Interior Point Methods for a Two-Group Discrete Time Influenza Model

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Abstract

We formulate a discrete time model to identify and evaluate the role of optimal control strategies on influenza transmission. We divide the population in two subgroups defined according to the contact activity or susceptibility levels. The individuals are identified as susceptible, infectious, treated, and recovered. The potential effect of antiviral treatment considering unlimited and limited resources is evaluated, where an isoperimetric constraint is incorporated in the presence of limited resources. The optimal control problem is solved by using the primal-dual interior-point method that enforces epidemiological constraints explicitly. Our goal is to determine how treatment doses should be distributed in each group when the objective is to minimize the number of infected and the cost of treatment.

1 Introduction

It is well known that every year millions of individuals get "flu" and thousands die from seasonal influenza. New specific vaccines are developed and distributed each year. In the case of seasonal influenza, the focus is on protecting high risk individuals. However, the cost associated with lost life and productivity due to influenza must also be considered [15]. Continuous time models have been used to study influenza outbreaks and the impact of different control policies [4, 8, 13, 24, 25]. Optimal control methods are used to evaluate the impact of control policies in epidemiology and other fields [16, 21]. In the case of influenza, the cost of antiviral treatment or the cost of isolation of infectious individuals has also been addressed using continuos time models [19, 20]. Recently, the evaluation of influenza public health interventions using discrete epidemiological models has also been proposed [6, 27, 28]. The fact that most epidemiological data is discrete particulary justifies the use of a discrete time formulation.

Here we explore the role of heterogeneity via a discrete time epidemiological model involving two interacting groups, since the goal is to explore the role of different contacts or susceptibility levels. An optimal control problem is formulated to evaluate the effect of antiviral treatment in scenarios involving limited or unlimited resources. This model extends the discrete single-group influenza model analyzed in [12]. The optimal control problem is solved using the primal-dual interior-point method, which to the best of our knowledge has not been previously used to solve control problems in epidemiology. The benefit of *interior point methods* is that the inclusion of explicit inequality constraints is natural and more efficient.

This manuscript is organized as follow; in the Section 2, we introduce the epidemiological model and the optimal control problem associated. Our goal is to reduce the number of infected individuals at a minimal cost of treatment during a single epidemic outbreak. In Section 3, we present the basic ideas of interior point methods and the algorithm that we use in order to solve our problem. The results of selected numerical simulations are presented in Section 4, by considering different scenarios such as different activity or susceptibility levels under limited or unlimited resources. Finally, we present some discussions and conclusions in Section 5.

2 Epidemiological Model

A discrete time Susceptible-Infectious-Recovered (SIR) model was analyzed in [12]. The susceptible, infectious and recover individuals are represented by S, I, and R respectively. Births and deaths from natural causes and disease induced deaths are ignored ($N = S + I + R$); The subindex t denotes the number of individuals of each class at time t, and the range of $t = 1, 2..., n$ where n denotes the final time. The fraction of susceptible individuals at time t that get infected at time $t + 1$ is modeled by the function

$$G_t = \rho \frac{I_t}{N_t},$$

where ρ is the susceptibility rate. It is assumed that infectious individuals recover with probability σ (per generation). The model (without control) is given by the following system of nonlinear difference equations:

$$\begin{aligned} S_{t+1} &= S_t(1-G_t) \\ I_{t+1} &= S_t G_t + (1-\sigma)\,(1-\delta) I_t \\ R_{t+1} &= R_t + \sigma\,(1-\delta)\,I_t. \end{aligned} \tag{1}$$

Since many disease dynamics such as measles and influenza are strongly correlated with age [7], we want to extend Model (1) by considering that the total population is divided into two age groups. Groups can be defined according to contact activity or susceptibility levels. We assume that people mix homogeneously within its group and proportionaly between groups; this is known as proportionate mixing [5]. Epidemiological models with age structure have been considered in [7, 9, 14]. Now we introduce the group-structured model.

Let $N_i(t)$ be the number of individuals in group i at time t, $(i = 1, 2)$ and q_{ij} be the probability that somebody from Group i has contact with somebody from group j. If we assume that both groups are connected $(q_{ij} > 0)$ and we consider proportionate mixing [7], we have

$$q_{ij} = q_j = \frac{C_j N_j}{C_1 N_1 + C_2 N_2}, \tag{2}$$

where C_i is the average contact number of individuals in group i. For the properties of the contact matrix [23]

$$q_1 + q_2 = 1.$$

Now we generalize the single population model SIR model (1) to a two-group model. Let $S_i(t)$, $I_i(t)$, and $R_i(t)$ denote the number of susceptible, infectious, and recovered individuals in the ith group, $i = 1, 2$. We consider a single outbreak and people remain in the same group. We assume that infectious individuals from group i naturally recover with probability σ_i. The fraction of susceptible individuals on group i at time t that get infected at time $t + 1$ is modeled by the function

$$G_i(t) = \rho_i \left(q_1 \frac{I_1(t)}{N_1(t)} + q_2 \frac{I_2(t)}{N_2(t)} \right), \tag{3}$$

where ρ_i is the susceptibility rate for individuals in group $i = 1, 2$. In Group 1. Figure 1 ilustrate the diseases dynamics.

The model is given by the system of difference equations

$$\begin{aligned} S_i(t+1) &= S_i(t)(1-G_i(t)) \\ I_i(t+1) &= S_i(t)G_i(t) + (1-\sigma_i)\, I_i(t) \\ R_i(t+1) &= R_i(t) + \sigma_i I_i(t). \end{aligned} \tag{4}$$

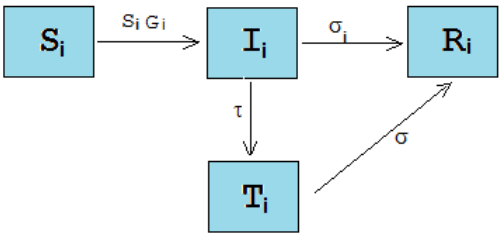

Figure 1: Diseases dynamics in Group i.

for $i = 1, 2$. The basic reproductive number is calculated by using the next generation operator [1], it is given by

$$R_0 = \frac{\rho_1 q_1}{1-(1-\sigma_1)(1-\delta_1)} + \frac{\rho_2 q_2}{1-(1-\sigma_2)(1-\delta_2)}.$$

Notice that there is a contribution from each group: it highlights that new infections can be generated from infected individuals in any group.

The next step is to include treatment as control policy in Model (4); we consider that a fraction $\tau_i(t)$ of infected individuals in group i gets treatment at time t. We assume that individuals (from any group) who get treatment recover with probability σ. Since treated individuals are still infectious with reduction parameter $0 < \epsilon_i < 1$, $i = 1, 2$ the function G_i given in (3) is modified as

$$G_i = \rho_i \left(q_1 \frac{I_1(t) + \epsilon_1 T_1(t)}{N_1} + q_2 \frac{I_2(t) + \epsilon_2 T_2(t)}{N_2} \right), \tag{5}$$

The model with control is given by the following system of difference equations:

$$\begin{array}{rcl} S_i(t+1) & = & S_i(t)(1 - G_i(t)) \\ I_i(t+1) & = & S_i(t)G_i(t) + (1-\tau_i(t))\,(1-\sigma_i)\,I_i(t) \\ T_i(t+1) & = & (1-\sigma)\,T_i(t) + \tau_i(t)\,(1-\sigma_i)\,I_i(t) \\ R_i(t+1) & = & R_i(t) + \sigma_i I_i(t) + \sigma T_i(t). \end{array} \tag{6}$$

Our goal is to minimize the number of infected individuals in both groups during the entire epidemic duration at a minimal cost; hence the optimal control problem is given by

$$\begin{array}{l} \min \dfrac{1}{2} \displaystyle\sum_{t=0}^{n-1} \left(B_{I_1} I_1(t)^2 + B_{\tau_1} \tau_1(t)^2 + B_{I_2} I_2(t)^2 + B_{\tau_2} \tau_2(t)^2 \right) \\ \text{s.t. Model (6), } 0 \le \tau_i \le 1 \end{array} \tag{7}$$

where n denotes the final time and the weight constants B_j for $j = \{I_i, \tau_i\}$ and $i = 1, 2$ represent the relative cost of treatment. We want to solve Problem (7) by considering

two scenarios: unlimited and limited doses of treatment. The first scenario is the problem given in (7). For the second one, we need to include the isoperimetric-constraint [20, 21]

$$\sum_{t=0}^{n-1} (\tau_1(t)I_1(t) + \tau_2(t)I_2(t)) = k, \tag{8}$$

where k represents the available number of treatment doses. A similar problem has been solved by considering limited vaccine for a continuous time influenza model [20] . The problem was solved by using the two-point boundary method; the authors remark that by including the isoperimetric-constraint, convergence issues have to be addressed. We will solve it by using the primal-dual interior-point method. We claim that the primal-dual interior-point method allows to include the new constraint more efficiently. Our goal is to determine how treatment doses should be distributed in each group in order to reduce the total number of infected at a minimal cost. In the next section we present the primal-dual interior point method.

3 Methodology

In this section, we present the methodology for solving unconstrained and constrained optimal control problems (7). Most of the optimal control problems on epidemiology are solved by using Pontryagin's maximum principle [16, 19, 20]. This principle provides the necessary conditions for finding an optimal solution [21], applying the two-point boundary method. We want to solve our problem by using the primal-dual interior-point method [3, 10, 22]. This technique has been applied successfully in different areas but to our knowledge, there is few evidences of applications on epidemiological problems. We present the basic ideas of primal-dual interior-point method in the next subsection.

3.1 Primal-Dual Interior-Point Method

Interior Point Methods (IPM) were introduced by Karmarkar in 1984 [17] for solving linear programming problems and his seminal work has been extended for solving large scale nonlinear programming problems. In particular we want to apply this method to our optimal control problem (7). Let us rewrite our Problem (7) as a nonlinear programming problem,

$$\begin{array}{ll} \min & f(y) \\ \text{s.t.} & E(y) = 0, \\ & y \geq 0, \end{array} \tag{9}$$

where

$$\begin{array}{rcl} \mathbf{y} & = & (S_1(1), I_1(1), T_1(1), \tau_1(0), \ldots, S_1(n), I_1(n), T_1(n), \tau_1(n-1), \\ & & S_2(1), I_2(1), T_2(1), \tau_2(0), \ldots, S_2(n), I_2(n), T_2(n), \tau_2(n-1)), \end{array} \tag{10}$$

and n is the final time. The objective functional is given by

$$f(y) = \frac{1}{2}\left(B_{I_1}\|\tilde{I_1}\|^2 + B_{\tau_1}\|\tau\|^2 + B_{I_2}\|\tilde{I_2}\|^2 + B_{\tau_2}\|\tau_2\|^2\right),$$

$f : \mathbb{R}^{8n} \to \mathbb{R}$, with $\tilde{I}_i = (I_i(0), I_i(1), \ldots, I_i(n-1))$ and $\tau_i = (\tau_i(0), \tau_i(1), \ldots, \tau_i(n-1))$ for $i = 1, 2$. From Model (6), we get the equality constraint $E : \mathbb{R}^{8n} \to \mathbb{R}^{6n}$,

$$E(y) = \begin{pmatrix} S_1(1) - S_1(0)(1 - G_1(0)) \\ I_1(1) - S_1(0)G_1(0) - (1 - \tau_1(0))\,(1 - \sigma_1)\,I_1(0) \\ T_1(1) - (1 - \sigma_2)\,T_1(0) - \tau_1(0)\,(1 - \sigma_1)\,I_1(0) \\ \vdots \\ S_1(n) - S_1(n-1)(1 - G_1(n-1)) \\ I_1(n) - S_1(n-1)G_1(n-1) - (1 - \tau_1(n-1))\,(1 - \sigma_1)\,I_1(n-1) \\ T_1(n) - (1 - \sigma_2)\,T_1(n-1) - \tau_1(n-1)\,(1 - \sigma_1)\,I_1(n-1) \\ S_2(1) - S_2(0)(1 - G_2(0)) \\ I_2(1) - S_2(0)G_2(0) - (1 - \tau_2(0))\,(1 - \sigma_1)\,I_2(0) \\ T_2(1) - (1 - \sigma_2)\,T_2(0) - \tau_2(0)\,(1 - \sigma_1)\,I_2(0) \\ \vdots \\ S_2(n) - S_2(n-1)(1 - G_2(n-1)) \\ I_2(n) - S_2(n-1)G_2(n-1) - (1 - \tau_2(n-1))\,(1 - \sigma_1)\,I_2(n-1) \\ T_2(n) - (1 - \sigma_2)\,T_2(n-1) - \tau_2(n-1)\,(1 - \sigma_1)\,I_2(n-1) \end{pmatrix}, \quad (11)$$

where G_i is given in (5). Hence the total population N is almost constant, we just have to consider S, I, and T because $R = N - S - I - T$. In the case of limited resources we need to include the isoperimetric constraint

$$\sum_{t=0}^{n-1} (\tau_1(t)I_1(t) + \tau_2(t)I_2(t)) = k,$$

where k represents the number of treatment doses available, it can be written as the inner product of $\boldsymbol{\tau}_i$ and $\tilde{\mathbf{I}}_i$, $(i = 1, 2)$

$$\boldsymbol{\tau}_1^T\tilde{\mathbf{I}}_1 + \boldsymbol{\tau}_2^T\tilde{\mathbf{I}}_2 - k = 0, \quad (12)$$

hence we modify the equality constraint given by (11) by adding the constraint (12), in this case $E : \mathbb{R}^{8n} \to \mathbb{R}^{6n+1}$.

Now we describe the primal-dual interior-point method used to solve problem (9). We define the Lagrangian associated to (9) as

$$L(y, w, z) = f(y) + E(y)^T w - y^T z,$$

where w and z are the lagrange multipliers associated with the equality and inequality constraint, respectively. Therefore the perturbed KKT conditions are given by

$$F_\mu(y,w,z) = \begin{bmatrix} \nabla_y L(y,w,z) \\ E(y) \\ YZe - \mu e \end{bmatrix} = 0, \tag{13}$$

where $\nabla_y L(y,w,z) = \nabla_y f + \nabla E^T w - z$, $Y = diag(y)$, $Z = diag(z)$, and $e = (1,\ldots,1) \in \mathbb{R}^{8n}$. The Newton's system associated with problem (9) is

$$F'_\mu(y,w,z)\Delta\nu = -F_\mu(y,w,z) \tag{14}$$

where

$$F'_\mu(y,w,z) = \begin{bmatrix} \nabla^2 L & \nabla E^T & -I \\ \nabla E & 0 & 0 \\ Z & 0 & Y \end{bmatrix} \quad \text{and} \quad \Delta\nu = \begin{bmatrix} \Delta y \\ \Delta w \\ \Delta z \end{bmatrix}.$$

The standard Newton's method assumptions for the convergence [10] of problem (9) are given by:

1. There exists $\nu^* = (y^*, w^*, z^*)$, solution to problem (9).
2. The jacobian matrix $F'_\mu(\nu^*)$ is nonsingular.
3. The jacobian operator F'_μ is locally Lipschitz continuous at ν^*.

To simplify the system (14), we derive a reduced system written as follows:

$$\begin{bmatrix} Y\nabla^2 L + Z & Y\nabla E^T \\ \nabla E & 0 \end{bmatrix} \begin{bmatrix} \Delta y \\ \Delta w \end{bmatrix} = \begin{bmatrix} -Y\nabla f - Y\nabla E^T W + \mu e \\ -E \end{bmatrix}, \tag{15}$$

with

$$\Delta z \;=\; \nabla^2 L\Delta y + \nabla E^T \Delta W + \nabla y + \nabla E^T W - z. \tag{16}$$

Therefore, the reduced system of equations (15) has some advantages over (14), there is a considerable size reduction in the system being solved ($16n \times 16n$) and the condition number of the associated matrix to the system is smaller that the one in system (14).

We use a *path-following* strategy [3] to solve (15). For $\mu > 0$ and working from the interior $(y,z) > 0$, we apply a linesearch Newton's method [22] to the perturbed KKT conditions (13). An optimal solution is reached when the perturbation parameter μ goes to zero. Let us present the primal-dual interior-point algorithm used to solve the nonlinear programming problem (9).

Algorithm 1 Primal-Dual Interior-Point Algorithm

1: Consider an initial interior point $v_0 = (y_0, w_0, z_0)$, i.e., $(y_0, z_0) > 0$, choose $\sigma \in (0, 1)$.
2: **for** $k = 0, 1, 2 \ldots$ until convergence **do**
3: Set the perturbed parameter $\mu_k = \sigma \frac{(y_k)^T z_k}{10n}$.
4: Solve the reduced system (15) for $\Delta\nu = (\Delta y, \Delta w)$, and solve (16) for Δz.
5: Maintain y, z positive. Calculate $\tilde{\alpha_k}$ according to

$$\tilde{\alpha_k} = \min\left(\frac{-1}{\min(Z^{-1}\Delta z, -1)}, \frac{-1}{\min(Y^{-1}\Delta y, -1)}\right)$$

6: Force a descent direction, For $i = 0, 1, 2, \ldots$, set $\alpha_{k+1} = \left(\frac{1}{2}\right)^i \tilde{\alpha_k}$ until

$$M(v_k + \alpha_{k+1}\Delta v) < M(v_k) + 10^{-4}\alpha_{k+1}\nabla M^T \Delta v$$

where $M = ||F_\mu||^2$, for F_μ as in (13).
7: Update $v_{k+1} = v_k + \alpha_{k+1}\Delta v$.
8: **If** $||F_\mu|| \leq \epsilon$, break,
9: **end for**

The numerical results of selected simulations generated by the implementation of the primal-dual interior-point method are discussed in the next chapter. Since the solution is based on Newton's method, the initial conditions are choosen carefully in order to get convergence.

4 Numerical Results

In this section we present some results of selected numerical simulations under various scenarios. First we consider both groups with the same population size under unlimited and limited treatment resources. In the first case, we consider no restrictions of antiviral treatment, in the second one we assume some restrictions in the treatment supply. Finally we present a more realistic scenario with different population sizes. For all simulations, we solve an optimal control problem by using the primal-dual interior-point method given in (3.1). In the case of limited resources, we include an isoperimetric constraint [20, 21]. For each case, the proportion of infected individuals generated in the absence of control or in the presence of control are compared. In these simulations the weight constants are selected in part to facilitate computational issues, IPM is sensitive to these values. We assume a moderate value of R_0, $(1.5 - 1.7)$. The final time, 180 days, is chosen for all simulations. The baseline parameter values are given in Table 1.

Table 1: Definition of parameters and baseline values.

Parameter	Value	Definition
σ_i	$\frac{1}{7}$	Recovering probability without treatment in Group $i = 1, 2$
σ	$\frac{1}{5}$	Recovering probability with treatment in each group
ϵ	0.3	Transmissibility reduction of the treated class
δ	0.001	Mortality rate
ρ_i	$0.135 - 1.9$	susceptibility rate for individuals in Group $i = 1, 2$
C_i	$0.003 - 0.01$	Average contact rate of individuals in Group $i = 1, 2$
B_j	$0.3 - 1$	Weigh constants in the objective function, $j = \{I_i, \tau_i\}$ and $i = 1, 2$

4.1 Unconstrained Formulation Problem

By considering the case of unlimited doses of treatment, we divide the total population into two groups with same population size and we consider three different scenarios. In the first one, both groups have the same activity level and same susceptibility, basically we want to validate our IPM algorithm. As we define in section 2, C_i and ρ_i are the average contact and the susceptibility levels for individuals in group $i = 1, 2$, respectively. For the second scenario, we assume that Group 1 is more active than Group 2, hence the average contact number is higher in Group 1 than Group 2 ($C_1 > C_2$) and both groups have the same susceptibility level ($\rho_1 = \rho_2$). For each scenario, Figures 2 - 8 show the control effort, the proportion of infected individuals and the final epidemic size in Group 1 on figures in the top (A, B, and C). The ones in the bottom (D, E, and F) show the control effort, the proportion of infected individuals and the final epidemic size in Group 2.

Scenario 1: Same Activity Level and Same Susceptibility
Since both groups have the same population size and similar behavior, the optimal control solution requires the implementation of the same amount of treatment on both groups (Figures 2A and 2D) and therefore we get the same reductions in the final epidemic size, 14% in each group, Figures 2C and 2F. The implementation of treatment strategy move the epidemic peak, without treatment is on day 50, while in the presence of treatment is around day 60 (Figures 2B and 2E).

Scenario 2: Same Activity Level, Higher Susceptibility in Group 1
Figures 3A and 3D show the optimal control solution when both groups with the same size population have the same activity level but Group 1 is more susceptible than Group 2. Since Group 1 has higher susceptibility, the optimal control solution requires the application of higher values of treatment in this group. The reduction in the final epidemic is given by 11% and 13% in Groups 1 and 2, respectively, (Figures 3C and 3F). This reduction is smaller in Group 1 because the number of infected individuals is higher in this group.

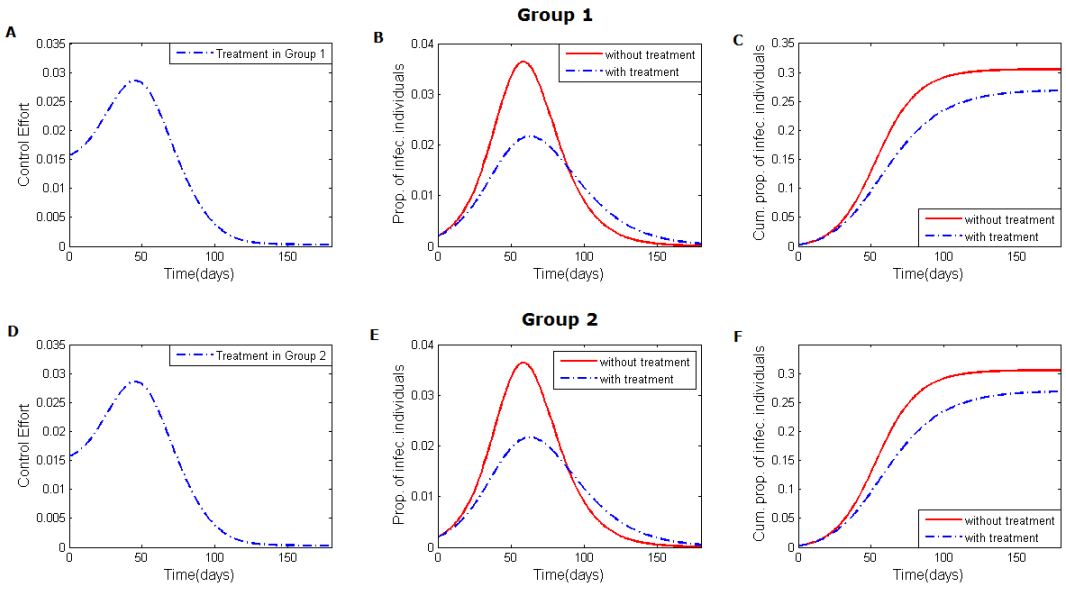

Figure 2: In the case of same population size in Group 1 and 2, the first scenario considers both groups with the same susceptibility and same activity level. Since both groups have similar behavior, the optimal control strategy requires the implementation of the same amount of treatment in both groups. The final epidemic size is reduced by 14% in each group.

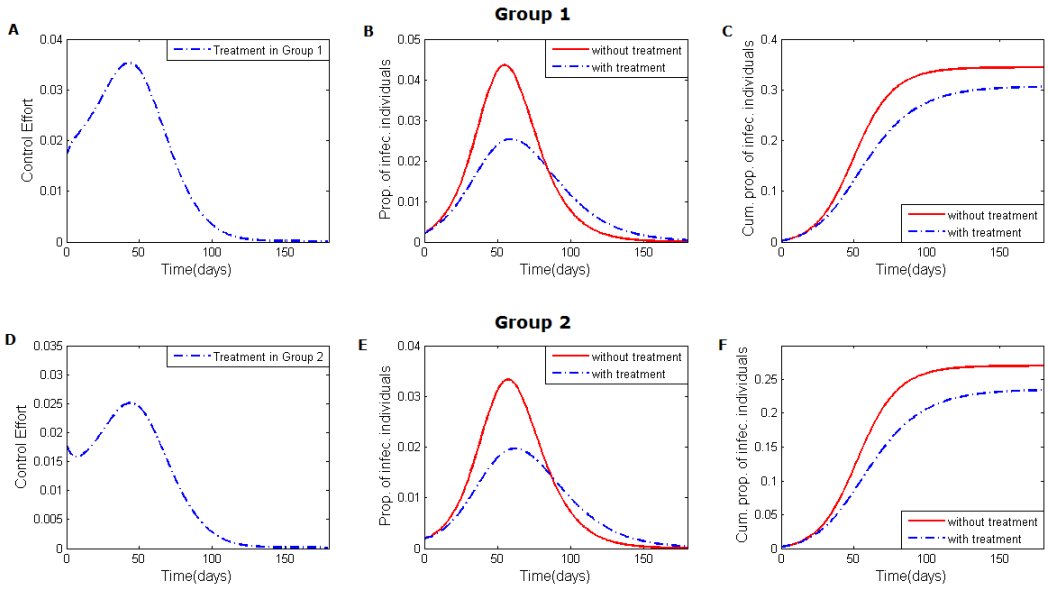

Figure 3: For Scenario 2, Group 1 is more susceptible than Group 1 but they have the same activity level. Since Group 1 is the high risk group, the optimal control strategy requires the implemetation of high control value in this group, however the number of infected individuals is higher in Group 1 and the reduction in the final epidemic size will be bigger in Group 2.

4.2 Constrained Treatment Strategy

In the case of limited resources, we solve the problem by including the isoperimetric constraint given in (8), where k represents the availability in treatment doses. We consider both groups with the same population size under three different scenarios. In Scenario 1 both groups have the same activity level and they are equally susceptible, i.e. $C_1 = C_2$ and $\rho_1 = \rho_2$. In the case of Scenario 2, they have the same susceptibility but Group 1 is more active than Group 2, $C_1 > C_2$. Finally for Scenario 3, we consider that both groups have the same activity level but Group 1 is more susceptible than Group 2, then $\rho_1 > \rho_2$. For each scenario we assume a moderate value of R_0 (1.5-1.8). For each case, we present the proportion of infected individuals generated in the absence of control or in the presence of control for different values of treatment doses k. Figures 4, 5, and 6 show the optimal control function, the proportion of infected individuals and the cumulative proportion of infected individuals in both groups under each scenario.

Scenario 1: Same Activity Level and Same Susceptibility in Each Group
Since both groups have the same behavior, the treatment should be distributed likewise on each population (Figures 4A and 4D). Three values of k are used, by assuming that 4%, 7%, and 11% of the infected individuals get treatment; the final epidemic size is reduced by 4.5%, 8.1%, and 14.7% for each value of k, respectively. When resources are highly limited 4% and 7%, Figures 4A and 4D show that the maximum effort in control is applied at the begining of the epidemic until all the resources are depleted (70 and 80 days, respectively).

Scenario 2: Same Activity Level, High Susceptibility in Group 1
Figure 5 shows the results for Scenario 2. The optimal control solution shows that more effort should be implemented in Group 1 (Figure 5A and 5C), since this is the high risk group; however the proportion of infected individuals is higher in Group 1 (Figures 5B and 5D). By using different values of k, 3%, 6%, and 13%, the final epidemic size in Group 1 is reduced by 2.4%, 5.8%, and 16% in each case; For Group 2, it is reduced by 3%, 7%, and 19%. Althoug the optimal solution allows the implementation of higher effort in Group 1, the reduction in the final epidemic size is higher in Group 2. For small values of k, (3% and 6%), Figures 5A and 5D show that in both groups, the maximum effort in control is applied at the begining of the epidemic, 55 and 75 days respectively.

Scenario 3: Same Susceptibility, High Activity Level in Group 1
Figure 6 shows that in the case of Scenario 3, Group 1 has more activity level than Group 2 but they have the same susceptibility, the optimal control solution requires the application of higher values of treatment in Group 1 (Figures 6A and 6D), however the number of infected individuals is the same in both groups (Figures 6B and 6E). For different values of k (4%, 7% and 14%), Figures 6C and 6E shows that the final epidemic size is reduced by 3%, 9% and 19% respectively.

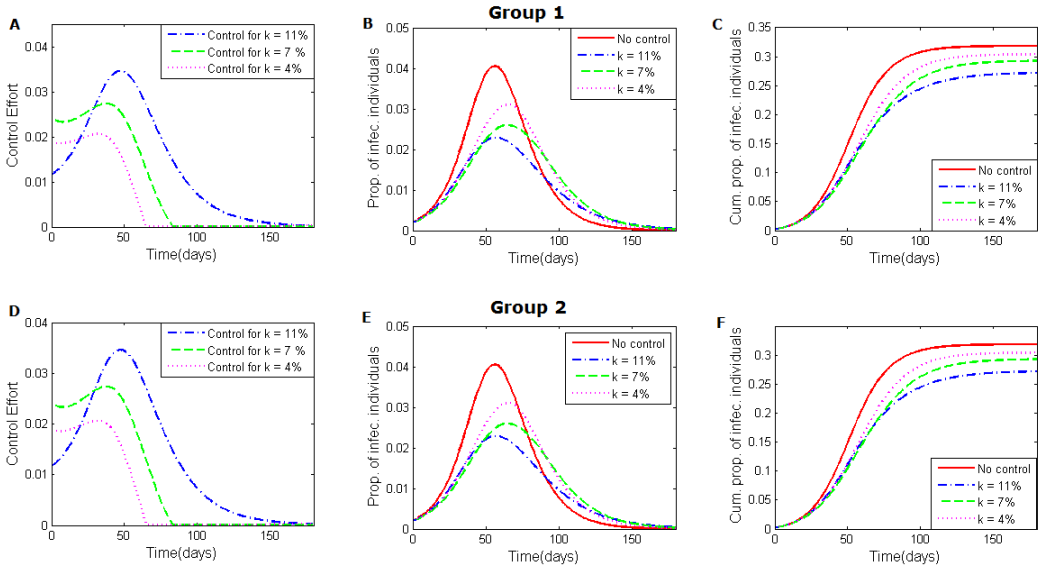

Figure 4: For Scenario 1, since both groups have similar behavior and same population size, the resources have to be distributed likewise. Figures A and D show that in the case of very limited resources (4 % and 7%),the maximum effort in control have to be implemented at the begining of the epidemic, until all the resources are spent.

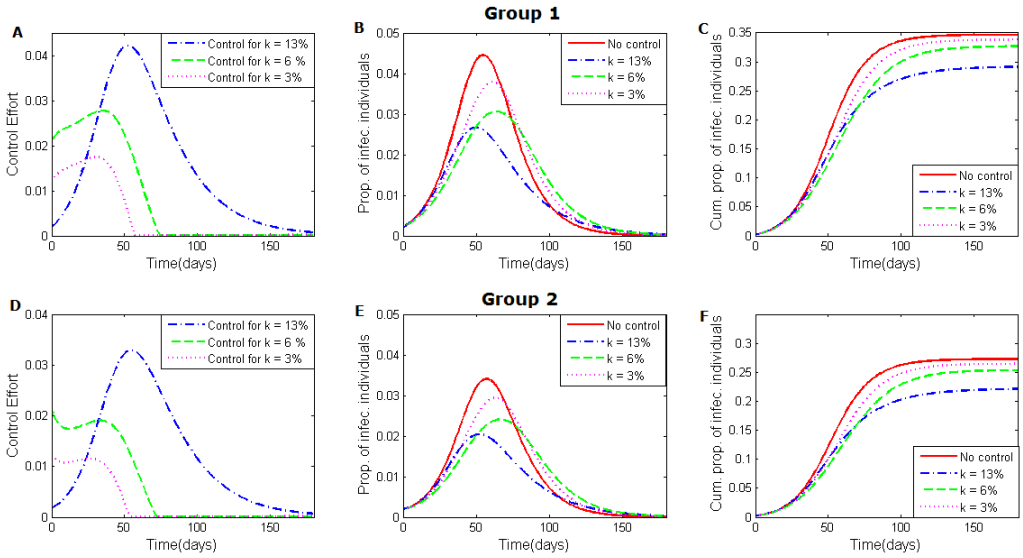

Figure 5: For Scenario 2, since Group 1 is the high risk one, more effort have to be applied in this group (Figure A and D) however for each value of k the reduction in the final epidemic size is higher in Group 2.

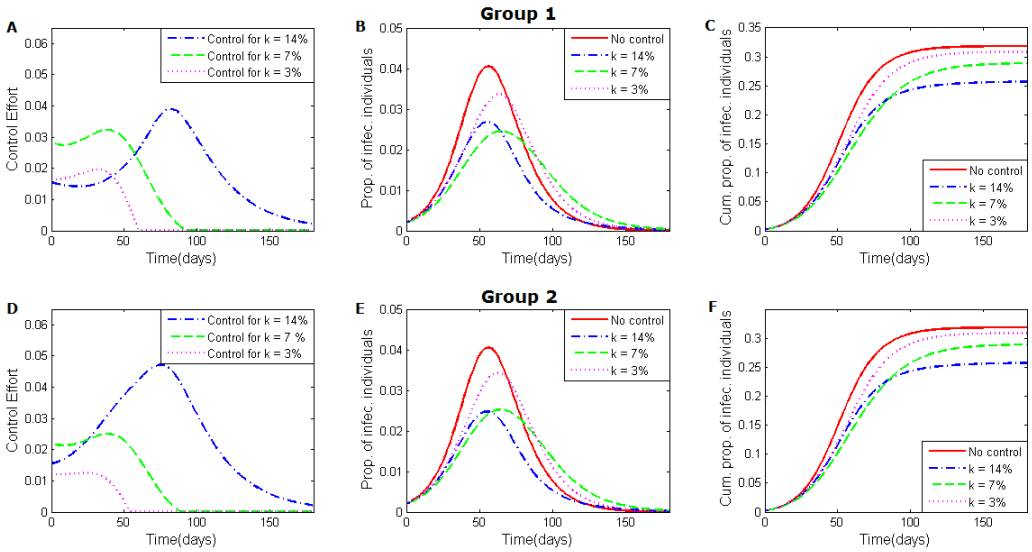

Figure 6: For Scenario 3, since Group 2 has high activity level, more control has to be implemented in this group, however since the susceptibility is the same for both groups, the number of infected individuals is alike for Group 1 and Group 2.

5 Seasonal Influenza

Finally, we consider a more realistic scenario, we divide the total population into two groups with different population sizes. Group 1 is given by 12.5% of the population aged 65 or more, and Group 2, 87.5% of the population aged less than 65 [5]. For these simulations we assume $R_0 = 1.5$ and we consider seasonal influenza, it is Group 1 is the high risk population ($\rho_1 > \rho_2$). For Scenario 1, we assume same activity level ($C_1 = C_2$); for Scenario 2 we assume that Group 2 is more active than Group 1($C_2 > C_1$).

Scenario 1: High Susceptibility in Group 1 and Same Activity in Both Groups

Figure 7 shows the results for Scenario 1. The optimal control solution shows that the amount of treatment that should be implemented is a little bit higher in Group 2 because it has a bigger population size (Figure 7A and Figure 7D). The final epidemic size in Group 1 is reduced by 10.7% with the implementation of the optimal control treatment. In the case of Group 2, is reduced by 25% (Figure 7C and Figure 7F).

Scenario 2: High Susceptibility and Less Activity Level in Group 1

The results for Scenario 2 are shown on Figure 8. since we have Group 2 as the more active one, then the optimal control requires more effort for this group than for the other; Figure 8D shows that we need to apply twice the treatment for Group 2 than for Group 1 (Figure 8A). The reduction in the final epidemic size is given by 8.2% and 24.9% in Groups 1 and 2 respectively.

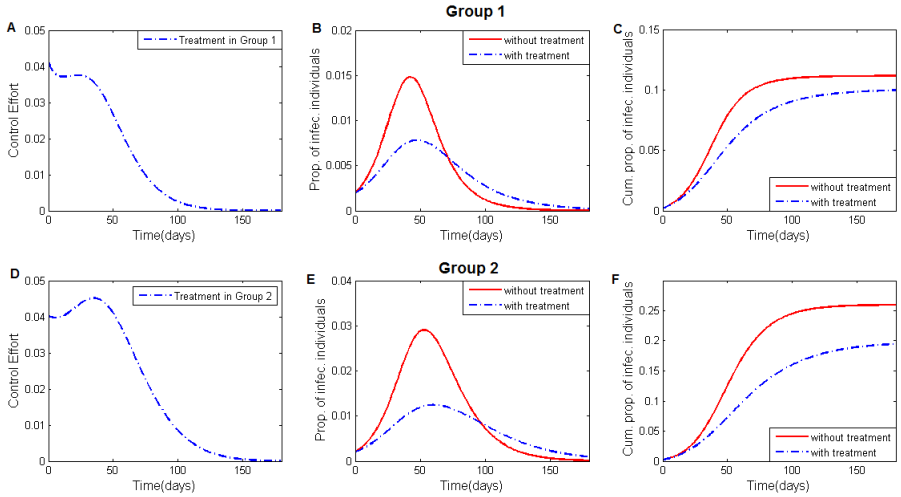

Figure 7: For Scenario 1, Group 1 (12.5 % of the total population) is the high risk population, both groups have the same activity level. Because of the size population, the control effort is a little big higher in Group 2 and therefore the reduction in the final epidemic size is higher in Group 2 (25%) than Group 1 (10.7%).

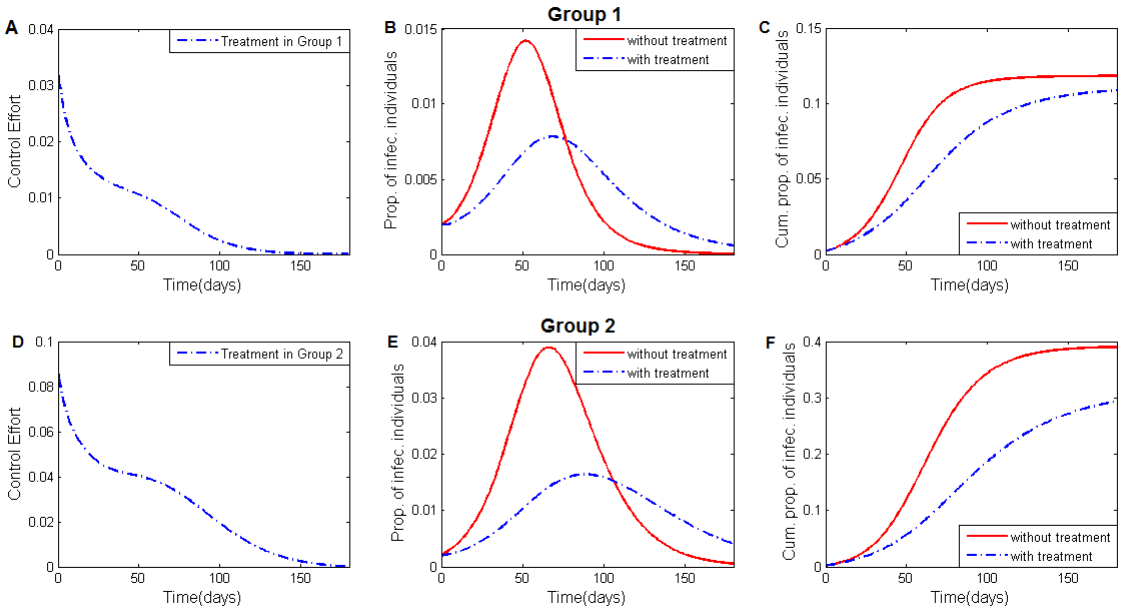

Figure 8: For Scenario 2, Group 1 (12.5 % of the population) is more susceptible but less active than Group 1. Since Group 2 is more active, more effort has to be applied in this group. Figure D shows that we need to apply twice the treatment for Group 2 than for Group 1 (Figure A).

6 Discussion

We present a two-age group discrete influenza model when the population is divided into susceptible, infected, treated, and recover individuals. An optimal control problem is formulated in order to reduce the number of infected individuals during a single influenza outbreak. We analyze different scenarios by considering same and different population sizes in each group. We also consider the case of unlimited resources by introducing an isoperimetric constraint. We solve the problem by using the primal-dual interior-point method (IPM), in contrast to the two point boundary method that is most used in optimal control problems in biological applications [11, 16, 19–21]. Interior Point Methods have become a popular choice for solving large scale constrained optimization problems. Its numerical advantages first demonstrated in the seminal work of Karmarkar [17], have led Interior point methodologies to be implemented in a variety of applications whose model induces a constrained optimization problem. This applications include fields in economics, machine learning, medical imaging, and geophysics [2, 18, 26] just to mention a few. As far as we know it has not been previously used to solve control problems in epidemiology. From our simulations we found that IPM allows to incorporate inequality constraints and the isoperimetric constraint in a more efficient way than the two point boundary method. However, we find that the solution is very sensitive to initial conditions since the IPM is based on Newton Method. We need to have good initial conditions in order to guarantee convergence.

In all scenarios, we find that the implementation of treatment reduces the number of infected individuals at a minimal cost. In the case of two groups with same population size and similar behavior, we get the same optimal control solution and therefore the same reduction in the final epidemic size. If one of the groups is more susceptible, more effort has to be implemented in that group but the reduction in final epidemic size will be bigger in the less susceptible group. In the case of limited resources, we found that the maximum effort in control have to be implemented at the beginning of the epidemic until all the resources are used.

The results are sensitive to the population size, in the case of small size population with high susceptibility (Group 1), the control effort is a bit higher in Group 2, (the one with big size population) when they have same activity level. However if we have a higher activity level in Group 2, the treatment has to be twice in this group even though Group 1 is more susceptible. We conclude than more effort has to be applied in the group with a higher activity level.

Acknowledgments

We would like to thank Dr. Carlos Castillo-Chavez, Executive Director of the Mathematical and Theoretical Biology Institute (MTBI), for giving us the opportunity to participate in this research program. We would also like to thank Co-Executive Summer Directors Dr. Erika T. Camacho and Dr. Stephen Wirkus for their efforts in planning and executing the day to day activities of MTBI. Finally, we want to give special thanks to Dr. Karen Rios-Soto, Dr. Jose Flores, and Nancy Hernadez for their comments and suggestions.

This research was conducted in MTBI at the Mathematical, Computational and Modeling Sciences Center (MCMSC) at Arizona State University (ASU). This project has been partially supported by grants from the National Science Foundation (NSF - Grant DMPS-0838705), the National Security Agency (NSA - Grant H98230-11-1-0211), the Office of the President of ASU, and the Office of the Provost of ASU. The first author was partially supported by international Fellowship from AAUW.

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