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Epidemiological features and trends of influenza incidence in mainland China: A population-based surveillance study from 2005 to 2015

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ABSTRACT

Objectives: To investigate epidemiological features and trends of influenza incidence with 1,173,640 cases in mainland China from 2005 to 2015.
Methods: Incidence and mortality data for influenza from 2005 to 2015 were provided by the data-center of China public health science and covered a population of about 1.3 billion people from 31 provinces and regions in mainland China. Joinpoint regression and exploratory spatial data analyses were used to examine the incidence trends from 2005 to 2015.
Results: The first upsurge in influenza cases occurred in 2009, and the highest incidence of influenza occurred in 2014 (15.9045 cases/100,000 people). The average incidence per year from 2009 to 2015 was threefold higher than that from 2005 to 2008 (10.5308 vs 3.4589 cases/100,000 people; incidence rate ratio = 3.0446). The joinpoint regression results showed that there was an increasing influenza incidence trend from 2005 to 2015 (annual change in percentage = 13.6%, 95%CI 2.2–26.3, p = 0.0236). The seasonal pattern analysis showed that influenza typically occurred in winter and spring during each monitoring year, peaking from November to March the next year.
Conclusions: This study will help governments to make valuable decisions in allocating scarce resources and providing strategies to limit the spread of influenza.

Introduction

Influenza remains an important infectious disease caused by the influenza virus worldwide. Global and country-specific influenza-associated epidemic and mortality estimates are useful to inform global public health priorities and provide information for influenza prevention. A global influenza study showed that among children age <5 years, 9,243–105,690 influenza-associated respiratory deaths occurred annually, which was important for national and international decision making on public health priorities. Coletti P. et al. studied the onset and peak times of regional epidemics on the basis of influenza-like illness time series in France from 1984 to 2014, and found that the spatial dynamics of influenza are associated with commuting (Coletti et al., 2018). The finding was different from the previously observed result as a general property of French influenza epidemics only to seasons exhibiting recurrent patterns, which can be applied to the incidence time series of different countries and different diseases. The children with age of >14 were examined in the 2016/2017 epidemic season, and the results demonstrated that children due to immature immunity are at particular risk for influenza (Cieslak et al., 2018). In the United States, Baltrusaitis et al. found that data from novel influenza surveillance systems can complement with traditional healthcare-based systems at multiple spatial resolutions (Baltrusaitis et al., 2018).

Some studies also were carried out to investigate the changes in influenza in mainland China. A study on the influenza infection in young children in eastern China showed that immunization for children with age of >6 months, and maternal and caregiver immunization for children under 6 months, can reduce influenza-associated hospitalizations in young children (Yu et al., 2019). The influenza surveillance in a rural region of mainland China detected

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influenza A (H1N1) pdm09 outbreak in the 2009/2010 influenza season (Zhang et al., 2014).

Although studies on influenza described country-specific influenza-associated epidemic and mortality estimates, these works are short-term ones or the results are outdated. Hence, this topic needs to be further investigated. Therefore, we carried out a large-scale epidemiological study and investigated the distribution characteristics of influenza from time, region and population in mainland China from 2005 to 2015. The trend and variation of influenza cases in mainland China were analyzed by using joinpoint regression. The influenza surveillance data at the provincial level was analyzed by exploratory spatial data analysis. This study aimed to explore the trend and variation, the spatial clustering of influenza, and the regularity of the clustering area that changes with time in mainland China, which would provide a theoretical basis for influenza prevention and control.

Methods

Data sources

Incidence and mortality data for influenza from 2005 to 2015 were provided by the data-center of China public health science, which is one part of the national scientific data sharing platform for population and health of the National science and technology infrastructure in China. On January 1, 2004, the notifiable infectious disease management system was established, which covered a population of about 1.3 billion people from 31 provinces and regions in mainland China. Influenza is one of the legally reportable infectious diseases in this management monitoring surveillance system.

Data extraction

Influenza data from Jan 1, 2005, to Dec 31, 2015, including the number of cases and deaths, the incidence and mortality of influenza, and patient data (sex, date of birth, occupation, and living address) were extracted in this study. To assess the epidemiological features and trends of influenza, we stratified the data by 31 provinces and areas, and the study period was divided into two stages, that is, 2005–2008 and 2009–2015, where an upsurge of influenza incidence in mainland China was observed in 2009.

Quality control

Influenza cases should meet the criteria issued by the Ministry of Health of the People's Republic of China. According to the 2004 Law of the People's Republic of China on the Prevention and Control of Infectious Disease, clinicians must complete a standardized infectious diseases card when they identify any probable, clinical, or laboratory-confirmed case of influenza. Once they received the disease card, the local epidemiologists did a field investigation using a standardized form, which includes basic demographic information, case classification, date of symptom onset, diagnosis, and death (if applicable) (Liu et al., 2018).

Statistical analysis

The definitions of incidence, mortality, case-fatality rate and incidence rate ratio (IRR) are described in Supplemental Table 1. Joinpoint regression software (version 4.3.1.0, the National Cancer Institute) was used to examine the incidence trends from 2005 to

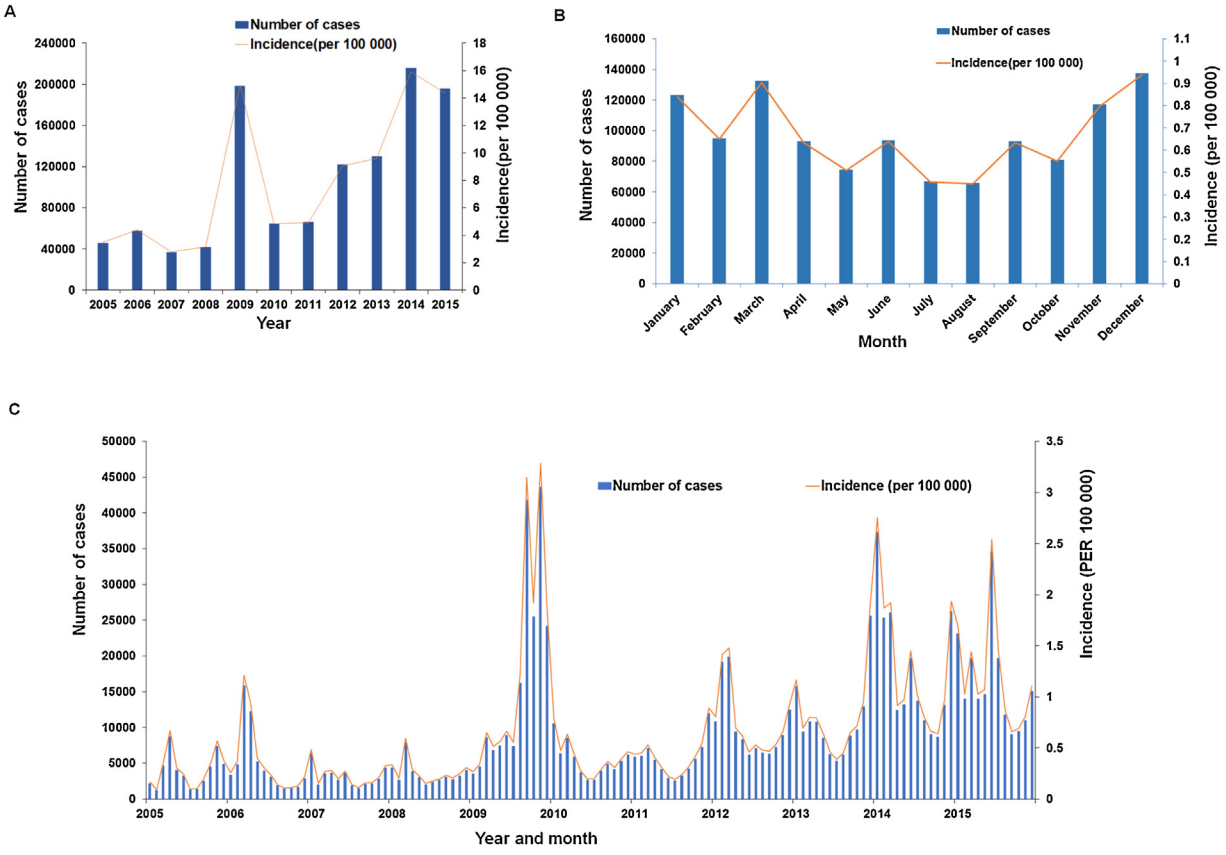

Figure 1. The incidence and number of influenza cases in mainland China.
(A) The incidence per 100,000 people and number of influenza cases by year from 2005 to 2015. (B) The incidence per 100,000 people and number of influenza cases by month from 2005 to 2015. (C) The incidence per 100,000 people and number of influenza cases by each month and year from 2005 to 2015.

Table 1
Annual incidence of influenza by 31 surveillance provinces or areas in China, 2005–2015.

Areas	Number of cases 2005–2015	Number of deaths 2005–2015	Case-fatality ratios (per 100 000 people)	Annualised mean incidence (per 100 000 people)			Incidence rate ratio (95% CI)	Annual percentage change (%) (95% CI)	p	Trend
				2005–2015	2005–2008	2009–2015				
Anhui	46097	7	15.1854	6.9095	1.6897	9.9253	5.88 (5.50 to 6.28)	29.2 (22.0 to 36.9)	<0.001	Increase
Beijing	24520	14	57.0962	12.2270	1.5362	17.1108	11.14 (9.72 to 12.62)	17.0 (−10.1 to 52.3)	0.2104	Stable
Chongqing	28679	3	10.4606	9.0700	5.3159	11.1324	2.09 (1.99 to 2.25)	−6.6 (−27.5 to 20.2)	0.5555	Stable
Fujian	38841	2	5.1492	9.6655	1.6464	14.0420	8.53 (7.80 to 9.25)	21.4 (5.8 to 39.3)	0.0109	Increase
Gansu	46009	1	2.1735	16.1258	11.0942	19.0099	1.71 (1.64 to 1.80)	5.4 (−4.5 to 16.4)	0.2610	Stable
Guangxi	36981	4	10.8164	7.1331	3.7929	9.0287	2.38 (2.23 to 2.49)	0.7 (−16.6 to 21.6)	0.0856	Stable
Guangdong	178109	11	6.1760	16.3169	5.4258	21.9192	4.04 (3.85 to 4.09)	24.4 (9.7 to 41.1)	0.0035	Increase
Guizhou	34101	2	5.8649	8.5303	7.5422	9.1206	1.21 (1.12 to 1.24)	−7.0 (−21.7 to 10.4)	0.3610	Stable
Hainan	3962	0	0.0000	4.1804	1.6879	5.5303	3.28 (2.68 to 3.90)	12.3 (−0.7 to 26.9)	0.0617	Stable
Hebei	165917	4	2.4108	21.2838	11.3910	26.6763	2.34 (2.28 to 2.40)	13.5 (9.1 to 18.1)	<0.001	Increase
Henan	87911	8	9.1001	8.4999	2.9842	11.6325	3.90 (3.74 to 4.07)	23.0 (15.7 to 30.8)	<0.001	Increase
Heilongjiang	4271	2	46.8274	1.0146	0.1473	1.5087	10.24 (7.79 to 13.48)	−2.1 (−23.8 to 25.6)	0.8494	Stable
Hubei	50166	3	5.9801	7.9501	2.8103	10.8567	3.86 (3.66 to 4.08)	4.5 (−15.1 to 28.7)	0.6404	Stable
Hunan	70308	7	9.9562	9.8556	2.8033	13.7351	4.90 (4.68 to 5.18)	2.8 (−16.0 to 25.7)	0.7679	Stable
Jilin	4900	1	20.4082	1.6278	0.3640	2.3430	6.44 (5.21 to 7.96)	21.1 (5.2 to 39.5)	0.0133	Increase
Jiangsu	30117	3	9.9612	3.5392	2.7334	3.9804	1.46 (1.37 to 1.54)	1.1 (−10.1 to 13.6)	0.8380	Stable
Jiangxi	46138	2	4.3348	9.4854	3.5142	12.7801	3.64 (3.43 to 3.84)	17.2 (7.9 to 27.3)	0.0019	Increase
Liaoning	8063	0	0.0000	1.6951	0.2035	2.5251	12.41 (9.97 to 15.43)	22.0 (5.3 to 41.2)	0.0136	Increase
Inner Mongolia	12622	3	23.7680	4.7022	2.8089	5.7499	2.05 (1.86 to 2.24)	0.7 (−12.5 to 15.8)	0.9164	Stable
Ningxia Hui Autonomous Region	11313	1	8.8394	16.4845	7.5473	21.2892	2.82 (2.57 to 3.18)	1.6 (−15.3 to 21.9)	0.8460	Stable
Qinghai	2697	1	37.0782	4.3799	2.3706	5.4817	2.31 (1.86 to 2.810)	15.5 (3.0 to 29.5)	0.0191	Increase
Shandong	30024	4	13.3227	2.8751	0.2640	4.3148	16.34 (14.39 to 18.63)	15.3 (−0.9 to 34.1)	0.0624	Stable
Shanxi	32568	1	3.0705	8.4925	0.9192	12.5873	13.69 (12.06 to 15.19)	30.9 (12.7 to 52.2)	0.0028	Increase
Shaanxi	27755	2	7.2059	6.7350	0.9324	10.0241	10.75 (9.63 to 12.00)	10.9 (−9.9 to 36.3)	0.2892	Stable
Shanghai	22950	1	4.3573	10.0180	1.0486	14.1530	13.50 (11.51 to 15.43)	26.2 (11.0 to 43.5)	0.0026	Increase
Sichuan	32304	4	12.3824	3.6102	3.2572	3.8135	1.17 (1.11 to 1.23)	−6.9 (−21.0 to 9.6)	0.3466	Stable
Tianjin	10075	5	49.6278	7.3383	8.1436	6.9743	0.86 (0.76 to 0.91)	0.8 (−10.8 to 13.8)	0.8898	Stable
Tibet	2616	0	0.0000	8.0891	18.7337	2.4790	0.13 (0.10 to 0.17)	−27.4 (−36.1 to −17.5)	0.0003	Decrease
Xinjiang Uygur Autonomous Region	12053	2	16.5934	5.1034	4.0222	5.6723	1.41 (1.29 to 1.54)	−0.2 (−13.9 to 15.8)	0.9818	Stable
Yunnan	27032	7	25.8952	5.3781	5.0779	5.5436	1.09 (1.03 to 1.15)	−8.7 (−22.0 to 7.0)	0.2279	Stable
Zhejiang	44541	2	4.4902	7.7462	4.1016	9.6620	2.36 (2.22 to 2.46)	10.1 (−2.8 to 24.6)	0.1143	Stable
Overall	1173640	107	9.1169	8.0025	3.4589	10.5308	3.04 (3.01 to 3.07)	13.6 (2.2 to 26.3)	0.0236	Increase

2015. The annual percentage changes (APCs) with their 95% confidence interval (CI) were obtained for each trend segment. A t-test was performed to assess whether an APC was significantly increased or decreased ($p < 0.05$). Global spatial autocorrelation analysis and local spatial autocorrelation were estimated by Geoda software (version 1.8). Spatial autocorrelation indicates whether clustering or dispersion is present in a map with values of Moran's I values. A positive Moran's I value indicates that the data are clustered, but a negative Moran's I value implies that the data are dispersed (Blazquez et al., 2018).

Local spatial autocorrelation at the provincial and autonomous level was reflected by the local indicators of spatial association (LISAs). LISA cluster graph presented four models, namely, high-high, low-low, high-low, and low-high models. The *z* test was used to assess the significant difference.

The spatial and temporal aggregation analysis of Chinese influenza from 2005 to 2015 was performed based on the discrete Poisson model at the provincial and autonomous region levels by using SaTScan 9.4 software (Kulldorff, 2006). The statistical value was log likelihood ratio (LLR), and the large LLR indicates a more likely gathering area. At the same time, the RR value of the region is calculated. Finally, the time-space scan results were visualized using ArcMap software (version 10.2).

The incidence rate ratio (IRR) with the 95% CI was estimated, and the difference was tested by Mann–Whitney U test in the period before and after the upsurge in 2009. The different proportions by sex and age were compared by χ^2 test.

Results

The trend of influenza incidence from 2005 to 2015

A total of 1,173,640 influenza cases and 107 death cases in mainland China were reported from Jan 1, 2005 to Dec 31, 2015. The average incidence was 8.0025 cases/100,000 individuals. The first upsurge in influenza cases occurred in 2009, with a high incidence of 14.9381/100,000 people (Figure 1A). After the upsurge in 2009, the annual incidence of influenza decreased to 4.8326/100,000 people in 2010 and 4.9316/100,000 people in 2011. Then, the annual influenza incidence continued to increase per year, and the highest influenza incidence occurred in 2014 (15.9045/100,000 people). The average incidence from 2009 to 2015 was threefold higher than that from 2005 to 2008 (10.5308/100,000 vs 3.4589/100,000 people, IRR = 3.04). The joinpoint regression showed an annual change in percentage of 13.6% (95% CI: 2.2–26.3, p = 0.0236), thereby indicating an increasing trend of influenza incidence from 2005 to 2015 (Table 1).

During the study period, the annual influenza incidences in 31 provinces and areas in mainland China exhibited three trends. (1) Eleven provinces and areas, including Jilin province, Liaoning province, Hebei province, Henan province, Fujian province, Jiangxi province, Shanghai, Shanxi province, Anhui province, Guangdong province and Qinghai province, showed significantly increasing incidence trends from 2005 to 2015. (2) The average influenza incidence decreased only in southwest China (including Tibet with the APC of −27.4% and 95% CI of −36.1 to −17.5). (3) The other provinces showed stable incidence trends from 2005 to 2015. The IRR values ranged from 0.13 (95% CI: 0.10–0.17) in Tibet to 16.34 (95% CI: 14.39–18.63) in Shandong province, thereby indicating differences in the annual influenza incidences not only in 31 provinces and regions of mainland China but also between the periods of 2005–2008 and 2009–2015 (Table 1).

The seasonal pattern of influenza

Influenza can occur throughout the year, but it possessed a semiannual seasonal peak. The seasonal pattern analysis showed that influenza typically occurred in winter and spring during each monitoring year. Nationally, the number of cases of influenza peaked from November to March the next year (Figure 1 B and C).

Geographical distribution characteristics of influenza

The results of the geographical distribution of influenza across mainland China in 2005–2015 demonstrated that the mean influenza case incidence ranged from 1.0146 cases/100,000 individuals to 21.2838 cases/100,000 people in the 31 provinces and areas. In the map, the areas with significantly high incidence in 2005–2015 were north (including Hebei province with 21.2838 cases/100,000 people), south (including Guangdong province with 16.3169 cases/100,000 people), and northwest China (including Gansu province with 16.1258 cases/100,000 people and Ningxia Hui Autonomous Region with 16.4845 cases/100,000 people). Meanwhile, the provinces or areas with significantly low incidence in 2005–2015 were northeast (including Heilongjiang province with 1.0146 cases/100 000 people, Jilin province with 1.6278 cases/100 000 people, and Liaoning province with 1.6951 cases/100 000 people) and east China (including Shandong province with 2.8751 cases/100,000 people) (Table 1, Figure 2A).

The geographical distribution of influenza incidence was similar before and after the upsurge in 2009, in which average the annual incidence was predominantly distributed in the north and southwest regions of mainland China. (Figure 2B and C).

Spatial autocorrelation analysis

The global spatial autocorrelation analysis results demonstrated a positive correlation among the years 2005, 2009, and 2014, with the Moran's I values of 0.2214 ($z = 2.8184$, $p = 0.013$), 0.2737 ($z = 2.7701$, $p = 0.008$), and 0.2654 ($z = 2.6684$, $p = 0.015$), respectively. These results indicated that the spatial clustering of influenza occurrence existed in 2005, 2009 and 2014. (Table 2).

Then, local spatial autocorrelation at the provincial and autonomous levels were further analyzed using a LISA cluster graph. The high-high aggregation of influenza incidence showed dynamic changes in mainland China during this period. The clustering areas were mainly distributed in northwest China from 2005 to 2006, changed to central China from 2009 to 2013, and then turned to southeast China from 2014 to 2015 (Figure 3).

Spatial and temporal aggregation analysis

Two spatial and temporal aggregation areas were revealed by using spatial and temporal aggregation analyses (Figure 4). The

Table 2
Global autocorrelation analysis of national influenza incidence, 2005–2015.

Year	Moran's I	Z	P	Correlation
2005	0.2214	2.8184	0.013	Positive correlation
2006	−0.0458	−0.1353	0.485	No correlation
2007	−0.0819	−0.4610	0.355	No correlation
2008	−0.0462	−0.1181	0.500	No correlation
2009	0.2737	2.7701	0.008	Positive correlation
2010	−0.0439	−0.1509	0.498	No correlation
2011	−0.0919	−0.7296	0.249	No correlation
2012	0.0849	1.0963	0.133	No correlation
2013	0.1431	1.6282	0.063	No correlation
2014	0.2654	2.6684	0.015	Positive correlation
2015	0.2164	2.3318	0.108	No correlation

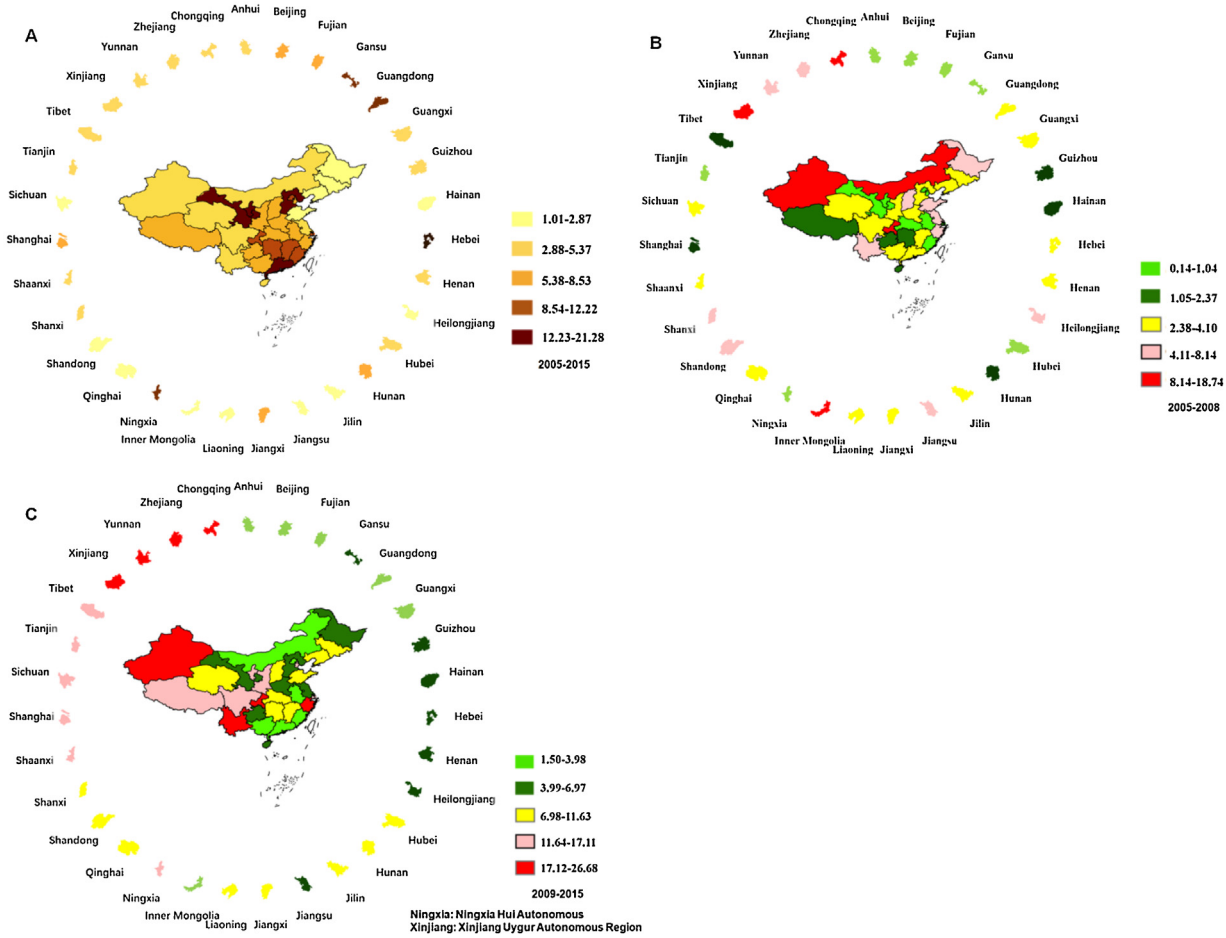

Figure 2. Spatiotemporal distribution of influenza incidence in mainland China (A) The center of the figure is the map of China. Each shape of the ring represents one different province, and the color of the shape in China map represents the average annual incidence of influenza. The different colors on the map represent different average annual incidence of influenza per 100,000 people in 31 Chinese provinces from 2005 to 2015. (B) Average annual incidence of influenza per 100,000 people in 31 Chinese provinces from 2005 to 2008. (C) Average annual incidence of influenza per 100,000 people in 31 Chinese provinces from 2009 to 2015.

first-level spatial and temporal aggregation areas distributed in east, central, and south China included Fujian, Zhejiang, Shanghai, Jiangxi, and Anhui; Hunan; and Guangdong, with the gathering time in 2014–2015, respectively. The actual number of cases reported in the region was 198,962, which was much higher than that of the number of expected cases, that is, 64,145 (RR = 3.53, LLR = 98945.92, $p < 0.001$). The secondary spatial and temporal aggregation areas covered seven provincial areas from 2012 to 2015. The areas were distributed in the north (including Shanxi, Hebei, and inner Mongolia), central (including Henan), and northwest China (including Ningxia Hui Autonomous, Gansu and Shaanxi). The actual number of cases reported in the region was 225,197, but the number of expected cases was 96,468 (RR = 2.65, LLR = 70203.30, $p < 0.001$).

Age, sex and occupation characteristics of influenza cases

We analyzed the pattern of reported influenza cases by age, sex, and occupation. Overall, males exhibited a higher influenza incidence than females in all age groups ($\chi^2 = 21995.290$, $p < 0.001$). The yearly incidence both in males and females peaked at two time points in 2009 and 2014 (Figure 5A). The yearly incidence among patients aged 0–14 was higher than that among the population aged 15-85 years old ($\chi^2 = 774355.327$, $p < 0.001$, Figure 5B).

Occupational data were available for 1,173,640 patients with influenza, including students (31.1788%), farmers (27.4037%), children (24.7385%), workers (2.0809%), service staff (1.0984%, including business services, childcare workers and nannies, and public place workers), medical staff (0.8039%), teachers (0.5687%), and others (12.1271%). (Figure 5C).

The influenza case fatality rate from 2005 to 2015

A total of 107 death cases, including farmers (31.7757%), children (17.7570%), students (6.5421%), workers (3.7383%), service staff (1.8692%), medical staff (0.9346%), and others (37.3831%), were reported in mainland China from 2005 to 2015, and no deaths of teachers were found (Figure 5C).

Discussion

Influenza is an acute respiratory illness with the highest burden experienced by young children, which causes substantial global morbidity and mortality annually (Lafond et al., 2016; Shi et al., 2017). Influenza-associated epidemic estimates with a large size population in a long period are useful to provide information for influenza prevention. Analyzing the epidemic of influenza in mainland China after the Spanish influenza pandemic in 1918 is important. In this study, we investigated the distribution characteristics and epidemic trend of 1,173,640 influenza cases in mainland China in the 11-year period. Our results demonstrated that China had an increasing influenza incidence trend from 2005 to 2015. After analyzing the data of a large population for a long

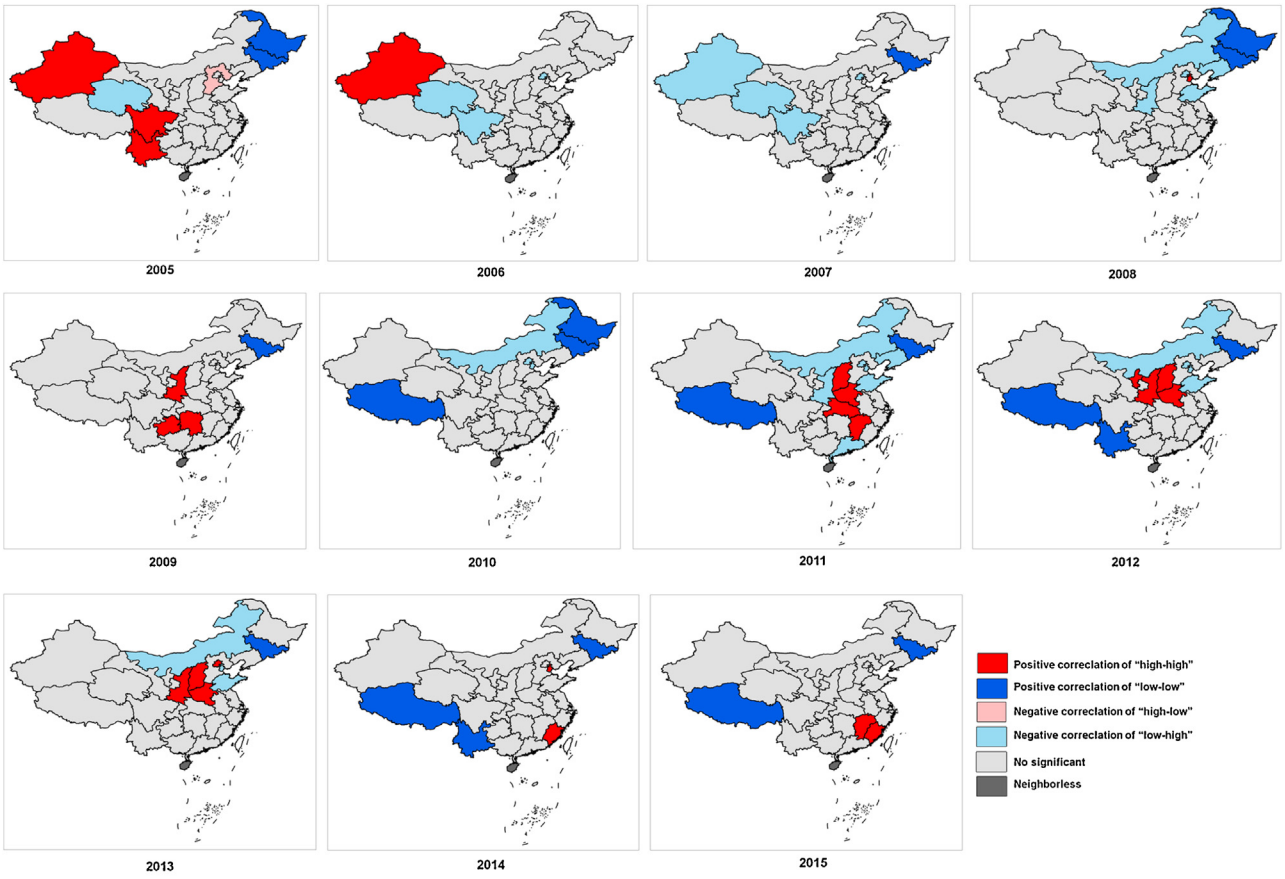

Figure 3. LISA cluster graph for influenza incidence in mainland China.
Spatial autocorrelation analysis of influenza incidence from 2005 to 2015, different colors in the map represent different spatial autocorrelation analysis results.

time, the changes found in influenza in mainland China will provide useful information for influenza prevention policy as well as scientific evidence.

Since the discovery of influenza type A virus in 1933 (Smith et al., 1995) and type B in 1940 (Francis, 1940), these viruses have become the major pathogens of acute respiratory illness. The type of major change in the influenza A viruses is known as antigenic shift, which infects humans when they have minimal or no immune protection to the new influenza A virus subtype (Paules and Subbarao, 2017). Influenza A virus may cause devastating outbreaks in domestic poultry or result in human influenza pandemics in a continuous manner (Bwj, 2008; Chou, 2014). In 2009, a new swine-origin influenza A, that is H1N1 virus, emerged in Mexico and the United States, which caused the first influenza pandemic of the 21 st century and spread worldwide to 30 countries (Smith et al., 2009), including China. We found the first upsurge of influenza in China from 2005 to 2015 occurred in 2009, with a high incidence similar to that in the other countries. Joinpoint regression further indicated that 2009 was a time point with a pandemic upsurge. Therefore, we divided the 11-year epidemic time into two stages, that is, 2005–2008 and 2009–2015. The average annual influenza incidence was threefold higher in the period from 2009 to 2015 than in 2005 to 2008 before the upsurge.

Four influenza pandemics, namely H1N1 Spanish influenza in 1918, H2N2 Asian influenza in 1957, H3N2 Hong Kong influenza in 1968, and H1N1 swine influenza in 2009, occurred in the past (Noh and Kim, 2013). Each influenza pandemic virus can arise directly from an avian host (1918) through both an avian virus and a circulating human strain (1957 and 1968) or from influenza virus in pigs (2009), which is transmitted among the human population and causes substantial morbidity and mortality (Cox and Subbarao, 1999; Kerkhove et al., 2012). The 1918–1919 pandemic led to mortality of >50 million people worldwide and was the most severe and devastating epidemic in modern history (Seiji, 2011). The 1957–1958 pandemic caused approximately 2 million deaths worldwide. The 1968-1969 pandemic killed approximately 1 million people. The number of A (H1N1) pdm09 respiratory deaths in the 2009–2010 pandemic was estimated to be between 123,000 and 203,000 (Lone et al., 2013). In our study, the results showed that there were 107 death cases were reported in mainland China from 2005 to 2015, including 93 death cases in the 2009–2010 pandemic.

The data from 11-year surveillance demonstrate that influenza incidence in mainland China increased and exhibited diversity and complexity. The results may be related to the following factors in China: a huge population and high residential density, unbalanced socio-economic development, influenza virus variability, relatively low immunity in special populations, geographic diversity, cold winter weather, low vaccination rate, poor access to the health care system, a large number of migrants, and a therapeutic drug shortage. For example, our results showed that Beijing had a high annual incidence between 2005 and 2015, which may be due to a large number of migrants (Goodwin and Sun, 2013). A significant increase in incidence of influenza was founded in the north areas of China, and the case fatality ratios declined from north and northwest China to south China, a trend that was similar to the geographical distributions of the effects of eco-environment development on life expectancy (Jiang et al., 2018). We also found that the clustering area of influenza was mainly distributed in the

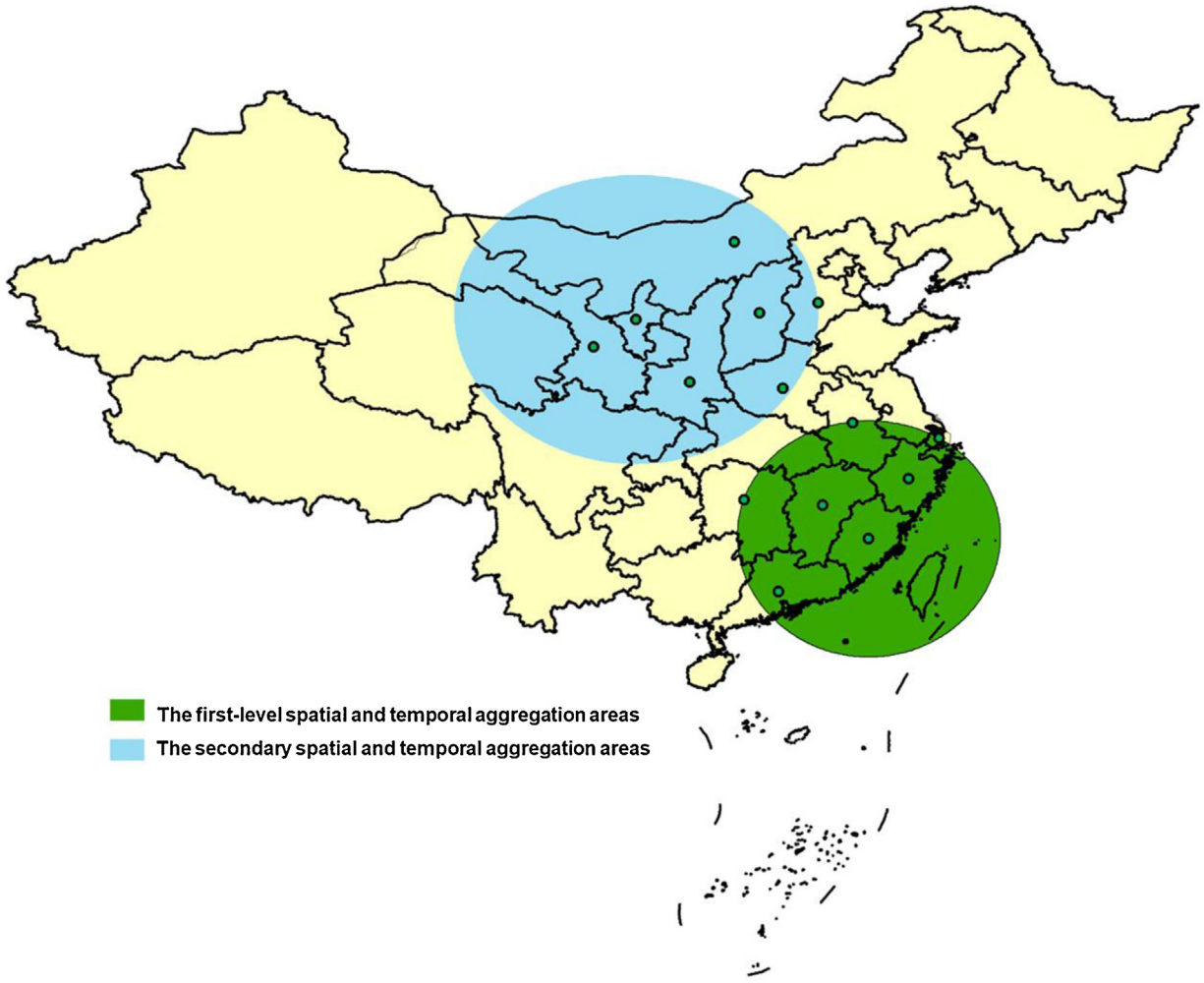

Figure 4. Spatial and temporal aggregation analysis of influenza cases in mainland China.
The two circles in the map represent different aggregation areas for influenza cases in mainland China from 2005 to 2015. The first-level spatial and temporal aggregation areas distributed in east, central, and south China, with the gathering time in 2014–2015. The secondary spatial and temporal aggregation areas covered seven provincial areas from 2012 to 2015, which are distributed in north, central, and northwest China.

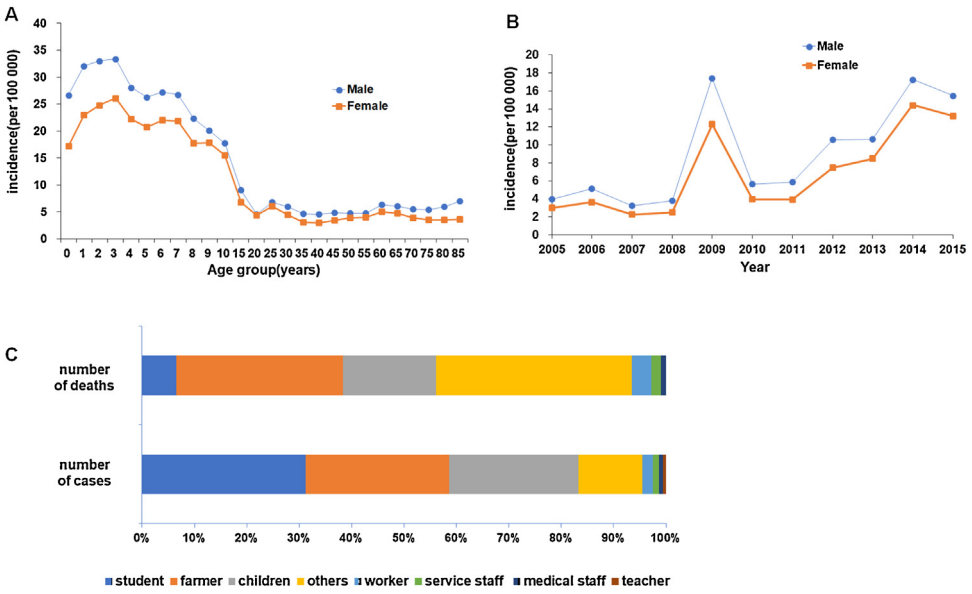

Figure 5. Population distribution of influenza cases in mainland China. (A) The average annual incidence of influenza per 100,000 people by sex and age from 2009 to 2015. (B) The yearly incidence of influenza per 100,000 people by sex from 2009 to 2015. (C) Overall number of influenza cases by occupation from 2009 to 2015.

northwest of China at first, changed to the central region in 2009–2013, and changed to southeast China in 2014–2015.

Children are much more infectious than adults and spread the virus until two weeks after infection (Keiko and Norio, 2006). Children and students, aged 0–14 years (especially 0–5 years), possessed the highest yearly incidence of influenza among patients, which was related to a slow build-up of immunity among young populations (Davila-Torres et al., 2015) and school life, mostly peaking in spring and winter (Wu et al., 2017). The results of occupation classification demonstrated that a high proportion from 2005 to 2015 occurred in farmers, who were less likely to know the main transmission route (either cough or talk face to face) (Lin et al., 2011).

Over the past centuries, global influenza pandemics periodically threatened the survival of global populations. Therefore, some measures should be taken to improve the quality of surveillance and the prevention of influenza virus infection as follows. (1) Strengthening surveillance. The most effective approach to tracking the changes in influenza viruses is facility-based surveillance in the outpatient or hospital (Gordon and Reingold, 2018). The clinical and demographic data of all the cases, including outcome and specimens from the samples of those who meet the case definition(s), need to be reported. (2) Reducing influenza transmission. Influenza can spread through repeated interspecies transmission from poultry to humans and from human to human. It is difficult to use routine long-term implementation to reduce the spread of respiratory viruses, but we can take some simple and low-cost interventions, such as hand-washing, the use of face masks, quarantine, and avoiding admissions, to reduce the transmission of influenza (Tom et al., 2008). (3) Improving the capacity of the public health system in early warnings of emerging infection diseases. Air travel can rapidly connect two cities on the planet, which can cause swift and broad dissemination of emerging infectious diseases and further poses threats to global health security (Findlater and Bogoch, 2018). (4) Promoting improved knowledge on influenza. Improved knowledge on influenza will reduce the influenza virus infection. We can reduce the infection risk of influenza by regular cleaning of high-touch surfaces (Zhang and Li, 2018). (5) Influenza vaccination administration. Annual influenza vaccination is considered the most effective tool for prevention of influenza virus infections in both humans and animals (Zoni et al., 2018). Seasonal influenza vaccination is recommended for subjects at high risk of contracting avian influenza H7N9 infection (Sivanandy et al., 2018). (6) The development of traditional Chinese herbal medicine (TCM) for anti-influenza therapy. TCM, such as the herb *Radix isatidis*, *honeysuckle, forsythia*, and compound formulas Lianhua-Qingwen and Maxin-Shigan Tang, can target the virus and the host simultaneously, thereby effectively inhibiting influenza-virus-induced inflammatory responses (Ding et al., 2017).

Limitations

Limitations do exist despite many important discoveries revealed in this study. Influenza is listed as a class C and H1N1 as a class B infectious disease in China. It is necessary to perform regular reporting of influenza to the Chinese Center for Disease Control and Prevention. Differentiating the clinical characteristics of influenza from those of other acute respiratory diseases is difficult, which may result in underestimating the true level of influenza to some extent.

Conclusions

In summary, our large-scale epidemiological study demonstrated that the annual influenza incidence in mainland China increased to certain extent, especially in 2014, and people became infected with influenza throughout the year, with peaks occurring in winter and spring during each monitoring year. The annual incidence was higher among males than females in all age groups, especially in children and students. This study will help governments to make valuable decisions in allocating scarce resources and providing strategies to limit the spread of influenza and other diseases.

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Role of the funding sources

The funder of this study did not take part in study design, data collection, or writing of this paper. The corresponding author accessed to all the data, and had final responsibility for its publication.

Ethical approval

The ethical approval was not required for this study.

Contributions

PYW designed the study, implemented the study protocol, and wrote the first manuscript. SSS and CJF directed statistical analyses of the data and designed the study. JC and YJL analyzed and interpreted the data. SYX also designed the study and revised the manuscript. All authors contributed to the discussion, reviewed and edited the manuscript, and approved the final manuscript.

Conflict of interest

The authors have declared that no competing interest exists.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2019.08.028.

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