Pulmonary tuberculosis notification rate in Shenzhen, China during 2010-2019: spatial-temporal analysis

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Abstract

Background: Pulmonary tuberculosis (PTB) is a chronic communicable disease of major public health and social concern. Though spatial-temporal analysis has been widely used to describe distribution characteristics and transmission patterns, few studies have been conducted to reveal the changes of small-scale clustering of PTB at the street level.

Objective: This study analyzed the temporal and spatial distribution characteristics and clusters of PTB at the street level in Shenzhen municipality to provide reference of PTB prevention and control.

Methods: A total of 58122 PTB cases from 2010 to 2019 were notified in Shenzhen. The annual notification rate of PTB decreased significantly from 64.97 per 100000 population in 2010 to 43.43 per 100000 population in 2019. PTB cases have shown seasonal variations with the peak in late spring and summer each year. The PTB notification rate was non-randomly distribution and spatially clustering with the Moran's I value of 0.134 (P<.05). One most likely cluster and ten secondary clusters were detected, and the most likely clustering area was centered at Nanshan Street of Nanshan District covering six streets, with the clustering time from January 2010 to November 2012.

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Conclusions: This study identified seasonal patterns and spatial-temporal clusters at the street level in Shenzhen municipality. Resources should be prioritized to high-risk areas for PTB prevention and control.

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ABSTRACT

Background:

Pulmonary tuberculosis (PTB) is a chronic communicable disease of major public health and social concern. Though spatial-temporal analysis has been widely used to describe distribution characteristics and transmission patterns, few studies have been conducted to reveal the changes of small-scale clustering of PTB at the street level.

Objective:

This study analyzed the temporal and spatial distribution characteristics and clusters of PTB at the street level in Shenzhen municipality to provide reference of PTB prevention and control.

Methods:

Data of reported PTB cases in Shenzhen from January 2010 to December 2019 was extracted from the China Information System for Disease Control and Prevention to describe the epidemiological characteristics. Time series, spatial autocorrelation and spatial-temporal scanning analyses were performed to identify the spatial and temporal patterns and high-risk areas at the street level.

Results:

A total of 58122 PTB cases from 2010 to 2019 were notified in Shenzhen. The annual notification rate of PTB decreased significantly from 64.97 per 100000 population in 2010 to 43.43 per 100000 population in 2019. PTB cases have shown seasonal variations with the peak in late spring and summer each year. The PTB notification rate was non-randomly distribution and spatially clustering with the Moran's I value of 0.134 (P<.05). One most likely cluster and ten secondary clusters were detected, and the most likely clustering area was centered at Nanshan Street of Nanshan District covering six streets, with the clustering time from January 2010 to November 2012.

Conclusions:

This study identified seasonal patterns and spatial-temporal clusters at the street level in Shenzhen municipality. Resources should be prioritized to high-risk areas for PTB prevention and control.

Keywords:

tuberculosis, spatial analysis, spatial-temporal cluster, Shenzhen

Introduction

Tuberculosis (TB), caused by the bacillus Mycobacterium tuberculosis, is a chronic communicable disease that is a major public health and social problem and one of the leading causes of death from a single bacterial pathogen worldwide [1] According to the World Health Organization (WHO) 2023 report, there were a globally estimated 7.5 million new TB cases and 1.3 million deaths caused by TB in 2022 [1] The 30 high TB burden countries accounted for 87% of all estimated incident cases across the world [1].

China has the third highest TB burden in the world in 2022, with an estimated 530000 new cases of TB, accounting for 7.1% of the global total [1]. To reduce the magnitude and burden of TB, China has been implemented several effective interventions such as adoption and implementation of the End-TB Strategy, expansion of directly observed therapy strategy (DOTs), and expansion of multidrug-resistant TB diagnosis and treatment centers. As a result, China has made a great progress of the annually reduced incidence of TB by 3.4% since 1990 [2]. However, TB remains a major public health problem in China.

Over the past decades, China's urbanization process, led by the nationwide economic reforms, has been accompanied by rapid growth of cities including Shenzhen due to the migration of young population from rural areas attracted by employment opportunities [3], contributing to large-scale domestic migrations. Rural labor migrants might change TB transmission patterns in the cities and their health problems including TB infection and active disease development might also be changed in the circumstance of the living city [4]. As a special economic zone, Shenzhen has developed amazingly in terms of economic scale and population growth. The massive influx of migrants to Shenzhen has brought serious challenges for the prevention and control of TB [3].

Identifying areas where TB is geographically concentrated is particularly essential for planning, implementing, monitoring and evaluation TB control programs and to inform the allocation of resources for targeted and effective interventions [5]. In recent years, spatial-temporal analysis has been widely used to describe distribution characteristics and transmission patterns of TB, demonstrating that TB has highly dynamics and spatially heterogeneous at provincial, national and international levels during certain periods of time [6, 7]. However, few studies have been conducted to reveal the changes of small-scale clustering of TB at the street level. In this study, we conducted a spatial-temporal cluster analysis to characterize distribution and patterns of pulmonary tuberculosis (PTB) at the street level in Shenzhen municipality, China from 2010 to 2019.

Methods

Study Setting

Shenzhen is a city located in southern China between 113°43' to 114°38' east longitude and 22°24' to 22°52' north latitude (Appendix), with 74 streets among ten districts in total. Thanks to the implementation of the reform and opening-up policies in the 1980s, Shenzhen has benefited greatly and developed quickly from a tiny fishery village of less than one million inhabitants to a modern metropolis with the permanent residents over ten million, making it one of the most developed municipalities in China [8]. Notably, over 70% of the residents in Shenzhen are migrants and most of these migrants are young, with only 3.22% of its population is 65 years old or above [8]. The gross domestic product (GDP) has increased amazingly more than 110 thousand times in the past 40 years, from less than 200 million Yuan in 1979 to approximately 2.69 trillion Yuan in 2019 [8].

Data Source

Data of reported PTB cases in Shenzhen from January 2010 to December 2019 was extracted from the China Information System for Disease Control and Prevention, which is established and operated by the Chinese Center for Disease Control and Prevention (CCDC). Each reported case contains demographic and medical information and is identified by the unique identity card number to avoid duplicate reports. Personal sensitive information like the name and phone number of all cases were blocked and excluded in this study to protect patient's privacy. The annual population data of each administrative street in every year were extracted from Shenzhen Statistical Yearbooks (2010–2019) of the Shenzhen Municipality Bureau of Statistics [8]. Basic map data were obtained from the Shenzhen Geographical Information Public Service Platform and the administrative number of the street was used as a reference at a 1:500000 scale to correlate and match the data of reported PTB cases in each street to establish the database.

As one of the most serious infectious diseases in China, each diagnosed PTB must be reported online within 24 hours after diagnosis. The Diagnostic Criteria for PTB (WS288-2017) issued by the Ministry of Health (the former National Health Commission) of the People's Republic of China in 2017 was used in the current study [9] that cases of PTB were diagnosed using radiography, pathogen detection, and pathologic diagnosis. All forms of PTB were included in this study, including bacteriologically confirmed and clinical diagnosed PTB, previously treated and new PTB, and childhood and adult PTB.

Ethical Statement

This study was approved by the Ethics Committee of Shenzhen Center for Chronic Disease Control and the permission of the PTB data used in the study was obtained from CCDC.

Data analysis

Descriptive and time series analysis. The epidemiological characteristics of PTB cases were analyzed. PTB cases reported from 2010 to 2019 were aggregated annually by age, sex, occupation, permanent residents and migrant population, and date of onset for PTB notification rate analysis. Comparison between different groups was tested using Chi-square tests or Fisher's exact tests. All statistical analyses were performed by SPSS 26 (SPSS Inc., Chicago, IL, USA) and a two-tailed *P* value less than .05 was considered statistically significant.

In addition, time series seasonal decomposition analysis was used to identify the seasonality of PTB notification rate in Shenzhen municipality. The time series of reported PTB cases were decomposed into seasonal variation, long-term trend, and random effect to explore the temporal patterns. The temporal patterns were determined by looking at the onset date of monthly registration of all reported PTB cases. The time series included 120 months from January 2010 to December 2019 and were examined by EXCEL.

Spatial autocorrelation analysis. In this study, the global index of spatial autocorrelation is selected as the Global Moran's *I* index, which was used to determine spatial autocorrelation and detect the spatial distribution pattern of PTB cases in Shenzhen municipality, China. The expression of the global Moran's *I* statistic is:

$$I=\frac{n\sum_{i=1}^{n}\sum_{j=1}^{n} w_{ij}(x_i-\acute{y})(x_j-\acute{y})}{\left(\sum_{i=1}^{n}\sum_{j=1}^{n} w_{ij}\right)\sum_{i=1}^{n}(x_{j}-\acute{x})^2}$$

where n is the number of units, and x_i and x_j are the attribute values of the unit i and unit j. The value of Global Moran's *I* index varies between -1 and 1, when |*I*| is larger, the autocorrelation is higher, and *I* = 0 indicates negative [10]. Both *Z* score and *P* value calculated by GeoDa 1.20 (Arizona State University, PHX, AZ, USA) are used to test the significance of Global Moran's *I* value.

Spatial-temporal scan analysis. Kulldorff's spatiotemporal scan statistical analysis was conducted to explore the spatial, temporal, and spatial-temporal clusters of PTB across different streets geographically and in different time periods [11]. The SaTScanTM 10.1 software (Kulldorff, Boston, MA, USA) is used for spatial-temporal scanning analysis, which is based on a moving column scanning window that contains geographical information with height corresponding to time [12]. According to previous studies [6], the maximum radius of the spatial scanning window and the maximum length of temporal scanning window was set as 11% of the population at risk and 30% of whole study period respectively in this study. Log likelihood ratio (*LLR*) of different circle centers and various radii was constructed to compare the notification rate of PTB inside and outside the scanning window [13]. The expression of *LLR* is:

$$LLR=\frac{\left(\frac{n_z}{u_z}\right)^{n_z}\left(\frac{n_g-n_z}{\mu_g-\mu_z}\right)^{(n_g-n_z)}}{\left(\frac{n_g}{\mu_g}\right)^{n_g}}$$

Where n_z signifies the observed count of events within the spatio-temporal window z, n_g denotes the total aggregate of events across the entirety of the study area, u_z represents the expected count of events within the particular spatio-temporal window z, while μ_g indicates the overall anticipated count of events within the study area. The larger the *LLR* value was, the more it was likely to be the cluster. Monte Carlo simulation test was used to evaluate whether the difference is statistically significant, and the relative risk (*RR*) is the estimated risk within the cluster divided by that outside the cluster [14, 15]. For each possible spatiotemporal cluster, when the *P* value is less than .05, a larger *LLR* value indicates the area covered by the dynamic scanning window is more likely to be a cluster region. The window with the largest *LLR* selected from all the scanning windows is the strongest cluster and the secondary clusters are the other windows with statistically significant LLR value. ArcMap software (Esri, Redlands, California, USA) was used to visualize the scanning results.

Results

Descriptive analysis of PTB cases

A total of 58122 PTB cases were notified in Shenzhen from 2010 to 2019, of which 38358 (66.00%) were male and over 60% were migrant population. 20795 cases (35.78%) were workers and 20629 (35.49%) unemployment by occupation. The mean age of the PTB patients was 34.73 years (standardized deviation: 14.13 years), with a range from 0 to 97 (Fig 1).

Figure 1. Characteristics of PTB cases from 2010 to 2019 in Shenzhen municipality, China

Temporal patterns of PTB cases

The annual average notification rate of PTB for the ten-year period was 51.63 per 100000 population. As shown in Fig 2, the total notification rate of PTB showed a significantly volatile downward trend over time from the highest of 64.97 per 100000 population in 2010 to the lowest of 43.43 per 100000 population in 2019 (P<.001). The monthly notification rates of PTB showed a trend of volatility and decline over the study period in Shenzhen municipality. PTB cases have shown seasonal variations with the highest number of PTB cases notified in May and July each year, then a steady decrease trend after July and a nadir in January and February (Fig 3).

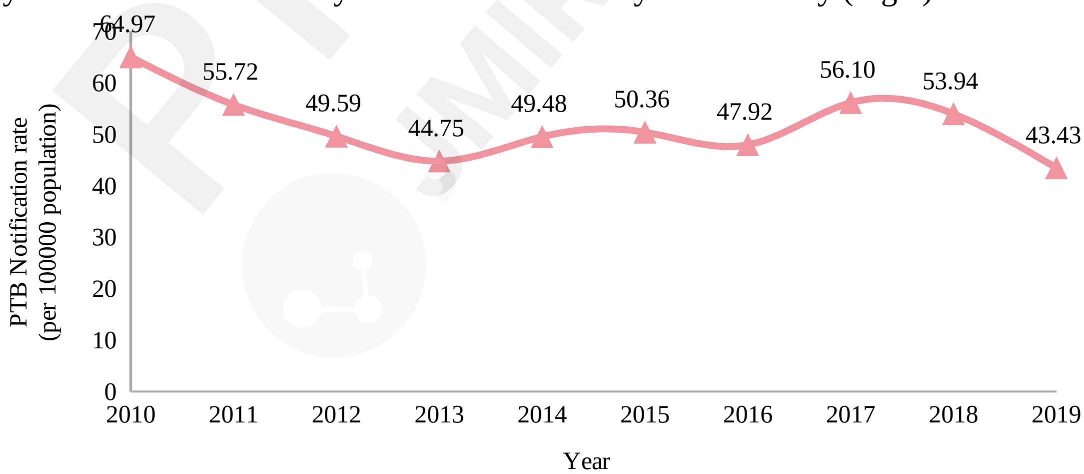

Figure 2. The variation trend of PTB notification rate (per 100000 population) from 2010 to 2019 in Shenzhen municipality, China

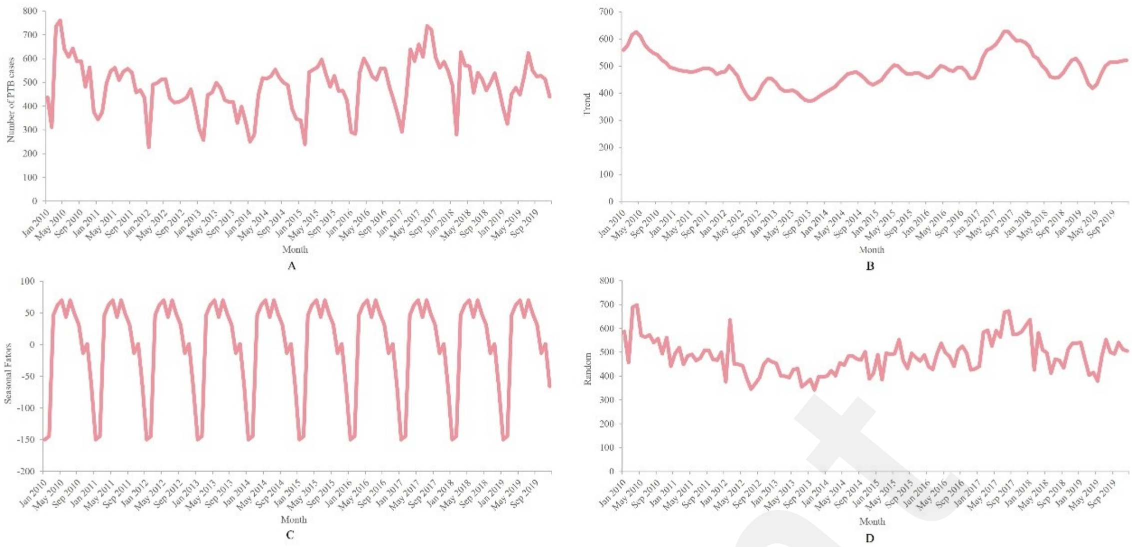

Figure 3. The seasonal distribution of monthly PTB cases from 2010 to 2019 in Shenzhen municipality, China

Spatial patterns of PTB cases

As displayed in Table 1, the global spatial autocorrelation analysis showed that the Moran's *I* value of PTB notification rate in Shenzhen municipality from 2010 to 2019 was positive (0.134) and the *P* value was less than .05, indicating that the notification rate of PTB in Shenzhen municipality was non-randomly distribution. Annually, except for the year of 2012 and 2014, there existed significant global spatial autocorrelation in the PTB notification rates in every year with the Moran's *I* value ranging from 0.130 to 0.353 (*P*<.05). Therefore, further spatial-temporal scan analysis of PTB was needed.

Table 1. Global spatial autocorrelation analysis of PTB notification rate from 2010 to 2019 in Shenzhen municipality, China

Year	Moran's *I* value	*Z*-score	*P* value[a]
2010	0.353	5.320	<.01
2011	0.179	2.748	<.01
2012	0.095	1.398	>.05
2013	0.143	2.103	<.05
2014	0.047	0.894	>.05
2015	0.130	1.851	<.05
2016	0.190	2.786	<.01
2017	0.217	3.065	<.01
2018	0.201	2.852	<.01
2019	0.155	2.361	<.01
2010-2019	0.134	1.894	<.05

[a]*P* value: The correlation is significant at a significant level of .05 (two-tailed).

Spatial clustering of PTB cases

Spatial clustering analysis of notified PTB cases every year from 2010 to 2019 found that the most likely clusters have changed dynamically over time. The most likely clusters of PTB in Shenzhen municipality from 2010 to 2014 were concentrated in the southwest regions, covering streets of Nanshan District and Baoan District. From 2015 to 2019, the most likely clusters are mainly distributed in the central and northern Shenzhen municipality, including Longhua District, Longgang District and Guangming District (Fig 4).

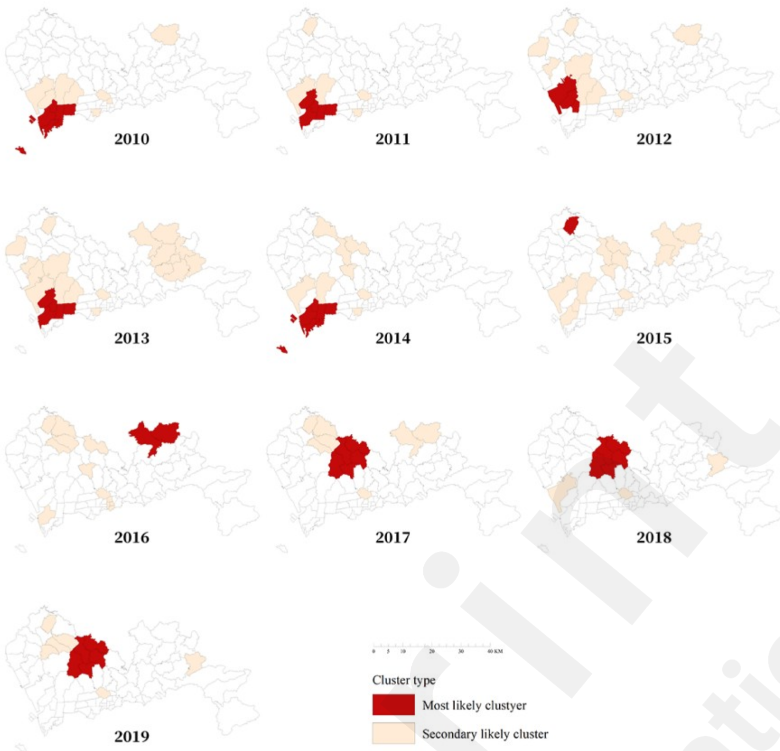

Figure 4. The spatial clusters of notified PTB cases from 2010 to 2019 in Shenzhen municipality, China

Temporal clustering of PTB cases

As presented in Table 2, the temporal clustering analysis in each year showed that PTB notification rates were concentrated in late spring and summer annually, ranging from March to August. The high aggregated time for PTB across the whole study period was observed from March 2010 to September 2010. During this period, there was a total of 4562 notified PTB cases and the risk of PTB related incidents was 53% (*RR*=1.53, *P*<.001) higher than that in other time periods.

Table 2. Temporal clustering of notified PTB cases from 2010 to 2019 in Shenzhen municipality, China

Year	Cluster time frame	Observed cases	Expected cases	RR[a]	LLR[b]	*P* value[c]
2010	1 March to 31 May	2136	1696.58	1.38	72.30	<.001
2011	1 July to 30 September	1642	1469.98	1.16	13.13	<.001
2012	1 February to 30 April	1500	1286.07	1.23	22.79	<.001
2013	1 April to 30 June	1430	1185.74	1.29	32.14	<.001
2014	1 June to 31 August	1600	1344.21	1.27	31.31	<.001
2015	1 April to 30 June	1714	1428.82	1.28	36.40	<.001
2016	1 April to 30 June	1693	1418.70	1.27	33.92	<.001
2017	1 July to 31	1458	1186.66	1.2	35.34	<.00

	August			9		1
2018	1 March to 31 May	1766	1517.62	1.23	26.28	<.001
2019	1 June to 31 August	1698	1460.91	1.23	24.88	<.001
2010-2019	1 March 2010 to 30 September 2010	4562	3072.58	1.53	334.01	<.001

[a]RR: relative risk.
[b]LLR: log likelihood ratios.
[c]*P* value: This is significant at a significant level of .05 (two-tailed).

Spatial-temporal clustering of PTB cases

The results of spatial-temporal clustering analysis for notified PTB cases in Shenzhen municipality from 2010 to 2019 were shown in Table 3 and Fig 5, indicating that the PTB notification rates were spatial-temporal clustered. Totally, one most likely cluster and ten secondary clusters were detected in this study. The most likely cluster area was distributed in the southwestern of Shenzhen municipality and the clustering time was from January 2010 to November 2012 (*RR*=1.96, *P*<.001) with a total of 3000 PTB cases were notified during this period. In addition, the area centered at Nanshan Street of Nanshan District (22.53 N, 113.94 E) with a radius of 6.39 k m covered six streets just like the most likely cluster in the purely spatial clustering analysis. Other ten secondary clusters were mainly located at the central and northwestern Shenzhen municipality - covering streets in Baoan District, Nanshan District, Longgang District, Guangming District and Longhua District - and several relatively small areas (clusters 1, 4 and 8) in Futian District and Luohu District. The main clustering time ranged from January 2010 to March 2013 except the secondary clusters 2, 5, 6 and 9.

Table 3. Spatial-temporal clustering of notified PTB cases from 2010 to 2019 in Shenzhen municipality, China

Cluster type	Cluster time frame	Coordinates/ Radius	N[a]	Observed cases	Expected cases	RR[b]	LLR[c]	*P* value[d]
Most likely cluster	1 January 2010 to 30 November 2012	(22.53 N, 113.94 E) / 6.39 km	6	3000	1573.33	1.96	527.74	<.001
Secondary cluster 1	1 April 2010 to 28 February 2013	(22.58 N, 114.09 E) / 0 km	1	441	143.58	3.09	198.21	<.001
Secondary cluster 2	1 February 2017 to 30 November 2018	(22.72 N, 114.02 E) / 8.98 km	7	1943	1258.93	1.56	163.27	<.001
Secondary cluster 3	1 January 2010 to 30 September 2012	(22.58 N, 113.99 E) / 4.49 km	2	888	458.81	1.95	158.79	<.001
Seconda	1 March	(22.52 N, 114.07	1	728	366.75	2.0	139.0	<.00

ry cluster 4	2010 to 31 January 2013	E) / 0 km				0	2	1
Secondary cluster 5	1 March 2015 to 30 November 2017	(22.77 N, 114.31 E) / 6.33 km	2	772	416.77	1.86	121.77	<.001
Secondary cluster 6	1 March 2013 to 30 November 2015	(22.78 N, 113.90 E) / 0 km	1	373	147.19	2.54	121.47	<.001
Secondary cluster 7	1 March 2010 to 30 June 2012	(22.63 N, 113.84 E) / 5.28 km	3	1516	1006.46	1.52	113.75	<.001
Secondary cluster 8	1 March 2010 to 30 September 2011	(22.55 N, 114.14 E) / 3.72 km	6	706	447.87	1.58	63.76	<.001
Secondary cluster 9	1 July 2017 to 30 September 2017	(22.63 N, 114.14 E) / 5.94 km	7	261	164.74	1.59	23.92	<.001
Secondary cluster 10	1 March 2010 to 31 July 2010	(22.73 N, 113.81 E) / 5.13 km	4	317	219.60	1.45	19.05	<.001

[a]N: number of prefectures in the cluster.
[b]RR: relative risk.
[c]LLR: log likelihood ratios.
[d]*P* value: This is significant at a significant level of .05 (two-tailed).

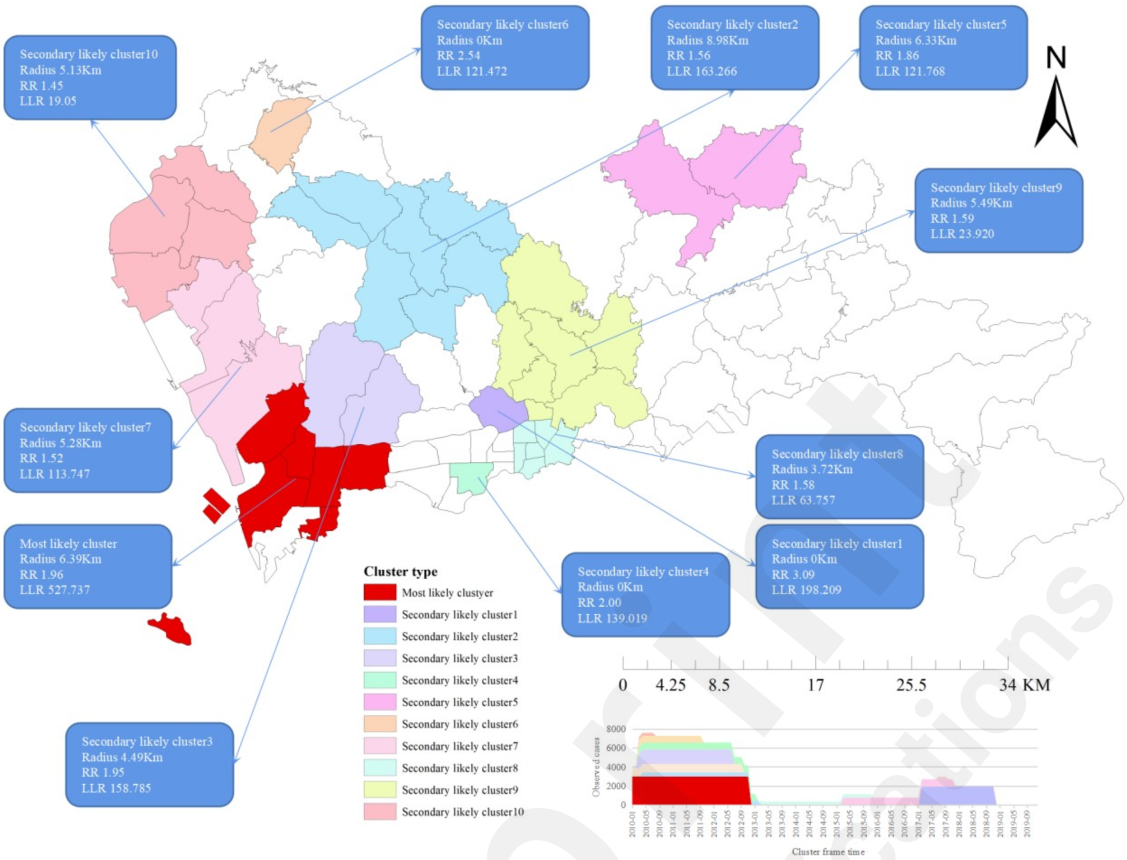

Figure 5. Spatial-temporal clustering of notified PTB cases from 2010 to 2019 in Shenzhen municipality, China

Discussion

Principal Findings

To the best of our knowledge, this is the first study to present a spatial-temporal cluster analysis of PTB at the street level in Shenzhen municipality using routinely collected PTB surveillance data, which identifies seasonal patterns and spatial-temporal clusters of PTB in Shenzhen.

The notification rate of PTB in Shenzhen municipality declined steadily during the ten-year study period, decreasing from the peak of 64.97 cases per 100000 population in 2010 to the lowest of 43.43 cases per 100000 population in 2019. This downward trend is in line with other municipal, provincial, and national studies [6, 16-19]. The achievement is due in large part to the great importance attached by the local government and health administrative department in Shenzhen to PTB control and prevention in recent years. First, financial support received from the government has increased continuously from RMB 28.2 million in the Twelfth Five-Year Plan (2011-2015) to about RMB 197.64 million in the Thirteenth Five-Year Plan (2016-2020) for TB control and prevention in Shenzhen. Following that, an integrated system under the collaboration of Centers for Disease Control and Prevention, tuberculosis-designated hospitals, and community health services centers was established and developed among the institutions with a clear division of labor and coordination [20]. In addition, a batch of molecular biological testing equipment for PTB diagnosis and treatment has been purchased and distributed to designated PTB medical institutions in various streets and districts of the city [20]. As a result, the diagnosis time of PTB and the possibility of pre-treatment transmission has declined, despite the percentage of cases detected and confirmed bacteriologically has increased. At the same time, PTB screening programs were added into the physical examination for the elderly aged 65 or above and for primary and secondary school students, and the rifampicin resistance testing was further strengthened on PTB patients [21]. In addition to the DOTs recommended by the WHO since 2000, Shenzhen has implemented a series of measures including providing free drug treatment and a certain degree of reimbursement for examination costs, so that PTB patients can be diagnosed and treated early to effectively curb the spread of disease. With the implementation of these targeted and effective measures, the PTB epidemic situation has improved greatly, though it is still a great challenge in Shenzhen municipality.

Via time series analysis, seasonal variations and cyclical trends were observed with apparent peaks in late spring and summer, especially in May and July. This is consistent with the findings of neighboring Guangzhou city [22]. Shenzhen has a subtropical monsoon humid climate, long summer and short winter, abundant sunshine, and abundant rainfall, with the average annual temperature and relative humidity of over 20 degrees Celsius and 80%, respectively. This is aligned with the transmission of respiratory infectious diseases and may be related to the spread of PTB. Previous studies indicated that lack of exposure to ultraviolet from sunlight and the poor ventilation in the indoor environment may increase the risk of PTB infection [23-25]. Consistent with other reports [17, 18], there were the least notified PTB cases in January and February. On one hand, this may be closely related to the massive public transportation and population flow during the Chinese Spring Festival usually in late January or February [22, 26], when many migrants left Shenzhen to return to their hometowns. On the other hand, people are busy celebrating the Lunar New Year, coupled with the frequent visits to relatives and friends during the period, and avoiding seeking medical care [17, 18]. These multiple factors resulted in a significant decline in PTB cases reported but an increased risk of transmission among the infectious source and the close contactors during the holiday, concentrating in late spring and summer after an incubation period of several months to half of a year, including a two-month interval from the symptom appearance to medical diagnosis [24]. This may be one of the contributors for the peak months in Shenzhen. In addition, the return of migrants and the delayed diagnosis should also be considered. Therefore, the detection and tracking of PTB patients should be strengthened during the Spring Festival, and suspected or confirmed cases should be transferred to designated medical institutions for further diagnosis and treatment as soon as possible, to shorten the delay time of treatment and reduce the risk of transmission. Health education should also be emphasized, and effective measures like actively wearing masks and opening windows for ventilation should be promoted, especially in crowded places.

Many studies have confirmed a spatial clustering distribution of PTB in a certain area [6, 17, 18, 27]. In this study, the global spatial autocorrelation analysis indicated that the notification rate of PTB in Shenzhen municipality displays an obvious spatial clustering distribution between 2010 and 2019. The results of advanced local spatial autocorrelation showed that the clusters of PTB at the street level had a dynamic change over time, from the southwest to the central and northern part of the city. The hotspots of PTB observed in the present study are basically aligned with the PTB notification rates in Shenzhen. PTB has long been known as ‘the disease of the poor’, and poverty has been considered as one of the causes of disease clustering [27-30]. However, previous study indicated that the incidence of PTB is higher in areas with better economic situation than in less developed areas because they are more attractive to population inflows [31]. Many migrants are at increased risk of ill health because of the backward conditions through which they travel and then work and live [32]. Migrant workers are usually not entitled to social welfares and health resources as local permanent residents, which made this specific population hard to access healthcare service [33, 34]. In this study, most of PTB cases are workers or unemployed, and they move with the economic development of local areas of the city. The regional economic development in the past 10 years started from Nanshan District and Baoan District in southwest Shenzhen, whose GDP ranked in the top three during the periods. With the change of urban planning, the GDP in the central and northern Shenzhen including Longhua District, Longgang District and Guangming District has grown rapidly recently, which has brought about a more obvious population agglomeration effect in these areas

[35]. Similar dynamics can also be found in Beijing [36] and Shanghai [37]. Understanding the interaction of TB transmission, population migration, and social development, albeit highly complex and dynamic, is essential for the control and prevention of TB [31].

Taking the role of time in the geographical distribution of PTB into account, the spatial-temporal scanning analysis was used to supplement the local spatial analysis. The results from the spatial-temporal clustering analysis of the PTB cases from 2010 to 2019 showed that the most likely cluster was concentrated in the southwestern Shenzhen, covering six streets of two districts, and the clustering period was from January 2010 to November 2012. In addition, most of the secondary clustering areas were also in this period, indicating that this period is the peak of PTB transmission in Shenzhen. The clusters identified by the spatial-temporal scanning analysis and the simple spatial clustering analysis were similar, which may show the robustness of our results. More importantly, these similar findings indicate that more effective and targeted measures should be urgently developed and implemented in the high-risk areas for PTB control and prevention in Shenzhen municipality.

Compared with the Guangdong provincial and China national findings in recent years [38, 39], Shenzhen has entered the low epidemic level of PTB. However, there is still far from the WHO goal of ending PTB. This requires stronger, more tailored and effective responses to achieve such an ambitious goal. First, the clustering results guide us to develop more accurate and effective interventions, with a focus on areas where PTB is concentrated, and to strengthen the deployment and implementation of corresponding actions to prevent and discover the outbreak and epidemic of PTB at the street level. PTB diagnosis, treatment, and care for migrants should be integrated into the general health services, while special efforts may be needed to reach migrants, for availability, accessibility, and quality of comprehensive medical services [40]. Screening for PTB contacts and selected high-risk groups should be linked to follow-up, strategies for preventive treatment or referral to the treatment program [40]. In addition, systematic and extensive health educational campaigns are needed for the provision of more accessible information to raise public awareness of PTB and improve public access to relevant health care services. Third, increasing the speed of referral of newly detected PTB patients to designated clinics is also crucial to minimize the risk of disease transmission and infections in the community.

Limitations

This is the first time to analyze the spatial-temporal clustering characteristics of PTB at the street level and identify the high-risk areas of PTB in Shenzhen municipality, which provides us with valuable information for future strategies and measures of PTB prevention and control. However, this study was subject to several limitations. First, our analysis was based on data extracted from the National Surveillance System and we were unable to preclude the possibility of missing cases' report. This might cause an underestimation of PTB epidemic in Shenzhen. Second, the current study only focused on the spatial and temporal patterns and clusters of PTB cases. Potential risk factors associated with PTB incidence like individual habits, socio-economic status, living conditions and environmental pollutant, were not evaluated in the present study. Further research should take these limitations into consideration.

Conclusions

This study identified spatial, temporal patterns and spatial-temporal clusters of PTB cases at the street level in Shenzhen municipality from 2010 to 2019. A volatile downward trend of PTB incidence over the study period was observed in Shenzhen municipality. The most likely clustering areas changed from the southwest to the central and northern part of the city, and the most likely clustering time was late spring and summer. Resources should be prioritized to high-risk areas for

PTB prevention and control.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions
PL and ZZ; methodology, PL and WC; software and analysis, PL; validation, WT and ZZ; formal analysis, PL and WC; resources, ZZ; writing—original draft preparation, PL, WC, LQ, CH and KL; writing—review and editing, WT and ZZ; visualization, PL; project administration, PL and ZZ. All authors read and approved the final manuscript.

Competing interests
None declared.

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Multimedia Appendix 1
Supplementary material

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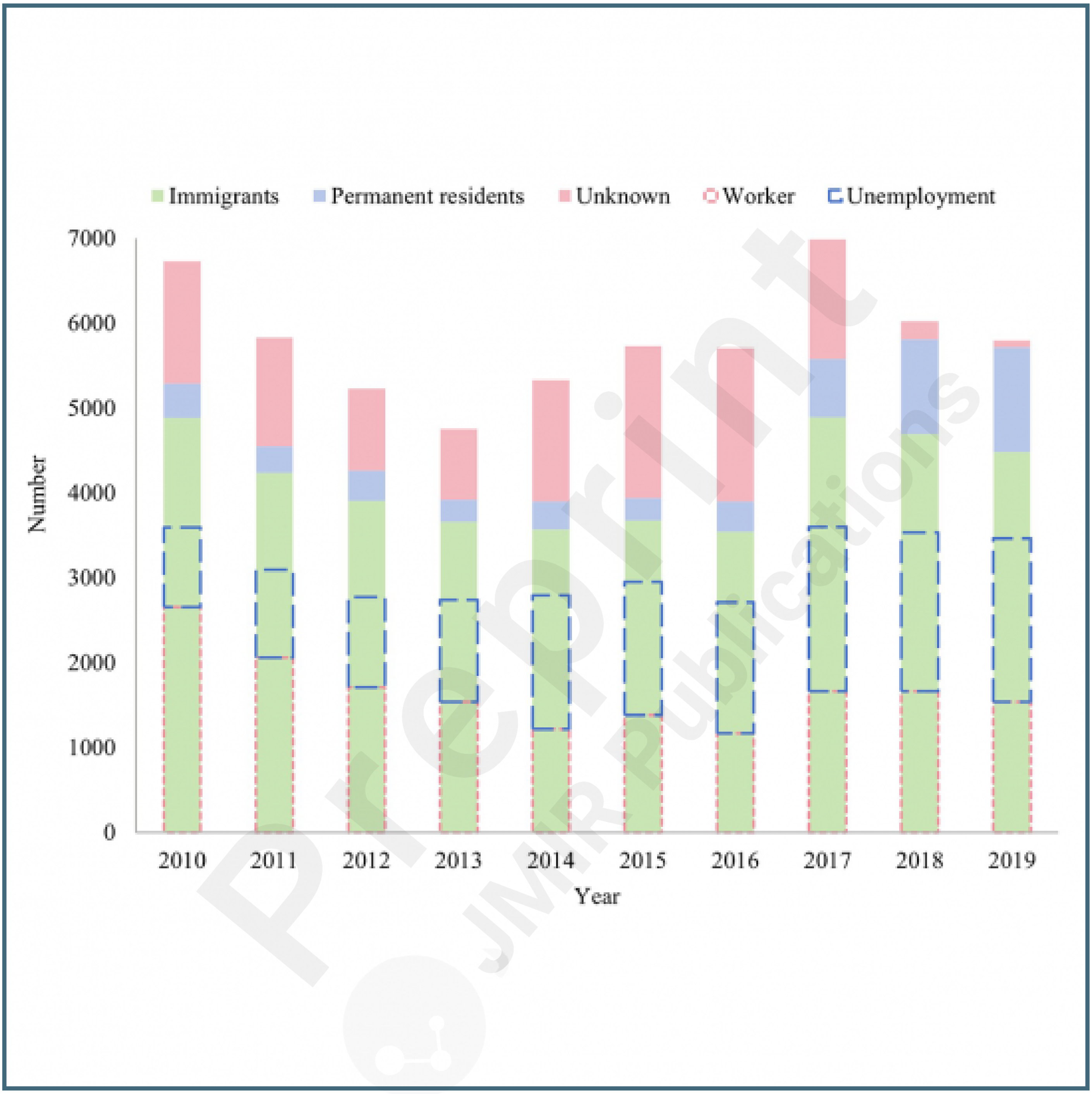
Abbreviations
PTB: Pulmonary tuberculosis
TB: tuberculosis
WHO: World Health Organization
DOTS: directly observed therapy strategy
CCDC: Chinese Center for Disease Control and Prevention
GDP: gross domestic product
LLR: log likelihood ratio
RR: relative risk

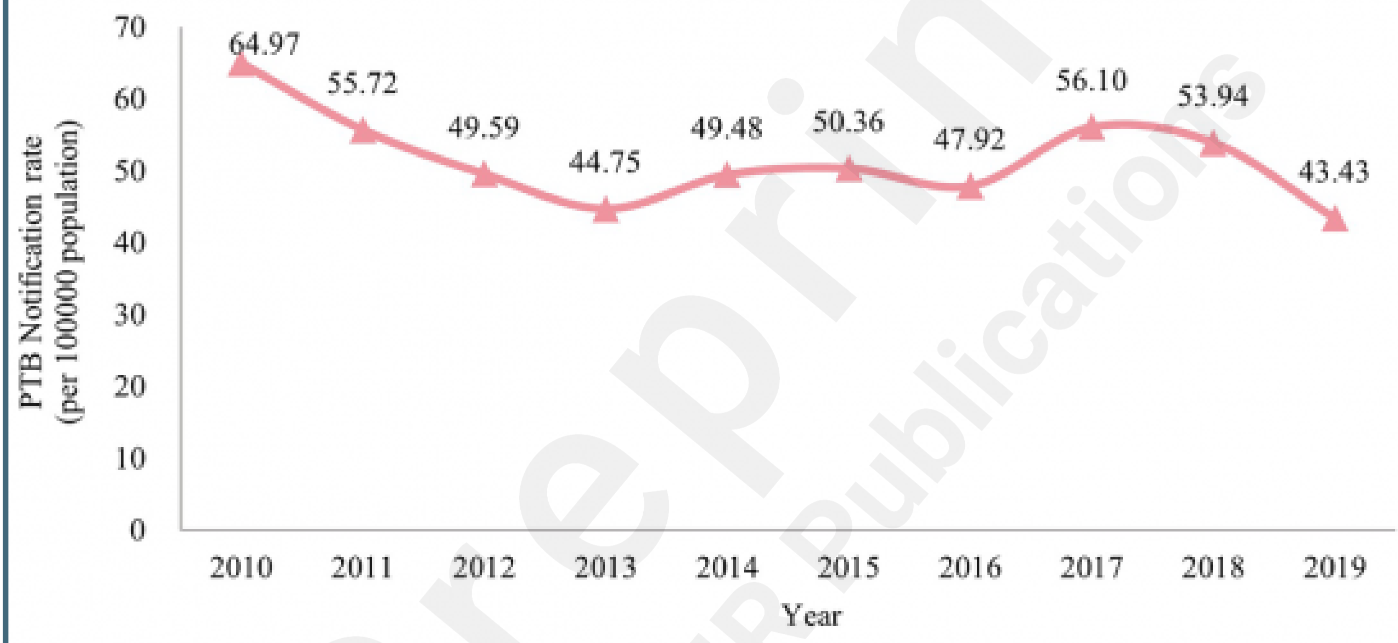
Supplementary Files

Figures

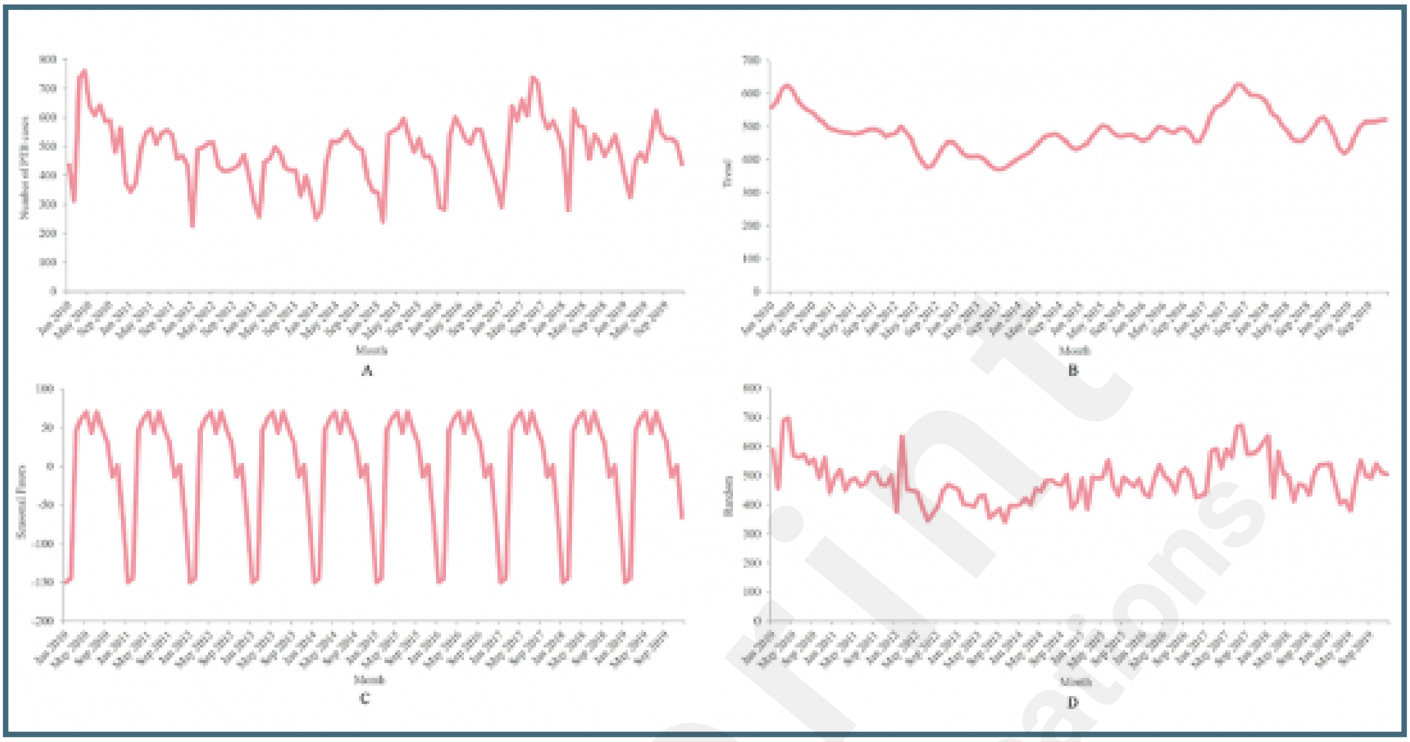
Characteristics of PTB cases from 2010 to 2019 in Shenzhen municipality, China.



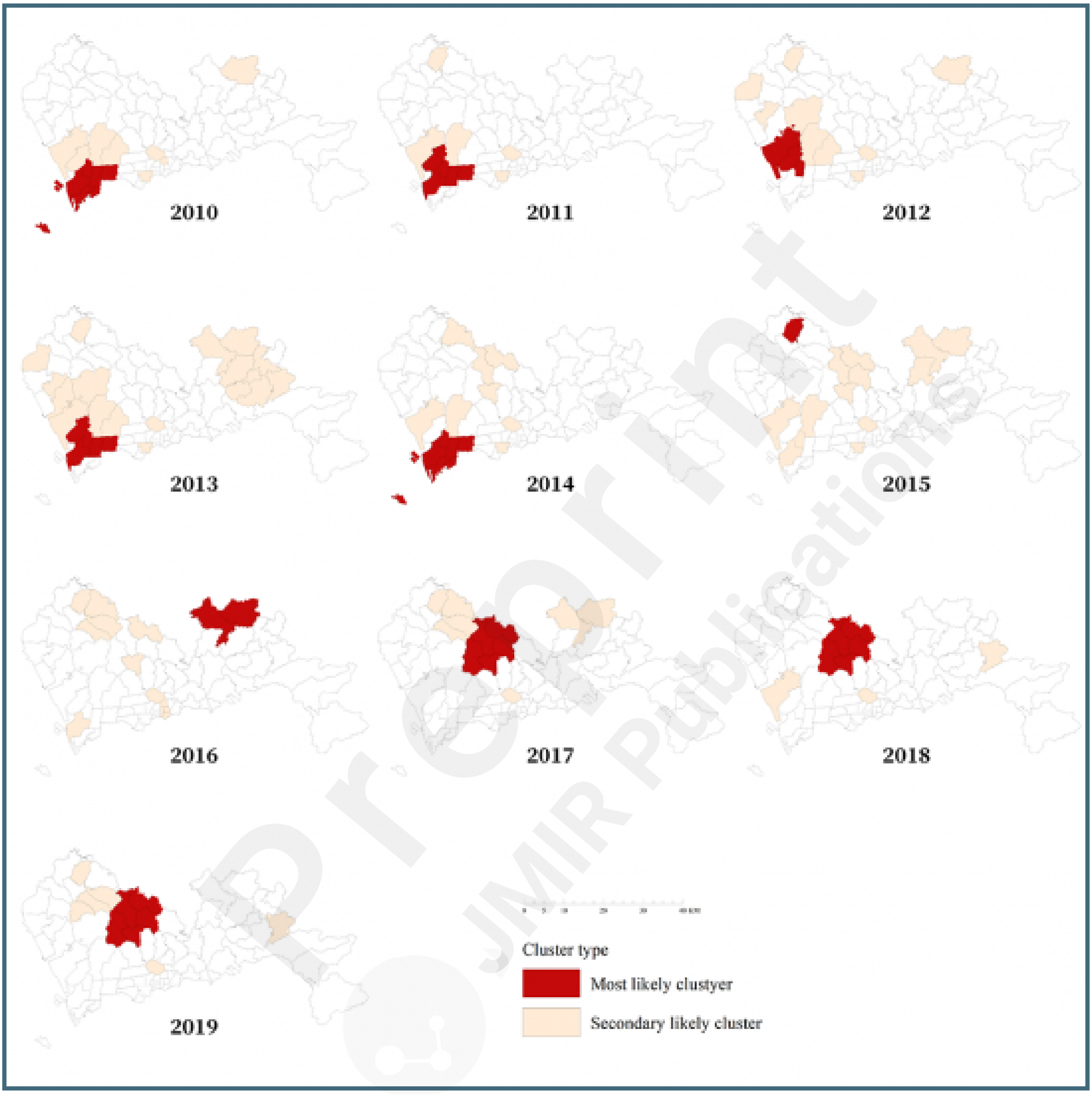
The variation trend of PTB notification rate (per 100000 population) from 2010 to 2019 in Shenzhen municipality, China.



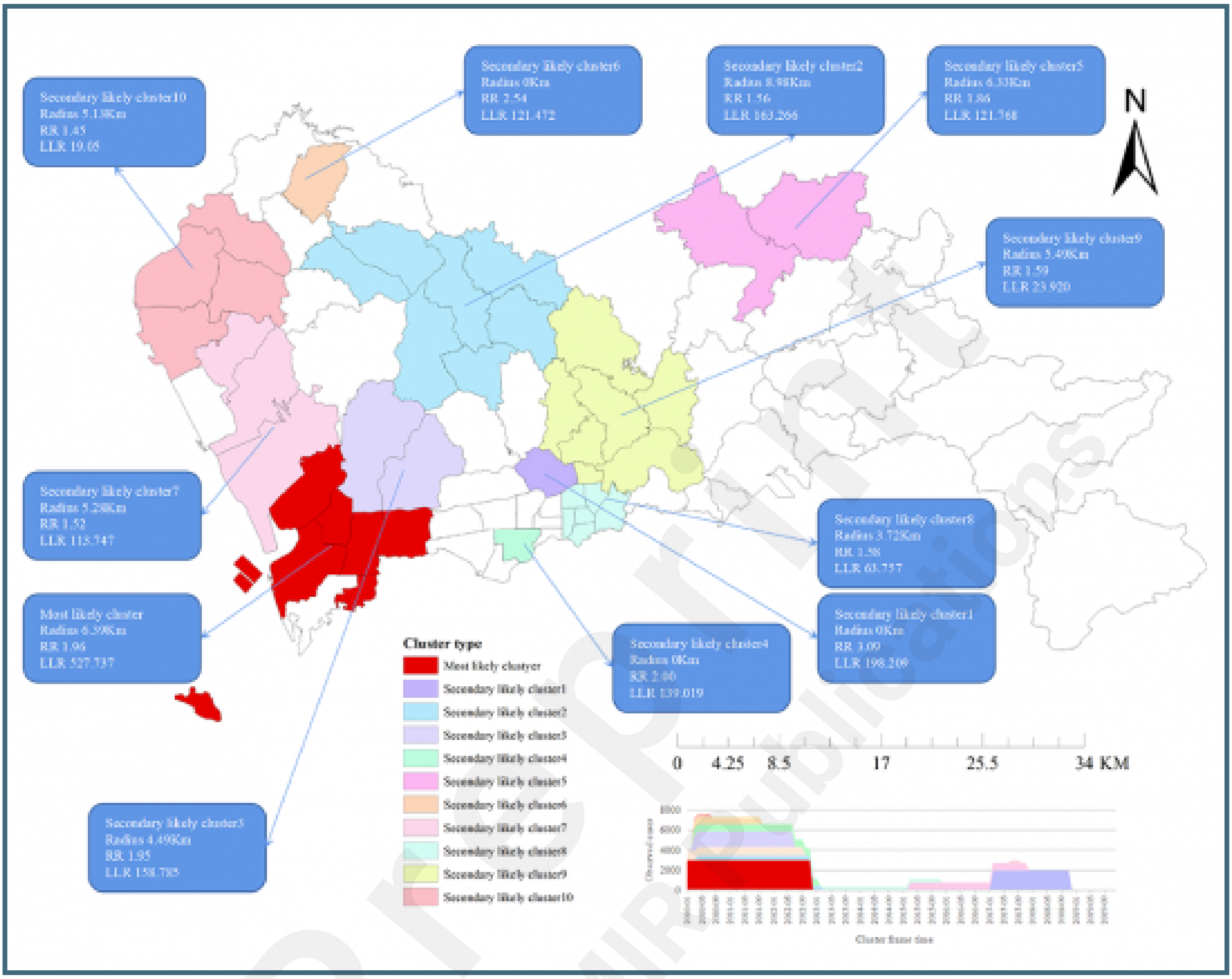
The seasonal distribution of monthly PTB cases from 2010 to 2019 in Shenzhen municipality, China.



The spatial clusters of notified PTB cases from 2010 to 2019 in Shenzhen municipality, China.



Spatial-temporal clustering of notified PTB cases from 2010 to 2019 in Shenzhen municipality, China.



Multimedia Appendixes

Supplementary figure. The location of Shenzhen Municipality in China.
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