Specific urban units identified in tuberculosis epidemic using a geographical detector in Guangzhou, China

Hongyan Ren¹*, Weili Lu¹,², Xueqiu Li³ and Hongcheng Shen³

Abstract

Background: A remarkable drop in tuberculosis (TB) incidence has been achieved in China, although in 2019 it was still considered the second most communicable disease. However, TB’s spatial features and risk factors in urban areas remain poorly understood. This study aims to identify the spatial differentiations and potential influencing factors of TB in highly urbanized regions on a fine scale.

Methods: This study included 18 socioeconomic and environmental variables in the four central districts of Guangzhou, China. TB case data obtained from the Guangzhou Institute of Tuberculosis Control and Prevention. Before using Pearson correlation and a geographical detector (GD) to identify potential influencing factors, we conducted a global spatial autocorrelation analysis to select an appropriate spatial scales.

Results: Owing to its strong spatial autocorrelation (Moran’s $I = 0.33$, $Z = 4.71$), the 2 km × 2 km grid was selected as the spatial scale. At this level, TB incidence was closely associated with most socioeconomic variables ($0.31 < r < 0.76$, $P < 0.01$). Of five environmental factors, only the concentration of fine particulate matter displayed significant correlation ($r = 0.21$, $P < 0.05$). Similarly, in terms of q values derived from the GD, socioeconomic variables had stronger explanatory abilities ($0.08 < q < 0.57$) for the spatial differentiation of the 2017 incidence of TB than environmental variables ($0.06 < q < 0.27$). Moreover, a much larger proportion ($0.16 < q < 0.89$) of the spatial differentiation was interpreted by pairwise interactions, especially those ($0.60 < q < 0.89$) related to the 2016 incidence of TB, officially appointed medical institutions, bus stops, and road density.

Conclusions: The spatial heterogeneity of the 2017 incidence of TB in the study area was considerably influenced by several socioeconomic and environmental factors and their pairwise interactions on a fine scale. We suggest that more attention should be paid to the units with pairwise interacting factors in Guangzhou. Our study provides helpful clues for local authorities implementing more effective intervention measures to reduce TB incidence in China’s municipal areas, which are featured by both a high degree of urbanization and a high incidence of TB.

Keywords: Tuberculosis, Geographical detector, Specific urban units, Pairwise interaction, Guangzhou, China

© The Author(s) 2022. Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

*Correspondence: renhy@igsnrr.ac.cn

1 State Key Laboratory of Resources and Environmental Information System, Institute of Geographic Sciences and Natural Resources Research, Chinese Academy of Sciences, Beijing 100101, China

Full list of author information is available at the end of the article
Owing to the progress made in providing essential TB services by health authorities in different countries worldwide, a large global drop in the number of newly diagnosed TB cases has been achieved [1]. Over the last 15 years, the incidence of TB has declined to 55.55 per 100,000 inhabitants in China; nevertheless, it was still the second most communicable disease in China in 2019 [4]. Among China’s southeast coastal provinces, which have a relatively low TB incidence and better socioeconomic development than China’s central and western regions, Guangdong presented the highest incidence, which is somewhat surprising based on its socioeconomic situation. This puzzle has increasingly attracted the attention of researchers [5].

Scholars from around the world have conducted considerable research into TB epidemics, including the risk factors affecting its transmission and the corresponding prevention and control measures [6–12]. These studies have shown that the survival, suspension, and spread of M. tuberculosis expelled by infected people were often prolonged and promoted by environmental factors (e.g., high temperature, appropriate humidity, and a certain concentration of airborne particulate matter), while the dispersal of its carriers (e.g., saliva and particulate matter) was inhibited by frequent precipitation and favorable vegetation coverage [13–15]. Meanwhile, the exposure and infection probability of susceptible populations, as well as the diagnosis and treatment of TB cases, are heavily influenced by a series of social and economic factors (e.g., higher population density, more frequent population flow, uneven household income, scarce medical resources, and a well-developed public transportation system) [9, 16, 17]. However, possible interactions or combinations among these potential influencing factors, the spaces where they tend to happen, and their relationships with the incidence of TB remain underexplored.

Moreover, many epidemiological studies have been conducted to identify the dominant influencing factors in some endemic areas at various spatial scales, including the country, province, city, county or district, township or street, village, and even regular grid, which was meaningful for health authorities designing and implementing targeted interventions to reduce the incidence of TB [6, 7, 9, 12, 16–20]. However, the key factors identified as influencing TB epidemics in the above investigations were different due to the different spatial scales used. There have been a number of studies on the optimal choice of scale, especially for regular grids [21–23]. To some extent, small spatial scales are often the final units where prevention and control measures can produce practical effects, and more research into the factors influencing the incidence and prevention of TB is required on a fine spatial scale, especially within a city or its internal areas [24, 25].

Therefore, this study was conducted to characterize the spatial patterns of the 2017 incidence of TB across the central areas of Guangzhou through spatial autocorrelation analysis, and a geographical detector (GD) was used to further identify specific urban units with potential socioeconomic and environmental factors affecting this disease’s spread on a fine scale. The aim here was to provide effective guidance for relevant government departments designing and implementing targeted prevention and control measures to reduce the incidence of this disease in highly urbanized regions with severe TB epidemics.

**Methods**

**Study area**

Guangzhou City is a typical representative of China’s megacities with more frequent population flows, more efficient and complex functional zones, more plentiful and fragmentized types of land uses, and more places or sites featured by variable microclimates [26]. The characteristics of its subtropical monsoon climate are obvious: warm and rainy, enough light and heat, an annual average temperature of 21–23 °C, and an average annual precipitation of 1800 mm. As the most important districts in Guangzhou City, the four central districts (i.e., Yuexiu, Haizhu, Tianhe, and Liwan) are featured by their higher population density, vigorous economic activities, more frequent population flows, comprehensive public facilities, and convenient public transportation [27], by which we consider them as the study area (Fig. 1).

**Data collection**

The TB epidemic data were obtained from Guangzhou Institute of Tuberculosis Control and Prevention, and included TB cases data from 2016 and 2017 (taking the newly diagnosed TB cases reported in 2017 as the dependent variable and existing cases reported in 2016 as a potential influencing factor). Relevant information included age, sex, permanent residence address, and occupation, as well as time of disease onset and diagnosis. Permanent residence address data was used in conjunction with geocoding (restapi.amap.com/v3/geocode) and coordinate deviation correction to produce cases data for a spatial point layer (Fig. 1) using ArcGIS 10.3 (ESRI, Redlands, CA, USA) software, in which the ratio of the number of TB cases to the total population in 2015 was calculated on a fine scale to indicate the TB incidence rates across the central districts. In 2017, the incidence of TB in Guangzhou was relatively high, with a total of 14,100 newly diagnosed cases, of which 4,313 were from the study area, accounting for 30.6% of the total, while this area only accounts for 4.5% of the entire area of Guangzhou.
According to previous studies [2, 7, 9, 12, 15–17, 28, 29], we gathered 18 potential factors from various data sources and then categorized them into two groups, listed in Table 1. Among 11 socioeconomic factors, the population-related factors included the incidence of TB in the previous year and the 1 km × 1 km gridded population density. The economic situation was analyzed based on the 1 km × 1 km gridded gross domestic product (GDP) per capita, and information with respect to officially appointed medical institutions included the medical resources that have been officially certified by local health departments to supply local residents with professional health services and to facilitate reimbursement of health service expenses to the patients. The road network, bus stops, and subway stations were selected to represent the condition of the public transportation system. With regard to potential influences of land use, the percentages of four typical kinds of land use in the central area—residential, commercial service, public service, and urban villages—were also calculated in this study. In addition to the above socioeconomic variables, five environmental conditions in 2017, including monthly mean values of the normalized difference vegetation index and the fine particulate matter concentration, as well as the average climatic conditions (temperature, precipitation, and humidity) from March to June, were simultaneously considered as potential variables influencing the prevalence of TB.

For the data of officially appointed medical institutions, medical points that do not serve the community (only designated personnel) were removed according to their service recipients. The officially appointed medical institutions were then divided into outpatient (Hosp11), inpatient and outpatient (Hosp12) types according to the range of medical institution services.

To facilitate statistical and spatial analysis, the dependent variable (2017 incidence of TB) and 18 independent variables, with different data types (vectors) or diverse resolutions (raster) as given in Fig. S1 (Additional file 1), were summarized and aggregated into a uniform spatial scale by using the spatial join, zonal statistics, and field calculation tools in ArcGIS 10.3 software.

Spatial scale
Owing to the constant changes of administrative divisions in China—in particular the districts, towns, streets, and villages—research units assigned by these divisions in relevant studies were likely to cause difficulties in conducting spatiotemporal analysis. To avoid this issue, replacing them with some regular grids is an appropriate solution [21]. In particular, these spatial grids are gradually considered as the final units where
prevention and control measures can produce practical effects in urban regions [24, 25].

In this study, a series of regular grids (1 km × 1 km–5 km × 5 km) were constructed, by which the optimal grid scale characterizing the spatial pattern of TB epidemic was selected based on Moran’s I and Z-scores [32]. Moran’s I was calculated as follows.

\[
I = \frac{\sum_{i,j} w_{ij} (x_i - \bar{x})(x_j - \bar{x})}{\sum_{i,j} w_{ij} x_i^2 - \left(\sum_{i} w_{ij} x_i\right)^2}
\]

(1)

where \( n \) is the number of grids in the study area, \( x_i \) and \( x_j \) represent the TB incidence rates in grids i and j, respectively. \( \omega_{ij} \) is the spatial weight. Global Moran’s I is generally tested by the Z-score/P-value, and the value varies from −1 to 1. A higher Moran’s I (larger Z-score and proper P-value) indicates greater similarity among attributes between adjacent spatial grids, which reveals that the TB epidemic is clustered in the region, whereas a low negative value indicates dissimilarity between adjacent grids and shows that the TB epidemic is discretely distributed in the region. In this study, Moran’s I and Z-scores of the TB incidence rates with different grid sizes were used to assess the optimal grid scales of the regional TB epidemic. Global Moran’s I was calculated using ArcGIS 10.3.

**Statistical analysis**

The geographical detector is a statistical tool (http://geodetector.cn/) for detecting spatial heterogeneity and its determinants [33]. In this study, the GD was used to detect the influence of the socioeconomic and eco-environmental factors on the incidence of TB on an appropriate grid scale. The method assumes that if the selected factors are associated with the 2017 incidence of TB, they have a similar spatial distribution. This coupling is calculated as follows:

\[
q = 1 - \frac{1}{N\sigma^2} \sum_{h=1}^{L} N_h \sigma_h^2
\]

(2)

where \( N \) and \( \sigma^2 \) are the total counts of grid units and the variance of the incidence of TB in 2017, respectively, and \( h = 1, 2, ..., L \), where \( L \) is the number of sub-areas of the study area divided by the detection factor \( X \). The number of strata \( L \) might be 2–10 or more, according to prior knowledge or a classification algorithm. Here, \( q \) measures the association between the 2017 incidence of TB and the detection factor \( X \), both linearly and nonlinearly, meaning that the explanatory power or ability of the detection factor \( X \) for the spatial heterogeneity of the gridded incidence of TB in 2017 is 100% × \( q \), where \( q \in [0,1] \). Note that \( q = 0 \) indicates that there is no coupling between the

---

**Table 1** Data collection and resources in this study

| Data group                  | Selected variables by previous studies | Data type   | Source                                                                 |
|-----------------------------|---------------------------------------|-------------|------------------------------------------------------------------------|
| Socioeconomic factor        | TB incidence rates in 2016 (Incid-2016) [9, 16] | Vector      | Guangzhou Center for Disease Control and Prevention                     |
|                             | Population density (Pop) in 2015 [9, 12, 15, 16] | Raster (1 km) | Resource and Environment Science and data center (https://www.resdc.cn/) |
|                             | Gross domestic product per capita (GDP) in 2015 [7, 15] | Raster (1 km) |                                                                                  |
|                             | Officially appointed medical institutions (Hosp) [2, 28] | Vector      | Guangzhou Municipal People’s Government (http://www.gz.gov.cn/)             |
|                             | Density of road network (Road_net) [17] | Vector      | Open Street Map (http://download.geofabrik.de/)                         |
|                             | Numbers of subway stations (Subway) [17] | Vector      |                                                                                  |
|                             | Counts of bus stops (Bus) [17] | Vector      |                                                                                  |
|                             | Percentage of residential land (Residential) [16] | Vector      | Tsinghua University (http://data.ess.tsinghua.edu.cn) [30]                |
|                             | Percentage of commercial service land (Commercial) [16] | Vector      |                                                                                  |
|                             | Percentage of land for public services (Pub-serv) [16] | Vector      |                                                                                  |
|                             | Percentage of urban village area (UV) [29] | Vector      | Our earlier study [31]                                                    |
| Environmental condition     | Monthly average of the normalized difference vegetation index (NDVI) [15] | Raster (1 km) | MODIS (https://modis.gsfc.nasa.gov/)                                     |
|                             | Monthly average of the fine particulate matter concentration (PM_{2.5}) [15] | Raster (1 km) | Socioeconomic Data and Applications Center (https://sedac.ciesin.columbia.edu/data/sets/browse) |
|                             | Average temperature from March to June (Temp) [13, 15] | Raster (1 km) | China Meteorological Data Service Center (http://data.cma.cn/)             |
|                             | Average precipitation from March to June (Prec) [13, 15] | Raster (1 km) |                                                                                  |
|                             | Average humidity from March to June (Humi) [13, 15] | Raster (1 km) |                                                                                  |

...
2017 incidence of TB and $X$, while $q=1$ indicates that this incidence is completely determined by $X$.

The interaction detection of the GD is also used to determine the explanatory ability of the interaction between any two factors for the spatial heterogeneity of the gridded incidence of TB in 2017. The interaction effects are judged by the following rules.

- **Enhance, nonlinear**: $q(X_1 \cap X_2 = X_3) > q(X_1) + q(X_2)$
- **Independent**: $q(X_1 \cap X_2 = X_3) = q(X_1) + q(X_2)$
- **Enhance, bi**: $q(X_1 \cap X_2 = X_3) > \max(q(X_1), q(X_2))$
- **Weaken, uni**: $\min(q(X_1), q(X_2)) < q(X_1 \cap X_2 = X_3) < \max(q(X_1), q(X_2))$

The enhancement effect of the interaction of variables is evaluated using the indicator $sq$ with the following equation.

$$sq = \frac{q(X_1) - \max(q(X_1), q(X_2))}{\max(q(X_1), q(X_2))} \times 100\%$$  \hspace{1cm} (3)

where $X_3 = X_1 \cap X_2$ indicates the interaction of the detection factors $X_1$ and $X_2$, $q(X_1 \cap X_2 = X_3)$ are the calculated $q$ values of factors $X_1$ and $X_2$. $\min(q(X_1), q(X_2))$, $\max(q(X_1), q(X_2))$ denote the minimum and maximum values of $q$ corresponding to $X_1$ and $X_2$. The larger $sq$ indicates that the greater the enhancement in the ability to explain the spatial heterogeneity of TB incidence when the two factors interact.

In addition to the above epidemiological characteristics, which were similar to those of the whole city of Guangzhou, several unique characteristics were also observed. The number of TB patients over 60 years old and the number of patients with the occupation of household/unemployed accounted for almost one-third of cases in the whole city. Meanwhile, about 40% of either the student or the cadre (and office clerk) TB cases in this city were reported within the four districts. Among the TB cases in the business and catering service (1,286 cases) of Guangzhou, more than half were located in the central districts (714 cases). In addition, the proportion of female cases in the central districts (31.0%) was slightly higher than the level of the whole city of Guangzhou (29.3%), while the proportion of male cases was slightly lower (69.0%). These analyses indicated that the incidence of TB in the study area shared some features of the incidence of TB in the whole city, but also possessed its own characteristics.

According to the Moran’s $I$ values derived from our global spatial autocorrelation analysis (Table 3), the 2017 incidence of TB in the central area was clearly spatially differentiated at various grid scales ranging from $1 \text{ km} \times 1 \text{ km}$ to $5 \text{ km} \times 5 \text{ km}$. Among these, the $2 \text{ km} \times 2 \text{ km}$ grid possessed the best ability to characterize the spatial distribution of the 2017 incidence of TB in the study area. Thus, the analyses that follow were conducted at this level.

### Results
#### Epidemiological characteristics

In 2017, 4,313 newly diagnosed TB cases were reported in Yuexiu, Tianhe, Haizhu, and Liwan, where the case density was 13.29 cases/km$^2$, compared to only 1.95 cases/km$^2$ in the whole city of Guangzhou. According to the proportion of TB patients’ occupation, age, and gender in the study area (Table 2), more than 72% of the total TB cases were reported among those with occupations of household/unemployed (33.1%), retired (23.9%), and commercial services (15.1%). Among the four age groups, the 19–45-year-old population accounted for the highest proportion, and the 0–18-year-old population had the lowest. The ratio of the number of male to female cases was about 7:3, which was consistent with the entire city of Guangzhou. These results show that the distribution of the TB epidemic in the four central districts was impacted by age, gender, and occupation.

### Individual effects of selected variables

The spatial distributions of 18 variables included in this study were clearly featured on the $2 \text{ km} \times 2 \text{ km}$ grid scale (Fig. 2). Meanwhile, the grids with a high incidence of TB in 2017 were surrounded by several grids that had experienced a relatively high incidence of TB in 2016, had more bus stops or subway stations, had more officially appointed medical institutions, had a higher population density, had a higher PM$_{2.5}$ concentration, and had lower NDVIs (Fig. 2). These results indicate that the spatial patterns of the gridded 2017 incidence of TB are likely associated with those of the 18 selected factors.

Meanwhile, the gridded incidence of TB in 2017 was closely associated with the majority of independent variables (Table 4). Among them, most of the socioeconomic factors presented significant positive relationships with this epidemic ($0.37 < r < 0.76$, $P < 0.001$), except for UV, GDP, and Pub-serv. In comparison with these socioeconomic factors, only one environmental variable (PM$_{2.5}$ concentration) was closely correlated with the gridded
incidence of TB in 2017 ($r < 0.21$, $P < 0.001$). As a whole, the 2017 incidence of TB in Guangzhou tended to be more heavily affected by socioeconomic factors than by environmental conditions.

In addition, the explanatory ability of each influencing factor, in terms of $q$-values as given in Table 4, was acquired using the GD. Among them, the majority of socioeconomic variables, excluding UV ($q_1 = 0.08$, $P > 0.10$) and Pub-serv ($q_1 = 0.02$, $P > 0.10$), possessed powerful explanatory abilities ($0.11 < q < 0.57$, $P < 0.10$) for the spatial differentiation of the gridded incidence of TB in 2017. In particular, three socioeconomic factors (i.e., the 2016 incidence of TB, the counts of officially appointed medical institutions, and the number of bus stops) accounted for about 44% of the spatial heterogeneity of the 2017 incidence of TB across the four central districts. In comparison, the environmental factors (e.g., the monthly averages of temperature, precipitation, and humidity) presented relatively lower explanatory abilities ($0.10 < q < 0.27$, $P < 0.10$), even though they were not closely associated with the 2017 incidence of TB. These results further illustrate that socioeconomic factors had greater impacts than environmental factors on the spatial heterogeneity of the gridded incidence of TB in 2017 in the central regions.

### Influences of pairwise interactions

According to the $q_3$ values varying from 0.16 to 0.89 (the lower left half in Fig. 3), the 153 pairwise interactions between the 18 individual variables presented...
much stronger abilities of interpreting the spatial differentiations of the gridded incidence of TB in 2017 than those of the 18 individuals alone (the diagonal grids from the left top to the right bottom in Fig. 3), resulting in obvious improvements termed by the $sq$ values ranging from 7.3% to 311.6% (the upper right half in Fig. 3). Then, the 153 pairwise interactions could be accordingly divided into three groups: 68 pairs ($sq < 50\%$), 49 pairs ($50\% < sq < 100\%$), and 36 pairs ($sq > 100\%$), among which about 55.6% of the total pairs showed notable enhancements ($sq > 50\%$). These results displayed that the pairwise interactions between selected potential influencing factors possessed much stronger explanatory abilities for the spatial differentiation of the gridded incidence of TB in 2017.

Furthermore, 153 pairwise interactions, in terms of the values of $q_3$ and Maximum ($q_1$, $q_2$), were further classified into five groups (by $q_3$ values) and three grades (by maximum values), yielding nine subgroups as given in Table 5. Among the 45 pairs within the first grade of Maximum ($q_1$, $q_2$), the majority (40 pairs, about 88.9%) presented moderately increased explanatory abilities from the level of below 0.2 to a slightly higher one ($0.2 < q_3 < 0.4$). Meanwhile, there were also larger proportions within Grade 1 (29 pairs, 63.0%) and Grade 2 (31 pairs, 50.0%) observed for their moderate enhancements of explanatory abilities from 0.2–0.4 and 0.4–0.6 to 0.4–0.6 and 0.6–0.8, respectively. In other words, the explanatory abilities of potential factors were more likely to be moderately enhanced to higher levels during the pairwise interaction.

**Discussion**

Using the GD and other spatial analysis tools, a series of potential influencing factors—and in particular their pairwise interactions—were clearly identified for the spatial differentiation of the gridded incidence of TB in 2017 in the four central districts of Guangzhou, from which several notable findings were obtained. This study provides useful clues for local authorities designing targeted intervention measures to control this disease in Guangzhou and similar municipal regions of China.

Occupational difference of the cases was an obvious characteristic of the 2017 incidence of TB. It has been reported that farmers and workers accounted for the largest proportion of TB cases in some regions of China (e.g., north-east Yunnan Province and Xi’an City) [34–36]. On the contrary, these occupations did not rank first
thus be seen that the TB cases in the study area possessed their own unique epidemiological characteristics in addition to those shared with cases across the entire city. Accordingly, these TB epidemic features should be considered to design regional appropriate intervention measures (e.g., adequate propaganda and education for these specific populations) to control this disease across the four central districts.

Previous studies have already pointed out that the dominant influencing factors on the distribution of infectious diseases tend to be different due to the varying research units [41, 42]. In our study, the 2 km × 2 km grid was chosen as the appropriate spatial scale on which the gridded TB incidence was spatially clustered, especially in the western part of Tianhe District and the junction area between the Haizhu, Liwan, and Yuexiu districts, owing to their grids having higher incidence. Moreover, the spatial relationship between the gridded TB incidence and most of the selected factors was also easily observed, so that the potential influences on the spatial distribution of the 2017 incidence of TB were sufficiently detected to identify the specific relevant urban units in this study area. The choice of an appropriate spatial scale is essential for identifying the spatial distribution of the incidence of TB and its influencing factors in the target region.

Local TB incidence is often determined by socioeconomic factors, such as the population at risk of spreading this disease, the density and mobility of the population, the transportation system, economic status of the region, and the medical service level on fine scales [7, 12, 16, 17]. Similar findings were obtained in our study: three socioeconomic variables (the 2016 incidence of TB, the counts of officially appointed medical institutions, and the number of bus stops) posed relatively large impacts on the spatial differentiation of the 2017 incidence of TB across the central region of Guangzhou. There was a four-fold increase in transmission risk from some TB patients to their close contacts, causing there to be a high exposure of the susceptible population [9], which may be a reasonable explanation for the strong effects of the 2016 incidence of TB. Another possible interpretation is that the recurrence of previous TB cases after treatment due to the increasing drug resistance of M. tuberculosis was very likely to increase the risk of transmission of TB in the regions with high incidence rates in the previous year [43, 44]. As far as the count of officially appointed medical institutions is concerned, its heavy influence on the TB epidemic was probably correlated with medical institutions being representative places where various patients aggregate to ask for health services, including potential TB patients and susceptible people with low immunity [28]. In addition, the number of bus stops was another non-negligible influencing factor for the TB epidemic.

### Table 4 Correlation coefficients between tuberculosis incidence and variables and the q-values derived from geographical detector analysis

| Variable type         | Variable name | r     | q values |
|-----------------------|---------------|-------|----------|
| Socioeconomic variables | Incid-2016  | 0.76*** | 0.57*** |
|                       | Hosp         | 0.67*** | 0.45*** |
|                       | Hosp11       | 0.65*** | 0.49*** |
|                       | Hosp12       | 0.54*** | 0.38*** |
|                       | Bus          | 0.69*** | 0.44*** |
|                       | Road-net     | 0.47**  | 0.26**  |
|                       | Pop          | 0.31*** | 0.23*** |
|                       | Subway       | 0.42*** | 0.19**  |
|                       | Commercial   | 0.37*** | 0.16*   |
|                       | Residential  | 0.37*** | 0.14**  |
|                       | GDP          | 0.16   | 0.11*   |
|                       | UV           | 0.17*  | 0.08    |
|                       | Pub-serv     | −0.01  | 0.02    |
| Environmental variables | Temp         | 0.01   | 0.27*** |
|                       | Prec         | 0.06   | 0.15*** |
|                       | Humi         | −0.07  | 0.10*   |
|                       | PM2.5        | 0.21** | 0.08    |
|                       | NDVI         | −0.11  | 0.06    |

r is the Pearson correlation coefficient. ***, **, * and indicates this value is significant at the level of 0.01, 0.05, and 0.10. Incid-2016 TB incidence in 2016, Pop population density, GDP gross national product per capita, Hosp counts of officially appointed medical institutions, Hosp11 outpatient hospitals of the officially appointed medical institutions, Hosp12 inpatient and outpatient hospitals of the officially appointed medical institutions, Road_net road network density, Subway counts of subway stations, Bus counts of bus stops, Residential percentage of residential land area, Commercial percentage of commercial service land, Pub-serv percentage of land for public services, UV percentage of urban village area, NDVI annual monthly average normalized differential vegetation index, PM2.5 annual monthly average PM2.5 concentration, Temp average temperature from March to June, Prec average precipitation from March to June, Humi average humidity from March to June.
Fig. 3 Illustration of the $q_3$ (the lower left half) and $sq$ (the higher right half) values for the pairwise interactions among the selected factors. Incid-2016 TB incidence in 2016, Pop population density, GDP Gross National Product per capita, Hosp Counts of officially appointed medical institutions, Hosp11 outpatient hospitals of the officially appointed medical institutions, Hosp12 inpatient and outpatient hospitals of the officially appointed medical institutions, Road_net Road network density, Subway Counts of subway stations, Bus Counts of bus stops, Residential Percentage of residential land area, Commercial Percentage of commercial service land, Pub-serv Percentage of land for public services, UV Percentage of urban village area, NDVI Annual monthly average normalized differential vegetation index, PM$_{2.5}$ Annual monthly average PM$_{2.5}$ concentration, Temp Average temperature from March to June, Prec Average precipitation from March to June, Humi Average humidity from March to June.

Table 5 The numbers and $sq$ values of 153 pairwise interactions in the nine subgroups

| Group 1 | Group 2 | Group 3 | Group 4 | Group 5 |
|---------|---------|---------|---------|---------|
| Grade 1 | Counts of pairs | 1 | 40 | 4 | \ | \ | 45 |
| sq (%)  | 159.7 | 49.3–283.9 | 159.1–311.6 | \ | \ | 49.3–311.6 |
| Grade 2 | Counts of pairs | \ | 15 | 29 | 2 | \ | 46 |
| sq (%)  | \ | 21.4–66.1 | 17.3–121.2 | 67.0–145.0 | \ | 21.4–145.0 |
| Grade 3 | Counts of pairs | \ | \ | 21 | 31 | 10 | 62 |
| sq (%)  | \ | \ | 9.5–31.7 | 7.3–65.1 | 42.9–57.7 | 7.3–65.1 |
| \ | 1 | 55 | 54 | 33 | 10 | 153 |

The $q_3$ groups: below 0.2, 0.2–0.4, 0.4–0.6, 0.6–0.8, and beyond 0.8. The Maximum ($q_1, q_2$) grades: below 0.2, 0.2–0.4, and 0.4–0.6. \ means that the group has no data.
because both the contact probability among individuals and the population mobility tended to be increased by a convenient public transportation system [17]. In general, the potential variables included in this study could reasonably be the dominant factors influencing the TB epidemic in the study area. Therefore, we cautiously suggest that: (i) the treatment of current TB cases, together with more effective methods dealing with the drug resistance, needs to be considered first to reduce their potential impacts on the incidence of TB during the next year; and (ii) more resources should be rationally allocated to reduce hospital infections and reinforce the propaganda and education for the individuals who often visit the hospital or take the bus.

In comparison to the individual variables, their explanatory abilities were strongly enhanced by their pairwise interactions [45, 46]. Rasam et al. and Ge et al. demonstrated that the interactions between public transportation condition, population density, and urban functional zones had much higher explanatory abilities for the TB epidemic’s spatial differentiations than each individual factor [16, 17]. Our study obtained similar findings; the individual explanatory abilities for the spatial differentiation of the incidence of TB in 2017 across the central region of Guangzhou were remarkably enhanced because of the pairwise interactions. In particular, the contributions of relatively weaker variables ($q<0.2$) had been significantly enhanced while interacting with bus stops, officially appointed hospitals (i.e., Hosp, Hosp11, and Hosp12), and the 2016 incidence of TB. Among these individual factors, UV, termed for the widely distributed units with crowded population in the low buildings clustered in the study area [29], is a typical urban unit impacting the transmission of $M. tuberculosis$ and TB infection [3, 47]. In general, the pairwise interactions made great contributions for interpreting the spatial differentiation of the 2017 incidence of TB across the four central districts. We strongly recommend that the regions with relatively weaker factors should be considered as targets in the prevention and control system, and that comprehensive intervention measures ought to be meticulously implemented in the regions with these paired factors in order to control TB in Guangzhou.

A few limitations should be mentioned here. First, although public transportation defined by bus stops and subway stations was included in this study, population mobility was not adequately considered due to the difficulty of collecting information about population flows, which might be addressed in the future through obtaining and processing either cell phone data or public transportation smart cards. Second, owing to the difficulty of collecting detailed population data with age structure, age-standardized incidence data were not calculated at the gridded scales, which could be possibly resolved through collecting detailed enough population data from the community- and building-based census data. Third, some potential variables related to health services (e.g., constant TB screening for community residents, household surveys, supervision and direction of anti-TB drugs, and follow-up visits for TB patients) supplied by multi-level medical institutions (i.e., township, street, village, and even community level) were not included because of the difficulty of directly calculating the gridded health services’ disparities in this study, which may be resolved in the future through quantifying health service supplies from the perspective of TB patients at various gridded levels because these variables have important effects on this disease. Finally, the TB case data over 10-year or longer periods should be obtained in the future so as to further consolidate and extend the current findings, which are only based on one year’s data.

Conclusions
A series of socioeconomic and environmental factors, together with their pairwise interactions, were identified as specific urban elements posing important impacts on the spatial differentiations of the gridded TB incidence across the four central districts of Guangzhou. We accordingly suggest that more attention should be paid to the zones with pairwise interactions of these influencing factors in Guangzhou. This study provides meaningful clues for local health authorities designing and implementing effective targeted intervention measures to control this disease in China’s municipal areas, defined by both high urbanization and severe TB epidemics.

Abbreviations
TB: Tuberculosis; Incid-2017: TB incidence in 2017; Incid-2016: TB incidence in 2016; Pop: Population density; GDP: Gross National Product per capita; Hosp: Counts of officially appointed medical institutions; Hosp11: Outpatient hospitals of the officially appointed medical institutions; Hosp12: Inpatient and outpatient hospitals of the officially appointed medical institutions; Road_net: Road network density; Subway: Counts of subway stations; Bus: Counts of bus stops; Residential: Percentage of residential land area; Commercial: Percentage of commercial service land; Pub-serv: Percentage of land for public services; UV: Percentage of urban village area; NDVI: Annual monthly average normalized differential vegetation index; PM$_{2.5}$: Annual monthly average PM$_{2.5}$ concentration; Temp: Average temperature from March to June; Prec: Average precipitation from March to June; Humi: Average humidity from March to June; $r$: The Pearson correlation coefficient.

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s40249-022-00967-z.
Acknowledgements
Not applicable.

Author contributions
HY and W-L conceived and designed the experimental concept. X-QL and H-CS helped collect data. HY and W-L analyzed the data and drafted the paper. HY, X-QL and H-CS revised the manuscript. All authors read and approved the final manuscript.

Funding
HY received the financial support from the National Natural Science Foundation of China (Grant no. 42071136, Grant no. 41571158).

Availability of data and materials
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1 State Key Laboratory of Resources and Environmental Information System, Institute of Geographic Sciences and Natural Resources Research, Chinese Academy of Sciences, Beijing 100101, China. 2 College of Resources and Environment, University of Chinese Academy of Sciences, Beijing 100190, China. 3 Guangzhou Chest Hospital, Guangzhou 510000, China.

Received: 2 December 2021   Accepted: 7 April 2022
Published online: 15 April 2022

References
1. World Health Organization. Global tuberculosis report 2021. https://www.who.int/publications/i/item/9789240037021. Accessed 17 January 2022.
2. Coulter C. Infection control guidelines for the management of patients with suspected or confirmed pulmonary tuberculosis in healthcare settings. Commun Dis Intell Q Rep. 2016;40(3):E362.
3. Wang T. The spatial epidemiology of tuberculosis in LinYi City, Shandong Province [Master]. Shandong University, 2012 (in Chinese).
4. National Health Commission of the People’s Republic of China. Chinese Health Statistical Yearbook: Peking Union Medical College Press; 2020. P. 274 (in Chinese).
5. National Health Commission of the People’s Republic of China. Chinese Health Statistical Yearbook: Peking Union Medical College Press; 2020. P. 283 (in Chinese).
6. Cui ZZ, Lin DW, Virasakdi C, Zhao JM, Mei L, Ou J, et al. Spatiotemporal patterns and ecological factors of tuberculosis notification: a spatial panel data analysis in Guangxi, China. PLoS One. 2019;14(5):e0212051.
7. Changmi I, Youngho K. Spatial pattern of tuberculosis (TB) and related socio-environmental factors in South Korea, 2008–2016. PLoS One. 2021;16(8):e0255727.
8. Ge EJ, Zhang X, Wang XM, Wei XL. Spatial and temporal analysis of tuberculosis in Zhejiang Province, China, 2009–2012. Infect Dis Poverty. 2016;5:11.
9. Rasam ARA, Shariff NM, Dony JF, Othman F. Spatial and Statistics for profiling risk factors of diseases: a case study of tuberculosis in Malaysia. IOP Conf. Ser. Earth Environ Sci. 2019;385(1): 012053.
10. Khualasiri H. Modelling mixed geographically weighted poison regression for tuberculosis disease in Surabaya. J Phys Conf Ser. 2020;1490(1): 012004.
11. Rasam ARA, Dony JF, Shariff NM. Local spatial knowledge for eliciting risk factors and disease mapping of tuberculosis epidemics. Environ- Behav Proceed J. 2020;50(2):45–7.
12. Hailu DM, Gemechu DD, Bernt L. Identifying geographical heterogeneity of pulmonary tuberculosis in southern Ethiopia: a method to identify clustering for targeted interventions. Glob Health Action. 2020;13(1):1785737.
13. Cong MY, Yun MY, Erkin A. Analysis on influence of climatic factors on the incidence of tuberculosis. Chin J Dis Control Prev. 2014;18(11):1051–4 (in Chinese).
14. Lai TC, Chiang CY, Wu CF, Yang SL, Liu DP, Chan CC, et al. Ambient air pollution and risk of tuberculosis: a cohort study. Occup Environ Med. 2016;73(1):56–66.
15. Yang LJ. Study on spatial distribution characteristics and relative factors of tuberculosis [Master]. Chinese Center for Disease Control and Prevention; 2020 (in Chinese).
16. Rasam ARA, Shariff NM, Dony JF. Geospatial-based model for diagnosing potential high-risk areas of tuberculosis disease in Malaysia. MATEC Web Conf. 2019;266:02007.
17. Ge E, Lai PC, Zhang X, Yang X, Li X, Wang H, et al. Regional transport and its association with tuberculosis in the Shandong province of China, 2009–2011. J Transp Geogr. 2015;46:232.
18. Liu MY, Li QH, Zhang YJ, Ma Y, Liu Y, Feng W, et al. Spatial and temporal clustering analysis of tuberculosis in the mainland of China at the prefecture level, 2005–2015. Infect Dis Poverty. 2018;7(1):106.
19. Wang L, Xu CD, Hu MG, Qiao JJ, Chen W, Li T, et al. Spatio-temporal variation in tuberculosis incidence and risk factors for the disease in a region of unbalanced socio-economic development. BMC Public Health. 2021;21(1):1817.
20. Li H, Ge M, Zhang MX. Spatio-temporal distribution of tuberculosis and the effects of geographical environmental factors in China. BMC Infect Dis. 2021. https://doi.org/10.21203/rs.3.rs-36641/v1.
21. Ren HY, Xu DY, Shi XM, Xu JW, Zhuang DF, Yang GH. Characterisation of gastric cancer and its relation to environmental factors: a case study in Shenqu County, China. Int J Environ Health Res. 2016;26(1):1–10.
22. Zheng L, Ren HY, Shi RH, Lu L. Spatiotemporal characteristics and primary influencing factors of typical dengue fever epidemics in China. Infect Dis Poverty. 2019;8(1):24.
23. Cui C, Wang BH, Ren HY, Wang Z. Spatiotemporal variations in gastric cancer mortality and their relations to influencing factors in s county, China. Int J Environ Res Public Health. 2019;16(5):784.
24. Li CY, Liu ZH. Review on the development of digital city management in China. Intelligent Build City Inform. 2017;2:28–35 (in Chinese).
25. Yan YJ. On grid management in city management. Urban Problems. 2006;02:76–9 (in Chinese).
26. Cui C, Ren HY, Zhao L, Zhuang DF. Street space quality evaluation in Yuexiu District of Guangzhou City based on multi-feature-fusion of street view imagery. J Geoinform Sci. 2020;22(06):1330–8 (in Chinese).
27. He SH. The study on the characteristics of commercial space agglomeration in the inner city of Guangzhou [Master]. South China University of Technology; 2019 (in Chinese).
28. Ito Y, Nagao M, Inumya Y, Matsumura Y, Mishima M. Risk factors for nosocomial tuberculosis transmission among health care workers. Am J Infect Control. 2016;44(5):596–8.
29. Ren HY, Wu W, Li TG, Yang ZC. Urban villages as transfer stations for dengue fever epidemic: a case study in the Guangzhou, China. PLoS Negl Trop Dis. 2019;13(4):e0007350.
30. Gong P, Chen B, Li X, Liu H, Wang J, Bai Y, et al. Mapping essential urban land use categories in China (EULUC-China): preliminary results for 2018. Sci Bull. 2020;65(3):182–7.
31. Zhao L, Ren HY, Cui C, Huang YH. A partition-based detection of urban villages using high-resolution remote sensing imagery in Guangzhou, China. Remote Sens. 2020;12(14):2334.
32. Anselin L, Getis A. Spatial statistical analysis and geographic information systems. Adv Spat Sci. 2010. https://doi.org/10.1007/8BF01581478.
33. Wang JF, Li XH, Christakos G, Liao YL, Zhang T, Gu X, et al. Geographical detectors-based health risk assessment and its application in the neural tube defects study of the Heshun Region, China. Int J Geogr Inform Sci. 2010;24(1):107–21.
34. Huang L, Abe EM, Li XX, Bergquist R, Xu L, Xue JB, et al. Space-time clustering and associated risk factors of pulmonary tuberculosis in southwest China. Infect Dis Poverty. 2018;7(1):91.

35. Du XT, Xiang XM, Wu R, Ma CF, Liu JF, Xiong YM. Analysis of the epidemiological characteristics of Tuberculosis in Xian City from 2005 to 2014. Mod Prev Med. 2016;43(16):3033–5 (in Chinese).

36. Wu QG, Lv DL, Guang HY, Tan WG, Che XL, Lv CR, et al. Analysis of epidemiological characteristics of pulmonary tuberculosis in Shenzhen from 2007 to 2016. J Trop Med. 2018;18(01):86–9 (in Chinese).

37. Shen HC, Du YH, Wu GF, Lei Y, Li TG, Liu JX. Epidemiological characteristics of newly reported pulmonary tuberculosis from 2008 to 2018 in Guangzhou, Chin J Antituberc. 2020;42(4):322–6 (in Chinese).

38. Wang W, Ye YN, Wu ZL, Zhong QH, Chen L, Huang F, et al. Analysis of the incidence trend and epidemic characteristics of tuberculosis in Foshan, 2010–2020. Dis Surveil. 2021;36(10):1039–45 (in Chinese).

39. Zhou CS, Tong XN, Wang JH, Lai SL. Spatial differentiation and the formation mechanism of population aging in Guangzhou in 2000–2010. Geogr Res. 2016;37(1):103–18.

40. Zhou C, Li Y, Tong X. Spatial change and influence factors of population aging in Guangzhou during 2000–2010. Acta Sci Natur Univ Sunyatseni. 2016;55(1):114–22 (in Chinese).

41. Danson FM, Graham AJ, Pleydell DRJ, Campos-Ponce M, Giraudoux P, Craig PS. Multi-scale spatial analysis of human alveolar echinococcosis risk in China. Parasitology. 2004;127(s1):S133.

42. Ricin S, Slaem G, Jungla E. Spatial variation of lung cancer death in France and spatial scales: importance of changing scale in health geography. Rev Epidémiol Santé Publique. 1999;47(5):411–20.

43. Pramudita A, Rumende CM, Fandayriti A. Fixed-dose combination antituberculosis therapy as a risk factor for tuberculosis recurrence: an evidence-based case report. Acta Med Indonesiana. 2017;49(2):175.

44. Mirsaedi M, Sadikot R. Patients at high risk of tuberculosis recurrence. Int J Mycobacteriol. 2018;7(1):1–6.

45. Ma T, Jiang D, Hao M, Fan PW, Zhang SZ, Qu GS, et al. Geographical detector-based influence factors analysis for Echinococcosis prevalence in Tibet, China. PloS Negl Trop Dis. 2021;15(7):e0009547.

46. Zheng C, Tao L, Li X, Wang J, Ma W. Individual and interactive effects of socio-ecological factors on dengue fever at fine spatial scale: a geographical detector-based analysis. Int J Envir Res Public Health. 2017;14(7):795.

47. Lai K, Xie W, Du YH, Lei Y, Wu GF, Yang JY, et al. Spatiotemporal characteristics on smear-positive pulmonary tuberculosis in Guangzhou city from 2014 to 2019. J Trop Med. 2021;21(06):782–5 (in Chinese).