Methods and Applications

Risk Assessment Method for Global Monkeypox Importation into China — May 2022–September 2025

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ABSTRACT

Introduction: In the context of globalization, the risk of cross-border transmission of infectious diseases is continuously increasing. There is an urgent need to develop a scientific, dynamic, and practical tool that captures regional heterogeneity in importation risk, thereby facilitating more targeted prevention and control measures at ports of entry.

Methods: We devised an extensible importation risk assessment framework by selecting key indicators through a Delphi expert consultation process and assigning their respective weights using the Analytic Hierarchy Process (AHP). Taking monkeypox (mpox) as a case study, we applied the framework to the global mpox epidemic spanning from May 2022 to September 2025 under three risk scenarios: Clade I, Clade II, and a non-clade-specific (aggregated) scenario. We then analyzed the temporal evolution of major source countries, the spatial distributions of provincial risk levels, and the association between clade-specific importation risk indices and domestically reported mpox cases across the study period.

Results: Our clade-stratified risk assessment framework demonstrates a high degree of consistency and reveals significant disparities between Clade I and Clade II in both international source contributions and provincial vulnerability. The importation risk associated with Clade I is predominantly influenced by Central African countries, particularly the Democratic Republic of the Congo and Uganda. In contrast, the risk related to Clade II is primarily associated with the United States and Southeast Asian nations, such as Thailand and the Philippines. Provincial importation risks generally adhere to a spatial pattern of "east-high, west-low": Shandong Province consistently exhibits a very high risk under Clade I, while Fujian Province maintains a very high risk under Clade II. Notably, the Clade II-specific risk index exhibited a statistically significant positive correlation with national mpox case counts (Spearman's ρ =0.50, P<0.05), whereas the non-clade-specific (aggregated) index did not (ρ =0.32, P=0.12).

Conclusion: This framework effectively captures the structural shift in the sources of mpox importation risk and the regional heterogeneity in risk levels across PLADs in China. It thereby provides a risk-driven decision-support framework for prioritizing port-of-entry screening and tailoring surveillance strategies to high-risk areas.

Globalization continues to raise the risk of cross-border infectious disease transmission (*1*). Since its discovery in 1958 (*2*), monkeypox (mpox) was long confined to Central and West Africa. It has two main clades: Clade I, prevalent in Central African countries like the Democratic Republic of the Congo (DR Congo), and Clade II, predominantly circulating in West African nations such as Nigeria and Ghana (*3*–*4*). In May 2022, Clade IIb sparked a global outbreak (*5*), prompting the World Health Organization (WHO) to declare a Public Health Emergency of International Concern (PHEIC) in July 2022 (*6*); that PHEIC ended in May 2023 (*7*). However, surging Clade I outbreaks in Central Africa led the WHO to declare a second PHEIC in August 2024 (*8*).

Existing frameworks for assessing infectious disease importation risk, such as those developed for coronavirus disease 2019 (COVID-19), dengue, and rabies, rely on aggregated case reports and travel flow data, not lineage- or clade-specific information (*9*–*12*). While useful for broad surveillance, they fail to capture how viral evolution (e.g., more transmissible or immune-evasive sub-lineages) changes importation risk. A few recent studies have begun incorporating variant data (*13*), but no standardized, quantitative, and operationally scalable framework for assessing the

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importation risk of specific viral lineages or clades. To address this, we developed a modular, extensible framework that explicitly incorporates lineage-related characteristics into cross-border transmission risk estimation. Through disease-specific parameterization, this framework has potential applicability to various infectious diseases. Taking mpox as a case study, we applied it to three scenarios: Clade I, Clade II, and a non-clade-specific aggregated scenario. Leveraging multi-source authoritative data from May 2022 to September 2025, we conducted a systematic analysis on the spatiotemporal evolution of primary risk-source countries across three phases (first wave, inter-epidemic interval, second wave) and the dynamic distribution of risk levels across 31 provincial-level administrative divisions (PLADs) in the mainland of China. Additionally, correlations between clade-specific risk indices and reported case counts were evaluated.

METHODS

Selection of Risk-associated Indicators and Data Processing

Key risk-associated indicators were selected through the Delphi method and expert consultation (see the "Selection of Risk-Associated Indicators and Data Collection" section of the Supplementary Material, available at https://weekly.chinacdc.cn/). Twenty experts participated: 10 in Microbiology and Biosafety, 8 in Epidemiology, and 2 in Health Management. All held at least an associate senior professional title, had expertise in public health, infectious disease prevention and control, epidemiology, virology, or biosafety, and completed both Delphi rounds (demographics in Supplementary Table S1, available at https://weekly.chinacdc.cn/). System consistency was assessed using mean, authority coefficient, coefficient of variation (CV), and Kendall coordination coefficient (Kendall's W). The Analytic Hierarchy Process (AHP) was applied to determine the weights of the selected indicators.

We systematically collected data on risk-associated indicators from multiple sources, including: public health system capacity and socioeconomic factors (2019); Global Health Security Index (GHSI, 2021); air passenger flows (study period), epidemiological characteristics of infectious diseases (2024), and geographic proximity from 206 countries or territories to 31 PLADs in China (time-invariant). All quantitative indicators were standardized to 1−5 scores based on percentile rank for quantitative one and predefined criteria (disease characteristics, historical importation patterns, and geographic proximity) for qualitative ones. Full details including definitions, ranges, scoring methodologies, and data sources are provided in Supplementary Material (see "Selection of Risk-Associated Indicators and Data Collection" section).

Development of the Risk Assessment Framework

Considering the reliability of epidemic data from source countries and the representativeness of air-travel entry modes, an automated framework for assessing the importation risk of infectious diseases was developed, incorporating an incidence adjustment coefficient (S) and a connectivity index (C). To facilitate its practical application, the framework has been deployed on an infectious disease surveillance and early warning information system platform, enabling the automated calculations of weekly provincial risk indices from standardized data sources (details in the Supplementary Material). The risk index for month "a" (IT_a) is:

$$IT_a = [\ln(N) \times S + 1] \times C \quad (1)$$

Where N represents the number of newly reported cases in month "a", S indicates the adjustment coefficient of the incidence rate, derived from 14 weighted indicators: 5 on source-country public health capacity (F_1–F_5, such as universal health coverage, public health budget, health workforce, etc.) and 9 on disease biology (F_6–F_{14}, such as symptom typicality, fatality rate, incubation period, etc.) affecting both the pathogen's international transmission potential and clinical detectability. There is no potential overlap or double-counting of information between S and N. We apply the form $\ln(N)\times S$ to adjust observed case counts and better estimate cross-border importation risk. C quantifies the connectivity between the source country and 31 PLADs in the mainland of China, calculated from eight indicators (F_{15} to F_{22}) using their weights and scores. The details on the calculations of S and C are given in the "Development of the risk assessment framework" and "Details of the Framework Development" sections in the Supplementary Material. In primary analysis, months with zero cases (N=0) were excluded to avoid undefined $\ln(N)$; in sensitivity analysis, we used $\ln(N+1)$ to retain all observations.

Although demonstrated here with mpox, this modular framework can be adapted to other infectious diseases by re-scoring the S-module indicators

according to their epidemiological characteristics.

Risk Assessment and Correlation Analysis

This study formulated three risk scenarios based on clade-specific geographical distributions: Clade I (17 African countries with Clade I circulation), Clade II (African countries with Clade II circulation plus all non-African countries, considering that most non-African cases were Clade IIb), and non-clade-specific (aggregated). Using WHO's monthly global mpox case data (May 2022–September 2025) and international air passenger data (2022–2023), the monthly importation risk indices for 31 PLADs were calculated. The identical formula was used across all scenarios. Besides defining the source-country scope based on the known geographical distribution of each clade to produce separate risk estimate for each scenario, we also assigned clade-specific values to the adjustment coefficient (S) to reflect clinical differences, primarily in the "common symptoms" indicator (F_6): Clade I scored 1 (systemic symptoms like high fever); Clade II scored 3 (easily recognizable symptoms like low-grade fever and localized rash). This approach ensures that each risk index accurately reflects the specific epidemiological and connectivity characteristics of its clade or scenario.

The study covered three phases: the first wave (May 2022–May 2023), inter-epidemic interval (June 2023–July 2024), and the second wave (August 2024–September 2025). For Clade I, the temporal trends in risk contributions from all 17 African source countries were tracked across phases; for Clade II and non-clade-specific scenarios, the top 20 source countries by cumulative risk were presented. Provincial risk indices were categorized into five levels using quintiles. Confirmed mpox case data in China from September 2023 to September 2025 were obtained from China CDC. Validation used two complementary approaches: 1) Spearman correlation between reported case counts and monthly cumulative risk (Clade II and non-clade-specific scenarios); 2) qualitative spatial validation for Clade I, checking whether the PLADs with confirmed Clade I importations (Zhejiang and Shandong) (*14*–*15*) aligned with "extremely high" risk classifications. All analyses used SPSSAU (version 24.0; SPSSAU Project Team, Chongqing, China) and R (version 4.3.1; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Risk-associated Indicators

Both consultation rounds achieved a 100% expert response rate. Based on expert feedback and group discussions, we developed an infectious disease importation risk assessment system comprising 2 primary, 4 secondary, and 22 tertiary indicators. The primary indicator X1 (epidemic situation in the source country) includes the epidemic detection capability (X1_1, F_1–F_5) and disease characteristics (X1_2, F_6–F_{14}). The primary indicator X2 (connectivity between source country and destination PLAD) includes the probability of importation from abroad (X2_1, F_{15}–F_{20}) and socioeconomic interactions (X2_2, F_{21}–F_{22}). The indicator importance rated by each expert are presented in detail in Supplementary Table S2 (available at https://weekly.chinacdc.cn/). The mean importance scores ranged from 3.650 to 4.950; coefficients of variation from 0.045 to 0.324; authority coefficients from 0.763 to 0.895. The Kendall's W was 0.443 (P<0.05), suggesting that the consultation results are reliable. The full statistics (mean, standard deviation, CV, authority coefficient) are summarized in Supplementary Table S3 (available at https://weekly.chinacdc.cn/). Details of the framework development can be found in the Supplementary Material. All secondary and tertiary indicator weights (Table 1) passed the consistency test [consistency ratio (CR)<0.1].

Risk Assessment

Clades show distinct imported risk source structures (Figure 1). In Clade I, dominant source countries shifted over time (Figure 1A). During the first wave, the Central African Republic, the DR Congo, and Sudan were primary contributors. The Central African Republic dominated in the early stage, then the DR Congo's contribution rose steadily. During the inter-epidemic interval, the DR Congo dominated almost exclusively, while contributions from other African countries decreased substantially. By the second wave, multi-center pattern emerged, with the DR Congo, Uganda, and Burundi led, while Kenya, Rwanda, Tanzania, and others also contributed significantly. For Clade II (Figure 1B), the United States remained a major risk source throughout all three phases. In the first wave, the primary contributors were the United States, Spain, and Nigeria. During the inter-epidemic interval, Nigeria's contribution declined substantially,

TABLE 1. Indicator weight distribution and testing.

First level indicator	Second level indicator	Weights	Third level indicator	Weights	Consistency check
Epidemic situation in the source country (X1)	Epidemic detection capability of source country (X1_1)	0.667	Effective universal health coverage in source country (F_1)	0.095	CI=0.043 CR=0.038 λ_{max}=5.172
			Public health budget of source country (F_2)	0.126	
			Health workforce in source country (F_3)	0.239	
			Pathogen diagnostic technology (F_4)	0.474	
			Global health security index (F_5)	0.069	
	Disease characteristics (X1_2)	0.333	Common symptom (F_6)	0.035	CI=0.049 CR=0.033 λ_{max}=9.388
			Case fatality rate (F_7)	0.135	
			Herd susceptibility (F_8)	0.253	
			Incubation period (F_9)	0.111	
			Infectiousness during incubation period (F_{10})	0.185	
			Communicable period (F_{11})	0.084	
			Classification of notifiable infectious disease (F_{12})	0.041	
			Classification of emerging infectious disease (F_{13})	0.050	
			Main routes of disease transmission (F_{14})	0.106	
Degree of connectivity between the source country and the PLAD in China (X2)	Probability of importation from abroad (X2_1)	0.750	Number of seats on flights from source country to the local area (F_{15})	0.355	CI=0.031 CR=0.024 λ_{max}=6.153
			Population migration index of the source country (F_{16})	0.117	
			History of similar disease importation from source country (F_{17})	0.158	
			Geographical location of the source country (F_{18})	0.062	
			Quantity of inbound overnight tourists received locally (F_{19})	0.084	
			Flight frequency from the source country to the local area (F_{20})	0.223	
	Socioeconomic interactions (X2_2)	0.250	Value of local imports and exports (F_{21})	0.333	CI=0 CR=0 λ_{max}=2
			Local international tourism revenue (F_{22})	0.667	

Note: The second level indicators under both primary indicators (X1 and X2) passed the consistency check (CI=0, CR=0, λ_{max}=2).
Abbreviation: CI=consistency index; CR=consistency ratio; λ_{max}=maximum eigenvalue of the judgment matrix.

and Thailand, Republic of Korea, and Vietnam emerged as primary sources. In the second wave, Nigeria rebounded, Thailand maintained high-risk, and the Philippines showed a notable rise. In the non-clade-specific scenario, the United States, Thailand, and the DR Congo were the primary risk sources across different phases, with shifting relative contributions over time (Supplementary Figure S1, available at https://weekly.chinacdc.cn/).

The risk of mpox importation into China exhibits significant spatiotemporal heterogeneity (Figure 2). For Clade I, cumulative risk increased gradually across three phases (range: 0–5 to 2–39) (Figure 2A). For Clade II, risk was higher during the first and second waves (range: 2–177 and 4–118, respectively), and dropped to 2–97 during the inter-epidemic interval

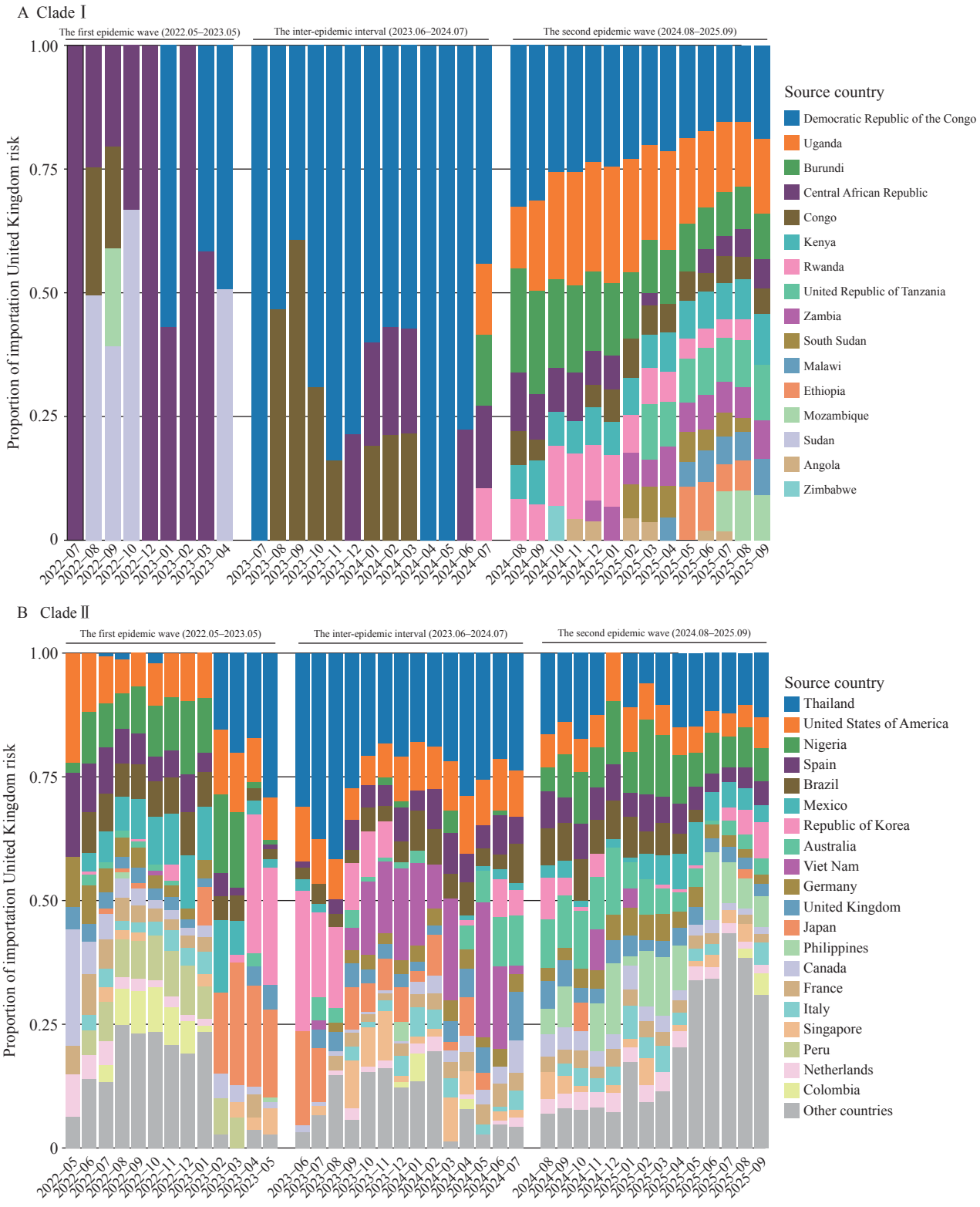


FIGURE 1. Clade-specific composition of source countries contributing to the risk of mpox importation across the three study phases. (A) Clade I: the proportions are calculated based on all identified source countries. (B) Clade II: the proportions are derived from the highest 10% of importation risk observations to highlight major source countries.
Abbreviation: mpox=monkeypox.

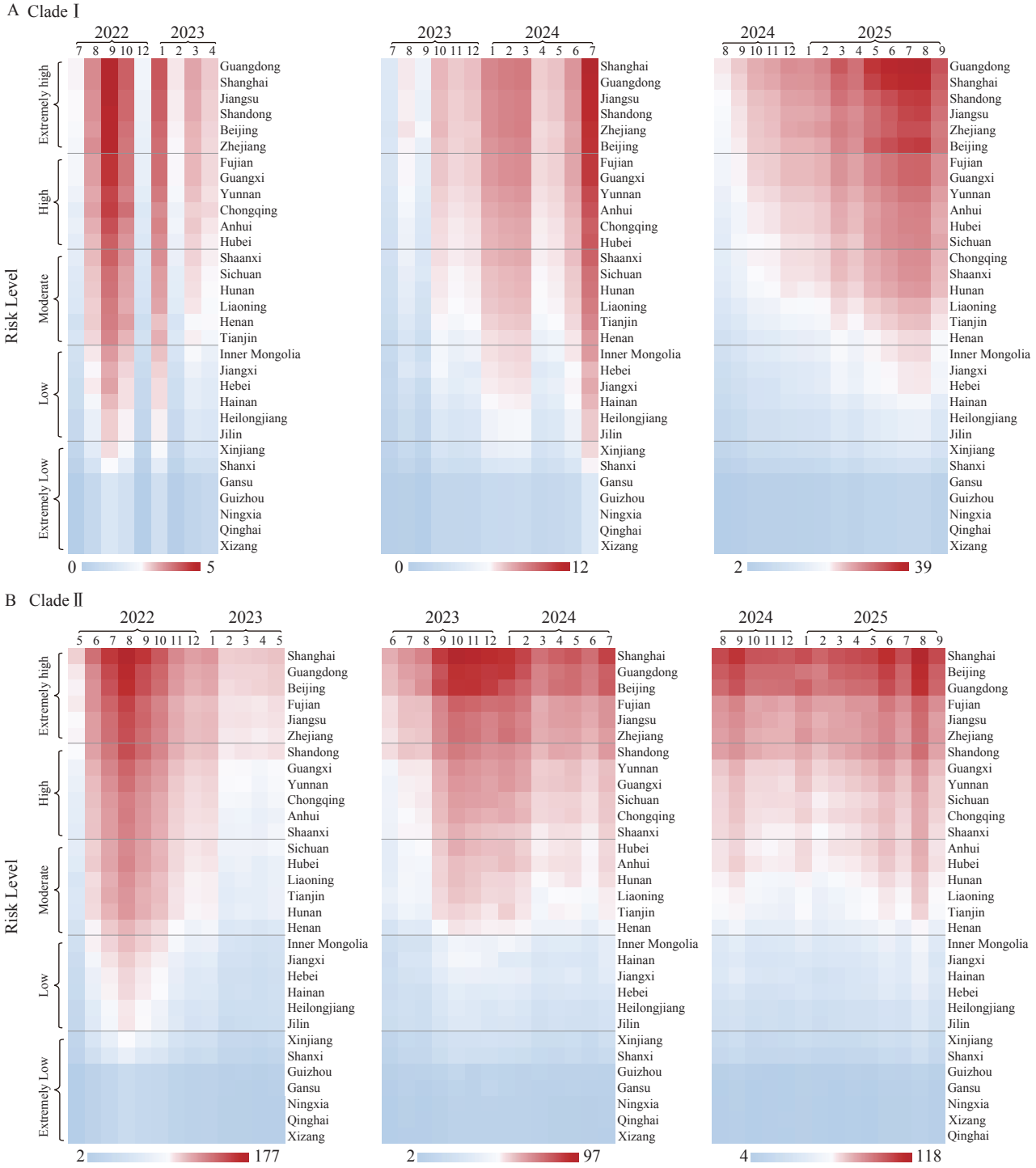


FIGURE 2. Importation risk of two mpox virus clades across 31 provincial-level administrative divisions (PLADs) in China. The heatmaps illustrate the estimated importation risks for (A) Clade I and (B) Clade II during the first epidemic wave (left panel), the inter-epidemic period (middle panel), and the second epidemic wave (right panel).
Note: Since the calculation of risk index is based on case data from source countries, and Clade I circulates in a limited number of countries, risk values could not be computed for certain months when no cases were reported in these source countries, resulting in temporal gaps in the Clade I time series.

(Figure 2B). Although overall provincial importation risk follows an "east-high, west-low" pattern, clade-stratified risks differ markedly in key PLADs. For instance, Shandong Province maintained extremely high-risk under Clade I but low-risk under Clade II, likely reflecting its role as a major maritime and air

gateway linking China with Africa. Conversely, Fujian Province consistently ranked as an extremely high-risk PLAD for Clade II, which is consistent with its extensive air links to Southeast Asia and other non-African countries that are the primary source regions of Clade II. Sichuan Province showed clade-dependent risk dynamics: high risk only during Clade I's second wave, but persistently high during both the inter-epidemic interval and second wave of Clade II. These patterns reveal that PLAD-level risk profiles arise from the interaction between each clade's geographical distribution and local international connectivity. As shown in Supplementary Table S4 (available athttps://weekly.chinacdc.cn/), the socio-geographic-mobility conditions (*A*) were the most important factors for nearly all country-PLAD pairs among Clade I source countries. In contrast, air travel conditions (*F*) dominated for high-risk PLADs (e.g., Shanghai, Guangdong, and Fujian) linked to major Clade II sources, particularly Thailand, the United States, the United Kingdom, and Australia. Provincial risk rankings in the non-clade-specific scenario generally resembled those in the Clade II scenario, but high-risk PLADs in Clade I (e.g., Shandong, Hubei) were significantly underestimated (Supplementary Figure S2, available at https://weekly.chinacdc.cn/).

Correlation Analysis

Time-series analysis revealed a significant positive correlation between national mpox case counts and the Clade II-specific importation risk index (ρ =0.50, P<0.05), but not for the non-clade-specific (aggregated) risk index (ρ =0.32, P=0.12) (Figure 3). Notably, Zhejiang and Shandong provinces, both reporting primary Clade I imported cases, were consistently assessed as having extremely high Clade I importation risk throughout the study period. Sensitivity analysis using ln(N+1) instead of ln(N) yielded near-identical risk estimates (Clade II: ρ =0.993; Clade I: ρ =0.995; both P<0.001), indicating the robustness of this risk assessment framework.

DISCUSSION

This study introduces the two predominant mpox virus clades into the importation risk assessment framework, revealing distinct risk patterns between Clade I and Clade II. For Clade I, risk sources shifted from the Central African Republic (first wave) to a multi-center pattern in the second wave, led by the DR Congo, Uganda, and Burundi. For Clade II, the United States remained a consistently major source

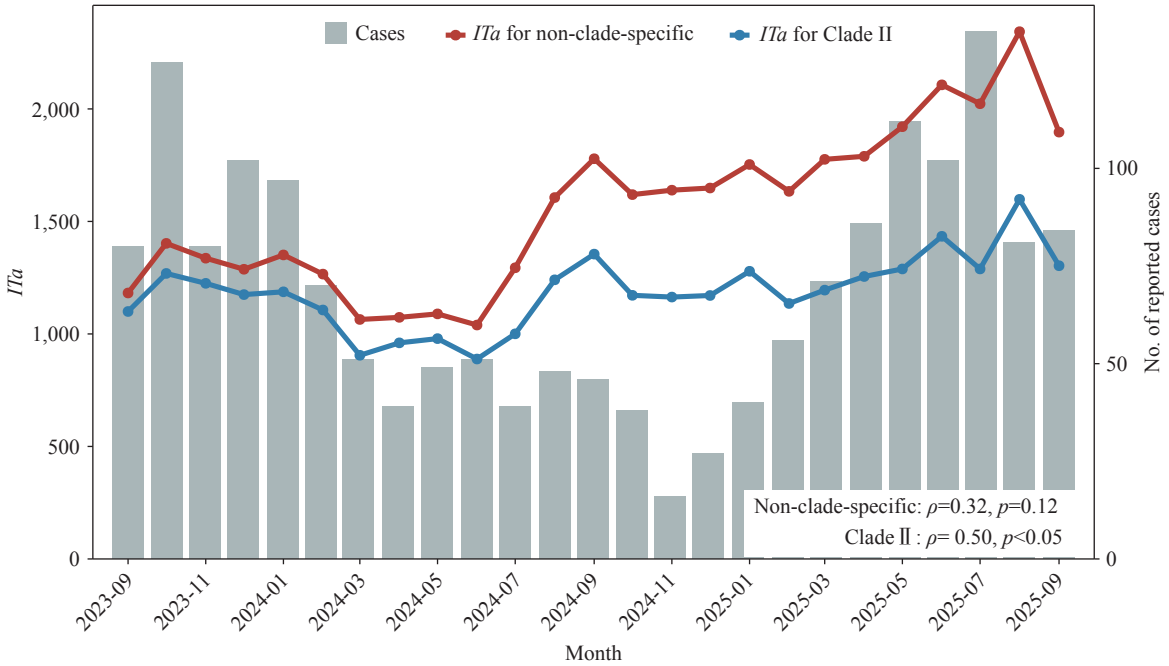


FIGURE 3. Temporal trends in the importation risk index and the number of reported mpox cases at the national level in China from September 2023 to September 2025.
Note: ρ denotes the Spearman correlation coefficient between IT_a and the reported number of mpox cases.

throughout all phases, but during the inter-epidemic interval, risk sources shifted toward Asian countries, particularly Thailand, Republic of Korea, and Vietnam. These dynamics align with the global epidemiological patterns documented by Cevik et al. They reported intensified Clade I outbreaks in Central Africa and the continued low-level Clade IIb circulation in non-endemic regions (*16*). The observed shift of Clade II risk sources towards Southeast Asia during the inter-epidemic interval is consistent with the regional surveillance data, which indicates sustained transmission in Thailand and neighboring countries (*17*).

Shandong Province had consistently very high importation risk under Clade I throughout all three phases, but low risk under Clade II. Fujian Province exhibited the opposite pattern. Non-clade-specific analysis substantially underestimated these differences, highlighting fundamental differences in geographical distribution and transmission dynamics between the two clades, as emphasized by Srivastava et al., and underscoring the need for clade-specific surveillance (*3*).

Clade II's risk index exhibited a statistically significant, moderate positive correlation with reported case counts (ρ =0.50, P<0.05), whereas the non-clade-specific aggregated index did not (ρ =0.32, P=0.12). This indicates that almost all mpox cases in China during 2023–2025 belonged to Clade IIb, except for a few in Shandong, Zhejiang, and Beijing (*14*–*15*,*18*). This is consistent with Clade IIb's global dominance outside Africa since 2022 (*19*). Thus, overseas importation risk is a crucial factor contributing to the observed domestic epidemic pattern. Factor decomposition analysis (Supplementary Table S4) further revealed that the spatial heterogeneity in provincial risk is shaped by different factors across clades: for Clade I, socio-geographic-mobility conditions (*A*) dominate due to minimal direct air links from African source countries; for Clade II, air travel conditions (*F*) serve as the most important factor for high-risk PLADs with direct flights from major source countries (e.g., Thailand, the United States, and Australia), while *A* remains dominant where such flights are limited. Temporal variation in risk ranking stems mainly from changes in source-country epidemic magnitude (*N*), accounting for the evolving contributions of different countries across the three study phases (Figure 1). In addition to the quantitative correlation, the spatial risk classifications of the framework are further supported by real-world events. During the study period, Zhejiang and Shandong provinces had documented Clade I importation cases (*14*–*15*), which were consistently classified in the highest risk quintile by the framework throughout all three phases, providing preliminary directional support for the framework's discriminative capacity under data-scarce conditions.

In comparison with existing frameworks, this study offers three potential improvements over previous approaches. Travel-volume-based models applied to COVID-19 and dengue estimate risk solely from air flows and source-country incidence, without considering detection capability or disease characteristics (*9*–*10*,*20*). AHP-based frameworks assess regional vulnerability in China, but concentrate on domestic transmission, not cross-border importation (*21*). The current framework integrates both the epidemic characteristics of the source country and the connectivity of the destination PLAD into a unified index, introduces clade-stratified differentiation to capture the divergent geographical footprints of pathogens, and provides provincial risk rankings across all 31 PLADs in China to guide the prioritization of resources at ports of entry. These findings have significant implications for public health. First, the framework supports regionally tailored surveillance strategies with scientific evidence. Second, the dynamic monitoring of the contributions from risk source countries allows for the timely adjustment to border screening and control measures as global outbreaks evolve. Third, the recent Clade Ib cluster in Yiwu City of Zhejiang Province demonstrates that international trade hubs remain vulnerable to rapid local transmission, highlighting the necessity for enhanced inbound surveillance targeting travelers from high-prevalence regions (*15*). China's comprehensive intervention framework, including early surveillance, mandatory case reporting, and timely treatment, has proven to be effective in containing imported cases and preventing community transmission (*22*).

This study has two main limitations. First, the China CDC reported imported and locally transmitted cases together, not separately. Since our risk index estimates only importation risk, secondary cases likely weakened the observed correlation, particularly during the second wave, when local clusters were more prevalent. This may partly account for the moderate magnitude of the Clade II correlation coefficient (ρ =0.50), despite its statistical significance. Nevertheless, the association indicates that the risk index captures meaningful spatiotemporal variability in

the early importation dynamics, which holds practical value for identifying PLADs that require intensified border screening and rapid-response preparedness. Second, in order to approximate the global distribution of Clade II, it was assumed that all mpox cases reported to WHO from non-African countries belonged to Clade II. While this assumption largely aligns with current epidemiological evidence, given that Clade IIb has dominated transmission outside Africa since 2022, it may overlook rare, undetected Clade I cases, potentially introducing misclassification bias. Future research could integrate multimodal traffic flow, social media sentiment, and environmental wastewater monitoring data, and extend the scope to other imported diseases.

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SUPPLEMENTARY MATERIALS

Selection of Risk-Associated Indicators and Data Collection

Details of the indicator selection: In the first round of the questionnaire, the total weight of the secondary indicators under each primary indicator and the total weight of the tertiary indicators under each secondary indicator were 1,000. Experts assigned weights to the secondary and tertiary indicators in the system. Indicators that were assigned zero weight by two or more experts, as well as meaningless indicators, were not included in the second round of the questionnaire. Indicators considered meaningful by the experts (which were both accessible and quantifiable) were added on this basis. In the second round of the questionnaire, experts assessed the importance, basis of judgment, and familiarity of all indicators. Any suggestion to delete an indicator was discussed in depth to decide whether to retain it.

Specific details of data collection are as follows: Data on the public health systems of various countries and territories were gathered from the Global Burden of Disease (GBD) database and the Global Health Security Index (GHSI) databases. These data encompassed the following indicators: effective universal health coverage (F_1), public health budget (F_2), and health workforce (F_3, sourced from the GBD database), as well as the Global Health Security Index (F_5, sourced from the GHSI database). F_1, F_2, F_3, and F_5 were scored using an inverse percentile rank: countries in the 81–100th percentile received a score of 1, and those in the 0–20th percentile received a score of 5, reflecting that stronger public health capacity leads to better case detection and lower underreporting risk. This system incorporates indicator data from 207 countries and territories. For the few territories with missing data, a score of 3 was used as a supplement. Data were missing for 3 countries in the 4 indicators of effective universal health coverage in the source country, public health budget in the source country, health workforce in the source country, and population migration index in the source country, and for 12 countries in the Global Health Security Index, and a score of 3 was used in this study as a proxy score for the missing values. This score represents 'neutral' or 'uncertain' status to avoid bias in scoring due to missing data and to ensure comparability of scores across countries.

Population movement data are sourced from the Official Aviation Guide (OAG) and the GBD database. These datasets encompass several key indicators, including the number of seats on flights from the source country to the destination region (F_{15}), flight frequency from the source country to the destination region (F_{20}, both sourced from OAG database), and the population migration index of the source country (F_{16}, sourced from the GBD database).

SUPPLEMENTARY TABLE S1. Experts' demographic information.

Characteristics	Demographics	Count
Gender	Male	16
	Female	4
Age (years)	0–44	8
	45–54	10
	55–64	2
Primary responsibility	Teaching & Research	16
	Clinical work	1
	Administrative management	1
	Other	2
Title of the job	Professor	13
	Associate professor	7
Education level	Doctoral/PhD	19
	Master	1
Professional field	Microbiology and Biosafety	10
	Epidemiology	8
	Health management	2

SUPPLEMENTARY TABLE S2. The importance scoring by each expert for each indicator.

Indicator	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
X1_1	4	5	5	4	4	5	5	4	5	5	5	5	4	5	5	5	5	5	5	5
X1_2	4	5	5	5	5	5	4	4	5	5	5	4	4	4	5	5	5	5	5	4
X2_1	3	5	5	5	5	5	5	5	5	5	5	5	4	4	5	3	5	5	5	4
X2_2	4	5	5	4	4	3	3	4	4	5	4	4	5	3	5	4	4	4	5	5
F_1	2	5	5	4	4	4	3	4	5	5	4	4	4	3	5	4	3	4	5	3
F_2	3	4	5	5	4	3	4	3	4	5	3	4	4	3	5	4	4	5	5	4
F_3	4	5	5	5	4	4	4	3	5	5	4	4	4	3	5	4	5	5	5	4
F_4	5	5	5	4	5	5	5	5	5	5	5	5	4	4	5	5	5	5	5	4
F_5	2	4	5	3	5	4	5	3	4	3	4	3	4	4	5	3	4	5	5	3
F_6	2	5	5	5	4	4	4	4	5	5	3	3	4	3	5	3	4	5	5	4
F_7	5	5	5	5	4	5	5	5	5	5	5	5	5	4	5	2	5	5	5	3
F_8	5	5	5	5	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
F_9	3	5	5	5	5	4	5	5	5	5	5	5	4	4	5	4	4	5	5	4
F_{10}	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	3
F_{11}	3	5	5	5	5	5	4	5	5	5	5	4	4	4	5	5	4	5	5	3
F_{12}	2	4	5	4	4	4	3	4	4	5	4	4	4	5	5	4	4	5	5	4
F_{13}	2	5	5	4	4	4	3	4	4	5	4	4	4	5	5	4	4	5	5	5
F_{14}	2	5	5	5	5	5	5	5	5	5	5	4	5	4	5	4	4	5	5	4
F_{15}	3	5	5	5	4	3	4	4	4	5	4	5	4	4	5	4	5	5	5	4
F_{16}	4	5	5	5	5	4	4	5	5	5	5	4	4	4	5	4	5	5	5	3
F_{17}	4	5	5	4	4	3	4	3	5	5	4	3	4	3	5	3	4	5	5	4
F_{18}	3	5	5	4	5	3	3	3	5	5	4	4	4	5	5	2	5	5	5	3
F_{19}	2	4	5	3	4	5	4	2	4	4	4	3	4	3	5	3	3	5	5	5
F_{20}	2	5	5	5	3	4	3	3	4	5	4	3	4	4	5	4	4	4	5	4
F_{21}	3	4	5	4	4	1	5	3	5	5	3	3	3	2	5	2	4	4	5	3
F_{22}	3	5	5	3	4	3	5	3	5	5	4	4	4	3	5	2	3	4	5	2

Note: Importance scores were defined as follows: 1 indicates very unimportant; 2 indicates unimportant; 3 indicates moderately importance; 4 indicates important; 5 indicates very important. Experts are denoted by letters A–T.

Socioeconomic data were obtained from the China Statistical Yearbooks Database (CSYD), and indicators included the number of inbound travelers to PLADs in China (F_{19}), value of local imports and exports (F_{21}), and local international tourism revenue (F_{22}). The scoring methodology for population movement and socioeconomic indicators (F_{15}, F_{16}, F_{19}, F_{20}, F_{21}, F_{22}) followed a positive percentile rank: countries or PLADs in the 0–20th percentile receive a score of 1, and those in the 81–100th percentile received a score of 5.

In the risk assessment framework, a historical disease importation indicator (F_{17}) was developed for each source country-disease-PLAD combination, based on the recorded number of similar infectious disease cases imported from source countries to destination PLADs between 2014 and 2015, as reported by the General Administration of Customs of China (GACC) and China CDC. The scoring rules are based on the frequency and magnitude of historical imports; if there are no records of imports for certain diseases, imports of diseases with the same transmission routes are taken into account, and additionally importation events with more than 10 cases in a two-year period are defined as "large-scale", otherwise they are considered as "small-scale". Specifically: a score of 1 is assigned if there is no record of similar disease importation; a score of 2 is given for small-scale importation of a similar disease but no record of this disease; a score of 3 for multiple or large-scale imports of a similar disease but no record of this disease; and a score of 4 for small-scale import record of the disease; records of multiple or large-scale importation of the disease were 5 points.

Furthermore, disease-related characteristic data were obtained for each recorded infectious disease from

SUPPLEMENTARY TABLE S3. Mean value, standard deviation, coefficient of variation, and authority coefficient of importance scores for each indicator.

Indicator	Mean value	Standard deviation	Coefficient of variation	Authority coefficient
X1_1	4.750	0.444	0.094	0.884
X1_2	4.650	0.489	0.105	0.881
X2_1	4.650	0.671	0.144	0.870
X2_2	4.200	0.696	0.166	0.816
F_1	4.000	0.858	0.215	0.823
F_2	4.050	0.759	0.187	0.816
F_3	4.350	0.671	0.154	0.823
F_4	4.800	0.410	0.085	0.886
F_5	3.900	0.912	0.234	0.800
F_6	4.100	0.912	0.222	0.853
F_7	4.650	0.813	0.175	0.894
F_8	4.950	0.224	0.045	0.895
F_9	4.600	0.598	0.130	0.893
F_{10}	4.850	0.489	0.101	0.891
F_{11}	4.550	0.686	0.151	0.876
F_{12}	4.150	0.745	0.180	0.864
F_{13}	4.250	0.786	0.185	0.868
F_{14}	4.600	0.754	0.164	0.894
F_{15}	4.550	0.605	0.133	0.834
F_{16}	4.100	0.788	0.192	0.803
F_{17}	4.150	0.988	0.238	0.843
F_{18}	3.850	0.988	0.257	0.813
F_{19}	4.000	0.858	0.215	0.788
F_{20}	4.350	0.670	0.150	0.820
F_{21}	3.650	1.182	0.324	0.763
F_{22}	3.850	1.040	0.270	0.781

authoritative sources including the Global Infectious Diseases and Epidemiology Network (GIDEON), WHO, and China CDC. These data encompassed the following indicators: pathogen diagnostic technology, common symptom, case fatality rate, herd susceptibility, incubation period, infectiousness during incubation period, communicable period, and the main routes of disease transmission, classification of infectious diseases. Scoring criteria for these indicators were predefined as follows. Pathogen diagnostic technology (F_4): score 1 if mature diagnostic techniques are available; score 2 if established but unverified; score 3 if techniques exist for similar pathogens only; score 4 if no techniques exist for similar pathogens; score 5 if the etiology is unknown. Common symptom (F_6): score 1 if high fever and widespread rash are present; score 3 if low-grade fever and localized rash are present; score 5 if fever and rash are absent. Case fatality rate (F_7): score 5 if <1%; score 3.75 if 1%–10%; score 2.5 if 10%–30%; score 1.25 if >30%. Herd susceptibility (F_8): score 1 if a limited population with high herd immunity; score 2 if a widespread population with high herd immunity; score 3 if generally susceptible with high herd immunity, or a limited population with low herd immunity; score 4 if a widespread population with low herd immunity; score 5 if generally susceptible with low herd immunity. Incubation period (F_9) and communicable period (F_{11}): score 1.25 if <3 days; score 2.5 if 3–7 days; score 3.75 if 7–14 days; score 5 if >14 days or uncertain. Infectiousness during incubation period (F_{10}): score 1 if no infectivity; score 3 if weak infectivity; score 5 if strong infectivity or uncertain. Notifiable disease classification (F_{12}): score 1 if Class A; score 3 if Class B; score 5 if Class C or other. Emerging disease classification (F_{13}): score 1 if not newly emerging in China; score 3 if newly emerging in

SUPPLEMENTARY TABLE S4. The most important factor driving these spatial and temporal variations of the risk index of the cross-border transmission of mpox (PLADs with top five cumulative risk), stratified by clades (May 2022–September 2025).

Clade	Source country	Cumulative *ITa*	The most important factor/PLAD1	The most important factor/PLAD2	The most important factor/PLAD3	The most important factor/PLAD4	The most important factor/PLAD5
Clade I	Democratic Republic of the Congo	2,329.7	Shanghai (A)	Guangdong (A)	Shandong (A)	Jiangsu (A)	Beijing (A)
	Uganda	1,203.8	Shanghai (A)	Zhejiang (A)	Hubei (A)	Guangdong (A)	Shandong (A)
	Burundi	842.9	Shanghai (A)	Guangdong (A)	Shandong (A)	Jiangsu (A)	Beijing (A)
	Central African Republic	660	Shanghai (A)	Guangdong (A)	Shandong (A)	Jiangsu (A)	Beijing (A)
	Congo	526.6	Zhejiang (A)	Shanghai (A)	Guangdong (A)	Shandong (A)	Jiangsu (A)
	Kenya	497	Guangdong (F)	Sichuan (F)	Shandong (A)	Hunan (A)	Shanghai (A)
	Rwanda	445.9	Shanghai (A)	Guangdong (A)	Shandong (A)	Jiangsu (A)	Beijing (A)
	United Republic of Tanzania	381.9	Guangdong (A)	Shanghai (A)	Shandong (A)	Beijing (A)	Jiangsu (A)
	Zambia	328.6	Shandong (A)	Zhejiang (A)	Shanghai (A)	Guangdong (A)	Jiangsu (A)
	South Sudan	201.7	Shanghai (A)	Guangdong (A)	Shandong (A)	Jiangsu (A)	Beijing (A)
Clade II	Thailand	2,405.1	Shanghai (F)	Beijing (F)	Zhejiang (F)	Yunnan (F)	Fujian (F)
	United States of America	2,042.5	Shanghai (F)	Guangdong (F)	Fujian (F)	Beijing (A)	Jiangsu (A)
	Nigeria	1,985	Beijing (A)	Guangdong (A)	Shanghai (A)	Shandong (A)	Jiangsu (A)
	Spain	1,916.5	Beijing (A)	Shanghai (A)	Zhejiang (A)	Jiangsu (A)	Chongqing (A)
	Mexico	1,790	Beijing (A)	Zhejiang (A)	Shanghai (A)	Guangdong (A)	Shandong (A)
	Brazil	1,696	Shanghai (A)	Jiangsu (A)	Chongqing (A)	Guangdong (A)	Shandong (A)
	Colombia	1,361.1	Shanghai (A)	Guangdong (A)	Shandong (A)	Jiangsu (A)	Beijing (A)
	The United Kingdom	1,357.3	Shanghai (F)	Beijing (F)	Guangdong (A)	Shandong (A)	Shaanxi (A)
	Canada	1,301.9	Shanghai (F)	Guangdong (A)	Fujian (A)	Beijing (A)	Shandong (A)
	Australia	1,252.2	Guangdong (F)	Shanghai (F)	Fujian (F)	Beijing (A)	Jiangsu (A)

Note: The IT_a is a product of epidemic magnitude ($\ln(N+1)\cdot S$) and the composite connectivity score C ($C=A+B+F$). Temporal variations in the risk contributed by each source country are primarily driven by fluctuations in N over time. Spatial variations across PLADs within the same source country are determined by C, as $\ln(N+1)\cdot S$ is country-specific and does not vary across provinces. The most important factor shown in each cell refers to the largest component of C for that country–PLAD pair. B did not appear as the most important factor for any pair due to its limited value range (0–0.25).

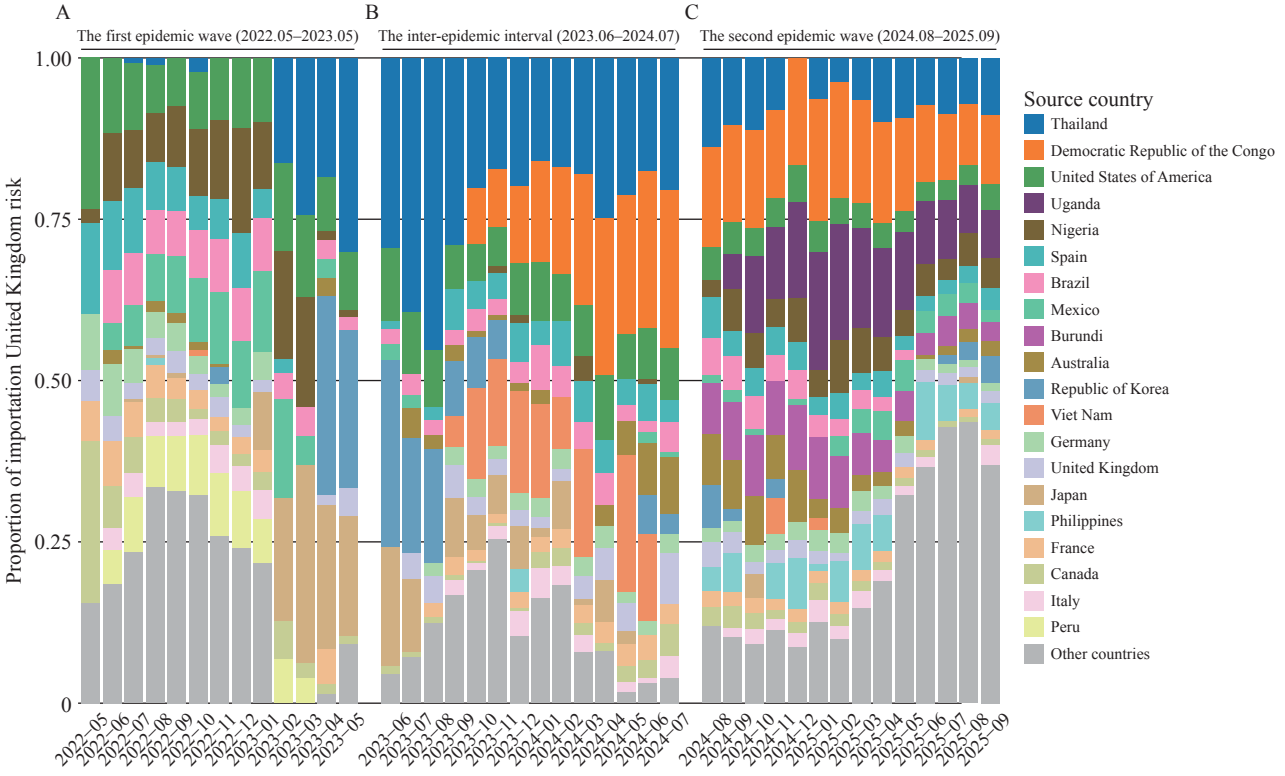
Abbreviation: mpox=monkeypox; IT_a=risk index of cross-border transmission of infectious diseases in month a; N=number of newly reported cases; S=adjustment coefficient of incidence rate; C=composite connectivity score; A=normalized socio-geographic and population mobility index of the destination PLAD; B=normalized historical importation record of similar infectious diseases from the source country; F=normalized air travel connectivity between the source country and the destination PLAD.

China; score 5 if newly emerging globally. Main transmission routes (F_{14}): score 1 for surface contact-borne; score 2 for bloodborne/sexually transmitted; score 3 for vector-borne; score 4 for gastrointestinal; score 5 for respiratory.

Geographic data were obtained from the Ministry of Natural Resources of the People's Republic of China and include indicators of the geographical location of the source country (F_{18}). Data were processed on a scale of 1 to 5 depending on the geographical proximity of the source country to China, far away from China (1.25); not sharing a land border with China but facing each other across the sea (2.5); not sharing a land border with China but coexisting on the same landmass (3.75); sharing a land border with China (*5*).

Development of the Risk Assessment Framework

Incidence rate correction coefficient (S): Given the potential for underreporting of infectious disease cases in the source country, it is deemed necessary to correct the incidence rate using the incidence rate correction coefficient



SUPPLEMENTARY FIGURE S1. Non-clade-specific of source countries contributing to mpox importation risk across the three study phases.
Abbreviation: mpox=monkeypox.

(S). This coefficient is determined by considering two factors: the epidemic detection capability of source country and the disease characteristics. This coefficient is calculated using 14 indicators, including effective universal health coverage in source country (F_1), public health budget of source country (F_2), and health workforce in source country (F_3) among others up to F_{14}. The specific calculation formula is as follows:

$$S = \frac{\sum_{i=1}^{14} a_i \times F_i \times b_i}{\ln 100} \quad (2)$$

Where a_i denotes the weight coefficient of the secondary indicators, b_i denotes the weight coefficient of the tertiary indicators, and F_i represents the score of the tertiary indicators (on a scale from 1 to 5).

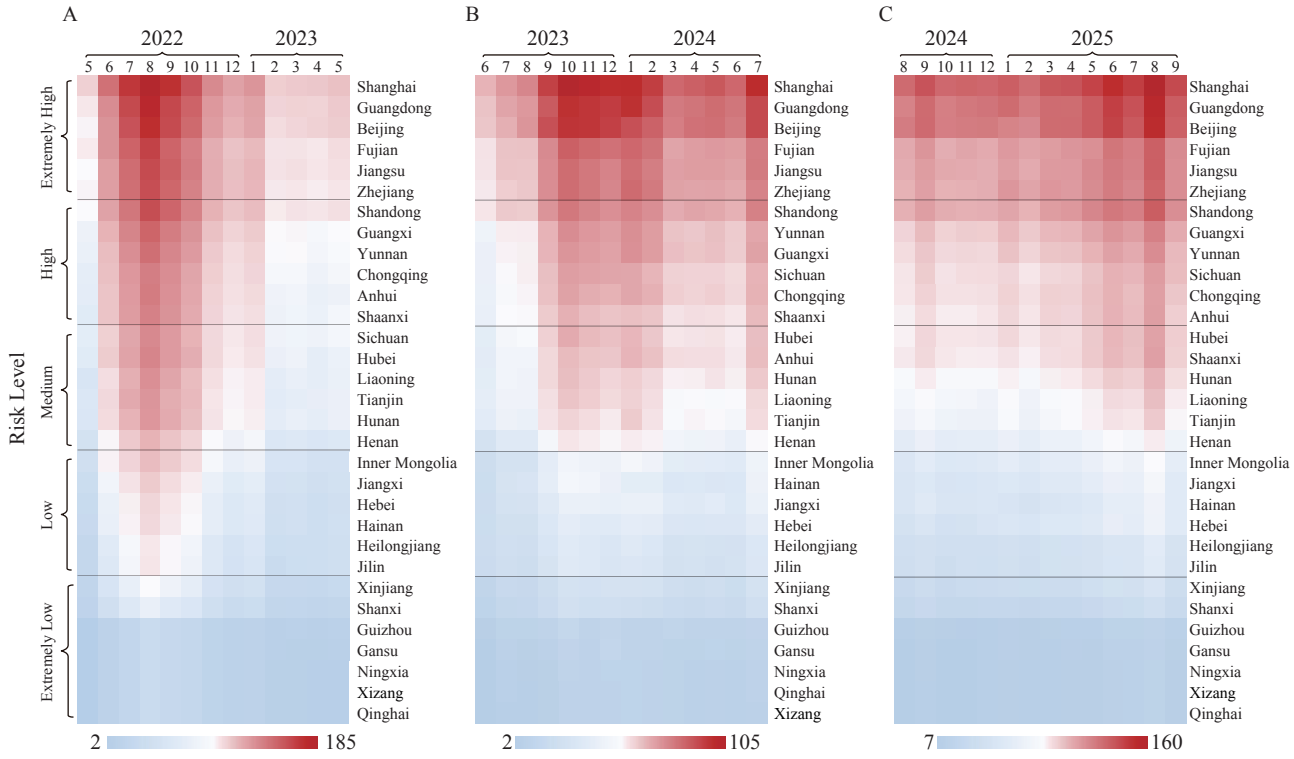
Source country to importing PLADs connectivity (C): C comprehensively considers aviation data and other factors potentially influencing connectivity, distinguishing between two aspects: the probability of importation from abroad and socioeconomic interactions. Use the following three parameters to calculate C by normalizing them to 0–1: air travel conditions (F), socio-geographic-mobility conditions (A), and history of similar disease imports from the source country (B).

A, B, and F are calculated as follows:

$$A, B, F = \sum_{i=1}^{n} a_i \times F_i \times b_i \quad (3)$$

A is calculated based on indicators F_{16}, F_{18}, F_{19}, F_{21} and F_{22}; B is computed using indicator F_{17}; F is calculated from indicators F_{15} and F_{20}. Where a_i denote the weight coefficient of the secondary indicators, b_i denote the weight coefficient of the tertiary indicators, and F_i represent the score of the tertiary indicators (on a scale from 1 to 5).

The F normalization formula is as follows:



SUPPLEMENTARY FIGURE S2. Importation risk of non-clade-specific across 31 PLADs in China.
Abbreviation: PLAD=provincial-level administrative division.

$$F' = \frac{F - F_{\min}}{F_{\max} - F_{\min}} \tag{4}$$

The same normalization method was used for A′ and B′.

The calculation of C is as follows:

$$C = A' + B' + F' \tag{5}$$

Details of the Framework Development

This system primarily evaluates the likelihood of infectious disease importation based on two key corrections: adjustments for the incidence rates in source countries and adjustments for the degree of connectivity between the source country and the PLAD in China.

Given the potential for underreporting of infectious disease cases in the source country, it is deemed necessary to correct the incidence rate using the incidence correction coefficient (S). This incidence rate correction coefficient S is determined by considering two factors: the epidemic detection capability of source country and the disease characteristics.

The epidemic detection capability of source country primarily considers the public health system of the source country, including factors such as the effective universal health coverage in source country (F_1), public health budget of source country (F_2), health workforce in source country (F_3), and pathogen diagnosis technology (F_4). In the process of establishing the evaluation system and creating the first-round questionnaire, we took into account the average education level of the source country to demonstrate the cognitive ability of the people in the source country with respect to diseases. Nevertheless, the questionnaire feedback indicated that two experts gave this indicator a weight of zero, suggesting that they regarded it as either unimportant or unable to reflect the intended aspect. Consequently, this indicator was deleted. Moreover, experts proposed adding the completeness of disease surveillance and early warning plans, systems, and capabilities. We hold that the Global Health Security Index can reflect this aspect to a certain degree. Consequently, the Global Health Security Index (F_5) has been newly incorporated. The gross domestic product (GDP) indicator of the source country was considered as potentially

indirectly reflecting the epidemic detection capability. However, in the second-round questionnaire, experts suggested deleting this indicator, as they believed it functions through public health budgets. We adopted this suggestion. Ultimately, the epidemic detection ability of the source country is represented by a total of five indicators, namely F_1 to F_5.

The characteristics of the disease considered include factors affecting detection and transmission, such as common symptoms (F_6), case fatality rate (F_7), herd susceptibility (F_8), incubation period (F_9), infectiousness during incubation period ($F10$), and communicable period (F_{11}). Additionally, the severity of the disease's impact may indirectly affect detection; hence, we also considered the classification of notifiable infectious disease (F_{12}) and the classification of emerging infectious disease (F_{13}). When formulating the evaluation framework and developing the initial questionnaire, the sequelae of the disease, whether it constitutes a Public Health Emergency of International Concern (PHEIC), and whether it is listed as a priority notifiable infectious disease were also considered in assessing the severity of the disease impact. However, each of these three indicators was assigned a weight of zero by two experts each, indicating that they deemed these indicators unimportant or not reflective. Consequently, these three indicators were removed. In the feedback from the first-round questionnaire, experts noted that the mode of transmission is an important characteristic of the disease and should be included as an indicator. Therefore, we added the main routes of disease transmission (F_{14}). Ultimately, the disease characteristics are represented by a total of nine indicators, namely F_6 to F_{14}.

The degree of connectivity between the source country and the PLAD in China determines the possibility of infectious disease import from another aspect. It consists of two parts: the possibility of importation from abroad and the socioeconomic interactions.

In terms of the possibility of importation from abroad, given that air travel serves as a significant mode of case importation, we considered aviation indicators such as the number of seats on flights from the source country to the local area (F_{15}) and the flight frequency from the source country to the local area (F_{20}). Additionally, we took into account other factors, including population migration index of the source country (F_{16}), history of similar disease importation from source country (F_{17}) and quantity of inbound overnight tourists received locally (F_{19}), to adjust for importation through non-aviation means. In establishing the assessment framework and developing the initial questionnaire, we also considered four additional indicators to correct for the likelihood of overseas importation: foreign direct investment from the source country, the number of personnel sent to contracted projects in the source country, the number of cases historically imported from the source country and the number of personnel dispatched for labor cooperation in the source country. We believed these indicators could potentially influence the risk of overseas importation. However, in the initial round of feedback from the questionnaire, each of these four indicators was assigned a weight of zero by at least two experts, indicating that they deemed the indicators unimportant or irrelevant. Consequently, we excluded these four indicators in the second round of questionnaire. Some experts suggested that the geographical location of the source country could influence the likelihood of overseas importation. Therefore, we added the geographical location of the source country (F_{18}) as a new indicator. Ultimately, the probability of importation from abroad is characterized by six indicators ranging from F_{15} to F_{20}.

The socioeconomic interactions component primarily aims to correct for importation through non-aviation means by assessing the degree of closeness between the local area and foreign regions. We considered the value of local imports and exports (F_{21}) and local international tourism revenue (F_{22}) as key indicators. In establishing the assessment framework and developing the initial questionnaire, we also considered the number of foreign businesses operating locally and the total foreign investment in the local area as indicators. However, four experts assigned a weight of zero to the number of foreign businesses, and three experts did the same for the total foreign investment, indicating that they deemed these indicators unimportant or irrelevant. Consequently, we excluded these two indicators in the second round of questionnaire. In the second round of feedback from the questionnaire, one expert noted that the value of local imports and exports may not fully align with population movements. While we found this suggestion to be valid, we decided to retain this indicator because no more suitable alternative was available, and it still provides insight into the local area's interactions with foreign regions. Consequently, the socio-economic exchanges are characterized by two indicators: F_{21} and F_{22}.