

Methods and Applications

Assessment of Cross-Border Monkeypox Importation Risk: A Modeling Study — Worldwide, 2022–2025

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ABSTRACT

Introduction: Monkeypox (mpox) has re-emerged as a significant global public health threat. This study developed a practical, rapid early-warning tool to quantify country-level mpox importation risk and identify potential sources of cross-border transmission.

Methods: We obtained weekly confirmed mpox case data and international passenger volume data spanning January 2022 through November 2025. We constructed an importation risk index (RI) that integrated epidemic intensity in source countries, passenger flows, and public health response capacity. Using a simplified ordinary differential equation framework, we derived a regional RI to estimate time-varying growth and acceleration parameters from surveillance time series. We then computed both real-time and baseline RI values and evaluated their lagged correlations with reported case counts.

Results: The RI demonstrated consistently strong lagged correlations with subsequent reported case counts. The real-time RI provided earlier alerts in 93.3% of countries, with a mean lead time of 4.23 weeks — approximately 3.7 weeks ahead of the baseline RI. The dominant sources of importation risk varied across countries, suggesting that this model can inform tailored, country-specific prevention and control strategies.

Conclusion: This cross-border risk assessment model provides an actionable framework for early warning and source attribution, supporting targeted surveillance and proactive allocation of public health resources. These findings underscore the critical importance of global health collaboration and timely data sharing.

Monkeypox (mpox) is caused by the monkeypox virus (MPXV) (1). Sustained human-to-human

transmission fueled a multinational outbreak, prompting the World Health Organization (WHO) to declare a Public Health Emergency of International Concern (PHEIC) in both 2022 and 2024 (2). The ongoing evolution of MPXV poses a persistent epidemic risk, necessitating continuous monitoring of viral mutations alongside the development of practical risk-warning tools (3–4).

Previous studies have assessed cross-border transmission risk using case data and passenger volumes between regions (5–7). However, delays in clinical consultation, sample processing, and case reporting frequently hinder timely public health responses. To address these gaps, we constructed a risk assessment model integrating airline network connectivity and healthcare control capacity to identify high-risk regions for mpox importation and enhance the speed and accuracy of risk assessments.

METHODS

Data Source and Preprocessing

Weekly confirmed mpox case data from January 2022 to November 2025 were obtained from the WHO dashboard (8). Monthly international air passenger data covering the same period were sourced from the Official Aviation Guide (OAG, www.oag.com).

Importation risk primarily originates from regions with high levels of epidemic activity. Countries with cumulative confirmed case counts exceeding 200 during the study period were selected for analysis; 48 countries met this criterion.

Risk Index Assessment

To address lags in data availability, we analyzed the importation risk index (RI) and its relationship to reported case counts. The RI is defined as follows:

$$RI_t: D_t \times F_t \times S_t \quad (1)$$

where D_t represents the weekly confirmed mpox case count reported by the source country at week t , normalized using min-max normalization across all source countries for each week to ensure cross-country comparability; F_t denotes the outbound air passenger volume from the source country to the destination country; S_t represents the stringency index of prevention and control measures, derived from the Global Health Security (GHS) Index — the GHS score was inverted ($100 - \text{GHS}$) so that higher values indicate weaker health security capacity (9); and t is the week of assessment. $\text{RI}(d, f, s)$ thus quantifies the risk of cross-border mpox importation.

For temporal harmonization, weekly confirmed case data served as the base temporal resolution. Monthly international air passenger data were uniformly disaggregated to the weekly level. The stringency index, a relatively stable country-level indicator, was assigned as each country's most recent available score. Where case or passenger data were unavailable due to reporting delays, linear interpolation was applied to fill gaps.

Given the observed outbreak time-series data $d \in D$ for a region, we defined the regional risk index (RRI) at time t as $\text{RRI} = \cdot v(t)$, where $v(t) \in \mathbb{R}^n$ is an n -dimensional vector representing multidimensional epidemic features of the region at time t , and $\epsilon \in \mathbb{R}^n$ is a weight vector balancing the contribution of each dimension to the RI. Equal weights were assigned to all dimensions. This parsimonious approach avoids subjective bias in the absence of empirical evidence favoring any single component and, because these dimensions capture complementary aspects of epidemic risk, provides a transparent and readily reproducible baseline.

To compute $v(t)$ explicitly, we constructed a simplified model guided by the principles of dynamic transmission modeling. Let $N(t)$ denote the number of infectious cases at time t in the source countries. We modeled $N(t)$ using the following ordinary differential equation:

$$\frac{dN(t)}{dt} = \lambda(t) N(t) \quad (2)$$

Here, $\lambda(t)$ is a time-varying coefficient encompassing the growth rate, control intensity, and effective reproduction number. A first-order linear approximation of $\lambda(t)$ was adopted for computational tractability and interpretability:

$$\lambda(t) = at + b \quad (3)$$

Within a sliding window of several weeks, the time-varying transmission coefficient can be reasonably approximated by a linear trend, as short-term changes in transmission intensity are generally monotonic. Parameter a captures the acceleration (or deceleration) of transmission, while b captures the baseline growth rate at the start of the window. Both parameters a and b were estimated from the time-series data ($d \in D$). Setting $\lambda(t^*) = 0$ yields the epidemic inflection point $t^* = -b/a$. Parameter a describes the acceleration of the infection rate under the combined influence of various factors. Denoting the total population of the region as P , we defined the following four-dimensional vector to characterize the epidemic risk situation:

$$v(t) = \left(|t - t^*|, \lambda(t), N(t), \frac{N(t)}{P} \right) \quad (4)$$

Lagged Correlation Assessment

The real-time RI is defined as the index computed using current case counts and passenger volume data, representing the best estimate under ideal data availability. The baseline RI (base RI) is defined as the index calculated under realistic reporting-delay conditions, with case data lagged by 4 weeks and air passenger data by 8 weeks, reflecting the data availability typical of routine surveillance settings.

We assessed the lagged correlation between the RI and reported case counts. Lead time was determined using an Exponentially Weighted Moving Average (EWMA) early-warning algorithm and was defined as the time difference (in weeks) between the RI triggering an alert and the reported case count triggering an alert.

RESULTS

We evaluated model effectiveness across three dimensions: risk index values, lag time, and primary sources of risk. Figure 1 shows that the mpox importation RI was highest in 2022, with peak values exceeding 1.0 in seven countries, primarily concentrated in Europe. During 2023 and 2024, peak RI values exceeded 1.0 in four and five countries, respectively, and the risk shifted toward East Asia. By 2025, overall importation risk remained low.

Among the 30 countries with the highest importation RI, reported case counts exhibited strong lagged correlations with RI values: 100% and 70.3% of countries showed correlation coefficients above 0.7 for

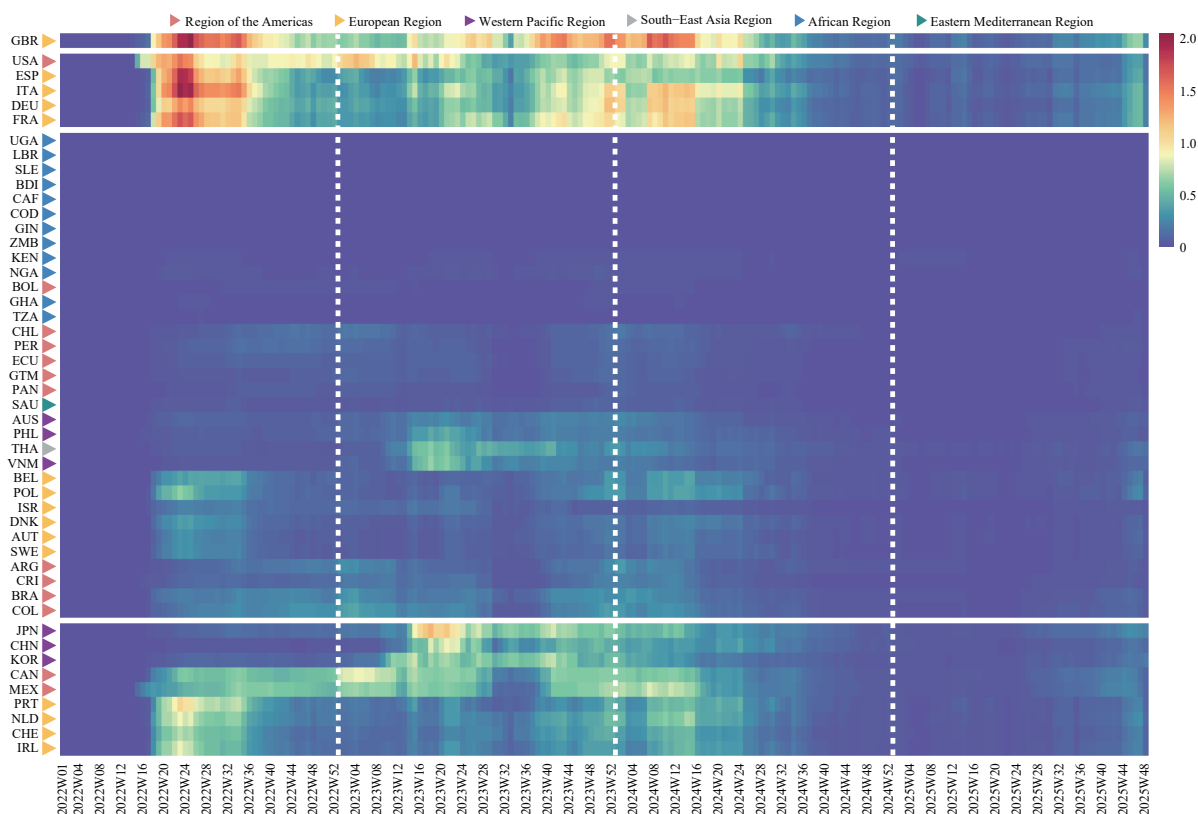


FIGURE 1. RI heatmap, 2022W01–2025W48.

Note: Forty-eight countries with cumulative cases greater than 200 are shown. The colors behind the row names correspond to different regions. White dashed lines separate different years.

Abbreviation: RI=risk index; ARG=Argentina; AUS=Australia; AUT=Austria; BDI=Burundi; BEL=Belgium; BOL=Bolivia; BRA=Brazil; CAF=Central African Republic; CAN=Canada; CHE=Switzerland; CHL=Chile; CHN=China; COD=Democratic Republic of the Congo; COL=Colombia; CRI=Costa Rica; DEU=Germany; DNK=Denmark; ECU=Ecuador; ESP=Spain; FRA=France; GBR=United Kingdom; GHA=Ghana; GIN=Guinea; GTM=Guatemala; IRL=Ireland; ISR=Israel; ITA=Italy; JPN=Japan; KEN=Kenya; KOR=Republic of Korea; LBR=Liberia; MEX=Mexico; NGA=Nigeria; NLD=Netherlands; PAN=Panama; PER=Peru; PHL=Philippines; POL=Poland; PRT=Portugal; SAU=Saudi Arabia; SLE=Sierra Leone; SWE=Sweden; THA=Thailand; TZA=United Republic of Tanzania; UGA=Uganda; USA=United States; VNM=Vietnam; ZMB=Zambia.

the real-time and baseline RIs, respectively (Table 1).

The real-time RI identified importation risks before a rapid increase in case counts in 93.3% of countries, with an average lead time of 4.23 weeks; by comparison, the baseline RI achieved a lead time of only 0.5 weeks (Figure 2). These findings demonstrate that both the real-time and baseline RIs can serve as effective early-warning tools, while underscoring the critical importance of timely surveillance data.

For most countries, importation risk was primarily driven by the United States, Australia, Spain, the Democratic Republic of the Congo, the United Kingdom, and Brazil (Figure 3). The dominant sources varied across recipient countries, indicating that this model can inform tailored, country-specific prevention and control strategies.

DISCUSSION

This risk assessment model offers a practical approach to quantifying and anticipating cross-border mpox importation risk by integrating epidemic intensity in source countries, cross-border passenger volumes, and contextual indicators of response capacity. The strong concordance between estimated importation risk and subsequent case trajectories supports the model's validity and robustness. This consistency was evident in both the trends and absolute levels of RI changes, confirming the reliability and stability of the risk assessment framework (10).

The cross-country variation in real-time RI lead time (0–15 weeks) reflects several interacting factors. Countries with well-established surveillance systems

TABLE 1. Lagged correlation between the importation risk index and reported cases, and the lead time for early detection of the increase in mpox cases.

No.	Country	Real-time risk index		Baseline risk index	
		<i>r</i>	Lead time (week)	<i>r</i>	Lead time (week)
1	ARG	0.96	9	0.96	4
2	AUT	0.99	3	0.86	0
3	BEL	0.99	2	0.69	0
4	BRA	0.99	3	0.84	0
5	CAN	0.95	0	0.31	-4
6	CHE	0.98	2	0.74	0
7	CHL	0.98	5	0.97	0
8	CHN	0.88	3	0.76	0
9	COL	0.99	7	0.99	1
10	CRI	0.83	15	0.41	12
11	DEU	0.98	0	0.46	-2
12	DNK	0.95	3	0.71	0
13	ECU	0.95	11	0.94	5
14	ESP	0.98	2	0.71	0
15	FRA	0.99	3	0.81	0
16	GBR	0.98	1	0.50	-3
17	GTM	0.89	14	0.89	10
18	IRL	0.90	4	0.87	0
19	ISR	0.95	2	0.63	0
20	ITA	0.96	1	0.72	0
21	JPN	0.86	4	0.84	0
22	KOR	0.87	8	0.89	0
23	MEX	0.98	7	0.97	1
24	NLD	0.98	1	0.52	-2
25	PER	0.99	3	0.92	-1
26	POL	0.98	5	0.97	-1
27	PRT	0.91	1	0.49	-1
28	SWE	0.90	2	0.74	0
29	THA	0.79	3	0.68	-2
30	USA	0.98	3	0.86	-2

Note: *r*, the optimal Pearson correlation coefficient from the lagged cross-correlation between the importation risk indices (real-time and baseline) and weekly reported case counts; lead time (weeks), the time difference between the RI triggering an early-warning alert and the reported case count triggering an alert, determined by the EWMA algorithm; positive values indicate the RI provided an earlier alert, negative values indicate a delayed alert.

Abbreviation: RI=risk index; EWMA=exponentially weighted moving average; mpox=monkeypox; ARG=Argentina; AUT=Austria; BEL=Belgium; BRA=Brazil; CAN=Canada; CHE=Switzerland; CHL=Chile; CHN=China; COL=Colombia; CRI=Costa Rica; DEU=Germany; DNK=Denmark; ECU=Ecuador; ESP=Spain; FRA=France; GBR=United Kingdom; GTM=Guatemala; IRL=Ireland; ISR=Israel; ITA=Italy; JPN=Japan; KOR=Republic of Korea; MEX=Mexico; NLD=Netherlands; PER=Peru; POL=Poland; PRT=Portugal; SWE=Sweden; THA=Thailand; USA=United States.

and short reporting delays (e.g., Germany and the United Kingdom) exhibited shorter lead times because their baseline RI already approximates real-time conditions, limiting the incremental predictive gain. Additionally, countries with diverse, multi-source

travel connectivity may aggregate risk signals across multiple importation pathways, enabling earlier detection (11). These findings underscore the importance of reducing surveillance reporting delays to maximize early-warning performance.

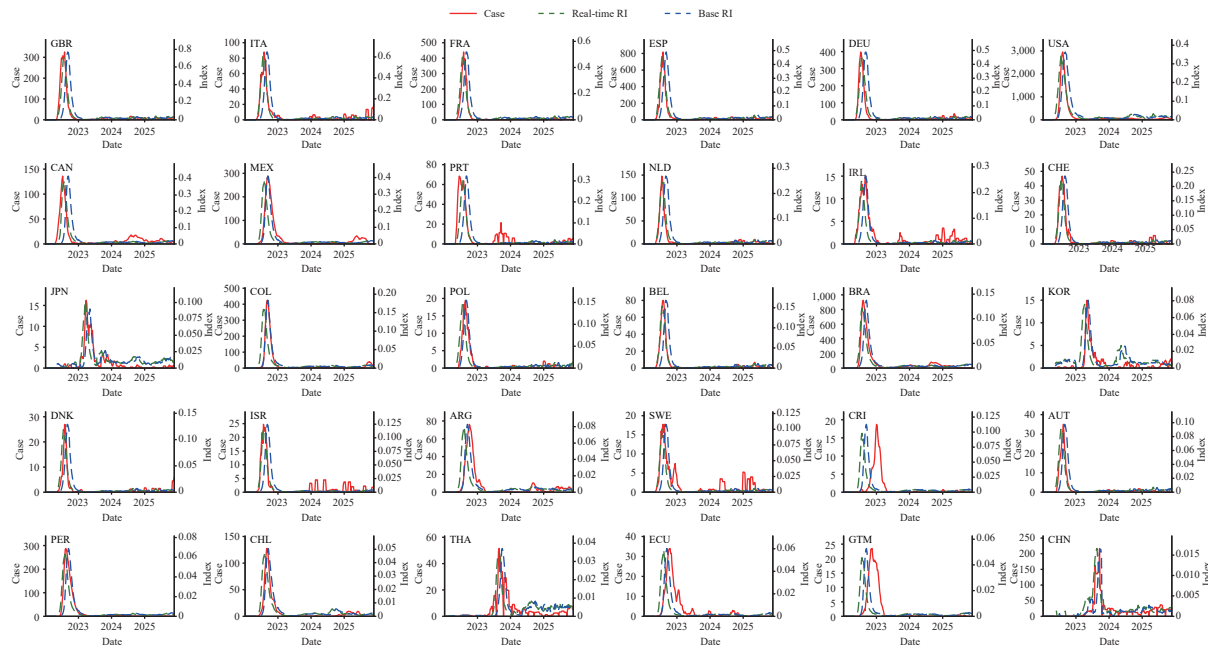


FIGURE 2. Country-specific time series of weekly cases and importation RI, 2022W01–2025W48.

Note: The weekly case series are shown as a red solid line (4-week moving average), the real-time RI as a green dashed line, and the baseline (base) RI as a blue dashed line. Cases are plotted on the left y-axis, while RI values are plotted on the right y-axis.

Abbreviation: RI=risk index; ARG=Argentina; AUT=Austria; BEL=Belgium; BRA=Brazil; CAN=Canada; CHE=Switzerland; CHL=Chile; CHN=China; COL=Colombia; CRI=Costa Rica; DEU=Germany; DNK=Denmark; ECU=Ecuador; ESP=Spain; FRA=France; GBR=United Kingdom; GTM=Guatemala; IRL=Ireland; ISR=Israel; ITA=Italy; JPN=Japan; KOR=Republic of Korea; MEX=Mexico; NLD=Netherlands; PER=Peru; POL=Poland; PRT=Portugal; SWE=Sweden; THA=Thailand; USA=United States.

The model demonstrates substantial early-warning value: compared with the baseline RI, the real-time RI provided an approximately four-week lead time. This advance warning can optimize public health resource allocation, reduce the economic impact of outbreaks, heighten public awareness, strengthen international cooperation, and inform evidence-based policy development. Further reductions in reporting delays would enable near-real-time situational awareness and extend the effective warning window (12), reinforcing the need for stronger international and multisectoral collaboration (13–14).

Beyond identifying when risk increases, the model helps pinpoint the sources of importation risk. For many countries, importation risk is concentrated among a set of major source countries, but the dominant sources differ across recipients. This heterogeneity supports tailored risk management strategies based on each country's connectivity profile (15). Our findings further suggest that even when overall global risk is low, localized or regional surges can rapidly reintroduce importation threats through highly connected travel nodes.

This study has several limitations. First, the RI relies on reported case counts and auxiliary indicators that may be affected by under-ascertainment, heterogeneous surveillance capacity, and reporting delays, potentially biasing estimates and limiting cross-country comparability. Second, the mobility component focuses exclusively on air travel and may underestimate risk in settings where land or sea crossings are substantial. Third, the linear approximation for $\lambda(z)$ may be inadequate during periods of rapid epidemic change; future work could explore piecewise-linear or nonlinear specifications to capture more complex trajectories. Fourth, equal weights were assumed for all regional risk index dimensions; future studies could leverage prior knowledge or empirical calibration data to optimize the weight vector and further enhance predictive accuracy.

Conflicts of interest: No conflicts of interest.

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Ethical Statement: All data used in this study are publicly available and do not involve personal

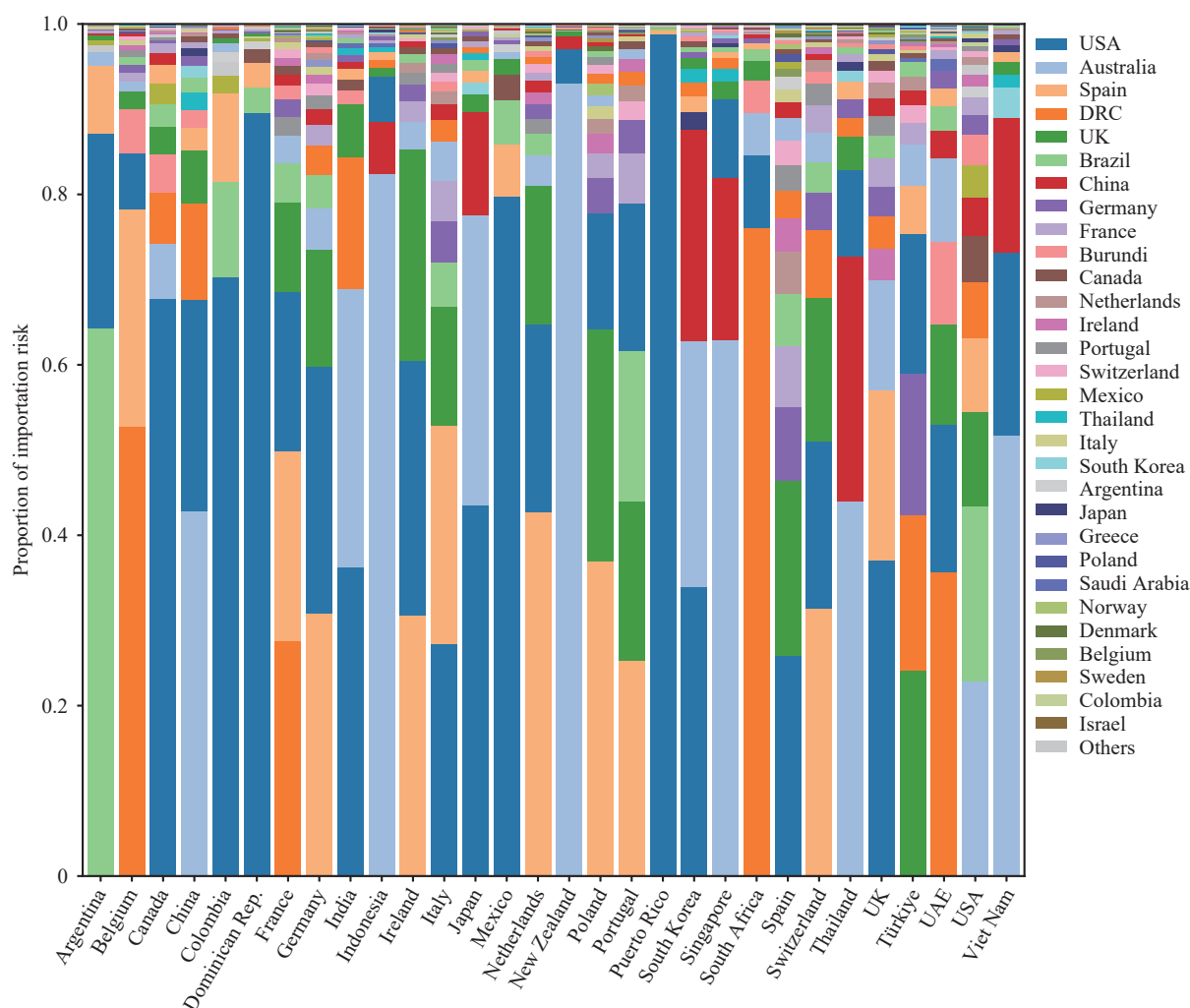


FIGURE 3. The proportion of importation risks for specific countries/regions.

Abbreviation: DRC=Democratic Republic of the Congo; UK=United Kingdom; USA=United States of America

information.

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