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Spatial-temporal distribution characteristics of pulmonary tuberculosis in eastern China from 2011 to 2021

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Abstract

China is still among the 30 high-burden tuberculosis countries in the world. Few studies have described the spatial epidemiological characteristics of pulmonary tuberculosis (PTB) in Jiangsu Province. This study aimed to study the temporal and geographical pattern of PTB and the factors affecting tuberculosis incidence. The registered incidence data of PTB patients in 95 counties of Jiangsu Province from 2011 to 2021 were collected from the Tuberculosis Management Information System. Three-dimensional spatial trends, spatial autocorrelation, and spatial-temporal scan analysis were conducted to explore spatial clustering pattern of PTB. From 2011 to 2021, a total of 347,495 newly diagnosed PTB cases were registered. The registered incidence rate of PTB decreased from 49.78/100,000 in 2011 to 26.49/100,000 in 2021, exhibiting a steady downward trend (χ^2 =414.22, P <0.001). PTB cases showed clear seasonal variations each year, and the peak of registrations occurred during the period from March to May. The average annual registered incidence rate of PTB was higher in the central region compared to either western or eastern regions. Moran's I indices of the registered incidence of PTB were all >0 (P <0.05) except in 2016, indicating a positive spatial correlation overall. Local autocorrelation analysis showed that "high-high" clusters were mainly distributed in northern Jiangsu, and "low-low" clusters were mainly concentrated in southern Jiangsu. The results of this study assist in identifying settings and locations of high tuberculosis risk and inform policy-making for PTB control and prevention.

Key Words: Pulmonary tuberculosis; Spatial autocorrelation; Spatial-Temporal Scan; China

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Introduction

China is ranked third among the 30 high tuberculosis (TB) burden countries in 2021, lower than the numbers of TB cases of Indonesia and India, The estimated number of TB patients accounted for 7.4% of the total global burden in 2021 (Bagcchi 2023). In order to effectively curb the epidemic of TB, China has continuously introduced TB prevention and control measures in the past decade, and positive progress has been made in the prevention and control of TB(China 2011;China 2019). The incidence rate of TB in China reported by the National Health Commission in 2021 was 45 cases per 100,000 persons (China 2022); this is ahead of schedule of the target of 55 cases per 100,000 persons derived in the Action Plan to Stop Tuberculosis (2019-2022) formulated by the Chinese government(China 2019). Despite this improvement, the number of reported TB deaths still ranks second among class A and B infectious diseases in China(C Liu et al. 2023).

Previous studies have found that the incidence of pulmonary tuberculosis (PTB) in different regions may be distinct due to geographical factors, climate, social economy, amongst others (Bie et al. 2021; Li et al. 2022; Li et al. 2021). The National Tuberculosis Epidemiological Sampling Survey is a cross-sectional investigation conducted nationwide using scientific methods to sample representative populations, thereby obtaining nationwide tuberculosis prevalence data at a specific point in time, The Fifth National Tuberculosis epidemiological Sampling survey uncovered that there were obvious regional differences in PTB incidence in China. For example, the PTB incidence in rural areas was significantly higher than that in the urban areas; in addition, the central and western regions have significantly higher incidence compared to eastern regions. PTB incidence in the western region is highest, approximately 1.7 and 2.4 times that of the central and eastern regions(Lixia et al. 2012). In areas with low PTB rate, the PTB incidence was also affected by floating migrant populations in recent years(Liu et al. 2022). Jiangsu Province is located in the eastern coastal of China, and there is considerable heterogeneity in climate and economic development within the province. With the rapid economic development and the increase of migrant population, PTB epidemics are frequently recorded in Jiangsu Province.

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Spatial epidemiology has been widely used in the infectious diseases in recent years to analyze links between disease distribution and change in different regions based on monitoring data. Studies from Iran(Kiani et al. 2021) and Kenya(Sifuna et al. 2019) have reported spatial clustering of PTB at the national and county levels. Prior research describes spatial clusters of PTB at the national, provincial, municipal and county levels in China (J Chen et al. 2019; Commission 2020; Yu et al. 2020). Thus far, there is no study on the spatial-temporal analysis of PTB in Jiangsu Province. Therefore, we conducted a temporal, spatial, and spatial-temporal analysis on PTB incidence at county level in Jiangsu Province from 2011 to 2021, and to providing more useful information for policy-making.

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Methods

Study area

Jiangsu Province is located at the eastern coast of China, in the Yangtze River Delta region, with a latitude and longitude of about 30°45 '-35°08' N, 116°21 '-121°56' E. The total area is 10,7200^2 kilometers. By the end of 2021, there were 95 counties in Jiangsu Province, with a permanent population of 85 million, and GDP per capita ranked first in China.

Data sources

The registered incidence data of PTB patients from 2011 to 2021 was obtained from the Tuberculosis Management Information System of Jiangsu Province (Q Liu et al. 2023; P Lu et al 2021;Q Liu et al. 2021); statistical analysis was conducted based on the current addresses of cases. The data of permanent residents from 2011 to 2021 were collected from the statistical yearbooks of each city. Vector maps of counties in Jiangsu Province were downloaded from the database of National Basic Geographic Information System.

Data processing

We calculated the registered incidence rate of PTB in 95 counties of Jiangsu Province from 2011 to 2021. The ArcGIS 10.7 software was used to construct a geographic information database of PTB incidence rate, including the name, code, latitude and longitude, and the registered incidence rate of PTB in each county, with the administrative division code as the matching field associated vector map.

Descriptive and time series analysis

The registered incidence rates of PTB in Jiangsu Province from 2011 to 2021 were computed and used in the three-dimensional spatial trend analysis by the ArcGIS 10.7 software. The spatial distribution map and the three-dimensional spatial trend analysis map of the annual registered

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incidence rate of PTB in the counties were subsequently drawn. The numbers of newly registered PTB cases were summarized by month, and the Excel 2013 software was used to draw the time series diagram.

Spatial autocorrelation analysis

Spatial autocorrelation analysis is often used to explore whether a certain feature of a spatial unit in a region is correlated with the feature of its neighboring spatial unit, and it is often employed to measure the clustering and dispersion degree of a feature of a spatial unit(Moore and Carpenter 1999). In this study, the geographic information data of registered PTB cases in Jiangsu Province from 2011 to 2021 were imported into Geoda1.18.0 software for global autocorrelation analysis and local autocorrelation analysis. The Moran's I is a common index in global autocorrelation analysis and used to quantify the overall distributional characteristics of a study area, as it represents the average aggregation degree of similar attributes in a study area. The value of the Moran's I ranges from -1 to 1. For a positive I: a larger value indicates a stronger spatial clustering pattern; For a negative I: a smaller value indicates a weaker spatial clustering pattern; A zero I suggests there is no spatial clustering(Zhang et al. 2023). The local spatial autocorrelation analysis was used to analyze the spatial differences in PTB registration incidence rates at the county level via the cluster map of local spatial correlation indicators. There are four types of clusters, namely, "high-high" clusters (high-incidence areas surrounded by high-incidence areas); "Low-low" clusters (low-incidence areas surrounded by low-incidence areas); "High-low" clusters (high-incidence areas surrounded by low-incidence areas); "Low-high" clusters (low-incidence areas surrounded by high-incidence areas)(Jin and Xu 2021).

Spatial-temporal scan analysis

The SaTScan10.1 software was used to perform spatial-temporal scan analysis based on the Poisson distribution model. A cylindrical shape scanning window with a base of space and a height of time was established. The log-likelihood ratio (LLR) was constructed according to the actual and expected number of PTB cases inside and outside of the scanning window to estimate the risk of PTB in the window, and the relative risk (RR) was calculated to evaluate the risk of

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each cluster. The larger the LLR, the more statistically significant the difference was, the higher the RR in this window, the more likely there were clustering areas(Kulldorff et al. 1998; Li et al. 2020). In this study, the maximum scanning time was set to 50% of the total study time, the maximum scanning space was set to 25% of the population, and the scanning interval was set to 1 year.

ArcGIS10.7 software was used for the three-dimensional spatial trend analysis and the visualization of the results. The significance level was set as 0.05.

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Results

Basic Information

A total of 347,495 newly diagnosed PTB cases were registered in Jiangsu Province from 2011 to 2021, and the registered incidence rate decreased from 49.78/100,000 in 2011 to 26.49/100,000 in 2021, showing an annual downward trend yearly ($\chi 2$ =414.22, P<0.001). A total of 4,456 multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB) cases were registered from 2011 to 2021. The registered incidence rate of MDR/RR-TB cases increased from 0.24/100 000 in 2011 to 0.62/100 000 in 2021, showing an overall upward trend ($\chi 2$=254.95, P<0.001) as shown in Table 1. The spatial distribution of annual registered incidence rate of PTB in Jiangsu Province from 2011 to 2021 showed that the areas with high registered incidence rate of PTB were mostly in the central, northwestern, and southwestern regions of Jiangsu Province, while the registered incidence rate was relatively low in the southeast area. The top three of the annual registered incidence rates of PTB were Huaian County (63.80/100,000), Gaochun County (58.09/100,000), and Xinyi County (58.09/100,000), as shown in Supplementary Figure 1 and Supplementary Figure 2. The temporal distribution of PTB cases showed seasonal fluctuations, with the peak mostly occurring from March to May each year, as shown in Supplementary Figure 3.

Three-dimensional trend analysis

The results of the three-dimensional trend map showed that the average annual registered incidence rate of PTB in Jiangsu Province from 2011 to 2021 was higher in the central Jiangsu and lower on either western or eastern Jiangsu, and showed a slow rise and then a downward trend from north to south, as shown in Figure 1.

Global spatial autocorrelation analysis

The Moran's I values of PTB registered incidence rate in Jiangsu Province were all higher than zero in each year, and the P values were all lower than 0.05 during the study period in other years except for 2016, indicating that there was a positive spatial correlation and a spatial clustering

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distribution in PTB registered incidence rate in Jiangsu Province except for 2016 (Table 2).

Local spatial autocorrelation analysis

The distribution pattern of registered incidence of PTB in Jiangsu Province was uneven. From 2011 to 2021, the "high-high" clustering areas were mainly located in the northern part of Jiangsu Province, especially Huai 'an, Lianyungang and Suqian cities. The number of "high-high" clustering areas was the largest in 2012, involving 13 counties. The number of "high-high" clustering areas showed a downward trend from 2014 to 2018, and began to increase after 2019. The "low-low" clustering areas were relatively concentrated, mainly in the southern areas such as Wuzhong and Wujiang districts of Suzhou City and Wujin district of Changzhou City. (Figure 2). There were " high-high" clustering areas in the registered incidence rate of MDR/RR-TB in Jiangsu Province from 2011 to 2021, with a dynamic distribution, with the number of counties involved concentrated in1 to 9, of which the largest number was 9 in 2021 and the smallest number was 1 in 2019. The LISA results of the annual registered incidence rate of MDR/RR-TB showed that there were seven " high-high" clustering areas. The number of counties and districts involved in "low-low" clustering areas ranged from 1 to 12, showing a dynamic distribution, of which the maximum number was 12 in 2012 and 2017, and the minimum number was 1 in 2015, as shown in Supplementary Figure 4.

Spatial-temporal scan analysis

The results of spatial-temporal scan analysis showed that there was a spatial-temporal clustering of the registered PTB incidence rate in Jiangsu Province from 2011 to 2021, and a total of 8 spatial-temporal clusters were identified (P <0.05). The cluster with highest confidence covered 23 counties, including all counties of Huai'an City, Tinghu County, Yandu County, Xiangshui County, Binhai County, Funing County, and Jianhu County of Yancheng City. Sucheng County, Shuyang County, Siyang County, and Sihong County of Suqian City, Guannan County and Guanyun County of Lianyungang City, Baoying County and Gaoyou County of Yangzhou City, Xinyi City of Xuzhou City, and Xinghua City of Taizhou City were all gathered from 2011 to 2015 (Table 3, Figure 3 and Supplementary Table 1).

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Discussion

Based on this geographic information system and spatial analysis, this study characterizes the spatial-temporal distribution of PTB cases in Jiangsu Province. This is the first study to estimate and summarize the spatial-temporal distribution characteristics of PTB at the county level in Jiangsu province. With the implementation of the World Health Organization's End TB Strategy by 2035, countries around the world are increasingly attaching importance to tuberculosis and making continuous efforts to achieve the goal of ending tuberculosis. Study of the spatiotemporal distribution of pulmonary tuberculosis can help reveal its geographical distribution, epidemic trends, and clustering patterns, thereby providing important basis for the development of more accurate tuberculosis prevention and control strategies. Analyzing the spatiotemporal clustering patterns of pulmonary tuberculosis at the county level can identify high-risk counties, which can assist health administrative departments in more effectively allocating TB control resources.

During the study period, the registered PTB incidence rate in Jiangsu Province decreased from 50 cases to 26.49 cases per 100,000 persons from 2011-2021. A downward trend by year was seen, consistent with the national trend of PTB incidence rate during the same period. The overall incidence rate in Jiangsu Province was significantly lower than the national average (Xue et al. 2023), indicating the high effectiveness of PTB prevention and control in Jiangsu, perhaps due to the province's increased attention to PTB prevention and control. The Jiangsu Provincial government released the 12th Five-Year Plan for Tuberculosis Prevention and Control in May 2012(Government 2012). The plan requires that medical institutions detect patients early, strict diagnosis and treatment standards, and improve the level of anti-tuberculosis related treatment(Martinez L et al. 2017). In the Jiangsu Provincial Tuberculosis Prevention and Control Plan (2018-2020) (Government 2018), Jiangsu took the lead in establishing a new comprehensive PTB prevention and control service model, distributing free supply of second-line anti-tuberculosis drugs to PTB patients, and offering free screening and diagnoses for PTB patients with suspicious symptoms. In the "14th Five-Year Plan" for PTB prevention and control in Jiangsu Province released in November 2021(Commission 2021), further feasible measures were taken to effectively control the epidemic of PTB and protect the health of the people. The analysis of this study reveals that the registered incidence rate of MDR/RR-TB in Jiangsu Province from 2011 to

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2021 was 0.49/100,000, indicating a low detection level. However, there has been an overall upward trend in the registered incidence, suggesting an improvement in the detection of MDR/RR-TB patients. The registered incidence rate showed a significant increase after 2017, which could be attributed to the implementation of the MDR/RR-TB project in Jiangsu Province in recent years. This project has played a vital role in enhancing the treatment management mode, detection level, and professional capabilities of the prevention and control personnel in Jiangsu Province.

Our study shows that the registered PTB incidence rate in Jiangsu Province has obvious seasonal variations. The number of registered PTB cases exhibits a clear downward trend from January to February and starts to approach its peak from March to May. There are several possible explanations for this seasonal trend, First, in autumn and winter, the decrease of UV exposure from outdoor sunlight and the increase of indoor activities may increase the chance of PTB infection (Martinez L et al. 2022; Ncayiyana JR et al. 2021).. Second, after the incubation period, the onset of PTB typically occurs from March to May. During the same time period, we also notice the high incidence of respiratory diseases in spring and also the peak of seeking medical treatment after the Spring Festival (Q Liu et al. 2022;Y Liu et al. 2023). Third, during the Spring Festival in China (January to February), patients are less motivated to seek medical treatment as they are busy celebrating the holiday (Yang et al. 2020). The seasonal trend observed in this study is consistent with the findings in other studies in Jiangsu Province(Q Liu et al. 2019), as well as previous studies in Chongqing Municipality(Yu et al. 2020) and Hubei Province(Zhang et al. 2023).

We also found substantial heterogeneity in terms of the average annual registered incidence rate of PTB within counties in Jiangsu Province during the study time period. The global spatial autocorrelation analysis found a positive spatial correlation in general and the overall spatial clustering distribution of registered PTB incidence rate in Jiangsu Province, suggesting that the incidence rate of PTB in Jiangsu Province is unevenly distributed at the county level. Further local spatial autocorrelation results identified some "high-high" clusters – such as Huai'an city, Suqian city, Lianyungang city – from 2011 to 2021. The distribution of these clusters, which were mainly located in northern Jiangsu, was relatively stable.. The annual registered incidence rates of PTB in

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these counties were high, and regional transmission is likely in these areas. Targeting areas with heavy and consistent 'high-high' clusters may be pertinent for reducing community-level tuberculosis transmission(Coleman M et al. 2022). The "low-low" clusters were mainly located in southern Jiangsu, including Wuzhong and Wujiang County of Suzhou City. Studies have shown that the PTB incidence rate is related to levels of local economic and social development, health resources, social culture, environment, and other factors. Better urban development and economic levels are important for controlling the incidence of PTB, which is supported by our findings as the economic level of northern Jiangsu is less developed than southern Jiangsu.

The spatial-temporal scan analysis identified 8 spatial-temporal clusters from 2011 to 2021, concentrated during the period of 2011-2018. There was no clear spatial-temporal clusters after 2019, indicating that the PTB burden in Jiangsu has been gradually reduced and the control of PTB has progressed. The identified clusters covered 23 counties, mainly located in the central and northern parts of Jiangsu Province, such as Huai'an, Yancheng, Suqian, and Yangzhou. The clustering pattern was the strongest from 2011 to 2015. Incidence rates of the identified clusters were higher than average levels from the whole province. Ongoing tuberculosis control measures should strengthen the surveillance and management of PTB in these areas.

There were several limitations in this study. First of all, the PTB registration incidence data were collected from the Tuberculosis Management Information System, and, similar to most TB registries, there may be missed diagnosis or notifications due to underreporting; this may result in underestimation of the estimated incidence. Second, relevant factors such as socioeconomic status, climatic conditions, and personal hygiene practices were not considered in this study. Third, this study was analyzed at the county level, and further studies at more refined (such as townships) levels are needed.

In conclusion, the registration incidence rate of tuberculosis in Jiangsu Province has shown a downward trend from 2011 to 2021, with peaks occurring from March to May each year. In this study, we have identified significant spatiotemporal clustering patterns and regional differences. Although the burden of tuberculosis in Jiangsu Province has been alleviated in recent years, disease control agencies should pay extra attention to the prevention and control of tuberculosis

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in "high-high" clustering areas and spatial-temporal cluster areas, potentially by increasing the special funding for PTB, enhancing the treatment and follow-up management of PTB patients, and expanding the active screening of PTB in communities.

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Authors' contributions

Qiao Liu and Bei Wang conceived the study; Ke Chen, Liang Chen and Qiao Liu analyzed the data and drafted the manuscript; Limei Zhu participated in the study design; Hao Yu and Qiao Liu implemented the field investigation; Leonardo Martinez and Tenglong Li participated in the study design and helped draft the manuscript. All authors contributed to the study and have read and approved the final manuscript.

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Availability of data and materials

Please contact the first author for data requests.

Conflicts of Interest

The authors declare no conflict of interest.

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483 Table 1. Registration of TB cases in Jiangsu Province from 2011 to 2021.

Year	Number of permanent residents at the end of the year (ten thousand people)	Number of registered TB cases	Registered TB incidence (per 100,000)	Number of registered MDR/RR-TB cases	Registered incidence of MDR/RR-TB (per 100,000)
2011	8022.99	39,935	49.78	196	0.24
2012	8119.81	39,781	48.99	334	0.41
2013	8192.44	36,963	45.12	365	0.45
2014	8281.09	36,301	43.84	308	0.37
2015	8315.11	34,129	41.04	377	0.45
2016	8381.47	31,412	37.48	370	0.44
2017	8423.5	29,615	35.16	515	0.61
2018	8446.19	27,562	32.63	456	0.54
2019	8469.09	25,662	30.3	486	0.57
2020	8477.26	23,605	27.85	522	0.62
2021	8505.4	22,530	26.49	527	0.62

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Table 2. Global autocorrelation analysis on the registered incidence rate of TB in Jiangsu province from 2011 to 2021.

Year	Moran's I	*Z*-Value	*P*-Value
2011	0.28	4.31	0.001
2012	0.32	4.95	0.001
2013	0.20	3.04	0.004
2014	0.17	2.66	0.006
2015	0.13	2.07	0.029
2016	0.09	1.61	0.061
2017	0.20	3.19	0.002
2018	0.13	2.25	0.021
2019	0.24	3.88	0.001
2020	0.24	3.69	0.001
2021	0.15	2.33	0.009
average	0.28	4.30	0.001

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Table 3. Spatial-temporal scan analysis of registered TB cases in Jiangsu province from 2011 to 2021.

Cluster Type	Cluster Time	Counties (n)	Radius（km）	Observed cases (n)	Excepted cases (n)	RR	LLR	*P*-Value
Most likely	2011 -2015	23	112.83	52085	36904.10	1.48	3137.82	0.001
Secondary	2011 -2015	1	0	2411	830.05	2.92	993.49	0.001
2nd Secondary	2011- 2015	13	91.35	32752	26691.71	1.25	698.06	0.001
3rd Secondary	2011- 2015	12	52.07	18942	14584.47	1.32	622.69	0.001
4th Secondary	2011- 2014	1	0	2445	2024.43	1.21	41.19	0.001
5th Secondary	2011- 2014	1	0	1383	1124.15	1.23	27.84	0.001
6th Secondary	2013-2015	1	0	1349	1120.46	1.20	21.94	0.001
7th Secondary	2018	1	0	320	235.15	1.36	13.75	0.001

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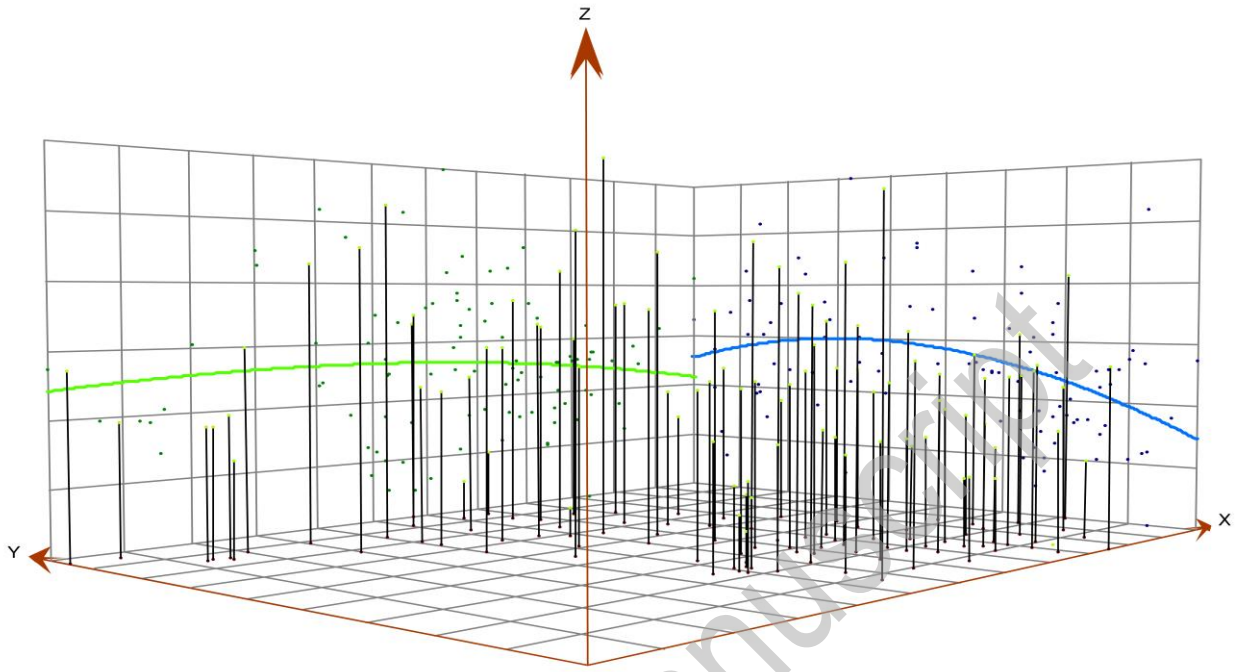

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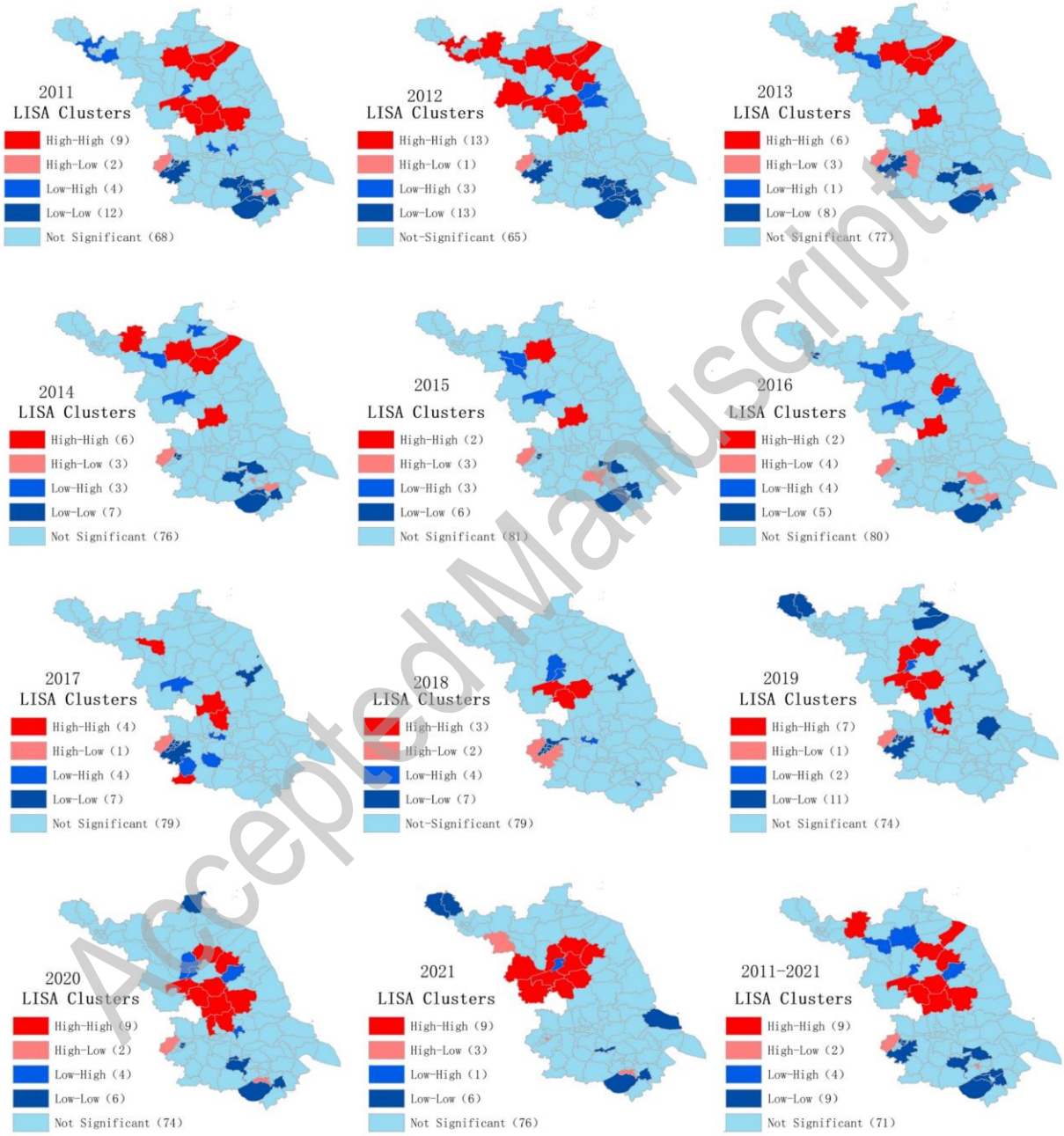

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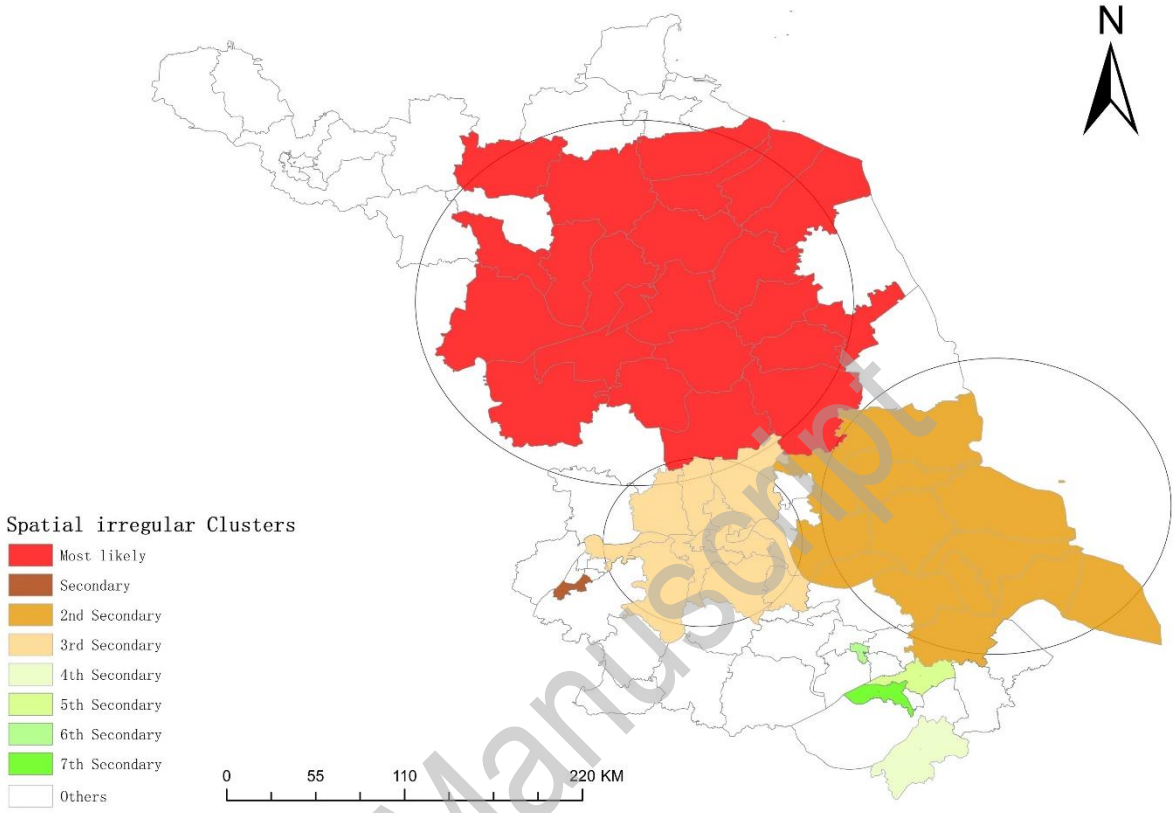

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