

THE LANCET

Infectious Diseases

Supplementary appendix

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Supplement to: Sharma A, Hill A, Kurbatova E, et al, for the Global Preserving Effective TB Treatment Study Investigators. Estimating the future burden of multidrug-resistant and extensively drug-resistant tuberculosis in India, the Philippines, Russia, and South Africa: a mathematical modelling study. *Lancet Infect Dis* 2017; published online May 9. [http://dx.doi.org/10.1016/S1473-3099\(17\)30247-5](http://dx.doi.org/10.1016/S1473-3099(17)30247-5).

Technical Appendix 1. Differential equations

The deterministic model consists of a series of differential equations that represent TB and HIV transmission, generation of resistance to TB medicines during treatment, and outcomes of TB and HIV infection based on underlying TB status. The differential equations used to model these states and outcomes are summarized below.

Susceptible

$$dS^n/dt = \Pi - (\lambda_L^n + \lambda_A^n + \mu^n + \tau)S^n + rN \left(1 - \frac{N}{k}\right)$$

$$dS^h/dt = \omega S^a + \tau S^n - (\lambda_L^h + \lambda_A^h + \mu^h + \theta)S^h$$

$$dS^a/dt = \theta S^h - (\lambda_L^h + \lambda_A^a + \mu^a + \omega)S^a$$

Latent TB infection

$$dL_i^n/dt = \lambda_{L,i}^n(S^n + L^n + R_t^n + R_u^n) - (\lambda_L^n + \lambda_A^n + v^n + \mu^n + \tau)L_i^n$$

$$dL_i^h/dt = \lambda_{L,i}^h(S^h + L^h + R_t^h + R_u^h) - (\lambda_L^h + \lambda_A^h + v^h + \mu^h + \theta)L_i^h + \tau L_i^n + \omega L_i^a$$

$$dL_i^a/dt = \lambda_{L,i}^a(S^a + L^a + R_t^a + R_u^a) - (\lambda_L^h + \lambda_A^a + v^a + \mu^a + \omega)L_i^a + \theta L_i^h$$

Active TB, not on treatment

$$dI_i^n/dt = \lambda_{A,i}^n(S^n + L^n + R_t^n + R_u^n) + v^n L_i^n + \alpha_u R_{u,i}^n + \alpha_t^n R_{t,i}^n + \delta_i^n D_i^n - (\chi^m + \phi_u^n + \mu_u^n)I_i^n + \sum \rho_{j,i}^n D_j^n$$

$$dI_i^h/dt = \lambda_{A,i}^h(S^h + L^h + R_t^h + R_u^h) + v^h L_i^h + \alpha_u R_{u,i}^h + \alpha_t^h R_{t,i}^h + \delta_i^h D_i^h - (\chi^m + \phi_u^h + \mu_u^h)I_i^h + \sum \rho_{j,i}^h D_j^h$$

$$dI_i^a/dt = \lambda_{A,i}^a(S^a + L^a + R_t^a + R_u^a) + v^a L_i^a + \alpha_u R_{u,i}^a + \alpha_t^a R_{t,i}^a + \delta_i^a D_i^a - (\chi^m + \phi_u^a + \mu_u^a)I_i^a + \sum \rho_{j,i}^a D_j^a$$

Active TB, on treatment

$$dD_i^n/dt = \chi^m I_i^n - (\mu_{t,i}^n + \phi_{t,i}^n + \delta_i^n + \sum \rho_{j,i}^n)D_i^n$$

$$dD_x^h/dt = \chi^m I_i^h - (\mu_{t,i}^h + \phi_{t,i}^h + \delta_i^h + \sum \rho_{j,i}^h)D_i^h$$

$$dD_x^a/dt = \chi^m I_i^a - (\mu_{t,i}^a + \phi_{t,i}^a + \delta_i^a + \sum \rho_{j,i}^a)D_i^a$$

Recovered from active TB, spontaneous

$$dR_{u,i}^n/dt = \phi_u^n I_i^n - (\lambda_L^n + \lambda_A^n + \alpha_u + \mu^n + \tau)R_{u,i}^n$$

$$dR_{u,i}^h/dt = \phi_u^h I_i^h - (\lambda_L^h + \lambda_A^h + \alpha_u + \mu^h + \theta)R_{u,i}^h + \tau R_{u,i}^n + \omega R_{u,i}^a$$

$$dR_{u,i}^a/dt = \phi_u^a I_i^a - (\lambda_L^h + \lambda_A^a + \alpha_u + \mu^a + \omega)R_{u,i}^a + \theta R_{u,i}^h$$

Recovered from active TB, treatment

$$dR_{t,i}^n/dt = \phi_{t,i}^n D_i^n - (\lambda_L^n + \lambda_A^n + \alpha^n + \mu^n + \tau)R_{t,i}^n$$

$$dR_{t,i}^h/dt = \phi_{t,i}^h D_i^h - (\lambda_L^h + \lambda_A^h + \alpha^h + \mu^h + \theta)R_{t,i}^h + \tau R_{t,i}^n + \omega R_{t,i}^a$$

$$dR_{t,i}^a/dt = \phi_{t,i}^a D_i^a - (\lambda_L^h + \lambda_A^a + \alpha^a + \mu^a + \omega)R_{t,i}^a + \theta R_{t,i}^h$$

Force of infection

$$\lambda_{L,i}^p = [p_L^{p,p} \beta_T (I_i^a + I_i^h) + p_L^{n,p} \beta_T I_i^n] / N$$

$$\lambda_{L,i}^n = [p_L^{p,n} \beta_T (I_i^a + I_i^h) + p_L^{n,n} \beta_T I_i^n] / N$$

$$\lambda_{A,i}^p = [p_A^{p,p} \beta_T (I_i^a + I_i^h) + p_A^{n,p} \beta_T I_i^n] / N$$

$$\lambda_{A,i}^n = [p_A^{p,n} \beta_T (I_i^a + I_i^h) + p_A^{n,n} \beta_T I_i^n] / N$$

$$\lambda_H = \beta_H (S^h + L^h + I^h + D^h + R_u^h + R_t^h) / N$$

Compartments:

S = Susceptible

L = Latent TB infection

I = Active TB, not on treatment

D = Active TB, on treatment

R = Recovered TB

Superscripts:

n = HIV negative

h = HIV positive not on ART

a = HIV positive on ART

m = MDR or non-MDR

p,n = HIV-positive to HIV-negative

p,p = HIV-positive to HIV-positive

n,n = HIV-negative to HIV-negative

n,p = HIV-negative to HIV-positive

Subscripts:

i = TB strain with particular drug resistance profile

j = TB strain with drug resistance profile other than i

u = not treated

t = treated

A = active TB

L = latent TB

H = HIV

T = TB

Rates:

Π = birth rate

λ = TB force of infection

μ = mortality rate

τ = HIV force of infection

ω = nonadherence rate for ART

θ = rate of starting ART

ν = reactivation rate for latent TB infection

α = relapse rate

δ = lost to follow up rate for TB on treatment

ρ = acquisition / amplification of drug resistance

χ = rate of initiating TB treatment

ϕ = TB cure rate

r = population growth rate

β = contact rate

Other:

N = total population

k = population cap

p = probability of acquiring latent TB infection or active TB on contact

Technical Appendix 2. Population growth

Population growth was modeled to follow a logistic growth function calibrated to population projections from the United Nations Population and Demographics.¹ Population growth follows the following differential equation:

$$dN/dt = rN \left(1 - \frac{N}{k}\right)$$

r , k were estimated using nonlinear regression via the NLS function in R. In our model, growth was modelled as additional births into the HIV negative susceptible compartment; Π was set to the overall mortality rate across all compartments. The data used for estimations of r and k were derived from UN projections, listed in Appendix Table 1 for each country.

Appendix Table 1. Country-specific population projections used for population growth calibration.

Year	South Africa	India	Philippines	Russia
1960	17,396,000	449,661,874	26,273,023	119,897,000
1961	17,949,962	458,691,457	27,164,618	121,236,000
1962	18,459,442	468,054,145	28,081,234	122,591,000
1963	18,936,138	477,729,958	29,016,770	123,960,000
1964	19,390,554	487,690,114	29,962,877	125,345,000
1965	19,832,000	497,920,270	30,913,931	126,745,000
1966	20,268,594	508,402,908	31,867,565	127,468,000
1967	20,707,258	519,162,069	32,826,602	128,196,000
1968	21,153,722	530,274,729	33,797,041	128,928,000
1969	21,612,522	541,844,848	34,787,588	129,664,000
1970	22,087,000	553,943,226	35,804,731	130,404,000
1971	22,602,373	566,605,402	36,851,055	131,155,000
1972	23,126,276	579,800,632	37,925,400	131,909,000
1973	23,655,908	593,451,889	39,026,082	132,669,000
1974	24,189,837	607,446,519	40,149,959	133,432,000
1975	24,728,000	621,703,641	41,295,129	134,200,000
1976	25,268,094	636,182,810	42,461,189	135,147,000
1977	25,805,575	650,907,559	43,650,333	136,100,000
1978	26,355,319	665,936,435	44,866,279	137,060,000
1979	26,940,793	681,358,553	46,113,992	138,027,000
1980	27,576,000	697,229,745	47,396,966	139,010,000
1981	28,254,655	713,561,406	48,715,592	139,941,000
1982	28,971,839	730,303,461	50,068,493	140,823,000
1983	29,724,004	747,374,856	51,455,037	141,668,000
1984	30,505,361	764,664,278	52,873,979	142,745,000
1985	31,307,880	782,085,127	54,323,651	143,858,000
1986	32,121,290	799,607,235	55,803,915	144,894,000
1987	32,933,081	817,232,241	57,312,794	145,908,000
1988	33,728,498	834,944,397	58,844,392	146,857,000
1989	34,490,549	852,736,160	60,391,168	147,721,000
1990	35,200,000	870,601,776	61,947,340	148,292,000
1991	35,933,108	888,513,869	63,509,940	148,624,000
1992	36,690,739	906,461,358	65,078,901	148,689,000
1993	37,473,796	924,475,633	66,654,954	148,520,000

1994	38,283,223	942,604,211	68,240,134	148,336,000
1995	39,120,000	960,874,982	69,835,713	148,375,726
1996	40,000,247	979,290,432	71,437,381	148,160,042
1997	40,926,063	997,817,250	73,042,605	147,915,307
1998	41,899,683	1,016,402,907	74,656,228	147,670,692
1999	42,923,485	1,034,976,626	76,285,225	147,214,392
2000	44,000,000	1,053,481,072	77,932,247	146,596,557
2001	44,909,738	1,071,888,190	79,604,541	145,976,083
2002	45,546,345	1,090,189,358	81,294,378	145,306,046
2003	46,127,031	1,108,369,577	82,971,734	144,648,257
2004	46,727,694	1,126,419,321	84,596,249	144,067,054
2005	47,349,013	1,144,326,293	86,141,373	143,518,523
2006	47,991,699	1,162,088,305	87,592,899	143,049,528
2007	48,656,506	1,179,685,631	88,965,508	142,805,088
2008	49,344,228	1,197,070,109	90,297,115	142,742,350
2009	50,055,701	1,214,182,182	91,641,881	142,785,342
2010	50,791,808	1,230,984,504	93,038,902	142,849,449
2011	51,553,479	1,247,446,011	94,501,233	142,960,868
2012	52,341,695	1,263,589,639	96,017,322	143,201,676
2013	53,157,490	1,279,498,874	97,571,676	143,506,911
2014	54,001,953	1,295,291,543	99,138,690	143,819,569
2015	54,490,410	1,311,050,530	100,699,400	143,456,920
2020	56,668,600	1,388,858,920	108,435,790	142,898,120
2025	58,436,200	1,461,625,230	116,151,400	141,205,240
2030	60,034,390	1,527,657,990	123,575,480	138,652,480
2035	61,551,460	1,585,349,850	130,555,570	135,673,910
2040	63,000,650	1,633,727,670	137,020,460	132,892,090
2045	64,347,870	1,673,618,770	142,920,700	130,588,310
2050	65,539,530	1,705,332,540	148,260,480	128,599,240
2055	66,492,950	1,729,354,060	152,971,280	126,654,850
2060	67,183,110	1,745,182,410	157,074,110	124,603,760
2065	67,636,310	1,752,843,330	160,517,590	122,534,290
2070	67,864,580	1,753,603,940	163,317,760	120,727,760
2075	67,878,330	1,747,945,830	165,483,850	119,439,110
2080	67,703,170	1,737,150,040	167,016,270	118,741,290
2085	67,374,090	1,722,039,440	168,032,680	118,471,060
2090	66,920,250	1,704,072,950	168,609,440	118,280,730
2095	66,355,290	1,683,339,040	168,814,270	117,937,540
2100	65,695,710	1,659,785,950	168,618,220	117,444,760

Life expectancy

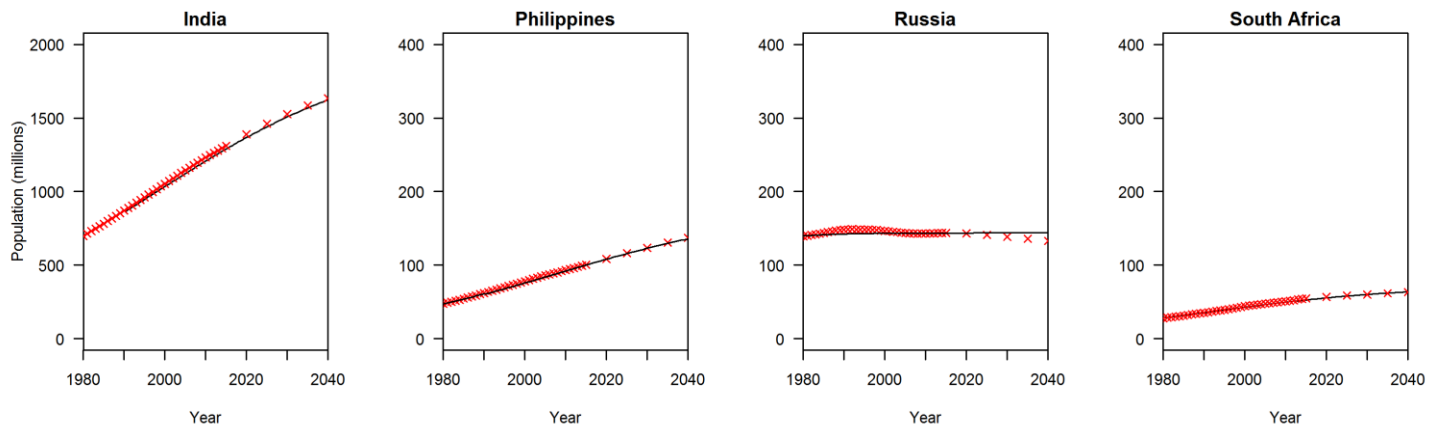
Changes in life expectancy were approximated for each country by fitting a linear regression function to time series data on life expectancy.² Life expectancy for years before 1960 was modeled to be the same as that of 1960. The general mortality rate of HIV negative persons in the Susceptible, Latent TB, or Recovered TB compartments was approximated by the inverse of life expectancy. Data used to calculate country-specific life expectancy are reproduced in Appendix Table 2.

Appendix Table 2. Country-specific annual life expectancy data used for modeled life expectancy.

Year	India	Philippines	Russia	South Africa
1960	41.17195	57.81193	66.05529	49.03629
1961	41.79049	58.12227	66.59702	49.42980
1962	42.41741	58.42885	67.02141	49.81329
1963	43.05273	58.73261	67.33990	50.19576
1964	43.69841	59.03307	67.56651	50.58176
1965	44.35351	59.33327	67.71885	50.97183
1966	45.01851	59.63624	67.81251	51.36302
1967	45.69093	59.94212	67.86015	51.74941
1968	46.36776	60.24546	67.87434	52.12600
1969	47.04700	60.54034	67.86712	52.49327
1970	47.72707	60.81324	68.13366	52.85068
1971	48.40741	61.04617	68.37659	53.19615
1972	49.08698	61.23110	68.30854	53.53363
1973	49.76029	61.36898	68.29463	53.87056
1974	50.42341	61.46534	68.32024	54.21341
1975	51.06793	61.53620	67.72390	54.57671
1976	51.68946	61.59959	67.48756	54.97446
1977	52.28463	61.67751	67.37634	55.41224
1978	52.84902	61.79000	67.39098	55.89261
1979	53.38071	61.94559	67.11439	56.41405
1980	53.87471	62.15476	67.03390	56.97307
1981	54.32854	62.42102	67.26390	57.56263
1982	54.74461	62.73241	67.80610	58.16720
1983	55.13234	63.07339	67.65268	58.76878
1984	55.49963	63.43344	67.20268	59.35244
1985	55.86090	63.79856	67.85683	59.91217
1986	56.23051	64.15373	69.38976	60.44951
1987	56.61844	64.48793	69.44000	60.95802
1988	57.03112	64.79163	69.46439	61.42380
1989	57.47305	65.05937	69.17171	61.82044
1990	57.94373	65.28807	68.90244	62.12007
1991	58.43822	65.48127	68.47439	62.29480
1992	58.94507	65.64846	66.87317	62.32517
1993	59.45293	65.79966	64.93585	62.19373
1994	59.95483	65.93885	64.46707	61.88798
1995	60.44437	66.07056	65.22122	61.37002
1996	60.91561	66.19776	66.19415	60.60546
1997	61.36956	66.32146	66.95073	59.61320
1998	61.80722	66.44217	66.78390	58.44302
1999	62.22707	66.56190	66.04366	57.15668
2000	62.63063	66.68212	65.34146	55.83688
2001	63.01985	66.80239	65.48780	54.57080

2002	63.39920	66.92166	65.08537	53.44120
2003	63.77454	67.03893	65.00756	52.52376
2004	64.14780	67.15420	65.42122	51.87376
2005	64.52388	67.26649	65.47000	51.55734
2006	64.90810	67.37476	66.64317	51.61371
2007	65.30044	67.47902	67.49756	51.99651
2008	65.69944	67.58078	67.84878	52.63602
2009	66.10263	67.68105	68.60488	53.46710
2010	66.50615	67.78332	68.85610	54.39076
2011	66.90417	67.89066	69.65854	55.29566
2012	67.28988	68.00707	70.36585	56.09832
2013	67.66041	68.13156	71.07317	56.73659

Population denominators for the country-specific median estimates are illustrated in Appendix Figure 1.



Appendix Figure 1. Modeled country-specific population projections. Solid lines represent modeled projections; red “X” denotes UN population projections.

Technical Appendix 3. Computational methods

The base R application³ was supplemented with several packages for this study. The R package deSolve⁴ was used to solve the differential equations, and epiR⁵ was used for calculation of partial rank correlation coefficients. Parallel processing using multiple cores was performed using foreach⁶ and doParallel⁷. plyr⁸ was used to append multiple dataframes into a single dataframe to compute median estimates and 95% prediction intervals.

Technical Appendix 4. History of HIV emergence and TB control programs

HIV emergence

Emergence of HIV was modeled by multiplying the susceptible HIV negative compartment by the proportion of PLHIV in a specified year; the product was added to the Susceptible, PLHIV not on ART compartment and subtracted from the Susceptible, HIV-compartment. Based on availability of HIV prevalence data, the HIV epidemic was modeled to begin in 1994 for Russia and 1990 for all other countries.

Initialization and incorporation of TB treatment and control programs

The initial state of the model assumed that 30% of the susceptible population had latent TB and all TB was fully drug susceptible. Simulations were run using a 1-year time step for 1000 years before 1960 to stabilize initial conditions representing the era before TB treatment became available, and then from 1960 to 2040 using a monthly time step to incorporate the rollout of TB control programs. TB treatment was modeled to become available starting in 1970 for non-MDRTB (i.e., TB without resistance to isoniazid and rifampicin), 1990 for MDRTB (i.e., TB with resistance to isoniazid and rifampicin) and pre-XDRTB (i.e., MDRTB with additional resistance to fluoroquinolones or second line medications), and 2000 for XDRTB (i.e., MDRTB with additional resistance to both fluoroquinolones and second line medications). DOTS was modeled to become available in 1995 in India,⁹ 1996 in South Africa,¹⁰ 1997 in the Philippines,¹¹ and 1994 in Russia.¹² GLC-approved treatment for MDRTB was modeled to expand beyond pilot phases in 2003 in the Philippines and 2005 in Russia.¹³ Because GLC-approved PMDT in India was limited to a pilot program in a limited geographical area, the model assumed that MDRTB treatment in India was only in non-GLC conditions. For Russia, the collapse of the United Soviet Socialist Republics was assumed to cause an immediate reduction in treatment initiation rates for non-MDRTB and MDRTB in 1991 followed by a period of recovery of this rate over 10 years. Appendix Table 3 summarizes these data for each modeled country.

Probability of initiating correct treatment for incident TB

There are insufficient empiric data that describe the length of time taken for a new incident TB case to initiate treatment based on the underlying resistance. In the absence of these empiric data, we used recently reported WHO case detection rates to approximate the probability of initiating correct treatment for incident TB relative as a proportion of the case detection rate (CDR).¹⁴ The case detection rate represents the proportion of smear positive TB cases that are notified in a year. Since the CDR does not account for TB notifications that might be lost to follow up after diagnosis before treatment, does not account for TB that might be detected in facilities that might not report to national TB programs, and does not account for smear-negative or extrapulmonary TB, we used a wide prior distribution of 0% to 100% of the reported CDR to estimate the proportion of incident TB cases that initiate treatment in a year. Because MDRTB cases encounter additional challenges in initiating treatment, including low availability of diagnostic centers and treatment facilities relative to non-MDRTB, we modeled the proportion of incident MDRTB cases that initiate treatment in a year to equal a proportion of incident non-MDRTB that initiated treatment in a year. These wide prior distributions for initiating correct treatment for non-MDRTB and MDRTB were calibrated to reported proportions from drug resistance surveys. Appendix Table 3 lists the case detection rates used for estimating treatment initiation rates; Appendix Table 6 lists the prior and posterior distributions for the probabilities of initiating correct treatment of TB relative to country case detection rates.

Appendix Table 3. Parameters used to model features of TB treatment and control programs, emergence of the HIV epidemic, and initiation of ART by country.

Country	Year when non-MDRTB treatment became available	Year when MDRTB and pre-XDRTB treatment became available	Year when XDRTB treatment became available	Annual case detection rate	Year when HIV epidemic began	Year when ART became available	Year when DOTS became available	Year when GLC-supported treatment became available
India	1970	1990	2000	0.6	1990	2003	1995	-
Philippines	1970	1990	2000	0.8	1990	2004	1995	2002
Russia	1970	1990	2000	0.8	1994	2004	1996	2005
South Africa	1970	1990	2000	0.75	1990	2003	1996	-

Technical Appendix 5. TB and drug resistance observed data for calibration.

The observed data used for calculating a joint likelihood function and subsequent calibration of model projections are presented in Appendix Tables 4 and 5.

If point estimates and confidence intervals were available, then a normal likelihood was generated for the percentage centered at the point estimate with variance approximated from the confidence intervals. For the percentage of MDR among incident TB and the percentage of XDR among incident MDRTB, if point estimates and confidence intervals were not available in drug resistance surveys, then reported numerators and denominators were used to generate a likelihood function based on beta distribution for the corresponding percentage assuming a design effect of two for the survey sample. Beta densities provide a flexible means of modeling unimodal distributions over a finite interval. A design effect of two is used as conventional approach to estimates point estimates and confidence intervals in the absence of information regarding survey design.

Modeled outputs should be calibrated to independent observations. The WHO estimates for TB incidence and HIV-positive TB incidence might not independent empirical observations. To ensure that our calibration process reflects the underlying stability of the model and not merely to annual consecutive WHO estimates, we calibrated the modeled outputs only to WHO estimates from year 2000 and year 2015 with the assumption that these estimates are independent. We assumed that estimates from serial drug resistance surveys are sufficiently independent.

Appendix Table 4. Country values for TB incidence and Incidence of TB cases who are HIV positive*.

Country	Year	TB incidence per 100 000			Incidence of TB cases who are HIV-positive per 100 000		
		Lower bound	Point estimate	High bound	Lower bound	Point estimate	High bound
India	2000	149	289	473	10	21	35
India	2015	112	217	355	4.4	8.6	14
Philippines	2000	238	368	526	0.26	0.43	0.64
Philippines	2015	277	322	370	3.3	4.3	5.4
Russia	2000	119	128	137	1.4	1.6	1.8
Russia	2015	69	80	92	6.5	7.9	9.4
South Africa	2000	379	585	836	221	349	506
South Africa	2015	539	834	1190	303	473	680

* Values were obtained from the WHO TB country profiles database.¹⁴

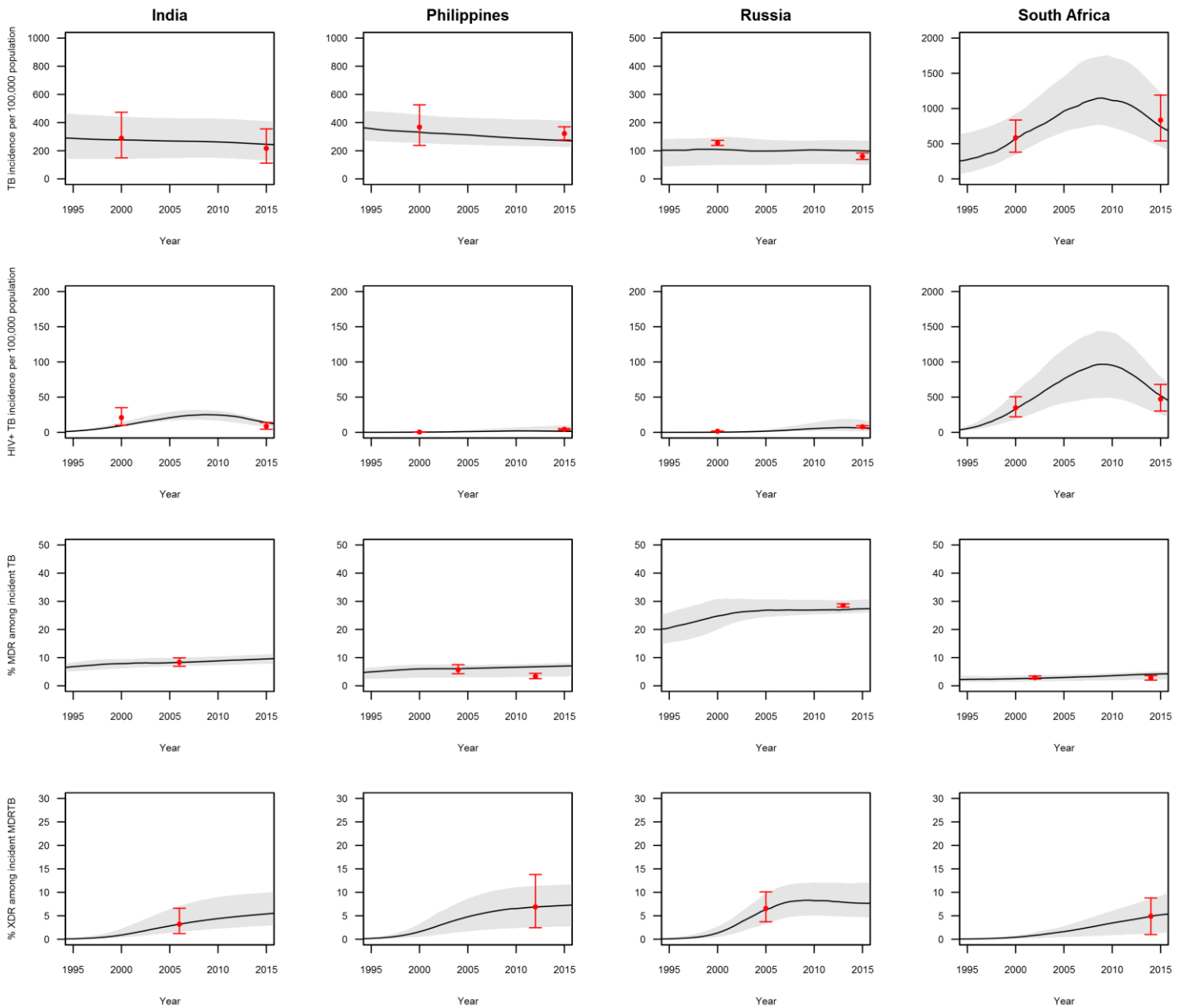
Appendix Table 5. Country values for % MDRTB among incident TB and % XDRTB among incident MDRTB.

% MDRTB among incident TB					
Country	Year	Lower bound	Point estimate	High bound	Source
India*	2006	0.069	0.084	0.099	¹⁵
Philippines	2004	0.043	0.057	0.075	¹⁶
Philippines	2012	0.0253	0.0335	0.0441	¹⁶
Russia*	2013	0.279	0.285	0.291	¹⁷
South Africa	2002	0.020	0.028	0.036	¹⁸
South Africa	2014	0.024	0.029	0.035	¹⁸

% XDRTB among incident MDRTB					
Country	Year	Lower bound	Point estimate	High bound	Source
India	2006	0.012	0.032	0.066	¹⁹
Philippines	2012	0.0246	0.0689	0.138	¹⁶
Russia*	2008	0.0193	0.0547	0.1069	¹⁹
South Africa	2014	0.010	0.049	0.088	¹⁸

*Imputed from subnational data.

The fitness of the final projections compared to the observed data are summarized in Appendix Figure 2.



Appendix Figure 2. Country-specific calibrated outcomes based on sampling and weighted resampling. The solid line represents the median projection, the gray shaded region represents 95% prediction intervals, and “X” denotes observed data. MDR = Multidrug-resistant; XDR = Extensively drug-resistant; TB = tuberculosis; HIV+ = HIV positive. Red dots and red lines respectively represent point estimates and bounds of observed data to which the model was calibrated.

Technical Appendix 6. Prior and posterior distributions.

Prior and country-specific posterior distributions are summarized in Appendix Table 6.

Appendix Table 6. Prior and country-specific posterior distributions for model variables.

Variable	Prior distribution			Posterior distributions												Source
				India			Philippines			Russia			South Africa			
	2.5%	50.0%	97.5%	2.5%	50.0%	97.5%	2.5%	50.0%	97.5%	2.5%	50.0%	97.5%	2.5%	50.0%	97.5%	
Contact rate for persons with TB*	2.374	3.650	4.932	2.417	3.379	4.791	2.439	3.514	4.804	2.454	3.700	4.939	2.342	3.105	4.725	20
Probability of initiating appropriate treatment for MDRTB [†] , Pre-XDRTB [‡] , and XDRTB [†] relative to case detection rate	0.025	0.448	0.900	0.169	0.379	0.808	0.124	0.231	0.456	0.474	0.752	0.953	0.050	0.102	0.248	Calibrated
Probability of initiating appropriate treatment for DS ^{**} TB and INHr/RR ^{††} TB relative to case detection rate	0.028	0.500	0.975	0.173	0.416	0.869	0.139	0.251	0.509	0.564	0.845	0.998	0.058	0.113	0.266	Calibrated
Effective contact rate for PLHIV ^{§§}	0.528	1.000	1.475	0.819	0.950	1.054	0.521	0.794	1.065	0.771	1.045	1.296	0.642	0.878	1.225	Calibrated
Probability of acquiring active TB from index case, PLHIV contact	0.098	0.265	0.432	0.107	0.258	0.429	0.098	0.256	0.434	0.103	0.255	0.434	0.095	0.207	0.423	20
Probability of acquiring LTBI ^{¶¶} from index case, PLHIV contact	0.413	0.533	0.654	0.415	0.529	0.649	0.411	0.536	0.649	0.412	0.546	0.651	0.415	0.535	0.655	20
Probability of acquiring TB from index case, HIV-negative contact	0.023	0.033	0.043	0.023	0.031	0.043	0.023	0.032	0.043	0.023	0.031	0.042	0.023	0.032	0.043	20
Probability of acquiring LTBI from index case, HIV-negative contact	0.473	0.514	0.556	0.476	0.517	0.557	0.473	0.516	0.557	0.473	0.509	0.557	0.473	0.517	0.557	20
Probability of reactivation of LTBI in 5 years, HIV-negative individual	0.013	0.029	0.046	0.015	0.030	0.044	0.016	0.031	0.046	0.012	0.022	0.040	0.013	0.029	0.045	21
Probability of reactivation of LTBI in 1 year, PLHIV not on ART ^{***}	0.042	0.093	0.145	0.049	0.110	0.145	0.042	0.091	0.144	0.042	0.104	0.145	0.042	0.090	0.144	22
Probability of death without TB treatment in 10 years, HIV-negative individual	0.634	0.700	0.766	0.636	0.695	0.766	0.634	0.704	0.767	0.632	0.697	0.764	0.635	0.700	0.765	23
Probability of death without TB treatment in 1 year, PLHIV not on ART	0.453	0.500	0.547	0.458	0.501	0.545	0.452	0.501	0.548	0.453	0.501	0.547	0.452	0.505	0.547	23
Probability of relapse among persons with spontaneously recovered TB in 1.5 years	0.091	0.100	0.109	0.091	0.102	0.109	0.091	0.100	0.109	0.090	0.099	0.109	0.091	0.100	0.109	24
Probability of treatment success for DS TB, HIV-negative, DOTS ^{†††}	0.790	0.809	0.829	0.790	0.808	0.829	0.790	0.810	0.829	0.790	0.810	0.829	0.790	0.810	0.829	25
Probability of treatment success for INHr/RR TB, HIV-negative, DOTS	0.629	0.687	0.745	0.634	0.687	0.744	0.628	0.691	0.745	0.629	0.687	0.741	0.628	0.687	0.747	25
Probability of treatment failure for DS TB, HIV-negative, DOTS	0.024	0.033	0.042	0.024	0.033	0.040	0.024	0.031	0.042	0.024	0.034	0.042	0.024	0.033	0.041	25
Probability of treatment failure for INHr/RR TB, HIV-negative, DOTS	0.079	0.120	0.160	0.079	0.110	0.160	0.079	0.108	0.157	0.090	0.134	0.161	0.079	0.114	0.158	25
Probability of ADR ^{§§§} from DS TB to MDRTB among treatment failures	0.228	0.356	0.484	0.227	0.367	0.487	0.225	0.312	0.478	0.237	0.393	0.484	0.225	0.337	0.483	25

Probability of ADR from DS TB to INHr/RR TB among treatment failures	0.153	0.270	0.388	0.148	0.261	0.381	0.152	0.243	0.385	0.157	0.285	0.389	0.153	0.262	0.385	25
Probability of ADR from INHr/RR TB to MDRTB among treatment failures	0.549	0.706	0.865	0.547	0.685	0.863	0.548	0.705	0.862	0.565	0.755	0.863	0.548	0.683	0.862	25
Probability of LTFU ^{***} during treatment for DS TB and INHr/RR TB, HIV-negative	0.036	0.067	0.098	0.038	0.071	0.098	0.036	0.067	0.097	0.040	0.072	0.096	0.037	0.067	0.098	25
Probability of death during treatment for DS TB and INHr/RR TB, HIV-negative	0.045	0.078	0.112	0.049	0.078	0.112	0.047	0.079	0.111	0.045	0.080	0.111	0.045	0.079	0.113	25
Probability of treatment success for DS TB and INHr/RR TB, PLHIV on ART, DOTS	0.663	0.689	0.717	0.663	0.688	0.713	0.662	0.690	0.717	0.662	0.692	0.716	0.662	0.690	0.717	26
Probability of treatment failure for DS TB and INHr/RR TB, PLHIV on ART, DOTS	0.019	0.032	0.045	0.019	0.033	0.044	0.019	0.033	0.045	0.018	0.031	0.045	0.019	0.031	0.045	27
Probability of LTFU during treatment for DS TB and INHr/RR TB, PLHIV	0.109	0.129	0.148	0.109	0.128	0.148	0.110	0.129	0.148	0.109	0.128	0.148	0.109	0.128	0.148	26
Probability of death during treatment for DS TB and INHr/RR TB, PLHIV on ART	0.087	0.122	0.157	0.092	0.122	0.158	0.087	0.123	0.158	0.086	0.115	0.155	0.088	0.122	0.158	27
Probability of treatment success for MDRTB, non-GLC	0.451	0.508	0.565	0.455	0.507	0.563	0.450	0.511	0.565	0.454	0.502	0.560	0.450	0.512	0.566	PETTS
Probability of death during treatment for MDRTB, non-GLC	0.081	0.117	0.154	0.083	0.117	0.153	0.082	0.117	0.154	0.081	0.121	0.152	0.082	0.120	0.153	PETTS
Probability of ADR to pre-XDRTB during treatment for MDRTB, non-GLC	0.071	0.106	0.141	0.071	0.105	0.141	0.072	0.106	0.141	0.072	0.107	0.140	0.073	0.105	0.141	PETTS
Probability of ADR to XDRTB during treatment for MDRTB, non-GLC	0.022	0.045	0.068	0.022	0.046	0.067	0.024	0.053	0.068	0.022	0.047	0.068	0.024	0.047	0.068	PETTS
Probability of treatment success for pre-XDRTB, non-GLC	0.133	0.200	0.267	0.130	0.193	0.263	0.130	0.198	0.269	0.136	0.209	0.267	0.130	0.195	0.267	PETTS
Probability of death during treatment for pre-XDRTB, non-GLC	0.118	0.183	0.248	0.119	0.177	0.248	0.118	0.191	0.249	0.117	0.177	0.246	0.117	0.180	0.246	PETTS
Probability of ADR to XDRTB during treatment for pre-XDRTB, non-GLC	0.285	0.366	0.448	0.284	0.361	0.442	0.284	0.368	0.449	0.287	0.368	0.451	0.288	0.369	0.450	PETTS
Probability of treatment success for XDRTB, non-GLC	0.047	0.102	0.158	0.048	0.096	0.158	0.047	0.099	0.158	0.046	0.093	0.157	0.049	0.102	0.158	PETTS
Probability of death during treatment for XDRTB, non-GLC	0.421	0.515	0.610	0.429	0.503	0.608	0.421	0.519	0.612	0.423	0.507	0.613	0.424	0.519	0.610	PETTS
Probability of LTFU during treatment for MDRTB, pre-XDRTB, or XDRTB, non-GLC	0.120	0.150	0.180	0.121	0.149	0.181	0.119	0.150	0.180	0.121	0.151	0.177	0.121	0.153	0.181	PETTS
Probability of treatment success for MDRTB, GLC****	0.505	0.557	0.610	-	-	-	0.507	0.556	0.609	0.505	0.555	0.608	-	-	-	PETTS
Probability of death during treatment for MDRTB, GLC	0.068	0.099	0.129	-	-	-	0.068	0.102	0.130	0.066	0.096	0.129	-	-	-	PETTS
Probability of ADR to pre-XDRTB during treatment for MDRTB, GLC	0.044	0.070	0.096	-	-	-	0.045	0.071	0.097	0.044	0.069	0.097	-	-	-	PETTS
Probability of ADR to XDRTB during treatment for MDRTB, GLC	0.006	0.019	0.032	-	-	-	0.006	0.020	0.032	0.006	0.021	0.032	-	-	-	PETTS
Probability of treatment success for pre-XDRTB, GLC	0.426	0.508	0.589	-	-	-	0.429	0.504	0.592	0.428	0.509	0.584	-	-	-	PETTS

Probability of death during treatment for pre-XDRTB, GLC	0.058	0.107	0.157	-	-	-	0.057	0.101	0.156	0.059	0.103	0.156	-	-	-	PETTS
Probability of ADR to XDRTB during treatment for pre-XDRTB, GLC	0.064	0.115	0.166	-	-	-	0.065	0.117	0.166	0.070	0.125	0.167	-	-	-	PETTS
Probability of treatment success for XDRTB, GLC	0.198	0.325	0.454	-	-	-	0.197	0.321	0.452	0.205	0.311	0.450	-	-	-	PETTS
Probability of death during treatment for XDRTB, GLC	0.124	0.238	0.353	-	-	-	0.124	0.232	0.350	0.122	0.225	0.349	-	-	-	PETTS
Probability of LTFU during treatment for MDRTB, pre-XDRTB, or XDRTB, GLC	0.167	0.201	0.235	-	-	-	0.168	0.200	0.235	0.174	0.201	0.236	-	-	-	PETTS
Probability of relapse for successfully treated TB, HIV-	0.011	0.016	0.021	0.011	0.016	0.021	0.011	0.016	0.021	0.011	0.016	0.021	0.011	0.016	0.021	28
Probability of relapse for successfully treated TB, PLHIV not on ART	0.031	0.041	0.051	0.030	0.042	0.050	0.031	0.041	0.051	0.031	0.042	0.052	0.031	0.041	0.051	28
Probability of relapse for successfully treated TB, PLHIV on ART	0.018	0.036	0.053	0.018	0.033	0.053	0.018	0.035	0.053	0.018	0.036	0.052	0.018	0.037	0.053	28
Probability of death, PLHIV not on ART	0.085	0.095	0.104	0.085	0.095	0.104	0.085	0.093	0.104	0.085	0.095	0.105	0.085	0.095	0.105	29
Probability of death, PLHIV on ART	0.030	0.034	0.037	0.030	0.033	0.037	0.030	0.033	0.037	0.030	0.034	0.037	0.030	0.033	0.037	29,30
Risk of stopping ART, PLHIV on ART	0.026	0.029	0.032	0.026	0.029	0.032	0.026	0.029	0.032	0.026	0.029	0.032	0.026	0.029	0.032	29,30
Relative risk of failure during TB treatment, INHr/RR TB to DS TB	6.977	9.500	12.036	7.126	9.376	11.869	6.920	9.579	12.067	7.047	9.204	11.989	7.093	9.594	12.090	31
Hazard ratio of TB incidence, PLHIV not on ART to PLHIV on ART	2.517	2.800	3.085	2.531	2.836	3.094	2.517	2.801	3.087	2.517	2.753	3.066	2.518	2.824	3.077	32
Hazard ratio of TB treatment success, PLHIV on ART to PLHIV not on ART	1.760	4.500	7.255	1.752	4.468	7.343	1.809	4.931	7.283	1.670	4.422	7.251	1.877	4.688	7.319	33
Hazard ratio of death during TB treatment, PLHIV on ART to PLHIV not on ART	0.308	0.450	0.592	0.307	0.430	0.581	0.306	0.453	0.592	0.307	0.443	0.589	0.308	0.450	0.595	33
Hazard ratio of ADR during treatment, non-DOTS to DOTS	3.931	8.080	12.251	4.005	6.781	12.073	3.762	5.190	11.467	7.383	10.796	12.454	3.788	6.511	11.481	34
Proportion of DS TB and INHr/RR TB treated in DOTS programs	0.028	0.500	0.975	0.031	0.560	0.990	0.056	0.672	0.981	0.029	0.380	0.944	0.034	0.601	0.976	Calibrated
Proportion of MDRTB, Pre-XDRTB, and XDRTB treated in GLC programs	0.028	0.500	0.975	-	-	-	0.012	0.395	0.962	0.015	0.463	0.952	-	-	-	Calibrated
Proportion of PLHIV not on ART who initiate ART	0.306	0.400	0.495	0.312	0.420	0.496	0.304	0.392	0.495	0.307	0.418	0.494	0.305	0.395	0.492	Calibrated

*TB = Tuberculosis. †MDRTB = Multidrug-resistant TB (TB resistant to isoniazid and rifampicin). ‡Pre-XDRTB = TB resistant to isoniazid, rifampicin, and either fluoroquinolones or second line injectable drugs. ††XDRTB = Extensively drug-resistant TB (TB resistant to isoniazid, rifampicin, fluoroquinolones, and second line injectable drugs). **DS = Susceptible to isoniazid and rifampicin. †††INHr/RR = Resistant to either isoniazid or rifampicin. ‡‡‡PLHIV = People living with HIV. ††††LTBI = Latent tuberculosis infection. †††††ART = Antiretroviral therapy. ††††††DOTS = Directly Observed Therapy, Short-course. ‡‡‡‡‡ADR = acquired drug resistance. †††††LTFU = Lost to follow up. ††††††GLC = Green Light Committee.

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