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Review

# Time and spatial distribution of multidrug-resistant tuberculosis among Chinese people, 1981–2006: a systematic review

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SUMMARY

*Objectives:* We aimed to investigate trends in the prevalence of multidrug-resistant tuberculosis (MDR-TB) among Chinese people from first report to 2006, and to detect the high prevalence regions in order to guide control efforts.
*Materials and methods:* The CBM, VIP, CNKI, and MEDLINE databases were searched through both keywords and subject headings. The literature was screened, and two investigators assessed the quality and extracted the data. Trends in MDR-TB prevalence in three groups – primary, acquired, and combined MDR-TB – were examined separately, using the Cochran–Armitage trend test. Differences were tested with the Kruskal–Wallis test. High prevalence provinces were explored through comparison of the 95% confidence interval (95% CI) with the national average level.
*Results:* Overall 169 studies were included, with 165 in Chinese and four in English. One hundred and sixteen studies concerned primary MDR-TB, 103 acquired MDR-TB, and 130 combined MDR-TB, with total positive *Mycobacterium tuberculosis* (MTB) isolates of 110 076, 25 187, and 150 233, respectively. The prevalences of MDR-TB in the three groups in 2005 were 2.64-, 6.20-, and 3.84-times that of 1985, respectively, all showing an upward trend ($p < 0.05$). The prevalences among the three groups were significantly different ($p < 0.05$), with acquired drug resistance (27.5%, 95% CI 26.9–28.1%) much higher than primary drug resistance (4.3%, 95% CI 4.2–4.4%), and combined resistance (9.9%, 95% CI 9.8–10.1%) in between. The top three prevalence regions for primary, acquired, and combined MDR-TB were distributed in the zone from the northeast to the southwest of China, with Hebei, Tibet, and Shanxi having an extremely high prevalence.
*Conclusions:* The prevalence of MDR-TB among the Chinese people has shown an upward trend since 1985. It is necessary to continue to monitor this trend in China. Special attention should be paid to provinces distributed in the zone from the northeast to the southwest of China for MDR-TB surveillance, research, and control.


## Introduction

In 2005, China ranked second behind India in the estimated number of tuberculosis (TB) incident cases, and multidrug-resistant tuberculosis (MDR-TB) was shown to be higher among new and previously treated cases in China than in India.[1] An estimated 489 139 MDR-TB cases emerged in 2006, with China, India and the Russian Federation carrying the highest numbers; China and India carried approximately 50% of the global burden and the Russian Federation a further 7%. In terms of the proportion of MDR-TB among all TB cases, China ranked second behind the Russian Federation, however in absolute numbers, China had the highest burden of cases in the world.[2]

Four large-scale cross-sectional surveys were carried out in China in 1979, 1985, 1990, and 2000 and the fifth national survey will be carried out in 2010. The surveys provide basic data for program development and evaluation. It has been reported in China that from 1979 to 2000, the prevalence of active pulmonary TB decreased from 717/100 000 to 346/100 000 and the prevalence of sputum smear-positive pulmonary TB decreased from 187/100 000 to 110/100 000.[3] However, with regard to the magnitude of drug resistance, the information has been limited; for example, 365 097 specimens were investigated in 2000 with only 392 *Mycobacterium tuberculosis* (MTB) isolates analyzed for drug resistance; the prevalences of MDR-TB among new, previously treated, and combined cases were 7.6%, 17.1%, and 10.7%, respectively.[3]

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China has taken part in The World Health Organization/International Union Against Tuberculosis and Lung Disease (WHO/IUATLD) Global Project on Anti-Tuberculosis Drug Resistance Surveillance (WHO Project) since 1996 with a small number of provinces/areas involved one after another; the information has just been for that local area in the survey year. However, it is necessary to understand national MDR-TB prevalence. Hence we collected all relevant studies to analyze the trends among Chinese people in order to provide basic information for MDR-TB control.

## Materials and methods

### *Data sources*

The Chinese CBM, VIP, and CNKI databases and the English MEDLINE database were searched through both keywords and subject headings. The keywords included *Mycobacterium tuberculosis*, drug resistance, multi-drug resistance, drug-resistant tuberculosis, multidrug-resistant tuberculosis, microbial susceptibility tests, and anti-mycobacterial susceptibility tests. The subject headings included *Mycobacterium tuberculosis*; drug resistance, multiple; tuberculosis, multidrug-resistant; microbial sensitivity tests; and drug resistance, bacterial. For MEDLINE, additional restrictions (China/Chinese/Hong Kong/Macao/Taiwan) were applied to limit objects to the Chinese people. All the databases were searched up to December 2006.

### *Study selection*

Studies were eligible for inclusion if MDR-TB was correctly defined or the results of anti-mycobacterial susceptibility tests were reported clearly for each anti-tuberculosis drug, including at least rifampin (R) and isoniazid (H). The identification of pulmonary TB was based on clinical symptoms, the results of chest X-ray, etiological detection, and pathological examination;[4] the improved Lowenstein–Jensen culture medium and absolute concentration indirect method for susceptibility tests were used in the studies.[5]

MDR-TB was defined as a TB case who had MTB resistant to at least R and H. Primary MDR-TB was defined as an MDR-TB case who had never been treated or who had been treated for less than one month with anti-tuberculosis drugs. Acquired MDR-TB was defined as an MDR-TB case who had been treated with anti-tuberculosis drugs for no less than one month. Combined MDR-TB was defined as an MDR-TB case regardless of the treatment history.

As previously reported,[6] China has a nationwide information system for disease control and prevention to which the diagnosed TB patient is reported by the clinician; the clinician has the responsibility of making sure that the information is complete, including the treatment history of the identified TB patient. We included the combined group in addition to the primary and acquired MDR-TB groups, to take account of quite a few papers in which susceptibility tests were carried out and the results were reported without consideration of patient treatment history.

Studies were excluded from the analysis if the total number of culture-positive MTB cases was not reported and/or it was not possible to retrieve the number of MDR-TB cases and/or the tests were carried out only for specific populations, such as the elderly, children, prisoners, etc.

### *Quality assessment*

Seven items were developed to assess the quality of included studies, based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[7,8] The items were: (1) whether the recruitment time of the objects was reported; (2) whether the recruitment place of the objects was reported; (3) whether the source of the data (e.g., medical records, diseases reporting system, survey, etc.) was reported; (4) whether the definition of MDR-TB was clear; (5) whether the procedures for anti-mycobacterial susceptibility testing were reported; (6) whether the object was of hospital origin or population origin; and (7) whether primary and acquired MDR-TB were defined properly. Items 1–6 were determined for all studies, whereas item 7 was only assessed for those studies reporting primary and acquired MDR-TB separately. If the answer was 'yes' for items 1–5 and item 7, a score of '1' was assigned, if the answer was 'no', a score of '0' was assigned. For item 6, if the object was population origin then it got a score of '1' and if it was of hospital origin it got a score of '0'. The mean average score for each region was calculated and the region graded accordingly (A to E in decreasing quality).

### *Quality control*

Two investigators were independently responsible for quality assessment and data extraction; if there was disagreement, a discussion to agreement would follow; if this failed, a third party was invited to make the judgment.

### *Statistical analyses*

MDR-TB prevalence (the statistical indicator) was defined as the proportion of MDR MTB isolates to the total number of culture-positive MTB over a certain period of time (e.g., 1 year), which equaled the number of MDR MTB isolates divided by the total number of culture-positive MTB, times 100%. We calculated this for the three groups of primary, acquired, and combined MDR-TB cases based on the literature reports. Data from the included studies carried out in the same region (special administrative region (SAR)/autonomous region (AR)/ municipality/province) were pooled.

Trends in MDR-TB prevalence in the three groups were examined separately using the Cochran–Armitage trend test. Differences in the prevalence of MDR-TB in the three groups were tested by Kruskal–Wallis test. High prevalence regions were explored through comparison of the 95% confidence interval (95% CI) with the national average level. A $p$-value of less than 0.05 was used to denote statistical significance. SPSS 13.0, Excel 2003 and CorelDRAW 12 software packages were used for the analyses.

## Results

One hundred and sixty-nine studies[9–177] were included, with 165 in Chinese and four in English (Figure 1).

The quality assessment results are shown in Table 1. Most areas located in the southwest, the north, and central China got low scores in the item totals, with Tibet the lowest. These are relatively less developed areas, demonstrating the gap in study report quality between the less developed and more developed areas of China.

One hundred and sixteen studies reported on primary MDR-TB, 103 on acquired MDR-TB, and 130 on combined drug resistance (data not shown), with totals of 110 076, 25 187, and 150 233 culture-positive MTB cases, respectively (Table 2). The earliest report was seen in 1981. It was not until 1985 that drug susceptibility test studies were reported consecutively in China. The number of positive MTB isolates varied over the period 1985–2006, with medians of 4795, 936, and 6666 for primary, acquired, and combined MDR-TB, respectively. There were more isolates in 1995–2004 compared to other periods (with the most in 1999 in all groups); this decreased after 2004, and the least for all groups were

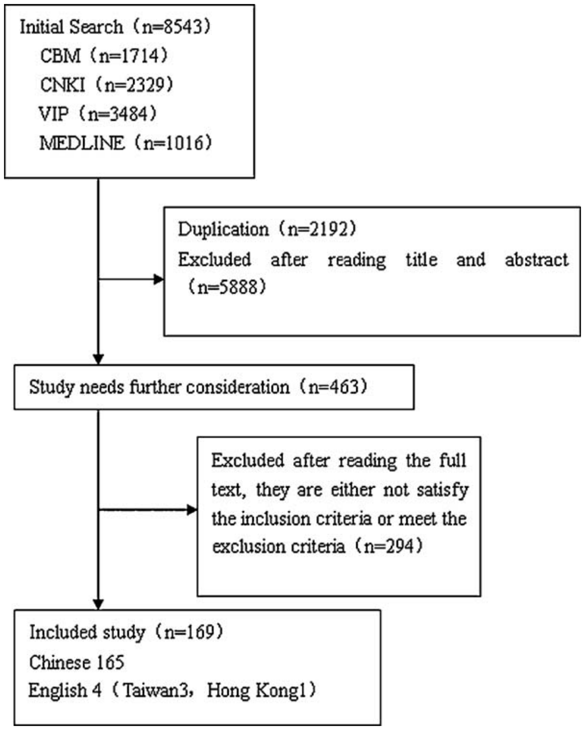


**Figure 1.** Flow chart of document retrieval and selection.

found in 2006 (10%, 23%, and 22% of the median for the three groups, respectively) (Table 2).

The culture-positive MTB totals for 1981–2006 in the different regions are shown in Figure 2. The top five regions were Hong Kong, Guangdong, Fujian, Henan, and Shanghai. With the exception of Henan, the other four are developed areas. Figure 2 reflects the great variation in reported culture-positive MTB in the different regions of China.

*Trends in MDR-TB prevalence*

Figure 3 shows the trends in MDR-TB prevalence of primary, acquired, and combined MDR-TB among Chinese people (national and local).

*National*

*Description*

Figure 3 shows that the primary MDR-TB prevalence remained below 4.0% before 1995, then increased gradually reaching 6.1% in 1996, then fluctuated upwards. It was higher than 4.0% after 1999 and reached 10.0% after 2005. A more significant rise was seen in 2006 than in 2005, with an increase of 44%.

The combined MDR-TB prevalence was stable below 5.0% before 1989; in 1990 it reached 15.9%, then fluctuated upwards to 19.1% in 2005, reaching 31.6% in 2006 (an increase of 65% from 2005 to 2006).

The acquired MDR-TB prevalence fluctuated upwards to reach 32.4% during 1985–1990 and was then around 30.0% until 2005; a noticeable increase to 51.0% then occurred in 2006 (an increase of 66% from 2005 to 2006).

**Table 1**
Evaluation of the included studies in 28 provinces/regions

| Items 1–6 | | | Item 7 | | | Items 1–7 | | |
|---|---|---|---|---|---|---|---|---|
| Province/region | Mean | Rank[a] | Province/region | Mean | Rank[b] | Province/region | Mean[c] | Rank[d] |
| Hong Kong | 6.00 | A | Hong Kong | 1.00 | A | Hong Kong | 7.00 | A |
| Guangdong | 5.03 | B | Taiwan | 1.00 | A | Taiwan | 6.00 | A |
| Taiwan | 5.00 | B | Ningxia | 1.00 | A | Ningxia | 6.00 | A |
| Ningxia | 5.00 | B | Guangxi | 1.00 | A | Guangxi | 6.00 | A |
| Guizhou | 5.00 | B | Zhejiang | 0.78 | B | Zhejiang | 5.48 | B |
| Guangxi | 5.00 | B | Liaoning | 0.67 | B | Guangdong | 5.48 | B |
| Gansu | 5.00 | B | Hunan | 0.67 | B | Liaoning | 5.34 | B |
| Henan | 4.75 | C | Shandong | 0.60 | B | Hunan | 5.05 | B |
| Zhejiang | 4.70 | C | Yunnan | 0.50 | C | Fujian | 5.04 | B |
| Liaoning | 4.67 | C | Xinjiang | 0.50 | C | Shanghai | 5.00 | B |
| Hubei | 4.67 | C | Tianjin | 0.50 | C | Henan | 5.00 | B |
| Beijing | 4.67 | C | Shanghai | 0.50 | C | Guizhou | 5.00 | B |
| Fujian | 4.62 | C | Inner Mongolia | 0.50 | C | Beijing | 5.00 | B |
| Sichuan | 4.60 | C | Guangdong | 0.45 | C | Sichuan | 4.93 | C |
| Shanghai | 4.50 | C | Fujian | 0.42 | D | Shandong | 4.93 | C |
| Hunan | 4.38 | D | Sichuan | 0.33 | D | Hubei | 4.89 | C |
| Tianjin | 4.33 | D | Shanxi | 0.33 | D | Tianjin | 4.83 | C |
| Shandong | 4.33 | D | Jiangsu | 0.33 | D | Jiangsu | 4.60 | C |
| Jiangsu | 4.27 | D | Jilin | 0.33 | D | Shanxi | 4.58 | C |
| Shanxi | 4.25 | D | Beijing | 0.33 | D | Yunnan | 4.50 | C |
| Hebei | 4.17 | D | Henan | 0.25 | D | Xinjiang | 4.50 | C |
| Yunnan | 4.00 | D | Hubei | 0.22 | D | Inner Mongolia | 4.50 | C |
| Xinjiang | 4.00 | D | Shanxi | 0.17 | D | Jilin | 4.33 | D |
| Shanxi | 4.00 | D | Tibet | 0.00 | E | Shanxi | 4.17 | D |
| Inner Mongolia | 4.00 | D | Hebei | 0.00 | E | Hebei | 4.17 | D |
| Jilin | 4.00 | D | Guizhou | 0.00 | E | Anhui | 4.00 | D |
| Anhui | 4.00 | D | Anhui | 0.00 | E | Tibet | 3.50 | E |
| Tibet | 3.50 | E | Gansu | NA | NA | Gansu | NA | NA |

NA: Not applicable.
Special Administrative Region (SAR): Hong Kong; Autonomous Region (AR): Ningxia (Hui nationality), Guangxi (Zhuang nationality), Xinjiang (Uygur nationality), Inner Mongolia (Mongolian) and Tibet (Tibetan nationality); Municipality: Beijing, Shanghai and Tianjin; Province: others.
[a] A (=6.00), B (≥5.00 and <6.00), C (≥4.50 and <5.00), D (≥4.00 and <4.50), E (<4.00).
[b] A (=1.00), B (≥0.60 and <1.00), C (≥0.45 and <0.60), D (>0 and <0.45), E (=0).
[c] Sum of mean of items 1–6 and item 7.
[d] A (≥5.50), B (≥5.00 and <5.50), C (≥4.50 and <5.00), D (≥4.00 and <4.50), E (0<4.00).

**Table 2**
Culture-positive MTB and MDR-TB isolates among Chinese people, 1981–2006

| Year | Primary | | Acquired | | Combined | |
|---|---|---|---|---|---|---|
| | Culture-positive (*N*) | MDR-TB (*n*) | Culture-positive (*N*) | MDR-TB (*n*) | Culture-positive (*N*) | MDR-TB (*n*) |
| 1981 | 232 | 1 | | | | |
| 1982 | | | | | | |
| 1983 | 301 | 1 | | | | |
| 1984 | | | | | | |
| 1985 | 1644 | 65 | 1472 | 73 | 2931 | 146 |
| 1986 | 2221 | 66 | 399 | 54 | 2620 | 120 |
| 1987 | 3554 | 90 | 371 | 42 | 3802 | 131 |
| 1988 | 2679 | 75 | 435 | 61 | 2961 | 119 |
| 1989 | 2670 | 58 | 245 | 41 | 2761 | 99 |
| 1990 | 4052 | 73 | 776 | 251 | 6507 | 1032 |
| 1991 | 4683 | 96 | 887 | 271 | 5264 | 360 |
| 1992 | 4468 | 92 | 328 | 73 | 4182 | 120 |
| 1993 | 6172 | 138 | 934 | 378 | 6825 | 650 |
| 1994 | 6011 | 143 | 1039 | 248 | 7383 | 453 |
| 1995 | 5645 | 154 | 318 | 58 | 5448 | 278 |
| 1996 | 7530 | 459 | 1900 | 601 | 12 149 | 1315 |
| 1997 | 7575 | 257 | 1422 | 349 | 10 466 | 616 |
| 1998 | 5673 | 124 | 654 | 104 | 8483 | 439 |
| 1999 | 9873 | 475 | 3881 | 1291 | 14 474 | 1751 |
| 2000 | 3990 | 226 | 1301 | 364 | 8179 | 810 |
| 2001 | 7466 | 616 | 1706 | 616 | 9951 | 1615 |
| 2002 | 9232 | 446 | 1811 | 458 | 11 882 | 1156 |
| 2003 | 4906 | 437 | 2399 | 802 | 8937 | 1292 |
| 2004 | 6391 | 286 | 1754 | 392 | 9546 | 1178 |
| 2005 | 2621 | 273 | 938 | 288 | 4039 | 772 |
| 2006 | 487 | 73 | 217 | 111 | 1443 | 456 |
| Total | 110 076 | 4724 | 25 187 | 6926 | 150 233 | 14 909 |

MTB, *Mycobacterium tuberculosis*; MDR-TB, multidrug-resistant tuberculosis.

*Test of statistical significance*

Drug susceptibility tests were reported consecutively after 1985 and the number of culture-positive MTB was the least in all groups in 2006. Hence we carried out statistical testing of the trend for 1985–2005 to show the time distribution of MDR-TB prevalence during the 20-year period in China, and compared it among the three groups to test the differences.

*The trends*

The primary MDR-TB prevalence showed a significant upward trend of 2.64-fold in 2005 compared with 1985 ($p < 0.05$). We further tested this for the 1980s, 1990s, and 2000s; the downward trend in 1985–1990 ($p < 0.05$) and the upward trend in 1991–2000 ($p < 0.05$) were significant, but the trend in 2001–2005 was not significant ($p = 0.95$).

The combined MDR-TB prevalence showed an upward trend of 3.84-fold in 2005 compared with 1985 ($p < 0.05$). Trends over the same three time periods (1980s, 1990s, and 2000s) were all significantly upward with $p < 0.05$, $p < 0.05$, and $p = 0.01$, respectively.

The acquired MDR-TB prevalence showed an upward trend of 6.20-fold in 2005 compared with 1985 ($p < 0.05$). The trend was significant in 1985–1990 (upward, $p < 0.05$), not significant in 1991–2000 ($p = 0.98$), and significant in 2001–2005 (downward, $p < 0.05$).

*Comparison among the three groups*

The prevalence in the primary, acquired, and combined MDR-TB groups was significantly different ($p < 0.05$). The weighted mean prevalence of MDR-TB was 4.3% (95% CI 4.2–4.4%) for primary, 27.5% (95% CI 26.9–28.1%) for acquired, and 9.9% (95% CI 9.8–10.1%) for combined MDR-TB. Comparisons between primary and acquired, and primary and combined, and acquired and combined all showed significant differences ($p < 0.05$ for each comparison). This demonstrates a wide gap between primary and acquired MDR-TB prevalence, with the latter much higher, and combined prevalence in between.

*Local*

Hebei, Shanxi, and Tibet were the provinces/regions with the greatest burden of primary, combined, and acquired MDR-TB, respectively (see below in the section on spatial distribution), and the trends in these areas are plotted in Figure 3.

The available data points show that the prevalence of MDR-TB was higher in these regions compared to the national level except for Shanxi in 2006.

The test of statistical significance indicated that the trend in primary MDR-TB in Hebei was upwards ($p < 0.05$), and the trends in combined MDR-TB in Shanxi and of acquired MDR-TB in Tibet were not significant ($p = 0.11$ and 0.70, respectively).

*Spatial distribution*

Figures 4, 5, and 6 show comparisons of MDR-TB prevalence in the different regions over the period 1981–2006 for primary, acquired, and combined MDR-TB. The *x*-axis represents the different regions and the *y*-axis represents MDR-TB prevalence (primary in Figure 4, acquired in Figure 5, and combined in Figure 6). The national data total is to the far right of the *x*-axis and the horizontal line across the national data total represents the average magnitude of MDR-TB prevalence in China. The circle is the point estimation of MDR-TB prevalence for the region, and the upper end of the vertical line through the circle is the upper limit of the 95% CI for corresponding MDR-TB prevalence and the lower end is the lower limit of the 95% CI.

Figure 4 shows that the regions having a primary MDR-TB prevalence higher than the national level (4.3%) were Hebei

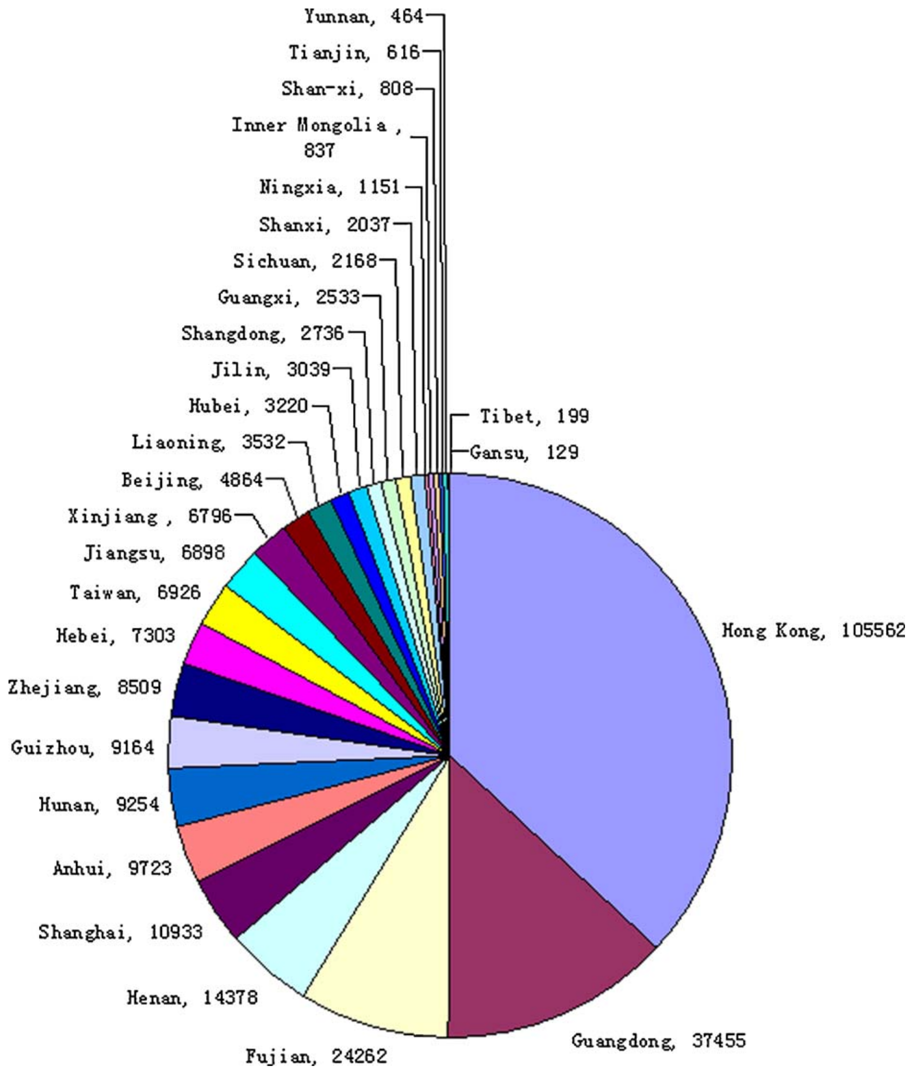


**Figure 2.** Positive MDR isolates in 28 provinces/regions, 1981–2006.

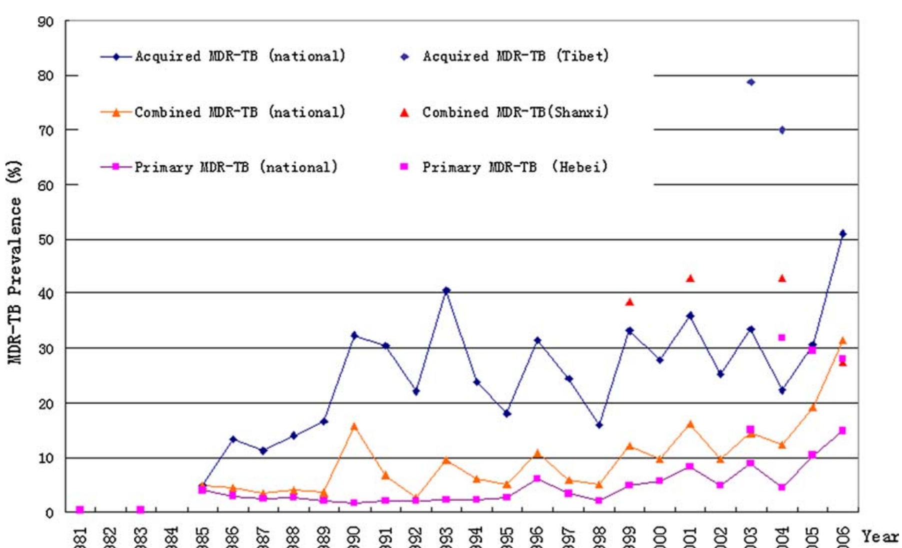


**Figure 3.** Trends in MDR-TB prevalence among Chinese people (national and high-burden local).

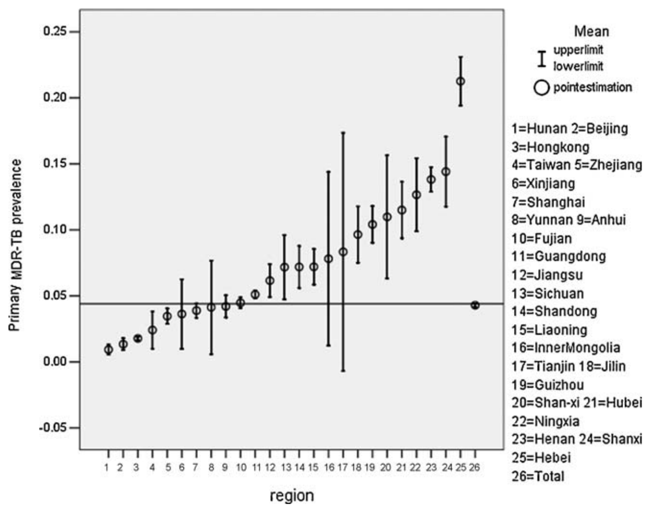


**Figure 4.** Comparison of primary MDR-TB prevalence among 25 regions, 1981–2006.

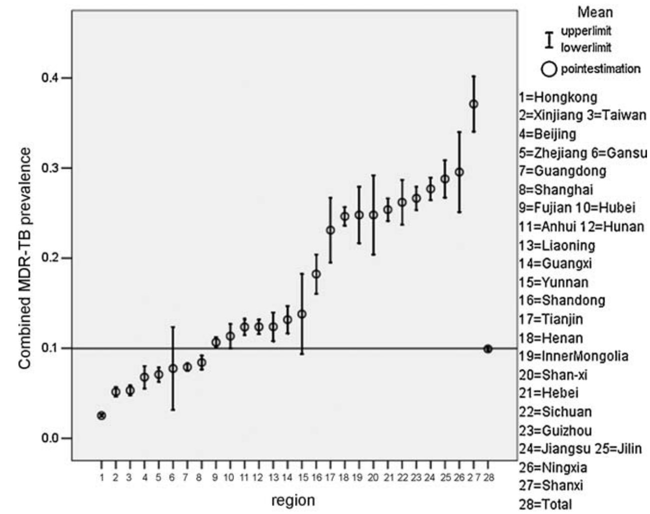


**Figure 6.** Comparison of combined MDR-TB prevalence among 27 regions, 1985–2006.

(21.3%), Shanxi (14.4%), Henan (13.8%), Ningxia, Hubei, Shanxi, Guizhou, Jilin, Liaoning, Shandong, Sichuan, Jiangsu, and Guangdong (the only province in the southeast of China with a higher prevalence), $p < 0.05$, with point estimates of the prevalence in descending order. Provinces 1 (Hunan) to 5 (Zhejiang) had the lower prevalences ($p < 0.05$), with Hunan the lowest (0.9%). For AR 6 (Xinjiang) to province 10 (Fujian) and AR 16 (Inner Mongolia) and municipality 17 (Tianjin), prevalence was not different from the national average level ($p > 0.05$).

Figure 5 shows that the regions having an acquired MDR-TB prevalence higher than the national level (27.5%) were Tibet (77.4%), Shanxi (54.9%), Sichuan (53.9%), Inner Mongolia, Ningxia, Hebei, Henan, Tianjin, Shanxi, Guizhou, Jilin, Beijing, and Shandong; $p < 0.05$, with the point estimate of prevalence in descending order. SAR 1 (Hong Kong) to province 7 (Hunan) had lower prevalences ($p < 0.05$), with Hong Kong the lowest (11.9%). For provinces 8 (Yunnan) to 14 (Hubei), prevalence was not different from the national average level ($p > 0.05$).

Figure 6 shows that the regions having a combined MDR-TB prevalence higher than the national level (9.9%) were province 11 (Anhui) to AR 14 (Guangxi) and provinces 16 (Shandong) to 27 (Shanxi) ($p < 0.05$), among which Shanxi (37.1%), Ningxia (29.6%), Jilin (28.8%), Jiangsu, Guizhou, Sichuan, Hebei, Shanxi, Inner

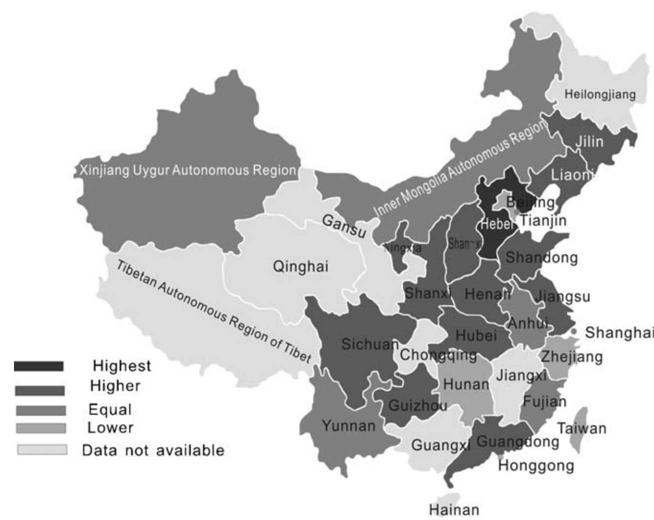


**Figure 7.** Comparison of primary MDR-TB prevalence with national level, 1981–2006.

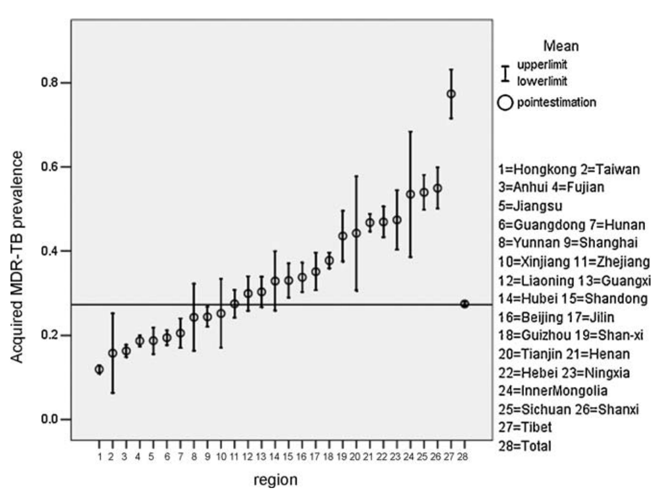


**Figure 5.** Comparison of acquired MDR-TB prevalence among 27 regions, 1985–2006.


**Figure 8.** Comparison of acquired MDR-TB prevalence with national level, 1985–2006.

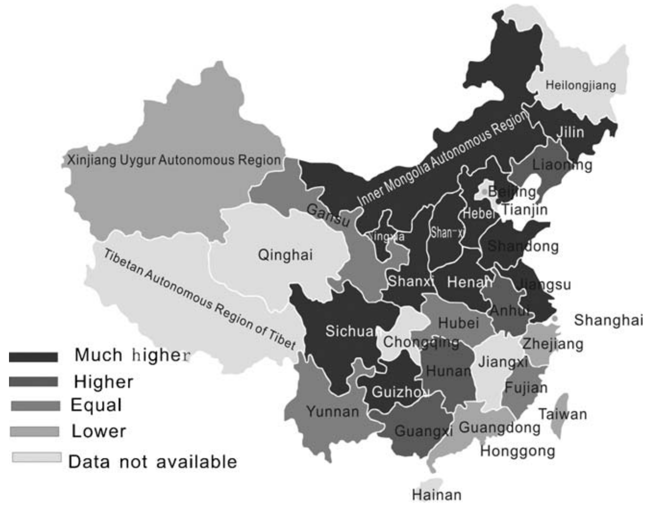


**Figure 9.** Comparison of combined MDR-TB prevalence with national level, 1985–2006.

Mongolia, Henan, Tianjin, and Shandong (with point estimates of the prevalence in descending order) had much higher prevalences ($p < 0.05$). SAR 1 (Hong Kong) to province 5 (Zhejiang), province 7 (Guangdong) and municipality 8 (Shanghai) had lower prevalences ($p < 0.05$), with Hong Kong the lowest (2.5%). Provinces 6 (Gansu), 9 (Fujian), 10 (Hubei), and 15 (Yunnan) had combined MDR-TB prevalence not different from the national average level ($p > 0.05$).

Figures 7, 8, and 9 are maps showing the results of Figures 4, 5, and 6, respectively.

Regions with the top three MDR-TB prevalences in the three groups were Jilin, Hebei, Henan, Ningxia, Shanxi, Sichuan, and Tibet, which are distributed in the zone from the northeast to the southwest of China. Hebei, Tibet, and Shanxi had extremely high prevalences of primary, acquired, and combined MDR-TB, respectively.

## Discussion

The disparity between economically developed and other developing/underdeveloped regions in the quality assessment of reports reflects the gap in scientific research between them. A strengthening of personnel development in health facilities of less developed areas is urgently required to improve their daily work and research capability (planning and reporting), in order to gain better control of this widespread disease.

The primary, acquired, and combined MDR-TB prevalences for 2005 were 2.64-, 6.20-, and 3.84-times those of 1985, respectively, and increased significantly in all groups during this period.

China has been involved in the WHO Project since 1996. Overall, the pooled MDR-TB prevalences are in agreement with the findings of the WHO Project, however there are differences in some years. The WHO Project in China has not been a countrywide survey and the number of provinces involved has varied from one (years 1997, 2001, 2002, and 2004) to four (years 1999 and 2005), with far fewer culture-positive MTB isolates in the WHO Project than in this review (12 894 vs. 110 076 of primary, 2277 vs. 25 187 of acquired, and 16 087 vs. 150 233 of combined MDR-TB cases).[2] This might, to some extent, have contributed to the differences. The number of positive MTB isolates in 2006 was the lowest during the period 1985–2006, which may be attributed to the lag between study completion and publication. There are risks of biased data in 2006 because of the small sample size, and it is necessary to follow up on the trends in recent years in order to better understand the epidemiology and results of efforts made to fight this disease, especially after 1990 in China. In 1996, the Chinese government enhanced TB control by changing its classification from a category C to a category B infectious disease (more strict requirements for infectious disease reporting, prevention and control in the disease prevention and treatment system for category B than C), and has recently paid special attention to fighting the three major infectious diseases of TB, hepatitis B, and AIDS in the community.

The prevalences in the three groups were significantly different, demonstrating the gap between primary and acquired MDR-TB prevalence. The magnitude of acquired MDR-TB is seriously high and implies an association between drug resistance and the therapeutic process. Primary MDR-TB deserves special focus, as it may result in resistance to pyrazinamide and ethambutol[178] and even an outbreak of MDR-TB.[179] It is reasonable that the combined prevalence is between the prevalences for primary and acquired MDR-TB, as it is the MDR-TB prevalence among cases regardless of treatment history (all cases).

Extremely drug-resistant TB (XDR-TB) is defined as TB with resistance to at least R and H, and resistance to a fluoroquinolone and a second-line injectable agent. This has been reported in China in several local special hospitals over the recent five years. However, according to a WHO report there are no data on XDR-TB for 2002–2007 at the national level.[2] A national survey of drug resistance was carried out in China during 2007–2008, however the final report is not yet available.

Guangdong is the only province in the southeast that had a higher primary MDR-TB prevalence than the national average level. This may be related to human migration, as Guangdong is located in the densest floating population area of China.[180] The top three prevalence provinces in the three MDR-TB groups are located in the zone from the northeast to the southwest of China, which are less developed areas compared to the southeast of China. Among them, Henan, Sichuan, and Hebei are populous provinces and Henan has a high burden of AIDS.[181] Tibet (Tibetan AR), is located in the southwest border area of China and has a plateau terrain. Our previous study suggested a high incidence of TB clustering in the Tibetan autonomous area in Sichuan Province;[6] the association between TB incidence and MDR-TB prevalence in the Tibetan nationality is a topic worth further exploration. Ningxia is an AR inhabited by those of Hui nationality; Shanxi is inland and a multi-ethnic province of China. Jilin is located in the northernmost part of the temperate zone and the northeast border area of China. Results suggest that there is an urgent need to focus on detection and prevention in high-risk people, intensive TB case management, and environmental disinfection in these regions.

The spatial distribution revealed in our study suggests that the prevalence of MDR-TB may be related to geography, although the evidence is not sufficient at present. And in China, the geography, apart from geographical position, is represented by factors such as economic development, population density and mobility, proportion of ethnic minorities and their characteristics, and distribution of relevant diseases (for example, AIDS), which should be addressed in future research to improve the management of MDR-TB.

In the 1990s, the directly observed treatment, short-course (DOTS) strategy was implemented step by step in China. It was reported that the Chinese government expended greater effort and higher budgets towards the lagging provinces to achieve nation-wide TB control targets,[182] and that the rate of DOTS coverage to counties increased from 68% in 2001 to 100% in 2005.[183] Is variation in the progress of DOTS implementation including drug supply to the different areas statistically significant? If it is, what is the magnitude of the effect on MDR-TB prevalence? Further investigations are needed.

Our study has limitations. Eligible published reports were not available for all of the 34 provinces/municipalities/ARs/SARs, not every study explored MDR-TB in all three investigated groups, and there were variations in the sum of culture-positive MTB isolates in the different regions and years. However, without long-term nationwide surveillance data, the results obtained here are so far the best source to show the magnitude of MDR-TB prevalence among the Chinese people in the past. The limitations should spur others to carry out further prospective studies to include the collection of high quality epidemiological and microbiological surveillance data, the monitoring of trends in MDR-TB, and the detection of key localities or groups of people for further research and better control in the future.

In conclusion, the prevalence of primary, acquired, and combined MDR-TB showed an upward trend from 1985 to 2005 among Chinese people. It is necessary to continue to monitor trends in MDR-TB prevalence, and special attention should be paid to regions distributed in the zone from the northeast to the southwest of China for MDR-TB surveillance, research, and control.

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