

Global Mpox spread due to increased air travel

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Abstract

Mpox is an emerging, infectious disease that has caused outbreaks in at least 91 countries from May to August 2022. We assessed the link between international air travel patterns and Mpox transmission risk on the one hand, and the relationship between the translocation of Mpox and human mobility dynamics on the other after travel restrictions due to the COVID-19 pandemic had been lifted. Our three novel observations were that: (i) more people travelled internationally after the removal of travel restrictions in the summer of 2022 compared to pre-pandemic levels; (ii) countries with a high concentration of the global air travel have most of recorded Mpox cases; and (iii) Mpox transmission include a number of previously non-endemic regions. These results suggest that international airports should be the primary location for monitoring of the risk of emerging communicable diseases, and they underscore the need for global collaboration with regard to proactive measures emphasizing real-time surveillance.

Keywords: Air traffic, Infectious disease, Mpox, Hotspot, Risk map.

Introduction

Mpox (previously known as monkeypox) is an infectious disease caused by the monkeypox virus, a member of the *Poxviridae* family (Damaso, 2023). The infection gives generally only mild symptoms and typically self-resolves except in at-risk patient groups with limited cellular immune response, children under 8-years of age, pregnant women and immunocompromised individuals (Guarner *et al.*, 2022). In the latter group, Mpox severity is significant and includes conjunctivitis, encephalitis, pneumonia, death and also foetal mortality (Burki, 2022; Guarner *et al.*, 2022). Fatality rates are greater in patients infected by the human immunodeficiency virus (HIV) (Simpson *et al.*, 2020).

Mpox is transmitted through body fluids or skin lesions as shown by Falendysz *et al.* (2017) during close physical contact with infected persons or animals, such as African rodents, mice, prairie dogs or non-human primates (Li *et al.*, 2023). In non-endemic areas, such as Europe and North America, preliminary genomic sequencing studies have identified the West African variant as the main virus lineage that has a case fatality rate of 1% (Burki, 2022). The Congo Basin variant of the monkeypox virus (which is not currently found outside Africa) has a fatality rate of up to 10% (Simpson *et al.*, 2020; Burki, 2022). The differences in virulence among monkeypox virus lineages highlight the outbreak risk of Mpox and its global health relevance.

Prior to 2018, Mpox infections rarely occurred outside West Africa, where the disease endemic (Vaughan *et al.*, 2020; Burki, 2022). Endemic countries, such as Nigeria and Ghana, have served as source of Mpox for international outbreaks through travel of infected people or live animal exports (Vaughan *et al.*, 2020; Guarner *et al.*, 2022). A significant turning point came in 2018 when the first confirmed case of human-to-human transmission outside Africa was reported in the United Kingdom. The transmission involved a healthcare worker who cared for a patient who had travelled from Nigeria (ECDC, 2018). In May 2022, the first Mpox outbreak was reported in the United Kingdom, originating from a British resident recently returning from a trip to Nigeria (Kraemer *et al.*, 2022). This coincided with the international relaxation of COVID-19 restrictions, which limited the number of flights and individuals travelling between countries (post-COVID-19 pandemic). The reduction of travel restrictions increased international air passenger flow via airline transportation, immediately returning to 68% of pre-COVID-19 pandemic levels (Kazda *et al.*, 2022; Kinoshita *et al.*, 2023). Understanding the dynamics of Mpox transmission, especially in the context of international travel, is crucial for effective outbreak control and prevention. Global changes facilitate the appearance of emerging diseases (Jones *et al.*, 2008) and the constant increase in connectivity (Baker *et al.*, 2022) amplifies the risk of future international epidemics and pandemics.

This project examined the spread of Mpox during the 2022 outbreak period, with a focus on temporal incidence, patterns of international travel, and global hotspots of transmission risk. It aimed to enhance our understanding of how the translocation of emerging diseases are influenced by international human mobility patterns. We hypothesized that international air passenger flow positively correlates with the translocation of Mpox infections. To test this hypothesis, we assessed the geographical and temporal patterns of airline networks and Mpox spread. We expect that our findings on global Mpox spread can help inform the formulation of public health measures within the airline networks.

Materials and methods

Data sources

Mpox data were downloaded from the GLOBAL.HEALTH monkeypox data repository (<https://www.monkeypox.global.health/>) for May and August for 2019 (pre-COVID-19) and 2022 (post-COVID-19) (Kraemer *et al.*, 2022). This repository indicates the emergence and rapid spread of the Mpox outbreaks and provides aggregated information for cases reported by the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC) in the United States (U.S.) and the European Centre for Disease Control and Prevention (ECDC) (websites accessed on Aug 22, 2023).

We collected international flight travel information from the OpenSky Network project (<https://opensky-network.org/>) on numbers of flights including origin and destination data (Schafer *et al.*, 2014). This network is a product of the Automatic Dependent Surveillance-Broadcast, which contains information directly transmitted by an aircraft, such as arrival and departure records, identification, coordinates, altitude and ground speed (Chevallier *et al.*, 2023). Analysing Mpox incidence data during the May-August 2022 period allowed us to capture major epidemiological signals of the outbreak, including its geographical patterns, early detection of cases, and the impact of international air travel during the summer months of the northern hemisphere with special reference to changes in COVID-19 travel restrictions.

Data analysis

We performed a descriptive analysis of Mpox cases to depict the cumulative and monthly case reports from each country and month as well as the travel history involved (origin and destination) using R statistic software version 4.1.2 (R Core Team, 2021). The Mpox incidence was calculated by dividing the cumulative confirmed cases by the population size of each country downloaded from the World Population Prospects 2022 (UNDESA, 2022), and we used log-transformation to ensure a standardized measure of Mpox cases per million (M) inhabitants. We used the ‘sf’ package of R (Pebesma, 2018) to conduct analyses of the number of cases imported via flights between countries. The ‘raster’ package (Hijmans & Van Etten, 2021) was applied to visualize the spatial distribution of overlap with confirmed Mpox cases reported and detect hotspot areas with a high frequency of Mpox transmission around the world. Finally, we compared the international air travel patterns to investigate air travel pre- and post-COVID-19 pandemic in each country. Air travel was then related to Mpox cases using generalized linear models to examine the relationship between the number of incoming flights with the number of confirmed Mpox cases.

Results

During the May-August 2022 period, Mpox outbreaks were reported in 91 countries, encompassing all continents except Antarctica. There was a total of 41,304 confirmed Mpox cases reported, and 89% of affected countries had not historically reported Mpox outbreaks. High Mpox case counts were observed in the U.S., Spain Brazil, and Germany (Figure 1). When controlling Mpox incidence by a country’s population size, Spain had the highest incidence per1M inhabitants (0.12 cases) followed by the Netherlands (0.06 cases) and the United Kingdom (0.05 cases) (Figure 2).

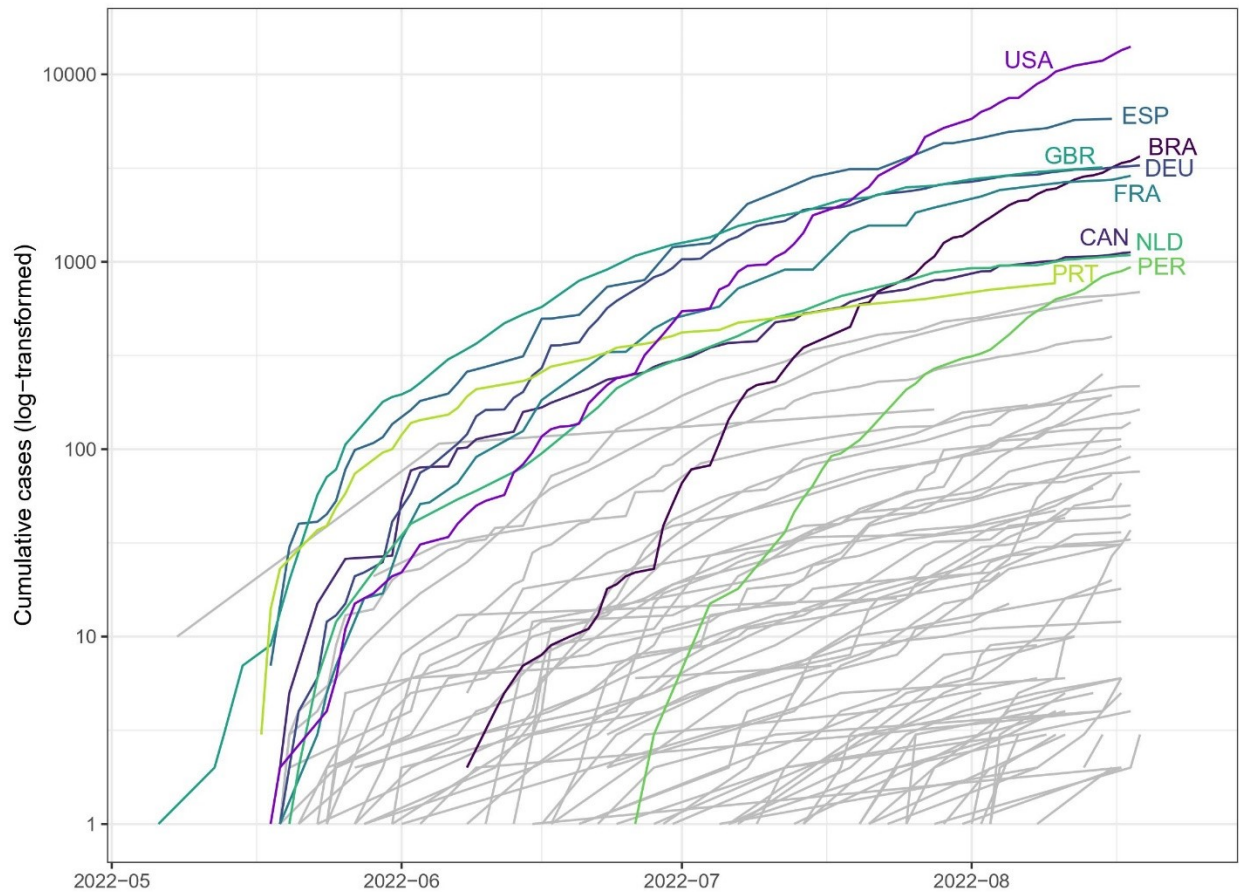


Figure 1. Log-transformed, cumulative cases (y-axis) in 91 countries during May-August 2022 (x-axis) Mpox cases by August 24, 2022, denoting the countries with a particular high number of cases: the U.S. (14,052 cases), Spain (5,792 cases), Brazil (3,658 cases), Germany (3,266 cases), the United Kingdom (3,193 cases), France (2,737), Canada (1,109 cases), the Netherlands (1,087 cases), Peru (889 cases) and Portugal (770 cases). Gray lines denote cases in all other affected countries.

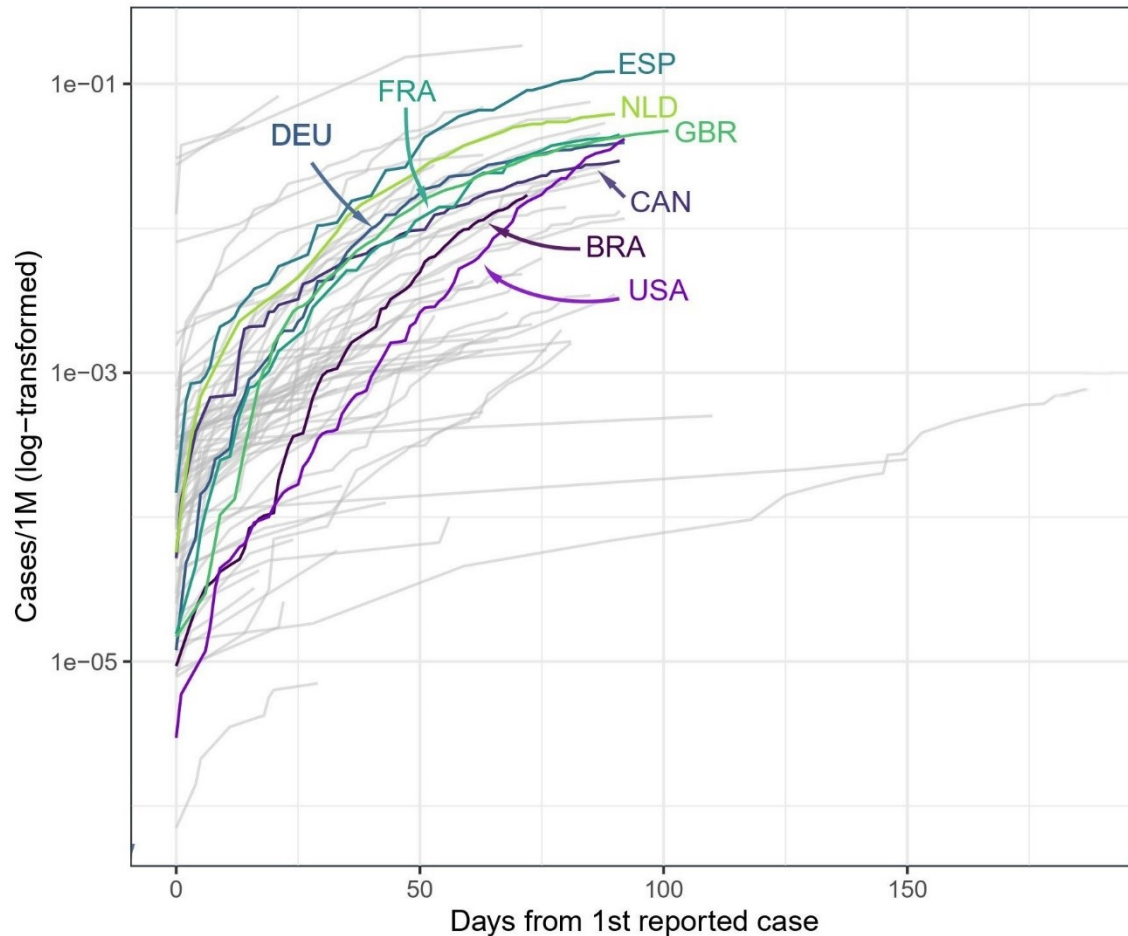


Figure 2. Log-transformed number of confirmed Mpox cases per million inhabitants (y-axis) in 91 countries since the first case detected (x-axis). Mpox case numbers/1M inhabitants in countries with high infection rates, including Spain (0.12), the Netherlands (0.06), the United Kingdom (0.05), France (0.05), Germany (0.05), the U.S. (0.05), Canada (0.04), Brazil (0.02). Gray lines denote cases in all other affected countries.

According to international air travel data in the summer of 2022 after the COVID-19 mobility restrictions had been lifted, the passenger flow surpassed pre-pandemic levels of air travel reported in 2019. Mpox patient flight histories revealed a biased origin of outbreak originating from patients returning from Europe and spreading to the rest of the world. (Figure 3). Indeed, air travel not only resumed in most countries (~79%) but the numbers often exceeded pre-pandemic travel (Figure 4). However, a decrease in air travel was detected in Russia, Thailand and Canada, which reported less than 100 Mpox cases, while Sweden, Italy, and the Czech Republic had air travel close to pre-pandemic levels and reported more than 100 Mpox cases. Importantly, the great majority of countries with increased travel reported more than 100 Mpox cases during the international Mpox outbreak.

International airports in Spain, the U.S. and Portugal became Mpox transmission hubs for the export of cases to the rest of Europe, the Americas, Australia, and Africa, while Germany played a key role in facilitating the spread to Asia. The amount of air travel was a strong predictor of

Mpox cases in non-endemic countries, with higher passenger flow linked to larger Mpox outbreaks (Figures 4 and 5). The levels of air passenger flow identified hotspot areas of likely Mpox outbreaks around the world, as shown in darker shades in Figure 5 A. As can be observed in the figure, most Mpox cases during the global outbreak were concentrated in the U.S., Spain, Brazil, the United Kingdom, Germany, and France, with secondary clusters of cases in Canada, the Netherlands, Peru, and Portugal (Figure 5A). The later heavier international connectivity by air travel led to significant global hotspots of Mpox emergence and spread, while countries exceeding pre-pandemic levels of air-passenger flow also reported the highest Mpox incidence (Figure 5B). The number of incoming flights was a strong, significant predictor of Mpox cases (i.e., $R^2=0.63$, Figure 5B).

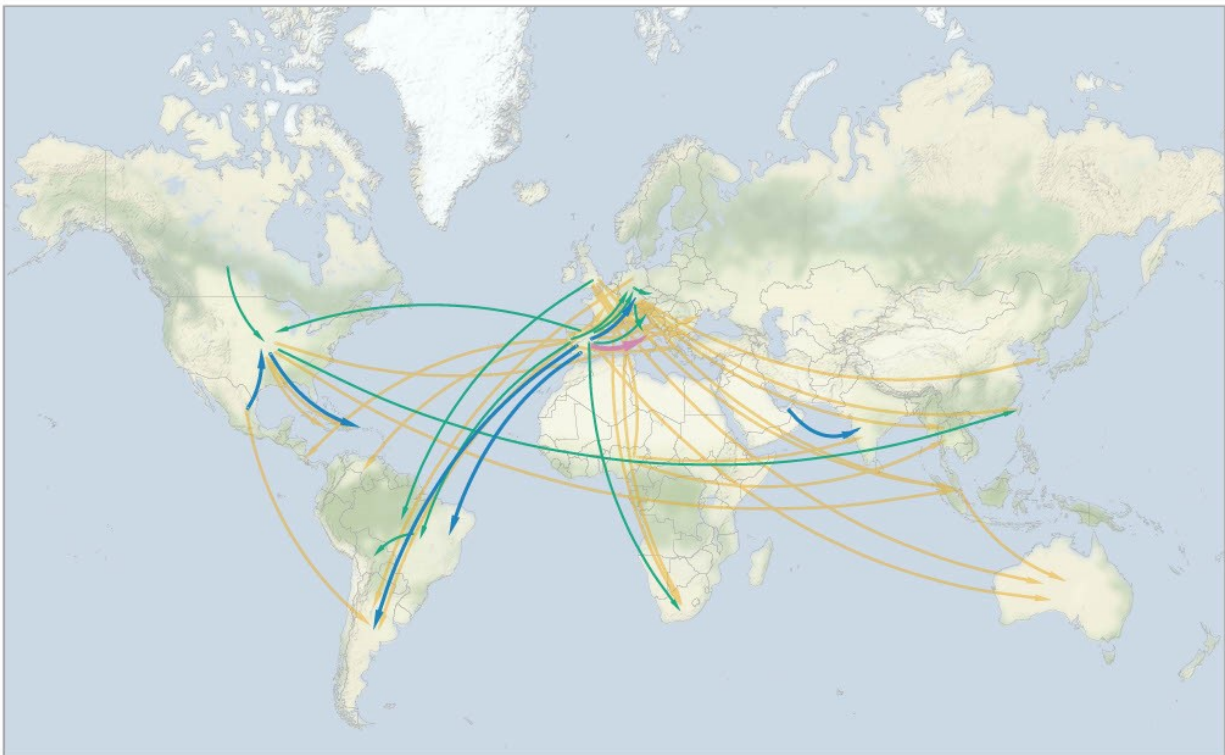


Figure 3. Mpox transmission hotspots. The number of cases imported via flights between countries is shown in different colours: one case (yellow), two cases (green), three cases (blue) and four cases (purple).

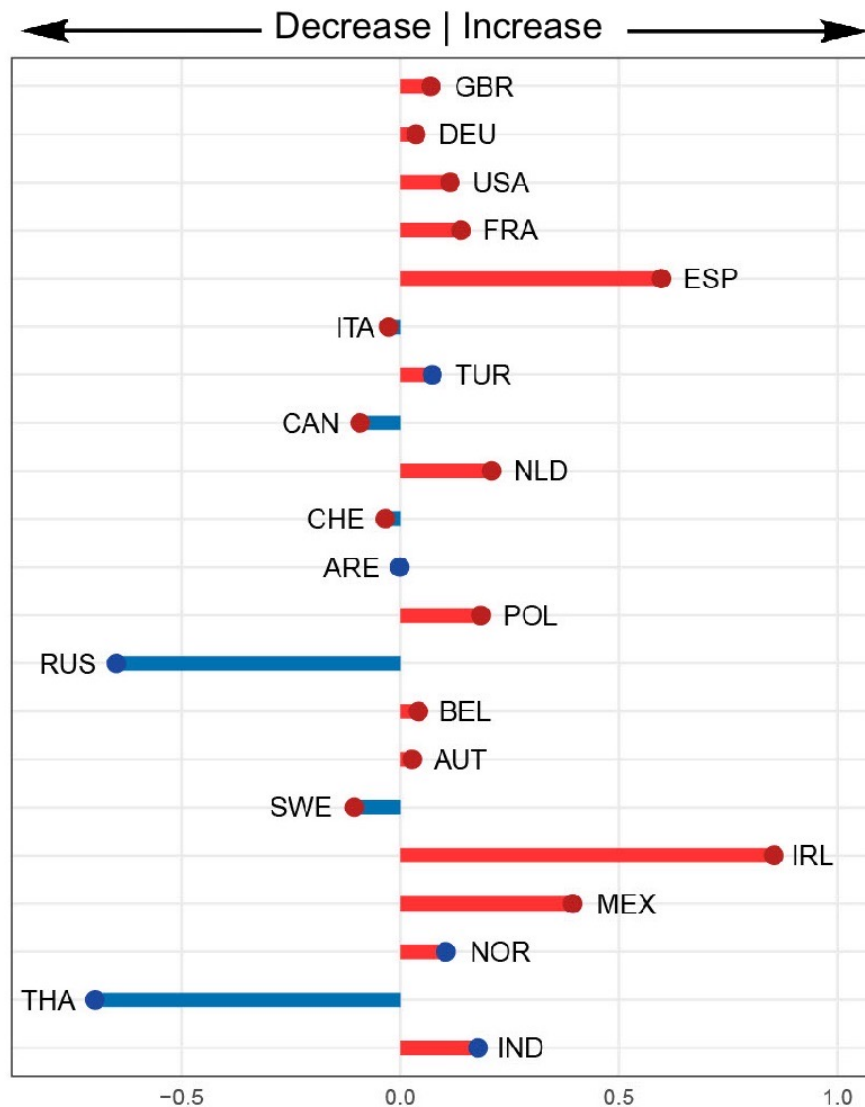


Figure 4. Change in international air travel patterns before (2019) and after (2022) the COVID-19 pandemic and Mpox cases in 2022. Red points denote countries reporting more than 100 Mpox cases. Blue points those reporting less than 100 Mpox cases. Red bars those with increased air travel. Blue bars those with a decreased air travel. Vertical line (0.0) denotes no change in air passenger flow.

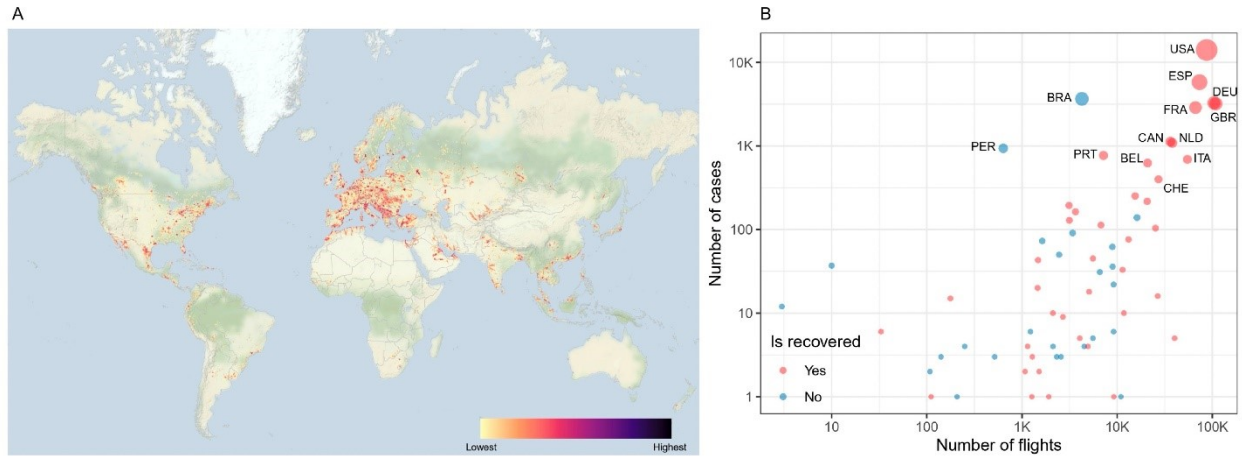


Figure 5. Mpox transmission hotspots predicted based on international air passenger flow.
A) Levels of passenger flow; B) Relationship between air travel and Mpox cases. Blue points indicate countries having not returned to pre-pandemic levels of passenger flow (not recovered). Red points indicate countries having exceeded pre-pandemic levels of passenger flow (recovered). Point size denote amount of Mpox cases.

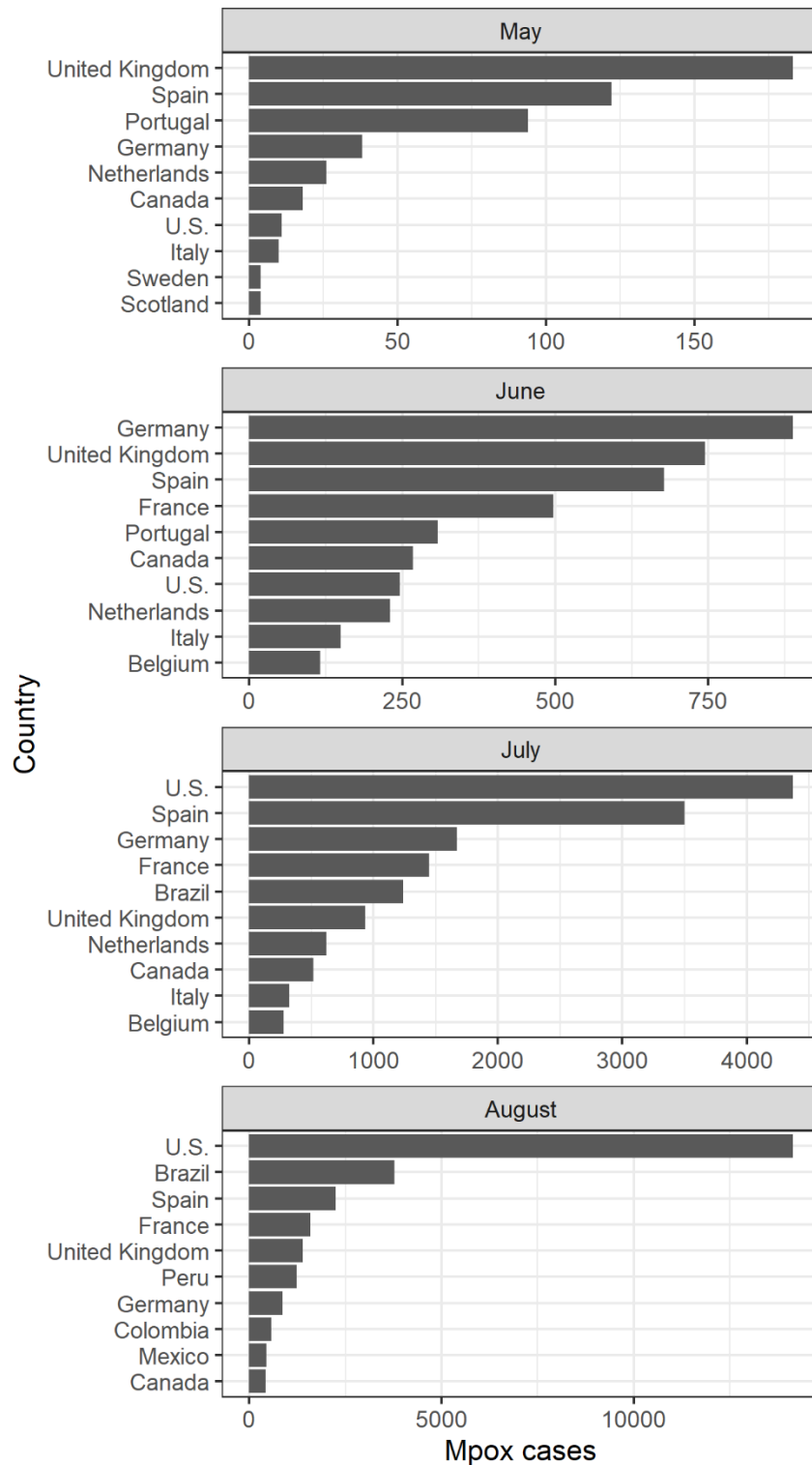


Figure 6. Count of confirmed Mpox cases detailed for the 10 countries with the highest transmission during the period May-August in 2022.

The Mpox incidence varied temporally and geographically (Figure 6). In May 2022, the highest number of confirmed cases was reported in Europe, including the United Kingdom (n=183),

Spain (n=122), Portugal (n=94), Germany (n=38) and the Netherlands (n = 26). In June 2022, Germany reported a substantial increase of confirmed cases (n=888) and the number of cases increased more than 300% in the United Kingdom (n=745), Spain (n=678), France (n=497) and Portugal (n=308). In July 2022, a high number of cases was reported in the U.S. (n=4,369) and Brazil (n=1,239). In August 2022, the U.S. accumulated the highest number of confirmed cases (n=14,140), followed by Brazil (n=3,780), Spain (n=2,245), France (n=1,593) and the United Kingdom (n=1,395).

In May 2022, 38.9% of the Mpox confirmed cases had a history of travel from Spain and only 5.6% from Nigeria, which was the only incidence reported from Africa (Figure 7). In June 2022, 36.8% of the Mpox confirmed cases had a history of travel departing from Spain, with 15.9% of all cases linked to departures from the U.S., Australia, Singapore, and Mexico (Figure 8). At least 25% of Mpox imported cases in South America originated in Spain and France (Figure 9). In August 2022, 17.6% of confirmed cases had a history of travel from the U.S. Late in the outbreak, Europe played a limited role in exporting Mpox cases, with six cases linked to a European origin in August 2022, the lowest compared with previous months (Figure 10).

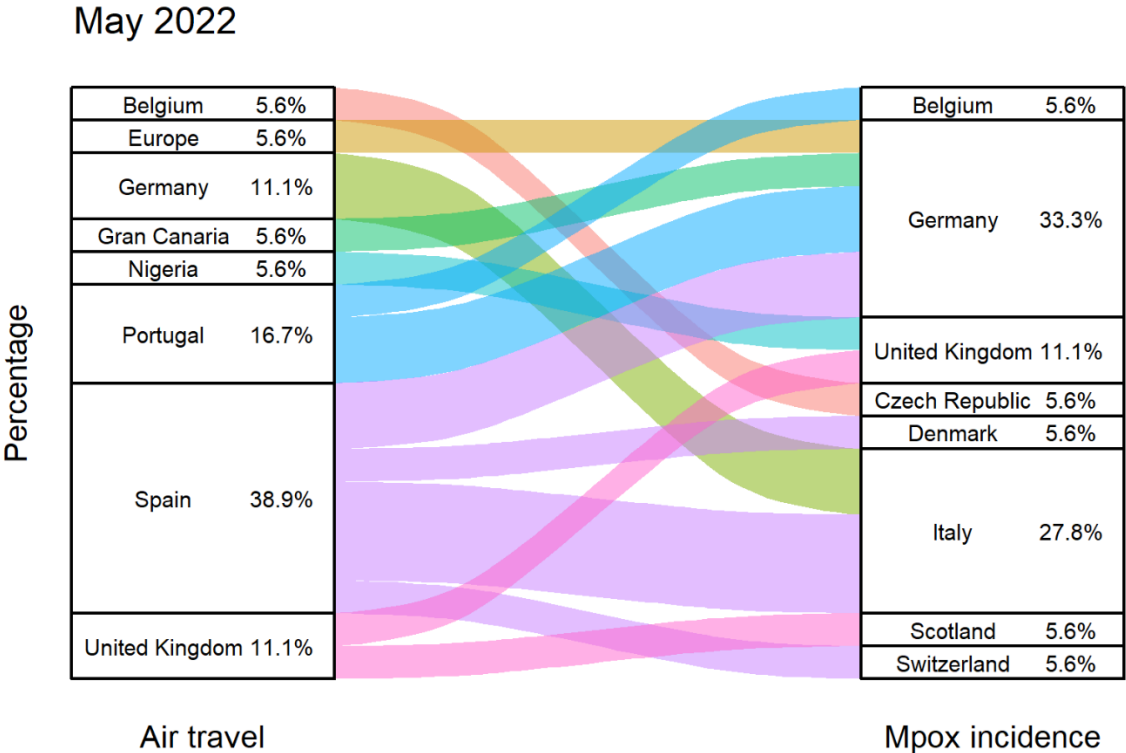


Figure 7. Air travel and Mpox spread globally May 2022. Left: Percentage of air travel between countries and their connectivity to other countries (color lines). **Right:** Mpox incidence in May 2022.

June 2022

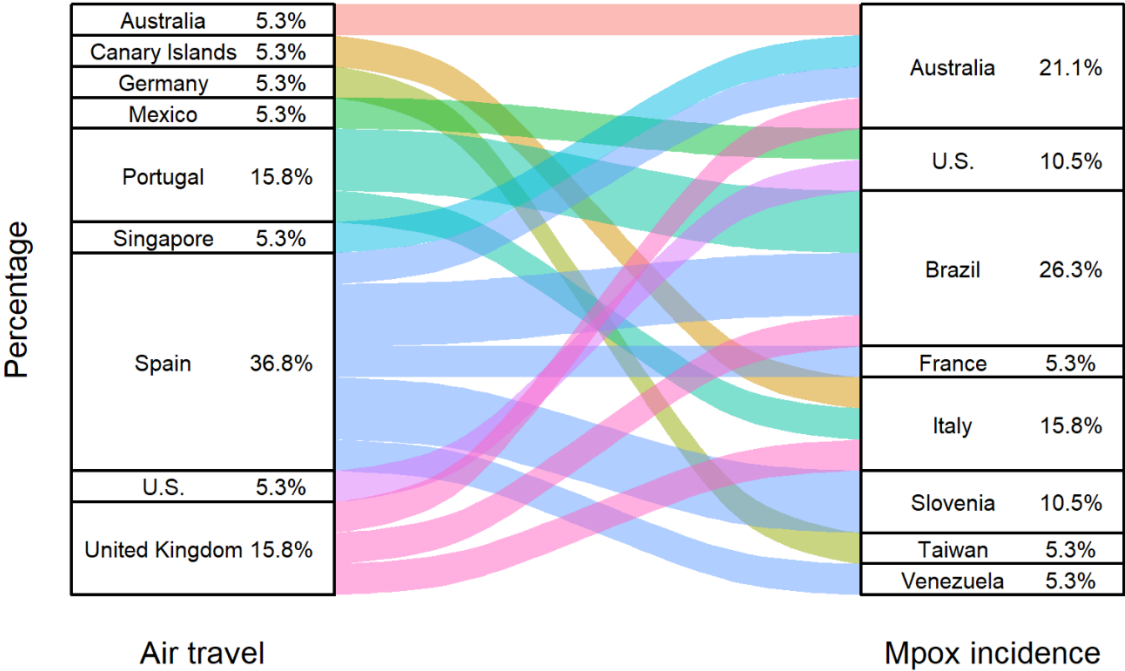


Figure 8. Air travel and Mpox spread globally June 2022. Left: Percentage of air travel between countries and their connectivity to other countries (colour lines). Right: Mpox incidence in June 2022.

July 2022

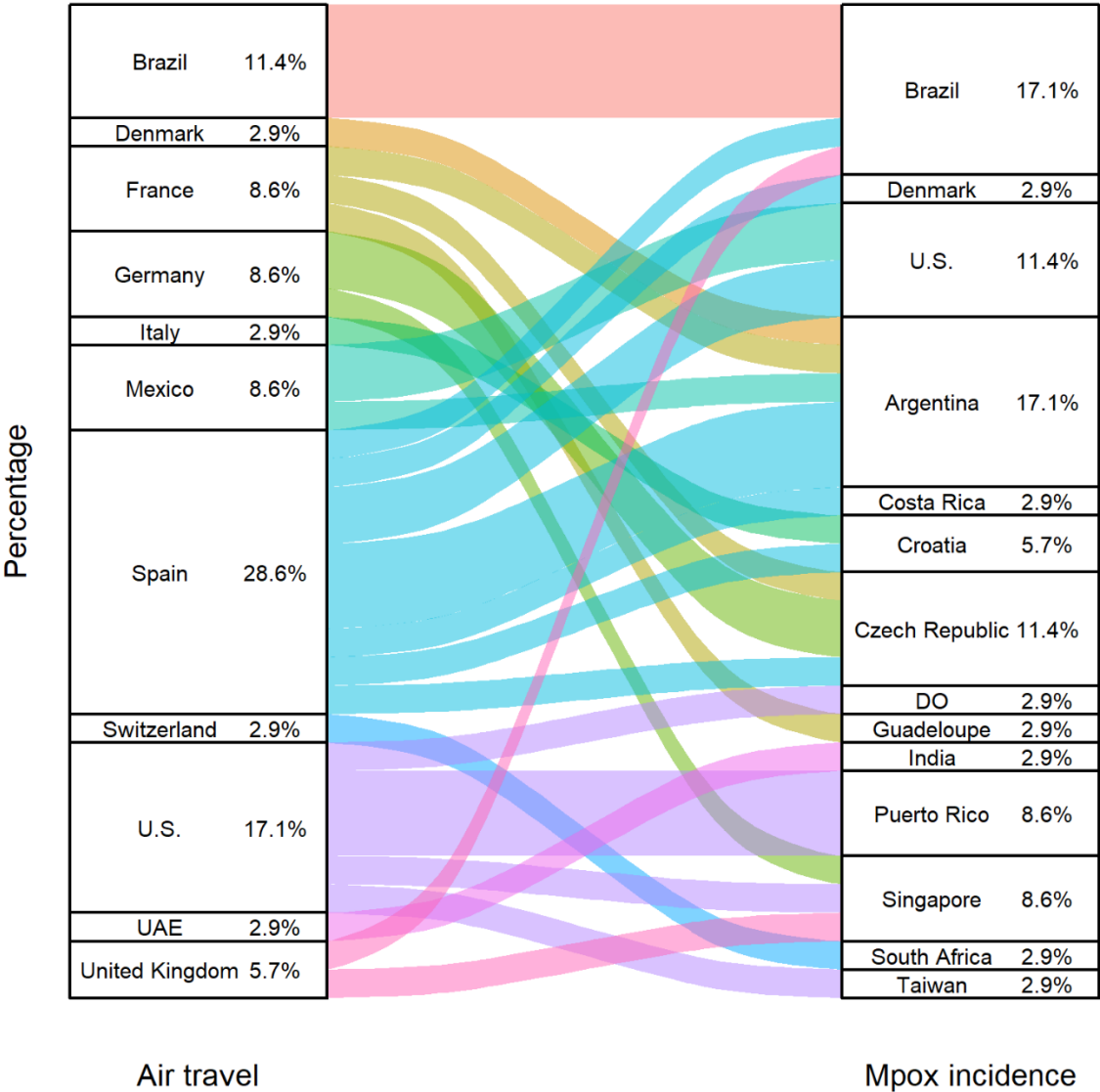


Figure 9. Air travel and Mpox spread globally July 2022. Left: Percentage of air travel between countries and their connectivity to other countries (colour lines). **Right:** Mpox incidence in July 2022. DO=Dominican Republic; UAE=United Arab Emirates.

August 2022

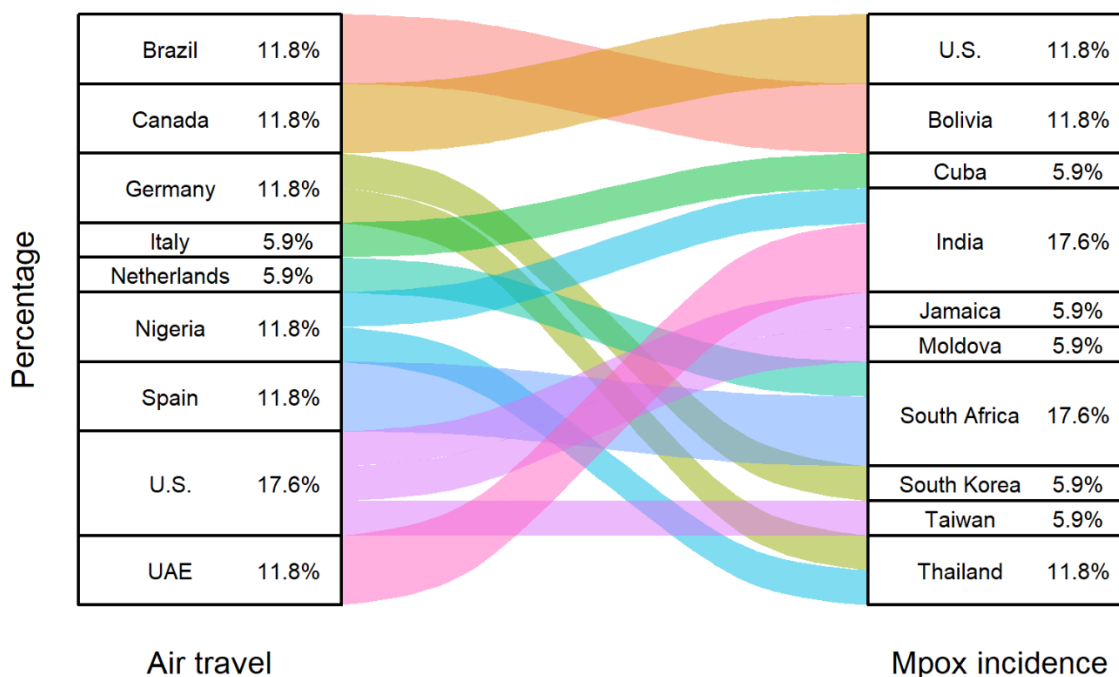


Figure 10. Air travel and Mpox spread globally August 2022. Left: Percentage of air travel between countries and their connectivity to other countries (colour lines). **Right:** Mpox incidence in August 2022. UAE=United Arab Emirates.

Discussion

Our findings regarding the Mpox outbreak of 2022 with European countries, especially Spain, playing a key role in its international spread, indicate that the number and direction of flights were associated with the fast spread in non-endemic localities (Betancort-Plata *et al.*, 2022; González-Val & Marcén, 2022). The relaxation of COVID-19 restrictions for international air travel in 2022 resulted in air travel exceeding pre-pandemic levels, which correlated with higher Mpox spread to non-endemic countries. There is therefore a need for effective global health strategies to prevent and control the international spread of infectious diseases informed by international air travel data.

This global outbreak demonstrated a concerning trend of the emergence of wildlife diseases of pandemic potential (WHO, 2022). The first case confirmed on May 6, 2022, in the United Kingdom was linked to recent travel history from Nigeria, an endemic country for Mpox (Kraemer *et al.*, 2022). The human Mpox cases confirmed by six laboratories in the United Kingdom between May 13 and 15 in 2022 lacked travel links to endemic countries, suggesting human-to-human community transmission in non-endemic localities (Burki, 2022; Guarner *et al.*, 2022; WHO, 2022). Community transmission was further supported by the fact that over 5,000 Mpox confirmed cases in non-endemic countries were reported, denoting the fast spread of the outbreak (Kozlov, 2022; Kraemer *et al.*, 2022). The Mpox outbreak revealed an exponential growth of community transmission globally (Kozlov, 2022), which was not immediately obvious due to delayed identification, tracing and isolation of patients.

Effective distance of contagion

The recent availability of air-travel data has facilitated epidemiologic applications of air travel models to predict disease arrival times and sites of origin. For instance, Brockmann & Helbing (2013) proposed the “effective distance” concept to denote air travel connections as a more effective distance to anticipate disease spread compared to geographic distance. This pioneer approach was employed to successfully anticipate the sites of origin and international spread of the H1N1 influenza, the 2003 severe acute respiratory syndrome (SARS), and the 2016 Chikungunya epidemic (Brockmann & Helbing 2013, Escobar *et al.*, 2016). We employed a network modelling approach to identify nodes with the highest likelihood of spreading cases to new regions. We used this information to map airport-level hotspots of transmission risk, which can inform future Mpox containment in view of the risk of future Mpox emergence (Figure 5).

The emergence of the 2022 Mpox outbreak and the introduction and spreading of Mpox to new countries, including specific super-spreading hotspots across Europe, the Americas, and South Asia, is in line with previous suggestions of the likely contribution of the relaxation of COVID-19 prevention measures to disease spread (Thornhill *et al.*, 2022). Previous studies have centred on local-level air travel data to estimate Mpox spread risk (e.g., Kinoshita *et al.*, 2022). Our global-level studies combining air travel data with Mpox importation data generated a data-driven, empirical estimate of Mpox spread (Figure 5). As shown in our Figures 1 & 2, our results overcame other assessments that identified the U.S. as a source of cases driven mainly by the volume of passengers from this country. That is, by controlling for air travel and Mpox incidence per capita, we found other countries having key contribution to the global spread of Mpox (Escobar *et al.*, 2016; Del Valle *et al.*, 2018).

We detected specific countries, cities, and airports with the highest likelihood of Mpox spread risk (Figure 5), which could help inform future travel restrictions to reduce epidemic spread. Grépin *et al.* (2021) found that implementing travel restrictions that reduce international travel by 40%–90% could likely have a positive impact in reducing the risk of infectious disease importation through airline networks. Nevertheless, Kinoshita *et al.* (2023) argue that the potential efficacy of travel restrictions to reduce the importation risk of Mpox through airline networks may have different magnitudes of effect among countries. We found that Brazil and Peru had higher Mpox incidence than expected, which could be explained by public health systems with limited capacity to block transmission. For instance, Brazil’s public health system dramatically worsened during the COVID-19 pandemic, leading to slow recovery when the Mpox outbreak occurred (Sott *et al.*, 2022). Consequently, despite passenger flow in this country not returning to pre-pandemic levels, Mpox effectively spread through community transmission, particularly among domestic travellers participating in mass gathering events (Luques *et al.*, 2023). Practical implementation of air travel interventions across airline networks may not be feasible in most areas after the detection of an emerging pathogen of pandemic potential due to the strong economic and social impact of travel restrictions (Meier *et al.*, 2022; Kinoshita *et al.*, 2023). Therefore, focused efforts to reduce air travel in high-risk airports would be more effective (Shi *et al.*, 2020), especially if combined with enhanced capacities and infrastructure for early disease detection, rigorous contact tracing, and effective isolation of first cases.

Caveats

An important challenge during the international outbreak was a likely delayed case identification and the lack of resources designated for early pathogen detection in some countries (Cui *et al.*, 2023). Delayed detection potentially resulted in an underestimation of the burden of Mpox. The rapid infection rate of Mpox requires large-scale screening and real-time monitoring for an accurate reconstruction of the numbers and spread of cases (Pliakos *et al.*, 2018; Cui *et al.*, 2023). Rapid, affordable and accessible diagnostic methods could significantly improve outbreak response and containment, reducing the potential public health impacts of Mpox in endemic and non-endemic countries (Bhatia *et al.*, 2021; Chang *et al.*, 2021). Furthermore, the primary lesson derived from the Mpox outbreak was the evident need for proactive global health collaboration (Kading *et al.*, 2018). Global collaboration should start by sharing, incorporating, analysing, and publishing economic and social data fundamental for decision-making during outbreak responses (Meier *et al.*, 2022; Kinoshita *et al.*, 2023). Global data sharing is needed considering that active infectious disease surveillance requires international cooperation among researchers, policymakers and public health officers (Bhatia *et al.*, 2021). Given the challenges of the Mpox outbreak, the global health community should push for active data sharing, enhanced public health infrastructure, global health diplomacy and the generation of novel tools in digital epidemiology for more effective and timely outbreak response.

Future directions

The rise of Mpox in ten African countries over the last five decades, totalling 1,347 confirmed cases and an additional ~28,800 suspected ones from the Democratic Republic of Congo, is likely tied to increased human-wildlife interaction with subsequent monkeypox virus spill-over to humans (Han *et al.*, 2020; Bunge *et al.*, 2022; Burki, 2022). Unlike smallpox, the monkeypox virus may exhibit both animal-to-human (spill-over), human-to-human (community) and human-to-animal (spill-back) transmissions (Henderson, 1999; Simpson *et al.*, 2020; Seang *et al.*, 2022). Current hypotheses suggest that spill-over leading to Mpox occurred in response to climate change, rainforest exploitation and highly mobile human populations (Simpson *et al.*, 2020). Nevertheless, the mechanisms behind wildlife-human spill-over of monkeypox virus and posterior community spread are poorly understood (Glidden *et al.*, 2021).

The limited knowledge of the patterns of Mpox transmission increases the risk of this virus becoming endemic where it currently circulates in wildlife. Our results suggest that international air travel modulates the likelihood of international disease spread. As such, international airports could play a crucial role by serving as places for monitoring the risk of emerging diseases. Future research should explore the effects of domestic flights on the spread of emerging diseases and the role of terrestrial and maritime human movement on the spread of infectious pathogens. Finally, the low transmissibility of the monkeypox virus, as compared with air-borne infections, allowed for a reliable recovery of case numbers in this international outbreak, which contributed to providing the epidemic signals that could help inform future models of emerging diseases.

Conclusion

Our project delved into the global spread of Mpox, emphasizing temporal incidence, international travel patterns and transmission risk hotspots. The summer of 2022 indicated a rapid global spread of Mpox, particularly affecting non-endemic countries, with increased air travel identified as a contributing factor. The recent Mpox international outbreak has clear geographical patterns, which were used to delineate hotspots of importation risk, aiming to

inform its prevention, control, and epidemiological surveillance. Air passenger flow is a predictor of hotspot areas of Mpox spread, which suggests a potential role of international airports as the first front to monitor the risk of disease emergence. This study underscores the need for proactive public health measures, emphasizing real-time epidemiological monitoring and global collaboration at the airport level.

Conflict of interest

The authors declare that they have no conflict of interest.

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Data availability statement

The code for this manuscript is available at <https://github.com/qiaohj/monkeypox>

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