The Spatial-temporal Analysis of the Tuberculosis in Chongqing, China, 2011-2018

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Abstract

Background : China is a country with a high burden of pulmonary tuberculosis (PTB), and the number of patient ranks second place in the world. Chongqing is the only municipality in the southwest of China directly under the Central Government, where the notification rate of PTB ranks top ten in China. This study analyzed the temporal and spatial distribution characteristics of PTB in Chongqing in order to take more powerful control measures.

Methods : A spatial-temporal analysis has been performed based on the data of PTB from 2011 to 2018, which was extracted from the National Surveillance System. Time series, spatial autonomic correlation and spatial-temporal scanning methods were used to identify the temporal trends and spatial patterns at county level.

Results : A total of 188,528 cases were included in this study. A downward trend was observed in the epidemic of PTB in Chongqing from 2011 to 2018. The peak of PTB notification was present in late winter and early spring season each year. By calculating the value of Global Moran's I and Local Getis's Gi*, we found that PTB was spatially clustered and some significant hot spots were detected in the southeast and northeast of Chongqing. One most likely cluster and three secondary clusters were identified by Kulldorff's scan spatial-temporal Statistic.

Conclusions : This study identified seasonal patterns and spatial-temporal clusters of PTB cases in Chongqing. The results provide us useful information for developing subsequent TB control measures.

Background

Tuberculosis (TB) is a chronic infectious disease caused by Mycobacterium tuberculosis (MTB). It is one of the top 10 causes of death[1]. In 2017, it was estimated that there were 10 million TB cases worldwide, with an incidence of 133 cases per 100,000 population. China contributed 9% of total cases in the world, ranking the second place after India[1]. In the 1990s, a tuberculosis control project, including directly observed treatment and short-course (DOTS) strategy, was implemented in 13 provinces of China[2]. Then the strategy had been expanded to the whole country by 2005[3]. After more than ten years efforts, China has reached the 2005 global tuberculosis control targets[4]. It is the only country with a high TB burden to make the achievements[5]. Although great achievements have been made, tuberculosis remains a major public health problem in China, especially in the relatively poor northern and western areas[6 – 7].

Chongqing is one of the four municipalities of China, located in the southwest of the country and the upper reaches of the Yangtze River. There are 39 districts and counties in Chongqing, of which 14 are national-level poor districts and counties[8]. In 2018, about 20,000 cases of PTB in Chongqing were reported to the National Infectious Disease Surveillance System, with the overall notification rate of 73.4 cases per 100,000 population, which was higher than the average of the whole country (59.3 cases per 100,000 population)[9]. A previous study of Chongqing pointed out that distribution of TB epidemic was uneven across the city[10], and a certain degree of seasonality was observed[11].

In recent years, spatial-temporal analysis has been widely used to describe the distribution characteristics and transmission patterns of tuberculosis in China[7,12–13]and other countries[14 – 18]. These studies demonstrated that TB has a highly complex dynamics and is spatially heterogeneous at the provincial, national, and international levels during certain periods of time[19]. As an area with high burden of PTB, few studies have been conducted in Chongqing to explore the spatial epidemiology at the county level. We conducted Geographical Information System (GIS) based spatial-temporal scan statistic to describe the geographic distribution pattern of pulmonary TB in Chongqing by using the surveillance data from 2011 to 2018.

Methods

Study setting

Chongqing is a mountainous city located in southwest China, with 27 districts and 12 counties. It covers an area of 82,400 square kilometers[20], of which 76% are mountains, 22% hills, 2% valleys and plains. The main stream of the Yangtze River runs through the city from west to east, with a flow of 665 kilometers. In 2018, there are 31 million permanent residents in Chongqing, of whom about 20 million were urban population, accounting for 65.5 percent of total residents. The gross domestic product (GDP) per capita was RMB 65,933 Yuan in 2018[21], which was 1.9 times higher than in 2011.

Data Collection And Management

The Chongqing TB surveillance data from January 2011 to December 2018 was extracted from the National Surveillance System for Notifiable Infectious Disease, which is established and operated by Chinese Center for Disease Control and Prevention (CDC). This surveillance system covers all counties of 32 provinces, autonomous regions and municipalities of China, and collects data of all TB cases reported by hospitals. We obtained these TB data from Chongqing Institute of Tuberculosis Control and Prevention, and were permitted to use.

Each case contains demographic information (e.g. age, gender, occupation, registered residence, current address, etc.) as well as medical information (e.g. date of onset, date of diagnosis, results of pathogen examination, etc.). Each case is identified by the unique identity card (ID) number to avoid repeated reports. In order to protect patients' privacy, asterisk was used to block the name and ID number of all cases when the data were extracted.

The effect of TB control was measured by the variation trend of pathogenic positive PTB notification rate and total TB notification rate. Pathogenic positive PTB includes smear positive (SS+) and smear negative but culture positive (S-C+). With the improvement of national infectious disease surveillance system, the rifampicin resistant tuberculosis (RR-TB) information has been added to the system since July 1, 2017 [22], so pathogenic positive PTB in 2017 and 2018 also included RR-TB cases. The overall PTB includes pathogenic positive TB, pathogenic negative TB and cases whose pathogenic examination not done.

A total of 188,528 cases of PTB were collected, and each case was geocoded by current address. Then them were matched to the county-level polygon maps of the geographic information (Geographic database from China CDC) at a 1:1,000,000 scale as the layer's attribute table by the same identified number. The longitude and latitude coordinates of the central point for each district and county were located though the Google geocoding service and the toolbox of Geoprocessing in ArcGIS v.10.6 (ESRI Inc, Redlands, CA, USA). The coordinates information were used for spatial-temporal analysis. This geocoding process has been widely applied in previous studies[7,19,23–24], and we used a similar approach.

The annual population data for each administrative district from 2011 to 2018 were obtained through the Chongqing Statistical Yearbook and the Basic Information System for Disease Prevention and Control.

Statistics Analysis

Time Series and Descriptive Analysis

The epidemiological characteristics of TB cases were analyzed at provincial level. TB cases reported from 2011 to 2018 were aggregated by age, gender, occupation and date of onset for TB notification rate analysis. Comparison between different demographic groups was carried out by Chi-square test or Fisher's exact test. The trend of the notification rate was tested using Cochran-Armitage test. All statistical analyses were performed using SPSS 22.0 (SPSS Inc., Chicago, IL, USA). The difference was considered significant if P-value was less than 0.05.

The temporal patterns were examined by looking at the onset month of all the TB cases. The time series included 96 months from January 2011 to December 2018 and was examined using EXCEL2016.

Spatial Autocorrelation Analysis

Spatial autocorrelation analysis is a spatial statistical method, which can reveal the regional structure of spatial variables. It can verify that an element attribute value is associated with an attribute value at an adjacent space point. It mainly includes global autocorrelation analysis and local autocorrelation analysis.

Global Moran's I values[25] calculated by ArcGIS 10.6 software (ESRI Inc., Redlands, CA, USA) was used to identify spatial autocorrelation and detect the spatial distribution pattern of TB in Chongqing, China. The range of Moran I value is between − 1 and 1. A positive Moran I value indicated that a positive correlation, and the larger the value, the more obvious the tendency to cluster is. While the Moran I value is less than zero, which indicates that the spatial distribution has negative correlation, it shows a discrete distribution. There is no spatial clustering when the value is zero, meaning that the data are randomly distributed[26]. Both Z-score and P-value are used to evaluate the significance of Moran's I[27].

Local Getis's Gi* statistic[28] is used to identify the local level of spatial autocorrelation and determine locations of clusters or hotspots. Value of Gi* in this study was calculated using ArcGIS 10.6 software (ESRI Inc., Redlands, CA, USA).

Spatial-temporal Scan Statistic

Kulldorff's spatial-temporal scan statistical analysis was used to identify the spatial, temporal and clusters of PTB across different counties geographically and different time period. SaTScanTM version 9.1.1 software (Kulldorff, Boston, MA, USA) was used based on the Poisson probability model [29]. The SaTScan™ software was developed by Martin Kulldorff together with Information Management Services Inc and could download on Web site (http://www.satscan.org/).

This method is based on creating a moving cylinder that contains geographical information with height corresponding to time[30]. The maximum radius of the bottom of the cylinder, which is the maximum area of scanning, was set in this analysis at 50 percent of the total population and the height corresponding to the time of the study area. Log likelihood ratio (LLR) of different circle centers and different radii was calculated to compare the notification rate of TB within the circular window and outside the circular window[31]. The larger the LLR value was, the more it likely to be the cluster. Monte Carlo simulation test was used to evaluate whether the difference is statistically significant. For each possible spatial-temporal cluster, when the P-value is less than 0.05, a higher LLR value indicates that the area covered by this dynamic scanning window is more likely to be a cluster region. The window with the largest LLR value is most likely cluster, and the secondary clusters are the other windows with statistically significant LLR value. Finally, ArcMap 10.6 software was used to visualize the scanning results.

Ethical Review

The TB data of Chongqing that support this study were collected though routine disease surveillance and they were available from the national surveillance system. These data were used with the approval of Ethics Committee of the Institute of Tuberculosis Control and Prevention, Chongqing, China. Not only the personal identifiable information of each case in our data analysis has been deleted, but also the availability of the data set is still restricted. However, with the permission of the National Center for Tuberculosis Control and Prevention (NCTB), the data is accessible from the corresponding author.

Results

Descriptive analysis of PTB cases

A total of 188,528 PTB cases were notified in Chongqing from 2011 to 2018. Among them, 32 percent (60,254 cases) were pathogenic positive. The annual average notification rate of all PTB and pathogenic positive PTB were 79 cases per 100,000 population and 25 cases per 100,000 population respectively. The total PTB notification rates decreased significantly from 88.8 cases per 100,000 population in 2011 to 73.4 cases per 100,000 population in 2018 (χ^2 trend = 732.178, P = 3.0096×10^{-161}) (Fig. 1). The annual average notification rate of male was significantly higher than that of female (χ^2 = 30273.043, P = 0.000). The notification rate of PTB was the highest among people over 60 years of age. More than half of the PTB patients were farmers, and the average proportion of farmer PTB patients was 54.3% between 2011 and 2018. The demographic characteristics of the PTB cases in Chongqing from 2011 to 2018 were shown in Table 1.

Table 1
Notification rates of PTB with different demographic characteristics in Chongqing from 2011 to 2018, (1/100,000)

Characteristics	2011	2012	2013	2014	2015	2016	2017	2018
Gender								
male	124.8	120.2	116.6	106.5	103.7	102.8	107.5	102.6
female	51.9	50.2	49.2	46.0	45.6	43.1	46.0	43.6
Age (year)								
0–14	7.2	5.8	5.5	4.4	4.6	4.0	4.3	4.5
15–29	119.9	108.0	105.2	96.8	90.7	88.6	96.2	87.3
30–44	80.5	85.5	80.2	70.5	65.4	60.7	59.8	54.1
45–59	109.4	96.9	88.1	82.0	82.0	82.5	84.2	83.7
≥60	124.2	119.7	125.5	117.4	121.3	115.6	132.8	127.9
Occupation								
Student	38.1	34.2	34.5	33.2	29.6	31.0	36.1	37.5
Teacher	66.4	50.2	54.2	47.8	39.3	42.7	40.2	45.1
Medical staff	90.0	116.5	85.8	110.4	85.7	97.7	93.1	85.2
Farmer	115.6	113.6	113.3	107.2	110.0	109.3	109.4	100.7
Others	79.2	76.7	72.9	64.1	60.7	58.1	66.8	66.2

Temporal Patterns Of Ptb Cases

An obviously temporal trend variation of PTB cases in Chongqing from 2011 to 2018 was showed in Fig. 2. The number of PTB peaked in the January and March each year, then showed a volatile downward trend after March, and declined to nadir in December.

Spatial Patterns Of Ptb Cases

The spatial variations of PTB notification rates between 2011 and 2018 at the county level in Chongqing were showed in Fig. 3. The highest notification rates were found in Pengshui county, Xiushan county, Chengkou county, Qianjiang district and Wulong district.

The global spatial autocorrelation analysis showed that the Moran's I values of PTB notification rates in each year from 2011 to 2018 were significantly different (Table 2), indicating that the notification rates of PTB in Chongqing were non-randomly distribution, and demonstrating that distribution of PTB was spatially autocorrelated in Chongqing over the period of eight years. The Moran's I value of annual PTB notification rate was positive, and the P value was less than 0.001. It pointed out that there was a global spatial positive autocorrelation in the notification rates of PTB in each year.

Table 2
Global spatial autocorrelation analyses for annul PTB notification rate in Chongqing, China from 2011 to 2018

Year	Moran's I	Z-score	P value
2011	0.489155	5.182869	< 0.001
2012	0.485119	5.139183	< 0.001
2013	0.594580	6.165923	< 0.001
2014	0.519618	5.541707	< 0.001
2015	0.577399	6.083351	< 0.001
2016	0.551651	5.847773	< 0.001
2017	0.413744	4.493974	< 0.001
2018	0.365869	4.079302	< 0.001

Spatial-temporal Clustering Analysis By Satscan

The notification rates of pulmonary tuberculosis during the period of 2011 to 2018 were analyzed by spatial-temporal scanning. The results showed that the notification rate of PTB was spatio-temporal clustering. One most likely cluster and three secondary clusters were been showed in Table 3 and Fig. 5.

The most likely cluster was mainly distributed in the southeast of Chongqing, which covered three counties and two districts: Xiushan county, Youyang county, Pengshui county, Qianjiang district, and Wulong district. The clustering time was from January 2015 to December 2018. A total of 14,787 cases were identified during this period. Our analysis results showed that the risk of PTB in these districts and counties was 2.08 times higher than that outside the hot spots. In addition, three statistically significant secondary clusters were also detected with high incidence of TB. These three secondary clusters distributed in different areas of Chongqing. They were 7 districts and counties in the central area, 5 districts and counties in the southwest area and 1 district in the western area. And the clustering time were from January 2011 to December 2013, January 2011 to December 2012, and January 2012 to December 2013, respectively.

Table 3
Significant high-rate PTB Clusters in Chongqing, China detected by SaTScan from 2011 to 2018

Cluster Type	Number of Clustering areas	Cluster districts and counties	Time frame	Observed cases	Expected cases	Relative risk	Log likelihood ratio	P-value
Most likely cluster	5	Xiushan, Youyang, Qianjiang, Pengshui, Wulong	2015–2018	14787	7427.77	2.08	2974.12	< 0.01
Secondary cluster 1	7	Dianjiang, Changshou, Liangping, Fengdu, Fuling, Zhongxian, Shizhu	2011–2013	13885	11925.43	1.18	163.79	< 0.01
Secondary cluster 2	5	Qijiang, Wansheng, Banan, Nanchuan, Nan'an	2011–2012	5693	5212.56	1.1	22.12	< 0.01
Secondary cluster 3	1	Dazu	2012–2013	1337	1153.37	1.16	13.99	< 0.01

Discussion

In our study, we first made a descriptive analysis of the epidemic situation of pulmonary tuberculosis in Chongqing, and then used the time series method to analyze the temporal patterns of PTB cases. Finally, we used the spatial analysis method to study the spatial patterns and Spatial-temporal clustering at the county level. The notification rate of PTB in Chongqing decreased steadily during the eight-year study period. The PTB notification rate had declined to 73.4.8 cases per 100,000 population in 2018 from the peak of 88.8 cases per 100,000 population in 2011. This downward trend was consistent with the studies of other provinces and cities, and the whole country[7,12,23,32]. It shows that the prevalence of pulmonary tuberculosis in Chongqing has been controlled to a certain extent. This is the results that in our city great importance has been attached to tuberculosis control and prevention by the Municipal Government Department and Health Administrative Department in recent years, and the intensity of all kinds of investment has been increased. First, the government released some good policies, such as the free treatment of tuberculosis patients was included in the projects in the public interest[33] to assess the completion of the work of the municipal government. Then Tuberculosis Control and Prevention Plan (2011–2015) was issued in February 2012, and effective measures were implemented. Second, tuberculosis control funding increased continuously. In 2018, the investment for tuberculosis control and prevention in Chongqing was RMB 1.03 per capita, which was approximately twice as much as the average of the country, ranking the sixth place among the provinces of China. Third, at the request of the Chongqing Municipal Tuberculosis Control Institute, a batch of molecular biology testing equipment and reagents for tuberculosis diagnosis and treatment were purchased and distributed by Chongqing Municipal Health Commission to designated TB hospitals in all districts and counties. The diagnostic time of pulmonary tuberculosis was shortened and the chance of transmission to others before treatment decreased. After the implementation of these effective measures, the tuberculosis epidemic situation in Chongqing has been improved significantly. But Chongqing is still one of the cities with high TB burden in China[34].

Through time series analysis, we found that the tuberculosis epidemic in Chongqing showed an obvious cyclical trend. TB onset was mainly concentrated in the first half of each year, especially between January and March. Chongqing has a subtropical monsoon humid climate, in which the coldest month has an average temperature of 4 to 8 degrees Celsius, and the average annual relative humidity is 70 to 80 percent. It is one of the regions with the least annual sunshine in China. To the best of our knowledge, lack of exposures to ultra violet from sunlight and the poor ventilation in indoor settings may increase the opportunity of infecting TB bacteria[35]. In late winter and early spring in Chongqing, residents close doors and windows, and reduce outdoor activities because of the cold, foggy and humid weather. This may be the reason for the largest number of PTB cases reported during this time period. The reason for the decrease in patients reported in February is that the Chinese Spring Festival usually falls in February, in which people are busy celebrating the lunar New Year, and ignoring to seek medical care. This seasonal pattern is the same as that of a national study[12,13], and studies in Guangxi Province[36], Xinjiang Uygur Autonomous Region[37], Zhaotong City of Yunnan Province [24,32] and other western regions, but a little different from that of studies in Zhejiang province[23], Hong Kong[38] and Taiwan[39], which are located in the eastern coastal area.

The field of spatial epidemiology has evolved rapidly in the past two decades[40,41], and it has been widely used in the study of tuberculosis[42–43]. The global spatial autocorrelation results in this study indicated that PTB in Chongqing shows an obvious spatial clustering distribution. And advanced local spatial autocorrelation analysis showed that the hot spots of PTB had a slight dynamic variation over time. The tuberculosis hotspots detected in this study are basically consistent with the notification rates of PTB in Chongqing. Pengshui County, Qianjiang District, Wulong District, Xiushan County and Youyang County located in the southeast of Chongqing, were the areas with high notification rates of PTB in the past 8 years. Their annual average notification rates from 2011 to 2018 ranks first, second, fourth, fifth and seventh, respectively. Chengkou and Wuxi counties located in the northeast of Chongqing were also hotspots, except in 2017. The reasons for these hot spots distribution may be as follows: these districts and counties were poor areas, with backward economy and shortage of health resources. The GDP of these districts and counties was the lowest in Chongqing. Most of the residents living there are ethnic minorities. Lack of funds for TB control and professionals has restricted the performance of local work. In addition, people living in these poor counties often have no fixed income and cannot afford the diagnosis and treatment of tuberculosis, leading to the continued spread of the disease. All these are the reasons of PTB clustering in adjacent areas[44]. Some changes, however, merit attention. For example, Kaizhou District has been removed from the hot spots since 2015. This indicates that the notification rate of PTB in Kaizhou District was significantly lower than that of neighboring hotspots. The reason for the decline of tuberculosis epidemic in Kaizhou District was that the local government department has paid more and more attention to TB control. First of all, the government leaders conducted investigations on local tuberculosis control work, and issued standardized construction, performance appraisal and other documents, which specified that every PTB patient must be found and cured. The TB screening of key groups, such as close contacts, Human immunodeficiency virus (HIV) infected people, the elderly, students and floating population, and extensive health education should be strengthened. The government will reward units and individuals that have made significant contributions to local TB control. Second, since 2014, a total of RMB 8 million has been invested in local TB control, including over 5 million special funds, 500,000 for salvaging poor patients, 450,000 for TB screening for the second grade students of senior high schools and more than 2 million for public health and personnel. Third, enhance talent introduction and training. For instance, more than 10 new professionals for TB control were recruited in 2015. Fourth, new equipment was purchased for rapid diagnosis, and an electronic medical record system was developed for patient medication management. Finally, work closely with education department and mass media to strengthen the promotion of tuberculosis control. After the implementation of all these powerful measures, TB control in Kaizhou District has achieved remarkable improvement. According to the result of global and local spatial analysis, we have initially identified that the southeastern region and the northeast region are the important regions for tuberculosis control and prevention in Chongqing.

Taking the role of time factors in the geographical distribution of diseases into consideration, we used spatial-temporal scanning analysis to supplement the simple spatial analysis. In the previous analysis of the spatial-temporal clustering characteristics of the national tuberculosis epidemic, we found that Chongqing was in the most likely cluster[7] from 2005 to 2011, and in another study, Chongqing was in the secondary cluster from 2005 to 2015[13]. These results show that although the burden of pulmonary tuberculosis in Chongqing is declining generally, it is still high. A spatial-temporal scan analysis of the PTB cases from 2011 to 2018 showed that the most likely cluster was concentrated in the southeast of Chongqing, covering two districts and three counties. The clustering time period was from 2015 to 2018. Obviously, it indicated that these counties and districts bore excess burden of PTB and had higher risk of disease transmission, so they are the most important areas for tuberculosis control in the next few years. More effective, stronger and targeted measures should be implemented to control TB transmission in these areas. During the study period, no spatial-temporal cluster was detected in the northeast region, which also showed that the tuberculosis prevention and control work in these regions has achieved satisfactory results since the implementation of the Eleventh Five-year Plan. However, according to the local autocorrelation analysis, there were still scattered hotspots in the northeastern region, hence the tuberculosis control in these areas should not be relaxed.

This is the first time to analyze the Spatial-temporal clustering characteristics at county level in Chongqing. The results of the analysis helped us to identify the high risk areas of PTB in the city. This is very important for our next step in tuberculosis control.

But there are some limitations in the study. First, our analysis was based on data obtained from the National Surveillance System, so it is possible that a small number of cases had not been captured, which might cause underestimation of PTB epidemic in Chongqing. Second, the geographical information of townships (the smallest unit of administrative division) of each district and county was not available, so we did not analyze the temporal and spatial characteristics of PTB at township level. Finally, potential risk factors, such as poverty[45], low education level[46], poor living conditions[47,48], inadequate access to medical services[49] and environmental pollution[50], which previously has been reported to be associated with a high incidence of tuberculosis, were not evaluated in this study. We will consider narrowing the geographical scale to the township level and incorporating relevant risk factors for further analysis.

Conclusions

This study identified seasonal patterns and spatial-temporal clusters of PTB cases at the county level in Chongqing from 2011 to 2018. The most likely clustering time was spring, and the most likely clustering areas were southeast and northeast regions of Chongqing. The spatial-temporal clustering results by SaTScan showed that southeastern Chongqing had higher TB burden and risks of TB transmission after 2015. Priorities should be focused to these areas in subsequent TB control measures.

Abbreviations

PTB: Pulmonary tuberculosis; TB: Tuberculosis; MTB: Mycobacterium tuberculosis; DOTS: Directly observed treatment and short-course; GIS: Geographical Information System; GDP: Gross Domestic Product; CDC: Center for Disease Control and Prevention; ID: identity card; SS+: Smear positive; S-C+: Smear negative but culture positive; RR-TB: rifampicin resistant tuberculosis; LLR: Log likelihood ratio; NCTB: National Center for Tuberculosis Control and Prevention; HIV: Human immunodeficiency virus

Declarations

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Authors' Contributions

Ya Yu, Wei Chen and Daiyu Hu conceived and designed the study. Ya Yu and Bo Wu collected data, performed the statistical analyses and wrote the main manuscript. Chengguo Wu and Qingya Wang helped to draft the manuscript. All authors read and approved the final version of the manuscript.

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Availability of data and materials

The data of TB patients that support the findings of this study cannot be shared publicly because the data contain sensitive patient information, and sharing local sensitive contagious disease data publicly without license is illegal. The Ethics Committee of the Institute of Tuberculosis Control and Prevention in Chongqing has imposed this restriction. Data are available from corresponding author for researchers who meet the criteria for access to confidential data.

Ethics Approval and consent to participate

This study was approved by the Ethics Committee of the Institute of Tuberculosis Prevention and Control, Chongqing, China. In this study, there was no access to individual information. A secondary analysis based on reported data has been conducted and informed consent from individuals was not required. All methods were performed in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

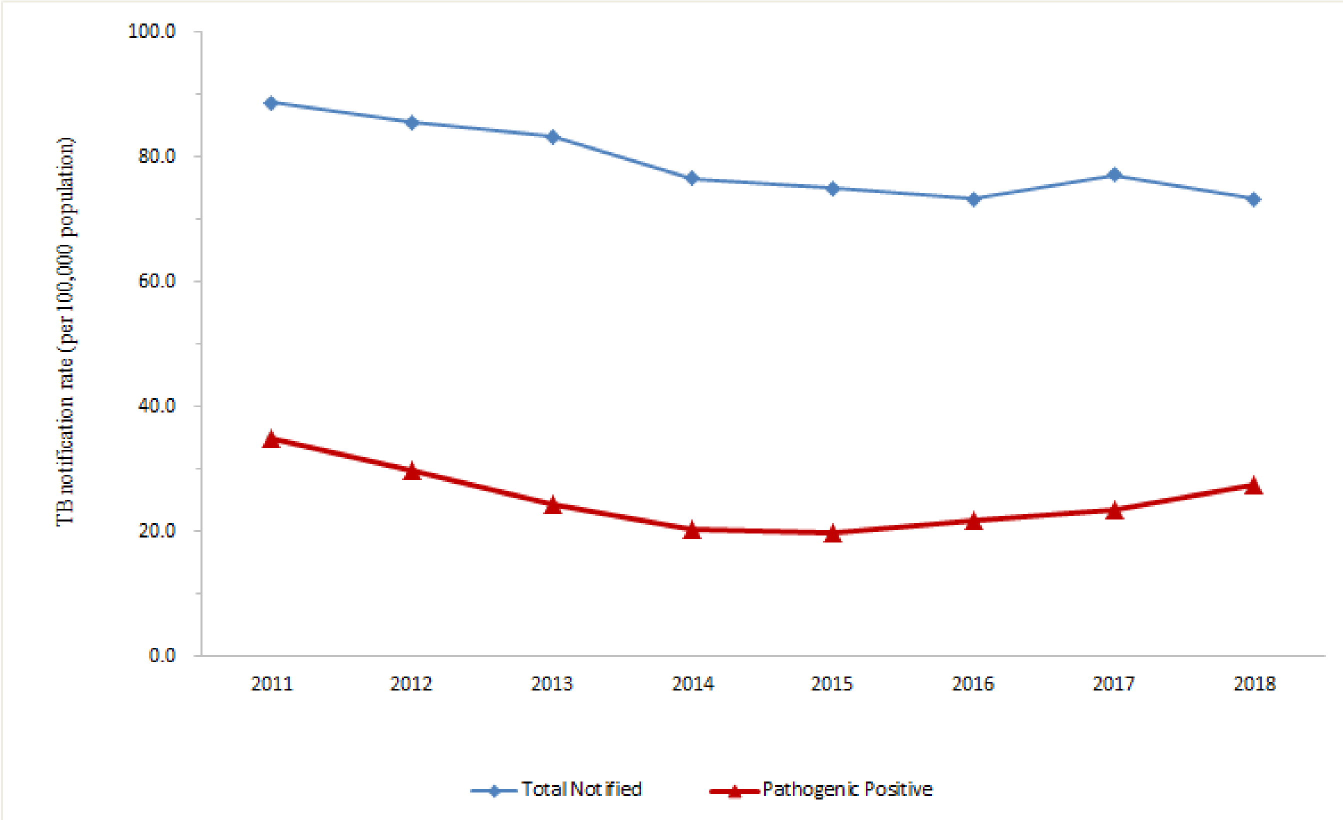

Figure 1

The variation trend of TB notifcation rate from 2011-2018.

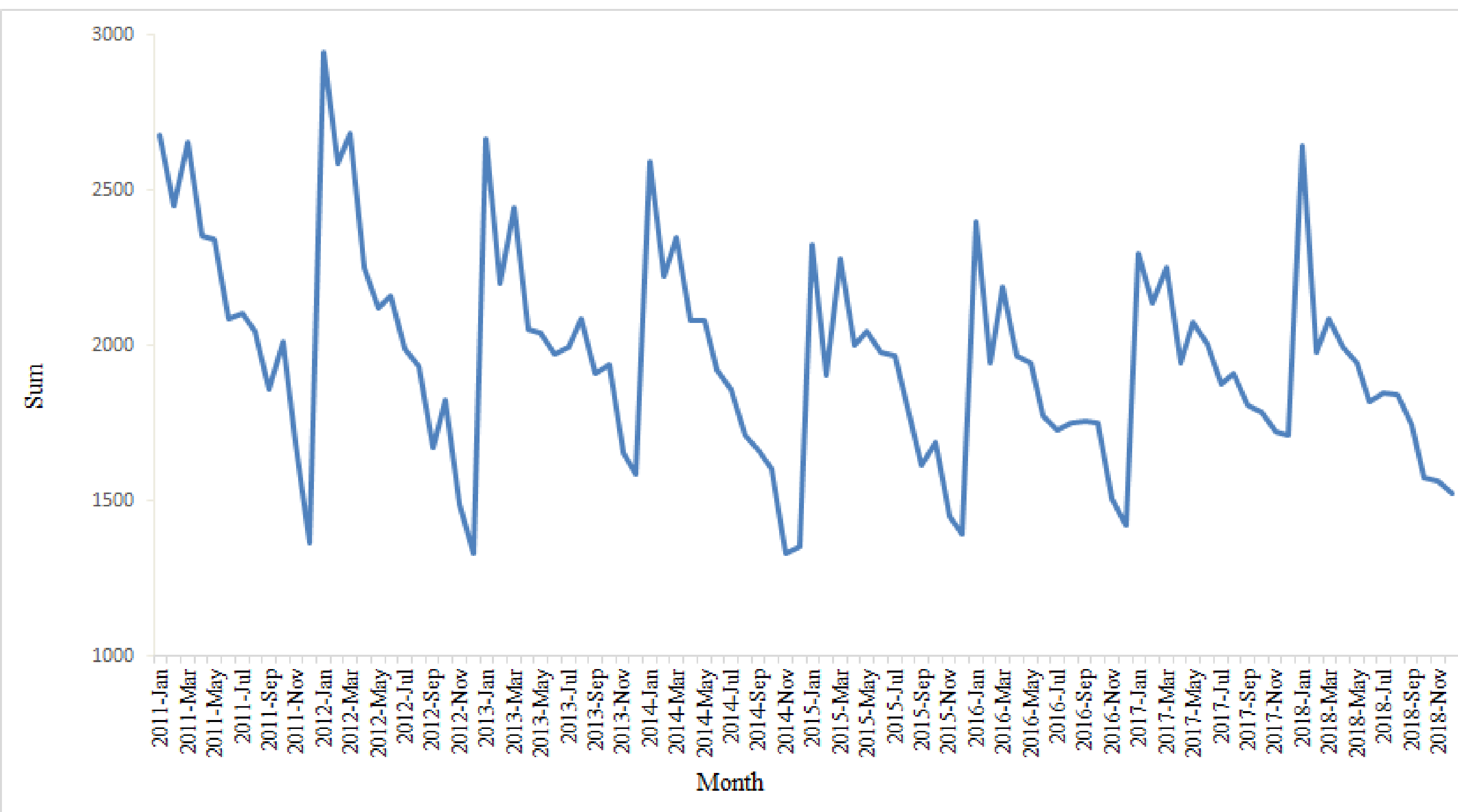

Figure 2

The monthly fluctuation of PTB cases in Chongqing from 2011 to 2018.

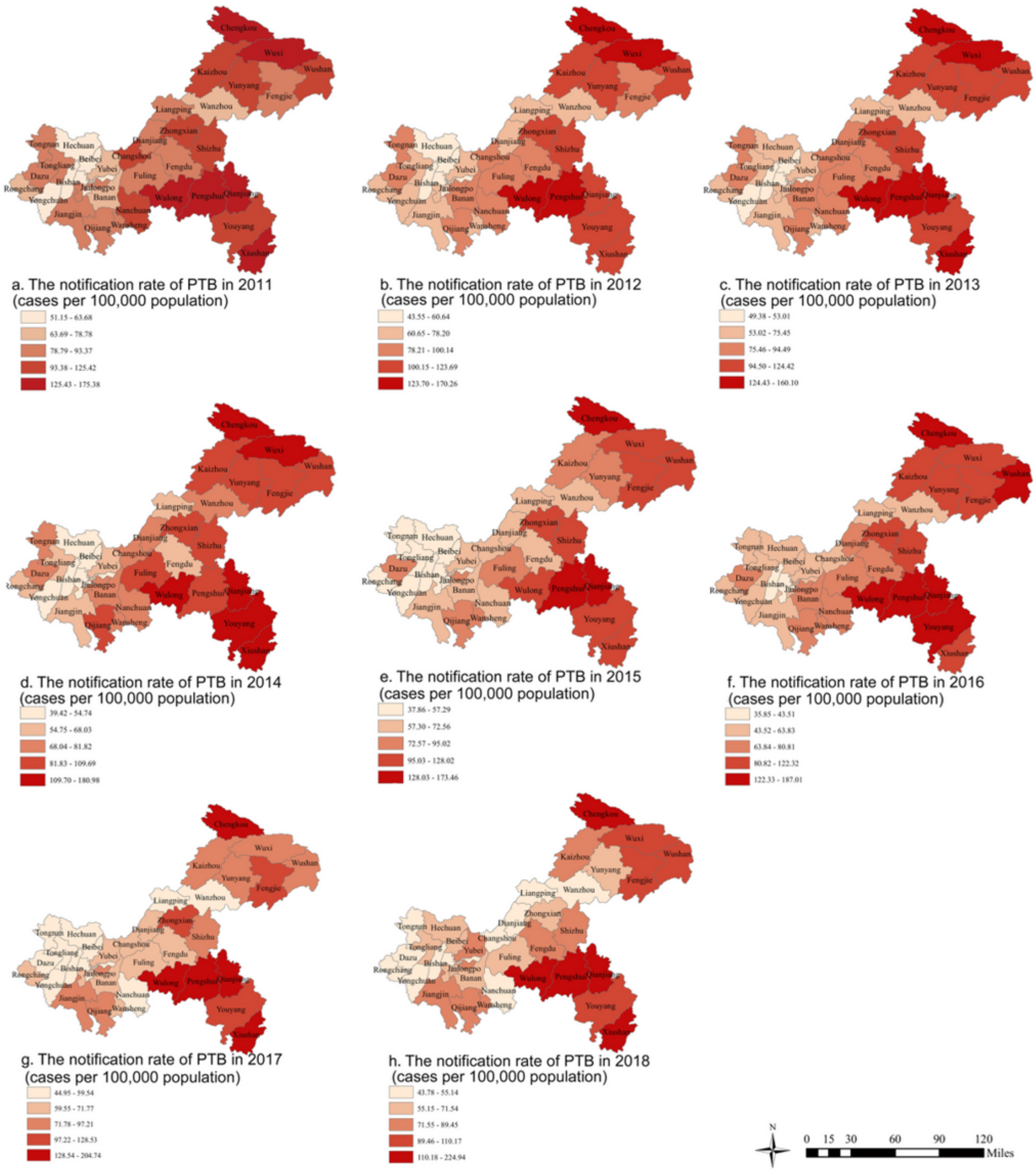

Figure 3

The notification rates of PTB at the county level in Chongqing, 2011–2018. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

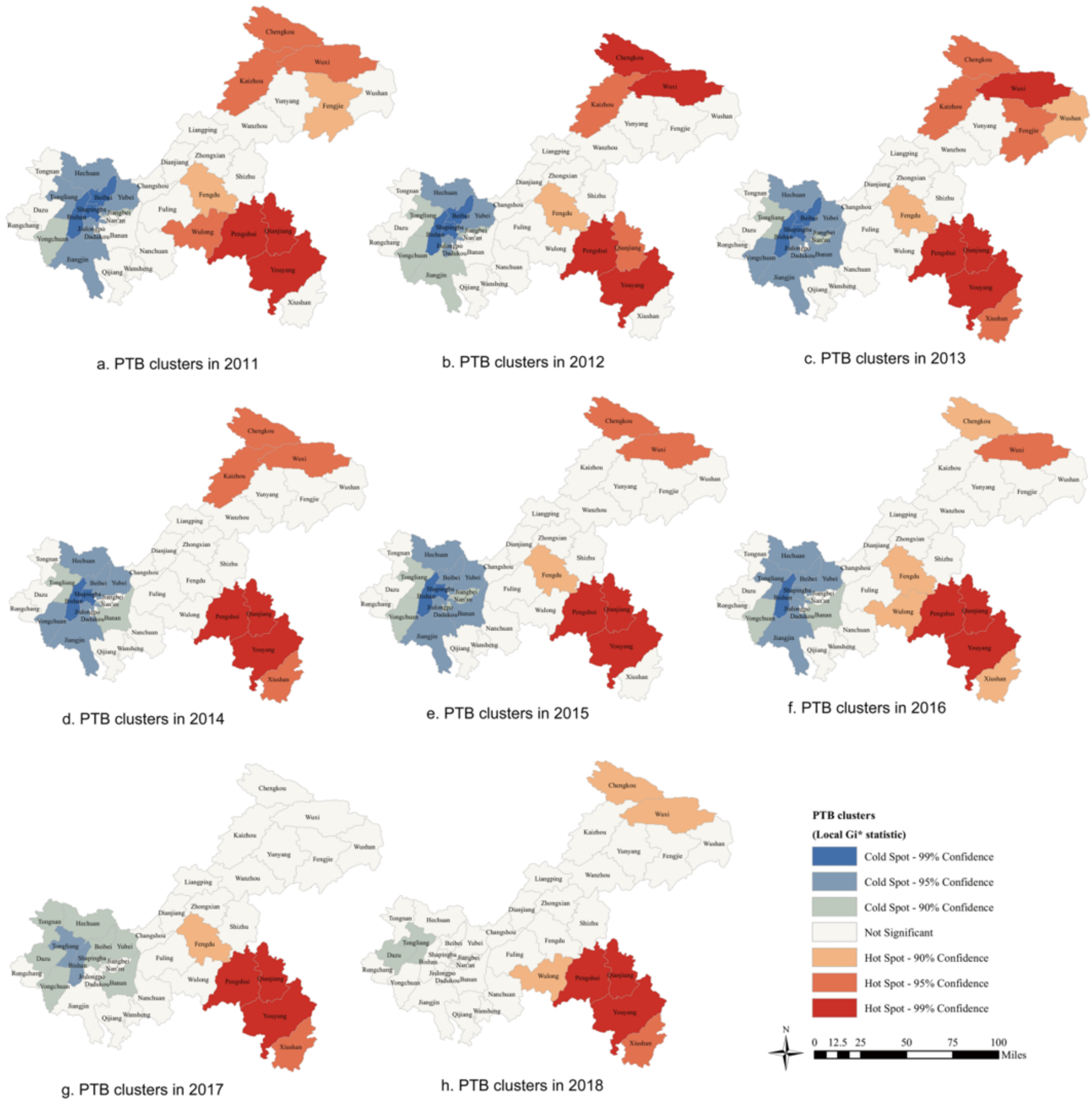

Figure 4

The spatial clusters of the PTB cases at the county level using the Local Gi* statistic. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

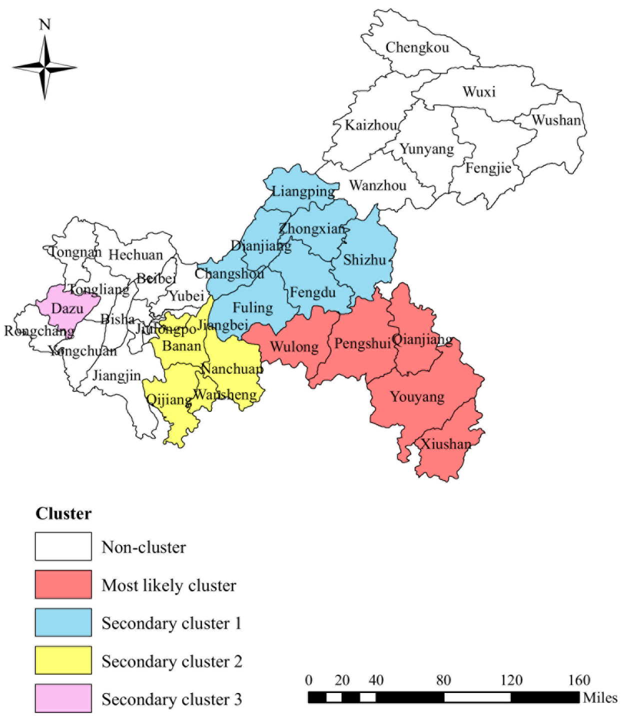

Figure 5

The space-time clusters of PTB cases at the county level in Chongqing, 2011-2018. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.