Original Paper

Analysis of spatial-temporal distribution and influencing factors of pulmonary tuberculosis in China, during 2008–2015

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Abstract

At present, the number of people with tuberculosis in China is second only to India and ranks second in the world. Under such a severe case of tuberculosis in China, prevention and control of pulmonary tuberculosis are urgently needed. This study aimed to study the temporal and geographical relevance of the pathogenesis of pulmonary tuberculosis and the factors affecting the incidence of tuberculosis. Spatial autocorrelation model was used to study the spatial distribution characteristics of pulmonary tuberculosis from a quantitative level. The research results showed that the overall incidence of pulmonary tuberculosis (IPT) in China was low in the east, high in the west and had certain seasonal characteristics. We use Spatial Lag Model to explore influencing factors of pulmonary tuberculosis. It indicates that the IPT is high in areas with underdeveloped economics, poor social services and low average smoking ages. Additionally, the IPT is high in areas with high AIDS prevalence. Also, compared with Classical Regression Model and Spatial Error Model, our model has smaller values of Akaike information criterion and Schwarz criterion. Besides, our model has bigger values of coefficient of determination (R^2) and log-likelihood ($\log L$) than the other two models. Apart from that, it is more significant than Spatial Error Models in the spatial dependence test for the IPT.

Introduction

Nowadays, China is one of the 22 countries with a high burden of tuberculosis. Tuberculosis is the first common cause of death from infectious diseases [1]. In China, its incidence is second only to viral hepatitis in legal infectious diseases. Despite the great progress that has been made in controlling tuberculosis over the past decades, China is still among the countries with the highest burden of tuberculosis [2]. Although the case-finding rate is higher than 85% [3] and the success rate of new smear-positive tuberculosis patients is higher than 90%, tuberculosis remains a major public health problem. The proportion of multi-drug resistant tuberculosis is still high, with 3.3% of new cases and 20% of retreatment cases have multi-drug resistant tuberculosis in the world [1]. The disease brings tremendous physical and psychological pain to the patient, which seriously affects their quality of life. It affects the therapeutic effect of the disease and physical recovery in turn [4]. Researches on infectious diseases such as tuberculosis are mostly limited to a single description of the incidence of diseases, neglecting the geographical relevance of the occurrence of tuberculosis and cannot make a certain discussion on the spatial distribution of disease from a quantitative level in China. While, tuberculosis as an infectious disease has certain links with the local environment, population, climate and so on. Its occurrence, development and epidemic are spatial phenomena with interactions and proliferation. In view of this, this study aims to investigate the clustering of pulmonary tuberculosis and study the influencing factors of the incidence of it, which in order to provide a theoretical basis for the formulation of public health policies in various regions, prevent and control tuberculosis and provide a reference for similar research.

Spatial information is used to extend the analysis of epidemic disease in spatial epidemiology [5, 6]. In order to predict the spatial-temporal trends of disease and the correlation between a disease and its latent factors, spatial epidemiology also explores the spatial distribution model [5, 7, 8]. Quantitative methods can present the distribution characteristics of disease objectively and scan statistics can describe the clustering characteristics in terms of both space and time [9–11].

A meta-analysis of Bauer *et al.* [12] found that, on a global scale, the overall quality of life of pulmonary tuberculosis patients is low. Not only the physical function is diminished, but also psychological, mental and social functions are greatly affected. In terms of social factors, Masumoto *et al.* [13] found that in addition to clinical factors, low socioeconomic status, including exposure to secondhand smoke and little social support, may be related to the quality of life of pulmonary tuberculosis patients through a cross-sectional survey. In terms of

personal factors, by conducting semi-structured interviews, Rondags *et al.* [14] found there are three main reasons for patients not complying with the treatment of pulmonary tuberculosis. The three main reasons include knowledge about tuberculosis, knowledge about tuberculosis treatment and choosing a healthcare treatment facility. In terms of environmental factors, Grange and Gandy [15] considered that analysis of the prevalence of tuberculosis must take into account the effects of changes in the environment and ecological factors and it was necessary to determine whether pathogenic microorganisms were evolving.

This paper is organised as follows. In the section Materials and methods, from both spatial and temporal perspectives, we will analyse the status and trends of the incidence of pulmonary tuberculosis (IPT) in China during 2008–2015. Then, apply local spatial autocorrelation analysis to explore the spatial relationship of the IPT. In the section Results, we establish Spatial Lag Model. The last section contains the conclusions, the highlights and limitations of our model.

Materials and methods

Data source

We have 14 categories of data from 31 provinces in China in 2014. The 14 categories of data are (1) the IPT (1/100 000), (2) the proportion of people who go to high school (HS)(1/10 000), (3) household consumption levels (HCL)(yuan), (4) population mortality (PM)(1/1000), (5) the number of health technicians per 10 000 people (HT)(person), (6) the number of beds in medical institutions per 10 000 people (BMI)(person), (7) per capital gross regional product (PGDP)(yuan), (8) population density (PD)(person/km^2), (9) the incidence of AIDS (IAIDS)(1/100 000), (10) the proportion of urban population (UP)(%), (11) the average age at which people start smoking (ASS), (12) the number of community health service centres (CHSC), (13) the number of social welfare enterprises (SWE), (14) operating number of public transport vehicles (PTV)(vehicle). All data comes from the National Bureau of Statistics of the People's Republic of China, the National Population and Health Science Data Sharing Platform.

Local spatial autocorrelation

It is important to examine spatial correlation and autocorrelation for spatial series [16]. Spatial autocorrelation refers to the spatial correlation of the same variable in different spatial positions. It is a measure of the degree of aggregation of spatial unit attribute values. Spatial autocorrelation is measured by using both global and local indicators. The global indicator is used to detect the spatial pattern of the entire area and a single value is used to reflect the degree of autocorrelation of the region. The local indicator calculates the degree of relevance of an attribute between each spatial unit and neighbouring unit [17]. The global indicator sometimes obscures the nonstationary of the local state [16]. Therefore, on many occasions, it is necessary to use local indicators to detect spatial autocorrelation.

In order to quantify the spatial relationship between the two provinces, we use the spatial weight matrix to represent it. Define a binary pairing spatial weight matrix to express the spatial relationship of 31 provinces in the following form:

$$W = \begin{bmatrix} \omega_{1,1} \cdots \omega_{1,31} \\ \vdots \quad \ddots \quad \vdots \\ \omega_{31,1} \cdots \omega_{31,31} \end{bmatrix}$$

where $\omega_{i,j}$ denotes the proximity relationship between the *i*th province and the *j*th province, $i, j = 1, 2, …, 31$. It can be measured according to the adjacency criterion or distance criterion [18].

There are many rules for determining the spatial weight matrix. We use rook neighbourhood to calculate statistics for local indicators of the IPT in China. The simple binary adjacency matrix for this research is:

$$\omega_{i,j} = \begin{cases} 1, & i \text{ is adjacent to } j. \\ 0, & \text{otherwise.} \end{cases}, \quad i, j = 1, 2, …, 31, \quad i \neq j \quad (1)$$

The *i*th province does not belong to its adjacency relationship with itself, which means $\omega_{i,i} = 0$.

After calculating the spatial weight matrix, we could calculate local indicators of the IPT in China. The most commonly used spatial autocorrelation local indicators are the Moran index and the G coefficient. The former was proposed by Anselin [19]. The formulas of spatial Moran index are as follows:

$$I_i = \frac{n(x_i - \bar{x}) \sum_{j=1}^{n} \omega_{i,j}(x_j - \bar{x})}{\sum_{i=1}^{n} (x_i - \bar{x})^2} \quad i, j = 1, 2, …, n \quad (2)$$

In the formula, $n = 31$, x_i, x_j denote the IPT in the *i*th and the *j*th province in 2014, $i \neq j$, $\omega_{i,j}$ denotes the neighbouring relationship between the *i*th and the *j*th province $\bar{x} = (1/n) \sum_{i=1}^{n} x_i$.

The formula for calculating the local Moran index I_i normalised statistic $Z(I_i)$ is as follows:

$$Z(I_i) = \frac{I_i - E(I)}{\sqrt{\text{Var}(I)}} \quad i = 1, 2, …, 31 \quad (3)$$

Here, $E(I)$ denotes the mean of I and $\text{Var}(I)$ denotes the variance of I.

The difference in the ability to detect spatial aggregation between the local Moran index and the local G coefficient is significant. The local G coefficient can detect the aggregated area more accurately; the local Moran index can generally detect the centre of the aggregated area, but the deviation from recognition of clustering range is greater and the detected range is smaller than the actual range [18]. In addition, the G coefficient has a spatial distribution pattern that can detect whether a regional unit belongs to a high-value cluster or a low-value cluster compared with the Moran index [20]. Therefore, next, we calculate the local G statistic G_i for the IPT in China in 2014 to detect spatial dependence within a small area. The formula for calculating the statistic G_i for the *i*th province is as follows:

$$G_i = \frac{\sum_{j=1}^{n} \omega_{i,j} x_j}{\sum_{j=1}^{n} x_j} \quad i, j = 1, 2, …, n \quad (4)$$

In the formula, n, x_j, $\omega_{i,j}$ denote the same as those in (2). The formula for calculating the local G coefficient G_i normalised statistic $Z(G_i)$ is as follows:

$$Z(G_i) = \frac{G_i - E(G)}{\sqrt{\text{Var}(G)}}.$$

Here, $E(G)$ denotes the mean of G and $\mathrm{Var}(G)$ denotes the variance of G.

Spatial Lag Model

After finding out the degree of correlation between the IPT in each province and its neighbouring provinces, we conducted a spatial regression analysis in order to further determine the influencing factors of the IPT in China. Spatial regression analysis is a spatial statistical analysis method for determining the interdependent quantitative relationship between two or more variables with spatial properties. Spatial regression analysis generally adopts three models: Classical Regression Model, Spatial Error Model and Spatial Lag Model.

In order to explore the influencing factors of the IPT. We get 13 influencing factors. Our influencing factors are (1) the proportion of people who go to HS (1/10 000), (2) HCL (yuan), (3) PM (1/1000), (4) number of HT per 10 000 people (person), (5) number of BMI per 10 000 people (person), (6) PGDP (yuan), (7) PD (person/km^2), (8) IAIDS (1/100 000), (9) proportion of UP (%), (10) the average ASS, (11) number of CHSC, (12) number of SWE, (13) operating number of PTV (vehicle). Since there are multi-collinearity among the 13 influencing factors, we use factor analysis to extract 4 common factors. These four common factors are analysed as independent variables. Spatial Lag Model was used in this research.

Spatial Lag Model reflects spatial interactions such as diffusion or overflow between adjacent space objects. It is as follows:

$$y(i) = \rho \sum_{j=1}^{31} \omega_{i,j} y(j) + \beta_0 + \beta_1 X_1(i) + \beta_2 X_2(i) + \beta_3 X_3(i) + \beta_4 X_4(i)$$

$$+ \, \varepsilon(i), \quad \varepsilon \sim N(\mathbf{0}, \Omega), \Omega = \sigma^2 E_{31 \times 31}, \quad i, j = 1, 2, \ldots, 31 \tag{5}$$

In the formula, $y(i)$ denotes the IPT in the ith province in 2014; $X_1(i) \sim X_4(i)$ denote four common factors C1, C2, C3, C4; $\beta_1 \sim \beta_4$ denote the regression coefficients of the independent variables $X_1(i) \sim X_4(i)$; $\varepsilon(i)$ are the random errors; ρ reflects the extent of spatial diffusion or spatial spillover; $\omega_{i,j}$ denotes the neighbouring relationship between the ith province and the jth province, which is the same with that in (2); Ω is a covariance matrix; $E_{31 \times 31}$ is an identity matrix with 31 rows and 31 columns.

Results

The data are tuberculosis data reported directly through the Infectious Diseases Network from 2008 to 2015. It includes information on tuberculosis patients registered and managed by the tuberculosis control agency.

IPT in 31 provinces of China during 2008–2015

Figure 1 shows that there is a significant difference in the IPT in 31 provinces. The darker the colour is, the higher the incidence is and the lighter the colour is, the lower the incidence is. The situation during 2008–2015 is generally characterised by low levels in the east and high levels in the west. It can be seen that the provinces with similar rates of pulmonary tuberculosis in our country have regional aggregation: there are clustering in Xinjiang, Tibet and Qinghai with a high IPT; there are clustering in Liaoning, Shandong and Jiangsu with a low IPT.

IPT in China during 2008–2015

In Fig. 2, the blue line denotes the IPT and the brown line denotes the number of persons with pulmonary tuberculosis. It can be seen that the IPT and the number of persons with pulmonary tuberculosis are roughly divided into two stages: from 2008 to 2011 and from 2012 to 2015. It can be seen that the incidence rate in the first stage shows a rapid decrease trend, while the incidence rate in the second stage shows a slow decrease trend. The trend of IPT and number of persons with pulmonary tuberculosis are nearly the same.

In Fig. 3a, from the seasonal changes, the IPT is lower in winter, higher in spring. Summer and fall showed a downward trend in volatility. From the year series, there are slight fluctuations. The overall trend is decreasing year by year. In Fig. 3b, the IPT has a decreasing trend and there is a cycle phenomenon.

Local spatial autocorrelation analysis

Since there are missing data and we only have complete data for 2014, we analyse the IPT in 2014 as an example.

Figure 4 shows that in 2014, there are three provinces with statistically significant (P <0.05) in HH (High High) region, including Xinjiang, Tibet and Qinghai. It indicates that the IPT in these provinces is high and the IPT in neighbouring provinces is still high. There are three provinces with statistical significance (P <0.05) in LL (Low Low) region, including Hebei, Beijing and Jiangsu. It indicates that the IPT in these provinces is low and the IPT in the neighbouring provinces is also low. There are two provinces with statistical significance (P <0.05) in LH (Low High) region, including Sichuan and Yunnan. It indicates that the IPT in these provinces is low, but the IPT in the neighbouring provinces is high. There are no statistically significant provinces in HL (High Low) region, indicating that there is no province with a high IPT having neighbouring provinces with a low IPT.

In Fig. 5, Xinjiang, Tibet, Qinghai, Sichuan and Yunnan are clustered areas with high IPT. Hebei, Beijing and Jiangsu are clustered areas with low IPT. In Fig. 6, hot spots (high incidence aggregation areas) are concentrated in the western part of China and cold spots (low incidence aggregation areas) are concentrated in the eastern part of China.

Analysis of influencing factors

We find that $P = 0.000$ <0.05, through Bartlett's Test of Sphericity. Therefore, there are multi-collinearity between influencing factors. We extract four common factors through factor analysis; use factor rotation to get the meaning of the four factors and then name the four factors. Table 1 shows the rotated component matrix. From Table 1, we can see that the first common factor reflects more information about HCL, HT, PGDP, UP, HS and PD. The second common factor reflects more information about CHSC, SWE and PTV. The third common factor reflects more information about the negative of IAIDS and ASS. The fourth common factor reflects more information about BMI and PM. Therefore, the first common factor reflects more information about the economic factor, the second common factor reflects the social service factor, the third common factor reflects the personal factor and the fourth common factor reflects more information about PM and the number of beds in medical institutions. The cumulative variance contribution rate of the four
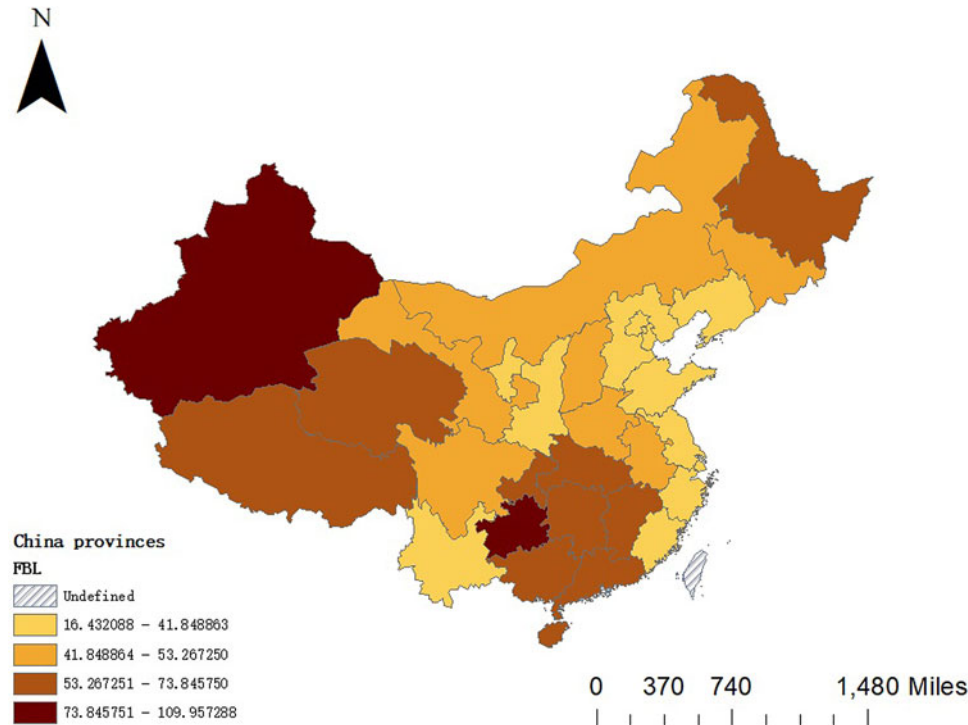
Fig. 1. Distribution of mean incidence of pulmonary tuberculosis in China during 2008–2015.
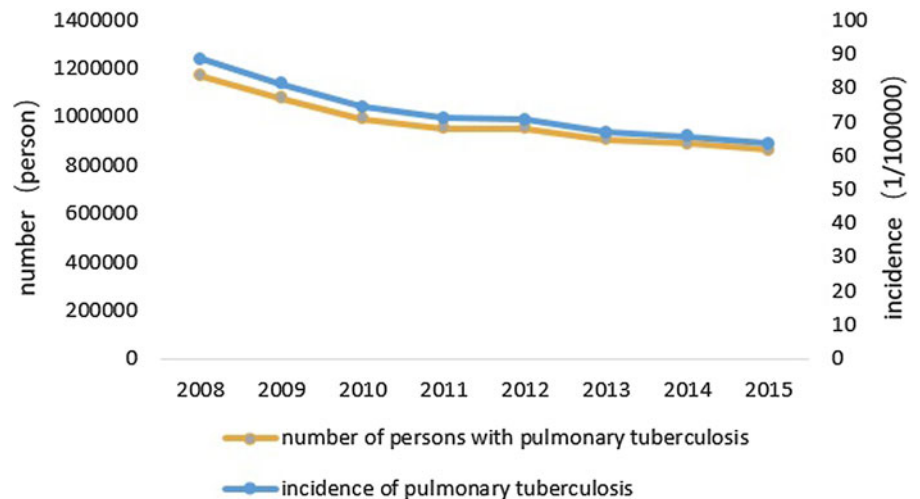

Fig. 2. Incidence of pulmonary tuberculosis and number of persons with pulmonary tuberculosis in China during 2008–2015.

common factors reaches 76.575%. Next, we use these four-factor scores as independent variables to build models.

In order to get the impact of these four common factors, Spatial Lag Model was used in this research.

Table 2 shows that C1, C2, C3 are significant except regional C4 when the significance level is 0.05. The IPT in 2014 was negatively correlated with C1, C2 and C3. It indicates that the IPT is high in economically underdeveloped areas. The IPT is high in areas with poor social services. The IPT is high in areas with low average smoking ages. Additionally, the IPT is high in areas with high AIDS prevalence.

In order to compare the regression effects of Classical Regression Model, Spatial Error Model and Spatial Lag Model, we used three models to regress separately and obtained the following results:

As can be seen from Table 3, the values of AIC and SC of Spatial Lag Model are all smaller than that in Classical Regression Model and Spatial Error Model. The values of R^2 and log L of Spatial Lag Model are all bigger than that in Classical Regression Model and Spatial Error Model. It means that the Spatial Lag Model fits better than two others. In Table 4, Spatial Lag Model passed the Robust LM tests with $P < 0.05$ while Spatial Error Model failed. Therefore, Spatial Lag Model has a better interpretation.

Discussions and conclusions

In this research, we analysed the IPT during 2008–2015 in terms of space, time and influencing factors comprehensively.
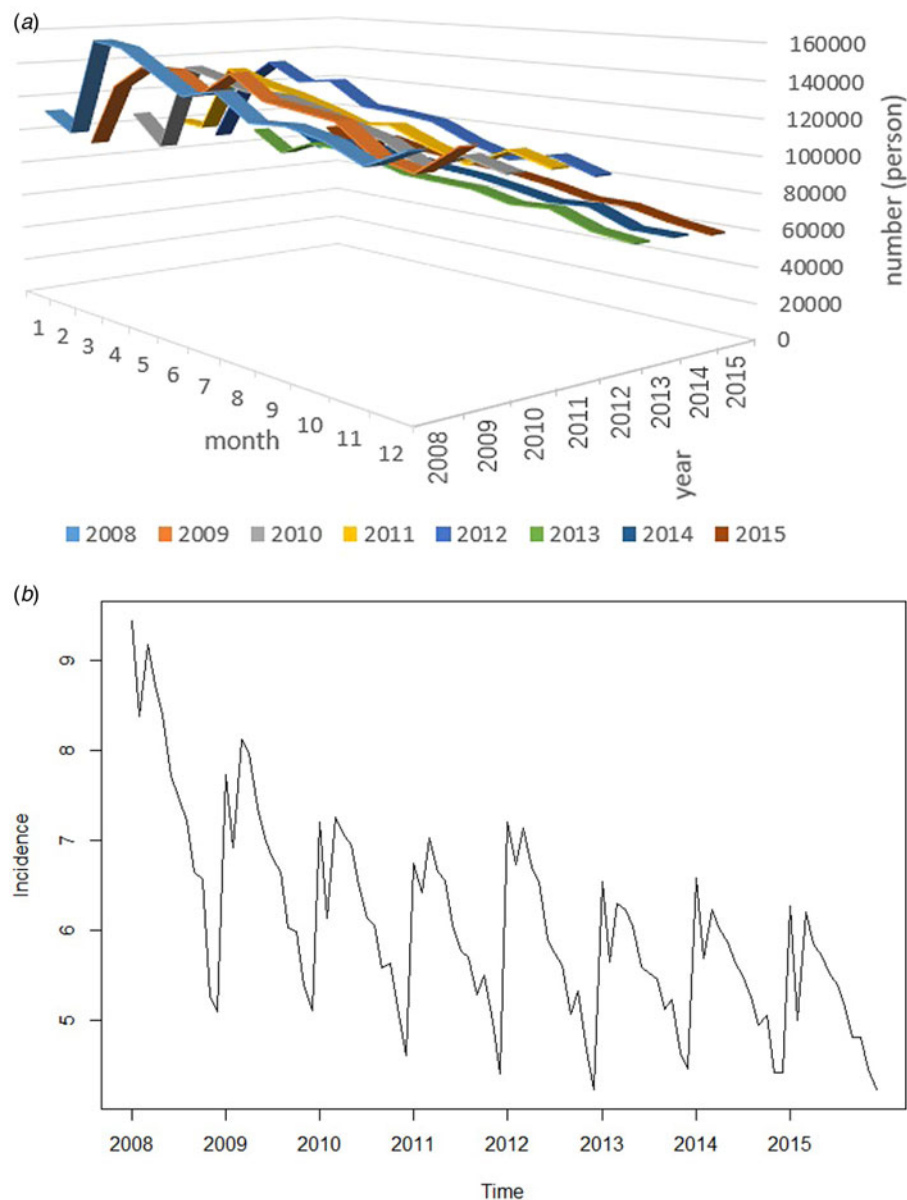
Fig. 3. Time trend. (a) Number of persons with pulmonary tuberculosis in 12 months during 2008–2015. (b) Time series of incidence of pulmonary tuberculosis during 2008–2015.

There is a significant difference in the incidence of tuberculosis in various provinces, which is characterised by low in the east and high in the west. It is related to the unbalanced economic development in some ways. The economic development in the east is higher than that in the west, making the entire system of medical care and prevention in the east more complete than in the west. Studies [21] show that people in areas with economic underdevelopment are more likely to get tuberculosis due to AIDS, drug use, application of immunosuppressive agents, alcoholism and poverty.

In particular, studies [22, 23] have shown that public transportation is closely related to the spread of Mycobacterium tuberculosis. It is also related to the incidence of tuberculosis. The terrain in the western region is complex, so the traffic is inconvenient, while the eastern region is plain and the transportation is more convenient.

At the same time, the overall quality of the population in the east is higher than that in the west and their awareness of prevention and treatment is stronger than that of the western residents

[24]. There are more AIDS patients in the western region. Tuberculosis is one of the most common opportunistic infections in AIDS patients. The two diseases affect each other and cause each other. AIDS patients have 30–50 times more likely to have tuberculosis than normal people [25]. Therefore, the incidence of tuberculosis is high in the west and low in the east.

From the analysis results, we can see that the incidence of tuberculosis is seasonal. The formation of the peak incidence of tuberculosis in the population has been analysed by Zhang *et al.* [26]. There are two main reasons. On the one hand, the spread of Mycobacterium tuberculosis in the population leads to an increase in the incidence of recent transmission. On the other hand, the immunity decreases and the incidence of latent infections in the population have increased. According to the survey, the peak incidence of tuberculosis is in spring, during the Chinese Lunar New Year period and the population movement is large, so that there are more opportunities for tuberculosis transmission, increasing the chance of infection of susceptible people [27]. The peak period in summer is mainly due to the
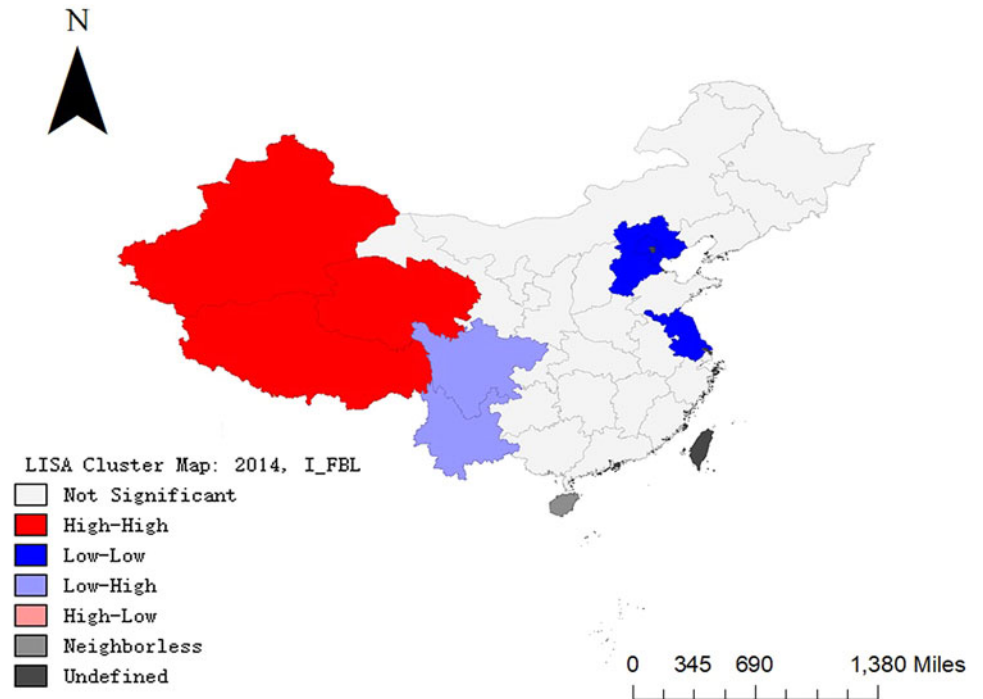
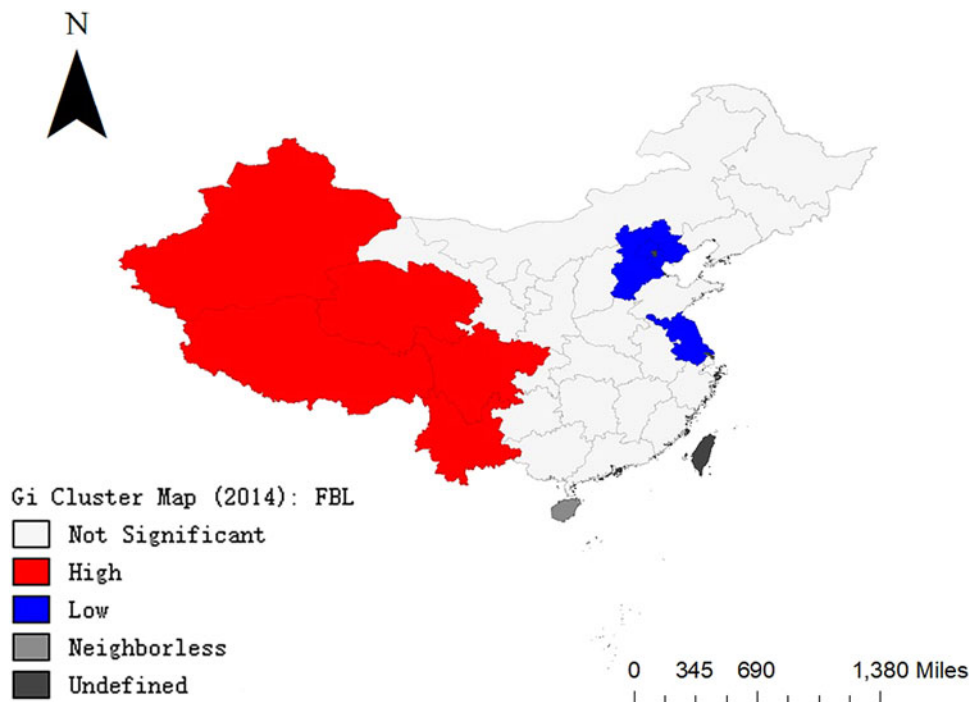**Fig. 4.** Results of local Moran index visualisation analysis in 2014.

Fig. 5. Results of local G coefficient visualisation analysis in 2014.

dryness of the air, the decrease of respiratory mucosal resistance and the cold weather of the air in the winter. The infected tuberculosis is in the incubation period and has a certain time from the onset to the diagnosis. The diagnosis was delayed, which led to the peak incidence of the report in spring or summer. Fundamentally speaking, the seasonal difference in the incidence is due to geographical and climatic reasons. The weather varies from season to season and the human immunity will be different.

The reason for the decrease in the IPT in recent years may be due to the fact that the state has always attached importance to the prevention and treatment of tuberculosis. The State Council issued the National Tuberculosis Prevention and Control Plan (2001–2010) in 2001 [28]. The scientific improvement of disease diagnosis and treatment methods, the disease screening rate and the increasing awareness rate of core information for tuberculosis prevention and control among the people have a
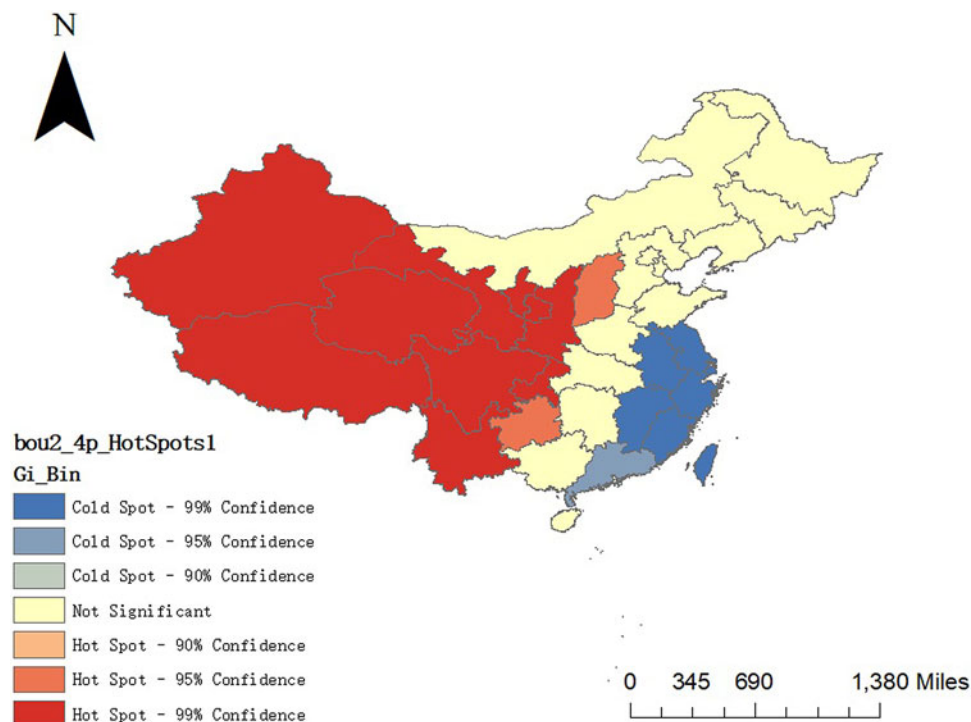
Fig. 6. Results of the hot and cold spot areas in 2014.

Table 1. Rotated component matrix

	Component 1 (C1)	Component 2 (C2)	Component 3 (C3)	Component 4 (C4)
HS	0.690	0.228	0.102	0.019
HCL	0.916	0.291	0.099	−0.047
PM	−0.402	0.265	−0.083	0.595
HT	0.813	−0.096	0.081	0.250
BMI	0.118	−0.147	−0.068	0.885
PGDP	0.898	0.204	0.143	−0.063
PD	0.711	0.234	0.086	−0.136
Negative of IAIDS	0.111	−0.058	0.827	−0.204
UP	0.932	0.205	0.116	−0.051
ASS	0.163	0.221	0.798	0.111
CHSC	0.168	0.902	0.063	−0.067
SWE	0.260	0.610	0.303	0.430
PTV	0.356	0.883	0.015	−0.028

great relationship with the decrease in the incidence of tuberculosis.

We have found the seasonality of tuberculosis incidence. This characteristic can remind residents to prepare for the prevention of pulmonary tuberculosis in advance. It can also remind the hospital to purchase tuberculosis-related drugs in advance. Additionally, it can remind the government to introduce relevant policies to prevent tuberculosis.

Through the spatial clustering of pulmonary tuberculosis, we can see which areas have a high IPT and which areas have a low IPT. At the same time, we need to focus on strengthening

treatment in areas with high IPT and prevention of tuberculosis in high incidence areas spreading to surrounding areas.

Through quantitative analysis, we analysed factors influencing the IPT. According to our conclusion, the government can improve the IPT by improving the level of economic development and regulating social services. Individuals can reduce the IPT by reducing smoking and the likelihood of being infected with AIDS.

In sum, our model has two highlights: (a) Compared with the other two models, Spatial Lag Model can fit the data better. The values of AIC and SC of Spatial Lag Model are all smaller and the values of R^2 and log L are all bigger than those in the other two

Table 2. Regression results of our model for the incidence of pulmonary tuberculosis in 2014

Variable	Coefficient	Std.Error	Z-value	P-value
ρ	0.32130	0.18282	2.06441	0.03898
Constant	85.92070	14.58680	5.89032	0.00000
C1	−16.31890	4.55901	−3.57949	0.00034
C2	−9.77808	4.61029	−2.12093	0.03393
C3	−9.74301	4.81508	−2.02344	0.04303
C4	1.09195	4.55564	0.23969	0.81057

Table 3. Comparison of regression results of three models

Index	SEM[a]	CRM[b]	SLM[c]
R^2	0.43518	0.42549	0.44854
log L[d]	−144.171909	−144.32800	−143.09000
AIC[e]	298.34400	298.65700	297.74400
SC[f]	305.51400	305.82700	305.34800

[a]Spatial error model.
[b]Classical regression model.
[c]Spatial lag model.
[d]Log likelihood.
[e]Akaike information criterion.
[f]Schwarz criterion.

Table 4. Results of the spatial dependence test for the incidence of pulmonary tuberculosis in 2014

Test	MI/DF	Value	P-value
Lagrange Multiplier (LM) (lag)	1	2.4259	0.11935
Robust LM (lag)	1	4.0264	0.04479
Lagrange Multiplier (LM) (error)	1	0.0043	0.94765
Robust LM (error)	1	1.6048	0.20522

models. (b) Compared with the Spatial Error Model, our model is more significant in the spatial dependence test for the IPT.

There are still some limitations to our model: (a) It ignores whether there are spillover effects in one area to a certain extent. (b) There are only 13 explaining variables in this research. In fact, there are a lot of influencing factors. Those are what the future work needs to further improve. From the perspective of space, the IPT varies significantly among regions in China. The overall situation is that the eastern part has low incidence and the western part has a high incidence. From the perspective of time, the IPT has been slowly decreasing in recent years. The IPT has certain seasonal characteristics: lower in winter, higher in spring and decreasing unsteadily in summer and autumn.

Conflict of interest. The authors declare no conflict of interest.

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