

# Epidemiological Characteristics and Associated Factors of Imported Respiratory Infectious Diseases in China, 2014 - 2018

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## Research Article

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# Abstract

## Background

With the progress of globalization, the international mobility of population is increasing, which facilitates the cross-border transmission of respiratory infectious diseases (RIDs). The aim of this study is to analyze the epidemiological characteristics and relative factors of imported RIDs for using high-tech and wisdom methods to early find and stop the important RIDs spread to China.

## Methods

The imported RIDs cases from 2014 to 2018 enrolled in this study were screened by the inbound sentinel network of customs and national notifiable disease reporting system in China. The spatial, temporal and population distribution of imported respiratory infectious diseases were analyzed. Seasonal index was calculated to describe the seasonality, and Pearson correlation coefficients were assessed to examine associations between independent variables and imported cases. Data analysis and visualization were carried out with R (version 4.0.5).

## Results

Among 1,409,265,253 inbound travelers, 31,302 (2.22/100,000) imported RIDs cases from 143 countries within 5 continents were reported. The incidence of imported RIDs in 2018 (2.77/100,000) was nearly 5 times that of 2014 (0.56/100,000). Among foreigners, the incidences were higher in male (5.11/100,000), 0–14 year old group (14.06/100,000), and Oceania (10.98/100,000). Influenza accounted for the majority of imported RIDs(90.64%), with obvious seasonality. The spatial distribution of imported RIDs was different between Chinese citizens and foreigners. With the increase of inbound travel volume and the number of influenza cases in source countries, the number of imported RIDs cases increased.

## Conclusions

Our study showed RIDs imported into China from 143 countries around the world. Therefore, it has great potential risks of transmitting important RIDs to China. So, it is urgent to strengthen the surveillance at customs for inbound population, and establish the wisdom surveillance and warning systems for preventing and stop imported RIDs spreading to China.

## Full Text

With the progress of globalization, especially the rapid development of air travel, the population mobile frequently, which facilitates the geographic spread of infectious diseases between different areas, especially for the emerging infectious diseases (EIDs)[1,2]. In 2018, the number of international trips

reached 1.4 billion which are more than 10% Chinese citizens[3]. Meanwhile, the speed and volume of cross-border spread of infectious diseases increase with population mobility increasing[1]. The 1918 influenza pandemic spreading to the world mainly by sea and land transportation, at that time international spread speed slower compared with the cross-border spread of infectious diseases today which can traverse the globe within one day[4-6]. Therefore, the surveillance, early warning, prevention and control of the cross-border spread of infectious diseases should be paid more attention.

In the past century, EIDs especially severe acute respiratory infectious diseases (RIDs), constantly occur worldwide, which have an enormous impact on human health and social development[2]. The rapid development of human society, convenient transportation, and frequent international exchanges have accelerated the cross-border spread of RIDs, which poses a significant challenge to the prevention and control. The Middle East Respiratory Syndrome (MERS) was first reported in Saudi Arabia in 2012, and continued to spread to other countries as a result of travel of MERS cases. As of 26 April 2016, a total of 1,728 laboratory-confirmed MERS cases have been reported in 27 countries around the world[7]. In 2015, Guangdong Province reported the first imported MERS case from South Korea, and rapid response and control were implemented quickly, avoiding the potential risk of onward spread and outbreaks[8,9].

Over the past decades, several international studies reported the relation between population mobility and infectious diseases spread[10-12]. Two previous studies had investigated the travel-related infections based on long-term surveillance data analysis, and reported the epidemiology of imported infections[13-15]. However, for imported RIDs, the detailed epidemiological characteristics and relative factors have not been further explored and analyzed. So that, we investigate the epidemiological characteristics and relative factors of imported RIDs for using high-tech and wisdom methods to early find and stop the important RIDs spread to China.

## Methods

### Data collection and resources

1. Imported RIDs surveillance data from Jan 1, 2014, to Dec 31, 2018, were collected from the entry–exit sentinel network of customs (EESNC) consisting of 272 quarantine sentry points distributed in 31 provinces of mainland China[13].
2. Domestic infectious disease surveillance data were obtained from National Notifiable Disease Reporting System (NNDRS) of Chinese Center for Disease Control and Prevention[16].
3. Global influenza weekly surveillance data among selected countries were downloaded from the FluNet website[17].
4. The statistics on gender, age and continent of foreigners coming to China each year were obtained from the China Statistical Yearbook[18]. However, these information of Chinese inbound passengers were not obtained, so the specific incidence by gender, age and continent of imported RIDs in Chinese was not calculated.

The imported RIDs information in our study were from the EESNC and NNDRS, and which is routine surveillance, and all cases information was anonymized.

## **Case definition**

The imported RIDs cases information was extracted and integrated from both EESNC and NNDRS. According to the Rules for the Implementation of Frontier Health and Quarantine Law of the People's Republic of China, all inbound passengers underwent routine infectious diseases screening when they passed through customs, which were reported through EESNC[19]. Symptomatic passengers were searched by fever screening and medical inspections, and other possible cases were found through self-declaration, on-board staff reports, and other methods. Suspector/suspected cases were transferred to epidemiological investigation and laboratory testing. For post-travel cases, medical staff identified the imported illness based on the diagnostic criteria of different infectious diseases and the travel history, which were reported through NNDRS[14].

## **Data management and quality control**

A unified criteria and definition was made for using the data, and data management was performed by two staff accordingly. The imported RIDs information was obtained by linking the two EESNC and NNDRS databases, and the duplicate individual information was removed. Although imported RIDs came from 143 countries, only 24 countries' travel volume to China was obtained from the China Statistical Yearbook. Due to the influenza accounted for over 90% of imported RIDs, we focused on analyzing imported influenza situation to explore the relationship between the number of imported RIDs and the epidemiology in original regions. Scatter plots by continents were mapped using the imported influenza data and annual influenza surveillance report data from source countries.

## **Statistical analysis**

Incidence per 100,000 travels were estimated as the number of imported cases divided by the number of inbound travelers. Seasonal index, which was used to describe the seasonality of imported respiratory infectious cases, was calculated by dividing each month number of imported RIDs by the respective yearly average number. The seasonal index was greater than 1, indicating the amount of that month is higher than the monthly average. A radar chart of the monthly seasonal indices of imported RIDs was plotted to clearly show the seasonal distribution characteristics. Continuous variables were summarized as median and range, and categorical variables were summarized as numbers and percentages. Pearson correlation coefficients were assessed to examine associations between independent variables and imported infections. Data analysis and visualization were conducted with R (version 4.0.5).

## **Results**

### **General Characteristics**

About 1,409.27 million passengers entered the mainland of China by different ways from 2014 to 2018, among them 87.60% was Chinese and 12.40% foreigner. Over the 5 years, 31,302 imported RIDs cases were reported, with a reported incidence of 2.22/100,000. The incidence of imported RIDs in 2018 (2.77/100,000) was nearly 5 times that of 2014 (0.56/100,000). The incidence of RIDs in foreigners (4.01/100,000) was high compared with that of Chinese (1.97/100,000). 2,0477 (65.42%) cases were male, and the median age was 32 years (IQR: 18–47). 27 kinds of pathogens were detected in the imported cases including influenza (90.64%), rhinovirus (3.21%), adenovirus (1.20%), tuberculosis (0.85%), and others (4.10%). Among foreigners, the incidence of imported RIDs was high in male (5.11/100,000), 0–14 year old group (14.06/100,000), and Oceania (10.98/100,000) (Table 1, Fig. 1).

Table 1  
 Characteristics of 31302 imported respiratory infectious diseases cases in China, 2014–2018

Variables	Total Cases		Chinese		Foreigner	
	N	(%)	N	(%)	N	(%)
<b>Sex</b>						
Male	20477	(65.42)	14935	(61.47)	5542	(79.09)
Female	10825	(34.58)	9360	(38.53)	1465	(20.91)
<b>Age</b>						
0~	7159	(22.87)	6293	(25.90)	866	(12.36)
15~	3419	(10.93)	2680	(11.03)	739	(10.55)
25~	11873	(37.93)	8660	(35.65)	3213	(45.85)
45~	7294	(23.30)	5453	(22.44)	1841	(26.27)
65~	1557	(4.97)	1209	(4.98)	348	(4.97)
<b>Disease</b>						
Influenza	28373	(90.64)	22267	(91.65)	6106	(87.15)
Rhinovirus	1004	(3.21)	776	(3.19)	228	(3.25)
Others*	1925	(6.15)	1252	(5.16)	673	(9.60)
<b>Year</b>						
2014	1383	(4.42)	967	(3.98)	416	(5.94)
2015	3090	(9.87)	2099	(8.64)	991	(14.14)
2016	5036	(16.09)	3337	(13.74)	1699	(24.25)
2017	13093	(41.83)	10868	(44.73)	2225	(31.75)
2018	8700	(27.79)	7024	(28.91)	1676	(23.92)
<b>Source continent</b>						
Africa	241	(0.77)	115	(0.47)	126	(1.80)
Americas	1079	(3.45)	468	(1.93)	611	(8.72)

\*: Other respiratory diseases including: Pulmonary tuberculosis, pneumococcal infection, Mycoplasma pneumoniae infection, Legionnaires' disease, Streptococcus infection, Chlamydia pneumoniae infection, Pertussis, Pneumococcal infection, Acute nodular pharyngitis, Adenovirus infection, Haemophilus influenzae infection, Respiratory syncytial virus infection, Chickenpox, Human metapneumovirus infection, coronavirus infection, parainfluenza virus infection, measles, mumps, bocavirus infection, rubella, scarlet fever, infectious atypical pneumonia, parvovirus infection, Middle East Respiratory Syndrome.

Variables	Total Cases		Chinese		Foreigner	
	N	(%)	N	(%)	N	(%)
Asia	16634	(53.14)	11871	(48.86)	4763	(67.97)
Europe	1507	(4.81)	831	(3.42)	676	(9.65)
Oceania	980	(3.13)	517	(2.13)	463	(6.61)
NA	10861	(34.70)	10493	(43.19)	368	(5.25)
<b>Imported province</b>						
Non-border province	2984	(9.54)	2563	(10.55)	421	(6.01)
Border province	28273	(90.32)	21690	(89.28)	6583	(93.95)
NA	45	(0.14)	42	(0.17)	3	(0.04)
<b>Entrance way</b>						
Air	15251	(48.72)	12160	(50.05)	3091	(44.11)
Land	9861	(31.51)	8961	(36.88)	900	(12.84)
Water	6020	(19.23)	3029	(12.47)	2991	(42.69)
NA	170	(0.54)	145	(0.60)	25	(0.36)
<b>Purpose</b>						
Tourism	10356	(33.08)	9047	(37.24)	1309	(18.68)
Business	1834	(5.86)	1369	(5.63)	465	(6.64)
Labour	1351	(4.32)	560	(2.31)	791	(11.29)
Studying	293	(0.94)	156	(0.64)	137	(1.96)
Visiting friends or relatives	626	(2.00)	310	(1.28)	316	(4.51)
Sailor	1538	(4.91)	545	(2.24)	993	(14.17)
Others	1937	(6.19)	1051	(4.33)	886	(12.64)
NA	13367	(42.70)	11257	(46.33)	2110	(30.11)
<b>Finding way</b>						

\*: Other respiratory diseases including: Pulmonary tuberculosis, pneumococcal infection, Mycoplasma pneumoniae infection, Legionnaires' disease, Streptococcus infection, Chlamydia pneumoniae infection, Pertussis, Pneumococcal infection, Acute nodular pharyngitis, Adenovirus infection, Haemophilus influenzae infection, Respiratory syncytial virus infection, Chickenpox, Human metapneumovirus infection, coronavirus infection, parainfluenza virus infection, measles, mumps, bocavirus infection, rubella, scarlet fever, infectious atypical pneumonia, parvovirus infection, Middle East Respiratory Syndrome.

Variables	Total Cases		Chinese		Foreigner	
	N	(%)	N	(%)	N	(%)
Fever screening	23997	(76.66)	19832	(81.63)	4165	(59.44)
Medical inspection	5246	(16.76)	3286	(13.53)	1960	(27.97)
Selfdeclaration	561	(1.79)	419	(1.72)	142	(2.03)
Reported by onboard staff	1468	(4.69)	743	(3.06)	725	(10.35)
Others	30	(0.10)	15	(0.06)	15	(0.21)
<b>Main Symptoms</b>						
Cough	12951	(41.37)	10170	(41.86)	2781	(39.69)
Fever	7592	(24.25)	5226	(21.51)	2366	(33.77)
Headache	4556	(14.55)	3426	(14.10)	1130	(16.13)
Chills	3116	(9.95)	2210	(9.10)	906	(12.93)
Facial flushing	1836	(5.87)	1421	(5.85)	415	(5.92)
Muscle pain	1105	(3.53)	832	(3.42)	273	(3.90)
*: Other respiratory diseases including: Pulmonary tuberculosis, pneumococcal infection, Mycoplasma pneumoniae infection, Legionnaires' disease, Streptococcus infection, Chlamydia pneumoniae infection, Pertussis, Pneumococcal infection, Acute nodular pharyngitis, Adenovirus infection, Haemophilus influenzae infection, Respiratory syncytial virus infection, Chickenpox, Human metapneumovirus infection, coronavirus infection, parainfluenza virus infection, measles, mumps, bocavirus infection, rubella, scarlet fever, infectious atypical pneumonia, parvovirus infection, Middle East Respiratory Syndrome.						

## Spatial Distribution

The imported RIDs came from 143 countries in 5 continents, mainly from Asia (53.14%) which entered developed coastal border areas in China. The main imported RIDs cases among Chinese back from Thailand (14.10%), South Korea (7.86%), Japan (7.17%), and Singapore (4.20%). The foreign cases were mainly from South Korea (12.80%), Japan (10.40%), Vietnam (7.64%) and Philippines (5.90%). Guangdong, Jiangsu and Shanghai were the main areas where cases have been imported (Fig. 1, Fig. 2).

## Temporal distribution

During 2014 to 2017, RIDs cases were mainly imported in July, with seasonal indices ranging from 2.95 to 10.10. In 2018, imported respiratory infectious cases were mainly concentrated in January-March, which was different from the previous importation peak in 2014–2017 (Fig. 3) .

## Correlation analysis

The Pearson correlation coefficient between number of imported cases and inbound travel volume was 0.874 (95% confidence interval [CI]: 0.727 to 0.945). A linear relationship was observed from the scatter plot, and a best-fitting line was calculated using the least squares method. The simple linear regression showed that the estimated coefficient for the slope of the line was 0.458, which indicated that, for every 10 thousand of inbound foreigners, the imported foreign respiratory infectious cases increased, on average, by 0.458 case. The results of the regression showed that the model explained 75.37% of the variance (adjusted  $R^2 = 0.7537$ ) and that the model was significant,  $F(1,22) = 71.37$ ,  $p < 0.001$  (Fig. 4).

It can be observed that the number of imported influenza cases increased with the increase of influenza reports from the source countries, but countries from different continents showed various imported epidemiological characteristics. Compared with other continents, the number of influenza cases imported to China from Asia countries was high, but the number of influenza cases reported by Asian countries is relatively small. Clear linear relationships were observed from countries in Americas and Oceania (Fig. 5).

## Discussion

The RIDs have huge impacts on people's health globally, and with the progress of globalization, the social, economic, cultural, and population exchanges of countries around the world have become more frequent, which poses a challenge to the prevention and control of cross-border transmission of RIDs[20, 21]. This study described the epidemiological characteristics of imported RIDs in China during 2014–2018, and reported the correlation on the number of imported RIDs cases with inbound population volume, and the number of influenza cases in the source countries. Influenza accounted for the majority of imported RIDs with obvious seasonality. The spatial distribution of imported RIDs was different between Chinese and foreigners. Among inbound foreigners, the incidence of imported RIDs was comparable high in male, 0–14 years old group, and Oceania. With the increase of inbound travel volume and number of influenza cases in source countries, the number of imported RIDs cases increased. We hope the findings can help to improve the surveillance and early warning of imported RIDs, promote the construction of joint prevention and control of infectious diseases among countries with high burden of RIDs, and protecting the health and safety of people around the world.

There are differences in the incidence of travel-related infectious diseases in different genders and age groups[22, 23]. The differences are relative to the type of infectious disease, the population, and the destination of travel[23]. In this study, males and the 0–14 age group have a higher risk of importation of RIDs, which is consistent with previous studies[24–27]. Males, accounting for the major of travelers, may be more susceptible to RIDs infection due to some risk behaviors and habits during the travel. Children may be more susceptible to respiratory infections due to the lack of proper protection against infectious diseases and lower immunity compared with adults[24–27]. Most children have been infected with at least one influenza virus by the age of 6 years old[29, 30]. Children infected with influenza during travel will increase the risk of infection to their parents and other relatives, which can be reduced by vaccination before travel[30].

The seasonal fluctuation of imported RIDs are observed in our study, which may be affected by several factors, e.g. international travel on holidays, and seasonality of RIDs in original areas[31]. The number of population traveling abroad increase during holidays, such as Chinese traditional spring festival from January to February and summer vacation for Chinese students from July to August, which promote the cross-border spread of RIDs. In addition, the seasonality of the influenza imported to China was similar to influenza in Asian countries, which accounted for the majority of imported RIDs. The import peak in January-March 2018 was different from that in 2014–2017, which might be mainly affected by the 2018 spring influenza pandemic in northern hemisphere countries[32].

Travel volume is an important factor influencing the number of RIDs cases imported[33, 34]. Passengers who contracted infectious diseases before or during travel spread the infectious diseases to another country by cross-border travel. Generally, the risk of imported infectious diseases increases with the increase of passenger volume. A previous study on the cross-border transmission of H1N1 revealed that the risk of importing H1N1 into countries that received more than 1,400 passengers from the endemic countries has increased significantly[35]. Travel volumes, especially the air travel data, are often used as an important variable for estimating the risk of cases importation at certain conditions[36]. Therefore, when emerging and reemerging infectious diseases outbreak, the cross-border spread of infectious diseases can be constrained effectively by scientific travel restriction, which has been proved in the practice of prevention and control of RIDs in recent years[37–40].

The number of imported cases is associated with the number of reported cases in source countries, which may be affected by prevalence of the disease and population of that country[41]. In general, the higher prevalence of infectious diseases in the source country, the higher risk of importation into neighboring countries. However, to estimate the risk of imported cases, the source countries' RIDs prevalence needs to be analyzed comprehensively with some other factors, such as travel restriction, cultural customs, social environment, travel distance, travel transportation and purpose. This study found that the average number of influenza case reports in the source countries of Asia is smaller than that in the Americas and European countries, but the number of importation cases from Asia countries is the highest. The travel volume variable can explain part of that variation, but other significant variables influencing on the importation of infectious diseases should be further explored.

In order to assess and predict the risk of importation, previous studies have developed some statistical models based on the data related to importation, such as international flights information, the epidemiology of selected diseases and demographic information of the source countries[42, 43]. Given the prerequisites of these models, it is often assumed that all residents have the same chance of infection, and all infected persons have the same chance of boarding the flights abroad. However, this assumption is difficult to come real, which is also the main reason for the difference between the predicted results of the model and the true results. Therefore, some other factors that can affect imported infectious diseases should be further studied and included in the analysis of the predictive models.

By the way, we think that there are additional factors that affect the epidemiological characteristics of imported RIDs, which need to be further explored. Vaccination status is one of the factors that influence imported RIDs. Also, environmental changes, e.g. temperature, humidity, air pollution, and sun exposure may also influence the RIDs spread[44]. Travel duration is often considered as another important factor of imported RIDs. Besides, due to the data mainly from EESNC and NNIDRS, it is possible to lose some information in our study, and might lead to inexactly calculated incidence of imported RIDs.

## Conclusions

The trend of imported RIDs incidence increased from 2014 to 2018. The gender, age, continent, inbound passenger volume and number of reported cases in original countries associated relatively with the incidence of imported RIDs. With the annual increase of international travel, the potential risk of RIDs spread to China rises accordingly. Therefore, it is urgent to strengthen the surveillance at customs for inbound population, and establish the wisdom surveillance and warning systems for imported RIDs to early find and stop the RIDs spreading to China. Furthermore, if the infectious diseases were controlled and eradicated at the original countries, the health and safety of people around the world will be protected effectively. So, it is very important for international community to support the important RIDs prevention and control for countries with limited resources.

## Declarations

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### Author's contributions

J-LW and TC designed and implemented the study, managed and analyzed the data, interpreted the data and wrote, reviewed and edited the manuscript. G-XH and L-PW designed the study, analysis, interpreted the data, wrote and edited the manuscript. D-YW convinced the idea, interpreted the data, critical review and edited the manuscript. L-LD, Y-JH provided support in data management and drafted and revised the manuscript. All authors read and approved the final manuscript.

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### Availability of data and materials

According to the requirement of the EESNC and NNDRS, the original data can be used only by our researchers and cannot be provided to others.

### **Ethics approval and consent to participate**

The information in our study were from the EESNC and NNDRS, and which is routine surveillance, and all cases information was anonymized.

### **Consent for publication**

All the authors have written the informed consent and agreed with the publication of this paper.

### **Competing interests**

The authors declare that they have no conflict of interest.

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## **Abbreviations**

EIDs: emerging infectious diseases;

RIDs: Respiratory Infectious Diseases;

MERS: Middle East Respiratory Syndrome;

EESNC: Entry–Exit Sentinel Network of Customs;

NNDRS: National Notifiable Disease Reporting System

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## Figures

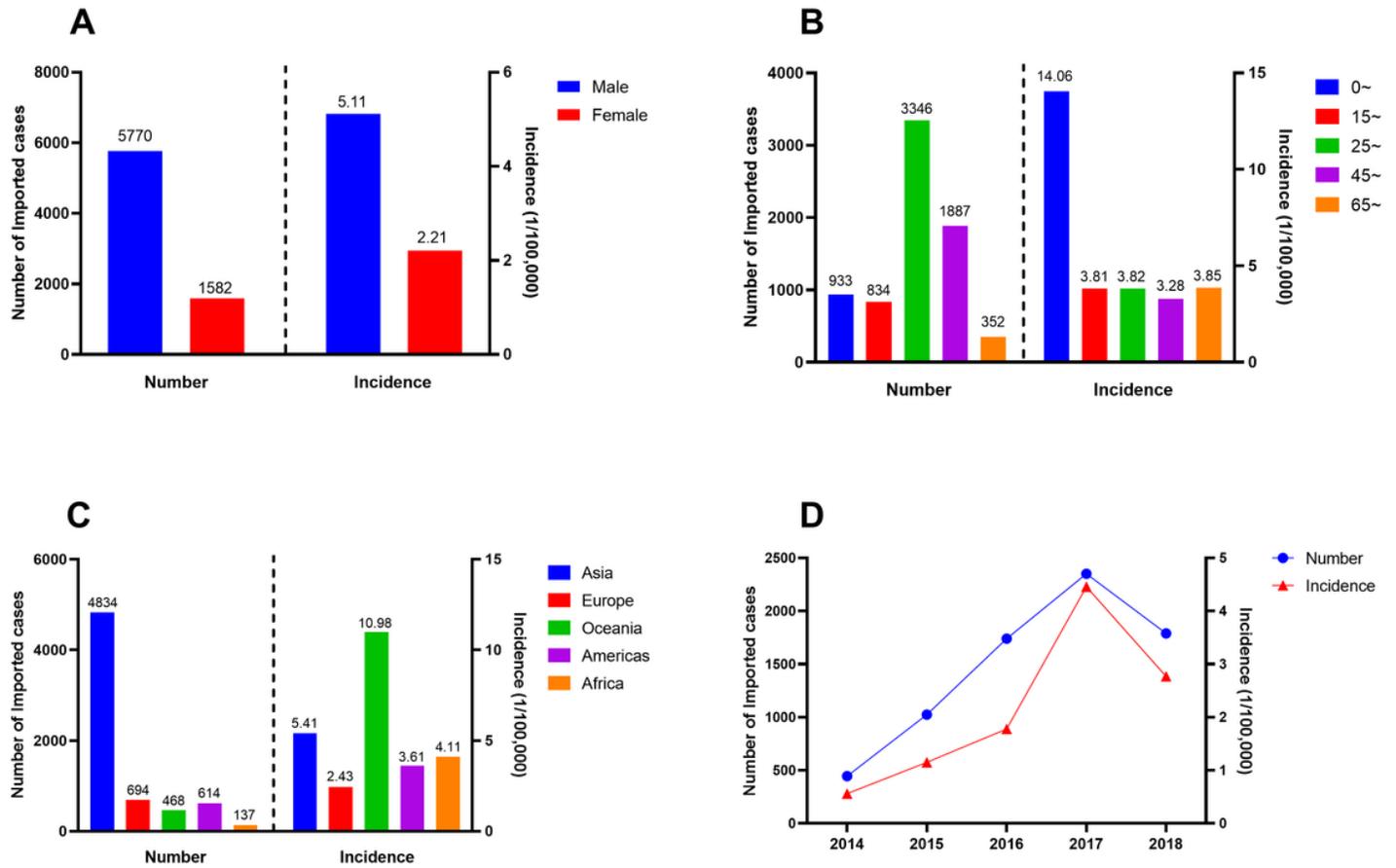
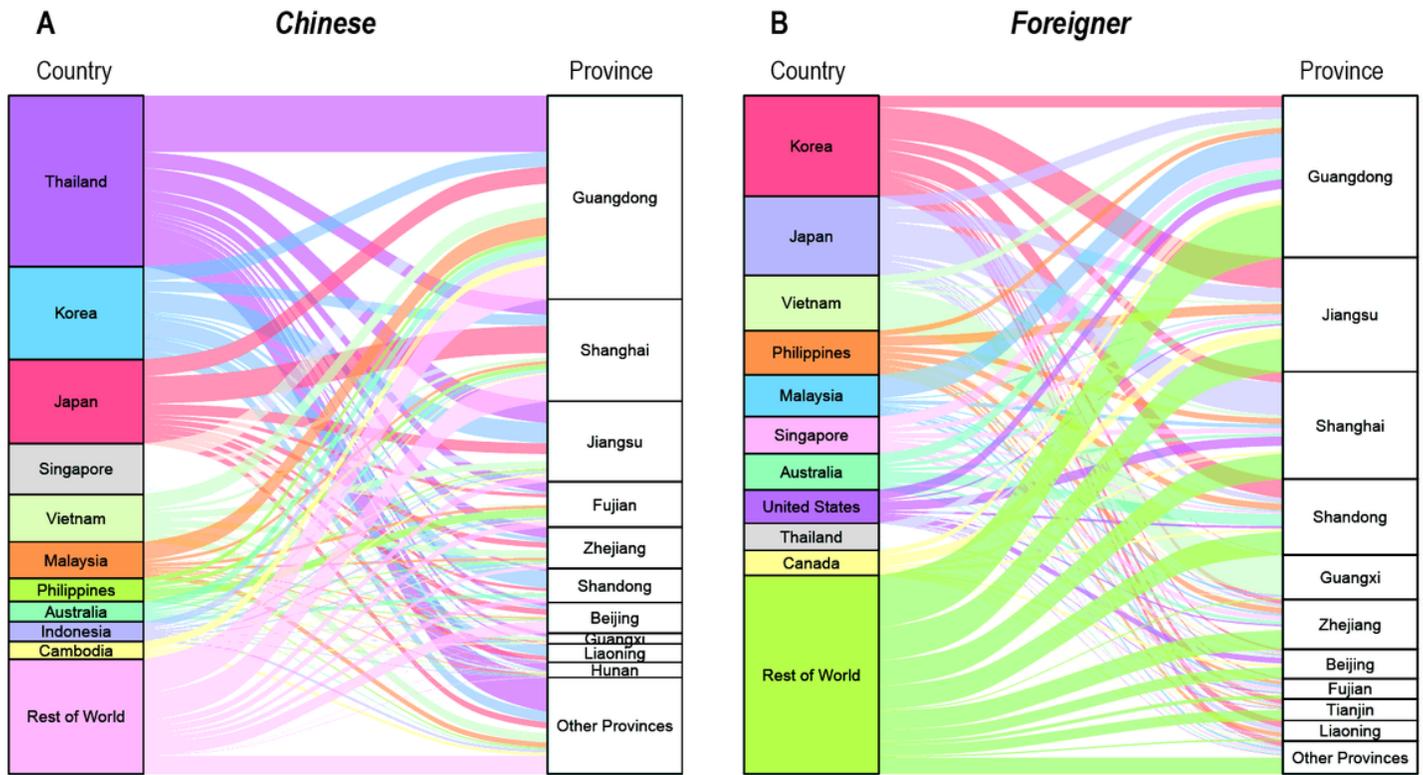


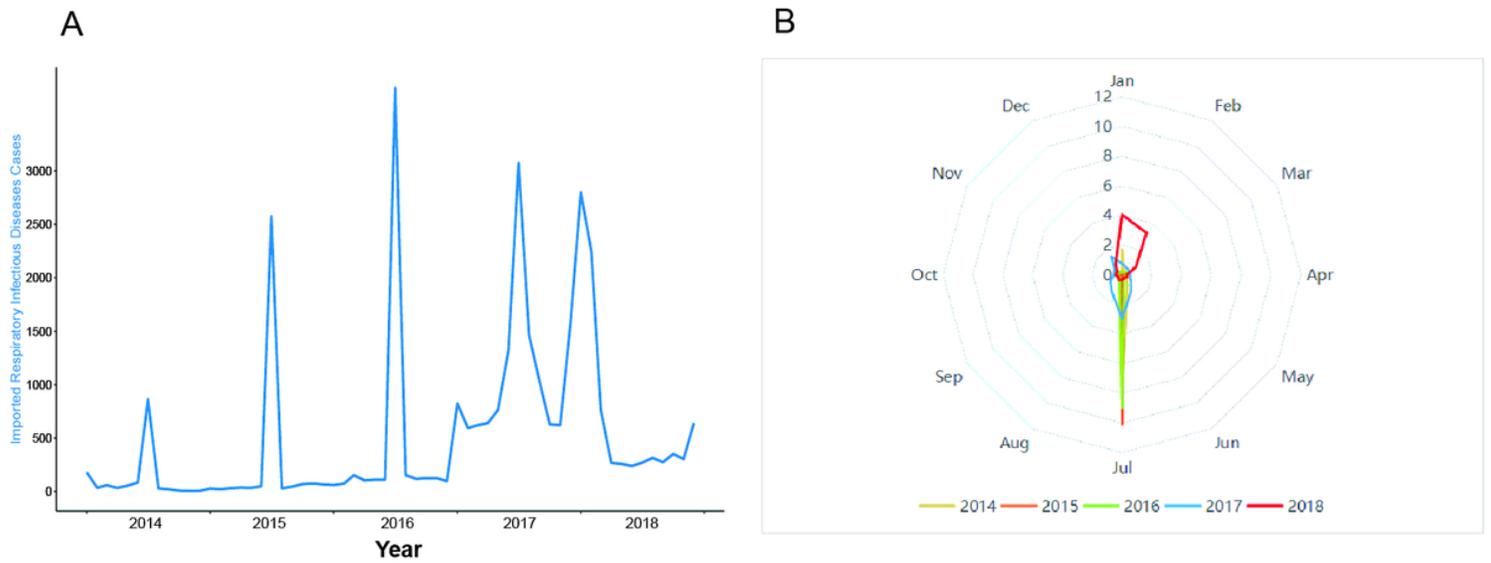
Figure 1

Caption not available with this version of the manuscript.



**Figure 2**

Caption not available with this version of the manuscript.



**Figure 3**

Caption not available with this version of the manuscript.

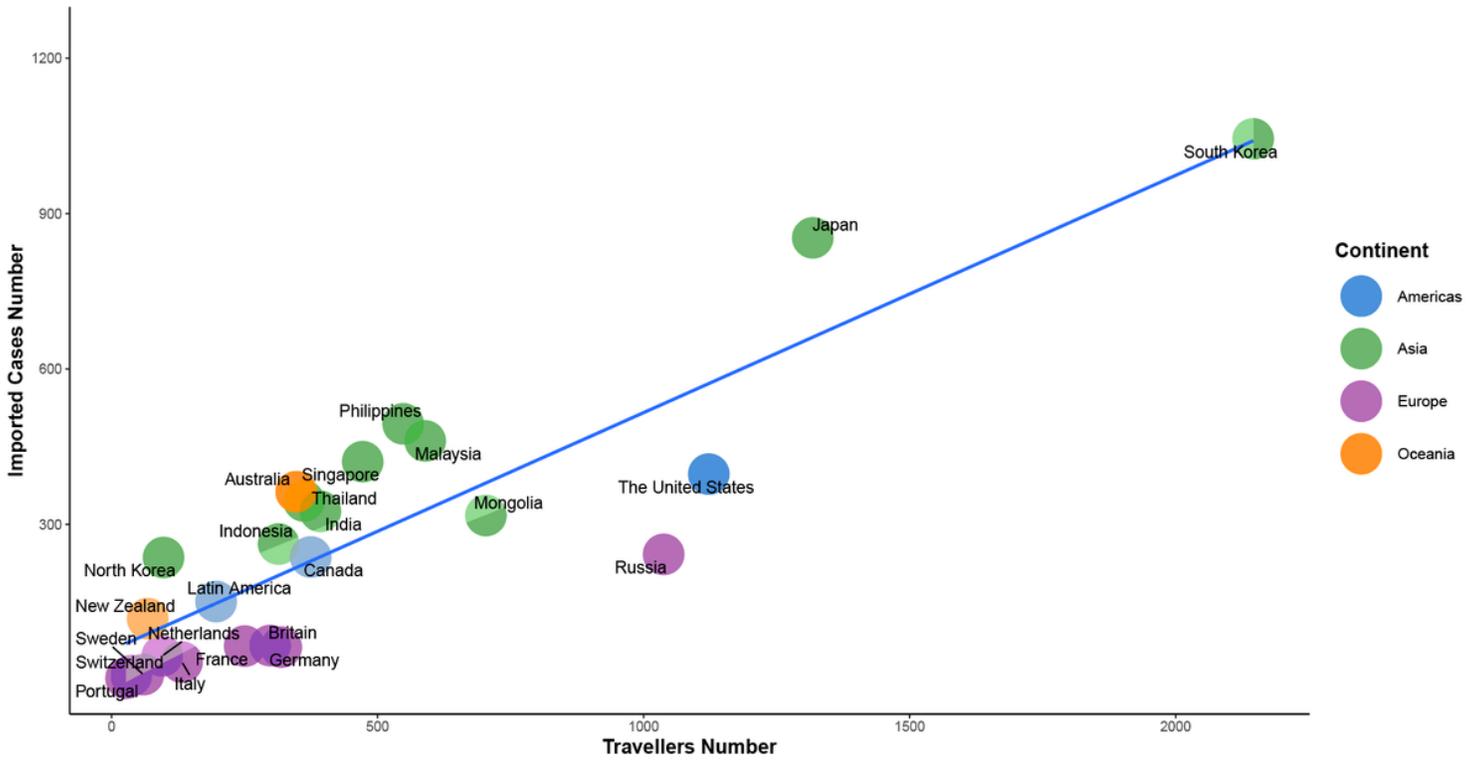


Figure 4

Caption not available with this version of the manuscript.

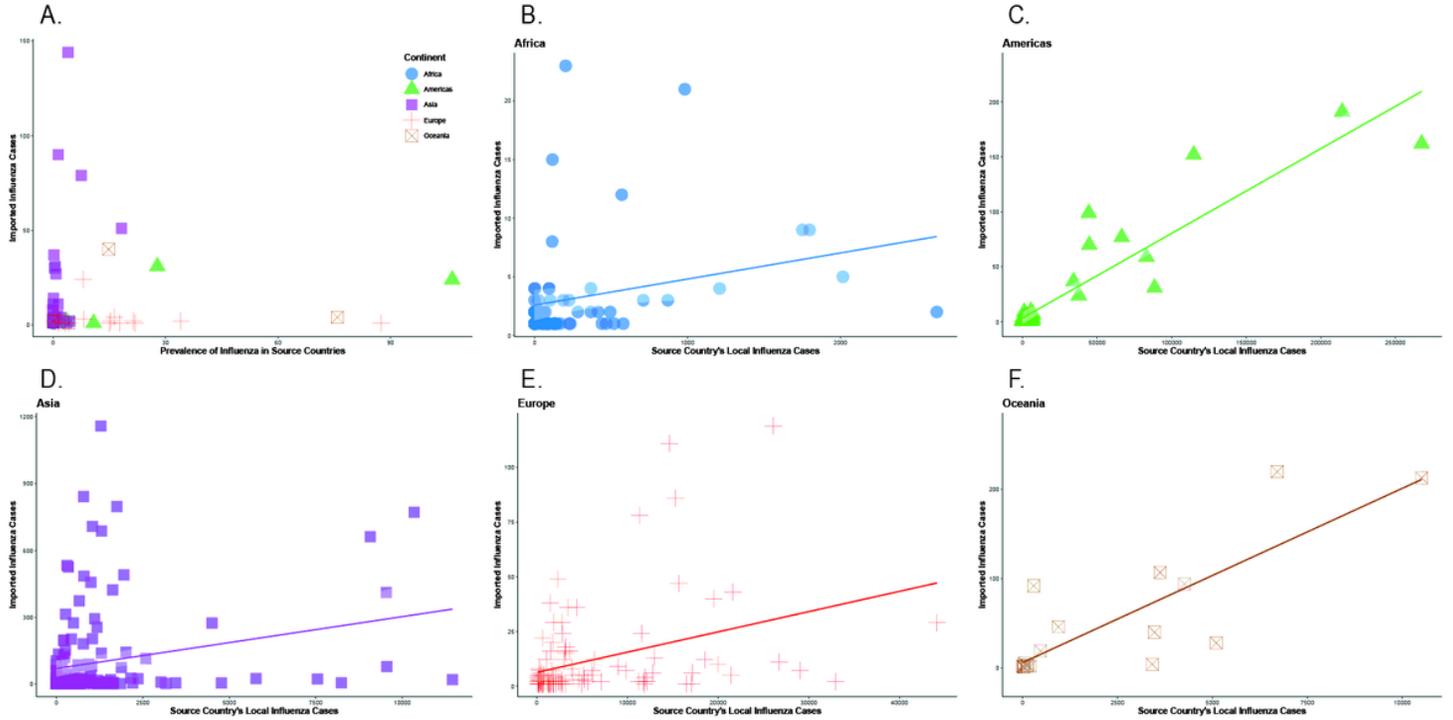


Figure 5

Caption not available with this version of the manuscript.