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Assessment of tuberculosis burden in China using a dynamic disease simulation model

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SUMMARY

SETTING: Although a preventable and treatable disease, tuberculosis (TB) is among the top 10 causes of death worldwide. A consequence of inadequately treated drug-susceptible TB (DS-TB) is multidrug-resistant TB (MDR-TB).

OBJECTIVES: To improve our understanding of the primary drivers of incidence and prevalence of DS- and MDR-TB in China.

METHODS: The Tuberculosis Disease Transmission Model (TBDTM) uses historical and current disease epidemiology and transmission trends and treatment effectiveness, and accounts for annual changes to these to estimate future DS-TB and MDR-TB burden.

RESULTS: The model shows that in China, by 2050, incidence, prevalence and mortality of DS-TB will decrease by 32%, 50% and 41%, respectively, whereas MDR-TB will increase by respectively 60%, 48% and 35%. Reduction in DS-TB is a result of high treatment and cure rates leading to a decrease in the prevalence of latent tuberculous infection (LTBI), while the increase in MDR-TB is attributed to inappropriate treatment, leading to high transmission of infection and increased LTBI prevalence.

CONCLUSIONS: These results demonstrate a reduction in DS-TB in China over the next 40 years, while MDR-TB will increase. Improvements in the diagnosis and treatment of MDR-TB are needed to counter this threat. The TBDTM tool has potential value in public health practice by demonstrating the impact of interventions and estimating their cost-effectiveness.

KEY WORDS: TB; MDR-TB; disease transmission model

ALTHOUGH a preventable and treatable disease, tuberculosis (TB) is among the top 10 causes of death worldwide.[1,2] The disease is endemic primarily in developing countries, with India and China accounting for 38% of the world's incident cases.[3] The 2000 United Nations (UN) Millennium Development Goal (MDG)[4] No 6 addresses TB, with the targets set by the Stop TB Partnership (Table 1). To meet these targets, the World Health Organization (WHO) and its partners, utilizing a multilayered strategy, have achieved significant reductions in the prevalence of drug-susceptible TB (DS-TB).[5] However, multidrug-resistant forms of TB remain a challenge. Lack of effective diagnostics, coupled with poor adherence and improper treatment practices, continue to fuel the spread of multidrug-resistant TB (MDR-TB).[5]

MDR-TB is defined as disease caused by strains of *Mycobacterium tuberculosis* resistant to the two predominant first-line drugs used to treat TB, isoniazid and rifampicin. MDR-TB is contracted either from an individual harboring the active form of this strain (primary) or it develops due to improper use of antituberculosis drugs in DS-TB patients (acquired). Recent estimates indicate that China accounts for 22% of the global burden of MDR-TB, and that with India the two countries account for nearly 50%.[6]

Due to the slow disease dynamics of the disease, simulation models are critical in forecasting the long-term evolution of the TB epidemic. Several mathematical simulation models for TB have been developed, examining natural transmission dynamics,[7–16] predicting future burden and evaluating TB control strategies.[10,17–23] However, few studies have attempted to provide a detailed epidemiological projection separately for DS-TB and MDR-TB for China.[10,12,17,24–30] A few models examining the epidemiological benefits of more effective TB interventions did carve out MDR-TB; however, these models, while focusing on the South-East Asia region, excluded China.[18,20]

A dynamic and adaptable TB disease transmission model was constructed that accounts for recent trends in TB incidence, prevalence and mortality in China as well as current and anticipated practices to prevent TB. This model evaluates whether the mid- and long-term goals of reducing the global burden of TB are likely to be met, and identifies key drivers that influence the future burden of MDR-TB and DS-TB separately.

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Table 1 Millennium Development Goals and Stop TB Partnership targets

Serial no.	Goals and targets
1	TB incidence should be falling by 2015
2	Reduce TB prevalence by 50% by 2015 compared to 1990 levels
3	Reduce TB mortality rate by 50% by 2015 compared to 1990 levels
4	Reduce global incidence of active TB to <1 case per 1 million persons by 2050

TB = tuberculosis.

The purpose of the present study was to apply this model to the current TB landscape in China to predict future incidence, prevalence and mortality of MDR-TB and DS-TB and help identify practical public health intervention strategies.

METHODS

A 'dynamic state transition model' has been developed that is similar to a Markov model but includes a 'loop back' that defines the incidence of DS-TB and MDR-TB as a function of the transmission rate among infected cases with active disease in the population. The prospective time horizon of the model is 40 years, starting in 2010. Actual patients did not participate in this study, and therefore no ethics review was required.

The model architecture (defined in Figure 1 and described in Table 2) differentiates between DS-TB and MDR-TB populations, tracks the movement between these populations, segregates the MDR-TB pool into primary and acquired MDR-TB populations and differentiates between the untreated and relapsed (previously treated) patient pools. Co-infection with the human immunodeficiency virus (HIV) was not explicitly considered, as such cases constitute a small proportion of all TB cases in China.[10]

The extent of transmission of the disease is described in Table 3. Active sputum smear-positive patients transmit infection to the susceptible population, and cease to do so only once they turn sputum smear-negative, when treated successfully—this stage is reached well before treatment completion.

Inputs for the model

Table 3 details the model inputs and sources, primarily from published literature. Given the granularity contained in the model, several China-specific inputs were not available in the published literature, particularly those related to latent tuberculous infection (LTBI), and the transition rates from latent to active states, which were derived in such a manner as to calibrate key model parameters (the 2008, 2009 and 2010 values of incidence, prevalence and mortality) with the published WHO Global TB Control 2011 report.[10] This calibration over a 3-year timeframe (Table 4) helped align the model with real world data for key parameters and characterize their growth rate over that period.

For the purpose of forecasting assumptions for

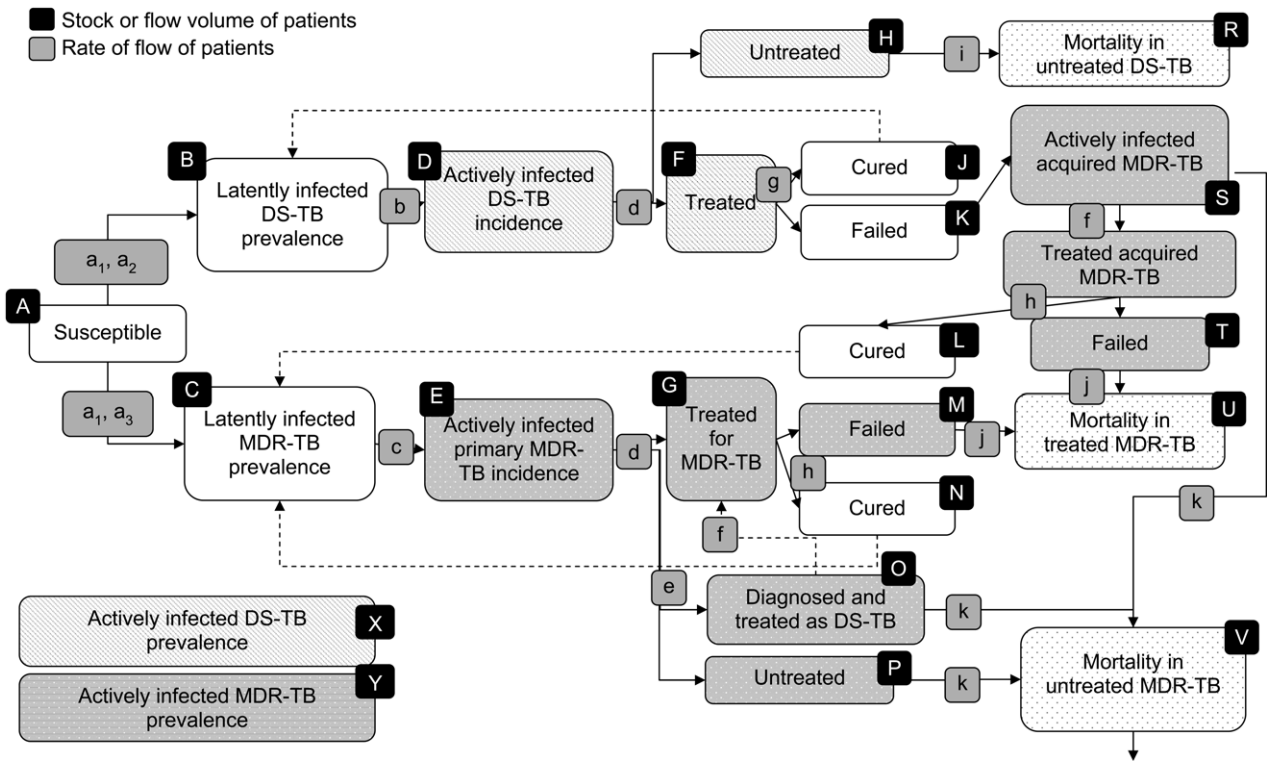

Figure 1 A schematic of the model architecture, showing key disease states and progression of patients between these disease states. DS-TB = drug-susceptible tuberculosis; MDR-TB = multidrug-resistant tuberculosis.

Table 2 Key elements of the model architecture

Tag	Type	Description
a	Rate	The flow of susceptible (unaffected) population into latently affected as a result of acquisition of infection. A substantial percentage of LTBI patients do not go on to develop the active form of the disease over a lifetime. This has been modeled as a function of the following three factors:
a_1		Effective infection transmission rate (susceptible patients infected per annum per active infected smear-positive case and who move to the latent pool; DS-TB and MDR-TB)
a_2		Months to sputum smear conversion for cured patients (DS-TB)
a_3		Months to sputum smear conversion for cured patients (MDR-TB)
b, c	Rate	Transition of patients from the latent pool to the active form of the disease; applied as an annual percentage of the prevalent latent pool. Separate transition rates applied to new, untreated individuals (b_1, c_1) and relapsed individuals (b_2, c_2)
g	Rate	The cure rate for DS-TB patients at the end of the treatment period
h	Rate	The cure rate for MDR-TB patients at the end of the treatment period
d	Rate	The percentage of active incident patients who are treated, applied in the respective year to the incident patients of that year and to the surviving incident patients of previous years
e, f	Rate	The treatment landscape of MDR-TB in emerging economies is characterized by inadequate testing for MDR-TB, thus resulting in incorrect diagnosis of MDR-TB patients as DS-TB, and the ensuing DS-TB treatment. MDR-TB treatment is begun for patients who have access to this treatment only after they fail DS-TB treatment 'e' represents the percentage of patients who are treated with DS-TB regimens 'f' represents the percentage of patients who, after being treated with DS-TB treatments and fail, are given MDR-TB treatment
i	Rate	Rate of mortality in untreated DS-TB
j	Rate	Rate of mortality in treated and failed MDR-TB (both primary and acquired)
k	Rate	Rate of mortality in untreated MDR-TB
A	Stock	The susceptible population, or those who have neither LTBI nor active TB
B	Stock	LTBI pool (naïve) comprises the population that has been infected with the disease but where the disease is yet to turn into its active form
C	Stock	While B represents the DS-TB populations, C represents the MDR-TB pools
X	Stock	The prevalence of active DS-TB patients comprises 1) untreated active patients [H], and 2) those who are currently undergoing treatment [F]
Y	Stock	The prevalence of active MDR-TB patients comprises 1) untreated active patients from both primary MDR-TB [P] and acquired MDR-TB [S], 2) those who are currently undergoing treatment [G] from within both primary and acquired MDR-TB pools, and 3) those who have failed MDR-TB treatment [M, T]
D	Flow	The annual incidence of active DS-TB patients from the latent DS-TB prevalent pool
E	Flow	The annual incidence of active MDR-TB patients from the latent MDR-TB prevalent pool
F	Flow	Patients who commence DS-TB treatment in any year Patients who commence MDR-TB treatment in any year Untreated active DS-TB patients alive
P	Stock	Untreated active MDR-TB patients alive
J	Flow	Cured DS-TB patients during a year who flow from the active pool to the latent pool
K	Flow	Failed DS-TB patients during a year
S	Stock	Prevalence of acquired MDR-TB patients alive, including 1) those who are untreated, 2) those who are being treated and 3) those who have failed treatment
L	Flow	Cured acquired MDR-TB patients during a year who flow from the active pool to the latent pool
T	Flow	Failed acquired MDR-TB patients during a year
M	Flow	Failed primary MDR-TB patients during a year
N	Flow	Cured primary MDR-TB patients during a year who flow from the active pool to the latent pool
O	Flow	MDR-TB patients mistakenly treated with DS-TB regimens
R	Flow	TB-related deaths from untreated DS-TB patients
U	Flow	TB-related deaths from failed MDR-TB patients
V	Flow	TB-related deaths from untreated MDR-TB patients

LTBI = latent tuberculous infection; DS-TB = drug-susceptible TB; MDR-TB = multidrug-resistant TB; TB = tuberculosis.

key input parameters for the period 2010–2050, the parameters have been placed in three categories:

Category A: Parameters that have seen a change over the years. Where such change is expected to continue, the trend is maintained until 2050. These parameters are:

1 Rate of incorrect diagnosis of MDR-TB: continued efforts to control the TB burden by local health authorities have led to a small but positive impact on the accurate diagnosis of MDR-TB. This declining trend in incorrect diagnoses of MDR-TB has been forecast to continue from 98% in 2010 to 90% in 2050.

2 Improvement in vaccine effectiveness factor, leading to a reduction in the rate of spread of infection. The childhood bacille Calmette-Guérin vaccination program has been able to cover almost the entire population in China for many years, creating a segment of the total population that may be less susceptible to LTBI (as compared to the pool that existed previously). This reduced susceptibility due to improved immunity has been modeled through a gradually decreasing rate of spread of infection per smear-positive TB patient from 6.5 in 2010 to 5.2 in 2050, by applying a change factor (vaccine effectiveness factor).

3 Annual transition rate from LTBI to active TB: to enable the calibration of the TB incidence in the model with WHO reports, the annual transition rate has been reduced by 25% from 2000 to 2010. To further align with the WHO incidence rate of TB, this decline was assumed to continue by an additional 10% (until 2017), and then hold constant thereafter.

Table 3 Model inputs and sources

Tag	Description	Values used in the model						Link/source
		2000	2010	2020	2030	2040	2050	
a_1	Effective infection transmission rate, susceptible patients infected per annum per active infected smear-positive case and who move to the latent pool (DS-TB and MDR-TB)*	6.5	6.2	6.0	5.7	5.5	5.2	[31] (value for 2000) *†
a_2	Months to sputum smear conversion for cured patients (DS-TB)	1	1	1	1	1	1	
a_3	Months to sputum smear conversion for cured patients (MDR-TB)	3	3	3	3	3	3	
b_1	Transition from new, untreated latently infected DS-TB individuals to active infection, % of such latent cases who transition to active cases during a year	0.27	0.20	0.18	0.18	0.18	0.18	Values assumed so as to calibrate model output with published data
c_1	Transition from new, untreated latently infected MDR-TB individuals to active infection, % of such latent cases who transition to active cases during a year	0.27	0.20	0.18	0.18	0.18	0.18	Values assumed so as to calibrate model output with published data
b_2	Transition from relapsed latently infected DS-TB individuals to active infection, % of such latent cases who transition to active cases during a year	0.53	0.40	0.35	0.35	0.35	0.35	Values assumed so as to calibrate model output with published data
c_2	Transition from relapsed latently infected MDR-TB individuals to active infection, % of such latent cases who transition to active cases during a year	0.53	0.40	0.35	0.35	0.35	0.35	Values assumed so as to calibrate model output with published data
d	Treatment rate for DS-TB							[10, 32] (some values have been assumed to calibrate model output with published data)
	% diagnosed out of incidence	33	98	98	98	98	98	
	% treated of diagnosed	68	99	99	99	99	99	
e	Incorrect diagnosis rate for MDR-TB,‡ % misdiagnosed out of total MDR-TB diagnosed	100	98	96	94	92	90	Values assumed so as to calibrate model output with published data
f	Retreatment rate for patients, initially treated for DS-TB and failed, % retreated with MDR–TB treatment after failure with DS-TB treatment	2	2	2	2	2	2	Values assumed so as to calibrate model output with published data
g	Cure rate for DS-TB, % successfully treated per total treated	99	99	99	99	99	99	[10]
h	Cure rate for MDR-TB, % successfully treated per total treated	56	56	56	56	56	56	[30, 33]
i	Disease-specific mortality rate of untreated DS-TB	10%–20%–30%–40%–42% in the first 5 years after incidence						Values assumed so as to calibrate model output with published data
j	Disease-specific mortality of failed MDR-TB	10%–20%–30%–40%–51% in the first 5 years after failure						Values assumed so as to calibrate model output with published data
k	Disease-specific mortality of untreated MDR-TB	10%–25%–35%–45%–55% in the first 5 years after incidence						Values assumed so as to calibrate model output with published data
i, j, k	General mortality rate for untreated and failed treatment active TB patients	6.35% per annum						Values assumed so as to calibrate model output with published data, and higher than general mortality rate of LTBI population to account for reduced survival of active compared to LTBI patients, even for non-TB causes
	General mortality rate for the latent pool, %	0.7	0.7	0.8	0.9	1.1	1.3	Values assumed so as to calibrate model output with published data
B	LTBI prevalence, % of total population with LTBI	40						Values assumed so as to calibrate model output with published data

*The effective transmission rates represent the number of people in the susceptible pool per annum (values for 2000) to whom tuberculous infection is transmitted by each smear-positive patient; patients who receive successful treatment cease to do so once they turn sputum smear-negative—this stage is reached well before treatment completion.

†It is recognized that DS and MDR strains of TB may have different 'fitness factors'. Estimates of the relative fitness of resistant strains have been obtained from in vitro competition studies of drug-resistant bacteria or derived from molecular epidemiological data.[34–36] The results of these empirical studies comparing the replicative potential of these strains have been heterogeneous and indicate a wide range of fitness costs associated with resistance.[37] Given that the impact on TB epidemiology of strain fitness is still under debate, the model does not differentiate between the transmission potential of drug-resistant and drug-susceptible strains.

‡Many MDR-TB patients are not tested for drug susceptibility, and while diagnosed with TB, are assumed to be drug-susceptible and treated as such. The extent of such incorrect diagnosis is measured by this metric.

DS-TB = drug-susceptible TB; MDR-TB = multidrug-resistant TB; TB = tuberculosis; LTBI = latent tuberculous infection.

Table 4 Comparison of the model output with WHO reports*

	2010 values		2009 values		2008 values	
Output parameters	WHO report	Our model	WHO report	Our model	WHO report	Our model
Incidence, per 100 000	78	78	81	81	84	84
Prevalence, per 100 000	108	108	112	113	119	119
Mortality, per 100 000	4.1	4.1	4.2	4.2	4.3	4.3

*From the WHO's Global Tuberculosis Control 2011 report.[3]
WHO = World Health Organization.

4 Birth rate and general mortality rate: these rates were adopted as per UN estimates, and were applied to LTBI patients.

Category B: Parameters where the 2010 value has been held constant in subsequent years given the relatively low likelihood of future change:

1 Increase in diagnosis rate from 33% (2000) to 98% (2010); this was retained at 98% until 2050.
2 Increase in treatment rate from 68% (2000) to 99% (2010); this was retained at 99% until 2050.

Category C: The following parameters were assumed to stay constant from 2000 to 2050:

1 Cure rate for DS-TB and MDR-TB at respectively 99% and 56%.
2 Percentage of cured patients who move to latent pool: 100%.
3 Treatment duration for DS-TB and MDR-TB at respectively 6 and 18 months.
4 Time to sputum smear conversion at respectively 1 and 3 months for DS-TB and MDR-TB.
5 Disease-specific mortality rates.
6 General mortality rate for active TB patients.

Sensitivity analyses have been carried out on key parameters (incorrect MDR-TB diagnosis rate, percentage of patients with access to MDR-TB treatment, infection spread rate and MDR-TB cure rate) to evaluate the impact of a change in these inputs on MDR-TB epidemiology. In these analyses, each of these input parameters was increased sequentially by 10%, and then by 20%, resulting in eight different configurations of these input parameters. However, the impact of any extraordinary developments (such as newer treatments, vaccines, diagnostic tools, policy changes, etc.) on the future of TB epidemiology was not incorporated into the base model.

Table 3 contains 1) a comprehensive list of the key inputs used in the model and their respective sources, and 2) a list of values for 2000, 2010, 2020, 2030, 2040 and 2050 for key parameters, as shown in the model; values for 2000 are used when 2010 values are not available for inputting into the future years.

RESULTS

Under current conditions, and assuming that present trends continue, significant decreases in the incidence, prevalence and mortality of TB are expected by 2015 compared to 1990 estimates (Table 5A). The first goal, a reduction in TB incidence by 2015, is likely to be met—in fact, incidence has been declining since at least 2000.[3] Furthermore, the expected prevalence and mortality are expected to be lower in 2015 than the 50% target set by the Stop TB Partnership as compared to 1990. In China, all MDG and Stop TB Partnership targets for 2015 are thus on track. The decline in incidence is a result of the declining pool of latently infected individuals; in 2000, 40% of the population was latently infected with TB and in 2015, 36% of the population is expected to be infected.

Despite the expectation of meeting the 2015 TB goals, the results mask deeper concerns. The incidence, prevalence and mortality related to TB will still remain high in 2015 (Table 5A), and at the current rate, the 2050 goal of reducing TB incidence to less than 1 per million is unattainable (Table 5B). Despite the advances in reducing the burden of DS-TB, MDR-TB threatens to become a much larger burden.

Table 5 TB incidence, prevalence and mortality in China*

Output parameters	1990	2015†	Change	Goal	Goal likely to be met
A 1990 and 2015					
Incidence (per 1 million)	1 338 563 (1165)	960 387 (688)	−28% (−41%)	NA	
			−1.5% (over previous year)	<0%	Yes
Prevalence (per 1 million)	3 758 426 (3271)	1 302 193 (933)	−65% (−71%)	(NA) −50%	Yes
TB mortality (per 1 million)	285 172 (248)	48 158 (34)	−83% (−86%)	(NA) −50%	Yes
	2010	2050†			
B 2010 and 2050					
Incidence (per 1 million)	1 067 381 (788)	790 126 (558)		NA (<1)	No
Prevalence (per 1 million)	1 457 681 (1076)	1 182 968 (835)		Goal not stated	NA
TB mortality (per 1 million)	54 991 (41)	64 806 (46)		Goal not stated	NA

*Includes both DS-TB and MDR-TB.
†Estimated by the model.
TB = tuberculosis; NA = not applicable; DS-TB = drug-susceptible TB; MDR-TB = multidrug-resistant TB.

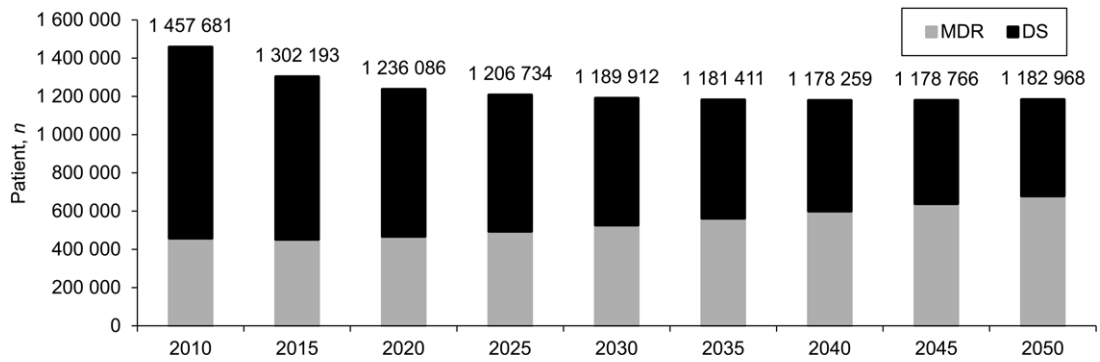

Figure 2 Comparison of prevalence of DS-TB and MDR-TB at 5-year intervals from 2010 to 2050. DS-TB = drug-susceptible tuberculosis; MDR-TB = multidrug-resistant tuberculosis.

MDR-TB paradox

In stark contrast to DS-TB, the epidemiological parameters for MDR-TB reflect a steep increase over the next 40 years (Figure 2 and Table 6). This increase is attributed to inadequate MDR-TB diagnosis, low correct treatment rates, long, suboptimal treatment regimens and poor patient adherence. As a consequence, the number of new (latent MDR-TB) infections will significantly increase (Figure 3).

Table 6 Incident cases, prevalent cases and deaths by TB type

Output parameters, type of TB	2010	2015	2050	% Change 2010–2050	% Change 2015–2050
Incidence					
DS-TB	997 204	891 151	677 678	−32	−24
Total MDR-TB	70 178	69 235	112 448	60	62
Primary MDR-TB	60 281	60 521	105 846	76	75
Acquired MDR-TB	9896	8714	6602	−33	−24
Prevalence					
DS-TB	998 549	848 751	502 727	−50	−41
Total MDR-TB	459 132	453 442	680 241	48	50
Primary MDR-TB	390 931	388 865	626 013	60	61
Acquired MDR-TB	68 201	64 576	54 228	−20	−16
TB deaths					
DS-TB	12 192	10 524	7152	−41	−32
Total MDR-TB	42 798	37 633	57 654	35	53
Primary MDR-TB	36 766	33 037	54 255	48	64
Acquired MDR-TB	6032	4597	3399	−44	−26

TB = tuberculosis; DS-TB = drug-susceptible TB; MDR-TB = multidrug-resistant TB.

On closer examination of the two components of MDR-TB, namely primary (85% of all MDR-TB) and acquired MDR-TB, different trends are seen (Table 6 and Figure 4). In contrast to primary MDR-TB, the model predicts a decline in the incidence, prevalence and mortality of acquired MDR-TB, attributed to its source, DS-TB.

To obtain a meaningful decline in MDR-TB epidemiology, there needs to be concurrent improvement in the following parameters: incorrect MDR-TB diagnosis rate, patients with access to MDR-TB treatment, infection spread rate and MDR-TB cure rate (Table 7).

DISCUSSION

The results of this TB model indicate that while the 2015 goals for TB will be achieved in China, the alarming MDR-TB epidemic is in sharp contrast to the reduction in the burden of DS-TB. While efforts

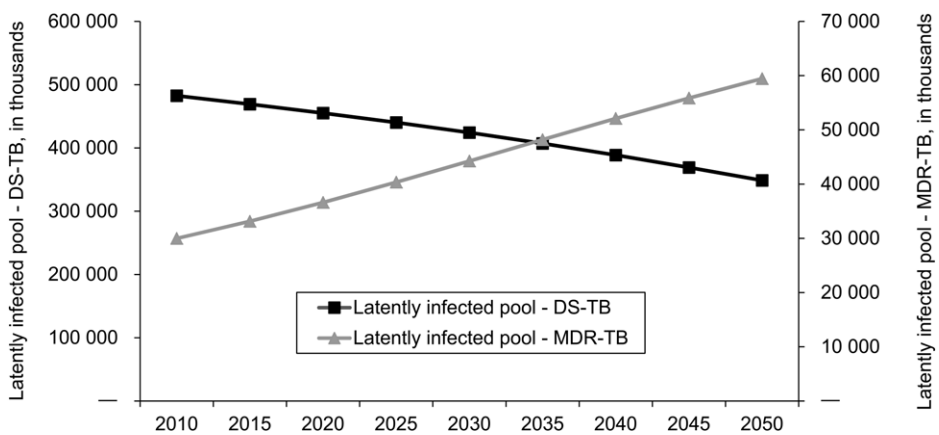

Figure 3 Trends in latently infected pools of DS-TB (left axis) and MDR-TB (right axis) at 5-year intervals from 2010 to 2050. DS-TB = drug-susceptible tuberculosis; MDR-TB = multidrug-resistant tuberculosis.

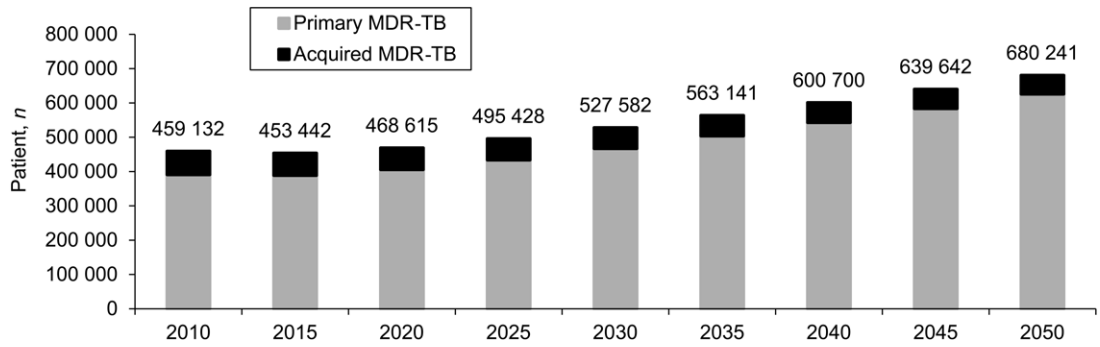

Figure 4 Comparison of prevalence of primary and acquired MDR-TB at 5-year intervals from 2010 to 2050. MDR-TB = multidrug-resistant tuberculosis.

deployed in meeting or exceeding the 2015 MDG goals are noteworthy, achievement of the 2050 goals will remain an elusive target unless the pace of public health interventions is accelerated.

The incidence of both DS-TB and MDR-TB is a function of the size of the pool of LTBI. For DS-TB, the LTBI pool will decrease as improved access and adherence to more efficacious (>95% cure rate) treatments are channeled through China's DOTS infrastructure. In contrast, the latent MDR-TB pool will increase (Figure 3) as a result of contact transmission from active MDR-TB patients. Factors contributing to continued transmission of MDR-TB include: 1) inadequate drug susceptibility testing capacity, leading to large numbers of unrecognized infectious individuals; 2) limited access to and delay in MDR-TB treatment, thus prolonging periods of infectiousness (only about 3000 patients are assumed to be correctly treated for MDR-TB each year in China, a fraction of the more than 60 000 incident MDR-TB patients in 2010);[6] 3) less efficacious (cure rate of 56%) and poorly tolerated drugs, leading to poor treatment outcomes; and 4) longer treatment duration, which may further adversely impact adherence.

The WHO has recognized the importance of the timely and accurate diagnosis of MDR-TB in its 2010 MDR-TB report, where it states:

> . . . since the vast majority of cases are undetected and do not receive adequate care, we expect a global decline in MDR-TB mortality as the coverage and quality of drug susceptibility testing and treatment programs improve globally.[6]

Furthermore, efforts need to be made to improve the effectiveness of current MDR-TB treatments by reducing treatment duration and/or time to sputum smear conversion, simplifying regimens, improving drug tolerability and thereby patient adherence, and introducing new, more potent treatments.

In addition, to meet the 2050 Stop TB goal in

Table 7 Sensitivity analysis

	Base values	Sensitivity analysis (absolute values)							
Sensitivity parameters									
Incorrect MDR-TB diagnosis rate, %*	90	72	72	72	72	54	54	54	54
Patients with access to MDR-TB treatment, %	2	2	22	22	22	22	41	41	41
Infection spread rate	5.2	5.2	5.2	4.16	4.16	4.16	4.16	3.12	3.12
MDR-TB cure rate, %	56	56	56	56	67	67	67	67	78
Sensitivity results									
Incidence									
Total MDR-TB	112 454	110 868	109 097	98 907	98 057	96 780	95 418	86 817	85 863
Primary MDR-TB	105 853	104 267	102 496	92 354	91 504	90 227	88 865	80 312	79 358
Acquired MDR-TB	6 601	6 601	6 601	6 553	6 553	6 553	6 553	6 505	6 505
Prevalence									
Total MDR-TB	680 275	650 506	623 710	581 752	559 965	531 075	506 510	474 016	444 210
Primary MDR-TB	626 052	596 283	572 023	530 311	509 252	480 362	458 807	426 539	398 066
Acquired MDR-TB	54 223	54 223	51 687	51 440	50 713	50 713	47 703	47 476	46 144
TB mortality									
Total MDR-TB	57 657	50 986	45 516	41 650	39 407	34 157	30 178	27 727	24 771
Primary MDR-TB	54 258	47 587	42 495	38 649	36 477	31 228	27 665	25 231	22 406
Acquired MDR-TB	3 399	3 399	3 021	3 001	2 930	2 930	2 513	2 496	2 365

*Many MDR-TB patients are not tested for drug susceptibility, and while diagnosed with TB, are assumed to be drug-susceptible and treated as such. The extent of such incorrect diagnosis is measured by this metric.
MDR-TB = multidrug-resistant TB; TB = tuberculosis.

China, a multi-pronged approach should target 1) curtailing new LTBI cases and 2) curbing the transition from the latent to the active state. For the latter, the daunting tasks of first identifying those with latent infection and then treating them en masse would need to be addressed.[38] For the former, more effective vaccines with broad uptake are needed,[10,18–23] as are improvements in the public health infrastructure and capacity, resulting in improved diagnostics, treatment access and adherence. In the absence of these actions, the disease will continue to spread.[18,22,39]

To construct an integrated epidemiological portrait of the TB epidemic from 2010 to 2050, this calibrated TB simulation model takes into consideration the source, course and transmission of infection, and is built upon current disease estimates and trend assumptions, but does not consider any extraordinary factors or new events, such as introduction of newer treatments, vaccines, diagnostic tools, policy changes, etc. These changes have not been factored into the inputs because the authors have no reliable basis for ascertaining their likelihood, timing or accurate magnitude.

Variability in the duration of LTBI,[18] while recognized and accounted for, is not explicitly modeled due to its limited impact on disease forecast. While it is recognized that HIV co-infection impacts the rate of spread of infection, the transition rate from latent to active disease, the treatment success rate and disease mortality, and that TB-HIV co-infection may see a substantial increase in the future, HIV co-infected patients have not been explicitly studied in the model, as 1) the number of such patients is small, 2) consensus values for HIV-specific input parameters are not readily available, and 3) accounting for these separately would place a much higher burden on relevant input parameters.

CONCLUSION

While this model demonstrates that great progress has been made in curbing TB, it also illustrates steep challenges that lie ahead in meeting 2050 WHO goals. This model could play an important role in quantifying the impact of new diagnostic tools, treatment innovations and critical public health interventions, e.g., incremental health care capacity, improved patient access, etc., and allow for greater rigor in assessing the relative impact of these improvements in limiting future disease burden.

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RÉSUMÉ

CONTEXTE : La tuberculose (TB), bien qu'une maladie pouvant être prévenue et traitée, appartient aux 10 causes principales de décès au niveau mondial. Une conséquence d'un traitement inadéquat d'une TB sensible aux médicaments (TB-DS) est une TB multirésistante aux médicaments (TB-MDR).

OBJECTIFS : Mieux comprendre les facteurs moteurs principaux de l'incidence et de la prévalence de la TB-DS et de -MDR en Chine.

SCHÉMAS : Le modèle de la transmission de la maladie tuberculeuse (TBDTM) utilise les incidences historique et actuelle de la maladie et les tendances de la transmission et les taux de succès du traitement, et tient compte des modifications actuelles de ces données pour estimer le fardeau futur de la TB-DS et de la TB-MDR.

RÉSULTATS : Ce modèle montre qu'en Chine, avant 2050, on notera une décroissance de 32% de l'incidence, de 50% de la prévalence et de 41% de la mortalité de la TB-DS, alors qu'il y aura une augmentation de 60% de l'incidence, de 48% de la prévalence et de 35% de la mortalité de la TB-MDR. Les réductions dans la TB-DS pourraient être dues à une diminution des patients atteints d'une infection latente tuberculeuse (LTBI), tandis que l'augmentation de la TB-MDR sera due au traitement inapproprié, entraînant une forte transmission de l'infection et la recrudescence de LTBI qui en résulte.

CONCLUSIONS : Les résultats démontrent une décroissance de la TB-DS en Chine au cours des 40 prochaines années et une recrudescence de la TB-MDR. Des améliorations dans le diagnostic et traitement des cas de TB-MDR seront nécessaires pour contrer cette menace. Cet outil TBDTM a une valeur potentielle en pratique de santé publique, en permettant de prévoir les résultats épidémiologiques de diverses interventions et estimer leur rapport coût-efficacité.

RESUMEN

MARCO DE REFERENCIA: Pese a que la tuberculosis (TB) es una enfermedad prevenible y se puede tratar, constituye una de las 10 principales causas de mortalidad en el mundo. Una consecuencia del tratamiento inadecuado de la TB normosensible (TB-DS) es la aparición de TB multidrogorresistente (TB-MDR).

OBJETIVOS: Comprender mejor la incidencia y la prevalencia de TB-DS y TB-MDR en la China.

MÉTODOS: El modelo de transmisión de la enfermedad tuberculosa (TBDTM) utiliza la incidencia histórica y la incidencia actual de la enfermedad, las tasas de tratamiento eficaz y las tendencias de la transmisión y considera las modificaciones anuales de estas medidas, con el propósito de calcular la carga futura de morbilidad por TB-DS y por -MDR.

RESULTADOS: El modelo puso en evidencia que entre antes del 2050 en la China se observará, con relación a la TB-DS, una disminución de un 32% de la incidencia, 50% de la prevalencia y 41% de la mortalidad, y, en relación con la TB-MDR, aumentará la incidencia un 60%, la prevalencia un 48% y la mortalidad un 35%. Los valores decrecientes de la TB-DS serán la consecuencia de una disminución de los pacientes con infección tuberculosa latente (LTBI), dada las altas tasas de tratamiento y de curación; al contrario la TB-MDR aumentará a medida de un tratamiento inadecuado, lo cual genera una alta tasa de transmisión de la infección y el consecutivo aumento de LTBI.

CONCLUSIÓN: Los resultados demuestran disminuciones anticipadas de TB-DS en la China durante los próximos 40 años, con una agravación de la TB-MDR. Será preciso contar con progresos en el diagnóstico y el tratamiento de la TB-MDR, a fin de afrontar este peligro. Esta herramienta de TBDTM puede ser muy útil en la práctica de salud pública con el objeto de prever los resultados epidemiológicos de las intervenciones y evaluar su rentabilidad.