
9. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Enhanced epidemiological summary: mpox in Ontario: January 1, 2024 to December 31, 2024. [Internet]. Toronto, ON: King's Printer for Ontario; 2025 [modified 2025 Jan 14; cited 2025 Feb 11]. Available from: https://www.publichealthontario.ca/-/media/Documents/M/24/mpox-ontario-enhanced-episummary.pdf?rev=7628048f46a343afac89e7ecee10f861&sc_lang=en&hash=19E1BE71D66967278DEE1872DA5AB3CC

10. Public Health Agency of Canada. Update on mpox in Canada – May 11, 2023 [Internet]. Statement. Ottawa, ON: Government of Canada; 2023 May 11 [cited 2025 Feb 11]. Available from: <https://www.canada.ca/en/public-health/news/2023/05/update-on-mpox-in-canada--may-11-2023.html>
11. World Health Organization (WHO). Global mpox trends [Internet]. Geneva: WHO; 2025 [cited 2025 Feb 11]. Available from: https://worldhealthorg.shinyapps.io/mpox_global/#section-fns2
12. World Health Organization (WHO). WHO Director-General declares mpox outbreak a public health emergency of international concern [Internet]. News release. Geneva: WHO; 2024 Aug 14 [cited 2025 Feb 11]. Available from: <https://www.who.int/news/item/14-08-2024-who-director-general-declares-mpox-outbreak-a-public-health-emergency-of-international-concern>
13. United Nations. WHO declares mpox virus a public health emergency of international concern [Internet]. News release. New York: United Nations; 2024 Aug 14 [cited 2025 Feb 11]. Available from: <https://news.un.org/en/story/2024/08/1153176>
14. Centers for Disease Control and Prevention (CDC). Mpox in the United States and around the world: current situation [Internet]. Atlanta, GA: CDC; 2025 [cited 2025 Feb 11]. Available from: <https://www.cdc.gov/mpox/situation-summary/index.html>
15. Subissi L, World Health Organization's (WHO) Incident Management Support Team (IMST). Overview of clinical characteristics of various MPXV clades [Internet]. Geneva: WHO; 2024 [cited 2025 Feb 11]. Available from: https://cdn.who.int/media/docs/default-source/consultation-rdb/overview-of-clinical-characteristics-of-various-clades.pdf?sfvrsn=78263ab0_3
16. Public Health Agency of Canada. Rapid risk assessment: clades 1a and 1b mpox virus (MPXV) multi-country outbreaks – public health implications for Canada [Internet]. Ottawa, ON: Government of Canada; 2024 [modified 2024 Oct 10; cited 2025 Feb 11]. Available from: <https://www.canada.ca/en/public-health/services/emergency-preparedness-response/rapid-risk-assessments-public-health-professionals/rapid-risk-assessment-clades-1a-1b-mpox-virus-multi-country-outbreaks-public-health-implications-2024.html>
17. World Health Organization (WHO). Mpox [Internet]. Geneva: WHO; 2024 [cited 2025 Feb 11]. Available from: <https://www.who.int/news-room/fact-sheets/detail/mpox>
18. Ogoina D, Damon I, Nakoune E. Clinical review of human mpox. Clin Microbiol Infect. 2023;29(12):1493-501. Available from: <https://doi.org/10.1016/j.cmi.2023.09.004>
19. Okwor T, Mbala PK, Evans DH, Kindrachuk J. A contemporary review of clade-specific virological differences in monkeypox viruses. Clin Microbiol Infect. 2023;29(12):1502-7. Available from: <https://doi.org/10.1016/j.cmi.2023.07.011>
20. Cowen EW, Tkaczyk ER, Norton SA, Leslie KS. Mpox-a rapidly evolving disease. JAMA Dermatol. 2023;159(4):424-31. Available from: <https://doi.org/10.1001/jamadermatol.2023.0041>
21. Sharif N, Sharif N, Alzahrani KJ, Halawani IF, Alzahrani FM, Díez IT, et al. Molecular epidemiology, transmission and clinical features of 2022-mpox outbreak: a systematic review. Health Sci Rep. 2023;6(10):e1603. Available from: <https://doi.org/10.1002/hsr2.1603>

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