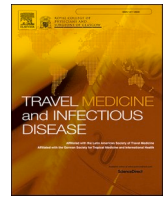


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Global spread of mpox Clade I: Implications for travel and public health

On August 15, 2024, the Swedish Public Health Agency announced that it has recorded the first case of mpox virus (MPXV) caused by Clade I variant outside Africa (<https://www.folkhalsomyndigheten.se/the-public-health-agency-of-sweden/communicable-disease-control/disease-information-about-mpox/one-case-of-mpox-clade-i-reported-in-sweden/>), which World Health Organization (WHO) declared a global health emergency on August 14, 2024 (<https://www.who.int/news/item/14-08-2024-who-director-general-declares-mpox-outbreak-a-public-health-emergency-of-international-concern>). Subsequently, several other cases outside of Africa were reported: in Thailand, in August (<https://www.aljazeera.com/news/2024/8/22/thailand-confirms-asias-first-known-case-of-new-mpox-strain>), one in India in late September (<https://www.bbc.com/news/articles/clyl1jlxr02o>), and the latest case, a 33-year-old man in German, whose viral strain was isolated on October 12 (<https://www.thenationalnews.com/health/2024/10/22/mpox-germany-reports-first-case-of-new-variant/>).

The infectious disease, formerly known as monkeypox, was first detected in humans in the Democratic Republic of the Congo (DRC) in 1970 [1]. There are two subtypes of the virus: Clade I and Clade II. The former, which is more lethal, has been endemic for decades in the Congo Basin in central Africa. The latter, less severe, has since been endemic in parts of West Africa.

The outbreaks were mostly caused by people who had contracted the virus from infected animals by eating bushmeat [2]. In recent years, human-to-human transmission has become more evident. This can occur through close physical contact, including respiratory droplets and contact with bodily fluids or contaminated materials. Symptoms of mpox typically begin with a high fever, accompanied by chills and general malaise. Muscle aches, or myalgia, are also common. The disease is notably characterized by the appearance of blister-like skin lesions, which start as small bumps and progress to larger, fluid-filled blisters. These blisters eventually crust over and fall off, often leaving behind discolored skin. Alongside these main symptoms, patients may experience headaches, fatigue, and swollen lymph nodes. Unlike the global outbreak of 2022 [3], the recent wave was driven by the Clade I and its new mutated variant, the so-called Clade Ib, first detected among sex workers in the remote mining town of Kamituga in the DRC's South Kivu province in September 2023 [4]. A phylogenomic reconstruction of all Clades and lineages of MPXV is described in Fig. 1. The spread of MPXV Clade Ib, especially in eastern DRC and neighboring regions, is driven by sustained human-to-human transmission, including sexual contact, similar to the previous global outbreak of Clade IIb. Studies highlight that sexual contact plays a significant role in transmission, with a notable proportion of cases involving individuals engaged in sex work. For instance, a study in Kamituga showed 29% of sub-Clade Ib cases reported involvement in sex work [5], while another study found 88% of hospitalized patients were involved in transactional sex [6]. Besides

sexual transmission, non-sexual contacts, such as those within households and healthcare settings, have also been reported as transmission pathways (<https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON522>). The implications for international travel are significant. Travelers to and from endemic regions, particularly those engaged in activities at higher risk of exposure such as humanitarian work, health care or sexual contact, are at increased risk. The mobility of populations between endemic and nonendemic areas could facilitate the spread of the virus, leading to potential outbreaks in previously unaffected regions. It is critical that health care providers be vigilant in evaluating travelers with symptoms consistent with mpox, particularly those returning from regions where Clade I or its subvariants are circulating. Pre-travel consultations should include discussions on mpox risk, vaccination recommendations, and preventive measures, especially for those visiting high-risk areas. In addition, travelers should be informed of the importance of seeking immediate medical attention if symptoms develop during or after travel to prevent further transmission. Strengthened surveillance at points of entry, combined with robust health education campaigns aimed at travelers, can play a key role in controlling the international spread of mpox. In response to the emerging threat, several countries have already implemented initial measures to prevent the spread of mpox. In Pakistan, for example, passengers are being screened at airports, and an isolation ward has been set up at a hospital in Peshawar after a case was confirmed in a traveler returning from a Gulf country (<https://www.sabcnews.com/sabcnews/pakistan-adopts-safety-measures-after-mpox-detected-in-peshawar/>). In Asia, China has introduced strict border controls for people showing symptoms or traveling from regions where mpox is prevalent, with airport authorities conducting surveillance and arranging isolation and testing. In Africa, South Africa has begun screening travelers at airports, while Kenya has begun testing travelers, reporting only mild cases so far. Nigeria has required all travelers entering the country to fill out a declaration form at the airport or online if they have recently visited parts of Africa affected by mpox (<https://www.bbc.com/pidgin/articles/c8rxe2l181po>). Current travel advisories and guidance related to mpox can be accessed at: <https://wwwnc.cdc.gov/travel/notices/level2/mpox-drc-neighboring-countries>.

To effectively address the growing mpox epidemic in Africa, several key actions by countries and stakeholders are essential: (i) educate clinicians on MPXV Clade I cases, focusing on both sexual and nonsexual transmission; (ii) strengthen surveillance, lab testing, epidemiological surveys, and contact tracing for timely reporting; (iii) provide vaccination guidance for travelers to affected areas; (iv) isolate suspected cases until a negative diagnosis, or if positive, until symptoms resolve, with contact tracing as per protocols; (v) maintain risk communication and collaborate with civil society to engage high-risk groups.

The experiences of past outbreaks, including Ebola, COVID-19, and

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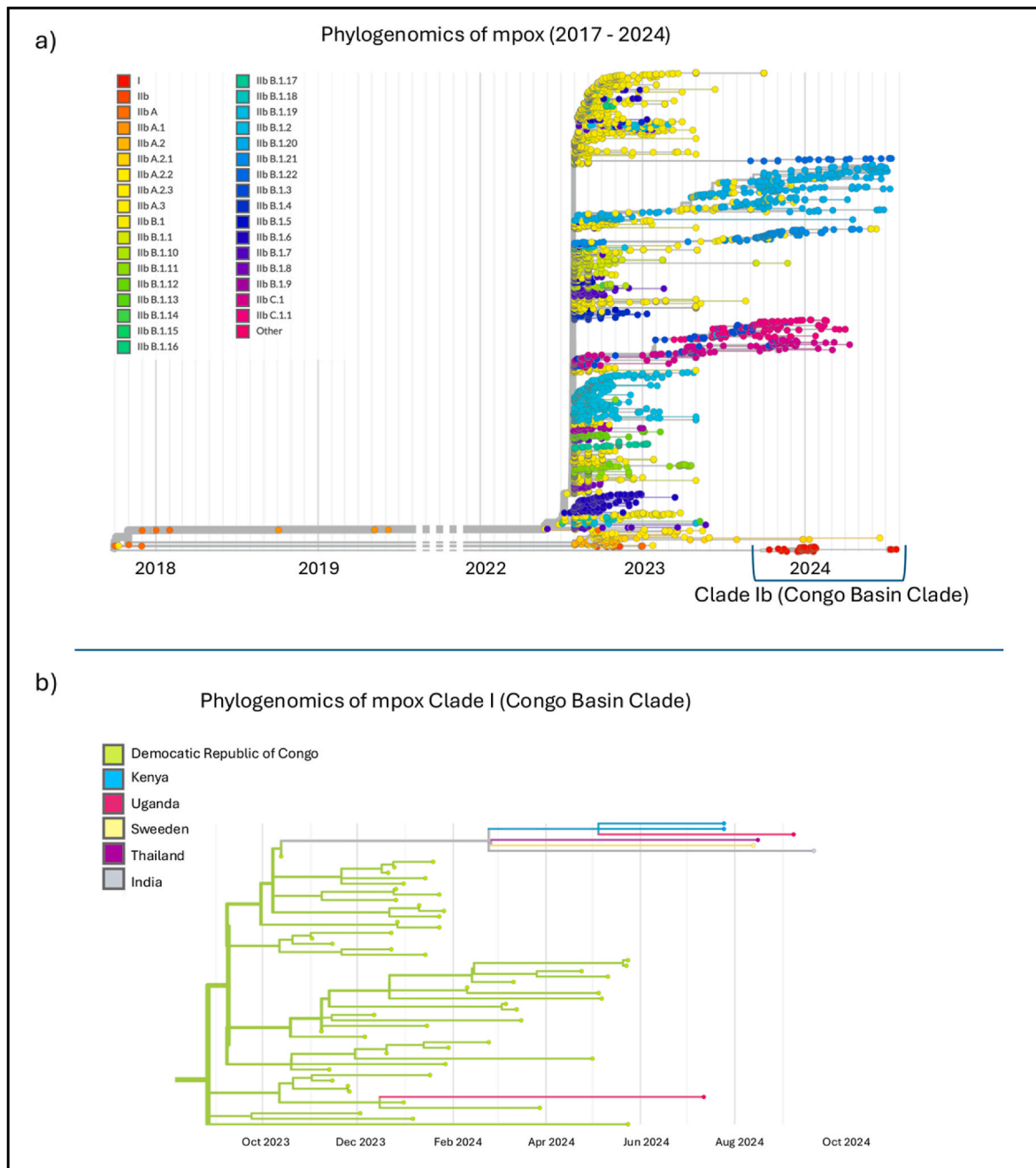


Fig. 1. A) Phylogenomic reconstruction of all Clades and lineages of mpox virus collected between October 2017 and October 2024 in the time-scaled phylogenetic tree constructed with all available genomes (last updated 2024-10-23). B) Highlight of the Clade Ib of mpox virus collected between October 2023 and October 2024 in the time-scaled phylogenetic tree constructed with 56 representative complete genomes (last updated 2024-08-14). Analysis was performed by using the Nextstrain/ncov tool available at the GitHub repository (<https://github.com/nextstrain/ncov>). Figure has been edited using the software GIMP 2.8 (available at <https://www.gimp.org/downloads/oldstable/>).

the 2022 multi-country mpox outbreak, offer crucial lessons that must not be forgotten. These crises have highlighted the importance of timely intervention, robust healthcare infrastructure, and international collaboration. The global community must unite in solidarity, recognizing that infectious diseases do not respect borders and that a threat to one region is a threat to all.

CRedit authorship contribution statement

Francesco Branda: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization.

Giancarlo Ceccarelli: Writing – review & editing, Writing – original draft, Investigation. **Antonello Maruotti:** Writing – review & editing, Writing – original draft. **Massimo Ciccozzi:** Writing – review & editing, Writing – original draft, Validation, Supervision. **Fabio Scarpa:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Formal analysis, Data curation.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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