SUPPLEMENTAL APPENDIX

Supplemental Table 1
Characteristics of institutional amplifiers in tuberculosis epidemics

<table>
<thead>
<tr>
<th>Region</th>
<th>Type of amplifier</th>
<th>Method of amplifier exposure</th>
<th>Typical durations of amplifier exposure</th>
<th>Method of amplification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Europe and Former Soviet Union</td>
<td>Prison wards</td>
<td>High incarceration rates⁹</td>
<td>5.2 years on average¹⁰</td>
<td>Release from prison¹¹</td>
</tr>
<tr>
<td>Southern Africa</td>
<td>Mines</td>
<td>Mines are the region’s largest employer, employing migrant workers¹²</td>
<td>Cyclic, 9 months/year on average¹³</td>
<td>Migrant labor from mines back to rural homelands¹³</td>
</tr>
<tr>
<td>South Asia, Latin America, and Southern Africa</td>
<td>Communal hospital wards</td>
<td>Admission to group wards (multi-person rooms) in crowded hospitals for therapy initiation¹⁴-¹⁶</td>
<td>Among tuberculosis patients, days to weeks for therapy initiation before outpatient continuation therapy¹⁷</td>
<td>Discharge to community¹⁴</td>
</tr>
</tbody>
</table>

* Numbers in parentheses are references.

MODEL EQUATIONS

We subdivided the population into civilian and amplifier populations, where the former was further organized into persons at risk (subscript i) and persons not at risk for amplification (subscript j). In the following equations, superscript a refers to persons in the amplifier, and subscripts s and r refer to non–multidrug-resistant tuberculosis (non-MDR TB) and MDR TB strains, respectively. The parameter definitions are provided in Supplemental Appendix, Table 1, and the state variables are susceptible persons (S), latently-infected persons (L), persons with active TB (T), those persons detected and in therapy (D), and those who have failed therapy (F). In simulations involving human immunodeficiency virus (HIV), the weighted average parameter values among HIV-negative and HIV-positive persons (Supplemental Appendix, Table 2) were used as the parameter values in the equations, where the HIV prevalence was used as the weight.

\[
\frac{dS_i}{dt} = \varepsilon S_i - \left( \lambda_s^* + \lambda_r^* + \delta + \mu_i \right) S_i
\]

\[
\frac{dS_j}{dt} = \gamma b + \delta S_j - \left( \lambda_s + \lambda_r^* + \delta + \mu_s \right) S_j
\]

\[
\frac{dS_j}{dt} = (1 - \gamma) b - \left( \lambda_s^* + \lambda_r + \delta + \mu_j \right) S_j
\]

\[
\frac{dS_a}{dt} = (1 - p_s) \lambda_s^* \left( S_s + x_s (L_s + L_s^*) \right) + n T_s + r k_s D_s + \varepsilon L_s
\]

\[
- \left( \lambda_s \lambda_r^* + v_s + \delta + \mu_j \right) L_a
\]

\[
\frac{dT_a}{dt} = p_s \lambda_s^* \left( S_s + x_s (L_s + L_s^*) \right) + \varepsilon L_s + \delta T_a
\]

\[
- \left( d^s + n_s + \delta + \mu_s + \mu_j \right) T_a
\]

\[
\frac{dT_a}{dt} = p_s \lambda_s \left( S_s + x_s (L_s + L_s^*) \right) + \varepsilon L_s + \delta T_a
\]

\[
- \left( d^s + n_s + \varepsilon + \mu_s + \mu_j \right) T_a
\]

\[
\frac{dT_a}{dt} = p_s \lambda_s \left( S_s + x_s (L_s + L_s^*) \right) + \varepsilon L_s + \delta T_a
\]

\[
- \left( d^s + n_s + \varepsilon + \mu_s + \mu_j \right) T_a
\]

\[
\frac{dL_s}{dt} = \left( 1 - p_r \right) \lambda_r \left( S_r + x_r (L_r + L_r^*) \right) + n T_r + r k_r D_r + \delta T_r
\]

\[
- \left( \lambda_s + \lambda_r \right) + v_r + \mu_j \right) L_r
\]

\[
\frac{dL_r}{dt} = \left( 1 - p_r \right) \lambda_r \left( S_r + x_r (L_r + L_r^*) \right) + n T_r + r k_r D_r + \delta T_r
\]

\[
- \left( \lambda_r \lambda_r \right) + v_r + \mu_j \right) L_r
\]

\[
\frac{dL_r}{dt} = \left( 1 - p_r \right) \lambda_r \left( S_r + x_r (L_r + L_r^*) \right) + n T_r + r k_r D_r + \delta T_r
\]

\[
- \left( \lambda_r \lambda_r \right) + v_r + \varepsilon + \mu_j \right) L_r
\]

\[
\frac{dL_r}{dt} = \left( 1 - p_r \right) \lambda_r \left( S_r + x_r (L_r + L_r^*) \right) + n T_r + r k_r D_r + \delta T_r
\]

\[
- \left( \lambda_r \lambda_r \right) + v_r + \varepsilon + \mu_j \right) L_r
\]

\[
\frac{dL_r}{dt} = \left( 1 - p_r \right) \lambda_r \left( S_r + x_r (L_r + L_r^*) \right) + n T_r + r k_r D_r + \delta T_r
\]

\[
- \left( \lambda_r \lambda_r \right) + v_r + \varepsilon + \mu_j \right) L_r
\]

\[
\frac{dF_i}{dt} = (1 - \alpha) \left( r (1 - k_a) D_a + (1 - \theta) \varepsilon D_a \right) + \varepsilon F_i
\]

\[
- \left( d_s + \delta + \mu_s + \mu_j \right) F_i
Natural history and TB control parameters used for simulation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Definition</th>
<th>HIV-negative value (range)</th>
<th>HIV-positive value (range)</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$</td>
<td>Per capita transmission rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Proportion of population at risk for amplifier entry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\epsilon$</td>
<td>Rate of entry to amplifier among those at risk for entry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\delta$</td>
<td>Rate of exit from amplifier</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\beta_{\text{per capita}}$</td>
<td>Proportion of newly infected persons experiencing primary progressive disease</td>
<td>0.14 (0.08–0.25)</td>
<td>0.67 (0.36–0.8)</td>
<td>(2, 19)</td>
</tr>
<tr>
<td>$k$</td>
<td>Proportion of treated cases cured</td>
<td>0.7 (0.6–0.85); 0.6 (0.5–0.95) lower for MDR TB</td>
<td>(6)</td>
<td></td>
</tr>
<tr>
<td>$\text{rate of natural self-cure}^1$</td>
<td></td>
<td>0.2 (0.15–0.25)</td>
<td>0.1 (0–0.15)</td>
<td>(2, 19)</td>
</tr>
<tr>
<td>$r$</td>
<td>1/culture conversion time</td>
<td>34 (8–181) days$^1$</td>
<td>1.13 × 10$^{-4}$ (10$^{-4}$–3 × 10$^{-4}$)</td>
<td>(20, 21)</td>
</tr>
<tr>
<td>$v$</td>
<td>Reactivation rate from latency</td>
<td>0.17 (0.04–0.2)</td>
<td></td>
<td>(2)</td>
</tr>
<tr>
<td>$x$</td>
<td>Proportion of latently-infected persons who are susceptible to primary progressive disease upon re-infection</td>
<td>0.35 (0.1–0.6)</td>
<td>0.75 (0.5–1.0)</td>
<td>(2)</td>
</tr>
<tr>
<td>$\mu_t$</td>
<td>Mortality rate caused by TB (multiplied by 0.5 (range 0–1) for treatment failures, $\mu_{\text{t}}$)</td>
<td>0.3 (0.2–0.4)</td>
<td>1.0 (0.75–1.0)</td>
<td>(1, 2)</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>Proportion of patients failing therapy who acquire resistance</td>
<td>0.07 (0.008–0.18)</td>
<td></td>
<td>(6)</td>
</tr>
<tr>
<td>$\phi$</td>
<td>Relative transmission fitness of MDR TB strains</td>
<td>0.5 (0.16–1.2)</td>
<td></td>
<td>(6, 7)</td>
</tr>
<tr>
<td>$\kappa$</td>
<td>Ratio of pulmonary to room ventilation rate</td>
<td>0.48 (0.4–0.6) m³/hour/520 (330–1,209) m³/hour</td>
<td>(5, 16)</td>
<td></td>
</tr>
</tbody>
</table>

The forces of infection in either environment, for both non-MDR and MDR TB strains, are as follows:

$$dF^n_s/\,dt = \alpha \left( r + \left( 1 - k_s \right)D^n_s + (1 - \theta)D^n_a \right) + r(1-k_s)D^n_s + (1-\theta)F^n_s$$

$$dF^a_s/\,dt = (1 - \alpha) \left( r + \left( 1 - k_s \right)D^n_s + (1 - \omega)D^a_s \right) + \delta F^a_s$$

$$dF^n_a/\,dt = (1 - \alpha) \left( r(1 - k_s)D^n_s + (1 - \omega)\delta D^n_s + \delta F^n_s \right) - (d + \epsilon + \mu_s + \mu_{\text{r}})F^n_a$$

$$dF^a_a/\,dt = \alpha \left( r(1 - k_s)D^n_s + (1 - \omega)\delta D^n_s + \delta F^n_s \right) - (d + \epsilon + \mu_s + \mu_{\text{r}})F^a_a$$

Sensitivity analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Definition</th>
<th>% Change in TB prevalence with 1% change in HIV-negative value</th>
<th>% Change in TB prevalence with 1% change in HIV-positive value</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$</td>
<td>Per capita transmission rate</td>
<td>1.7719</td>
<td>0.0084</td>
<td></td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Proportion of population at risk for amplifier entry</td>
<td>1.8053</td>
<td>0.0457</td>
<td></td>
</tr>
<tr>
<td>$\epsilon$</td>
<td>Rate of entry to amplifier among those at risk for entry</td>
<td>0.0260</td>
<td>0.0017</td>
<td></td>
</tr>
<tr>
<td>$\delta$</td>
<td>Rate of exit from amplifier</td>
<td>-1.0432</td>
<td>-0.0106</td>
<td></td>
</tr>
<tr>
<td>$\beta_{\text{per capita}}$</td>
<td>Proportion of newly infected persons experiencing primary progressive disease</td>
<td>1.8233</td>
<td>0.0876</td>
<td></td>
</tr>
<tr>
<td>$k$</td>
<td>Proportion of treated cases cured</td>
<td>-0.5903</td>
<td>-0.0948</td>
<td></td>
</tr>
<tr>
<td>$\text{rate of natural self-cure}^1$</td>
<td></td>
<td>-0.0532</td>
<td>0.8302</td>
<td></td>
</tr>
<tr>
<td>$r$</td>
<td>1/culture conversion time</td>
<td>-0.5903</td>
<td>-0.0948</td>
<td></td>
</tr>
<tr>
<td>$v$</td>
<td>Reactivation rate from latency</td>
<td>0.0532</td>
<td>0.8302</td>
<td></td>
</tr>
<tr>
<td>$x$</td>
<td>Proportion of latently-infected persons who are susceptible to primary progressive disease upon re-infection</td>
<td>0.6105</td>
<td>0.0131</td>
<td></td>
</tr>
<tr>
<td>$\mu_t$</td>
<td>Mortality rate caused by TB (multiplied by 0.5 (range 0–1) for treatment failures, $\mu_{\text{t}}$)</td>
<td>-0.9401</td>
<td>-0.0318</td>
<td></td>
</tr>
<tr>
<td>$\alpha$</td>
<td>Proportion of patients failing therapy who acquire resistance</td>
<td>-5.9984 × 10$^{-4}$</td>
<td>-0.0030</td>
<td></td>
</tr>
<tr>
<td>$\phi$</td>
<td>Relative transmission fitness of MDR TB strains</td>
<td>0.0030</td>
<td>0.0420</td>
<td></td>
</tr>
<tr>
<td>$\kappa$</td>
<td>Ratio of pulmonary to room ventilation rate</td>
<td>-5.9984 × 10$^{-4}$</td>
<td>-0.0030</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2**

*TB = tuberculosis; HIV = human immunodeficiency virus; MDR = multidrug resistant.

**Table 3**

*Percentage change in overall population TB prevalence upon a 1% increase in the listed parameter while all other parameters are held at their modal values from Table 2 and the amplifier parameters listed in the main manuscript for Russian prisons, along with 1% general population HIV prevalence. The figure excludes those parameters for which a univariate sensitivity analysis is already presented in the main manuscript figures, i.e., proportion of population at risk of amplifier entry. TB = tuberculosis; HIV = human immunodeficiency virus; MDR = multidrug resistant.
REFERENCES