

Vital Surveillances

Epidemiological Characteristics and Spatiotemporal Cluster Analysis of Multidrug-Resistant and Rifampicin-Resistant Tuberculosis Among Older People — China, 2019–2025

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ABSTRACT

Introduction: Multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB) in older individuals remains a significant public health challenge in China. This study evaluated the epidemiological characteristics and spatiotemporal patterns of MDR/RR-TB in individuals aged ≥ 65 years in China between 2019 and 2025.

Methods: Data were obtained from the China Information System for Disease Control and Prevention (CISDCP). Spatiotemporal distribution and demographic characteristics of MDR/RR-TB cases in China were analyzed using descriptive epidemiological methods. Global Moran's I and local indicators of spatial association were employed to assess spatial clustering, and spatiotemporal scanning was performed using the SaTScan software to detect high-risk clusters.

Results: From 2019 to 2025, 21,569 patients with MDR/RR-TB aged ≥ 65 years were registered across 31 provincial-level administrative divisions nationwide [1.72% of all pulmonary tuberculosis (PTB) in older patients]. The notification rate of MDR/RR TB among older people declined in 2022 and then rebounded in 2025. The proportion of MDR/RR-TB among older patients with PTB increased. The patients were predominantly male (73.3%) in the 65–69-year age group. Of the cases, 46.0% were retreated, and 83.3% underwent molecular diagnostic testing. Heilongjiang and Gansu were persistent high-high cluster areas, whereas Xinjiang presented the highest risk. Spatiotemporal scanning identified significant clusters in Xinjiang, the three northeastern provinces, Chongqing-Guizhou, and Ningxia-Shaanxi-Gansu.

Conclusions: The proportion of MDR/RR-TB among older patients with PTB in China increased significantly. The clusters were mainly located in the central-western and northeastern regions. We recommend strengthening drug resistance surveillance,

expanding molecular testing coverage in high-risk areas, and optimizing treatment strategies for retreated patients.

China is among the countries with the highest burden of drug-resistant tuberculosis globally. In 2024, newly diagnosed multidrug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB) cases in China will account for approximately 7.1% of the global total and rank second worldwide (1). China's population is rapidly aging. In 2024, the number of people aged ≥ 65 years reached 220 million (15.6% of the total population), making China a veritable aging society. Older adults are particularly vulnerable to TB because of their declining immune function, multiple comorbidities, and prior *Mycobacterium tuberculosis* infections (2). MDR/RR-TB poses even greater challenges for this population, including complex treatment regimens, a high incidence of adverse reactions, and poor outcomes (3).

Previous studies have focused primarily on MDR/RR-TB in the general population or in specific regions (4–6), with limited nationwide research on the epidemiological patterns and spatiotemporal distribution of drug-resistant tuberculosis in older patients. Thus, this study analyzed the epidemiological characteristics, spatial distribution, and spatiotemporal clustering of MDR/RR-TB among older adults in China from 2019 to 2025.

METHODS

Data Source

Data on older patients with MDR/RR-TB from 31 provincial-level administrative divisions (PLADs) in China (2019–2025) were obtained from the China Information System for Disease Control and Prevention (CISDCP). All personal identifiers were

removed to ensure anonymity and only aggregated provincial data were used. Data on age, sex, residence, treatment history, drug sensitivity diagnostic type, and drug sensitivity testing methods were collected. All cases were diagnosed according to the Chinese national health industry standard, "Diagnosis for Pulmonary Tuberculosis (WS 288-2017)" (7). As the study involved the analysis of de-identified secondary surveillance data, ethical approval and informed consent were waived in accordance with national regulations. Detailed information on the data reporting specifications, quality control, data cleaning, and drug resistance detection methods is provided in [Supplementary Material](https://weekly.chinacdc.cn/) (available at <https://weekly.chinacdc.cn/>).

Global Moran's *I* and local indicators of spatial association (LISA) were used to evaluate spatial autocorrelation. The LISA results were classified into -high, -low, high-, and -low, with statistical significance assessed at $P < 0.05$ after 999 permutations. For spatiotemporal cluster detection, we performed a retrospective scan using SaTScan (version 10.2.5; Martin Kulldorff, Boston, MA, USA) based on a discrete Poisson model. The maximum spatial cluster size was set to 50% of the at-risk population and the maximum temporal cluster size was set to 50% of the study period. Statistical significance was assessed using 999 Monte Carlo replications, and clusters with $P < 0.05$ were considered statistically significant. All statistical analyses were performed using the R (version 4.2.1; R Foundation, Vienna, Austria). Spatial mapping was conducted using the ArcGIS Desktop software (version 10.8; Esri, Redlands, California, USA).

RESULTS

Sociodemographic Characteristics

From 2019 to 2025, 21,569 older patients with MDR/RR-TB were registered among the 31 PLADs in China. The population comprised 15,817 men (73.3%) and 5,752 women (26.7%), with a male-to-female ratio of 2.7:1. The mean age was 71.5 ± 6.6 years, with the largest proportion of cases (41.0%) occurring in the 65–69-year age group, followed by the 70–74-year age group (29.6%), 75–79-year age group (17.6%), and ≥ 80 -year age group (11.7%).

Most cases (90.5%) involved local residents, whereas the migrant population accounted for only 9.5%. Nearly half of patients (46.0%) had a history of prior

tuberculosis treatment. Molecular diagnostics were the primary method for detecting rifampicin resistance, which was used in 83.3% of cases (Table 1).

Temporal Trends

Between 2019 and 2022, the registration rate for pulmonary tuberculosis (PTB) among older individuals (≥ 65 years) in China declined significantly from 114.46 to 79.98 per 100,000 (average annual decline, 11.26%). Over the same period, the registration rate of MDR/RR-TB in this population decreased from 1.79 to 1.14 per 100,000 people (average annual decline, 13.96%). From 2023 to 2025, both rates rebounded. The PTB registration rate increased to 90.68 per 100,000 (average annual decline, 0.61%) over the full period. By contrast, the MDR/RR-TB registration rate increased to 1.79 per 100,000 (average annual growth rate, 4.16%) (Figure 1A).

The proportion of MDR/RR-TB among older patients with PTB declined from 1.57% to 1.43% between 2019 and 2022, then increased to 1.97% in 2025, representing a 25.7% increase from the 2019 level (Figure 1B).

TABLE 1. General characteristics of registered MDR/RR-TB cases among adults aged ≥ 65 years in PLADs in China (2019–2025).

Characteristic	Total (N=21,569), n (%)
Age (years)	
65–69	8,854 (41.0)
70–74	6,382 (29.6)
75–79	3,806 (17.6)
≥ 80	2,527 (11.7)
Sex	
Male	15,817 (73.3)
Female	5,752 (26.7)
Residence	
Local	19,524 (90.5)
Migrant	2,045 (9.5)
Treatment history	
New	11,657 (54.0)
Retreated	9,912 (46.0)
Drug sensitivity diagnostic type	
Molecular	17,971 (83.3)
Phenotypic	3,598 (16.7)

Abbreviation: MDR/RR-TB=multidrug-resistant and rifampicin-resistant tuberculosis; PLADs=provincial-level administrative division.

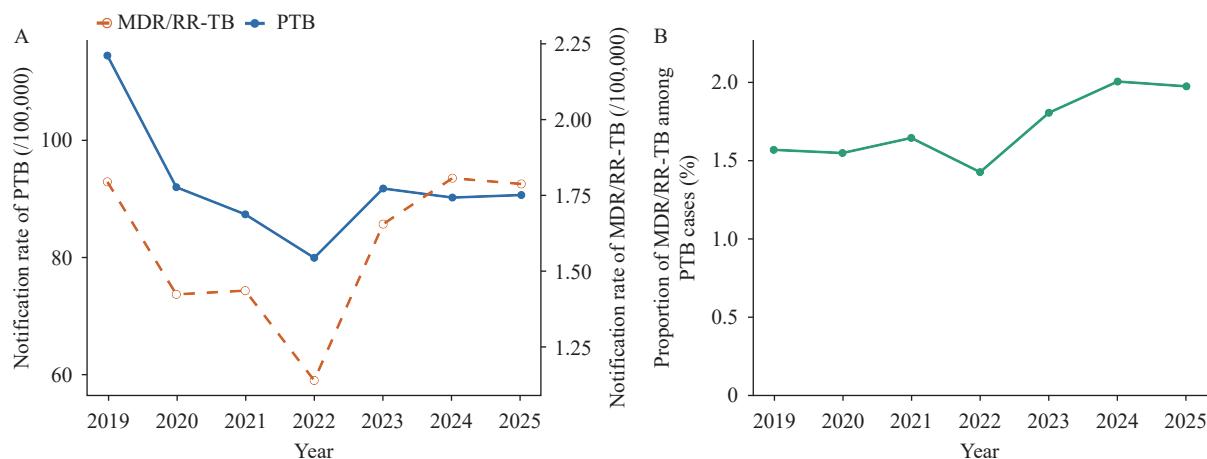


FIGURE 1. Registration trend of PTB and MDR/RR-TB among adults aged ≥ 65 years in PLADs in China (2019–2025). (A) Notification rate of PTB and MDR/RR-TB; (B) MDR/RR-TB proportion in notified PTB cases.

Note: In panel A, the left y-axis (blue) shows the notification rate of PTB per 100,000 population aged ≥ 65 years; the right y-axis (orange) shows the notification rate of MDR/RR-TB per 100,000 population aged ≥ 65 years. Solid lines with filled circles represent PTB and dashed lines with open circles represent MDR/RR-TB. The notification rate was calculated as follows: (notified cases in a given year/mid-year population aged ≥ 65 years) $\times 100,000$. In panel B, the solid line with filled circles indicates the proportion of MDR/RR-TB among notified PTB cases, calculated as (notified MDR/RR-TB cases $\div$ notified PTB cases) $\times 100\%$.

Abbreviation: PTB=pulmonary tuberculosis; MDR/RR-TB=multidrug- and rifampicin-resistant tuberculosis; PLADs=provincial-level administrative divisions; TB=tuberculosis.

Spatial Analysis

From 2019 to 2025, provincial MDR/RR-TB notification rates exhibited marked spatial heterogeneity and temporal dynamics. Global Moran's I values ranged from 0.058 to 0.486 across years, with significant positive spatial autocorrelation detected in all years, except 2022 ($P=0.195$) (all $P<0.05$) (Table 2).

LISA analysis revealed that high-high clusters were primarily distributed in Heilongjiang Province (persisting throughout 2019–2025) and Gansu Province (2019, 2020, 2021, 2023, 2024, and 2025), with further expansion to Xinjiang, Xizang, and Qinghai in 2020. Low-high clusters were observed in Sichuan (2020), Xizang (2021), Anhui (2023), Qinghai (2024), and Inner Mongolia (2025). The low-low clusters included multiple central-eastern provinces, including Jiangsu, Anhui, Shandong, Henan, Hebei, and Zhejiang (Table 2). In addition, Anhui Province exhibited a high-low clustering pattern in 2022.

Spatiotemporal Cluster Analysis

The SaTScan spatiotemporal scanning analysis identified 10 statistically significant high-rate clusters from 2019 to 2025 (Table 3). The cluster with the highest relative risk was Xinjiang [2019–2021, relative risk (RR)=7.92], followed by another cluster in

Xinjiang (2023–2024, $RR=7.45$). The three northeastern provinces had two clusters (2023–2025, $RR=2.51$; 2019–2021, $RR=1.89$). Chongqing and Guizhou formed a cluster (2023–2025, $RR=2.28$), whereas Chongqing alone constituted a cluster (2019–2021, $RR=2.13$). The Ningxia-Shaanxi-Gansu region has two clusters (2024–2025, $RR=1.72$; 2019–2020, $RR=1.49$). Jiangxi (2024–2025, $RR=1.49$) and Anhui (2023–2024, $RR=1.34$) were identified as clusters (Table 3).

DISCUSSION

The proportion of MDR/RR-TB among PTB cases increased from 1.57% to 1.97%, with notification rates declining more slowly than those of PTB. MDR/RR-TB exhibited distinct spatiotemporal clustering: Heilongjiang and Gansu were persistent high-burden areas, Xinjiang presented the highest risk, the three northeastern provinces showed recurrent clustering, and Anhui and other eastern provinces emerged as hotspots.

Temporal trend analysis revealed that the notification rates for both PTB and MDR/RR-TB among older adults declined rapidly from 2019 to 2022. Although China launched the "Action Plan to Stop Tuberculosis (2019–2022)," prioritizing drug-resistant tuberculosis and emphasized enhanced

TABLE 2. Global and local spatial autocorrelation of MDR/RR-TB notification rates among adults aged ≥ 65 years in PLADs in China (2019–2025).

Year	Global aggregation analysis			Localized areas of aggregation			
	Moran's <i>I</i>	Z	P	High–high agglomeration	High–low agglomeration	Low–high agglomeration	Low–low agglomeration
2019	0.058	2.016	0.044	Gansu Heilongjiang Xinjiang Xizang Qinghai			Jiangsu Anhui Jiangsu Anhui
2020	0.486	4.965	<0.001	Gansu Heilongjiang Gansu Heilongjiang		Sichuan	Shandong Henan Hebei
2021	0.220	2.409	0.016	Heilongjiang	Anhui	Xizang	Henan Hebei
2022	0.108	1.294	0.195	Heilongjiang			Shanxi Hebei
2023	0.174	2.205	0.027	Heilongjiang			Hebei
2024	0.104	1.469	0.142	Heilongjiang			
2025	0.375	3.531	<0.001	Heilongjiang Jilin		Inner Mongolia	Jiangsu Anhui Shandong

Abbreviation: MDR/RR-TB=multidrug-resistant and rifampicin-resistant tuberculosis; PLADs=provincial-level administrative divisions.

TABLE 3. Spatiotemporal clusters of MDR/RR-TB notification rates among adults aged ≥ 65 years in PLADs in China (2019–2025).

Cluster number	PLADs (location IDs)	Time (year)	Number of MDR/RR-TB cases	Expected cases	RR	LLR	P
1	Xinjiang	2019–2021	816	106.49	7.92	964.025	<0.001
3	Jilin Liaoning Heilongjiang	2023–2025	2,062	871.73	2.51	619.914	<0.001
1	Xinjiang	2023–2024	451	61.66	7.45	511.592	<0.001
2	Chongqing Guizhou Jilin	2023–2025	1,115	503.30	2.28	284.167	<0.001
3	Liaoning Heilongjiang	2019–2021	1,354	740.10	1.89	213.101	<0.001
1	Chongqing	2019–2021	483	229.78	2.13	107.109	<0.001
3	Ningxia Shaanxi Gansu	2024–2025	541	317.98	1.72	65.661	<0.001
3	Ningxia Shaanxi Gansu	2019–2020	389	262.05	1.49	27.099	<0.001
1	Jiangxi	2024–2025	283	190.87	1.49	19.530	<0.001
1	Anhui	2023–2024	402	302.22	1.34	15.143	<0.001

Abbreviation: RR=relative risk; LLR=log likelihood ratio; MDR/RR-TB=multidrug-resistant and rifampicin-resistant tuberculosis; PLADs=provincial-level administrative divisions.

screening, the coronavirus disease 2019 (COVID-19) pandemic (2020–2022) severely disrupted timely medical consultations for individuals with suspected TB cases, resulting in a substantial decline in case detection, especially among older individuals (8). After the pandemic ended in 2023, notification rates for both conditions rebounded, with MDR/RR-TB recovering faster than PTB, resulting in an approximately 25% increase in the proportion of MDR/RR-TB among older patients with tuberculosis

compared to 2019. Although molecular diagnostics have been increasingly used since 2019 (Supplementary Table S1, available at <https://weekly.chinacdc.cn/>), their detection effect was masked during the pandemic owing to reduced healthcare access. This divergence may be attributed to post-pandemic recovery of diagnostic services that led to catch-up detection of previously missed MDR/RR-TB cases and pandemic-related treatment interruptions that likely increased acquired resistance among retreatment

patients. Although PTB detection has stabilized, the number of MDR/RR-TB cases has continued to increase, suggesting differing transmission dynamics between drug-resistant and drug-sensitive TB. Therefore, TB control efforts should prioritize older patients with MDR/RR-TB, focusing on standardized management and drug resistance screening, especially among retreatment patients.

Of the older patients with MDR/RR-TB, 73.3% were male, and 41.0% were aged 65–69 years, consistent with data reported in China (9). A higher proportion of men may be linked to increased exposure to *M. tuberculosis* (10), whereas the predominance of the 65–69-year age group may reflect an elevated risk of latent infection reactivation and a higher prevalence of comorbidities such as diabetes (11–12). Molecular diagnostics accounted for 83.3% of the detections, highlighting the significant role of technologies such as GeneXpert MTB/RIF in identifying drug-resistant cases (13).

Drug resistance in tuberculosis is clinically classified into primary resistance, which is more common among new patients, and acquired resistance, which is typically observed in retreatment cases. In this study, 54.0% of the older patients with MDR/RR-TB were new cases, whereas 46.0% were retreatment cases. The high proportion of new cases suggests the substantial burden of primary resistance in this population. However, without molecular epidemiological data, determining whether this reflects recent transmission, endogenous reactivation, or reinfection remains challenging, especially considering the high latent infection rate in the older population. Meanwhile, 46.0% of the patients were retreated, indicating that treatment failure or improper treatment remains significant (14–15). Therefore, prevention and control require strengthening early and rapid screening of all newly diagnosed patients to ensure timely initiation of appropriate treatment, while simultaneously enhancing standardized retreatment regimens and case management to improve adherence and prevent further development of acquired resistance.

The spatial distribution of MDR/RR-TB notification rates showed significant clustering. Heilongjiang and Gansu were persistent high-high cluster areas. In Heilongjiang, the contributing factors may include a cold climate, prolonged indoor gatherings, a high proportion of the older population, limited primary-level detection capacity, and the ongoing transmission of resistant strains. This clustering is partly attributable to a substantial burden

of retreatment cases, among which 61.5% of patients with MDR/RR-TB had received retreatment and 60.3% had experienced non-standard hospitalization (16). In Gansu, economic underdevelopment, uneven healthcare distribution, and poverty are likely contributors. In 2020, high-high clusters extended westward to Xinjiang, Xizang, and Qinghai, which were likely influenced by the pandemic. During its early phase, the western regions, which were less affected by strict control measures, maintained relatively stable case detection rates, resulting in higher notification rates than regions with more significant declines. Xinjiang exhibited the highest risk ($RR=7.92$), which was attributable to its heavy baseline burden and active screening strategies (17). The three northeastern provinces formed clusters in both 2019–2021 and 2023–2025, with the latter potentially linked to release of accumulated cases and ongoing transmission. Other regions (Chongqing, Guizhou, Ningxia, Shaanxi, Gansu, Jiangxi, and Anhui) also exhibited clustering, although at a lower risk. Multiple central-eastern provinces exhibited low-low clustering, forming a stable low-burden belt associated with better economic development and healthcare accessibility (18).

This study has some limitations. Passive surveillance may result in under-reporting or diagnostic delays. In addition, provincial-level analysis could not identify intra-provincial clusters; prefecture-level analysis was limited by low case counts and was therefore not conducted, as the results would be unstable. Future studies should address prefecture-level heterogeneity within hotspot provinces as data accumulate.

A shifting epidemiological landscape of MDR/RR-TB was observed among older individuals in China. Following the COVID-19 pandemic, notification rates rebounded rapidly, and drug resistance proportions continued to increase, with significant clustering in the central-western and northeastern regions. Current risk patterns included persistent high-high clusters in Heilongjiang and Gansu, extremely high risk in Xinjiang, recurrent clustering in the three northeastern provinces, and emerging hotspots in the eastern provinces. Therefore, we recommend implementing differentiated control strategies within a risk-stratified framework, investigating the drivers of sustained transmission, developing region-specific action plans, and adopting tailored measures (enhanced surveillance, active screening, and optimized treatment) for different cluster types. These strategies emphasize moving beyond a "one-size-fits-all" model to address the complex heterogeneity of MDR/RR-TB across spatial,

temporal, and demographic dimensions.

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SUPPLEMENTARY MATERIAL

Data Reporting Specifications, Data Cleaning, Quality Control, and Drug Resistance Detection Methods

Data reporting and management: Designated institutions are required to complete case registration within 24 hours of diagnosis and enter follow-up and treatment outcome data within 48 h. The China Information System for Disease Control and Prevention (CISDCP) incorporates automated logic checks and duplication detection to ensure data integrity.

Data cleaning and quality control: Laboratory quality control strictly adheres to the guidelines outlined in China's "National Technical Specifications for Tuberculosis Prevention and Control" (2020 edition). For data cleaning, records with the following issues were excluded to ensure accuracy and consistency:

1. Identification of non-tuberculous mycobacteria (NTM) cases.
2. Contradictory drug susceptibility testing (DST) results, such as cases labeled "sensitive" despite evidence of resistance.
3. Cases exhibiting isoniazid monoresistance were excluded to focus on MDR/RR-TB.

Drug resistance detection methods: According to the National Tuberculosis Control Program (NTP), rifampicin drug susceptibility testing (DST) is universally recommended for all patients with bacteriologically confirmed pulmonary tuberculosis.

The primary detection methods were as follows:

1. Molecular diagnostic methods for rapid detection include GeneXpert MTB/RIF and line probe assays.
2. Phenotypic DST methods, including the proportion method and absolute concentration method, performed on *Mycobacterium tuberculosis* strains isolated from culture.

In China, DST coverage among patients with bacteriologically confirmed TB increased from 81.8% in 2019 to over 90% during 2020–2025, reflecting substantial improvement in detection capacity.

SUPPLEMENTARY TABLE S1. Annual drug susceptibility testing methods for MDR/RR-TB cases among older individuals aged ≥65 years in China (2019–2025).

Year	Molecular biology testing (n)	Traditional phenotypic DST (n)	Total DST (n)	Molecular testing proportion (%)
2019	2029	935	2,964	68.45
2020	1,850	666	2,516	73.53
2021	2,069	674	2,743	75.43
2022	1,851	405	2,256	82.05
2023	2,960	452	3,412	86.75
2024	3,514	305	3,819	92.01
2025	3,665	194	3,859	94.97

Abbreviation: DST=drug susceptibility testing; MDR/RR-TB=multidrug- and rifampicin-resistant tuberculosis.

Molecular biology testing includes rapid molecular diagnostics such as GeneXpert MTB/RIF and line probe assays. Traditional phenotypic DST refers to culture-based methods such as the proportion method and absolute concentration method. Molecular testing proportion (%) = (molecular biology testing / total DST) × 100%.