Optimal Control on a discrete time Influenza Model

Paula A. González-Parra
Computational Science Program, University of Texas at El Paso

Mathematical and Theoretical Biology Institute
MTBI/SUMS
Institute for Strengthening Understanding of Mathematics and Science

Computational Science

Outline

- Introduction
- Discrete Epidemiological model
- Control problem
- Strategies
- Numerical results
- Conclusions

http://health.utah.gov/epi/diseases/flu/Graphics/influenza_germ.JPG

Introduction

- In April of 2009 the World Health Organization (WHO) announced the emergence of a novel strain of A-H1N1 influenza. In June of 2009 WHO declared the outbreak to be a pandemic.
- Different continuous time approaches have been used to study single influenza outbreaks.
- The identification of optimal control strategies that involve antiviral treatment and isolation have also been studied in the continuous case.
- We introduce a optimal control problem in order to minimize the number of infected and dead individuals via the use of the most ``cost-effective'' policies involving social distancing and antiviral treatment using a discrete time epidemic framework.

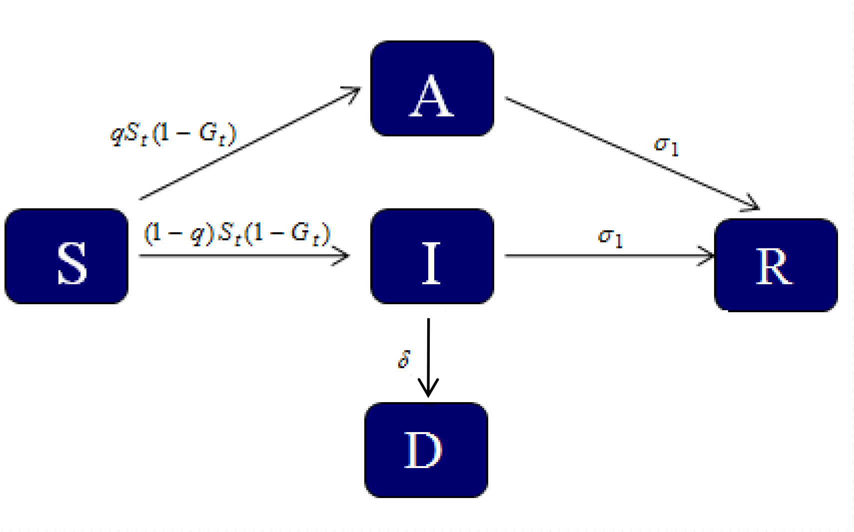
http://i.telegraph.co.uk/telegraph/multimedia/archi
395/swine-flu-treatmen_1395505c.jpg

http://clovetwo.com/archives/2009
/8/23
/healthnfitness/sf_05distance.jpg

Discrete SAIR model

The model is given by the system of difference equations:

$$
\begin{aligned}
S_{t+1} &= S_t G_t \\
A_{t+1} &= qS_t(1-G_t) + (1-\sigma_1)A_t \\
I_{t+1} &= (1-q)S_t(1-G_t) + (1-\sigma_1)(1-\delta)I_t \qquad (1) \\
R_{t+1} &= R_t + \sigma_1(1-\delta)I_t \\
D_{t+1} &= D_t + \delta I_t
\end{aligned}
$$



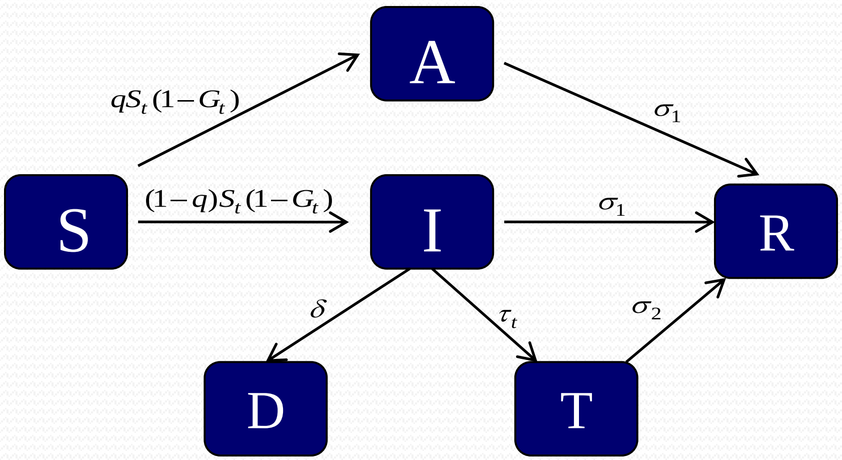
where

$$G_t = e^{-\beta \frac{I_t + m A_t}{N}}$$

Discrete SAITR model

The model is given by the system of difference equations:

$$
\begin{aligned}
S_{t+1} &= S_t G_t \\
A_{t+1} &= qS_t(1-G_t) + (1-\sigma_1)A_t \\
I_{t+1} &= (1-q)S_t(1-G_t) + (1-\tau_t)(1-\sigma_1)(1-\delta)I_t \\
T_{t+1} &= (1-\sigma_2)T_t + \tau_t(1-\sigma_1)(1-\delta)I_t \\
R_{t+1} &= R_t + \sigma_1(1-\delta)I_t + \sigma_2 T_t \\
D_{t+1} &= D_t + \delta I_t
\end{aligned}
\qquad (2)
$$



where

$$G_t = e^{-\beta(1-x_t)\frac{I_t + m A_t + \rho T_t}{N}}$$

Final Epidemic Size

In the absence of controls we get the final size relation

$$\ln\left(\frac{S_0}{S_\infty}\right) = R_0\left(1-\frac{S_\infty}{N}\right) \qquad (3)$$

with the basic reproductive number given by

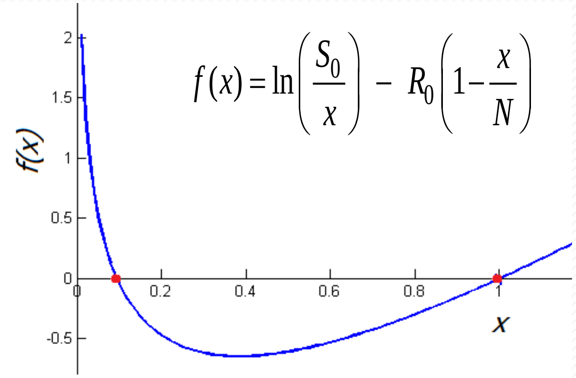
$$R_0 = \beta\left(\frac{1-q}{1-(1-\sigma_1)(1-\delta)} + m\frac{q}{\sigma_1}\right).$$

- The addition of controls replace (3) by the inequality

$$\ln\left(\frac{S_0}{S_\infty}\right) \le R_0\left(1-\frac{S_\infty}{N}\right) \qquad (4)$$

- **Result** : If S_∞ is a solution of (2) and S_∞^{wc} satisfies the inequality (3) then

$$S_\infty^{wc} \ge S_\infty$$



Optimal Control Problem

The goal is to minimize the number of infected and dead individuals with the judicious (cost effective) use of social distancing and antiviral treatment measures over a finite interval $[0, T_f]$. We compare three different Strategies:

- Strategy 1 : Only Social Distancing,

minimize $\frac{1}{2}\sum_{t=0}^{T_f-1}\left[B_0 I_t^2 + B_1 D_t^2 + B_2 x_t^2\right]$

subject to model (1) and $0 \le x_t \le x_{max}$

$$
\begin{aligned}
S_{t+1} &= S_t G_t \\
A_{t+1} &= qS_t(1-G_t) + (1-\sigma_1)A_t \\
I_{t+1} &= (1-q)S_t(1-G_t) + (1-\sigma_1)(1-\delta)I_t \\
R_{t+1} &= R_t + \sigma_1(1-\delta)I_t \\
D_{t+1} &= D_t + \delta I_t
\end{aligned}
$$

- Strategy 2 : Only Antiviral Treatment,

minimize $\frac{1}{2}\sum_{t=0}^{T_f-1}\left[B_0 I_t^2 + B_1 D_t^2 + B_3 \tau_t^2\right]$

subject to model (2), and $0 \le \tau_t \le \tau_{\max}$

$$S_{t+1} = S_t G_t$$
$$A_{t+1} = qS_t(1-G_t) + (1-\sigma_1)A_t$$
$$I_{t+1} = (1-q)S_t(1-G_t) + (1-\tau_t)(1-\sigma_1)(1-\delta)I_t$$
$$T_{t+1} = (1-\sigma_2)T_t + \tau_t(1-\sigma_1)(1-\delta)I_t$$
$$R_{t+1} = R_t + \sigma_1(1-\delta)I_t + \sigma_2 T_t$$
$$D_{t+1} = D_t + \delta I_t$$

- Strategy 3 : Dual of Social Distancing and Treatment.

minimize $\frac{1}{2}\sum_{t=0}^{T_f-1}\left[B_0 I_t^2 + B_1 D_t^2 + B_2 x_t^2 + B_3 \tau_t^2\right]$ (5)

subject to model (2), $0 \le \tau_t \le \tau_{\max}$ and $0 \le x_t \le x_{\max}$

Numerical Solution

The discrete Hamiltonian associated with problem (5) is given by:

$$H_t = B_0 I_t^2 + B_1 D_t^2 + B_2 x_t^2 + B_3 \tau_t^2 + \boldsymbol{\lambda}_{t+1}^T \mathbf{y}_{t+1}$$

Where $\mathbf{y}_t = (S_t, A_t, I_t, T_t, R_t, D_t)^T$ and $\boldsymbol{\lambda}_{t+1} \in \mathbb{R}^6$ are the state and adjoint variables.

The adjoint equations are defined as

$$\lambda_t^i = \frac{\partial H_t}{\partial y_t^i}, \quad i = 1, 2, \ldots, 6, \qquad (6)$$

and the optimality conditions are:

$$\frac{\partial H_t}{\partial x_t} = 0, \quad \frac{\partial H_t}{\partial \tau_t} = 0. \qquad (7)$$

Adjoint Equations For Strategy 3:

The adjoint equations associated with problem (5) are:

$$\lambda_t^1 = G_t \lambda_{t+1}^1 + \left(q\lambda_{t+1}^2 + (1-q)\lambda_{t+1}^3\right)(1-G_t)$$

$$\lambda_t^2 = S_t G_t \frac{\beta m}{N}(1-x_t) L_{t+1} + (1-\sigma_1)\lambda_{t+1}^2 + \sigma_1 \lambda_{t+1}^5$$

$$\lambda_t^3 = B_0 I_t + S_t G_t \frac{\beta}{N}(1-x_t) L_{t+1} + (1-\delta)\left[(1-\sigma_1)\left((1-\tau)\lambda_{t+1}^3 + \tau\lambda_{t+1}^4\right) + \sigma_1 \lambda_{t+1}^5\right] + \delta\lambda_{t+1}^6$$

$$\lambda_t^4 = S_t G_t \frac{\beta\rho}{N}(1-x_t) L_{t+1} + (1-\sigma_2)\lambda_{t+1}^4 + \sigma_2 \lambda_{t+1}^5$$

$$\lambda_t^5 = \lambda_{t+1}^5$$

$$\lambda_t^6 = B_1 D_t + \lambda_{t+1}^6$$

where $L_{t+1} = -\lambda_{t+1}^1 + q\lambda_{t+1}^2 + (1-q)\lambda_{t+1}^3$

Optimality Conditions

The optimality conditions are:

$$\frac{\partial H_t}{\partial \tau_t} = (1-\sigma_1)(1-\delta) I_t \left(\lambda_{t+1}^4 - \lambda_{t+1}^5\right) + B_3 \tau_t = 0$$

$$\frac{\partial H_t}{\partial x_t} = B_2 x_t + S_t G_t a_t \left(\lambda_{t+1}^1 - q\lambda_{t+1}^2 - (1-q)\lambda_{t+1}^3\right) = 0$$

where

$$G_t = e^{-\beta(1-x_t)\frac{I_t + m A_t + \rho T_t}{N}}, \quad a_t = \frac{\beta}{N}\left(I_t + m A_t + \rho T_t\right).$$

Algorithm: (Forward-Backward method)

- Step 1. The initial guess $\boldsymbol{x}$, $\boldsymbol{\tau}$ and condition $\boldsymbol{y_0}$ is selected.
- Step 2. Solve the state equations (1 or 2) forward in time.
- Step 3. Solve the adjoint equations (6) backward in time with the transversality conditions,
$$\lambda_t^i\left(T_f\right)=0$$
- Step 4. Solve the optimality condition (7) .
- Step 5. Check convergence. If $\dfrac{\left\|\mathbf{u}-\mathbf{u}_{old}\right\|}{\left\|\mathbf{u}\right\|}\leq 0.001,$ stop; else go to Step 2.

Numerical Results

- We present the results of selected simulations generated by the numerical implementation of Strategy 1, 2 and 3.

- We compare the number of infected individuals generated by low R_0 (1.3 - 1.8) or high R_0 (2.4 - 3.2) with no controls or in the presence of single or dual optimal controls.

- A sensitivity analysis is also carried out by studying the robustness of our simulations in relationship to the weight constants and the upper bounds of controls.

Implication of social distancing and antiviral treatment (moderate R_0)

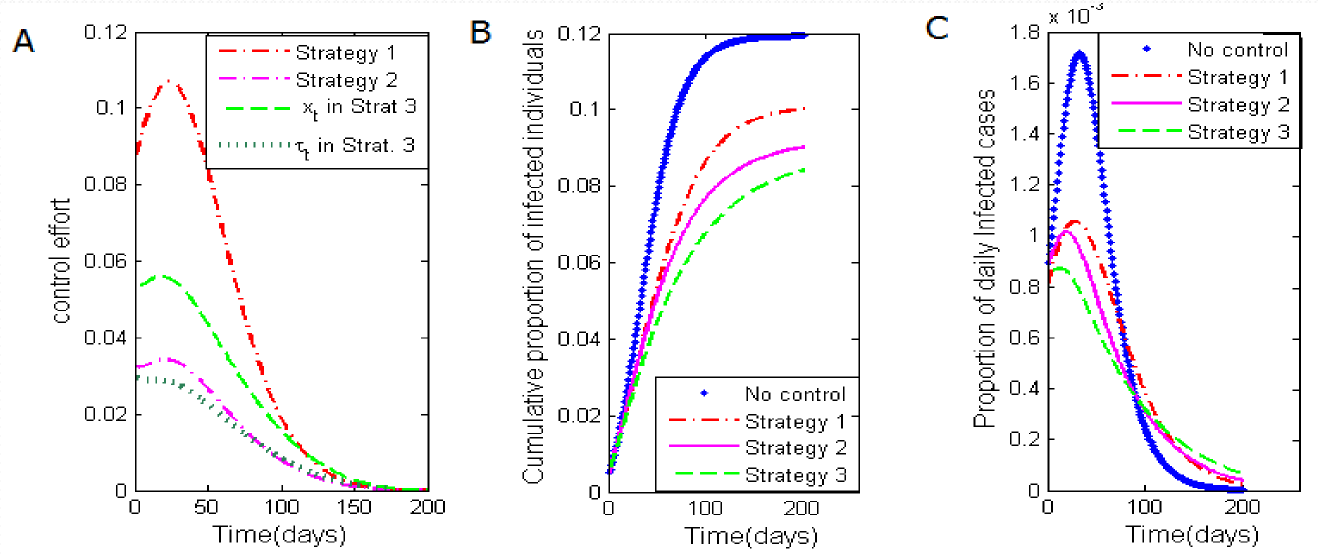


Figure 1: For Ro = 1.3, The optimal control solution does not required the application of the permitted maximum values. However, there is a strong impact in the reduction of the final epidemic size by the application of each strategy. Strategy 3 has the most significant reduction, almost 32%

Implication of social distancing and antiviral treatment (high R_0)

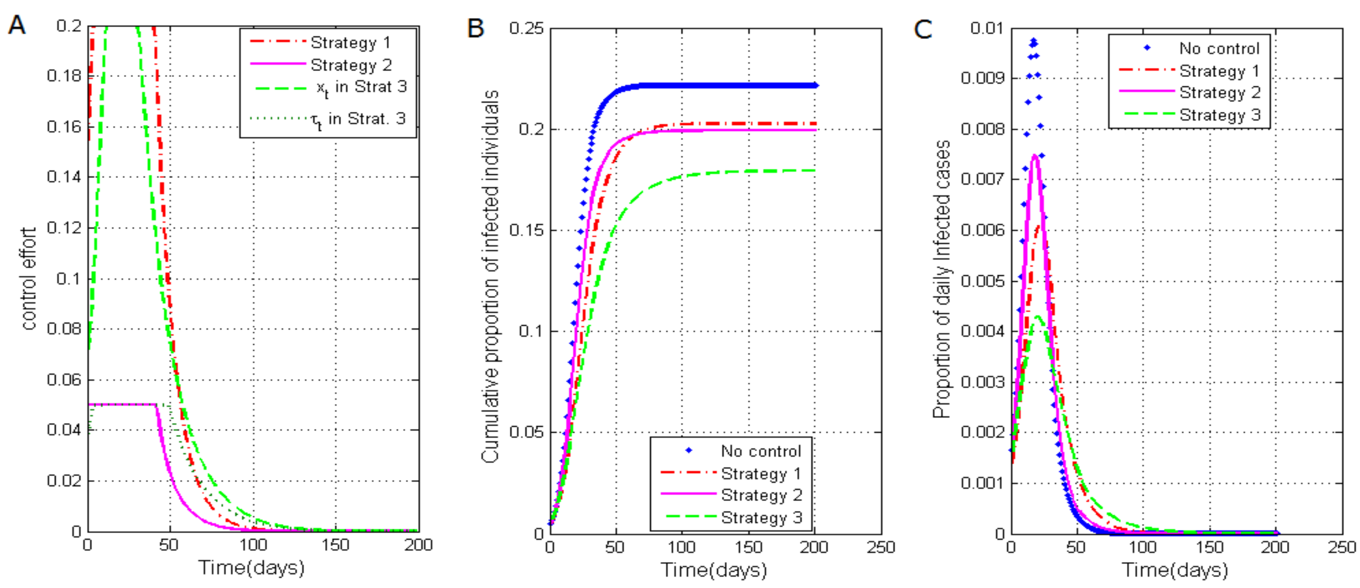


Figure 2: For Ro = 2.4, the optimal solution requires the implementation of the highest permitted values for each control. Strategy 3 produces a reduction of less than 22%. Even when there is a maximum control implementation, the effort is not enough and the reduction in the final epidemic size is less significant

Comparison of final epidemic size vs. R_0

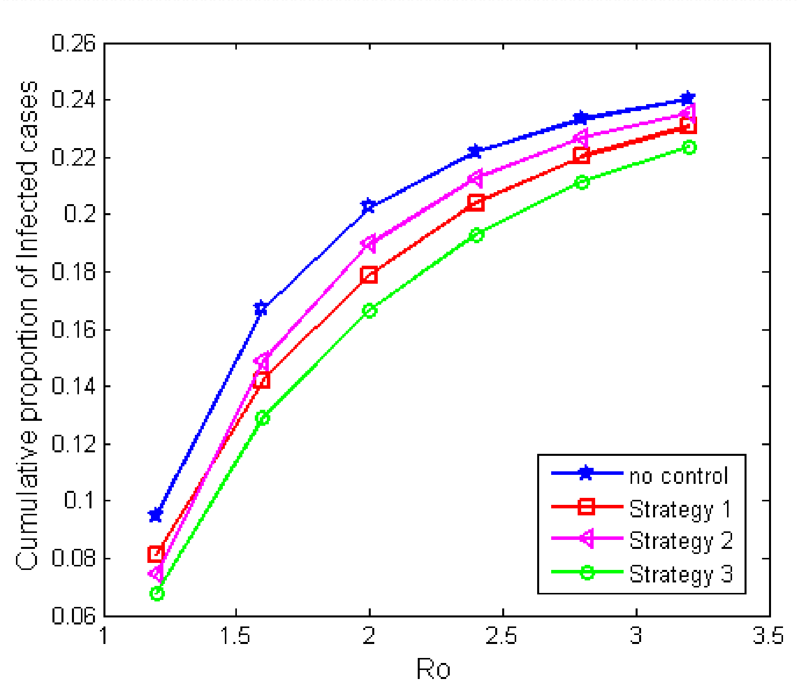


Figure 3: **B**y fixing the weights B2 and B3 of each control function, the results show that Strategy 3 yields the highest reduction of the final epidemic size (more than 31% for small values of R_0).

Effect of weight constants

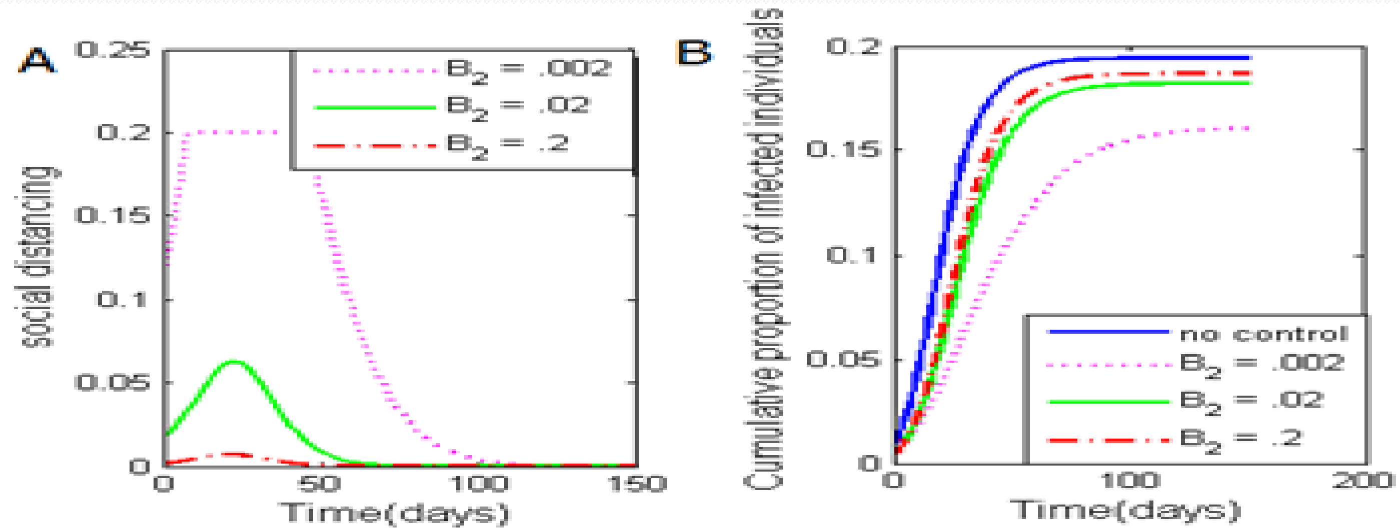


Figure 4: In Strategy 1, the value of the weight constant B2 is varied. For a small value of B2 the optimal solution permits the implementation of high values of social distancing and we obtain a high reduction in the final epidemic size (20%). For a large value of B2 the reduction in the final epidemic size is not significant (7.5%).

For Strategy 2:

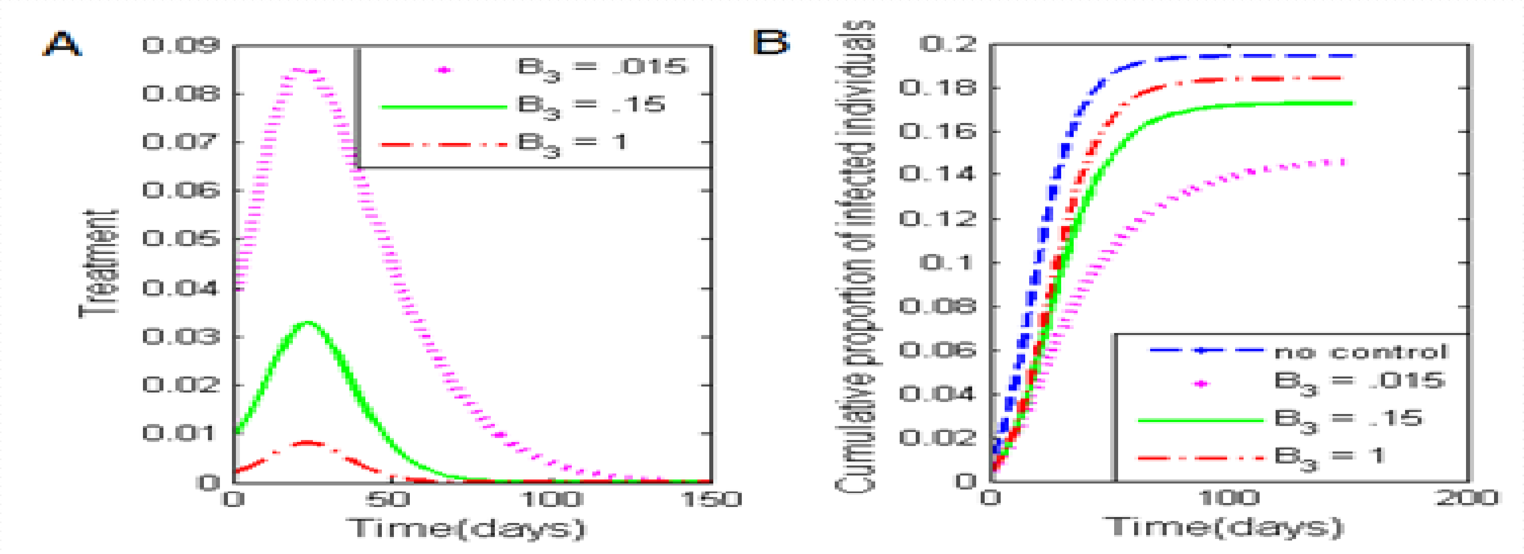


Figure 5: by increasing the cost on antiviral treatment, B3, the optimal solution permits the application of smaller value for treatment. We obtain an increase in the cumulative proportion of infected cases. In contrast, when the cost is moderate the optimal solution permits the implementation of high values of treatment and we get a strong impact in the reduction of the final epidemic size 30%.

Final Epidemic size for Strategies 1 and 2:

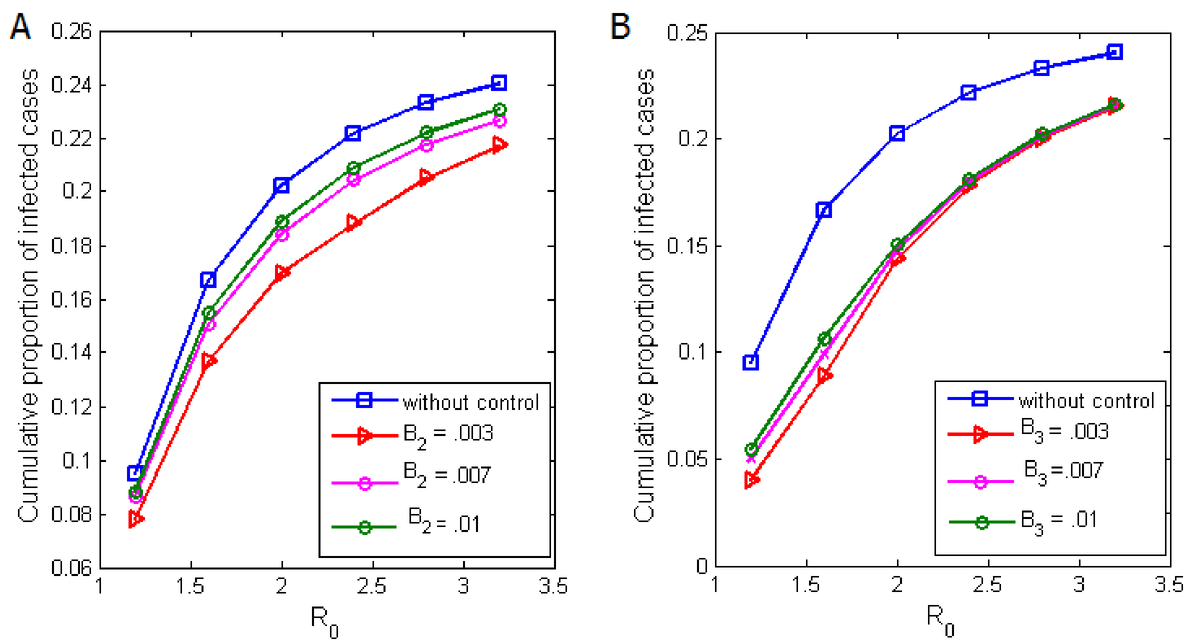


Figure 6: The final epidemic size vs. R_0 for Strategies 1 and 2 by changing the weight constants for social distancing and antiviral treatment. When we have a moderate cost of social distancing, there is a reduction in the final epidemic size for every value of R_0 for (A); however, by changing B_3 there is not a significant difference in the final epidemic size . $R_0 > 2.5$ (B).

The effect of upper bound on the optimal control

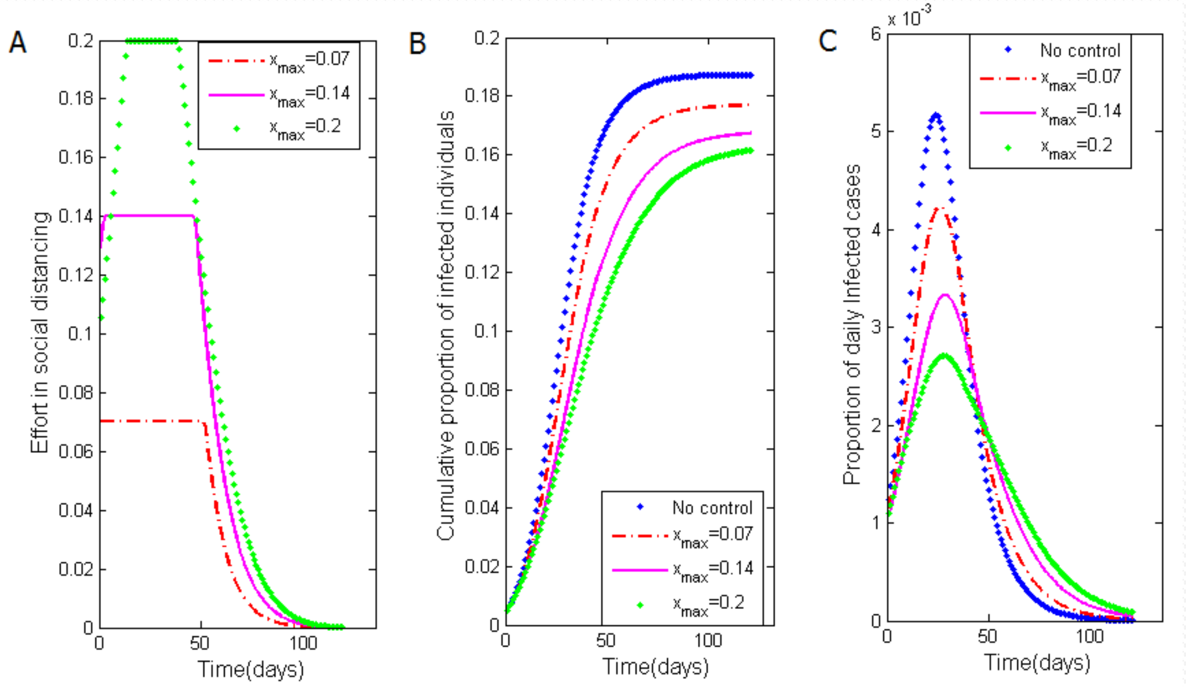


Figure 7: When the resources are limited and the upper bound is smaller x_{max} = 0.07, the reduction of the final epidemic size is small (5%).However, if the upper bound is high there is a stronger impact in the reduction of the final epidemic size, (20%).

Upper bound for Strategy 2

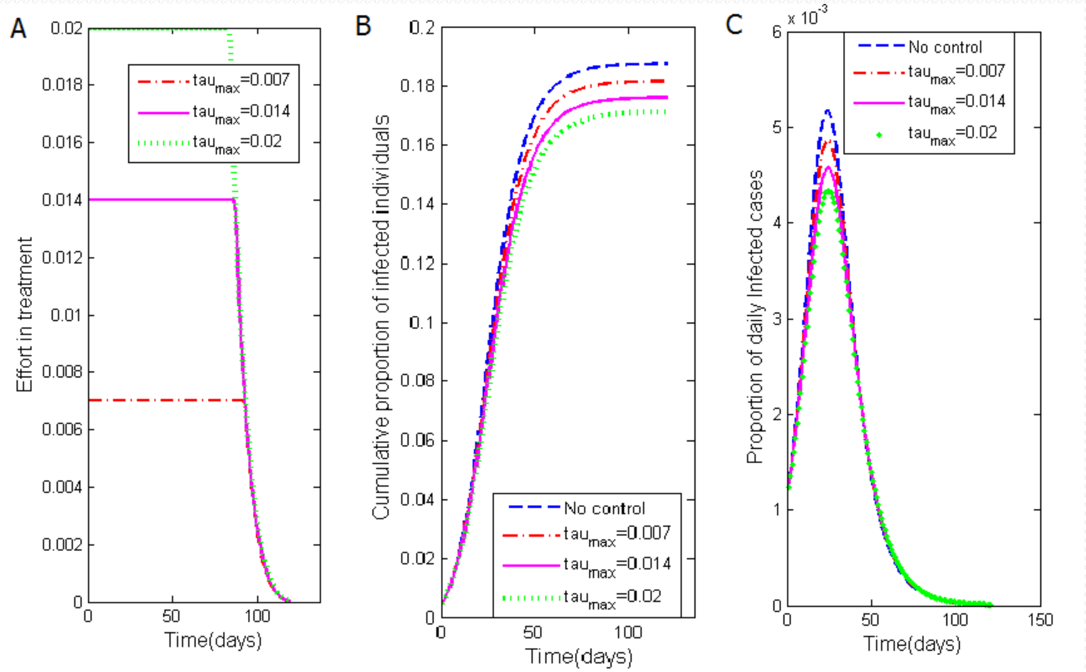


Figure 8: The impact of the control in Strategy 2 is reduced when the resources are limited. For a small upper bound, $\tau_{max} = 0.007$, we get a small reduction of the final epidemic size 5%. When the upper bound is $\tau_{max} = 0.02$, the final epidemic size is reduced by 13%.

Conclusions

- The use of single and dual strategies (social distancing and antiviral treatment) results in the reduction on the cumulative number of infected individuals.
- We compare the impact of relative costs on the effort carried out in the implementation of each single strategy (weight constants on controls) and also the use of limited resources (control upper bounds).
- Dual strategies have stronger impact in terms of the reduction in the final epidemic size, but it is more cost-expensive.
- Future work: we want to include a time delay in the application of policies

Acknowledgments

This project has been supported by grants from the National Science Foundation (NSF - Grant DMPS-0838705), the National Security Agency (NSA - Grant H98230 -09-1-0104), the Alfred P. Sloan Foundation; and the President and Provost Offices at Arizona State University. The Mathematical and Theoretical Biology Institute now hosted at the Mathematical, Computational and Modeling Science Center at ASU would like to give thanks to everybody involve with the program for the past 15 years.

Special thanks to Sunmi Lee, Aprillya Lanz and Carlos Castillo – Chavez for their support and contributions.

Thank you!