Intervention Impacts in Joined-Up HIV and TB Epidemics

(Report on on-going joint work with K. Herman, M. Chen, and M. Kgosimore)

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The Problem

- **TB is one of the biggest infectious killers of PLWHIV, leading up to half of all HIV-related deaths in some places**

- **PLWHIV are up to 50 times more likely to develop TB in their lifetime than HIV-negative people**

- **ART reduces the rate of developing TB but PLWH on HRT still have a massively increased risk of developing TB (4-8 times of HIV-negative)**

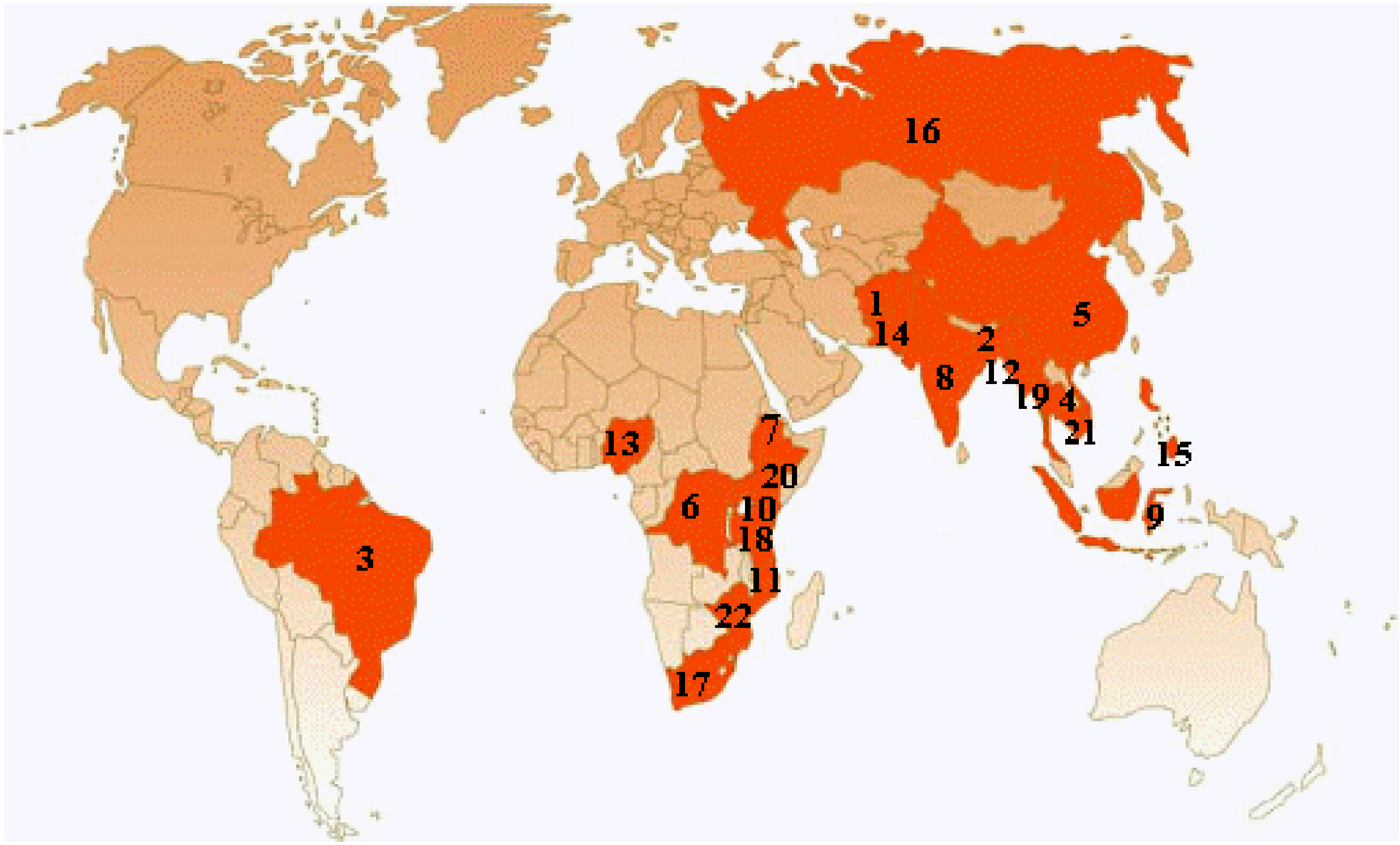
- 2006 HIV/TH Report Card for 22 TB High Burden Countries
- Ayles (2006): TB finding/TB Prevention in HIV infected populations

Outline

- **Brief Background Motivation**
  - **Global TB/HIV Epidemiology overview**
  - **Interventions**
- **Math Model**
  - **Interaction diagram**
  - **Equilibria**
- **Numerical experiments**

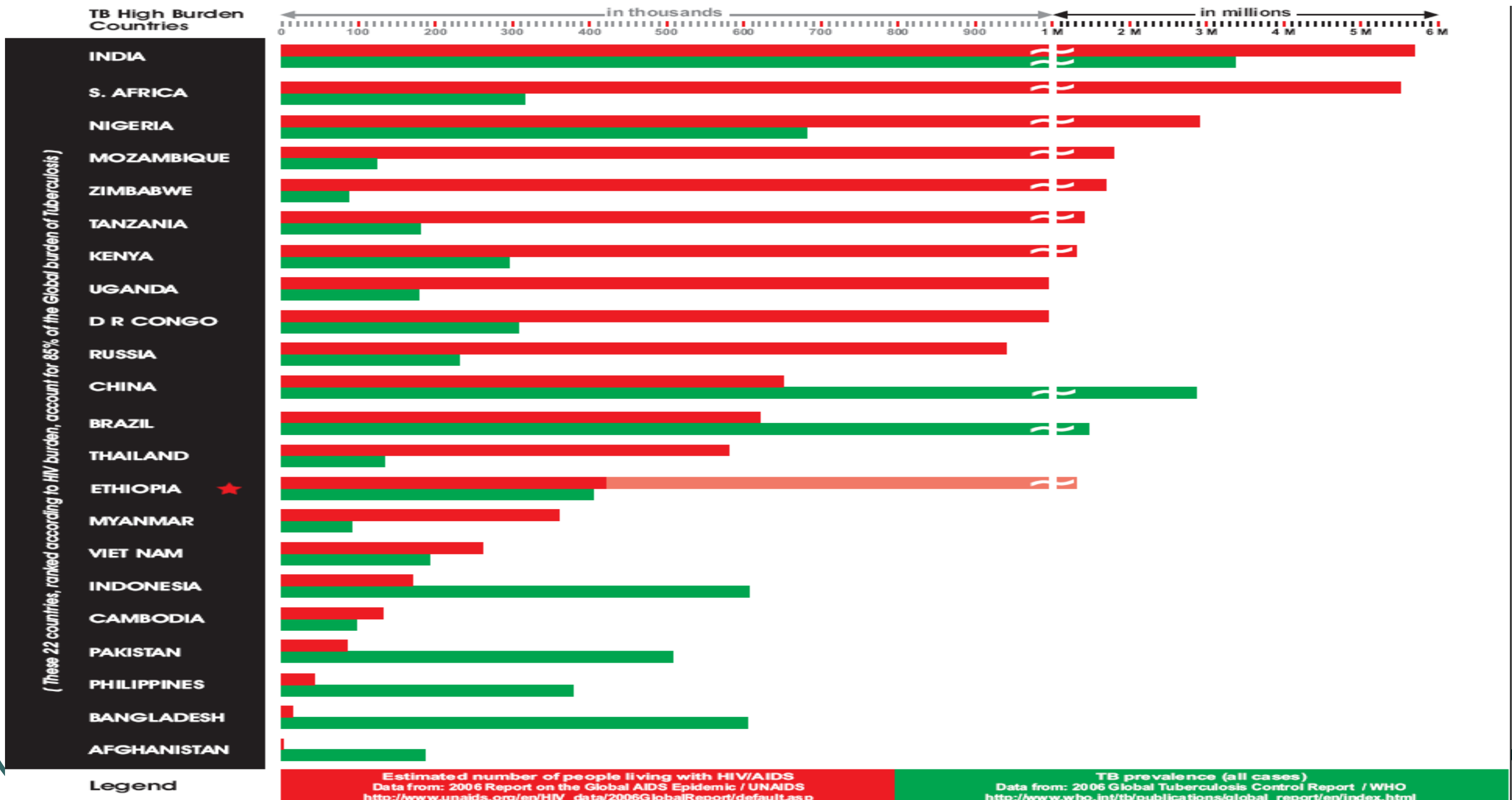
The Global TB Picture

The Top 22 Countries accounting for 85% TB Burden – TB Rank



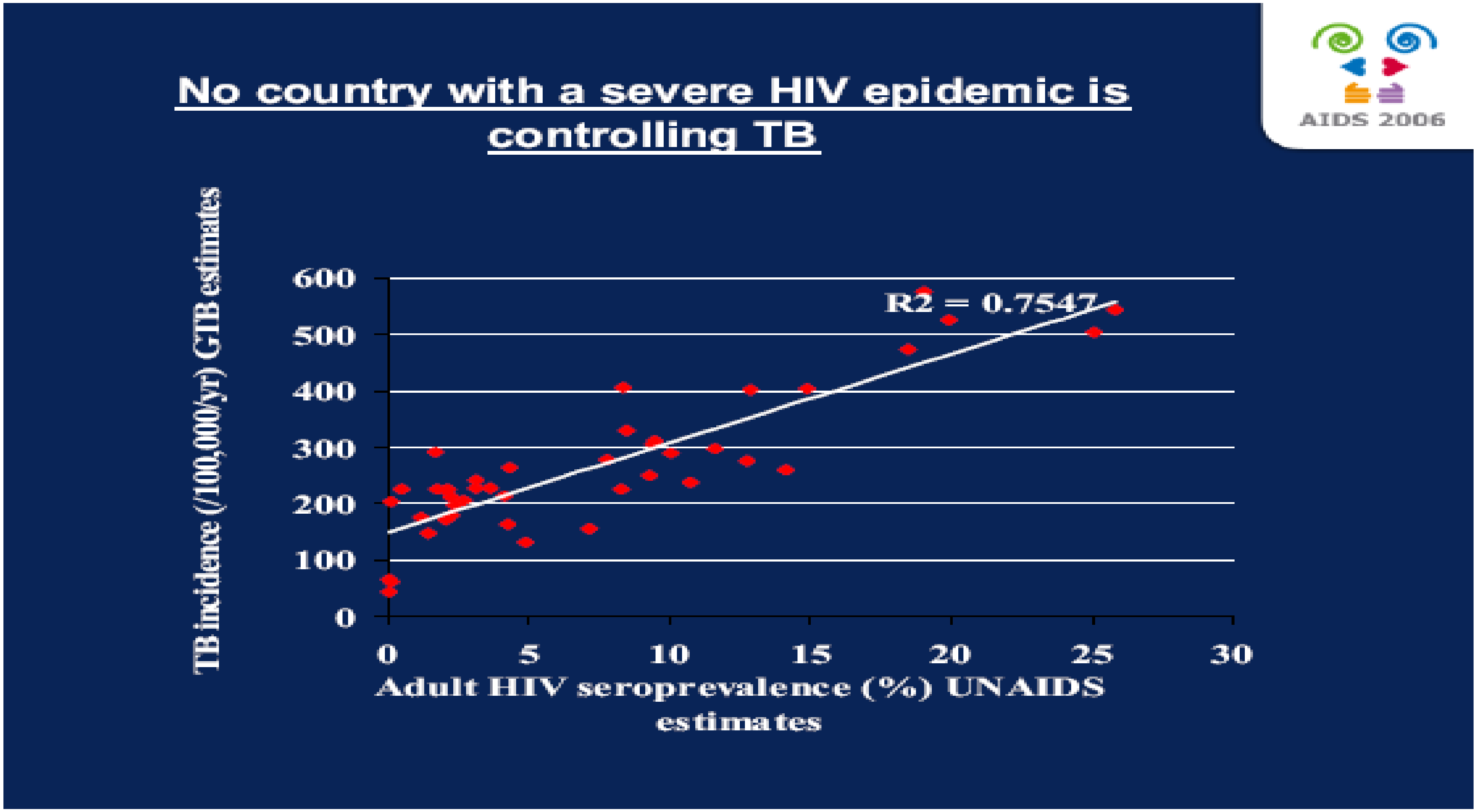
The Global TB/HIV Picture

The Top 22 Countries accounting for 85% TB Burden – HIV Rank



The Global TB/HIV Picture

Correlation - the sad truth



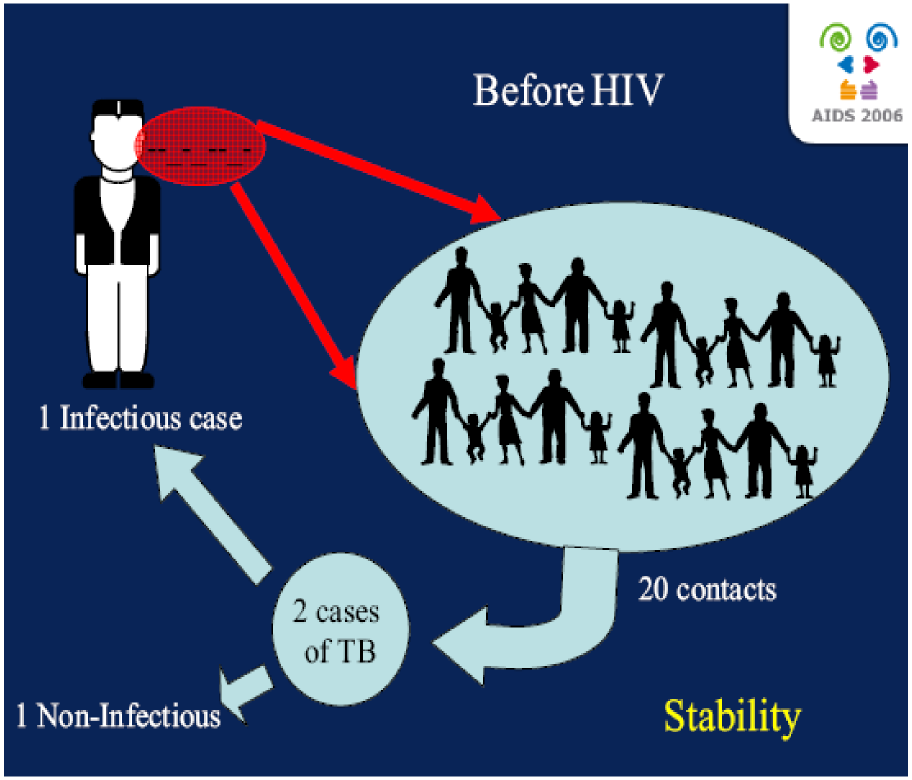
Summary of Current Situation

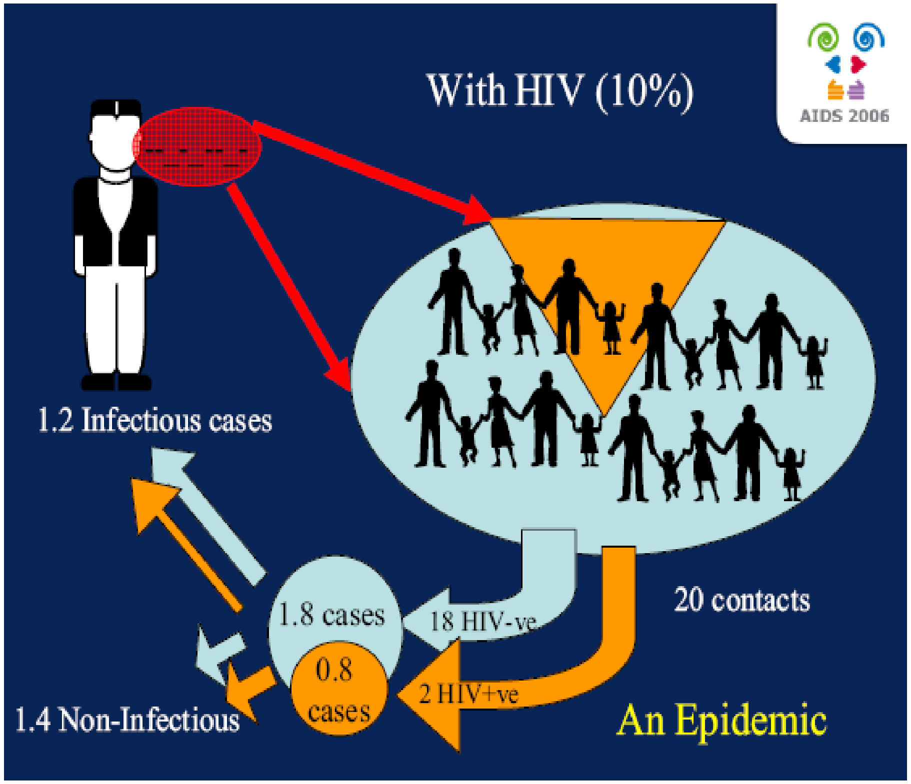
- Two to three million people around the world die of TB each year
- Someone is infected with TB every second
- One third of the world population is infected with TB (the prevalence in the US is 10-15%)
- Twenty two countries in South East Asia and Sub Saharan Africa account for 85% total cases around the world
- 70% untreated actively infected individuals die

How HIV fuels the TB Epidemic

- HIV promotes progression to active TB both in people with recently acquired and with latent TB
- HIV is the most powerful known risk factor for reactivation of latent TB to active disease
- The annual risk of developing active TB in a PLWH who is co-infected with TB is 5 – 15%.
- HIV increases the rate of recurrent TB, which may be due to either endogenous reactivation or exogenous re-infection.
- Increasing TB cases in PLWH pose an increased risk of TB transmission to the general community.

How HIV fuels the TB Epidemic





Interventions

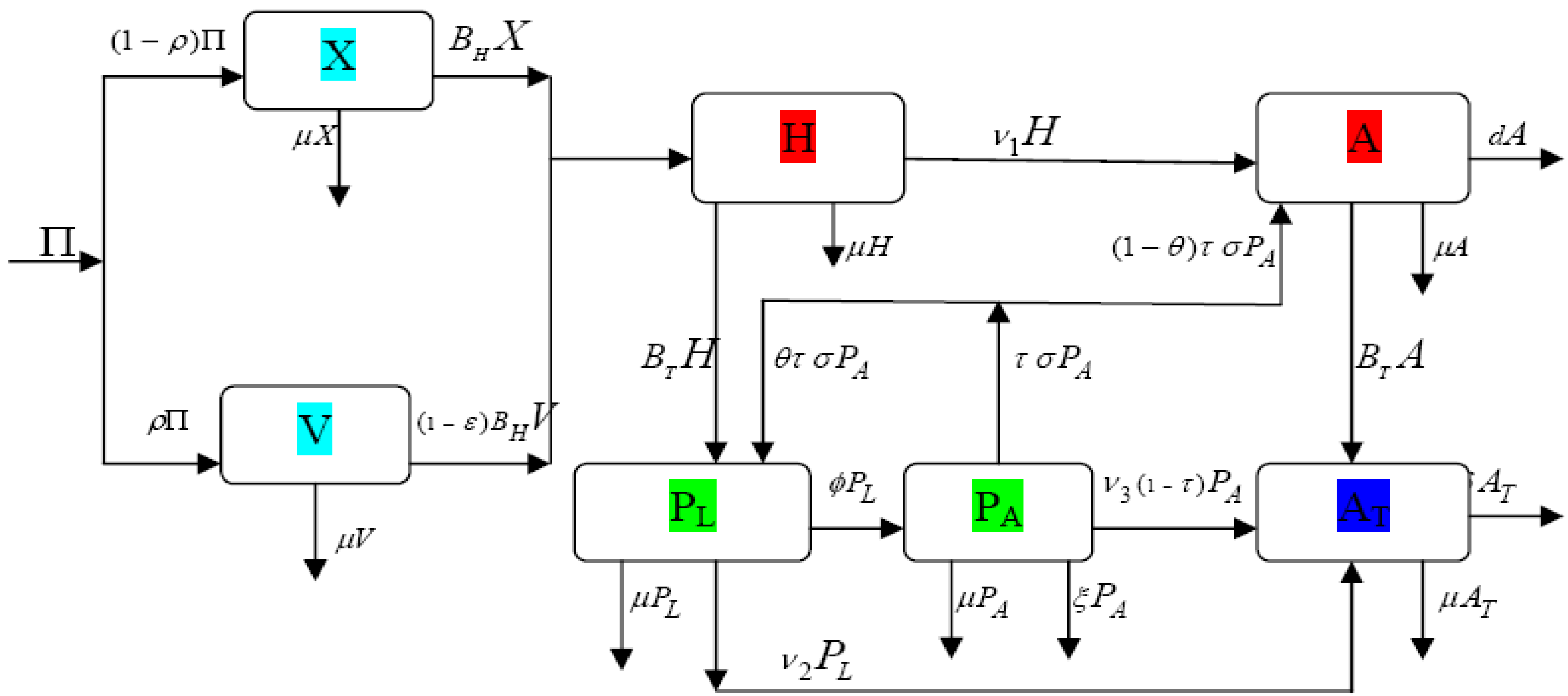
Tuberculosis treatment
Interventions to increase tuberculosis case detection and cure rates
Cotrimoxazole prophylaxis, HIV-positive TB patients
BCG immunization
Preventive tuberculosis treatment
Interventions to reduce HIV incidence**: (a) condom distribution + STD treatment for commercial sex workers (CSWs) (b) Blood safety measures (c) Mother to child transmission prevention (nevirapine) (d) Voluntary counselling and testing (e) STD treatment
Antiretroviral treatment

Associated Costs

Intervention	Approximate number eligible	Total annual cost (US$ millions)	Total cost as % government health budget
Tuberculosis treatment	70,000	15	3
Interventions to increase tuberculosis case detection (CD) and cure rates (CR)	140,000 (CD) 70,000 (CR)	??	??
Cotrimoxazole prophylaxis, HIV-positive tuberculosis patients	28,000-42,000	0.4-0.6	0.1
Preventive tuberculosis treatment	150,000	3.8-7.2	0.9-1.7
Interventions to reduce HIV incidence:			
(a) Mother to child transmission prevention (nevirapine)	900,000	3.6-6.3	0.8-1.5
(b) Voluntary counselling and testing	15,000,000	210-450 or 21-45 per 1% coverage	49-105 or 4.9-10.5
Antiretroviral treatment	200,000*	220 or 22 per 1% coverage	50.9 or 5.1

*based on assumption of provision to symptomatic individuals with late-stage disease. Provision to the entire HIV-infected population could increase the numbers eligible by a factor of approximately 10.

A Mathematical Model



$$B_H = \frac{c_H\beta_H H + c_L\beta_L P_L + c_A\beta_A P_A}{N} \text{ and } B_T = \frac{\kappa^A\beta^A P_A + \kappa^T\beta^T A_T}{N}$$

A Mathematical Model

$$\frac{dX}{dt} = \pi(1-\rho) - \mu X - B_H X$$

$$\frac{dV}{dt} = \pi\rho - \mu V - (1-\varepsilon)B_H V$$

$$\frac{dH}{dt} = B_H X + (1-\varepsilon)B_H V - (\mu + \upsilon_1)H - B_T H$$

$$\frac{dA}{dt} = \upsilon_1 H + (1-\theta)\tau\sigma P_A - (\mu + d)A - B_T A$$

$$\frac{dP_L}{dt} = B_T H + \theta\tau\sigma P_A - (\mu + \phi + \nu_2)P_L$$

$$\frac{dP_A}{dt} = \phi P_L - (\mu + \nu_3(1-\tau) + \xi + \tau\sigma)P_A$$

$$\frac{dA_T}{dt} = \nu_2 P_L + \nu_3(1-\tau)P_A + B_T A - (\mu + \delta)A_T$$

The Reproduction Numbers

$$R_0 = \frac{c_H \beta_H}{\mu + \nu_1}$$

$$R_{0T} = \frac{\kappa^A \beta^A}{\mu + \nu_3(1-\tau) + \sigma\tau + \xi},$$

$$R_{Hv} = (1 - \rho\epsilon) R_0.$$

$$R_{0TA} = \frac{\kappa^T \beta^T}{\mu + d}$$

Endemic Equilibria

$$\alpha = \frac{d\nu_1}{\mu + d}$$

$$\zeta = \left(\frac{d}{\mu + d}\right)\left(\frac{\nu_1}{\mu + \nu_1}\right)$$

- Case I $\quad c_H\beta_H = \alpha$

  and $\quad (1-\rho)\zeta \neq 1$
- Case II $\quad (1-\epsilon)c_H\beta_H = \alpha$

  and $\quad \rho\zeta \neq 1$
- Case III $\quad (1-\epsilon)c_H\beta_H < \alpha < c_H\beta_H$
- Case IV $\quad c_H\beta_H < \alpha$
- Case V $\quad \alpha < (1-\epsilon)c_H\beta_H$

Endemic Equilibria

- (a) (Cases I and III): If $(1-\varepsilon)R_0 < \zeta \le R_0$ and $R_{Hv} < 1$, then and there is a unique endemic equilibrium
- (b) (Cases II and V): If $\zeta \le (1-\varepsilon)R_0$ and $R_{Hv} > 1$, then there is a unique endemic equilibrium; while if $\zeta \le (1-\varepsilon)R_0$ and $R_{Hv} \le 1$, then there is no endemic equilibrium
- (c) Case IV: If $R_0 < \zeta$, then $R_{Hv} < 1$ and there are two endemic equilibria.

Numerical Experiments

Initial Class Variables

Class	Initial Value	Reason
X	30 000000	50% Southern Africa Approximate Total Population
V	0	None Yet
H	4 000 000	14 % HIV prevalence
A	120 000	10%H
P_L	1 600 000	40% TB prevalence
P_A	315 000	10% P_L
A_T	31 500	10% active TB patients also have AIDS

Numerical Experiments

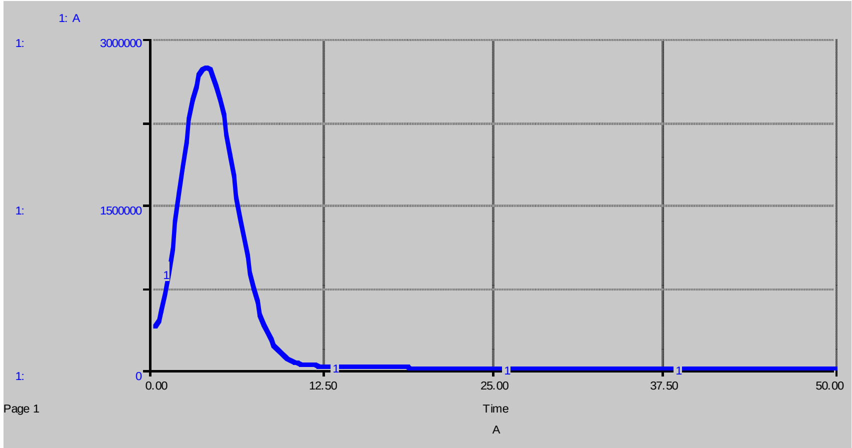
Parameter Values

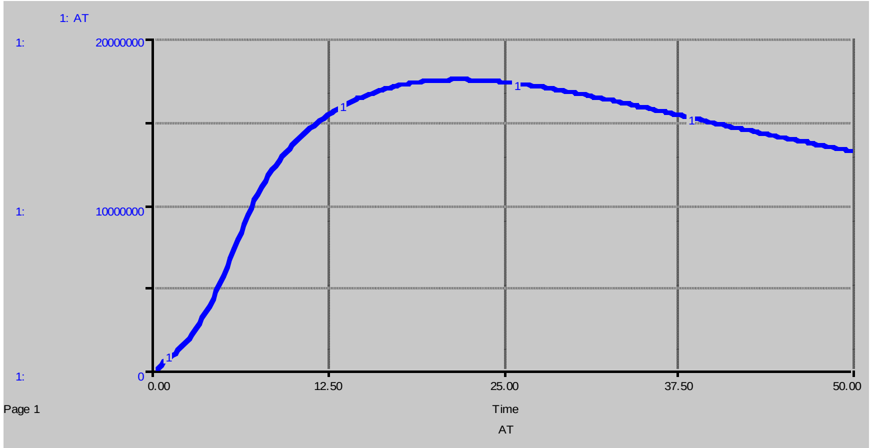
Parameter	Initial Value	Reason/Reference
Π	$0.02 * X^0$	Lungu
ρ	$0 \le \rho \le 1$	Vaccine coverage (proportion)
ε	$0 \le \varepsilon \le 1$	Vaccine effectiveness
c_H	4	Gumel, Lungu
c_L	4	Gumel, Lungu
c_A	4	Gumel, Lungu
κ^A	13	CCC, WHO
κ^T	13	CCC, WHO
β_H	.45	Gumel
β_L	.45	Gumel
β_A	.45	Gumel
β^A	.22	CCC
β^T	.22	CCC
μ	.03	Lungu, WHO
d	.01	Lungu
ξ	.01	CCC
δ	.01	Estimate
σ	.7	DOTS success rate
τ	$0 \le \tau \le 1$	Treatment parameter
θ	$0 \le \theta \le 1$	Proportion of TB cured with delayed AIDS onset
ν_1	0.05	Lungu, WHO
ν_2	0.05	Lungu, WHO
ν_3	0.25	Lungu, WHO
φ	.08	CCC

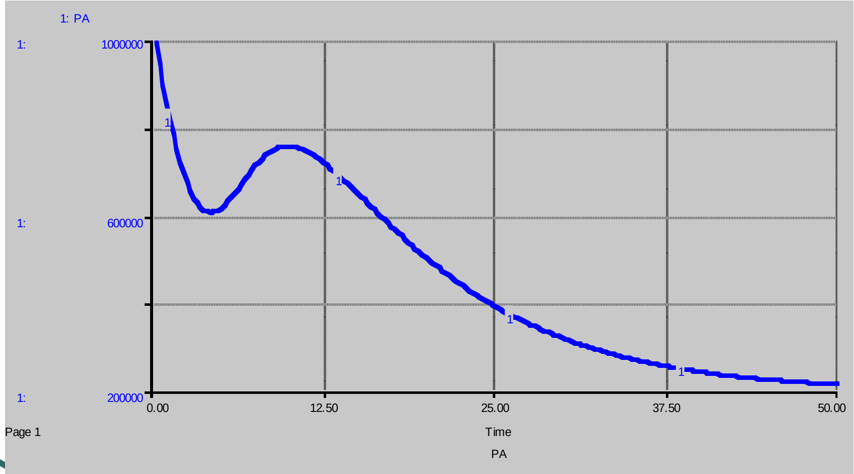
Castillo-Chavez and Sung, 2004; Gumel, Moghadas, and Mickens, 2002; Lungu, Kgosimore, and Nyabadza, 2006

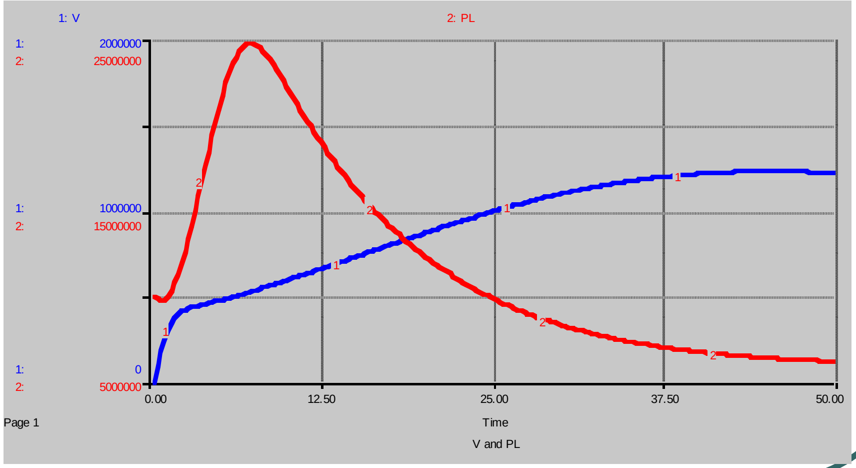
Numerical Experiments

Typical Class Profiles









Summary

- ART is (practically) impossible to afford – especially for the countries most affected – unless something drastic happens
- Perhaps there is hope: ‘We can start saving lives NOW through collaborative HIV-TB programmes, strengthening health systems and the research and development of new ways to prevent, diagnose and treat TB among PLWH.’
- (According to our model) TB treatment alone, and well as with HIV incidence reduction, could lower the TB/HIV burden
- Our model supports the WHO recommendation to “Work within the HIV community to reduce TB by:
  - increasing TB treatment – find and treat more cases
  - reducing latent-to-active prevention’

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