A model for Tuberculosis epidemics
endemicity and control strategies

Mimmo Iannelli
University of Trento

Roma, January 24, 2018

A collaboration with:

- Bedr'Eddine Ainseba

  Institute of Mathematics Bordeaux, Bordeaux University

- Zhilan Feng

  Department of Mathematics, Purdue University

- Fabio Milner

  School of Mathematical and Statistical Sciences, Arizona State University

Some references:

- B. Ainseba, Z. Feng, M. Iannelli and F. A. Milner,
  Control Strategies for TB Epidemics, *SIAM J. Appl. Math., 77 (2017), pp. 82-107.*

- B. Ainseba, M. Iannelli,
  Optimal control of an SIR structured problem, *Math. Modelling of Natural Phenomena, 7 (2012), pp. 12-27.*

- Z. Feng, M. Iannelli and F. A. Milner,
  A two strain tuberculosis model with age of infection, *SIAM J. Appl. Math., 62 (2002), pp. 1634-1656.*

- V. Barbu, M. Iannelli,
  Optimal control of population dynamics, *J. Optim. Theory Appl., 102 (1999), pp. 1-14.*

- V. Barbu, M. Iannelli,
  Controlling the SIS Epidemics, *Proceedings of the Conference on Mathematical Models in Medical and Health Sciences, Nashville, Tennessee, edited by M. A. Horn, G. Simonett, G. F. Webb, 1998.*

About Tuberculosis

Key facts on tuberculosis
(WHO fact sheet, January 2018)

- Tuberculosis (TB) is one of the top 10 causes of death worldwide.
- In 2016, 10.4 million people fell ill with TB, and 1.7 million died from the disease
- In 2016, an estimated 1 million children became ill with TB and 250 000 children died of TB
- TB is a leading killer of HIV-positive people: in 2016, 40% of HIV deaths were due to TB.
- Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. WHO estimates that there were 600 000 new cases with resistance to rifampicin.
- Globally, TB incidence is falling at about 2% per year. This needs to accelerate to a 4-5% annual decline to reach the 2020 milestones of the End TB Strategy.
- An estimated 53 million lives were saved through TB diagnosis and treatment between 2000 and 2016.
- Ending the TB epidemic by 2030 is among the health targets of the Sustainable Development Goals.

About Tuberculosis

Disease details

- Tuberculosis (TB) is caused by bacteria (Mycobacterium tuberculosis) that most often affect the lungs. Tuberculosis is curable and preventable.
- TB is spread from person to person through the air. When people with lung TB cough, sneeze or spit, they propel the TB germs into the air. A person needs to inhale only a few of these germs to become infected.
- About one-quarter of the world's population has latent TB, which means people have been infected by TB bacteria but are not (yet) ill with the disease and cannot transmit the disease.
- People infected with TB bacteria have a 5-15% lifetime risk of falling ill with TB. However, persons with compromised immune systems, such as people living with HIV, malnutrition or diabetes, or people who use tobacco, have a much higher risk of falling ill.
- When a person develops active TB disease, the symptoms (such as cough, fever, night sweats, or weight loss) may be mild for many months. This can lead to delays in seeking care, and results in transmission of the bacteria to others. People with active TB can infect 10-15 other people through close contact over the course of a year. Without proper treatment, 45% of HIV-negative people with TB on average and nearly all HIV-positive people with TB will die.

About Tuberculosis

Disease details

- Tuberculosis (TB) is caused by bacteria (Mycobacterium tuberculosis) that most often affect the lungs. Tuberculosis is curable and preventable.
- TB is spread from person to person through the air. When people with lung TB cough, sneeze or spit, they propel the TB germs into the air. A person needs to inhale only a few of these germs to become infected.
- About one-quarter of the world's population has latent TB, which means people have been infected by TB bacteria but are not (yet) ill with the disease and cannot transmit the disease.
- People infected with TB bacteria have a 5-15% lifetime risk of falling ill with TB. However, persons with compromised immune systems, such as people living with HIV, malnutrition or diabetes, or people who use tobacco, have a much higher risk of falling ill.
- When a person develops active TB disease, the symptoms (such as cough, fever, night sweats, or weight loss) may be mild for many months. This can lead to delays in seeking care, and results in transmission of the bacteria to others. People with active TB can infect 10-15 other people through close contact over the course of a year. Without proper treatment, 45% of HIV-negative people with TB on average and nearly all HIV-positive people with TB will die.

About Tuberculosis

From observation data we have the fraction of infected individuals of age-of-infection θ showing symptoms of the disease

$$p(\theta) = \begin{cases} 0.06 & \theta \in [0,1), \\ 0.084 & \theta \in [1,2), \\ 0.093 & \theta \in [2,3), \\ 0.097 & \theta \in [3,4), \\ 0.098 & \theta \in [4,5), \\ 0.099 & \theta \in [5,6), \\ 0.1 & \theta \in [6,\infty), \end{cases}$$

Thus, if $i(\theta, t)$ is the density of infected individuals with age of infection θ at time t, then

$$p(\theta) i(\theta, t)$$

is the density of infectious individuals with age of infection θ at time t.

The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t) d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)] S(t) + \displaystyle\int_0^\infty \kappa(\theta) i(\theta, t)\, d\theta \\ \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu\ i(\theta, t) + \gamma(\theta) i(\theta, t) = m_I(\theta), \\ i(0, t) = \lambda(t) S(t), \\ S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t) d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)]\, S(t) + \displaystyle\int_0^\infty \kappa(\theta) i(\theta, t)\, d\theta \\[2ex] \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu\ i(\theta, t) + \gamma(\theta) i(\theta, t) = m_I(\theta), \\[2ex] i(0, t) = \lambda(t) S(t), \\[2ex] S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

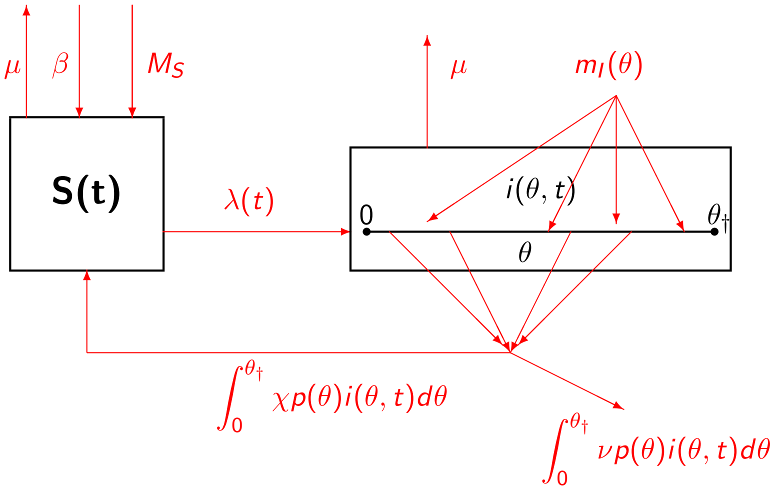
The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t) d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)]\, S(t) + \displaystyle\int_0^\infty \kappa(\theta) i(\theta, t)\, d\theta \\ \\ \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu\ i(\theta, t) + \gamma(\theta) i(\theta, t) = m_I(\theta), \\ \\ i(0, t) = \lambda(t) S(t), \\ \\ S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

The model



μ
β
M_S
μ
$m_I(\theta)$
S(t)
$\lambda(t)$
$i(\theta, t)$
0
$\theta_\dagger$
θ
$\int_0^{\theta_\dagger} \chi p(\theta) i(\theta, t) d\theta$
$\int_0^{\theta_\dagger} \nu p(\theta) i(\theta, t) d\theta$

The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t) d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)]\, S(t) + \displaystyle\int_0^\infty \kappa(\theta) i(\theta, t)\, d\theta \\ \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu\; i(\theta, t) + \gamma(\theta) i(\theta, t) = m_I(\theta), \\ i(0, t) = \lambda(t) S(t), \\ S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t) d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)]\, S(t) + \displaystyle\int_0^\infty \kappa(\theta) i(\theta, t)\, d\theta \\ \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu\ i(\theta, t) + \gamma(\theta) i(\theta, t) = m_I(\theta), \\ i(0, t) = \lambda(t) S(t), \qquad\qquad m_I(\theta) = M\phi_I q_I(\theta) \\ S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t) d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)] S(t) + \displaystyle\int_0^\infty \kappa(\theta) i(\theta, t)\, d\theta \\ \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu\; i(\theta, t) + \gamma(\theta) i(\theta, t) = m_I(\theta), \\ i(0, t) = \lambda(t) S(t), \\ S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t)d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)]\, S(t) + \displaystyle\int_0^\infty \kappa(\theta) i(\theta, t)\, d\theta \\[2ex] \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu\ i(\theta, t) + (\chi + \nu) p(\theta) i(\theta, t) = m_I(\theta), \\[2ex] i(0, t) = \lambda(t) S(t), \\[2ex] S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t) d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)]\, S(t) + \displaystyle\int_0^\infty \chi p(\theta) i(\theta, t)\, d\theta \\ \\ \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu\ i(\theta, t) + (\chi + \nu) p(\theta) i(\theta, t) = m_I(\theta), \\ \\ i(0, t) = \lambda(t) S(t), \\ \\ S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t) d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)] S(t) + \displaystyle\int_0^\infty \kappa(\theta) i(\theta, t)\, d\theta \\ \\ \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu\ i(\theta, t) + \gamma(\theta) i(\theta, t) = m_I(\theta), \\ \\ i(0, t) = \lambda(t) S(t), \\ \\ S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t) d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)] \, S(t) + \displaystyle\int_0^\infty \kappa(\theta) i(\theta, t) \, d\theta \\ \\ \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu \; i(\theta, t) + \gamma(\theta) i(\theta, t) = m_I(\theta), \\ i(0, t) = \lambda(t) S(t), \qquad \lambda(t) = \dfrac{1}{N(t)} \displaystyle\int_0^\infty \rho(\theta) p(\theta) i(\theta, t) \, d\theta, \\ S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

The model

We shall consider a population of otherwise healthy individuals, of size $N(t)$ at time $t \geq 0$, some of whom are infected by a single drug-sensitive strain of *Mycobacterium tuberculosis*.

$$N(t) = S(t) + \int_0^\infty i(\theta, t) d\theta$$

$$\begin{cases} S'(t) = M_S + \beta N(t) - [\mu + \lambda(t)]\, S(t) + \displaystyle\int_0^\infty \kappa(\theta) i(\theta, t)\, d\theta \\ \dfrac{\partial}{\partial t} i(\theta, t) + \dfrac{\partial}{\partial \theta} i(\theta, t) + \mu\ i(\theta, t) + \gamma(\theta) i(\theta, t) = m_I(\theta), \\ i(0, t) = \lambda(t) S(t), \qquad \lambda(t) = \dfrac{1}{N(t)} \displaystyle\int_0^\infty \rho(\theta) p(\theta) i(\theta, t)\, d\theta, \\ S(0) = S_0 > 0, \quad i(\theta, 0) = i_0(\theta) \geq 0. \end{cases}$$

$$c(\theta)\delta(\theta)\frac{p(\theta) i(\theta, t)\, d\theta}{N(t)}$$

The model

the transformed and scaled model

$$\begin{cases} n'(t) = 1 + (\mathcal{R}_d - 1)n(t) - \nu \displaystyle\int_0^\infty p(\theta)u(\theta,t)d\theta, \\ \dfrac{\partial}{\partial t}u(\theta,t) + \dfrac{\partial}{\partial \theta}u(\theta,t) + u(\theta,t) + \gamma(\theta)u(\theta,t) = \phi_I \; q_I(\theta), \\ u(0,t) = \left(1 - \dfrac{U(t)}{n(t)}\right) \displaystyle\int_0^\infty \rho(\theta)p(\theta)u(\theta,t)d\theta, \\ u(\theta,0) = u_0(\theta) \geq 0, \quad n(0) = n_0 > 0 \end{cases}$$

- demographic reproduction number $\mathcal{R}_d = \dfrac{\beta}{\mu}$
- scaled total population $n(t)$
- scaled infected $u(\theta, t)$
- scaled total infected $U(t) = \displaystyle\int_0^{\theta_\dagger} u(\theta, t)d\theta$

The model

the transformed and scaled model

$$
\begin{cases}
n'(t) = 1 + (\mathcal{R}_d - 1)n(t) - \nu \displaystyle\int_0^\infty p(\theta)u(\theta,t)d\theta, \\
\dfrac{\partial}{\partial t}u(\theta,t) + \dfrac{\partial}{\partial \theta}u(\theta,t) + u(\theta,t) + \gamma(\theta)u(\theta,t) = \phi_I \; q_I(\theta), \\
u(0,t) = \left(1 - \dfrac{U(t)}{n(t)}\right) \displaystyle\int_0^\infty \rho(\theta)p(\theta)u(\theta,t)d\theta, \\
u(\theta,0) = u_0(\theta) \geq 0, \quad n(0) = n_0 > 0
\end{cases}
$$

- demographic reproduction number $\mathcal{R}_d = \dfrac{\beta}{\mu}$
- scaled total population $n(t) \longrightarrow \dfrac{\mu N(t)}{M}$
- scaled infected $u(\theta,t) \longrightarrow \dfrac{i(\theta,t)}{M}$
- scaled total infected $U(t) = \displaystyle\int_0^{\theta_\dagger} u(\theta,t)d\theta$

The endemic state

$$
\begin{cases}
1 + (\mathcal{R}_d - 1)n^* - \nu \displaystyle\int_0^\infty p(\theta)u^*(\theta)d\theta = 0 \\
\dfrac{d}{d\theta}u^*(\theta) = -(1 + \gamma(\theta)u^*(\theta) + \phi_I \; q_I(\theta), \\
u^*(0) = \left(1 - \dfrac{U^*}{n^*}\right) \displaystyle\int_0^\infty \rho(\theta)p(\theta)u^*(\theta)d\theta, \\
U^* = \displaystyle\int_0^\infty u^*(\theta)d\theta.
\end{cases}
$$

The endemic state

For any set of parameters, with $\phi_I > 0$, there exists a unique steady state:

$$u^*(\theta) = v^* K_0(\theta) + \phi_I \int_0^\theta \frac{K_0(\theta)}{K_0(s)} q_I(s) ds,$$

where

$$K_0(\theta) = e^{-\theta} e^{-\int_0^\theta \gamma(\sigma) d\sigma},$$

is the probability of remaining infected at age θ, and v^* is the (unique) solution of

$$b(\Pi_0 v + \Pi_I \phi_I)(\mathcal{R}_0 v + \mathcal{R}_I \phi_I) = (Q - \nu \mathcal{J}_0 v)((\mathcal{R}_0 - 1)v + \mathcal{R}_I \phi_I)$$

The endemic state

Significant parameters:

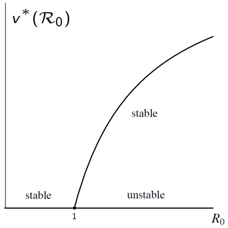
- epidemiological reproduction numbers:
  - $\mathcal{R}_0 = \int_0^\infty \rho(\theta) p(\theta) K_0(\theta) d\theta$
  - $\mathcal{R}_I = \int_0^\infty \rho(\theta) p(\theta) \int_0^\theta \frac{K_0(\theta)}{K_0(s)} q_I(s) ds d\theta.$
- expected duration of latency:
  - $\Pi_0 = \int_0^\infty K_0(\theta) d\theta$
  - $\Pi_I = \int_0^\infty \int_0^\theta \frac{K_0(\theta)}{K_0(s)} q_I(s) ds d\theta.$
- expected duration of infectivity:
  - $\mathcal{J}_0 = \int_0^\infty p(\theta) K_0(\theta) d\theta$
  - $\mathcal{J}_I = \int_0^\infty p(\theta) \int_0^\theta \frac{K_0(\theta)}{K_0(s)} q_I(s) ds d\theta.$

The endemic state

the role of $\mathcal{R}_0$

If $\phi_I = 0$ then

$$u^*(\theta) = v^*(\mathcal{R}_0) K_0(\theta)$$

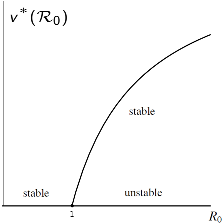


The endemic state

the role of $\mathcal{R}_0$

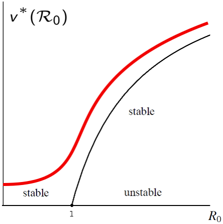
If $\phi_I = 0$ then

$$u^*(\theta) = v^*(\mathcal{R}_0) K_0(\theta)$$



If $\phi_I > 0$ then

$$u^*(\theta) = v^*(\mathcal{R}_0) K_0(\theta) + \phi_I \int_0^\theta \frac{K_0(\theta)}{K_0(s)} q_I(s) ds$$



The endemic state

stability of the endemic state by the characteristic equation

$$\rho\hat{K}_1(\lambda) = \frac{\lambda + 1 + \rho\mathcal{K}^*}{\Big(\lambda + 1\Big)\Big(1 - h^* - \frac{\nu\mathcal{K}^* h^*}{\lambda + b}\Big) + (\chi + \nu)\mathcal{K}^*}$$

proving (for small ν) that all roots have $\Re\lambda < 0$

Screening strategies

We consider two possible interventions

- screening of the resident population
- screening of the immigrant group

$$\begin{cases} n'(t) = 1 + (\mathcal{R}_d - 1)n(t) - \nu \displaystyle\int_0^\infty p(\theta)u(\theta,t)d\theta, \\ \dfrac{\partial}{\partial t}u(\theta,t) + \dfrac{\partial}{\partial \theta}u(\theta,t) + u(\theta,t) + \gamma(\theta)u(\theta,t) = \phi_I \; q_I(\theta), \\ u(0,t) = \left(1 - \dfrac{U(t)}{n(t)}\right) \displaystyle\int_0^\infty \rho(\theta)p(\theta)u(\theta,t)d\theta, \\ u(\theta,0) = u_0(\theta) \geq 0, \quad n(0) = n_0 > 0 \end{cases}$$

$\sigma(t)$: the fraction of individuals screened per unit time

$$\sigma \in \mathcal{U} = \{f \in L^\infty(0,T); 0 \leq f(t) \leq \sigma_{max}\}$$

Screening strategies

We consider two possible interventions

- screening of the resident population
- screening of the immigrant group

$$\begin{cases} n'(t) = 1 + (\mathcal{R}_d - 1)n(t) - \nu \int_0^\infty p(\theta)u(\theta,t)d\theta, \\ \frac{\partial}{\partial t}u(\theta,t) + \frac{\partial}{\partial \theta}u(\theta,t) + [1 + \gamma(\theta) + \sigma(t)(1 - p(\theta))]\, u(\theta,t) = \phi_I \; q_I(\theta), \\ u(0,t) = \left(1 - \frac{U(t)}{n(t)}\right) \int_0^\infty \rho(\theta)p(\theta)u(\theta,t)d\theta, \\ u(\theta,0) = u_0(\theta) \geq 0, \quad n(0) = n_0 > 0 \end{cases}$$

Screening strategies

We consider two possible interventions

- screening of the resident population
- screening of the immigrant group

$$\begin{cases} n'(t) = 1 + (\mathcal{R}_d - 1)n(t) - \nu \displaystyle\int_0^\infty p(\theta)u(\theta,t)d\theta, \\ \dfrac{\partial}{\partial t}u(\theta,t) + \dfrac{\partial}{\partial \theta}u(\theta,t) + [1+\gamma(\theta)]\,u(\theta,t) = (1-\sigma(\theta))\phi_I\;q_I(\theta), \\ u(0,t) = \left(1 - \dfrac{U(t)}{n(t)}\right)\displaystyle\int_0^\infty \rho(\theta)p(\theta)u(\theta,t)d\theta, \\ u(\theta,0) = u_0(\theta) \geq 0, \quad n(0) = n_0 > 0 \end{cases}$$

Screening strategies

respective cost functions

- screening of the resident population
- screening of the immigrant group

treatment of active-TB individuals $\tau_+ \dfrac{M}{\mu} \chi \displaystyle\int_0^T \int_0^\infty p(\theta) u^\sigma(\theta, t) d\theta dt,$

treatment of non-infectious screened $\tau_- \dfrac{M}{\mu} \displaystyle\int_0^T \sigma(t) \int_0^\infty (1 - p(\theta)) u^\sigma(\theta, t) d\theta dt.$

social cost of the disease $\zeta \displaystyle\int_0^T \int_0^\infty u^\sigma(\theta, t) d\theta dt,$

fixed cost of the screening procedure $\dfrac{\alpha}{2} \displaystyle\int_0^T \sigma^2(t) dt,$

cost of screening the population $c \dfrac{M}{\mu} \displaystyle\int_0^T \sigma(t) n^\sigma(t) dt.$

Screening strategies

respective cost functions

- screening of the resident population
- screening of the immigrant group

$$C_I(\sigma) = \int_0^T \int_0^\infty [A(\theta) + \sigma(t)B(\theta)]\, u^\sigma(\theta, t) d\theta dt$$

$$+ \int_0^T \left[\frac{\alpha}{2}\sigma^2(t) + c\ \sigma(t) n^\sigma(t)\right] dt,$$

where

$$A(\theta) = \zeta + \tau_+ \chi p(\theta), \qquad B(\theta) = \tau_-(1 - P(\theta))$$

Screening strategies

respective cost functions

- screening of the resident population
- screening of the immigrant group

treatment of active-TB individuals $$\tau_+ \frac{M}{\mu}\chi \int_0^T \int_0^\infty p(\theta) u^\sigma(\theta,t) d\theta dt,$$

treatment of non-infectious screened $$\tau_- \frac{M}{\mu}\phi_I \int_0^T \sigma(t) \int_0^\infty (1-p(\theta)) q_I(\theta) d\theta dt.$$

social cost of the disease $$\zeta \int_0^T \int_0^\infty u^\sigma(\theta,t) d\theta dt,$$

fixed cost of the screening procedure $$\frac{\alpha}{2} \int_0^T \sigma^2(t) dt,$$

cost of screening the population $$c\frac{M}{\mu}\phi_I \int_0^T \int_0^\infty \sigma(t) q_I(\theta) d\theta dt.$$

Screening strategies

respective cost functions

- screening of the resident population
- screening of the immigrant group

$$C_{II}(\sigma) = \int_0^T \int_0^\infty A(\theta) u^\sigma(\theta, t) d\theta dt$$

$$+B \int_0^T \sigma(t) dt + \frac{\alpha}{2} \int_0^T \sigma^2(t) dt$$

where

$$A(\theta) = \zeta + \tau_+ \chi p(\theta), \quad B = \phi_I(\tau_+ - \tau_-) \int_0^\infty p(\theta) q_I(\theta) d\theta + \phi_I(\tau_- + c)$$

Screening strategies

About existence and uniqueness of an optimal control

either (local existence and uniqueness)

V. Barbu, M. Iannelli,
Controlling the SIS Epidemics, Proceedings of the Conference on Mathematical Models in Medical and Health Sciences, Nashville, Tennessee, edited by M. A. Horn, G. Simonett, G. F. Webb, 1998.

or (existence)

B. Ainseba, M. Iannelli,
Optimal control of an SIR structured problem, Math. Modelling of Natural Phenomena, 7 (2012), pp. 12-27.

Numerics

Numerical scheme for the state equation (strategy I)

$$\begin{cases} u_j^0 = u_0(jh), \\ U^i = h\sum_{j=1}^{N_a} u_j^i, \\ V^i = h\sum_{j=1}^{N_a} \rho_j p_j u_j^i, \\ u_0^i = \left(1 - \dfrac{U^i}{N^i}\right) V^i, \\ \dfrac{u_{j+1}^{i+1} - u_j^i}{h} + u_{j+1}^{i+1} + \sigma^{i+1}(1 - p_{j+1}) u_{j+1}^{i+1} \\ \qquad\qquad + (\chi + \nu) p_{j+1} u_{j+1}^{i+1} = \phi_I \; q_{j+1}, \\ W^{i+1} = h\sum_{j=1}^{N_a} p_j u_j^{i+1}, \\ \dfrac{N^{i+1} - N^i}{h} = 1 - bN^{i+1} - \nu W^{i+1}. \end{cases}$$

Numerics

discrete cost function (strategy I)

$$C_{Ih} = h^2 \sum_{i=0}^{N_t-1} \sum_{j=0}^{N_a-1} \left[(\zeta + \tau_+ \chi p_j) + \tau_-(1-p_j)\sigma^i \right] u_j^i + h \sum_{i=0}^{N_t-1} \left[\frac{\alpha}{2} {\sigma^i}^2 + c\sigma^i N^i \right]$$

discrete adjoint equation (strategy I)

$$\begin{cases} z_j^{Nt+1} = 0, \\ z_{Na+1}^i = 0, \\ w^{Nt+1} = 0, \\ -\dfrac{z_{j+1}^{i+1} - z_j^i}{h} + z_j^i + \sigma^i(1-p_j)z_j^i + (\chi+\nu)p_j z_j^i + \nu h p_j w^i \\ \qquad\qquad\qquad = (-\dfrac{V^i}{n^i} + (1 - \dfrac{U^i}{n^i})\rho_j p_j) z_1^{i+1} - (A_j + B_j\sigma^i) \\ -\dfrac{w^{i+1} - w^i}{h} + bw^i = \dfrac{U^i V^i}{2(n^i)^2} z_1^{i+1} - hc\sigma^i \end{cases}$$

discrete gradient (strategy I)

$$\frac{\partial C_{Ih}}{\partial \sigma^i}(\sigma) = \sum_{j=0}^{N_a-1} (1-p_{j+1}) u_{j+1}^i z_{j+1}^i + \alpha\sigma^i + cw^i$$

Numerics

The algorithm (strategy I)

- **Step 1** Choose an initial screening effort σ_0 and a tolerance $\varepsilon > 0$;
- **Step 2** solve the discrete state system with σ_0;
- **Step 3** solve the discrete adjoint system with σ_0;
- **Step 4** compute the cost $C_{Ih}(\sigma_0)$ and the gradient $\dfrac{\partial C_{Ih}}{\partial \sigma}(\sigma_0)$;
- **Step 5** compute the next iteration screening effort using a gradient descent method $\sigma_{n+1} = \sigma_n - \rho \dfrac{\partial C_{Ih}}{\partial \sigma}(\sigma_n)$. Here ρ represents the path of descent, which is internally chosen by the routine "Uming" of the International Mathematics and Statistics Library (IMSL);
- **Step 5** if $\|\sigma_{n+1} - \sigma_n\| < \varepsilon$ then stop; else go to Step 1.

Data from Italy 2012

resident population

$$N = 59.54 \times 10^6, \quad \beta = 0.009, \quad \mu = 0.01 \quad (\mathcal{R}_d = 0.9 < 1)$$

$$\nu = 0.065, \quad \chi = 1.34, \quad \rho = 0.81, \quad I_0 = 4.9 \times 10^4$$

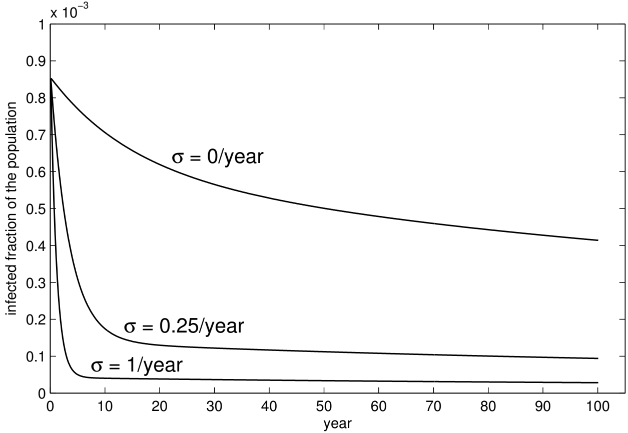
$$\mathcal{R}_0 = 0.54 < 1$$

immigrant population

$$M = 0.37 \times 10^6, \quad M_I = 2.4 \times 10^3,$$

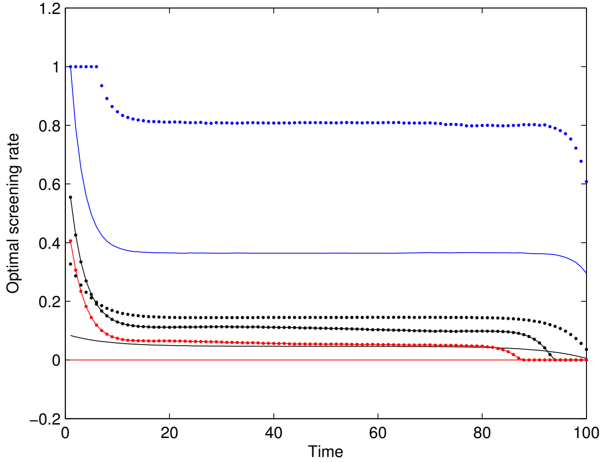
Simulations

strategy I: fixed screening rate



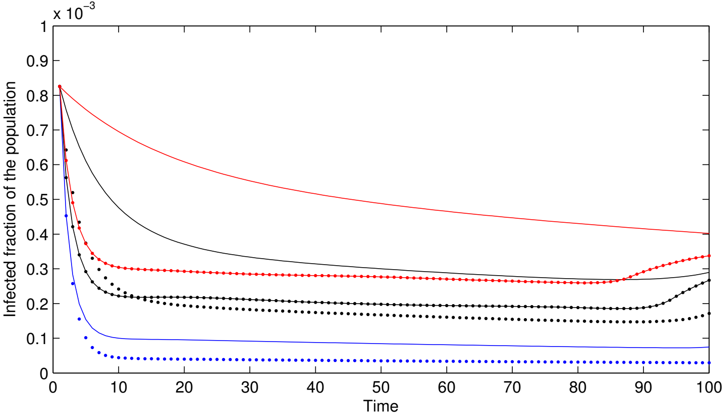
Simulations

in decreasing order: same social cost and, increasing fixed cost of screening + increasing single cost



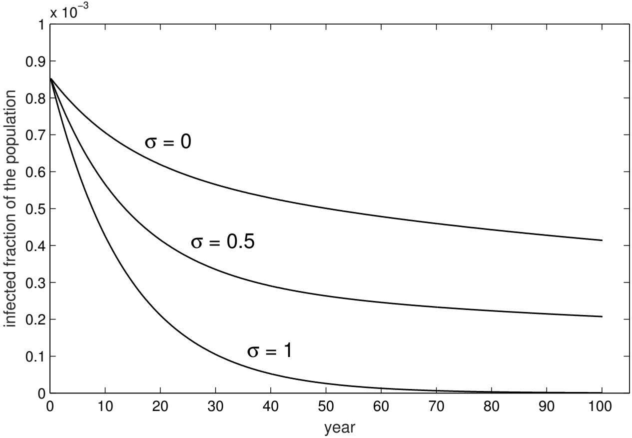
Simulations

the respective infected fractions



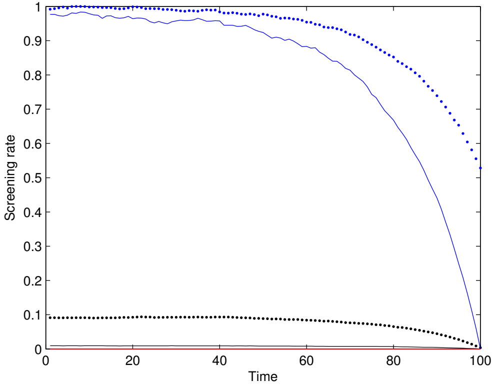
Simulations

strategy II: fixed screening rate



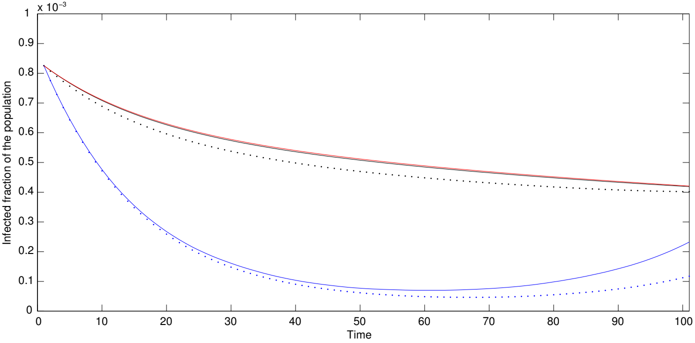
Simulations

in decreasing order: same social cost and, increasing fixed cost of screening + increasing single cost



Simulations

the respective infected fractions



Simulations

Summary with respective efficacy (*difference between the cost when no control is performed and the cost of the particular strategy, normalized by the cost without control*)

ζ	α	c	Efficacy Strategy I	Efficacy Strategy II
200	0	0	0.904	0.725
200	0.1	0	0.745	0.320
200	1	0	0.523	0.032
200	10	0	0.240	0.003
200	0.1	0.1	0.353	0
200	0.1	0.2	0.195	0
200	0.1	1	0	0
20	0.1	1	0	0

THANK YOU FOR YOUR ATTENTION