Vital Surveillances

Spatiotemporal Transmission Characteristics of Global Monkeypox — Worldwide, January 2022–September 2025

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ABSTRACT

Introduction: Since 2022, the global monkeypox (mpox) epidemic has undergone clade replacement from clade IIb to clade Ib, accompanied by a geographic shift in the epidemic's epicenter. However, systematic analyses spanning the entire epidemic cycle from 2022 to 2025 remain limited. Integrating global epidemiological and genomic data is essential for determining spatiotemporal transmission dynamics.

Methods: Global mpox surveillance data, mpox virus whole-genome sequences, and demographic data were collected. Retrospective spatiotemporal scan statistics were used to identify significant transmission clusters. Phylogenetic trees were used to characterize evolutionary relationships among clades, and haplotype network analysis was used to infer transmission pathways.

Results: A total of 165,244 mpox cases were reported globally, showing a two-phase pattern. From January 2022 to August 2023, clade IIb predominated, accounting for 96.18% of cases in Europe and the Americas. From September 2023 to September 2025, the epicenter shifted to Africa, where clade Ib became dominant; during this phase, Africa accounted for 71.48% of global cases. Spatiotemporal scan analysis identified 10 significant clusters, with the highest relative risk observed in the West African cluster in 2025. Phylogenetic analyses linked clade IIb to the European and American phases, whereas clade Ib was associated with the African phase. The haplotype network suggested that Africa is the core transmission region of clade Ib, with Europe serving as a dissemination hub.

Conclusion: Mpox evolved from IIb-driven global dissemination to Ib-dominated regional clustering in Africa, with clade replacement driving the geographic shifts. The current risk is concentrated in Africa, underscoring the need for strengthened surveillance, genomic tracing, equitable access to resources, and targeted interventions.

Since May 2022, the mpox virus (MPXV) clade IIb, originating in Africa, has triggered a global outbreak affecting more than 100 countries. This outbreak marked a fundamental shift in mpox from a regionally endemic zoonotic disease to a sustained global public health threat characterized by human-to-human transmission (*1*). The World Health Organization (WHO) declared it a Public Health Emergency of International Concern (PHEIC) in July 2022 and terminated this status in May 2023. However, from late 2023 to 2024, the renewed transmission and international spillover of clade Ib, originating in Africa, prompted the WHO to redeclare a PHEIC in August 2024. Although this status was lifted in September 2025, the ongoing global transmission risk continues to be emphasized (*2*).

Although extensive studies have examined the global outbreak of MPXV driven by clade IIb (*3*), and the subsequent African resurgence associated with clade Ib (*4*–*5*), a systematic analysis of the complete epidemic trajectory from 2022 to 2025 remains lacking. Previous studies have largely focused on individual clades, specific regions, or limited time periods (*6*–*7*) and have failed to capture the macro-level intercontinental shift in epidemic centers driven by alternating clade dominance, as well as the micro-level mechanisms of viral adaptive evolution.

This study aimed to conduct an integrated analysis of the global mpox epidemic from January 2022 to September 2025 by combining macroepidemiological evidence (spatiotemporal distribution of cases) with microvirological insights (genomic evolutionary characteristics). The findings provide a robust scientific basis for global surveillance systems and differentiated prevention and control strategies.

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METHODS

Data Sources

Confirmed global mpox case data were obtained from the WHO website. Viral clade distribution and whole-genome sequence data were retrieved from the Global Initiative on Sharing All Influenza Data (GISAID) database. The population data for each country were sourced from the World Bank.

Analytical Methods

Spatial distribution maps were generated using ArcGIS 10.8.1 (Environmental Systems Research Institute, Inc., Redlands, California, USA). Bar charts and heatmaps were produced using the "ggplot2" and "pheatmap" packages in R (version 4.4.2, R Foundation for Statistical Computing, Vienna, Austria). A retrospective spatiotemporal scan analysis was conducted using SaTScan v10.2 (Information Management Services, Inc., Rockville, Maryland, USA) under a Poisson model, with a maximum spatial window of 30% of the at-risk population, a temporal window of 6–12 months, and a minimum cluster size of 1,000 cases. Cluster strength was assessed using the log-likelihood ratio, observed-to-expected ratio, and relative risk (*RR*), with $P<0.05$ considered statistically significant.

The eligible MPXV whole-genome sequences were filtered using GISAID (GISAID Initiative, Munich, Bavaria, Germany). Multiple sequence alignments were performed using the Multiple Alignment using Fast Fourier Transform (MAFFT) software (Osaka University, Suita, Osaka, Japan). Phylogenetic trees were constructed using IQ-TREE 2.0 (University of Vienna, Vienna, Austria) with the maximum-likelihood method and 1,000 bootstrap replicates, and visualized using iTOL v7 (biobyte solutions GmbH, Heidelberg, Baden-Württemberg, Germany). Quality-controlled whole-genome sequences from clade Ib were used to construct haplotype networks with the modified Templeton-Crandall-Singh (TCS) algorithm in fast Haplotype Networker (fastHaN), and visualization was performed with tcsBU (University of Porto, Porto, Portugal).

RESULTS

Epidemiological Overview of Global Monkeypox

Between January 2022 and September 2025, 165,244 mpox cases were reported across 135 countries. Regarding clade distribution (Table 1), clade IIb was predominantly detected in Europe and the Americas, whereas clades Ia, Ib, and IIa were mainly concentrated in Africa, with sporadic detections in other regions.

The global mpox epidemic exhibited a pronounced two-phase pattern (Supplementary Figure S1 and Supplementary Table S1, available at https://weekly.chinacdc.cn/). During the first phase (January 2022–August 2023), clade IIb predominated, with rapid expansion beginning in May 2022 and peaking in August 2022. In total, 96.18% of cases occurred in Europe and the Americas. In the second phase (September 2023 to September 2025), the epidemic center shifted to Africa, where clade Ib became the dominant strain and a new peak emerged in May 2025. During this phase, Africa accounted for 71.48% of global cases, while the Western Pacific, Eastern Mediterranean, and South-East Asian regions reported persistently low incidence levels.

Country-level heatmaps (Figure 1) show that Europe and the Americas experienced concentrated mpox outbreaks between June and August 2022, with Spain (6.02/100,000 in July) and Luxembourg (4.43/100,000 in August) reporting the highest monthly mpox incidence. From September 2023 onward, mpox incidence markedly increased in the Democratic Republic of the Congo (DRC), followed by Burundi and Uganda, with increases after August 2024. In early 2025, a new cluster emerged in West Africa, and Sierra Leone reached a peak incidence of 26.37/100,000 in May, the highest globally.

Spatiotemporal Clustering Analysis

A retrospective spatiotemporal scan analysis identified 10 significant transmission clusters with substantial heterogeneity in their spatial and temporal distributions. The five highest-risk clusters (Table 2), in chronological order, were as follows: a European cluster involving 19 countries from May to October 2022 (centered in the United Kingdom); a North American cluster from June to November 2022 (centered in the United States); a South American cluster involving nine countries from July to December 2022 (centered in Bolivia); a Central and Eastern African cluster from September 2024 to August 2025 (centered in the Democratic Republic of the Congo); and a West African cluster comprising Guinea, Sierra Leone, and Liberia from April to September 2025, which showed the highest *RR* (*RR*=86.69, $P<0.001$).

TABLE 1. Global distribution of mpox virus clades from January 2022 to September 2025.

MPXV clade	Number of countries	Countries	WHO region distribution (*n*, %)
Ia	15	Benin, Cameroon, Central African Republic, China, Democratic Republic of the Congo, Denmark, Gabon, Ireland, Liberia, Netherlands, Republic of the Congo, Sierra Leone, Sudan, Turkey, USA	AFRO: 8 (53.33); AMRO: 1 (6.67); EMRO: 1 (6.67); EURO: 4 (26.67); WPRO: 1 (6.67)
Ib	34	Angola, Australia, Belgium, Brazil, Burundi, Canada, China, Democratic Republic of the Congo, Ethiopia, France, Germany, India, Ireland, Italy, Japan, Kenya, Malawi, Oman, Pakistan, Qatar, Republic of the Congo, Rwanda, South Africa, South Sudan, Sweden, Switzerland, Tanzania, Thailand, Uganda, United Arab Emirates, UK, USA, Zambia, Zimbabwe	AFRO: 14 (41.18); AMRO: 3 (8.82); EMRO: 4 (11.76); EURO: 8 (23.53); SEARO: 2 (5.88); WPRO: 3 (8.82)
IIa	9	Cote d'Ivoire, Denmark, France, Ghana, Guinea, Liberia, Netherlands, Sierra Leone, USA	AFRO: 5 (55.56); AMRO: 1 (11.11); EURO: 3 (33.33)
IIb	72	Argentina, Australia, Austria, Belgium, Benin, Brazil, Cambodia, Cameroon, Canada, Central African Republic, Chile, China, Colombia, Costa Rica, Cote d'Ivoire, Czech Republic, Democratic Republic of the Congo, Denmark, Dominican Republic, Ecuador, Egypt, Ethiopia, Finland, France, Georgia, Germany, Ghana, Guinea, Hungary, Iceland, India, Indonesia, Ireland, Israel, Italy, Japan, Jordan, Lithuania, Luxembourg, Mexico, Nepal, Netherlands, Nigeria, North Macedonia, Oman, Pakistan, Paraguay, Peru, Philippines, Poland, Portugal, Republic of the Congo, Romania, Russia, Rwanda, Republic of Korea, Sierra Leone, Singapore, Slovakia, Slovenia, South Africa, Spain, Sudan, Sweden, Switzerland, Thailand, Togo, Turkey, UK, USA, Venezuela, Vietnam	AFRO: 14 (19.44); AMRO: 13 (18.06); EMRO: 5 (6.94); EURO: 28 (38.89); SEARO: 4 (5.56); WPRO: 8 (11.11)

Note: MPXV clade information was obtained from sequences available in the GISAID database as of September 30, 2025. n denotes the number of countries in each WHO region where a given MPXV clade was identified. The percentage (%) was calculated as the number of countries with that clade in each WHO region divided by the total number of countries with that clade across all WHO regions.
Abbreviation: MPXV=mpox virus; WHO=World Health Organization; SEARO=South-East Asia Region; EMRO=Eastern Mediterranean Region; EURO=European Region; AMRO=Region of the Americas; WPRO=Western Pacific Region; AFRO=African Region; USA=United States of America; UK=United Kingdom.

Phylogenetic and Haplotype Analyses

Phylogenetic analysis exhibited strong concordance between the staged evolution of the global mpox epidemic and the evolutionary dynamics of distinct viral clades (Figure 2A). Clade IIb showed extensive intercontinental dissemination and high genetic diversity in 2022, followed by a gradual decline after 2023, consistent with the epidemic phase dominated by Europe and the Americas. Conversely, clade Ib showed a highly localized transmission core in Africa, particularly in the Democratic Republic of the Congo and Uganda, with limited genetic diversity, reflecting the Africa-centered second phase of the epidemic. Clades Ia and IIa displayed more restricted transmission ranges than the other clades, indicating substantial differences in transmission adaptability among the MPXV clades.

Haplotype network analysis of clade Ib further showed that the DRC was the persistent core of regional transmission, while Uganda experienced short-term, high-intensity outbreaks. Other countries primarily showed sporadic importations or limited local transmission chains that were rapidly interrupted, indicating that clade Ib remained largely Africa-centered with limited global dissemination capacity (Figure 2B).

DISCUSSION

This study represents the first comprehensive integration of macroepidemiological and microvirological evidence to characterize the complete global mpox epidemic trajectory from January 2022 to September 2025. The results reveal a clear two-phase spatiotemporal pattern. We determined the intrinsic linkage between viral clade replacement (IIb to Ib) and intercontinental shifts in epidemic epicenters and addressed key gaps in previous studies that focused on single clades or localized spatiotemporal scales.

During the first phase, clade IIb drove a rapid expansion in Europe and the Americas, which was closely associated with dense social networks among men who have sex with men and high levels of international mobility (*8*–*10*). In the second phase, the epidemic center shifted to Africa, where clade Ib predominated and showed strong regional clustering. This pattern likely reflects Africa's role as a traditional reservoir of clade I mpox, which is characterized by

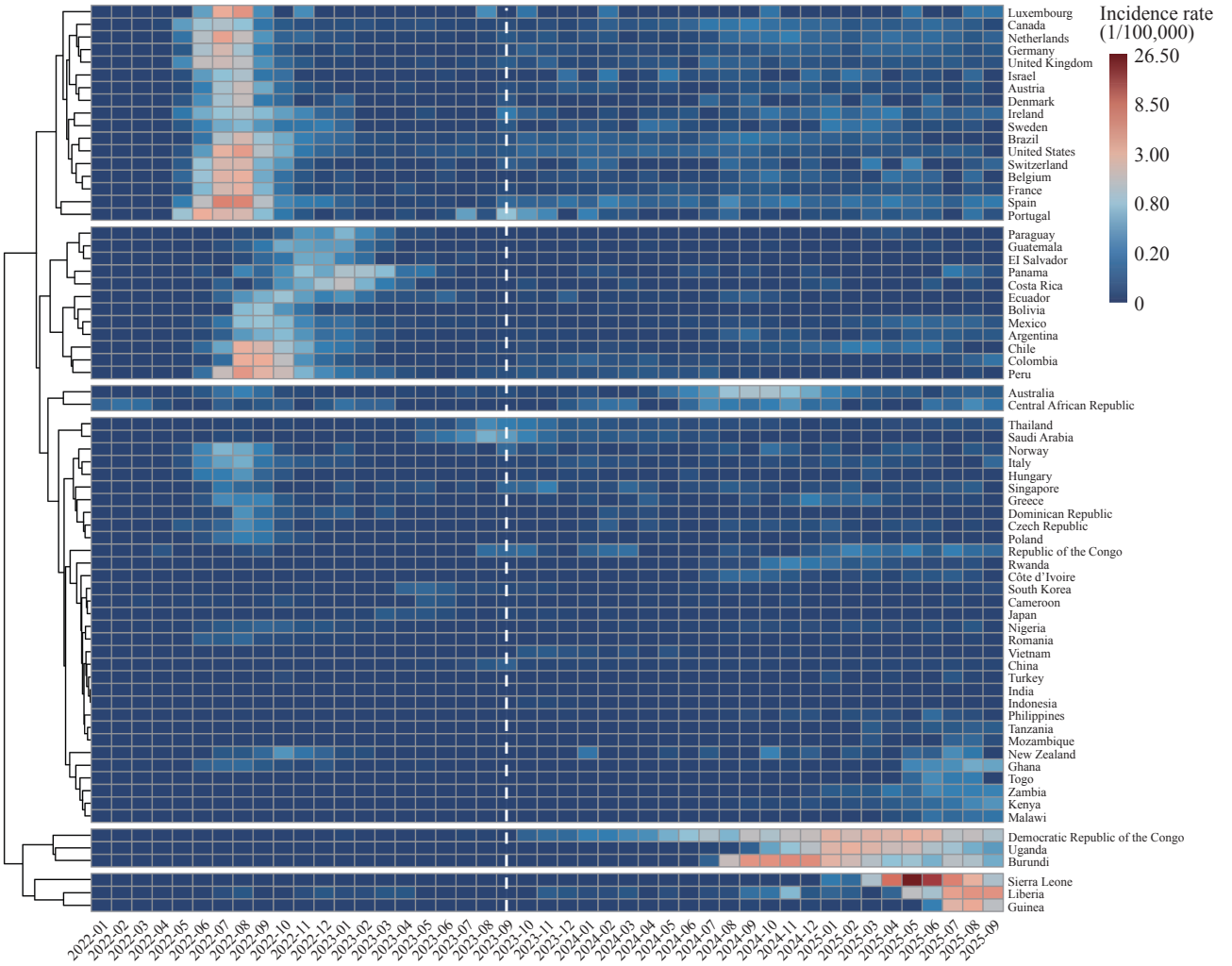

FIGURE 1. Heatmap of monthly mpox incidence rates among countries that reported more than 50 cumulative cases from January 2022 to September 2025.
Note: Countries with more than 50 cumulative cases were included, covering more than 99% of all reported mpox cases globally. Monthly incidence rates were calculated using the formula $\ln(x\times10^5+0.1)$. Hierarchical clustering of rows and columns was performed using the complete linkage method with Euclidean distances. A total of 69 countries were included, with rows representing countries and columns representing months. Color gradients indicate the magnitude of monthly incidence rates, with red indicating higher incidence and blue indicating lower incidence.

sustained zoonotic transmission cycles (*11*). Moreover, clade Ib transmission is primarily associated with close heterosexual contact (*12*), involves geographically constrained social networks, and emerges after widespread clade IIb circulation, when partial population immunity from prior infection or vaccination may have limited its interregional spread (*13*). The lack of widespread intercontinental dissemination of clades Ia and IIa further underscores the marked differences in transmission adaptability among MPXV clades. Notably, the West African cluster identified in 2025 exhibited the highest RR. This finding suggests that this region has become a current transmission hotspot, potentially driven by limited public health resources and insufficient surveillance capacity (*14*–*15*).

This study had several limitations. First, although 14,089 MPXV whole-genome sequences were retrieved from the GISAID during the study period, these genomes represent only a small proportion of the global mpox burden (165,244 cases across 135 countries from January 2022 to September 2025) (Supplementary Table S3, available at https://weekly.chinacdc.cn/). Therefore, the genomic dataset may not fully represent the global pandemic. This constraint likely reflects pronounced heterogeneity across countries and regions in sampling intensity, sequencing capacity, surveillance practices, and the timeliness of

TABLE 2. Characteristics of the five highest-risk mpox transmission clusters worldwide from January 2022 to September 2025.

Cluster	Time frame	Locations included	Number of cases	Observed/ expected	Relative risk	Log likelihood ratio	*P*
1	2022/5/1 to 2022/10/31	United Kingdom (cluster center), Ireland, Netherlands, Belgium, Luxembourg, France, Denmark, Germany, Switzerland, Andorra, Iceland, Spain, Portugal, Monaco, Czech Republic, Austria, Sweden, Slovenia, San Marino	23,409	20.98	24.28	50,544.05	<0.001
2	2022/6/1 to 2022/11/30	USA (cluster center), Canada, Mexico	34,641	22.47	28.16	78,303.17	<0.001
3	2022/7/1 to 2022/12/31	Bolivia (Plurinational State of) (cluster center), Paraguay, Peru, Brazil, Uruguay, Argentina, Chile, Ecuador, Colombia	21,460	16.98	19.36	41,871.78	<0.001
4	2024/9/1 to 2025/8/31	Democratic Republic of the Congo (cluster center), Rwanda, Burundi, Uganda	36,774	34.56	44.16	98,765.45	<0.001
5	2025/4/1 to 2025/9/30	Guinea (cluster center), Sierra Leone, Liberia	7,111	83.00	86.69	24,548.58	<0.001

sequence submission. Such spatiotemporal sampling imbalance may introduce ascertainment bias, thereby affecting regional comparisons and the interpretation of temporal trends. Specifically, given the widespread global circulation of clade IIb and the relatively high number of well-assembled sequences submitted from high-burden regions, the dataset likely provides a comprehensive representation of its genetic diversity. However, the limited sequencing capacity in Africa, further compounded by the exclusion of low-coverage sequences, may mean that the true diversity and extent of clade Ib transmission are not fully captured. These imbalances underscore the urgent need to enhance equity and balance in global genomic surveillance. Second, the inference of spatiotemporal transmission was limited by imperfect temporal and geographic concordance between epidemiological investigations and available genomic data. Nevertheless, the principal evolutionary patterns identified in this study are broadly consistent with the observed phase-specific macroepidemiological features. Specifically, clade IIb showed extensive intercontinental dissemination and relatively high genetic diversity by 2022, aligning with the Europe- and Americas-dominated phases, followed by a gradual decline after 2023. In contrast, clade Ib exhibited a more localized transmission focus in Africa with comparatively limited diversity, which is consistent with the subsequent Africa-centered phase. Taken together, this concordance supports the robustness of the core conclusions; however, inferences for regions with sparse genomic sampling should be interpreted with caution.

Currently, clade Ib continues to circulate in Africa, with sporadic importations and limited local transmission. In 2025, an additional outbreak driven by clade IIb occurred in Sierra Leone, indicating that the mpox epidemic caused by clade IIb persists. The G.1 lineage (A.2.2.1) detected in Sierra Leone carries a high proportion of apolipoprotein B mRNA-editing enzyme catalytic polypeptide-like 3 (APOBEC3)-type mutations, suggesting potential human adaptation (*16*). However, whether this lineage has acquired enhanced transmissibility remains to be determined. Future mpox prevention and control efforts should adopt a framework of global collaboration; prioritize Africa, particularly West Africa, for enhanced surveillance, genomic sequencing, and molecular tracing; and promote equitable access to vaccines and antiviral therapies. Targeted interventions tailored to distinct transmission patterns and high-risk populations are essential to prevent the recurrence of global pandemics.

Conflicts of interest: No conflicts of interest.

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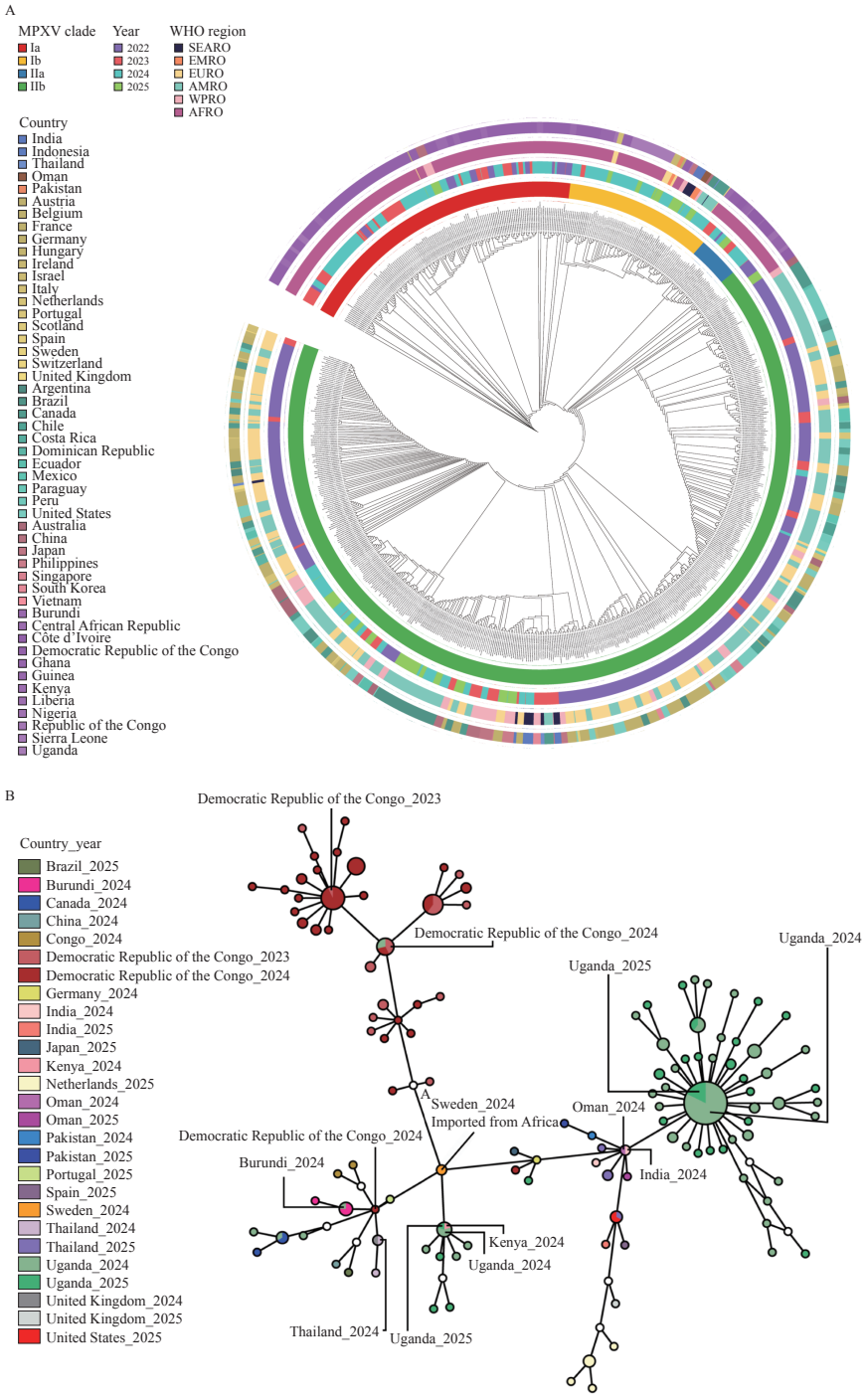

FIGURE 2. Phylogenetic analysis of four MPXV clades and haplotype network characterization of MPXV clade Ib. (A) Phylogenetic tree constructed from complete genomes of four MPXV clades; (B) Haplotype network analysis of MPXV clade Ib (January 2022 to September 2025).

Note: For (A), a total of 14,089 MPXV whole-genome sequences available from GISAID during the study period were retrieved. The sequences were filtered according to the following criteria: 1) genome length ≥190,000 base pairs; 2) absence of "warn/alert" flags; 3) no insertions or gaps ≥200 nucleotides; 4) absence of "stop/truncation" annotations; and 5) only countries with >50 cumulative mpox cases were included. After a multistep sampling procedure and removal of sequences with genome coverage <95% (Supplementary Table S2, available at https://weekly.chinacdc.cn/), the final dataset comprised 730 sequences, including 183 clade Ia, 45 clade Ib, 10 clade IIa, and 492 clade IIb genomes. For (B) MPXV clade Ib whole-genome sequences available from GISAID during the study period were retrieved. Sequences with genome coverage >95% were retained. A total of 245 sequences were included for haplotype network construction.

Abbreviation: MPXV=mpox virus.

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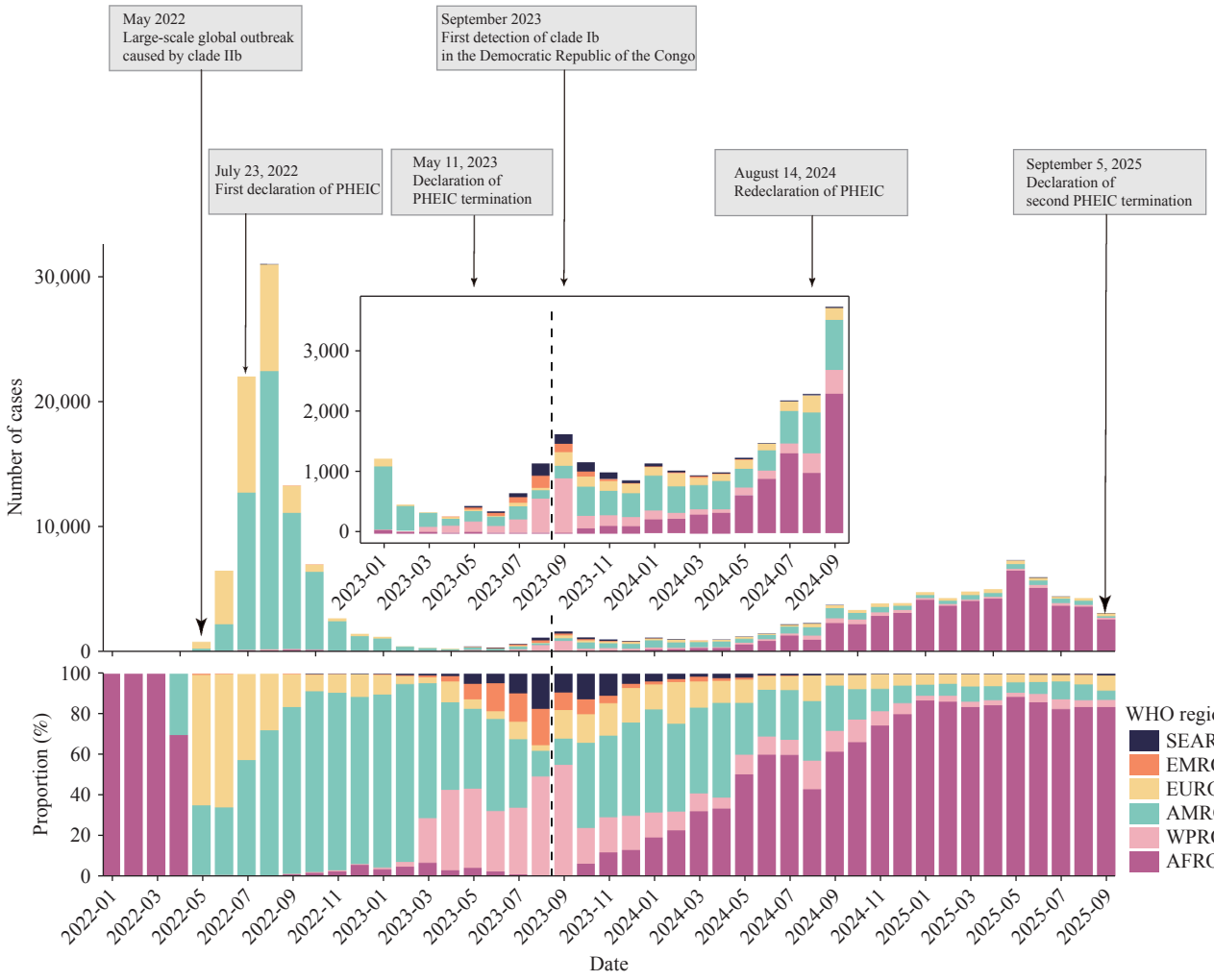
SUPPLEMENTARY MATERIAL



SUPPLEMENTARY FIGURE S1. Monthly trends and regional composition of newly reported mpox cases across the six WHO regions from January 2022 to September 2025.
Note: Six colors represent WHO regions: SEARO, EMRO, EURO, AMRO, WPRO, and AFRO.
Abbreviation: WHO=World Health Organization; SEARO=South-East Asia Region; EMRO=Eastern Mediterranean Region; EURO=European Region; AMRO=Region of the Americas; WPRO=Western Pacific Region; AFRO=African Region.

SUPPLEMENTARY TABLE S1. Comparison of the epidemiological characteristics of mpox between two epidemic phases, from January 2022 to August 2023, and from September 2023 to September 2025.

Epidemiological characteristic	The first phase (January 2022 to August 2023)	The second phase (September 2023 to September 2025)
Dominant pathogen	Clade IIb	Clade Ib
Onset of epidemic increase	May 2022	March 2024
Peak period	August 2022	May 2025
Peak case count	31,008 cases	7,343 cases
Cumulative cases	89,870 cases	75,374 cases
Predominant epidemic regions (proportion)	Region of the Americas and European Region (96.18%)	African Region (71.48%)

SUPPLEMENTARY TABLE S2. Sampling procedure and dataset of genomic sequences used for phylogenetic analysis.

MPXV clades	Total	Round 1 (Random sampling approximately 20%)	Round 2 (20% random sampling from clade IIb, others unchanged)	Round 3 (Removal of sequences with coverage less than 95%)
Clade Ia	1,049	210	210	183
Clade Ib	589	118	118	45
Clade IIa	39	10	10	10
Clade IIb	12,412	2,482	496	492
Total	14,089	2,820	834	730

SUPPLEMENTARY TABLE S3. Number of sequences and reported cases in countries included in the analysis.

Country	Number of sequences included in this study	Reported case count	Included sequences/ case count, (%)
Argentina	2	1,376	0.15
Australia	13	1,769	0.73
Austria	3	381	0.79
Belgium	3	907	0.33
Brazil	39	14,328	0.27
Burundi	14	4,483	0.31
Canada	32	2,236	1.43
Central African Republic	9	180	5.00
Chile	5	1,677	0.30
China	10	3,618	0.28
Costa Rica	2	232	0.86
Côte d'Ivoire	5	167	2.99
Democratic Republic of the Congo	203	30,615	0.66
Dominican Republic	3	83	3.61
Ecuador	4	629	0.64
France	3	4,539	0.07
Germany	95	4,532	2.10
Ghana	5	785	0.64
Guinea	2	1,040	0.19
Hungary	1	88	1.14
India	2	51	3.92
Indonesia	6	88	6.82
Ireland	17	320	5.31

Continued

Country	Number of sequences included in this study	Reported case count	Included sequences/ case count, (%)
Israel	1	378	0.26
Italy	12	1,233	0.97
Japan	11	256	4.30
Kenya	2	624	0.32
Liberia	2	940	0.21
Malawi	2	122	1.64
Mexico	10	4,862	0.21
Netherlands	8	1,557	0.51
Nigeria	4	1,384	0.29
Oman	2	7	28.57
Pakistan	2	29	6.90
Paraguay	3	130	2.31
Peru	24	3,959	0.61
Philippines	9	334	2.69
Portugal	13	1,255	1.04
Republic of the Congo	12	128	9.38
Sierra Leone	2	5,345	0.04
Singapore	2	81	2.47
Republic of Korea	6	188	3.19
Spain	5	9,028	0.06
Sweden	2	373	0.54
Switzerland	2	651	0.31
Thailand	7	960	0.73
Uganda	20	8,209	0.24
United Kingdom	10	4,354	0.23
USA	148	35,590	0.42
Vietnam	1	211	0.47
Total	800	156,312	0.51