Letter to the Editor

The Spatiotemporal Dynamic Distributions of New Tuberculosis in Hangzhou, China

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Pulmonary tuberculosis (TB) remains a global health threat worldwide, despite the availability of effective antibiotics for drug-sensitive TB for decades. This is in part due to the ongoing transmission from cases of undiagnosed TB[1] and drug-resistant TB (DR-TB)[1]. China has the second largest number of multidrug-resistant TB (MDR-TB) cases worldwide, which is estimated at 73,000 MDR-TB or rifampicin-resistant TB (RR-TB) cases and accounts for 13% of the global burden[1]. The results of China's Fifth National TB Epidemiological Survey indicated that the prevalence of TB in the western region was more than three times the eastern region and twice the central region[2]. However, whether TB distributions appeared in the same way in smaller regions at county level is still unclear.

Previous studies argued that TB demonstrated highly complex dynamics and spatially heterogeneity at the national[3] and provincial level[4] in China. Hangzhou, one of the most developed cities in eastern China, is experiencing the largest population migration in history. Human activities may help TB transmission span the boundaries of an individual area, thereby making the prevalence more complicated[5]. The latest studies on the spatial distributions of TB at county level in Hangzhou were quite few[6]. Ge et al. reported the unevenly distributed TB cases in Zhejiang province from 2009 to 2012[6]; however, more detailed information about Hangzhou remained uncertain. Thus, it is of great significance to identify whether the heterogeneity of spatiotemporal distributions existed in Hangzhou.

We are targeting new TB patients with three main reasons: 1) to avoid data repetition from already treated patients; 2) to try to identify the new areas with high TB burden; 3) to target new cases which were usually associated with TB transmissions recently and new outbreaks. We investigated the spatiotemporal dynamics distributions of new TB using a finer scale at county level and examined the spatiotemporal patterns of TB distributed in Hangzhou between 2009 and 2018. Briefly, information of new smear-positive TB patients was exported from 'China TB information management system'. Medical records with the status 'completed' were selected, excluding those marked with 'diagnostic changes' and 'Hong Kong SAR, China, Macao SAR, China, Taiwan, China, and foreign countries'. Geographic information of patients was transformed into longitude and latitude coordinates using Google map online. These coordinates were imported into ArcGIS to produce a point file. In addition, Kernel Density Analysis could be operated under the default parameters (ArcToolbox > Spatial Analyst > Kernel Density Analysis). The 'population field' could be 'none' and the output pixel size was 0.0001. The search radius (which usually was 0.01) could be adjusted to try to achieve a better view. The GIS-based spatial analysis exploring the geographic distribution patterns of TB could provide scientific reference for local policymakers to establish a more precise TB prevention and control strategy.

From January 1, 2009 to December 31, 2018, 43,204 patients were diagnosed with culture-positive TB in Hangzhou. Migrants with TB were significantly younger (P = 0.001) and were more likely engaged in physical labor (P < 0.0001). Residents with TB were most likely farmers or herdsmen (P < 0.0001) (Table 1). Figure 1A showed the total number of TB cases in each month, and Figure 1B exhibited mean TB case per day by month. It revealed a strong seasonal pattern with a large number of TB appearances in March and April and then fell until it hit its lowest point in December (Figure 1A and B). Figure 1C showed the trends of TB incidence rate per 100,000 population on county level every year. Gongshu had the highest incidence rates (more than 95 per 100,000 population) in

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2009, and the overall incidence rates of each county was decreasing year by year from 2009 to 2018 (Figure 1C). The mean incidence rate of TB in Hangzhou from 2009 to 2018 was 51.42 per 100,000 population. In the first 5 years, Gongshu had the highest mean incidence rate of 84.54 (Figure 2A), and in the later 5 years, higher mean incidence rates extended to more districts: Yuhang, Gongshu, Binjiang, and Chunan (Figure 2A). However, the mean incidence rates of Yuhang, Gongshu, and Chunan were the highest among all districts from 2009 to 2018 (Figure 2A).

We performed kernel density estimation to identify patterns of spatial aggregation of TB patients[7]. Kernel density estimation every two years indicated that most patients were located in populated centers of cities or counties. Nevertheless, several high density points also appeared in remote rural areas in mountainous southwest Hangzhou. In addition, high density areas were extending from urban centers to the surroundings during the past decade (Figure 2B).

The seasonal pattern of TB cases suggested that warm spring may be related to high incidence; however, cold winter may help the spread of TB transmission slowly. This pattern has also been reported previously in other studies[6]. Moreover, more studies should be done to figure out the relationships between TB transmission and temperature alterations. In the present study, we presented dynamic descriptions of TB at county level and discovered that the overall TB incidence rate was decreasing in Hangzhou over the decade. However, TB patients are more prevalent in urban areas, and this seems to be increasingly evident. The reasons can be attributed to the following. Reason number one is the aging of the population at the national level and the fact that low fertility and

Table 1. Characteristics of new TB patients in Hangzhou, China, 2009–2018 (*n* = 43,204)

Patients imformation	Resident (*n* = 28,822)	Migrant (*n* = 14,382)	Frequency		*P*
			n	%	
Gender					
Male	19,379	9,725	29,104	67.36	0.424
Female	9,443	4,657	14,100	32.64	Reference
Age, years					
≤ 20	1,909	1,490	3,399	7.87	Reference
21–39	9,344	8,274	17,618	40.78	0.001
40–59	7,866	3,013	10,879	25.18	< 0.0001
60–79	7,847	1,301	9,148	21.17	< 0.0001
≥ 80	1,856	304	2,160	5.00	< 0.0001
Occupation					
Commercial service	1,695	1,175	2,870	6.64	Reference
Domestic service	2,312	1,738	4,050	9.37	0.101
Farmer/Herdsman	13,927	3,875	17,802	41.20	< 0.0001
Physical labor	4,205	5,445	9,650	22.34	< 0.0001
Teacher	204	47	251	0.58	< 0.0001
Student	1,718	910	2,628	6.08	< 0.0001
Retired	3,077	551	3,628	8.40	< 0.0001
Cadre staff	1,374	574	1,948	4.51	< 0.0001
Medical staff	287	53	340	0.79	< 0.0001
Other	23	14	37	0.00	0.703
Sputum smear results					
Positive	9,683	4,233	13,916	32.21	< 0.0001

mortality rates of China are expected to accelerate[8]. Aging leads to more individuals being of an age in which reactivation of latent TB is more likely to occur. Second reason is the rapid urbanization of China in recent decades. The influx of increased population from rural areas, called 'migrants', to central cities like Hangzhou has been increasing. Migrant patients with TB accounted for 33.29% of TB cases in this study (Table 1), and they lived temporarily around the urban center of Hangzhou (Shangcheng and Xiacheng) (Figure 2A). A larger number of them engage in physical labor (Table 1), and they know little about TB disease and public health policies and have limited health care insurances and are more likely to delay seeking help when they get sick[9]. Therefore, they should be managed in priority groups by local government in infectious management.

In addition, kernel density analysis revealed several high density points in rural areas far away from TB-designated hospitals (Figure 2B). Geographic accessibility is not the determinant factor for patients accessing health care services timely; however, it plays a critical role in patients' therapeutic outcomes[10]. The mountainous southwest areas of Chunan and Jiande have complex terrain structures and inconvenient transportations and are far away from TB-designated hospitals (Figure 2B). High density points were found in these areas and they should be paid more attention.

However, some limitations of the present study should be noted. First, and most importantly, our ability to reliably infer patterns of TB dynamic distributions in terms of time and space was dependent on the exact time of onset of TB-related symptoms and the residential addresses we collected which were provided by patients on the day of admission. The time of registration was acquired from patients according to how they remembered it, and the residential address may change later for migrant patients. Second, our studies only included culture-positive TB patients, and this was somewhat limited actually.

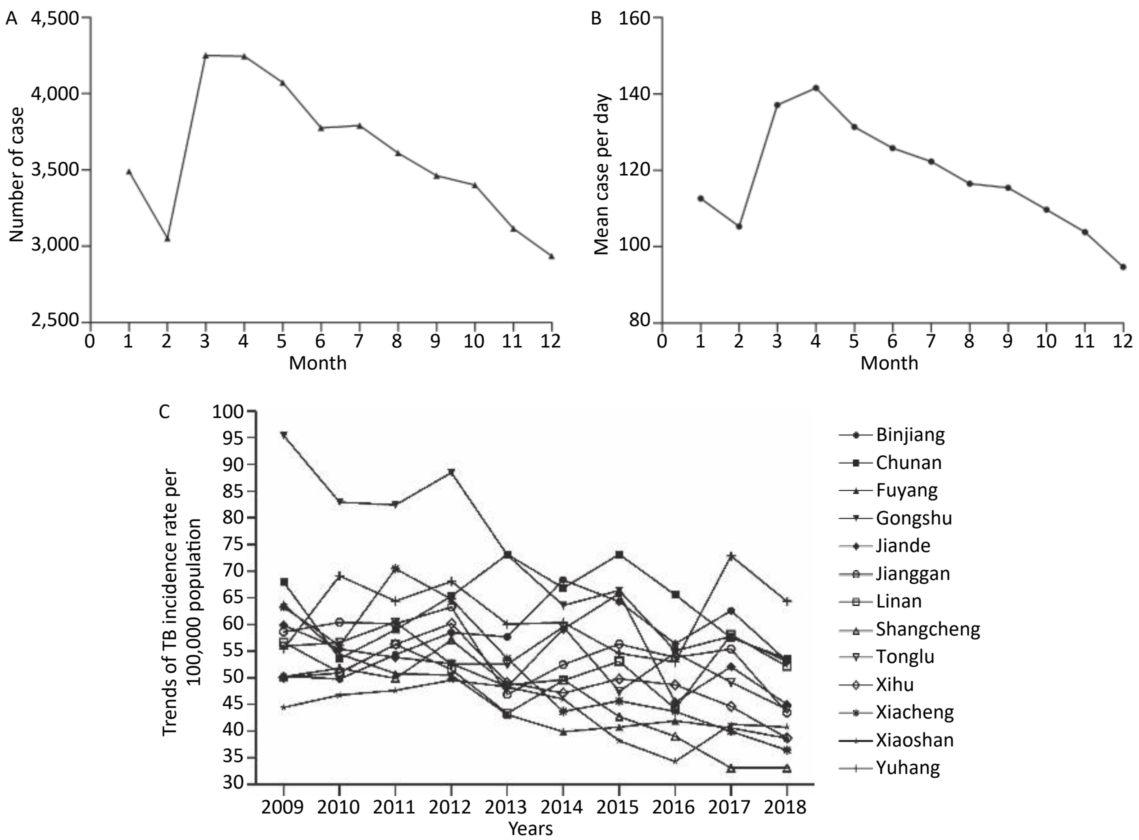

Figure 1. Time distributions of new smear positive TB cases enrolled in this study. Total number of TB case in each month (A). Mean TB case per day by month (B). Trends of TB incidence rate per 100,000 population on county-level every year (C).

In conclusion, we demonstrated the dynamic time-space analysis of TB in Hangzhou from 2009 to 2018. The trend of TB incidence rate per 100,000 population was decreasing year by year. However, the mean incidence rates of Yuhang, Gongshu, and Chunan were still higher than other districts. In addition, kernel density estimation demonstrated that urban centers had more patients, and ranges of high density tended to expand gradually over the past decade. Furthermore, TB-designated hospitals distributed unevenly, and this may increase risks of TB transmission and costs of TB treatment for patients in rural areas.

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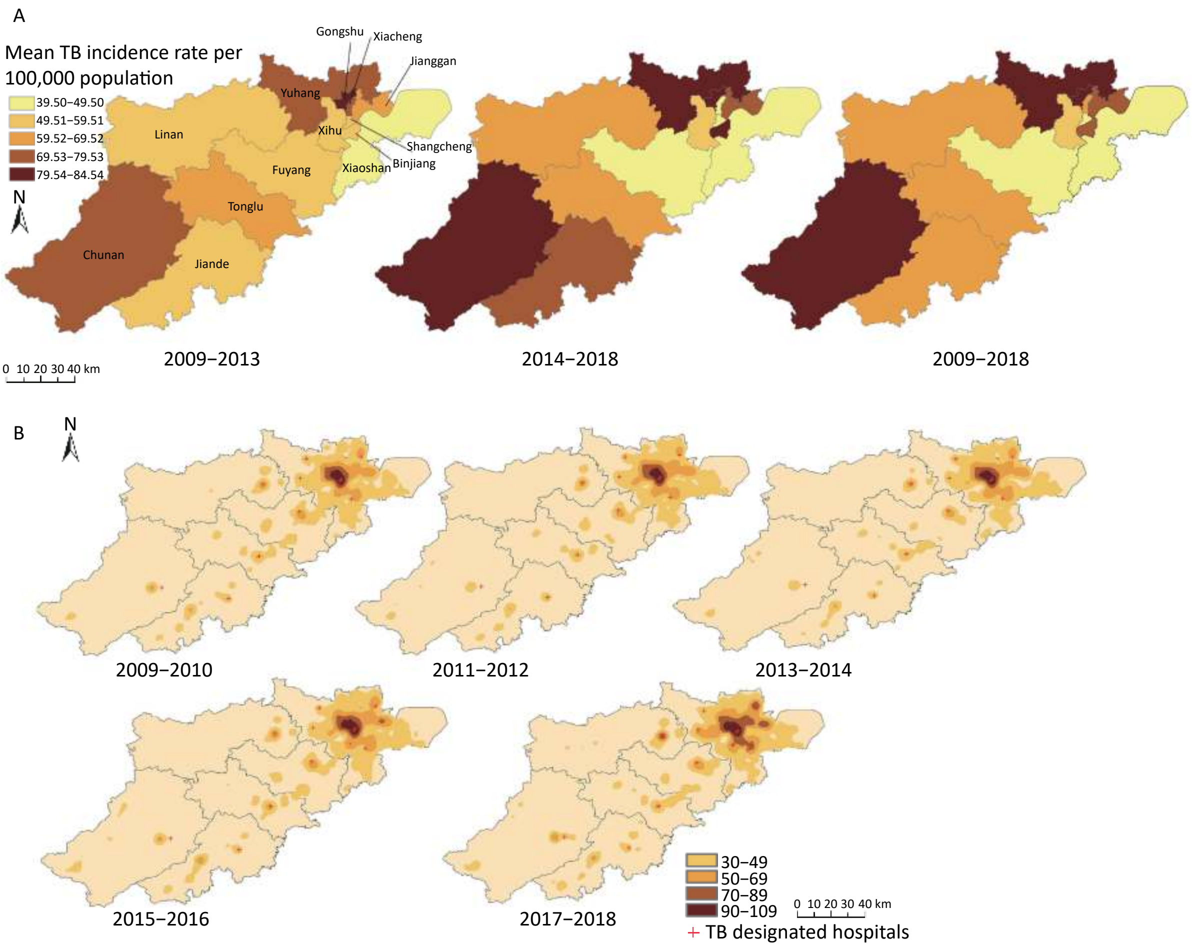

Figure 2. Space distributions and kernel density estimation of TB in Hangzhou, China 2009–2018. Mean TB incidence rate per 100,000 population (Mean TB case/ mean population) by districts in Hangzhou (A). Changes of kernel density estimation for TB case every two years in Hangzhou (B).

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