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# Trends in Drug Resistance and Epidemiological Patterns of Tuberculosis in Elderly Patients in Wenzhou, China (2014-2023)

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**Purpose:** This study aimed to elucidate the epidemiological features, drug resistance patterns, and temporal trends among elderly tuberculosis (TB) patients in Wenzhou, China, from 2014 to 2023, providing insights for targeted TB control strategies.

**Patients and Methods:** Data were extracted from 10,993 TB patients registered in the Laboratory Information System of Wenzhou Central Hospital and the Tuberculosis Information Management System of the Chinese Center for Disease Control and Prevention. Patients were divided into elderly (≥60 years, n=2,727) and non-elderly (<60 years, n=8,266) groups. Sociodemographic, clinical, and phenotypic drug susceptibility testing data were analyzed using chi-square tests. Temporal trends in drug resistance were assessed via Joinpoint regression to estimate annual percentage changes (APC).

**Results:** The elderly group had higher proportions of males (79.65% vs 69.66%), Han ethnicity (99.63% vs 96.35%), and lesions involving ≥3 lung fields (42.35% vs 32.62%), but lower proportions of migrants (20.32% vs 51.20%), urban residents (41.03% vs 53.41%), employed individuals (8.98% vs 32.91%), and pulmonary cavitation (46.75% vs 53.54%). The overall drug-resistant tuberculosis (DR-TB) rate was similar between the elderly and non-elderly groups (20.76% vs 20.30%). However, the elderly group had lower rates of streptomycin (SM) resistance (11.07% vs 12.62%), rifampicin (RFP) resistance (6.20% vs 8.06%), and multidrug-resistant tuberculosis (MDR-TB) (5.39% vs 7.10%). From 2014 to 2023, the overall DR-TB rate among elderly patients decreased from 31.58% to 20.64% (−34.63%), with a significant decline in MDR-TB (APC of −9.9%). Resistance to isoniazid (INH) decreased from 2016 to 2023 (APC −4.0%), and RFP resistance decreased from 2014 to 2021 (APC −10.7%). Significant decreases were also observed among migrant populations (APC −10.1%, 2014–2020), urban residents (APC −8.7%, 2014–2021), and unemployed individuals (APC −4.3%, 2014–2023).

**Conclusion:** Our study revealed that drug resistance among elderly TB patients in Wenzhou has decreased over the past decade, particularly for MDR-TB and key first-line drugs. However, the elderly group still exhibited distinct epidemiological and drug resistance profiles compared to younger patients. These findings offer clear suggestions for public health policy-making and clinical practice, which can help further reduce the burden of tuberculosis and drug resistance in the elderly population.

**Keywords:** tuberculosis, elderly population, drug resistance, epidemiology, joinpoint regression model

## Introduction

Tuberculosis (TB) is widely acknowledged as an extremely harmful infectious disease that contributes significantly to illness and death across the globe.[1,2] Although there has been notable advancement in controlling TB on a worldwide scale over



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recent decades, it continues to pose a substantial public health challenge, especially in low- and middle-income nations.[3] The most recent report from the World Health Organization (WHO) estimates that in 2023, around 10.8 million individuals were diagnosed with TB worldwide, with a significant number of these cases arising in countries heavily impacted by the disease, such as China.[4] The rise and swift dissemination of drug-resistant TB (DR-TB) present a daunting obstacle to existing treatment approaches and public health initiatives, threatening the progress achieved in combating TB.[5–7]

Among various susceptible populations, the elderly exhibit a significantly elevated risk of TB infection due to immunocompromised status, high prevalence of chronic disorders, and reactivation of latent tuberculosis infection.[8,9] Previous studies have demonstrated that elderly TB patients frequently present with atypical symptoms, which may lead to misdiagnosis or underdiagnosis, thereby contributing to subsequent delays in treatment initiation.[10,11] Compared with younger patients, elderly TB patients experience poorer treatment outcomes and higher mortality rates, a phenomenon closely associated with their physiological characteristics and comorbid conditions.[12] For instance, studies from India have revealed that elderly TB patients demonstrate significantly higher treatment failure and mortality rates than their younger counterparts, primarily attributable to multiple comorbidities and poor treatment adherence.[13,14] Similar findings have been reported in studies conducted in Lishui, Zhejiang Province, China,[15] the Western Pacific Region[8] and Taipei, China.[16] Collectively, these studies untangle the unique challenges faced by the elderly population regarding TB diagnosis, treatment adherence, and clinical management.

The genetic mutations in Mycobacterium tuberculosis (MTB) play a crucial role in the development of drug resistance. Specific mutations in genes such as *rpoB* for rifampicin resistance, *katG* and *inhA* for isoniazid resistance, and *rrs* for streptomycin resistance have been well-documented.[17] These mutations can lead to changes in the target sites of the drugs or alter the drug uptake mechanisms, rendering the drugs ineffective. Understanding these genetic mutations helps to appreciate the complexity of drug resistance and the need for effective diagnostic tools and treatment strategies. In terms of TB treatment regimens, the standard first-line regimen typically includes isoniazid, rifampicin, pyrazinamide, and ethambutol for an initial period of 2 months, followed by isoniazid and rifampicin for an additional 4 months. However, the emergence of drug resistance has led to the development of alternative regimens, which often involve the use of second-line drugs such as fluoroquinolones and bedaquiline.[18] The commonly used diagnostic tests for TB include sputum smear microscopy, culture, and molecular methods such as the Xpert MTB/RIF assay, which can rapidly detect MTB and rifampicin resistance.[19] These diagnostic tools are essential for early detection and appropriate treatment of TB, but their effectiveness may vary in different populations, including the elderly.

Since 1999, China has entered an aging society, with a continuous increase in the elderly population, projected to exceed 250 million by 2030.[20] Zhejiang Province is one of China's most populous provinces, and Wenzhou, as an important city in Zhejiang, has a substantial elderly population. By the end of 2023, the population aged 60 and above in Wenzhou reached 1.8031 million, accounting for 22.03% of the total population, indicating that Wenzhou has entered a moderately aging society.[21] This demographic shift not only exerts immense pressure on medical resources but also poses new challenges for TB control.[22] To address the TB burden, the Chinese government has implemented various TB control programs, including the Directly Observed Treatment, Short-course (DOTS) strategy, the strengthening of TB surveillance systems, and the promotion of public awareness campaigns.[23,24] These efforts have contributed to the overall decline in TB incidence in China, but the situation among the elderly remains a concern. This study aims to analyze the epidemiological characteristics, drug resistance patterns, and their changing trends among elderly TB patients in Wenzhou from 2014 to 2023, providing scientific evidence for targeted TB control strategies.

# Materials and Methods

## Study Population and Data Collection

This study was conducted at Wenzhou Central Hospital, a designated tuberculosis diagnosis and treatment center in Wenzhou City. Data were extracted from the Tuberculosis Information Management System (TBIMS) of the Chinese Center for Disease Control and Prevention and the hospital's laboratory information system, including sociodemographic details (gender, age, ethnicity, household registration, current residence, and employment status), phenotypic drug susceptibility testing (pDST) results, pulmonary imaging findings, and TB treatment records. From January 1, 2014, to December 31, 2023, TBIMS recorded 39,356 TB cases in Wenzhou City. After excluding 9,819 cases diagnosed solely by molecular methods without mycobacterial culture confirmation, 117 cases identified as non-tuberculous mycobacterial infections upon culture, and 18,427 culture-negative cases lacking pDST results, the final study cohort comprised 10,993 patients with MTB culture isolation and available pDST results.

## Definitions

Patients were categorized into two groups based on age: the elderly group (aged≥60 years) and the non-elderly group (aged<60 years).

Drug resistance was classified as follows: Any drug resistance refers to resistance to a particular anti-tuberculosis drug. Mono-resistant tuberculosis (MR-TB) is defined as resistance to one first-line anti-tuberculosis drug. Polydrug-resistant tuberculosis (PDR-TB) is characterized by resistance to two or more first-line anti-tuberculosis drugs, excluding simultaneous resistance to isoniazid and rifampicin. Multidrug-resistant TB (MDR-TB) is defined as resistance to at least isoniazid and rifampicin.[25]

New cases were defined as patients who had not previously received anti-tuberculosis treatment or had received treatment for less than one month. Retreatment cases refer to patients who have received irregular anti-TB treatment for more than one month, as well as those who have failed initial treatment and have relapsed.[25]

## Bacteriologic Examinations and Drug Susceptibility Testing

Upon patient admission, 3–5 mL of sputum or bronchoalveolar lavage fluid samples were collected and pre - treated with NALC-NaOH. The pre-treated samples were then inoculated into BACTEC MGIT liquid culture tubes or Löwenstein-Jensen solid media and incubated at 37°C. For culture-positive isolates, smears were prepared and subjected to Ziehl-Neelsen acid-fast staining, followed by microscopic examination. If mycobacteria were identified, an MPB64 antigen test was performed to confirm the strain as MTB. Phenotypic drug susceptibility testing for MTB was conducted using the MGIT liquid culture method, following the instructions provided with the instruments and reagents. The concentrations of the four first-line anti-tuberculosis drugs (FLDs) were set as follows: Streptomycin (SM) at 1.0μg/mL, Isoniazid (INH) at 0.1μg/mL, Rifampin (RFP) at 1.0μg/mL, and Ethambutol (EMB) at 5.0μg/mL. The culture-positive MTB samples were inoculated into MGIT liquid culture tubes containing the respective drug concentrations, with control tubes without drugs also being set up. The culture tubes were placed into the MGIT 960 instrument and cultured at 37°C, with the instrument automatically monitoring the fluorescence signals in the culture tubes to determine bacterial growth. When the fluorescence signal in the control tube reached the preset threshold, the instrument automatically read the results of the drug-containing culture tubes, and the sensitivity of MTB to different drugs was determined based on the changes in fluorescence signals.

## Statistical Analysis

Categorical variables, including gender (male/female), ethnicity (Han/others), migrant population (yes/no), place of residence (urban/rural), employment status (employed/unemployed), number of involved lung fields (≤2/≥3), pulmonary cavity (yes/no), treatment type (new treatment/retreatment), and drug resistance patterns, were summarized using frequencies and percentages. The chi-square test was employed to compare the differences in demographic, clinical characteristics, and drug resistance patterns between the elderly group and the non-elderly group. A P value of less than 0.05 was considered statistically significant.

The Joinpoint regression model was utilized to analyze the annual changes in the drug resistance rate of elderly tuberculosis patients from 2014 to 2023. The trend was expressed as the annual percentage change (APC), which was estimated by fitting a simple linear log regression model. The Z test was conducted to determine whether the APC was significantly different from zero. Specifically, an APC with P≥0.05 was deemed stable, whereas a significant positive or negative APC (P<0.05) indicated an increase or decrease. All statistical analyses were performed using SPSS software (version 26.0) and Joinpoint regression software (version 5.3.0.0).

# Results

## Sociodemographic and Clinical Characteristics of TB Patients

In this study, we analyzed the sociodemographic and clinical characteristics of elderly and non-elderly TB patients in Wenzhou from 2014 to 2023. A total of 10,993 patients were included, with 2,727 (24.80%) in the elderly group and 8,266 (75.20%) in the non-elderly group. Regarding gender distribution, male patients accounted for 72.14% of the total (7,930/10,993), with a higher proportion in the elderly group compared to the non-elderly group (79.65% vs 69.66%, P<0.001). In terms of ethnicity, Han Chinese patients constituted 97.16% of the total (10,681/10,993), with a higher proportion in the elderly group compared to the non-elderly group (99.63% vs 96.35%, P<0.001). For migration status, the non-elderly group had a higher proportion of migrants compared to the elderly group (51.20% vs 20.32%, P<0.001). Regarding place of residence, the non-elderly group had a higher proportion living in urban areas compared to the elderly group (53.41% vs 41.03%, P<0.001). In terms of occupation, the non-elderly group had a higher proportion of employed individuals compared to the elderly group (32.91% vs 8.98%, P<0.001). Regarding pulmonary involvement, the elderly group had a higher proportion of cases with ≥3 lung fields involved compared to the non-elderly group (42.35% vs 32.62%), but a lower proportion of pulmonary cavities (46.75% vs 53.54%). Regarding treatment category, new cases accounted for 89.30% of the total (9,817/10,993), with no significant difference between the elderly and non-elderly groups (88.38% vs 89.61%, P=0.071) (Table 1).

## Drug Resistance Profiles in Elderly and Non-Elderly Patients with TB

Among patients with TB, the elderly group (n=2727) and the non-elderly group (n=8266) exhibited similar rates of DR-TB, with no significant difference observed (20.76% vs 20.30%, P=0.609). In terms of specific drug resistance, the elderly group had a lower rate of streptomycin (SM) resistance compared to the non-elderly group (11.07% vs 12.62%, P=0.033), while the rate of isoniazid (INH) resistance was higher in the elderly group (15.33% vs 14.30%, P=0.187), although this difference was not statistically significant. The elderly group also had a significantly lower rate of rifampicin (RFP) resistance (6.20% vs 8.06%, P=0.001), while the rate of ethambutol (EMB) resistance did not differ significantly between the two groups (3.37% vs 3.76%, P=0.349). Regarding types of drug resistance, the elderly group had a higher rate of MR-TB (10.96% vs 9.50%, P=0.026), while the rate of PDR-TB did not differ significantly between the groups (4.40% vs 3.70%, P=0.101). The incidence of MDR-TB was lower in the elderly group (5.39% vs 7.10%, P=0.002). Additionally, the proportion of patients simultaneously resistant to isoniazid and rifampicin (INH+RFP) was

**Table 1** Sociodemographic and Clinical Characteristics of Elderly and Non-Elderly TB Patients in Wenzhou from 2014 to 2023

| **Characteristics** | | **Total, n = 10,993 (%)** | **Elderly Group, n = 2727 (%)** | **Non-Elderly Group, n = 8266 (%)** | ***P*-value** |
|---|---|---|---|---|---|
| Gender | Male | 7930 (72.14) | 2172 (79.65) | 5758 (69.66) | < 0.001 |
| | Female | 3063 (27.86) | 555 (20.35) | 2508 (30.34) | |
| Ethnicity | Han | 10681 (97.16) | 2717 (99.63) | 7964 (96.35) | < 0.001 |
| | Others | 312 (2.84) | 10 (0.37) | 302 (3.65) | |
| Migrant | Yes | 4786 (43.54) | 554 (20.32) | 4232 (51.20) | < 0.001 |
| | No | 6207 (56.46) | 2173 (79.68) | 4034 (48.80) | |
| Residence | Urban | 5534 (50.34) | 1119 (41.03) | 4415 (53.41) | < 0.001 |
| | Rural | 5459 (49.66) | 1608 (58.97) | 3851 (46.59) | |
| Occupation | Employed | 2965 (26.97) | 245 (8.98) | 2720 (32.91) | < 0.001 |
| | Unemployed | 8028 (73.03) | 2482 (91.02) | 5546 (67.09) | |
| Number of lesions involving lung fields | ≤ 2 | 7142 (64.97) | 1572 (57.65) | 5570 (67.38) | < 0.001 |
| | ≥ 3 | 3851 (35.03) | 1155 (42.35) | 2696 (32.62) | |
| Pulmonary cavity | Yes | 5701 (51.86) | 1275 (46.75) | 4426 (53.54) | < 0.001 |
| | No | 5292 (48.14) | 1452 (53.25) | 3840 (46.46) | |
| Treatment category | New cases | 9817 (89.30) | 2410 (88.38) | 7407 (89.61) | 0.071 |
| | Retreated cases | 1176 (10.70) | 317 (11.62) | 859 (10.39) | |

similar between the two groups (1.69% vs 1.84%, P=0.605), while the proportion simultaneously resistant to streptomycin, isoniazid, and rifampicin (SM+INH+RFP) was significantly lower in the elderly group (1.72% vs 2.55%, P=0.013). The incidence of resistance to all four drugs (SM+INH+RFP+EMB) was also lower in the elderly group (1.47% vs 2.15%, P=0.026) (Table 2).

## Temporal Trends of Drug Resistance in Elderly TB Patients in Wenzhou, 2014-2023

From 2014 to 2023, the overall incidence rate of DR-TB among elderly TB patients in Wenzhou decreased from 31.58% to 20.64% (−34.63%). MR-TB decreased from 13.82% to 9.92% (−28.20%), PDR-TB increased from 5.26% to 5.90% (+12.06%), and MDR-TB significantly declined from 12.50% to 4.83% (−61.39%). Resistance rates to first-line drugs also changed: SM from 14.47% to 13.67% (−5.53%), INH from 26.32% to 13.67% (−48.04%), RFP from 12.50% to 6.43% (−48.53%), and EMB from 6.58% to 4.29% (−34.80%). Demographically, male rates decreased from 30.51% to 20.42% (−33.08%), female from 26.47% to 21.43% (−19.05%), Han ethnicity from 31.79% to 20.70% (−34.88%), migrants from 37.50% to 23.08% (−38.46%), non-migrants from 30.00% to 20.46% (−31.80%), urban patients from 25.00% to 16.87% (−32.53%), and rural patients from 35.42% to 23.67% (−33.16%). Unemployed patients' rates decreased from 34.53% to 21.04% (−39.08%). Employed patients' rates increased from 16.67% in 2015 to 17.78% in 2023 (+6.67%). Regarding pulmonary involvement, patients with ≤2 lung fields involved saw rates drop from 28.74% to 19.63% (−24.07%), and those with ≥3 lung fields involved experienced a decline from 35.38% to 18.95% (−46.43%). For pulmonary cavity status, patients with cavities had rates decrease from 37.14% to 18.18% (−51.05%), and those without cavities saw a rate decrease from 26.83% to 22.60% (−15.78%). In terms of treatment category, new cases' rates dropped from 23.77% to 20.17% (−15.13%), and retreated cases' rates significantly declined from 63.33% to 26.92% (−57.49%) (Table 3).

**Table 2** Drug Resistance Patterns in Elderly and Non-Elderly TB Patients

| Drug Resistance Pattern | Elderly Group, n = 2727 (%) | Non-Elderly Group, n = 8266 (%) | *P*-value |
|---|---|---|---|
| DR-TB | 566 (20.76) | 1678 (20.30) | 0.609 |
| Any resistance | | | |
| Any SM | 302 (11.07) | 1043 (12.62) | 0.033 |
| Any INH | 418 (15.33) | 1182 (14.30) | 0.187 |
| Any RFP | 169 (6.20) | 666 (8.06) | 0.001 |
| Any EMB | 92 (3.37) | 311 (3.76) | 0.349 |
| MR-TB | 299 (10.96) | 785 (9.50) | 0.026 |
| SM | 111 (4.07) | 384 (4.65) | 0.209 |
| INH | 159 (5.83) | 312 (3.77) | < 0.001 |
| RFP | 14 (0.51) | 58 (0.70) | 0.291 |
| EMB | 15 (0.55) | 31 (0.38) | 0.220 |
| PDR-TB | 120 (4.40) | 306 (3.70) | 0.101 |
| SM+RFP | 2 (0.07) | 5 (0.06) | 1.000* |
| SM+INH | 95 (3.48) | 245 (2.96) | 0.174 |
| SM+EMB | 0 (0) | 2 (0.02) | 1.000** |
| RFP+EMB | 6 (0.22) | 16 (0.19) | 0.789 |
| INH+EMB | 10 (0.37) | 20 (0.24) | 0.279 |
| SM+INH+EMB | 7 (0.26) | 18 (0.22) | 0.711 |
| MDR-TB | 147 (5.39) | 587 (7.10) | 0.002 |
| INH+RFP | 46 (1.69) | 152 (1.84) | 0.605 |
| SM+INH+RFP | 47 (1.72) | 211 (2.55) | 0.013 |
| INH+RFP+EMB | 14 (0.51) | 46 (0.56) | 0.791 |
| SM+INH+RFP+EMB | 40 (1.47) | 178 (2.15) | 0.026 |

**Notes:** *By Continuity correction chi-square test. **By Fisher's Exact Test.

**Abbreviations**: DR-TB, drug-resistant tuberculosis; MR-TB, mono-resistant tuberculosis; PDR-TB, polydrug-resistant tuberculosis; MDR-TB, multidrug-resistant tuberculosis; SM, streptomycin; INH, isoniazid; RFP, rifampicin; EMB, ethambutol.

**Table 3** Temporal Trends of Drug Resistance Rate Among Elderly TB Cases in Wenzhou from 2014 to 2023

| Characteristics | Drug Resistance Rate (%) | | | | | | | | | | Change[a] (%) 2014–2023 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | |
| DR-TB (Total) | 31.58 | 17.39 | 23.90 | 23.21 | 22.22 | 17.67 | 19.93 | 17.14 | 19.53 | 20.64 | −34.63 |
| Type | | | | | | | | | | | |
| MR-TB | 13.82 | 8.70 | 11.22 | 15.00 | 12.38 | 8.33 | 10.70 | 8.57 | 12.46 | 9.92 | −28.20 |
| PDR-TB | 5.26 | 2.17 | 6.34 | 2.50 | 4.13 | 3.67 | 4.06 | 4.86 | 4.71 | 5.90 | 12.06 |
| MDR-TB | 12.50 | 6.52 | 6.34 | 5.71 | 5.71 | 5.67 | 5.12 | 3.71 | 2.36 | 4.83 | −61.39 |
| First-line drugs | | | | | | | | | | | |
| SM | 14.47 | 5.43 | 14.15 | 10.36 | 13.97 | 7.67 | 12.18 | 9.14 | 9.76 | 13.67 | −5.53 |
| INH | 26.32 | 15.76 | 17.56 | 17.14 | 16.51 | 14.33 | 13.65 | 12.57 | 12.79 | 13.67 | −48.04 |
| RFP | 12.50 | 6.52 | 6.83 | 6.79 | 5.71 | 7.00 | 5.17 | 4.57 | 4.04 | 6.43 | −48.53 |
| EMB | 6.58 | 2.72 | 4.88 | 2.86 | 2.54 | 2.67 | 2.58 | 2.57 | 3.70 | 4.29 | −34.80 |
| Gender | | | | | | | | | | | |
| Male | 30.51 | 17.81 | 23.08 | 20.27 | 21.86 | 17.62 | 18.81 | 17.89 | 20.09 | 20.42 | −33.08 |
| Female | 26.47 | 15.79 | 27.78 | 34.48 | 23.53 | 17.86 | 24.53 | 13.85 | 17.46 | 21.43 | −19.05 |
| Ethnicity | | | | | | | | | | | |
| Han | 31.79 | 17.03 | 24.14 | 23.30 | 22.22 | 17.67 | 20.00 | 17.14 | 19.32 | 20.70 | −34.88 |
| Others | | 50.00 | | | | | | | 50.00 | | |
| Migrant | | | | | | | | | | | |
| Yes | 37.50 | 24.39 | 27.78 | 28.79 | 28.28 | 24.75 | 11.76 | 22.58 | 10.00 | 23.08 | −38.46 |
| No | 30.00 | 15.38 | 23.08 | 21.50 | 19.44 | 14.07 | 24.85 | 16.61 | 20.22 | 20.46 | −31.80 |
| Residence | | | | | | | | | | | |
| Urban | 25.00 | 25.76 | 22.78 | 21.28 | 22.86 | 16.80 | 16.24 | 13.41 | 16.33 | 16.87 | −32.53 |
| Rural | 35.42 | 12.71 | 24.60 | 24.19 | 21.90 | 18.29 | 22.73 | 20.43 | 22.67 | 23.67 | −33.16 |
| Occupation | | | | | | | | | | | |
| Employed | | 16.67 | 8.70 | 27.78 | 20.00 | 8.33 | 17.65 | 17.24 | 33.33 | 17.78 | 6.67 |
| Unemployed | 34.53 | 17.47 | 25.82 | 22.54 | 22.41 | 18.06 | 20.08 | 17.13 | 18.15 | 21.04 | −39.08 |
| Number of lesions involving lung fields | | | | | | | | | | | |
| ≤ 2 | 28.74 | 19.42 | 23.53 | 21.79 | 22.11 | 18.60 | 24.05 | 16.67 | 19.63 | 21.82 | −24.07 |
| ≥ 3 | 35.38 | 14.81 | 24.42 | 25.00 | 22.40 | 16.41 | 14.16 | 17.81 | 19.40 | 18.95 | −46.43 |
| Pulmonary cavity | | | | | | | | | | | |
| Yes | 37.14 | 20.00 | 20.00 | 26.15 | 27.10 | 16.41 | 19.57 | 21.12 | 17.57 | 18.18 | −51.05 |
| No | 26.83 | 15.60 | 28.00 | 20.67 | 17.50 | 18.60 | 20.30 | 13.76 | 21.48 | 22.60 | −15.78 |
| Treatment category | | | | | | | | | | | |
| New cases | 23.77 | 10.60 | 21.11 | 22.08 | 22.18 | 15.95 | 18.60 | 16.20 | 18.05 | 20.17 | −15.13 |
| Retreated cases | 63.33 | 48.48 | 44.00 | 30.00 | 22.58 | 27.91 | 31.03 | 27.59 | 32.26 | 26.92 | −57.49 |

**Notes**: The drug resistance rate (%) was calculated as follows: (Number of cases in each DR-TB subgroup / Total number of corresponding elderly TB cases in the same year)*100%. For instance, the drug resistance rate (%) among elderly male TB cases in 2014 was calculated as: (Number of DR-TB cases in elderly males in 2014 / Total number of elderly male TB cases in 2014)*100%. [a]The % changes were calculated as follows: (incidence in 2023 - incidence in 2014) / incidence in 2014.
**Abbreviations**: DR-TB, drug-resistant tuberculosis; MR-TB, mono-resistant tuberculosis; PDR-TB, polydrug-resistant tuberculosis; MDR-TB, multidrug-resistant tuberculosis; SM, streptomycin; INH, isoniazid; RFP, rifampicin; EMB, ethambutol.

## Annual Percentage Change and Joinpoint Regression Model of Drug Resistance Among Elderly TB Patients in Wenzhou, 2014-2023

The Joinpoint regression model analysis revealed that from 2014 to 2023, the incidence rate of MDR-TB among elderly TB patients in Wenzhou significantly decreased, with an APC of −9.9% (95% CI: −15.4% to −4.1%, P=0.005). Among first-line anti-TB drugs, resistance to INH significantly decreased from 2016 to 2023, with an APC of −4.0% (95% CI: −7.1% to −0.7%, P=0.027). Resistance to RFP significantly decreased from 2014 to 2021, with an APC of −10.7% (95% CI: −19.3% to −1.2%, P=0.035). In terms of demographic characteristics, the resistance rate among migrant populations significantly decreased from 2014 to 2020, with an APC of −10.1% (95% CI: −18.7% to −0.7%, P=0.040). Urban residents experienced a significant decrease in resistance rates from 2014 to 2021, with an APC of −8.7% (95% CI: −12.8% to −4.4%, P=0.004). Unemployed individuals showed a significant decrease in resistance rates from 2014 to 2023, with an APC of −4.3% (95% CI: −8.4% to −0.1%, P=0.048). Additionally, retreated cases had a significant decrease in resistance rates from 2014 to 2018, with an APC of −20.1% (95% CI: −26.5% to −13.2%, P=0.001). Other variables, including MR-TB, PDR-TB, overall DR-TB rates, as well as resistance to SM and EMB, and resistance rates stratified by gender, ethnicity, rural residence, pulmonary involvement, and new cases, showed changes across different periods but did not reach statistical significance (P>0.05) (Table 4).

**Table 4** Annual Percentage Change in Drug Resistance Rate of Elderly Tuberculosis in Wenzhou from 2014 to 2023

| Variables | Period | APC (95% CI) | Test Statistic (t) | *P*-value |
|---|---|---|---|---|
| Type | | | | |
| DR-TB (Total) | 2014–2021 | −5.9 (−13.3, 2.2) | −1.894 | 0.117 |
| | 2021–2023 | 9.0 (−35.6, 84.6) | 0.421 | 0.691 |
| MR-TB | 2014–2017 | 2.5 (−33.6, 58.3) | 0.146 | 0.890 |
| | 2017–2023 | −3.9 (−14.4, 7.8) | −0.894 | 0.412 |
| PDR-TB | 2014–2019 | −5.4 (−29.7, 27.3) | −0.484 | 0.649 |
| | 2019–2023 | 12.0 (−18.7, 54.3) | 0.908 | 0.406 |
| MDR-TB | 2014–2023 | −9.9* (−15.4, −4.1) | −3.834 | 0.005 |
| First-line drugs | | | | |
| SM | 2014–2021 | −4.0 (−18.5, 13.2) | −0.632 | 0.555 |
| | 2021–2023 | 15.6 (−57.0, 211.0) | 0.378 | 0.721 |
| INH | 2014–2016 | −16.5 (−38.1, 12.7) | −1.545 | 0.183 |
| | 2016–2023 | −4.0* (−7.1, −0.7) | −3.108 | 0.027 |
| RFP | 2014–2021 | −10.7* (−19.3, −1.2) | −2.870 | 0.035 |
| | 2021–2023 | 16.1 (−46.3, 150.9) | 0.498 | 0.640 |
| EMB | 2014–2019 | −17.1 (−32.0, 1.0) | −2.436 | 0.059 |
| | 2019–2023 | 16.8 (−9.3, 50.5) | 1.579 | 0.175 |
| Gender | | | | |
| Male | 2014–2019 | −7.0 (−17.2, 4.4) | −1.623 | 0.166 |
| | 2019–2023 | 2.6 (−11.7, 19.2) | 0.438 | 0.679 |
| Female | 2014–2017 | 7.5 (−35.5, 79.2) | 0.364 | 0.731 |
| | 2017–2023 | −7.5 (−19.3, 6.1) | −1.461 | 0.204 |
| Ethnicity | | | | |
| Han | 2014–2021 | −6.0 (−13.7, 2.4) | −1.852 | 0.123 |
| | 2021–2023 | 9.0 (−37.0, 88.8) | 0.405 | 0.702 |
| Migrant | | | | |
| Yes | 2014–2020 | −10.1* (−18.7, −0.7) | −2.753 | 0.040 |
| | 2020–2023 | 2.3 (−36.0, 63.4) | 0.123 | 0.907 |
| No | 2014–2019 | −7.0 (−22.2, 11.1) | −1.053 | 0.341 |
| | 2019–2023 | 3.7 (−15.8, 27.7) | 0.447 | 0.674 |
| Residence | | | | |
| Urban | 2014–2021 | −8.7* (−12.8, 4.4) | −5.035 | 0.004 |
| | 2021–2023 | 7.8 (−18.9, 43.2) | 0.675 | 0.530 |
| Rural | 2014–2019 | −7.2 (−23.5, 12.6) | −0.992 | 0.367 |
| | 2019–2023 | 4.7 (−19.0, 35.4) | 0.463 | 0.663 |
| Occupation | | | | |
| Employed | 2015–2023 | 2.2 (−9.2, 15.0) | 0.436 | 0.676 |
| Unemployed | 2014–2023 | −4.3* (−8.4, −0.1) | −2.335 | 0.048 |
| Number of lesions involving lung fields | | | | |
| ≤ 2 | 2014–2021 | −4.2 (−10.6, 2.6) | −1.599 | 0.171 |
| | 2021–2023 | 7.3 (−31.5, 68.1) | 0.405 | 0.702 |
| ≥ 3 | 2014–2020 | −9.9 (−22.2, 4.2) | −1.839 | 0.125 |
| | 2020–2023 | 6.8 (−27.1, 56.4) | 0.443 | 0.677 |

(*Continued*)

**Table 4** (Continued).

| Variables | Period | APC (95% CI) | Test Statistic (t) | *P*-value |
|---|---|---|---|---|
| Pulmonary cavity | | | | |
| Yes | 2014–2016 | −15.5 (−56.4, 63.9) | −0.653 | 0.543 |
| | 2016–2023 | −3.9 (−10.2, 2.9) | −1.491 | 0.196 |
| No | 2014–2021 | −5.8 (−14.8, 4.3) | −1.503 | 0.193 |
| | 2021–2023 | 19.4 (−34.9, 119.2) | 0.752 | 0.486 |
| Treatment category | | | | |
| New cases | 2014–2021 | −3.3 (−14.4, 9.3) | −0.701 | 0.515 |
| | 2021–2023 | 7.5 (−46.7, 116.9) | 0.266 | 0.801 |
| Retreated cases | 2014–2018 | −20.1* (−26.5, −13.2) | −6.919 | 0.001 |
| | 2018–2023 | 3.9 (−3.6, 11.9) | 1.314 | 0.246 |

**Abbreviations**: APC, annual percentage change; DR-TB, drug-resistant tuberculosis; MR-TB, mono-resistant tuberculosis; PDR-TB, polydrug-resistant tuberculosis; MDR-TB, multidrug-resistant tuberculosis; SM, streptomycin; INH, isoniazid; RFP, rifampicin; EMB, ethambutol.

## Discussion

As a high-burden region for TB, China is also experiencing rapid population aging, making the burden of TB among the elderly an increasingly severe public health concern.[26,27] Conducting a comprehensive study on the epidemiological characteristics and drug resistance patterns of TB in the elderly is crucial, as it provides important insights into the nature of TB in this vulnerable population. In Wenzhou, no such studies have been conducted previously. Our study focuses on the period from 2014 to 2023 in Wenzhou City, filling this gap by analyzing the epidemiological features, drug resistance patterns, and temporal trends of TB in the elderly.

The findings of our study highlight significant sociodemographic differences between elderly and non-elderly TB patients in Wenzhou. The elderly group demonstrates a higher proportion of male patients, consistent with global trends, as evidenced by aligned conclusions from studies such as Patra S et al in India,[13] An Q et al in Shandong, China,[28] Oshi DC et al in Nigeria,[29] and Duong KL et al in Vietnam.[30] This increased susceptibility to tuberculosis among elderly males may be attributed to cumulative environmental exposures over time, occupational hazards, or smoking-related lung damage.[31–33] The overwhelming majority of Han Chinese patients reflects the local ethnic composition, consistent with the findings of Li SJ et al,[34] although the significantly higher proportion of elderly individuals may suggest differences in healthcare access, cultural practices, or migration patterns over the past few decades. The proportion of elderly patients with lesions involving ≥3 lung fields was higher, similar to the findings of Gupta D et al in North India.[35] Consistent with previous studies, non-elderly patients exhibit higher rates of migration, urban residence, and employment, highlighting the role of mobility and urbanization in tuberculosis transmission among younger, economically active populations.[36–38] This contrasts sharply with elderly groups, who may face age-related vulnerabilities such as immunosenescence and comorbidities,[39] coupled with lower occupational engagement. The proportion of pulmonary cavitation was higher in the non-elderly group, consistent with multiple studies, likely due to the stronger immune response in young patients leading to easier liquefaction and discharge of caseous necrosis.[40,41] The lack of significant differences in treatment categories suggests that both groups predominantly represent incident TB rather than relapse, emphasizing the need for robust primary prevention strategies. These findings underscore the importance of age-tailored TB control programs. For elderly populations, targeted screening for high-risk subgroups (eg, males, long-term residents) and integration with geriatric care could improve early detection. For non-elderly groups, interventions addressing migrant health and occupational exposure in urban settings are critical.

Our study found that the overall incidence of DR-TB was similar between the elderly and non-elderly groups, but there were differences in resistance patterns. The resistance rates to SM and RFP were lower in the elderly group than in the non-elderly group, with statistically significant differences. However, the proportion of single drug resistance to INH and the incidence of MR-TB were higher in the elderly group, and these differences were also statistically significant. Additionally, the incidence of PDR-TB was higher in the elderly group, although this difference was not statistically significant. Similar findings were reported by An Q et al,[28] who observed that the elderly group had lower resistance rates to SM and RFP, with statistically significant differences. However, the incidence of MDR-TB and PDR-TB was slightly lower in the elderly group, without statistical significance. In contrast, Wang Z et al[42] showed that the elderly group had lower resistance rates to SM, RFP, and INH, with statistically significant differences, and a lower incidence of MDR-TB. However, the incidence of PDR-TB was higher in the elderly group, with statistically significant differences. The study by Lisson Y et al[43] in Australia showed that elderly patients had the highest rate of INH resistance, while the study by Lee EG et al[44] in South Korea showed that the elderly group had lower resistance rates to SM, INH, RFP, and EMB compared to the non-elderly group. The differences across studies may be related to various background factors, such as regional variations in treatment practices, diversity of MTB strains, or limitations in study design (eg, retrospective data collection, survival bias in the elderly cohort).[45,46] Therefore, understanding the resistance patterns of elderly patients in our region is essential. It is noteworthy that the incidence of MDR-TB was significantly lower in the elderly group compared to the non-elderly group, consistent with previous studies that show MDR-TB is more prevalent in younger patients.[44,47] This may be attributed to several factors: First, young people have more frequent social interactions and often live in densely populated areas, which increases the transmission rate of TB.[48] Second, the proportion of migrant populations is higher among young people, and their high mobility can lead to poor treatment adherence, thereby increasing the risk of drug-resistant TB.[49,50] Additionally, the higher proportion of pulmonary cavitation in the non-elderly group suggests that cavitation may be more likely to harbor drug-resistant strains, according to some studies.[51] These findings remind us that when formulating TB control strategies, it is essential to consider the differences in resistance patterns and social behaviors between different age groups. Targeted efforts should be made to strengthen resistance monitoring and treatment management for the elderly population, while optimizing TB prevention measures and treatment adherence interventions for younger individuals to effectively curb the spread of DR-TB.

From 2014 to 2023, the trend of drug resistance among elderly TB patients in Wenzhou highlighted both the significant progress in TB control and the challenges that remain, with the COVID-19 pandemic emerging as a potential influencing factor in the later stages of the study. The overall rate of DR-TB declined significantly, with notable reductions in MDR-TB and drug resistance among retreatment patients. This underscores the effectiveness of enhanced TB management strategies, including strict adherence to standardized treatment protocols, improved monitoring, increased accessibility of rapid molecular diagnostics, and the implementation of directly observed treatment, short-course (DOTS).[52–54] Additionally, the substantial decrease in resistance to first-line drugs such as INH and RFP indicates improved effectiveness and patient adherence to treatment regimens. The significant decline in drug resistance among migrant populations and rural residents is likely related to improved access to medical services in Wenzhou and public health activities targeting elderly TB patients. However, challenges persist. The incidence of PDR-TB increased by 12.06%, and resistance to SM only decreased by 5.53%, suggesting the need for further investigation into the underlying causes. The stagnation in the decline of drug resistance among new cases (with an overall decrease of 15.13%) indicates that the spread of drug-resistant strains remains a concerning issue. Moreover, the outbreak of COVID-19 in 2020 had a negative impact on TB control efforts,[55] which may explain some of the fluctuations in trends observed after 2020. Joinpoint regression analysis further supports this conclusion: the drug resistance rate among migrants decreased significantly before 2020 (APC of −10.1%), but stabilized afterward, coinciding with mobility restrictions and reduced access to healthcare for migrant populations during the pandemic. Similarly, the drug resistance rate in urban areas declined sharply before 2021 (APC of −8.7%) but then entered a stable phase, likely due to the shift of public health focus toward COVID-19 control. For retreatment cases, the drug resistance rate decreased significantly from 2014 to 2018 (APC of −20.1%), but progress slowed after 2018, indicating that pandemic-related disruptions in healthcare may have hindered the continuity of complex retreatment regimens. Moving forward, it is essential to continue strengthening drug resistance surveillance and diagnostic capabilities, optimizing treatment regimens, and enhancing public health education.[56] Additionally, it is crucial to ensure stable resource allocation for TB control efforts, especially in the face of public health emergencies such as the COVID-19 pandemic, to guarantee uninterrupted and standardized treatment for TB patients.[57]

This study has several limitations. First, the exclusion of 18,427 culture-negative cases may introduce selection bias and potentially affect the generalizability of the findings. Additionally, as the study was conducted solely in the Wenzhou region, its conclusions may have geographical applicability constraints. Future studies should consider employing more comprehensive diagnostic approaches (eg, combining molecular diagnostic techniques with culture methods) to minimize bias

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caused by diagnostic uncertainty and validate the current findings in broader populations. Second, this study utilized the liquid pDST system provided by BD. However, since BD has not yet commercialized second-line drug susceptibility testing (SLD-DST) reagents,[58] routine SLD-DST could not be performed. This limitation confined the analysis to FLDs resistance patterns, making it difficult to comprehensively assess drug resistance characteristics in the elderly population, particularly the epidemiological trends of extensively drug-resistant tuberculosis (XDR-TB). The absence of SLD-DST data prevented accurate estimation of XDR-TB prevalence in the elderly population and direct comparisons with studies from other regions or countries, which may diminish the guiding value of this study's findings for XDR-TB prevention and control strategies. Future research should routinely incorporate SLD-DST to provide more comprehensive drug resistance data for clinical decision-making and public health policy formulation. Third, this study did not analyze the impact of comorbidities on drug resistance and treatment outcomes in elderly TB patients. Future studies should incorporate these variables to more comprehensively understand the epidemiological characteristics and resistance trends in this population.

## Conclusion

Our study demonstrates that drug resistance among elderly TB patients in Wenzhou has decreased over the past decade, particularly for MDR-TB and key first-line drugs. However, the elderly group still exhibits distinct epidemiological and drug resistance profiles compared to younger patients. These findings highlight the importance of continuous monitoring and targeted interventions, providing clear suggestions for public health policy-making and clinical practice to further reduce the burden of TB and drug resistance in the elderly population.

## Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Ethics Approval

This study received approval from the Medical Ethics Committee of Wenzhou Central Hospital (batch No. L2025-02-024). The research data were obtained from the Tuberculosis Information Management System (TBIMS) of the Chinese Center for Disease Control and Prevention and the hospital's laboratory information system, with permission from the hospital's administration department. Given that this is a retrospective study, all data were anonymized before analysis, which led to the Medical Ethics Committee granting a waiver for patient informed consent. The research methods used in this study adhere to the ethical guidelines set forth in the Declaration of Helsinki.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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