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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 ($P\geq0.01$). 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	−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	−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	−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	−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	−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	−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	−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	−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	−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	−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	−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	−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	−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	−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	−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	−13.4	−14.8%	−2.2% (−3.5 to −0.9)	<0.01	Decrease

Abbreviation: CI=confidential interval.

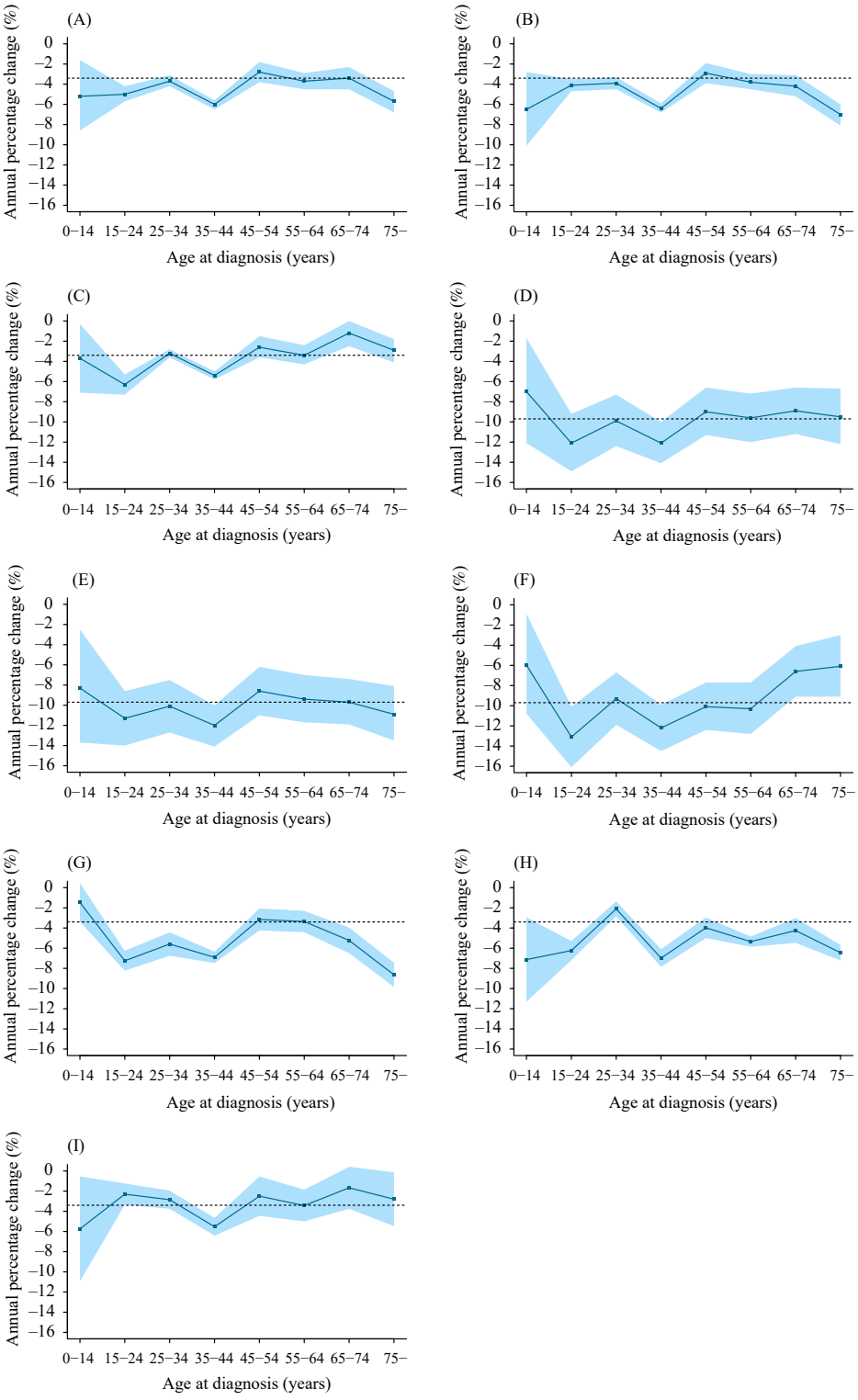

FIGURE 1. Average annual percentage change of pulmonary tuberculosis notification rates by age group in China, 2008–2018. (A) PTB; (B) PTB in male; (C) PTB in female; (D) Smear-positive PTB; (E) Smear-positive PTB in male; (F) Smear-positive PTB in female; (G) PTB in eastern; (H) PTB in central; (I)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

1. World Health Organization. Global TB database [Internet]. https://www.who.int/tb/data/en/. [2020-2-18].
2. United Nations, Department of Economic and Social Affairs Population Division. World Population prospects 2019 [Internet]. 2019. https://population.un.org/wpp/DataQuery/. [2019-12-20].
3. National Bureau of Statistics. China statistical yearbook 2019. Beijing: China Statistics Press. 2019. http://find.nlc.cn/search/showDocDetails?docId=8240639012058037117&dataSource=ucs01&query=%E4%B8%AD%E5%9B%BD%E7%BB%9F%E8%AE%A1%E5%B9%B4%E9%89%B4. (In Chinese).
4. Janssens JP, Rieder HL. An ecological analysis of incidence of tuberculosis and per capita gross domestic product. Eur Respir J2008 2008;32(5):1415 – 6. http://dx.doi.org/10.1183/09031936.00078708.
5. Duan Chengrong. New Characteristics of Migrant Population in China. China Population Today 2016;6:9 – 12. http://dx.doi.org/CNKI:SUN:DDZG.0.2016-06-004.
6. Disease Prevention and Control Bureau of the Ministry of Health, Department of Medical Affairs, Ministry of Health, Chinese Center for Disease Control and Prevention. Guidelines for implementing the national tuberculosis control program in China (2008). Beijing: China Union Medical University Press. 2009. (In Chinese).
7. Ministry of Health of the People's Republic of China. WS 288-2008 Diagnostic criteria for pulmonary tuberculosis. Beijing: People's Medical Publishing House. 2008. http://www.csres.com/detail/189569.html. (In Chinese).
8. Li T, Du X, Liu XQ, Li YH, Zhao YL. Implementation performance of tuberculosis control in China: 2011–2020. China CDC Wkly 2021;3(12):252 – 5. http://dx.doi.org/10.46234/ccdcw2021.073.
9. Ding C, Wang ST, Shangguan YW, Feng XW, Guo WR, Shi P, et al. Epidemic trends of tuberculosis in China from 1990 to 2017: evidence from the global burden of disease study. Infect Drug Resist 2020;13:1663 – 72. http://dx.doi.org/10.2147/IDR.S249698..
10. World Health Organization. Global tuberculosis report 2019. Geneva: WHO. 2019. https://book.douban.com/subject/35072660/.
11. Prevention and control of tuberculosis in facilities providing long-term care to the elderly. Recommendations of the advisory committee for elimination of tuberculosis. MMWR Recomm Rep 1990;39(RR-10):7-13. https://pubmed.ncbi.nlm.nih.gov/2165558/.
12. Ghotbi N, Nishimura S, Takatsuka N. Japan's national tuberculosis control strategies with economic considerations. Environ Health Prev Med 2005;10(4):213 – 8. http://dx.doi.org/10.1007/BF02897713.
13. Huang F, Xia YY, Chen H, Wang N, Du X, Chen W, et al. The impact of the COVID-19 epidemic on tuberculosis control in China. Lancet Reg Health West Pac 2020;3:100032. http://dx.doi.org/10.1016/j.lanwpc.2020.100032.

Perspectives

Neglected Zoonotic Monkeypox in Africa but Now Back in the Spotlight Worldwide

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On July 23, 2022, the World Health Organization (WHO) Director-General, Dr. Tedros Adhanom Ghebreyesus claimed monkeypox a Public Health Emergency of International Concern (PHEIC), the 7th such an event in the 21st century (*1*). This is an alarming challenge to the world while we are still combating the coronavirus disease 2019 (COVID-19) pandemic. Until mid-August, approximately 40 thousand cases had been reported in more than 89 nations and regions worldwide (*2*).

Monkeypox was named upon its first discovery in monkeys in 1958 and was first identified in humans in 1970 (*3*). Monkeypox is usually a self-limiting disease caused by monkeypox virus (MPXV), a member of the *Orthopoxvirus* genus in the family *Poxviridae* (*4*). MPXV is phylogenetically divided into two clades: West African clade as Clade two (II) and Congo Basin (Central Africa) clade as Clade one (I). The Clade II strain of MPXV is linked to the current monkeypox outbreak. Monkeypox presents with fever, an extensive characteristic rash and usually swollen lymph nodes (*4*). However, the largest study of 2022 confirmed monkeypox cases to date identified new clinical symptoms that were similar to those of syphilis and other sexually transmitted infections and could easily lead to misdiagnosis (*5*). MPXV is not so tightly host restricted and employs wild rodents as primary reservoirs with occasional spillover leading to cases of MPXV infections in humans (*4*). Animal-to-human (zoonotic) transmission can occur from direct contact with the blood, bodily fluids, or cutaneous or mucosal lesions of infected animals. Human-to-human transmission can result from close contact with respiratory secretions, skin lesions of an infected person, or recently contaminated objects (*4*). Detection of viral DNA by polymerase chain reaction (PCR) is the preferred laboratory test for monkeypox. The best diagnostic specimens are directly from rashes — skin, fluid, or crusts, or biopsy where feasible (*6*).

Monkeypox is a viral zoonotic disease that occurs primarily in tropical rainforest areas of Central and West Africa and is occasionally exported to other regions (*4*). In 2003, the first monkeypox outbreak outside of Africa was in the United States of America and was linked to pet importation from Africa (*4*). In recent years, the monkeypox epidemic in Central and West Africa has been relatively active, and multiple cases of monkeypox have also been identified in several non-endemic countries (*4*). MPXV in Africa was grossly neglected by international community for over five decades prior to the global outbreak that has affected wealthy countries in North America and Europe since May 2022 (*1*). With these cases spreading worldwide, without epidemiological links with outbreaks among men who have sex with men (MSM), it warrants urgent public health control measures to contain the spread of the MPXV and investigate the underlying pathophysiology, including genetic modification of the virus (*6*).

In 1980, smallpox was eradicated under vaccination, and its related vaccine programs were gradually discontinued. Vaccination against smallpox with a first generation vaccinia virus-based smallpox vaccine was shown to be 85% effective in preventing monkeypox in the past (*4*). Since the smallpox vaccine can also prevent monkeypox, the termination of the smallpox vaccine program at the time also caused a surge in monkeypox-endemic areas.

The recent gradual lifting of COVID-19-related travel restrictions in West and Central Africa may have contributed to an increase in monkeypox cases. No cases of monkeypox infection have been found in the mainland of China, nor has the virus been found in animal hosts. However, on June 24, 2022, the first confirmed case of monkeypox appeared in Taiwan, China, which sounded the alarm for us. Most of the population in China (especially those born after 1981) have no history of smallpox vaccination and lack immune protection background against MPXV, which results in a large population susceptible to monkeypox. With the country's trade with Africa and the increasing number of African workers and tourists, the risk of importation of monkeypox has also increased objectively. In addition, MPXV is a zoonotic virus that can infect rodents and a variety of wild animals, recent reports indicated that the establishment of a reservoir of MPXV in animal populations in a previously non-

endemic region is now a distinct possibility and would make control and eradication much more challenging (*4*,*7*). The clinical symptoms of some people infected with MPXV are very similar to those of smallpox, and the pathogens are not easy to distinguish. The possibility of smallpox or monkeypox bioterrorism in the world increases the threat to public health and social security. We can learn from the experience of the COVID-19 pandemic, prepare technical reserves as early as possible, take the initiative to respond, and prevent endemic monkeypox before it occurs in China. Therefore, in order to effectively control and prevent monkeypox in China, specific real-time PCR and serological detection techniques have been successfully established in China CDC, which were successfully applied in the China-Sierra Leone Joint BSL-3 Laboratory to detect monkeypox cases and conduct molecular traceability in 2017 (*8*). In 2018, the experts in China CDC compiled and formulated the "Technical Plan for Emergency Response to Monkeypox Epidemic". On June 6, 2022, China CDC released: "Monkeypox Prevention and Control Technical Guidelines (2022 Edition)". In addition, "Guidelines for the Diagnosis and Treatment of Monkeypox (2022 Edition)" was jointly issued on June 14, 2022 by the National Health Commission and the State Administration of Traditional Chinese Medicine. The prevention of monkeypox in China should focus on the quarantine of entry personnel and imported animals. At present, it is recommended to control the human-to-human transmission of monkeypox through early detection and diagnosis of cases, isolation, and contact tracing as much as possible, and mass vaccination of the population is not currently recommended to prevent monkeypox. We should seriously study and treat monkeypox, but people should not panic.

Neglected zoonotic monkeypox has been restricted in Africa for fifty years but now it is back in the spotlight worldwide. Many questions surrounding the basic biology of MPXV demand answers to lay the foundations for developing effective strategies and tools to manage the disease. Scientists have always attached importance to the basic research on *Orthopoxvirus* and the research and development of prevention and control products. In recent years, several specific diagnostic reagents, novel therapeutic drugs, and preventive vaccines for monkeypox have been approved for commercial use in Europe and the USA. While vaccines and specific therapies have been approved to prevent and treat monkeypox, they are not currently used worldwide. It is imperative to strengthen relevant basic research funds, especially cooperation between industry, academia and research, and to strengthen the R&D and application reserves of safe and effective vaccines and drugs for monkeypox. In addition, assessment of potential routes for zoonotic and reverse-zoonotic transmission of MPXV is encouraged based on the clear One Health framework. To our knowledge, we are currently facing many challenges and difficulties against the global monkeypox epidemic, such as different economic and technological levels among nations and regions, uneven vaccine and drug reserves and distribution, difficulty monitoring and management of MSM activities, atypical clinical manifestations and the risk of cryptic spread, so the MPXV evolution in large populations brings a lot of uncertainty to prevention and control. These challenges also shed light on global preparedness for future emerging infectious diseases or unknown Diseases X or even pandemics.

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REFERENCES

1. Taylor L. Monkeypox: WHO declares a public health emergency of international concern. BMJ 2022;378:o1874. http://dx.doi.org/10.1136/bmj.o1874.
2. CDC. 2022 monkeypox outbreak global map. 2022. https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html. [2022-8-15].
3. Ladnyj ID, Ziegler P, Kima E. A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo. Bull World Health Organ 1972;46(5):593-7. https://pubmed.ncbi.nlm.nih.gov/4340218/.
4. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, et al. The changing epidemiology of human monkeypox-A potential threat? A systematic review. PLoS Negl Trop Dis 2022;16(2):e0010141. http://dx.doi.org/10.1371/journal.pntd.0010141.
5. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, et al. Monkeypox virus infection in humans across 16 countries-April-June 2022. N Engl J Med 2022;387(8):679 – 91. http://dx.doi.org/10.1056/NEJMoa2207323.
6. Looi MK. Monkeypox: what we know about the 2022 outbreak so far. BMJ 2022;378:o2058. http://dx.doi.org/10.1136/bmj.o2058.
7. Seang S, Burrel S, Todesco E, Leducq V, Monsel G, Le Pluart D, et al. Evidence of human-to-dog transmission of monkeypox virus. Lancet 2022;400(10353):658 – 9. http://dx.doi.org/10.1016/S0140-6736(22)01487-8.
8. Ye F, Song JD, Zhao L, Zhang Y, Xia LX, Zhu LW, et al. Molecular evidence of human monkeypox virus infection, Sierra Leone. Emerg Infect Dis 2019;25(6):1220 – 2. http://dx.doi.org/10.3201/eid2506.180296.

Perspectives

A Secure Supply of Antiretroviral Medicines for People Living with HIV During the COVID-19 Pandemic — China's Experience

Yan Zhao[1]; Mengjie Han[1,#]; Yuting Lian[1]; Qiang Wang[1]; Xiumin Gan[1]; Lan Yu[1]; Chuntao Ma[1]

The occurrence of acute infectious diseases or severe natural disasters has a negative impact on the medical system (*1*). A survey of 105 countries by the World Health Organization (WHO) from March to June 2020 found that health services were disrupted in 90% of countries due to the coronavirus disease 2019 (COVID-19) pandemic, with low- and middle-income countries being the most affected. Human immunodeficiency virus (HIV) treatment continuity and healthcare service delivery were also affected by the COVID-19 pandemic (*2–3*).

In public health emergencies where social distancing and isolation regulations prevent people living with human immunodeficiency virus (PLHIV) from going to their regular clinics and hospitals for treatment, they may not receive timely medical services, leading to an increased risk of disruption of antiretroviral therapy (ART) (*4–6*). China has taken rigorous measures to contain the COVID-19 pandemic outbreak since early 2020. Lockdowns in cities have resulted in PLHIV who had travelled away from their hometowns being unable to return home and access HIV services from their usual healthcare providers (*7*).

In China, more than 95% of PLHIV have taken free medication provided by government programs from clinics they have chosen themselves. The emergency measures have been summarized to maintain essential health services and continuous ART during the COVID-19 pandemic. We hope to share the experience of minimizing the antiretroviral supply risk and improve service in the future.

RAPID JUDGMENT AND RESPONSE IN EMERGENCY PERIOD

Since the outbreak of COVID-19 in China, the Chinese government has taken the strictest measures to prevent the spread of COVID-19. Wuhan, one of the cities most affected by the outbreak, was quarantined starting on January 23, 2020 (*8*). This coincided with the Chinese Spring Festival, which saw increased travel nationwide. PLHIV were stranded in different cities from where their regular clinics were located and were at risk of having access to antiretroviral (ARV) drugs interrupted.

The National Center for AIDS/STD Control and Prevention (NCAIDS) immediately recognized the negative impact of COVID-19 control measures such as quarantine on PLHIV's access to ARV medicines. On January 26, 2020, NCAIDS issued an official notice ensuring that all ART clinics across the country could provide ARV to PLHIV stranded in other cities. Regardless of where they were, they could always obtain their medication from local clinics and be provided with a month's dose immediately. This information was released to the public through official websites and social media. Subsequently, the addresses and telephone numbers of more than 5,000 clinics were published to assist PLHIV in seeking help nearby. In addition, NCAIDS developed an app to collect PLHIV's requests. PLHIV who needed help could input their location and contact information into the system then local staff would provide assistance. This system helped roughly 1,100 PLHIV within a month of its launch. PLHIV's request for help came mainly from Hubei, Jiangsu, Sichuan, and Hebei provinces. A survey launched by UNAIDS and the BaiHuaLin Alliance of PLHIV in February 2020 assessed community needs for ARV medicines (*9*). In addition to those stranded in other cities, PLHIV who had stayed onsite also had difficulties accessing HIV services due to COVID-19 control measures such as road or community closures. In response, healthcare workers, including local CDC staff and nurses, helped deliver life-saving medicines during these difficult times. In places where hospitals and healthcare workers were overwhelmed with COVID-19 patients, resulting in insufficient supply at ART clinics, CDC staff, volunteers, and community-based organizations (CBO) supported reaching PLHIV at risk of running out of their medications through offering home deliveries.

In the Joint United Nations Programme on HIV

and AIDS (UNAIDS) press release on February 6, 2020, UNAIDS commended NCAIDS for acting quickly to ensure that PLHIV who were not in their hometowns during lockdown could receive their monthly refills of ART. "China has made extraordinary efforts to contain the outbreak, and I have full confidence in China's ability to bring the epidemic under control," said Winnie Byanyima, Executive Director of UNAIDS (*10*). "I applaud the efforts of NCAIDS to support people living with HIV and affected by the lockdowns to get their medicines — we must ensure that everyone who needs HIV treatment gets it, no matter where they are," said Winnie Byanyima, on February 19, 2020 (*9*).

MULTIPLE MEASURES IN REGULAR EPIDEMIC PREVENTION AND CONTROL PERIOD

By the end of March 2020, the COVID-19 situation in China was essentially under control, while other countries were still experiencing the continued impact of COVID-19. For China, guarding against inbound cases and domestic resurgences of the epidemic at home were the most important issues for national COVID-19 epidemic prevention and control (*8*,*11*). Stable guarantee measures had to be formulated for the safe supply of ARV drugs.

Sustained Production, Procurement, and Distribution of ARV Medicine

From early 2020, COVID-19 complicated the supply of ARV medicines in many forms, including the supply of active pharmaceutical ingredients (API), pharmaceutical production and transportation, and other aspects. Under the guidance of the Bureau of Disease Control and Prevention of the National Health Commission, NCAIDS combed the entire chain of medicine production and supply. We found that domestic production of API and foreign import of API, such as tenofovir and efavirenz, were blocked during the COVID-19 control period. Through the State Council's Joint COVID-19 Prevention and Control Mechanism, the National Health Commission worked with the Ministry of Industry and Information Technology and local authorities, where pharmaceutical enterprises were located, to solve various problems in production.

The ARV drug supply system consists of domestic manufacturing and importation. The ARV medicine supply system was established in 2004. Currently, all ARV medicines are bid on annually and distributed to provincial drug administration agencies. To ensure a continuous supply of drugs, drug agencies at the provincial level established a mechanism for drug demand forecasting and early stock warning. In the first half of 2020, the quarterly delivery of ARV medicines was interrupted due to supply chain disruptions, and some PLHIV were only able to receive medications for one or two months. The procurement work in 2020 was initiated in advance and successfully completed the drug procurement of all varieties.

Implementation of Multi-Month Dispensing Policy

The Chinese National Free ART Guidelines indicate that PLHIV can receive a quarterly amount of ARV medication after three months of treatment. In 2020, the pandemic caused a shortage in the ART supply chain, but normal supplies were quickly restored through multisectoral efforts.

UNAIDS called on countries to adopt multi-month dispensing (MMD), specifically indicating the follow-up time interval for PLHIV at ART. In 2020, to alleviate the risk of exclusive supply of each variety, some varieties were supplied by two companies simultaneously through bidding. The quarterly medicine supply was restored by the end of 2020 (*12*).

Emergency Plan and Early Warning Mechanism

Due to persistent reoccurrences of COVID-19 cases in various locations, at the beginning of 2021, the National Health Commission required ARV medicine administrations from all provincial-level administrative divisions to establish dynamic monitoring and early warning mechanisms for free ARV medicines to maintain supply and demand. All levels of ARV medicine administration were to appoint responsible persons, monitor drug consumption and stock every month, and reserve all types of drugs for at least one quarter. If the stock is insufficient to meet treatment needs for one month, the ARV medicine administrations must promptly report to NCAIDS. Provincial ARV medicine administrations should regularly update the drug supply plan to ensure that pharmaceutical factories organize production and delivery on time. A standby warehouse should be prepared to ensure continued supply during temporary outbreaks of COVID-19.

Guidance for PLHIV

To help PLHIV get the relevant information in time, all ART clinics were suggested to take measures such as online appointments and peak shifting interviews. ART clinics were asked to actively contact PLHIV with whom they had not regularly followed up. Continuous medicine supply was ensured through mailing and borrowing drugs for non-resident PLHIV when isolation and traffic control occurred. At the same time, all clinics were to publish their contact telephone numbers and provide healthcare and psychological support. Personal information and data of PLHIV were also protected. To inform PLHIV on how to prevent COVID-19, maintain hygiene habits, get vaccinated, and maintain ART, NCAIDS regularly issued patient guidance on official websites and official accounts.

ART PROGRESS UNDER COMPREHENSIVE MEASURES

Under the shelter of the above comprehensive measures, imported drugs have been stored for at least 6 months, and domestic drugs have been distributed quarterly. The provincial drug administration agencies have reported their drug reserves to NCAIDS every month, so as to timely capture the possible supply risks. In areas where the COVID-19 epidemic fluctuates, the emergency mechanism of drug supply will be launched as soon as possible, and PLHIV stranded in other cities could apply for drugs at local designated clinics.

We compared treatment data from 2019 to 2021. The treatment coverage of PLHIV in China increased from 89.7% in 2019 to 92.6% in 2021. The ART program in China has developed steadily. The numbers of PLHIV on treatment at the end of 2019, 2020, and 2021 were 863,000, 978,000, and 1,066,000, respectively (Figure 1). The rate of virological suppression (viral load ≤1,000 copies/mL) has continuously remained above 95% in recent 3 years.

Although the experience described in this article may have some flaws to be further improved, we hope that it will provide some insight into the ARV supply chain to other countries or regions seeking to manage ART in accordance with the public health model. Given the changeable epidemic situation, we will continue to optimize the management process, ensuring that PLHIV still have access to essential HIV services and a stable drug supply.

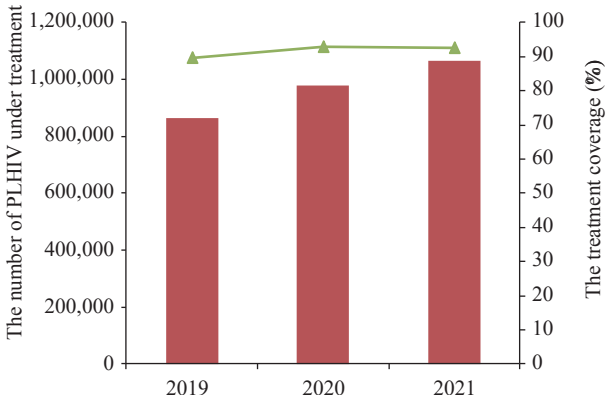

FIGURE 1. Antiretroviral therapy progress from 2019 to 2021.
Abbreviation: PLHIV=people living with human immunodeficiency virus.

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REFERENCES

1. Bogart LM, Ojikutu BO, Tyagi K, Klein DJ, Mutchler MG, Dong L, et al. COVID-19 related medical mistrust, health impacts, and potential vaccine hesitancy among black americans living with HIV. J Acquir Immune Defic Syndr 2021;86(2):200 – 7. http://dx.doi.org/10.1097/QAI.0000000000002570.
2. Kambugu A. The impact of COVID-19 on the HIV pandemic worldwide. CROI 2021 2021. http://www.croiwebcasts.org/console/player/47953?mediaType=slideVideo&. [2021-12-15].
3. Armstrong WS, Agwu AL, Barrette EP, Ignacio RB, Chang JJ, Colasanti JA, et al. Innovations in human immunodeficiency virus (HIV) care delivery during the coronavirus disease 2019 (COVID-19) pandemic: policies to strengthen the ending the epidemic initiative-a policy paper of the infectious diseases society of America and the HIV medicine association. Clin Infect Dis 2021;72(1):9 – 14. http://dx.doi.org/10.1093/cid/ciaa1532.
4. Jewell BL, Mudimu E, Stover J, Brink DT, Phillips AN, Smith JA, et al. Potential effects of disruption to HIV programmes in sub-Saharan Africa caused by COVID-19: results from multiple mathematical models. Lancet HIV 2020;7(9):e629 – 40. http://dx.doi.org/10.1016/S2352-3018(20)30211-3.
5. Geretti AM, Stockdale AJ, Kelly SH, Cevik M, Collins S, Waters L, et al. Outcomes of coronavirus disease 2019 (COVID-19) related hospitalization among people with human immunodeficiency virus (HIV) in the ISARIC World Health Organization (WHO) clinical characterization protocol (UK): a prospective observational study. Clin

Infect Dis 2021;73(7):e2095 – 106. http://dx.doi.org/10.1093/cid/ciaa1605.
6. Xu Z, Zhang C, Wang FS. COVID-19 in people with HIV. Lancet HIV 2020;7(8):e524 – 6. http://dx.doi.org/10.1016/S2352-3018(20)30163-6.
7. Wu XF, Ye YQ. A public health perspective on preventing and controlling the spread of coronavirus disease 2019. China CDC Wkly 2020;2(14):237 – 40. http://dx.doi.org/10.46234/ccdcw2020.060.
8. Wang C. One year in: lessons from China's fight against COVID-19. China CDC Wkly 2021;3(7):128 – 9. http://dx.doi.org/10.46234/ccdcw2021.033.
9. UNAIDS. UNAIDS and China working together during the COVID-19 outbreak to ensure that people living with HIV continue to get treatment. https://china.un.org/en/131014-unaids-and-china-working-together-during-covid-19-outbreak-ensure-people-living-hiv-continue. [2020-2-19].
10. UNAIDS. UNAIDS is working with partners in China to ensure that HIV services continue during the novel coronavirus outbreak UNAIDS. 2020. https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2020/february/20200206_coronaVirus_PS. [2020-2-6].
11. Liu T, Sun JF, Wen MY, Zhang YP, Luo XD, Liu XX, et al. Experiences and lessons of combating COVID-19 that Chinese experts shared with the world. China CDC Wkly 2020;2(43):848 – 50. http://dx.doi.org/10.46234/ccdcw2020.225.
12. UNAIDS. Prevailing against pandemics by putting people at the centre — World AIDS Day report 2020. 2020.

Notes from the Field

The First Imported Case of Monkeypox in the Mainland of China — Chongqing Municipality, China, September 16, 2022

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Monkeypox is a zoonotic viral disease caused by the monkeypox virus (MPXV), and historically, all outbreaks have been linked to Africa; however, monkeypox has been posing an alarming challenge to the world in 2022 (*1*) as approximately 60,000 cases have been reported in more than 100 nations and regions worldwide (*2*). Currently, many cases of monkeypox were identified in many nonendemic countries outside of Central and West Africa, and human-to-human transmission has occurred frequently, especially among men who have sex with men (MSM) presenting new clinical symptoms similar to syphilis and other sexually transmitted infections (*3*). The World Health Organization (WHO) has declared monkeypox a Public Health Emergency of International Concern (PHEIC) on July 23, 2022. Here, we report the first imported case of monkeypox in the mainland of China on September 16, 2022.

A 29-year-old salesman of Chinese nationality visited Germany during September 2–8, 2022, and had MSM behavior in Berlin on September 2. He subsequently traveled to Spain, and then returned Chongqing Municipality, China on September 14, 2022. The man suffered from dry and itchy throat and had a fever on September 9 with red rashes and pustules displayed on his right thigh (Figure 1A). On September 11, he visited a private clinic and took anti-inflammatory medication. On September 14, he was isolated in a coronavirus disease 2019 (COVID-19) quarantine spot in Chongqing. He self-reported that he displayed monkeypox-like clinical manifestations and was then identified as a suspected case of monkeypox by Chongqing CDC.

Clinical specimens, including blister fluid, nasopharyngeal and oropharyngeal swabs, and a blood sample were collected on September 14, and the primary screening of MPXV based quantitative real-time polymerase chain reaction (qPCR) showed positive results among these specimens, which were then sent to National Institute for Viral Disease Control and Prevention (IVDC), China CDC on September 16. Several qPCR (*4*–*5*) and whole genome sequencing (DNBSEQ-G99 by MGI Tech Co., Ltd. China and Oxford/Nanopore) were performed. The qPCR results showed that monkeypox genome and West Africa strain was detected as positive in the specimens of the case (Table 1). In addition, the swab of blister fluid was directly used for transmission electron microscopy. The result revealed that typical mulberry-shaped particles were visualized with diameters ranging from 150 to 200 nm, a characteristic of MPXV (Figure 1B). Gene sequencing suggests that MPXV strain in this case (China-CQ202209) belongs to B.1 branch of the West African linage, and it was highly homologous to strains from Germany collected on June 21, 2022 (GISAID ID: EPI_ISL_13889435) (Figure 1C). These results confirmed the first imported monkeypox case in the mainland of China, making this the fifth confirmed monkeypox infection in humans reported in China. Other imported cases of monkeypox human infection were reported in Taiwan, China (*6*) and Hong Kong Special Administrative Region, China (*7*).

Neglected zoonotic monkeypox is now back in the spotlight worldwide and the alarm for China's prevention and control has been sounded to prevent MPXV import and transmission (*1*). The Chinese technical plan for monkeypox prevention and control has been released for guidance and reference since July 1, 2022 (*8*). It is essential to control the human-to-human transmission of monkeypox through early detection, early reporting, early isolation, and early treatment. It is necessary to further strengthen symptomatic surveillance in travelers and immigrants from endemic and epidemic areas. In addition, the keys to control the epidemic of MPXV include the following: enhancing health education among general populations and strengthening the management of both high-risk people (such as inbound travelers who have had close contact with infected persons or wildlife) and key demographics (such as MSM).

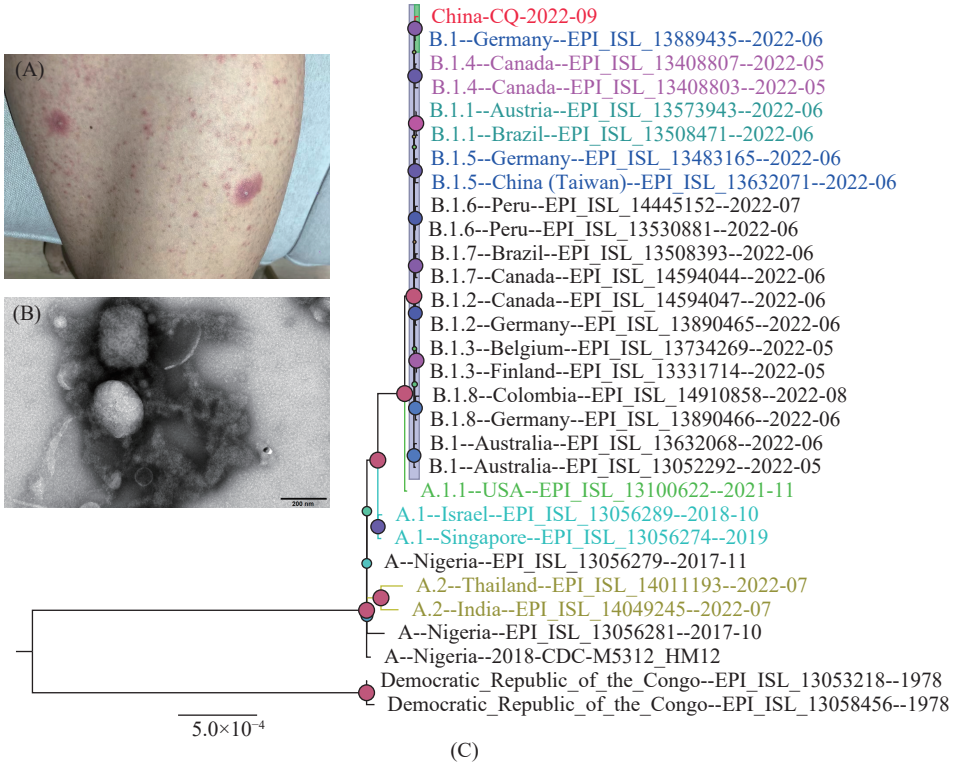

FIGURE 1. Clinical manifestations and laboratory evidence of the first imported monkeypox case in the mainland of China. (A) Rash and pustules displayed on the right thigh of the imported case. (B) Electron microscopy of MPXV-CQ-2022 in the swabs of blister fluid. (C) Phylogenetic tree based on the full-length genome sequences of MPXV.

TABLE 1. Detection of MPXV among the specimens of Chongqing imported case by qPCR.

Specimen	Ct-F3L	Ct-J2R	Ct-D14L	MPXV	West Africa strain of MPXV
Blister fluid swab	20.76	ND	ND	Positive	ND
Oropharyngeal swab	27.81	31.29	Neg	Positive	Positive
Nasopharyngeal swab	31.00	33.25	Neg	Positive	Positive
Blood	33.65	35.54	Neg	Positive	Positive

Abbreviation: MPXV=monkeypox virus; qPCR=quantitative real-time polymerase chain reaction; ND=not determined; Neg=negative.

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REFERENCES

1. Tan W, Gao GF. Neglected Zoonotic Monkeypox in Africa but Now Back in the Spotlight Worldwide. China CDC Wkly 2022. http://dx.doi.org/10.46234/ccdcw2022.166.
2. CDC. 2022 monkeypox outbreak global map. 2022. https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html [2022-9-15].
3. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, et al. Monkeypox Virus Infection in Humans across 16 Countries — April–June 2022. N Engl J Med 2022;387(8):679 – 691. http://dx.doi.org/10.1056/NEJMoa2207323.
4. Ye F, Song JD, Zhao L, Zhang Y, Xia LX, Zhu LW, et al. Molecular Evidence of Human Monkeypox Virus Infection, Sierra Leone. Emerg Infect Dis 2019;25(6):1220 – 2. http://dx.doi.org/10.3201/eid2506.180296.
5. Li Y, Zhao H, Wilkins K, Hughes C, Damon IK. Real-time PCR assays for the specific detection of monkeypox virus West African and Congo Basin strain DNA. J Virol Methods 2010;169(1):223 – 7. http://dx.doi.org/10.1016/j.jviromet.2010.07.012.
6. Yang ZS, Lin CY, Urbina AN, Wang WH, Assavalapsakul W, Tseng SP, et al. The first case of monkeypox virus infection detected in Taiwan: awareness and preparation. Int J Infect Dis 2022;122:991 – 5. http://dx.doi.org/10.1016/j.ijid.2022.07.051.
7. WHO. 2022 Monkeypox Outbreak: Global Trends. 2022. https://worldhealthorg.shinyapps.io/mpx_global/#2_Global_situation_update [2022-9-17].
8. Health Emergency Response Office. Notice of the General Office of the National Health Commission on the issuance of the Technical Guidelines for monkeypox Prevention and Control (2022 edition). 2022. http://www.nhc.gov.cn/yjb/s3577/202207/acd6016aaca543e29c16deb9b5ea3303.shtml. [2022-9-17]. (In Chinese).

Methods and Applications

Development and Application of a Multidrug-Resistant Tuberculosis Case Management System — Yunnan Province, China, 2017–2020

Jinou Chen[1,&]; Yunzhou Ruan[2,&]; Kai Wang[3]; Ling Li[3]; Yunbin Yang[1]; Rui Yang[1]; Lin Xu[1,#]

ABSTRACT

Introduction: Treatment and case management of multidrug-resistant tuberculosis (MDR-TB) is a significant challenge in tuberculosis (TB) control and prevention. This pilot study aims to apply and test a new electronic information system in order to help bolster case management of MDR-TB.

Methods: The MDR-TB Case Management System (CMS) was developed and piloted in the Yunnan Tuberculosis Clinical Center (TCC) in 2017. Next, 5 sites in Yunnan were randomly selected and sampled as pilots in 2018. The real-time regular follow-up rate (RFUR) was calculated for pilot sites. Loss to follow-up (LTFU) rates of MDR-TB treatment cohorts between pilot and non-pilot sites were compared by a chi-square test. LTFU for MDR-TB treatment cohorts was then assessed by univariate and multivariate binary logistic regression.

Results: The average regular follow-up rate was 90.7% in TCC and 73.7% in five other pilot sites of Yunnan Province respectively. The average LTFU rate for pilot sites (9.0%) was lower than non-pilot sites (20.6%, $P<0.01$). The risk of LTFU during MDR-TB treatment reduced 61.7% in CMS pilot cases (adjusted odds ratio: 0.38, 95% confidence interval: 0.23–0.60) compared with non-pilot cases.

Conclusions: As a significant supplement to the Tuberculosis Information Management System, the CMS strengthened the collection, analysis, and utilization of strategic information for MDR-TB cases. The system improved case management by embedding it as a tool of the Comprehensive Supportive Care service model.

INTRODUCTION

The emergence of multidrug-resistant tuberculosis (MDR-TB) was a major public health threat and challenge for the End TB Strategy proposed by the World Health Organization (WHO). The WHO reported 157,000 MDR-TB cases in 2020 worldwide (*1*). About 95% of identified MDR-TB patients were enrolled in treatment using second-line drug therapy; however, unfavorable treatment outcomes were high, as treatment success for MDR-TB is only 59.3%. These unfavorable outcomes include loss to follow-up (LTFU, 14.3%), death (13.3%), and treatment failure (9.1%). China in particular has seen a major challenge posed by limited treatment success (54%) and high loss to follow-up rate (31.9%) (*1*). A simulated mathematical model showed that, if TB response is maintained at the current level, the prevalence of MDR-TB will triple by 2050 (*2*).

A previous qualitative study showed that barriers to MDR-TB treatment success included the long treatment course, poor treatment adherence, catastrophic financial barriers to treatment, adverse effects to second-line drugs, and lack of support from family, doctors, and peers (*3*). Even further, without an electronic system that can integrate all key strategic information, it is very technically difficult to conduct timely monitoring of disease progression and manage patients' follow-up on a long-term basis.

To overcome the barriers of MDR-TB treatment, the Yunnan CDC (YNCDC) collaborated with Family Health International (FHI 360) in 2017, under the technical guidance of the Tuberculosis Prevention and Control Center of the China CDC, to develop and implement the Control and Prevention of MDR-TB program (CAP-TB). The program introduced a patient-centered, Comprehensive Supportive Care (CSC) services model to strengthen MDR-TB care (*4*). Based on this CSC framework, the program developed an integrated, supportive information system for MDR-TB patient management: the MDR-TB Case Management System (CMS, Figure 1A). This study aims to introduce the CMS in pilot areas and evaluate whether the system helps improve treatment management of MDR-TB.

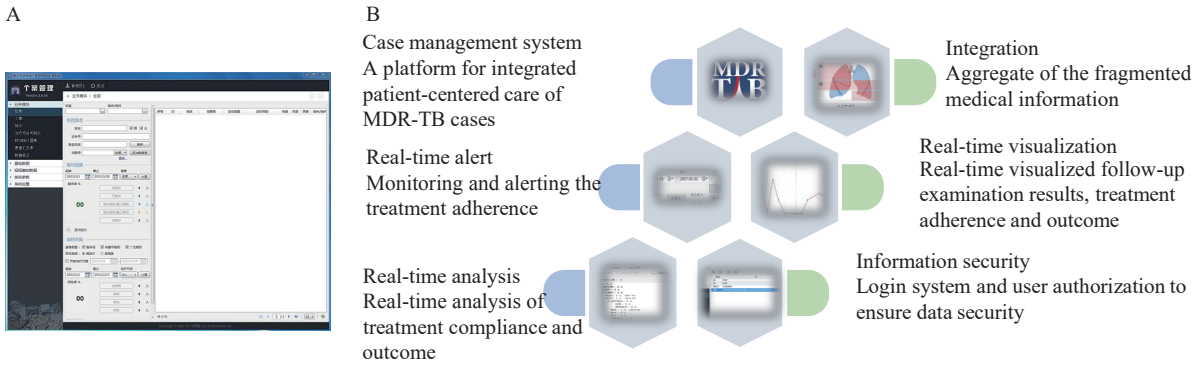

FIGURE 1. The interface and features of CMS for multidrug-resistant tuberculosis in Yunnan pilot, 2017–2020. (A) The interface and modules of CMS. (B) The features of CMS.
Abbreviation: CMS=case management system; MDR-TB=multidrug-resistant tuberculosis.

METHODS

Development of the CMS

The Yunnan CDC and FHI 360 designed and developed the CMS under the guidance of the China CDC in 2017. The CMS was developed based on the Microsoft Visual Studio (version 12.00, Microsoft, Redmond, American). The required supporting software included the Microsoft. NET Framework (version 4.7.1, Microsoft, Redmond, American) and Microsoft Visual Studio (version 12.00, Microsoft, Redmond, American). The CMS was designed based on the concept of case management. An integrated, patient-centered system means dependable communication and coordination throughout the entire process of MDR-TB care, which best meets the healthcare needs of TB patients. The integrated system intensifies information aggregation and data visualization, and includes useful features ranging from warnings about adverse reactions and timely reminders for upcoming appointments to tracking patients throughout treatment (Figure 1B).

Features of the CMS

The integrated, patient-centered supportive information CMS was finalized in 2017.

It includes 5 key functionalities:

Case management: The CMS includes the functions of case listing, case filtering, case detailing, and case registration. It is used to collect the clinical data of diagnosed MDR-TB patients who have enrolled in treatment and provide continuous care throughout the entire treatment course. The CMS records demographic and socioeconomic background, diagnosis information, medical history, clinical indicators, treatment and supportive care records, as well as results from patient intake assessment tools — including mini nutritional assessments, social support instruments, and depression and anxiety tests.

Case information retrieval: The CMS can filter and search a registered case by one or multiple conditions. Case information aggregates longitudinal and horizontal data for the entire treatment course. The longitudinal data refers to the individual record across follow-up visits made by the patients. The horizontal data indicates clinical data of individual patients from various departments of the hospital, such as diagnosis and treatment for inpatients; clinical summary reports for outpatients, radiology, and chest X-rays; laboratory blood tests; and sputum smears and cultures.

Follow-up query and alert: Based on the treatment regimen and follow-up algorithm for MDR-TB care, the CMS can automatically generate a list of patients who are expected to attend treatment visits within a particular period of time, use queries to identify whether the patients have attended their scheduled visits on time or not, and track whether they have completed sputum tests and other required examinations for treatment monitoring. The CMS can also alert the case manager about patients who have failed to show up for their scheduled visits.

Real-time analysis and visualization: The CMS monitors critical indicators of adherence and treatment. The CMS also generates real-time statistical analysis and visualization of sputum test results, treatment adherence, and adverse reactions — either at individual or population levels. Even further, the CMS can automatically determine treatment outcomes according to the CMS status of patients and sputum tests performed.

Share and transfer CMS data: In order to make it

easier for users to carry out further statistical analysis or share data with others, the system supports exporting, importing and printing of data.

The CMS was designed to monitor critical indicators of real-time regular follow-up rate (RFUR). In practice, a standard MDR-TB regimen is a treatment course of 18–20 months in accordance with the Chinese National Tuberculosis Program (CNTP). The regimen contains an intensive phase of 6 months and a continuous phase of 12–14 months. All MDR-TB patients are expected to pay for clinical visits for treatment monitoring (including sputum smear microscopy and cultures, chest X-rays, routine blood tests, and liver-kidney function tests) each month during the intensive phase and every two months in the continuous phase.

Regarding the population level, the *RFUR* in a fixed period t (normally one month) can be calculated with the following equation

$$RFUR_t = \frac{No.\ actual\ visits_t}{No.\ expected\ visits_t} \quad (1)$$

According to the individual treatment regimen, the *expected visits* is defined as the number of patients expected to visit during a particular period t (e.g., from May 1st, 2021 to May 31st, 2021). The *actual visits* is defined as the actual number of patients who have both visited the TB care facility and had monitoring treatment tests performed during the given period (e.g., May 2021).

The calculation of $RFUR_t$ is a dynamic process, depending on not only different periods of time t but also the change of the population cohort in the given period t, which refers to the new patients introduced into the treatment cohort or patients whose treatment outcomes occurred and left the cohort. The *expected visits* included the number of patients returning to visit on time (within one week before or after the expected date of visit), the patients coming ahead of schedule (before one week of the expected date of visit), the patients with delayed visits (after one week of the expected date of visit), and the patients who did not return to visit (within two weeks before or after the expected date of visit).

The comparison of the features between the paper-based reports, the Tuberculosis Information Management System (TBIMS) and the CMS, is presented in Table 1.

The Pilot Study of the CMS

The pilot study for the application of the CMS was initiated in the Yunnan Tuberculosis Clinical Center (TCC) in 2017. Then, this study applied a simple randomized sampling method: sampling 5 prefectures (Baoshan, Honghe, Lincang, Dehong and Pu'er), from 16 overall prefectures of Yunnan Province, who implemented the pilot between 2018 and 2019. Another 11 prefectures of Yunnan were defined as non-pilot sites. Meanwhile, 5 cities (Jinan, Urumqi, Zhenjiang, Yichang, Wuhan) in 4 provincial-level administrative divisions (PLADs) carried out the CAP-TB program synchronously.

TABLE 1. The comparison of different features between the paper-based reports, the national TBIMS and the CMS for MDR-TB.

Feature	Paper-based reports	TBIMS	CMS
Utilization	Collected case and patient data for record	Electronic report and surveillance of the TB disease in a large-scale population	The supplementary of TBIMS to enhance the case management
Content	Paper-based MDR-TB case report	Web-based MDR-TB case report and registration	Integrated demographic, socioeconomic, epidemiological, clinical, treatment, treatment adherence, nutritional and psychological assessment; also available for 9-month short regimen for MDR-TB
Data collection	Collected data by paper- and pencil	Collected data based on website	Collected data by CMS client computer
Data storage	Stored data by paper-based records	Data were automatically uploaded to data center	Data were locally stored by SQL file
Data transmission	Mail or delivery	Data transmitted by network service	Data transmitted by packaged SQL file
Real-time statistical analysis	Unavailable	Simple statistics on website	Real-time statistical analysis in CMS client. CMS computed adherence rate, in-time adherence rate, and treatment outcome
Real-time visualization	Unavailable	Unavailable	Real-time analysis and visualized for adherence of treatment and the follow-up examination results
Real-time alert	Hard to track patients	Hard to track patients	Surveillance and alert to the poor compliance patients

Abbreviation: TBIMS=Tuberculosis Information Management System; CMS=case management system; MDR-TB=multidrug-resistant tuberculosis; SQL=structured query language.

Data Analysis

The real-time RFUR was extracted from the CMS; then, real-time RFUR was evaluated in TCC and 5 sites of the pilot study between 2017 and 2020, respectively. The coverage and use of the CMS in Yunnan was calculated between 2017 and 2020.

Data from the pilot and non-pilot sites of the MDR-TB treatment cohort between 2017 and 2019 were extracted from the TBIMS. The LTFU rates for pilot and non-pilot sites were compared by a chi-square test. The potential factors associated with LTFU for MDR-TB treatment cohorts were categorized and described by proportion, then assessed by univariate and multivariate binary logistic regression.

Statistical analyzes were done by using R software (version 4.0.2, R Core Team, Vienna, Austria). The statistical significance level was set as $P<0.05$.

RESULTS

At the pilot sites, the CSC model for MDR-TB was implemented with supportive care services put in place. Based on the CMS data from the Yunnan pilot sites, the average MDR-TB RFUR was 90.7% in TCC and 73.7% at the prefecture-level sites (Figure 2A).

In 2020, use of the CMS was scaled up to all 16 prefectures of Yunnan Province. With the YNCDC endorsement, utilization of the CMS has become the standard of care for MDR-TB control in the province. The coverage rate of the CMS reached 100% in Yunnan. The CMS was also extended beyond Yunnan to reach four additional PLADs in China.

Under the CSC model, the patient-centered CMS contributed to improved patient regular follow-up of the MDR-TB treatment. The average LTFU rate was 9.0% for the treatment cohort in pilot sites, which was significantly lower ($P<0.05$) than non-pilot sites (20.6%) between 2017 and 2019 (Figure 2B).

Across the 816 patients in the MDR-TB treatment cohort (Table 2), the risk of LTFU reduced by 61.7% during CMS pilot implementation [adjusted odds ratio (aOR): 0.38, 95% confidence interval (CI): 0.23–0.60] compared with non-pilot sites (Figure 2C–D).

DISCUSSION

In the fight against the MDR-TB epidemic, it is critical to strengthen effective MDR-TB detection and ensure treatment completion as the world works towards reaching a cure. Poor treatment adherence and undesirable outcomes exacerbate transmission of MDR-TB across populations. The CSC model and CMS filled the gap by providing patient-centered, individualized care to improve treatment adherence. The CMS responded to the needs of the patients and managed to tackle critical challenges in MDR-TB control.

Embedded in the three-in-one system of TB care delivery, the CMS strengthened communication and collaboration between CDCs, designated hospitals, and community healthcare service institutions. As a platform that encourages real-time cooperation and information sharing, CMS strengthened coordination between different TB stakeholders.

The CMS integrated and unified fragmented clinical data spread across different systems, enabling users to access all key strategic information in one interface. The CMS also provided a multi-dimensional view of the patient's entire medical history. With the CMS in place, case management of MDR-TB was optimized with increased precision, timeliness, and effectiveness. Use of the CMS has been demonstrated to be an effective measure for data-driven quality assurance and quality improvement of the supportive care delivered to the patients. The powerful real-time analysis function, visualization, and tracking of key indicators allowed users to promptly identify and address potential barriers to treatment adherence.

Previous studies provided evidence that digital technology could promote treatment adherence and improve outcomes for TB. A systematic review showed that treatment outcomes among drug-susceptible tuberculosis can be strengthened through effective adherence interventions such as patient education and counseling; management of incentives and enablers; provision of psychological interventions, reminders and tracers; and use of digital health technologies (*5*). Another systematic review showed that medication monitoring increased the probability of cure (relative risk 2.3, 95% CI: 1.6–3.4) (*6*). Although short message service (SMS) and video-observed therapy (VOT) as interventions reported comparable treatment completion when compared with directly observed treatment (DOT), more evidence and high-quality studies are needed to illustrate how such digital technology could strengthen patient compliance (*7*–*8*).

This study was subject to some limitations. Although the data of the Yunnan cohort was used for the evaluation of the CMS, more evidence is needed for the generalization of the CMS across different

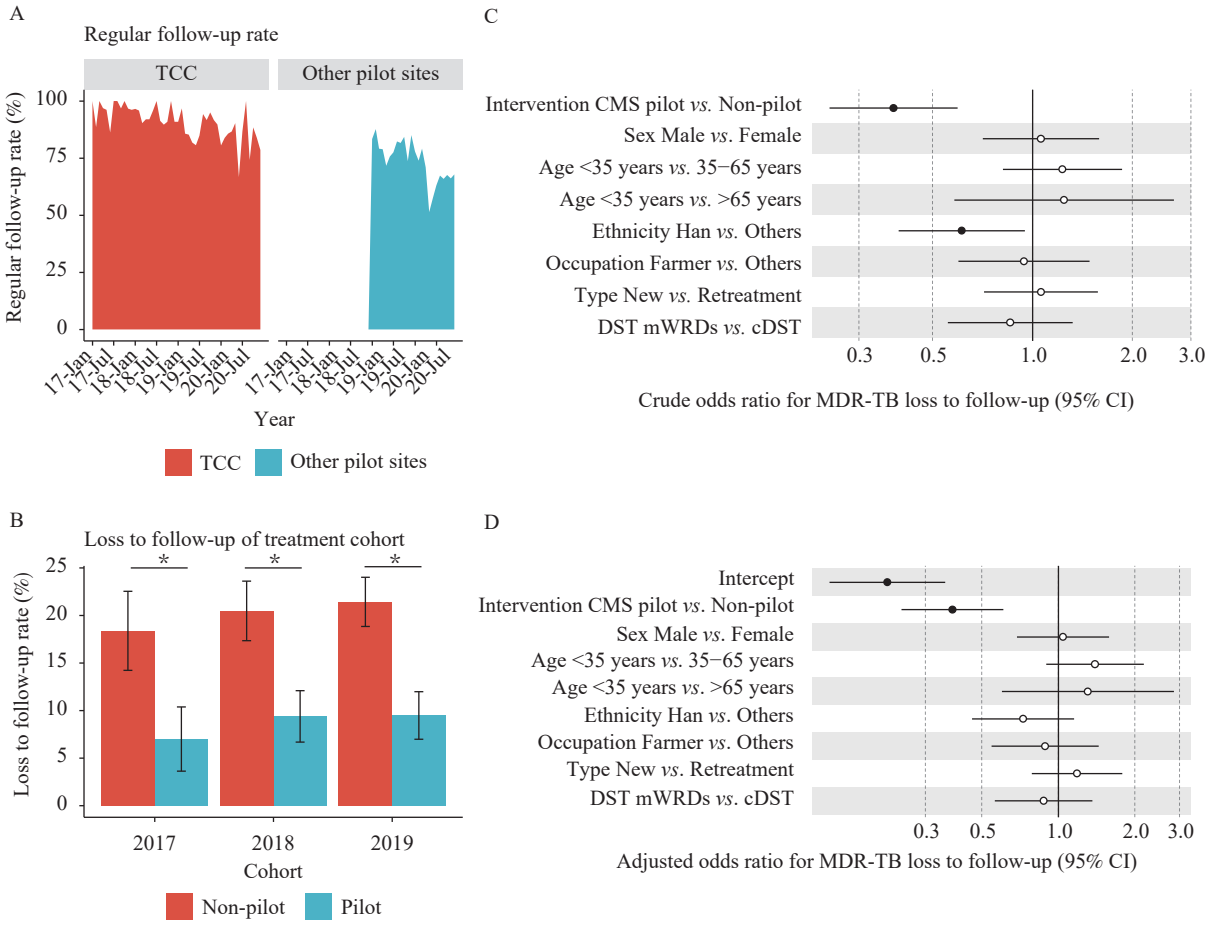

FIGURE 2. The MDR-TB regular follow-up rate and loss to follow-up rate in treatment cohort, and the factors associated with loss to follow-up in Yunnan, 2017–2020. (A) Illustration of the MDR-TB regular follow-up rate in TCC and pilot sites of Yunnan, 2017–2020. (B) Comparison of loss to follow-up rate between the MDR-TB treatment cohorts in the pilot and non-pilot sites of Yunnan, 2017–2019. (C) Crude odds ratio of the factors associated with the loss to follow-up for the MDR-TB patients in Yunnan, 2017–2019. (D) Adjusted odds ratio of the factors associated with the loss to follow-up for the MDR-TB patients in Yunnan, 2017–2019.

Note: The asterisk in Figure 2B presented that the loss to follow-up rate was significantly different in the pilot and non-pilot treatment cohort (P<0.05). The point and interval in Figure 2C–D presented the univariate and multivariate logistic regression odds ratio and its 95% confidence interval, respectively. The solid circle was regression coefficient P<0.05, otherwise, the hollow circle was regression coefficient $P\geq0.05$.

Abbreviation: CMS=case management system; MDR-TB=multidrug-resistant tuberculosis; TCC=tuberculosis clinical center; mWRDs=molecular WHO-recommended rapid diagnostic tests; cDST=conventional drug susceptibility test.

settings. Application scenarios for the CMS should still be according to specific health care resource allocation, the diverse barriers of MDR-TB treatment, and CSC model best practices. The CMS is just a tool and a platform for strengthening MDR-TB case management to meet the requirements of the CSC model and supportive care for MDR-TB treatment. There also remains a need for more investigations to understand the association between adherence intervention and favorable outcomes of MDR-TB. Next, the exchange of data between the CMS and other systems sometimes proves difficult. The CMS thus needs to be further technically enhanced to increase its compatibility and connectivity with existing systems, such as the National Notifiable Disease Reporting System (NNDRS), the TBIMS, hospital information systems (HIS), laboratory information systems (LIS), and the National Project of Basic Public Health Service (BPHS). A comprehensive information system could close such gaps in digital technology. This more advanced system should be underpinned by the concepts of case management and patient-centered care, and should be able to monitor and manage lifelong disease and health issues through a unified dataset that can automatically exchange and share information (*9*).

TABLE 2. The characteristics of the MDR-TB treatment cohort categorized by treatment outcome of Yunnan, 2017–2019.

Characteristic	Loss to follow-up N (%)	Other treatment outcome N (%)	Overall N (%)	χ^2	*P*
Overall	132 (16.2%)	684 (83.8%)	816 (100.0%)		
Treatment cohort					
2017	20 (15.2%)	124 (18.1%)	144 (17.6%)	0.89	0.64
2018	45 (34.1%)	238 (34.8%)	283 (34.7%)		
2019	67 (50.8%)	322 (47.1%)	389 (47.7%)		
Intervention					
Non-pilot	104 (78.8%)	401 (58.6%)	505 (61.9%)	19.07	<0.01
CMS pilot	28 (21.2%)	283 (41.4%)	311 (38.1%)		
Sex					
Male	91 (68.9%)	480 (70.2%)	571 (70.0%)	0.08	0.77
Female	41 (31.1%)	204 (29.8%)	245 (30.0%)		
Age (years)					
<35	39 (29.5%)	233 (34.1%)	272 (33.3%)	1.02	0.60
35–64	83 (62.9%)	403 (58.9%)	486 (59.6%)		
≥65	10 (7.6%)	48 (7.0%)	58 (7.1%)		
Ethnicity					
Han	102 (77.3%)	462 (67.5%)	564 (69.1%)	4.91	0.03
Other minorities	30 (22.7%)	222 (32.5%)	252 (30.9%)		
Occupation					
Farmer	104 (78.8%)	532 (77.8%)	636 (77.9%)	0.07	0.79
Others	28 (21.2%)	152 (22.2%)	180 (22.1%)		
Type of case					
New	44 (33.3%)	237 (34.6%)	281 (34.4%)	0.08	0.77
Retreatment	88 (66.7%)	447 (65.4%)	535 (65.6%)		
DST					
mWRDs	100 (75.8%)	498 (72.8%)	598 (73.3%)	0.49	0.48
cDST	32 (24.2%)	186 (27.2%)	218 (26.7%)		

Abbreviation: MDR-TB=multidrug-resistant tuberculosis; CMS=case management system; DST=drug susceptibility test; mWRDs=molecular WHO-recommended rapid diagnostic tests; cDST=conventional drug susceptibility test

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REFERENCES

1. World Health Organization. Global tuberculosis report 2021. Geneva: WHO; 2021. https://www.who.int/publications/i/item/9789240037021.
2. Li BY, Shi WP, Zhou CM, Zhao Q, Diwan VK, Zheng XB, et al. Rising challenge of multidrug-resistant tuberculosis in China: a predictive study using Markov modeling. Infect Dis Poverty 2020;9(1):65. http://dx.doi.org/10.1186/s40249-020-00682-7.
3. Hutchison C, Khan MS, Yoong J, Lin X, Coker RJ. Financial barriers and coping strategies: a qualitative study of accessing multidrug-resistant tuberculosis and tuberculosis care in Yunnan, China. BMC Public Health 2017;17(1):221. http://dx.doi.org/10.1186/s12889-017-4089-y.

4. Ruan YZ, Li L, Xu L, Zhao YL, Zhong L, Xu ZX, et al. Practical experiences of delivering multidrug-resistant tuberculosis comprehensive supportive care services in China. China CDC Wkly 2021;3(26):566 – 8. http://dx.doi.org/10.46234/ccdcw2021.146.
5. Nunn AJ, Phillips PPJ, Meredith SK, Chiang CY, Conradie F, Dalai D, et al. A trial of a shorter regimen for rifampin-resistant tuberculosis. N Engl J Med 2019;380(13):1201 – 13. http://dx.doi.org/10.1056/NEJMoa1811867.
6. Ngwatu BK, Nsengiyumva NP, Oxlade O, Mappin-Kasirer B, Nguyen NL, Jaramillo E, et al. The impact of digital health technologies on tuberculosis treatment: a systematic review. Eur Respir J 2018;51(1):1701596. http://dx.doi.org/10.1183/13993003.01596-2017.
7. Subbaraman R, de Mondesert L, Musiimenta A, Pai M, Mayer KH, Thomas BE, et al. Digital adherence technologies for the management of tuberculosis therapy: mapping the landscape and research priorities. BMJ Glob Health 2018;3(5):e001018. http://dx.doi.org/10.1136/bmjgh-2018-001018.
8. Riquelme-Miralles D, Palazón-Bru A, Sepehri A, Gil-Guillén VF. A systematic review of non-pharmacological interventions to improve therapeutic adherence in tuberculosis. Heart Lung 2019;48(5):452 – 61. http://dx.doi.org/10.1016/j.hrtlng.2019.05.001.
9. Wang N, Li T, Du X, Li Y, Sun MM, Huan ST, et al. Effectiveness of the integrated TB surveillance system — China, 2018-2019. China CDC Wkly 2020;2(12):190-3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8393169/.

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