SUPPLEMENTAL APPENDIX

SUPPLEMENTAL TABLE 1
Characteristics of institutional amplifiers in tuberculosis epidemics*

Region	Type of amplifier	Method of amplifier exposure	Typical durations of amplifier exposure	Method of amplification
Eastern Europe and Former Soviet Union	Prison wards	High incarceration rates[9]	5.2 years on average[10]	Release from prison[11]
Southern Africa	Mines	Mines are the region's largest employer, employing migrant workers[12]	Cyclic, 9 months/year on average[13]	Migrant labor from mines back to rural homelands[13]
South Asia, Latin America, and Southern Africa	Communal hospital wards	Admission to group wards (multi-person rooms) in crowded hospitals for therapy initiation[14–16]	Among tuberculosis patients, days to weeks for therapy initiation before outpatient continuation therapy[17]	Discharge to community[14]

*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.

$$dS_i^a / dt = \varepsilon S_i - \left(\lambda_s^a + \lambda_r^a + \delta + \mu_i\right) S_i^a$$

$$dS_i / dt = \gamma b + \delta S_i^a - \left(\lambda_s + \lambda_r + \varepsilon + \mu_i^a\right) S_i$$

$$dS_j / dt = (1-\gamma) b - \left(\lambda_s + \lambda_r + \mu_j\right) S_j$$

$$dL_{is}^a / dt = (1-p_i)\lambda_s^a \left(S_i^a + x_i\left(L_{is}^a + L_{ir}^a\right)\right) + n_i T_{is}^a + rk_s^a D_{is}^a + \varepsilon L_{is} - \left(x_i\left(\lambda_s^a + \lambda_r^a\right) + v_i + \delta + \mu_i\right) L_{is}^a$$

$$dL_{ir}^a / dt = (1-p_i)\lambda_r^a \left(S_i^a + x_i\left(L_{is}^a + L_{ir}^a\right)\right) + n_i T_{ir}^a + rk_{ra} D_{ir}^a + \varepsilon L_{ir} - \left(x_i\left(\lambda_s^a + \lambda_r^a\right) + v_i + \delta + \mu_i\right) L_{ir}^a$$

$$dL_{is} / dt = (1-p_i)\lambda_s \left(S_i + x_i\left(L_{is} + L_{ir}\right)\right) + n_i T_{is} + rk_s D_{is} + \delta L_{is}^a - \left(x_i\left(\lambda_s + \lambda_r\right) + v_i + \varepsilon + \mu_i\right) L_{is}$$

$$dL_{ir} / dt = (1-p_i)\lambda_r \left(S_i + x_i\left(L_{is} + L_{ir}\right)\right) + n_i T_{ir} + rk_r D_{ir} + \delta L_{ir}^a - \left(x_i\left(\lambda_s + \lambda_r\right) + v_i + \varepsilon + \mu_i\right) L_{ir}$$

$$dL_{js} / dt = (1-p_j)\lambda_s \left(S_j + x_j\left(L_{js} + L_{jr}\right)\right) + n_j T_{js} + rk_s D_{js} - \left(x_j\left(\lambda_s + \lambda_r\right) + v_j + \lambda_j\right) L_{js}$$

$$dL_{ir} / dt = (1-p_j)\lambda_r \left(S_j + x_j\left(L_{js} + L_{jr}\right)\right) + n_j T_{jr} + rk_r D_{jr} - \left(x_j\left(\lambda_s + \lambda_r\right) + v_j + \lambda_j\right) L_{jr}$$

$$dT_{is}^a / dt = p_i \lambda_s^a \left(S_i^a + x_i\left(L_{is}^a + L_{ir}^a\right)\right) + v_i L_{is}^a + \varepsilon T_i^s - \left(d^a + n_i + \delta + \mu_i + \mu_{ti}\right) T_{is}^a$$

$$dT_{ir}^a / dt = p_i \lambda_r^a \left(S_i^a + x_i\left(L_{is}^a + L_{ir}^a\right)\right) + v_i L_{ir}^a + \delta T_i^r - \left(d^a + n_i + \varepsilon + \mu_i + \mu_{ti}\right) T_{ir}^a$$

$$dT_{ir} / dt = p_i \lambda_r \left(S_i + x_i\left(L_{is} + L_{ir}\right)\right) + v_i L_{ir} + \delta T_{ir}^a - \left(d + n_i + \varepsilon + \mu_i + \mu_{ti}\right) T_{ir}$$

$$dT_{js} / dt = p_j \lambda_s \left(S_j + x_j\left(L_{js} + L_{jr}\right)\right) + v_j L_{js} - \left(d + n_j + \mu_j + \mu_{tj}\right) T_{js}$$

$$dT_{jr} / dt = p_j \lambda_r \left(S_j + x_j\left(L_{js} + L_{jr}\right)\right) + v_j L_{jr} - \left(d + n_j + \mu_j + \mu_{tj}\right) T_{jr}$$

$$dD_{is}^a / dt = d^a \left(T_{is}^a + F_{is}^a\right) + \theta\varepsilon D_{is} - \left(r + \delta + \mu_i + \mu_{ti}\right) D_{is}^a$$

$$dD_{ir}^a / dt = d^a \left(T_{ir}^a + F_{ir}^a\right) + \theta\varepsilon D_i^r - \left(r + \delta + \mu_i + \mu_{ti}\right) D_{ir}^a$$

$$dD_{is} / dt = d\left(T_{is} + F_{is}\right) + \omega\delta D_{is}^a - \left(r + \varepsilon + \mu_i + \mu_{ti}\right) D_{is}$$

$$dD_{ir} / dt = d\left(T_{ir} + F_{ir}\right) + \omega\delta D_{ir}^a - \left(r + \varepsilon + \mu_i + \mu_{ti}\right) D_{ir}$$

$$dD_{js} / dt = d\left(T_{js} + F_{js}\right) - \left(r + \mu_j + \mu_{tj}\right) D_{js}$$

$$dD_{jr} / dt = d\left(T_{jr} + F_{jr}\right) - \left(r + \mu_j + \mu_{tj}\right) D_{jr}$$

$$dF_{is}^a / dt = (1-\alpha)\left(r(1-k_{sa}) D_{is}^a + (1-\theta)\varepsilon D_{is}\right) + \varepsilon F_{is} - \left(d_a + \delta + \mu_i + \mu_{tfi}\right) F_{is}^a$$

$$dF_{ir}^{a}/dt = \alpha\left(r\left(1-k_s^a\right)D_{is}^{a} + (1-\theta)\varepsilon D_{is}\right) + r\left(1-k_r^a\right)D_{ir}^{a} + (1-\theta)\varepsilon D_{ir} + \varepsilon F_{ir} - \left(d_a + \delta + \mu_i + \mu_{tfi}\right)F_{ir}^{a}$$

$$dF_{is}/dt = (1-\alpha)\left(r\left(1-k_s\right)D_{is} + (1-\omega)\delta D_{is}^{a}\right) + \delta F_{is}^{a} - \left(d + \varepsilon + \mu_i + \mu_{tfi}\right)F_{is}$$

$$dF_{ir}/dt = \alpha\left(r\left(1-k_s\right)D_{is} + (1-\omega)\delta D_{is}^{a}\right) + r\left(1-k_r\right)D_{ir} + (1-\omega)\delta D_{ir}^{a} + \delta F_{ir}^{a} - \left(d + \varepsilon + \mu_i + \mu_{tfi}\right)F_{ir}$$

$$dF_{js}/dt = (1-\alpha)r\left(1-k_s\right)D_{js} - \left(d + \mu_j + \mu_{tfj}\right)F_{js}$$

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

$$\lambda_s = \beta f_i\left(T_{is} + T_{js} + D_{is} + D_{js} + z\left(F_{is} + F_{js}\right)\right)/N_c$$

$$\lambda_r = \varphi\beta f_i\left(T_{ir} + T_{jr} + D_{ir} + D_{jr} + z\left(F_{ir} + F_{jr}\right)\right)/N_c$$

$$\lambda_s^a = \kappa q f_j\left(T_{is}^a + D_{is}^a + zF_{is}^a\right)$$

$$\lambda_r^a = \varphi\kappa q f_j\left(T_{ir}^a + D_{ir}^a + zF_{ir}^a\right)$$

Supplemental Table 2
Natural history and TB control parameters used for simulation*

Parameter	Definition	HIV-negative value (range)	HIV-positive value (range)	Sources
b	Population birth rate	Set to maintain constant population		–
γ	Proportion of population at risk for amplifier entry	Varied in simulation		–
ε	Rate of entry to amplifier among those at risk for entry	Varied in simulation		–
δ	Rate of exit from amplifier	Varied in simulation; inverse length of stay in amplifier		–
β	Per capita transmission rate	9.8 (7.0–12.6)		(1)
f	Fraction of active TB cases who are infectious	0.65 (0.5–0.65)	0.3 (0.19–0.4)	(2)
z	Relative proportion of treatment failures who are infectious vs. active cases	0.25 (0–0.5)		(1)
μ	Background (non-TB) mortality rate	0.015 (0.01–0.04)	0.098 (0.093–0.103)	(2, 18)
d	Detection and treatment initiation rate	83 (40–172) weeks	18 (9-30) weeks	(19)
p	Proportion of newly infected persons experiencing primary progressive disease	0.14 (0.08–0.25)	0.67 (0.36–0.8)	(2)
k	Proportion of treated cases cured	0.7 (0.6–0.85); ×0.6 (×0.5–×1) lower for MDR TB		(6)
n	Rate of natural self-cure	0.2 (0.15–0.25)	0.1 (0–0.15)	(2)
r	1/culture conversion time	34 (8–181) days^{-1}		(20, 21)
v	Reactivation rate from latency	1.13×10^{-4} (10^{-4}–3×10^{-4})	0.17 (0.04–0.2)	(2)
x	Proportion of latently-infected persons who are susceptible to primary progressive disease upon re-infection	0.35 (0.1–0.6)	0.75 (0.5–1.0)	(2)
μ_t	Mortality rate caused by TB (multiplied by 0.5 (range 0–1) for treatment failures, μ_{tf})	0.3 (0.2–0.4)	1.0 (0.75–1.0)	(1, 2)
α	proportion of patients failing therapy who acquire resistance	0.07 (0.008–0.18)		(6)
φ	Relative transmission fitness of MDR TB strains	0.5 (0.16–1.2)		(6, 7)
κ	Ratio of pulmonary to room ventilation rate	0.48 (0.4–0.6) m^3/hour/520 (330–1,209) m^3/hour		(5, 16)
θ, ω	Proportion not lost to treatment follow-up at entry to (θ), or upon exit from (ω), amplifier	Varied in simulations		–

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

Supplemental Table 3
Sensitivity analysis*

Parameter	Definition	% Change in TB prevalence with 1% change in HIV-negative value	% Change in TB prevalence with 1% change in HIV-positive value
β	Per capita transmission rate	1.7719	
f	Fraction of active TB cases who are infectious	1.8053	0.0084
z	Relative proportion of treatment failures who are infectious vs. active cases	0.0457	
μ	Background (non-TB) mortality rate	0.0260	0.0017
d	Detection and treatment initiation rate	–1.0432	–0.0106
p	Proportion of newly infected persons experiencing primary progressive disease	1.8233	0.0876
k	Proportion of treated cases cured	–0.9715	
n	Rate of natural self-cure	–0.5903	–0.0030
r	1/culture conversion time	–0.0948	
v	Reactivation rate from latency	0.0532	0.8302
x	Proportion of latently-infected persons who are susceptible to primary progressive disease upon re-infection	0.6105	0.0131
μ_t	Mortality rate caused by TB (multiplied by 0.5 (range 0–1) for treatment failures, μ_{tf})	–0.9401	–0.0318
α	Proportion of patients failing therapy who acquire resistance	-5.9984×10^{-4}	
φ	Relative transmission fitness of MDR TB strains	0.0030	
κ	Ratio of pulmonary to room ventilation rate	0.0420	

*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.

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