

## Preplanned Studies

## Age-Specific Pulmonary Tuberculosis Notification Rates — China, 2008–2018

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### Summary

#### What is already known about this topic?

The incidence of tuberculosis (TB) was declining in China but has plateaued in recent years.

#### What is added by this report?

Notifications of pulmonary TB declined by 27.7% between 2008 and 2018, with an average crude decline of 3.4% per year and an average age-adjusted decline of 4.3% per year. Notifications decreased faster among older people, but slower in western China; the combination of trends led to an inflection in 2016 in the overall notification trend from decreasing to stable.

#### What are the implications for public health practice?

Population ageing and geographic disparities slowed tuberculosis control progress in China. Enhanced, targeted, and proactive responses are recommended to achieve the End TB targets.

Tuberculosis (TB) remains a major public health threat in China, which has the second largest number of TB patients worldwide. The incidence of TB had been declining, but with China's rapid pace of ageing, the incidence began to plateau, and the annual decline in TB after 2015 was half of what it was during the previous two decades (1). People are getting older. In 2018, 1.9% of the population was 65 years or above; by 2035, 20.7% of the population will be 65 or older, and by 2050, 26.1% will be (2). In addition to ageing, the coronavirus disease 2019 (COVID-19) pandemic has also brought great challenges to TB control — older people are at the highest risk of severe disease and adverse outcomes from both TB and COVID-19. A better understanding of age-specific TB incidence will provide reference points for improving targeted strategies. According to the China's law of infectious diseases control, pulmonary TB (PTB) must be reported to the national TB Management Information System (TBIMS), which provides a profile of the PTB epidemic.

In this study, we analyzed age-specific PTB rates reported in TBIMS from 2008 to 2018 and conducted a joinpoint regression analysis to evaluate the impact of ageing on the potential to achieve the World Health Organization (WHO) End TB Strategy targets. We found an overall decline of 27.7% during the study period with an annual crude percentage change of -3.4% and an annual age-adjusted change of -4.3%. The rates of decline were greater among older people and were lower in central and western China compared with eastern China. In 2016, there was an inflection point in which the decline plateaued, potentially cancelling tuberculosis control progress in China. Targeted responses, including enhanced surveillance, age-sensitive analysis, and early screening and preventative therapy, are recommended.

The study data came from all 31 provincial-level administrative divisions (PLADs) in the mainland of China. Annual population data were collected from the China Statistical Yearbook. We determined annual crude and age-adjusted notification rates using the 2008 population as a reference. We determined the average crude and age-adjusted annual percentage change (APC) using exponential linear regression and joinpoint regression. Comparison of declines by subgroup was based on both crude and age-adjusted APCs. Joinpoint regression identified a joinpoint that divided the crude and age-adjusted notification rates into two periods that we used in subsequent analyses. A trend was defined as an increase or decrease if it had a statistically significant difference ( $P < 0.01$ ), and as stable if it had a non-significant difference ( $P \geq 0.01$ ). Statistical analyses were done with R (version 3.6.0, R Development Core Team, Vienna, Austria) and Joinpoint Regression Program, (version 4.7.0, Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD, USA).

Between 2008 and 2018, a total of 9,242,525 PTB cases were notified to TBIMS, for an average notification rate of 62.1 cases per 100,000. Notification rates were higher for males, increased with age, and were disproportionately distributed by

geographical region (Table 1). A total of 42% of PTB cases were smear-positive.

Among individuals 15 years or older, annual notification rates for males were significantly higher than for females, particularly among older adults (Table 1). A significant decrease was observed in PTB notification rates, with an absolute change of -21.0 cases per 100,000 during the study period — a relative change of -27.7% and an average annual percentage change of -3.4% (95% confidential interval, CI: -3.9 to -3.0). Decreases were observed in all groups, but were faster among males, people younger than 45, smear-positive patients, eastern China, and central China (Table 1).

Among children (<15 years), the average annual percentage change was significantly greater in males, in central China, and in western China compared with the overall average. Among 15 to 64-year-olds, changes were greater in 35 to 44-year-olds, 15 to 24-year-olds except in western China, 25 to 34-year-old females, and people in central China and western China. Among people 65 years and older, the average annual percentage change was greater in males, in eastern China, and in central China. Children 0 to 14 years old in eastern China and 65 to 74-year-olds in western China were the only groups without a significantly decreasing trend (Figure 1).

The year 2016 was an inflection point between decreasing and stable incidences. Before 2016, the crude annual percentage change showed a faster decline in smear-positive PTB (-11.7%, 95% CI: -13.7 to -9.6) than in PTB (-3.9%, 95% CI: -4.3 to -3.5) and a faster decline in eastern China (-5.3%, 95% CI: -5.9 to -4.8) than in central China (-3.7%, 95% CI: -4.2 to -3.3) and western China (-3.5%, 95% CI: -4.5 to -2.5). After 2016, no statistically significant change was identified. Trends in central and eastern China were different from national level and western China trends. In central China, TB declined rapidly after 2015, while in eastern China the rate of decline slowed but didn't stop. Age-adjusted joinpoint analyses showed consistent regression patterns but with faster declines. The annual percentage change of age-adjusted rates were -4.3% (95% CI: -4.8 to -3.8) at the national level, -5.5% (95% CI: -6.1 to -4.9) in eastern China, -5.0% (95% CI: -5.2 to -4.8) in central China, and -3.1% (95% CI: -4.4 to 1.8) in western China (Table 2).

## DISCUSSION

Our study found that the pulmonary tuberculosis

notification rate declined by 27.7% in China between 2008 and 2018, with an annual decline of 3.4% until 2016, when the decline plateaued. Age, sex, and regional disparities had significant impacts on distribution and notification trends. Age-specific analyses showed the highest notification rate in people 65 years and above. As noted, joinpoint analysis showed an inflection in the declining trend in 2016. Given few proactive strategies, China may face a slower decline or a plateau in PTB incidence in the coming years, or possibly a resurgence like some countries experienced during the 1990s. Great attention should be paid to trends and demographic characteristics of TB patients.

China is rapidly moving toward an ageing society, with high-paced economic development and achievement of universal health coverage. According to a World Population Prospects 2019 estimate, China's fertility rate was approximately 1.7 — lower than the regeneration rate of 2.1. The percentage of the population over 65 years increased from 8.3% in 2008 to 11.9% in 2018 (3) and may exceed 20% in 2035 (2). This rapid ageing has brought great challenges to TB control in China. The TB notification rate in people 65 years and above was more than twice that of the entire population. Although the rate of decline in older people seems higher, age standardization reduced the annual decline rate by 0.9% in 2008 to 2016 and 0.5% in 2016 to 2018. Standardization impact may be even greater over the longer term due to the acceleration of population ageing.

Western China changed from decrease to plateau (and close to increase) in TB notifications, which contributed to the national plateau after 2016. Economic disparities and consequential disparities in health awareness and health service accessibility could be important reasons. According to JP Janssen and colleague's analysis, TB incidence is linearly related to per capita gross domestic product (4). During recent decades, large-scale population flow has occurred from western and central China into eastern China because of unbalanced economic development. Considering most migrant populations are under 40 years of age (5), interregional migration may aggravate demographic, and consequently TB, disparities in the different regions.

Many factors may be responsible for a faster decline in the notification rate of smear-positive PTB patients. In 2008, China launched national guidelines (6) and standardized diagnostic criteria (7), which strengthened diagnosing, reporting, and treating of smear-negative

TABLE 1. Notified pulmonary tuberculosis cases, rates, and change and trend analysis of rates in China, 2008–2018.

Group	Number of total notified cases	Average notification rate (1/100,000)	Annual notification rate (1/100,000)															Change between 2008 and 2018		Trend analysis	
			2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Absolute change	Relative change	Average annual percentage change (95% CI)	P value	Trend			
Total	9,242,525	62.1	75.6	71.4	67.9	65.7	64.5	60.9	58.6	56.6	54.6	53.8	54.7	54.7	-21.0	-27.7%	-3.4% (-3.9 to -3.0)	<0.01	Decrease		
Sex																					
Male	6,441,130	84.4	103.1	97.1	92.4	89.8	87.8	82.6	79.6	76.9	74.0	73.3	73.6	73.6	-29.5	-28.6%	-3.5% (-4.0 to -3.1)	<0.01	Decrease		
Female	2,801,395	38.6	46.4	44.3	42.2	40.3	40.0	38.1	36.4	35.3	34.2	33.4	34.8	34.8	-11.6	-24.9%	-3.2% (-3.8 to -2.6)	<0.01	Decrease		
Age (years)																					
0–14	59,017	2.3	3.3	3.3	2.5	2.4	2.3	1.9	1.6	1.6	1.8	1.9	2.4	2.4	-0.9	-26.9%	-5.2% (-8.6 to -1.6)	<0.01	Decrease		
15–24	1,425,718	58.1	71.2	69.9	68.1	65.6	61.9	56.8	53.4	48.3	47.7	46.4	46.5	46.5	-24.7	-34.7%	-5.0% (-5.7 to -4.2)	<0.01	Decrease		
25–34	1,318,915	62.2	77.0	72.4	69.5	65.7	62.8	59.8	58.2	56.6	55.6	54.0	53.5	53.5	-23.5	-30.5%	-3.7% (-4.2 to -3.1)	<0.01	Decrease		
35–44	1,331,405	51.9	67.6	64.8	61.8	58.1	55.2	50.1	49.2	44.3	41.0	38.5	37.5	37.5	-30.1	-44.6%	-6.0% (-6.5 to -5.6)	<0.01	Decrease		
45–54	1,543,716	70.5	88.9	80.3	75.1	72.0	70.6	68.3	64.6	64.9	65.5	65.4	64.8	64.8	-24.1	-27.1%	-2.8% (-3.8 to -1.8)	<0.01	Decrease		
55–64	1,616,223	99.8	126.8	116.5	108.6	104.7	105.1	101.5	93.7	90.0	86.3	83.8	89.3	89.3	-37.5	-29.6%	-3.7% (-4.5 to -2.9)	<0.01	Decrease		
65–74	1,275,541	147.7	189.0	172.9	161.5	141.2	153.9	146.4	142.9	144.8	126.5	130.2	130.8	130.8	-58.2	-30.8%	-3.4% (-4.5 to -2.3)	<0.01	Decrease		
75–	671,990	129.7	185.8	172.8	163.8	142.0	132.8	126.9	118.4	121.4	104.2	106.0	106.4	106.4	-79.4	-42.7%	-5.7% (-6.8 to -4.7)	<0.01	Decrease		
TB category																					
New pulmonary tuberculosis	9,130,914	61.3	74.2	70.1	66.8	64.8	63.7	60.3	58.1	56.2	54.2	53.4	54.2	54.2	-20.0	-26.9%	-3.3% (-3.8 to -2.9)	<0.01	Decrease		
Smear-positive pulmonary tuberculosis	3,856,327	25.9	40.0	38.3	36.3	31.6	26.6	23.0	19.8	17.5	16.4	16.3	20.5	20.5	-19.5	-48.8%	-9.7% (-12.5 to -6.8)	<0.01	Decrease		
Region																					
Eastern	2,910,810	47.9	61.0	58.2	55.6	51.3	49.7	46.1	44.8	43.2	41.2	40.0	38.5	38.5	-22.6	-37.0%	-4.7% (-5.1 to -4.3)	<0.01	Decrease		
Central	3,255,461	69.5	84.4	80.8	76.8	73.9	73.1	69.1	66.7	64.5	61.1	58.7	56.4	56.4	-28.0	-33.2%	-3.9% (-4.2 to -3.7)	<0.01	Decrease		
Western	3,076,254	75.6	90.3	82.6	78.3	78.9	77.7	74.5	69.7	67.4	67.1	68.7	76.9	76.9	-13.4	-14.8%	-2.2% (-3.5 to -0.9)	<0.01	Decrease		

Abbreviation: CI=confidential interval.

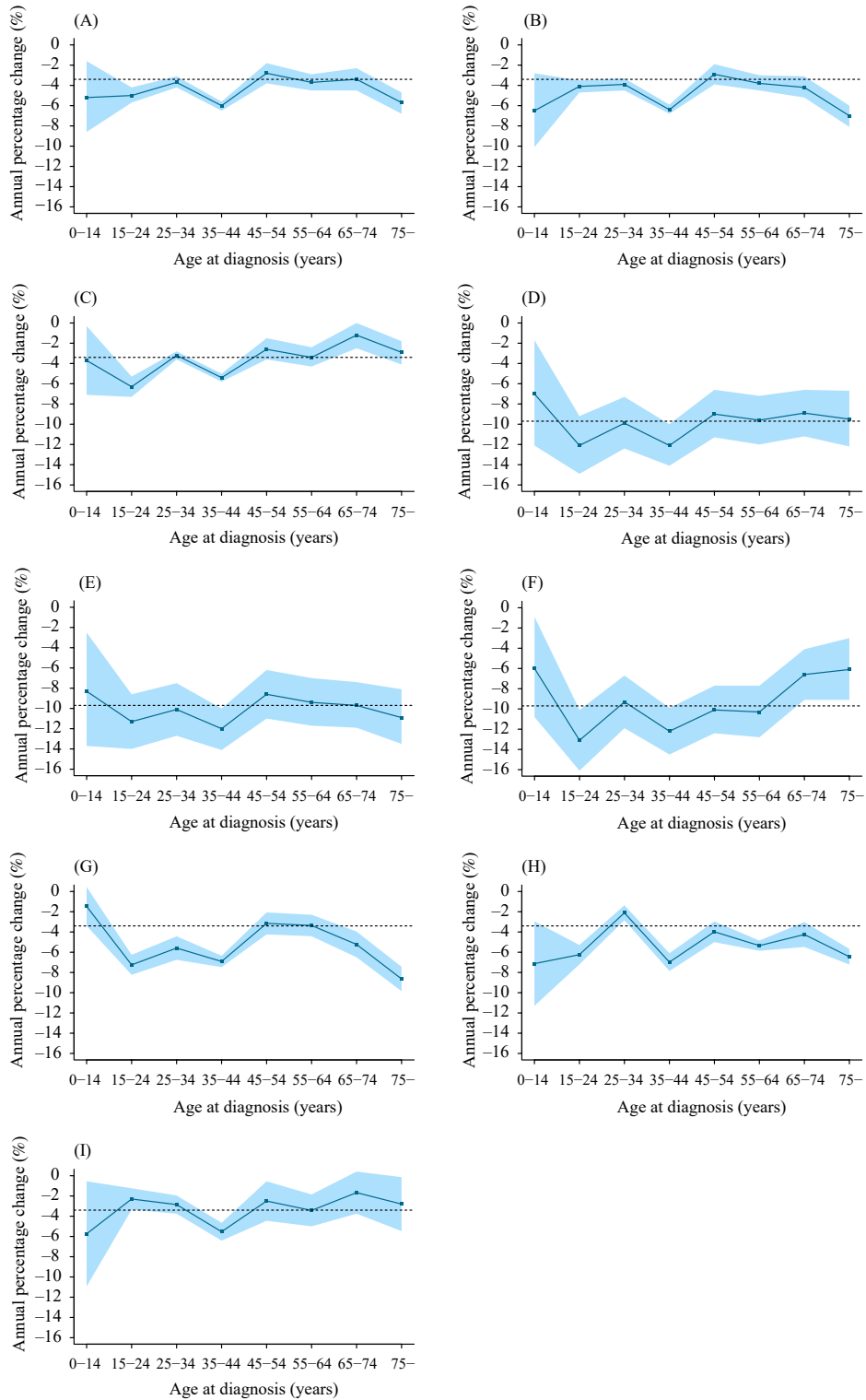


FIGURE 1. Average annual percentage change of pulmonary tuberculosis notification rates by age group in China, 2008–2018. (A) PTB; (B) PTB in male; (C) PTB in female; (D) Smear-positive PTB; (E) Smear-positive PTB in male; (F) Smear-positive PTB in female; (G) PTB in eastern; (H) PTB in central; (I) PTB in western.

Note: Dots and shaded areas represent the annual percentage change (% per year) and 95% CIs in pulmonary tuberculosis notification rates by age group in China during 2008–2018. The dashed line represents the average annual percentage change in all age groups in pulmonary tuberculosis (–3.4%) and smear-positive pulmonary tuberculosis (–9.7%). PTB is pulmonary tuberculosis.

Abbreviation: PTB=pulmonary tuberculosis; CI=confidence interval.

TABLE 2. Joinpoint analysis of crude and age-adjusted pulmonary tuberculosis notification rates in China, 2008–2018.

Group	Joinpoint regression						Annual percentage change (95% CI) from 2008 to 2018
	Trend 1: decrease			Trend 2: stable and decrease			
	Period	Annual percentage change (95% CI)	Trend	Period	Annual percentage change (95% CI)	Trend	
Crude rate	2008–2016	-3.9% (-4.3 to -3.5)*	Decrease	2016–2018	0.2% (-3.8 to 4.3)	Stable	-3.4% (-3.9 to -3.0)
Sex							
Male	2008–2016	-4.0% (-4.4 to -3.6)*	Decrease	2016–2018	-0.1% (-4.2 to 4.2)	Stable	-3.5% (-4.0 to -3.1)
Female	2008–2016	-3.8% (-4.2 to -3.4)*	Decrease	2016–2018	0.9% (-3.1 to 5.2)	Stable	-3.2% (-3.8 to -2.6)
TB category							
New pulmonary tuberculosis	2008–2016	-3.8% (-4.2 to -3.4)*	Decrease	2016–2018	-0.0% (-4.0 to 4.2)	Stable	-3.3% (-3.8 to -2.9)
Smear-positive pulmonary tuberculosis	2008–2016	-11.7% (-13.7 to -9.6)*	Decrease	2016–2018	11.1% (-13.6 to 42.9)	Stable	-9.7% (-12.5 to -6.8)
Region							
Eastern	2008–2013	-5.4% (-6.0 to -4.8)*	Decrease	2013–2018	-3.8% (-4.5 to -3.0)*	Decrease	-4.7% (-5.1 to -4.3)
Central	2008–2015	-3.7% (-4.2 to -3.3)*	Decrease	2015–2018	-4.3% (-6.2 to -2.5)*	Decrease	-3.9% (-4.2 to -3.7)
Western	2008–2016	-3.5% (-4.5 to -2.5)*	Decrease	2016–2018	7.5% (-2.2 to 18.2)	Stable	-2.2% (-3.5 to -0.9)
Age-adjusted rate	2008–2016	-4.8% (-5.2 to -4.4)*	Decrease	2016–2018	-0.3% (-4.6 to 4.1)	Stable	-4.3% (-4.8 to -3.8)
Sex							
Male	2008–2016	-4.9% (-5.3 to -4.5)*	Decrease	2016–2018	-0.6% (-4.9 to 4.0)	Stable	-4.4% (-4.9 to -3.9)
Female	2008–2016	-4.5% (-4.9 to -4.1)*	Decrease	2016–2018	0.3% (-3.9 to 4.7)	Stable	-3.9% (-4.5 to -3.4)
TB category							
New pulmonary tuberculosis	2008–2016	-4.6% (-5.0 to -4.2)*	Decrease	2016–2018	-0.5% (-4.7 to 4.0)	Stable	-4.1% (-4.6 to -3.7)
Smear-positive pulmonary tuberculosis	2008–2016	-12.6% (-14.6 to -10.6)*	Decrease	2016–2018	10.4% (-14.3 to 42.3)	Stable	-10.2% (-12.6 to -7.8)
Region							
Eastern	2008–2013	-6.5% (-7.8 to -5.2)*	Decrease	2013–2018	-4.1% (-5.6 to -2.6)*	Decrease	-5.5% (-6.1 to -4.9)
Central	2008–2015	-4.7% (-5.1 to -4.4)*	Decrease	2015–2018	-5.2% (-6.9 to -3.6)*	Decrease	-5.0% (-5.2 to -4.8)
Western	2008–2016	-4.4% (-5.3 to -3.5)*	Decrease	2016–2018	6.7% (-2.6 to 16.9)	Stable	-3.1% (-4.4 to 1.8)

\*  $P < 0.01$ , an average annual percentage change had significant difference from zero.  
Abbreviation: CI=confidential interval.

TB patients. Enhancement programs such as health education and patient-awareness augmentation also contributed greatly to shortening diagnosis time and lessening TB patients' symptoms. Meanwhile, the reform of China's TB service delivery model from traditional TB-specific facilities to designated general hospitals may have influenced the examination and detection of smear-positive patients (8).

The End TB Strategy requires a decline in the TB incidence rate of at least 10% before 2025. Based on our analysis, achieving the End TB 2020/2025

milestones and the National Tuberculosis Program 13th Five Year Plan targets is on pace. However, the current rate of decline is too slow to achieve the End TB 2035 milestone. While the scientific community looks for new vaccines and drugs to accelerate this process, we must also proactively address new challenges like population ageing and regional disparities.

The annual rate of decline rate that we found is similar to modeling results from the Global Burden Disease study (1990–2017) (9), but higher than

average levels in Western Pacific countries or worldwide (10). China is shifting from a high to a moderate epidemic of TB, similar to what was seen in developed countries in the 1950s. At that stage, in addition to implementation of standardized chemotherapy and treatments, most developed countries implemented various policies such as large-scale active screening, active targeted screening in key populations, and preventive treatment. For example, the United States (11) and Japan (12) both launched active screening strategies for elderly people during this period, as highlighted in the WHO End TB Strategy relevant guidelines. China has started exploring active screening pilot projects in key populations. Successful experiences will help spread these good practices to other regions.

There are limitations to our study. We did not consider HIV and drug-resistance in our analyses. The impact of COVID-19 on the TB epidemic could not be evaluated at the time of the study. Other studies showed that COVID-19 temporarily decreased the TB notification rate in China (13). Whether COVID-19 will profoundly influence TB notification will need to be evaluated in a future study.

Our dynamic analysis and monitoring of surveillance data demonstrated demographic changes and TB epidemiological trends in China. Age-specific transitions and decreased pace of TB case notifications due to population ageing and geographic disparities may significantly influence TB control progress in the future. Maintenance of the current strategy will have limited impact on reducing future TB incidence; only additional screening and preventative therapy for older people will enable China to reach its targets on time.

**Conflicts of interest:** No conflicts of interest reported.

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