Optimal Control for a Discrete Time Influenza Model

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Abstract. We formulated a discrete time model in order to study optimal control strategies for a single influenza outbreak. In our model, we divided the population into four classes: susceptible, infectious, treated, and recovered individuals. The total population was divided into subgroups according to activity or susceptibility levels. The goal was to determine how treatment doses should be distributed in each group in order to reduce the final epidemic size. The case of limited resources is considered by including an isoperimetric constraint. We found that the use of antiviral treatment resulted in reductions in the cumulative number of infected individuals. We proposed to solve the problem by using the primal-dual interior-point method that enforces epidemiological constraints explicitly.

Keywords: Influenza, Optimal Control, Interior-Point methods, Epidemiology.

1 Introduction

Continuous time models have been used to study influenza outbreaks and the impact of different control policies [4,9,15]. In the case of influenza, the cost of antiviral treatment or the cost of isolation of infectious individuals has also been addressed using continuous time models [11,12]. Recently, the evaluation of influenza public health interventions using discrete epidemiological models has been proposed [2]. We explore the role of heterogeneity via a discrete time epidemiological model involving two interacting groups. An optimal control problem is formulated to evaluate the effect of antiviral treatment in scenarios involving limited or unlimited resources. The optimal control problem is solved using the primal-dual interior-point method, which to the best of our knowledge has not

L.F. Castillo et al. (eds.), *Advances in Computational Biology*,
Advances in Intelligent Systems and Computing 232,
DOI: 10.1007/978-3-319-01568-2_33,

been previously used to solve control problems in epidemiology. This method allows an efficient inclusion of explicit inequality constraints. In this paper, we introduce the epidemiological model and the optimal control problem in Section 2, the basic ideas of interior point methods are introduced in Section 3. 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.

2 Problem Formulation

The dynamics of many diseases such as measles and influenza are strongly correlated with age [3]. Epidemiological models with age structure have been considered for the continuous case in [3,5,10]. We divide the population into 2 subgroups. 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 [3], we have $q_{ij} = q_j = \frac{C_j N_j}{\sum_{k=1}^{m} C_k N_k}$, where C_i is the average number of contacts per unit of time. Let $S_i(t)$, $I_i(t)$, $T_i(t)$, and $R_i(t)$ denote the number of susceptible, infectious, treated and recovered individuals in the ith group. 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. We consider that the fraction of infected individuals in group i who get treatment each generation is modeled by $\tau_i(t)$. Since treated individuals are still infectious, the fraction of susceptible individuals on group i at time t that get infected at time $t + 1$ is modeled by the function:

$$G_i = \rho_i \sum_{j=1}^{2} \left(q_j \left(\frac{I_j(t) + \epsilon_j T_j(t)}{N_j} \right) \right), \tag{1}$$

where ϵ_j represents the effectiveness of treatment for individuals on group j, with $0 < \epsilon_j \leq 1$. We assume that individuals (from any group) who get treatment recover with probability σ. The model with control is given by the following system of difference equations:

$$\begin{aligned} S_i(t+1) &= S_i(t)(1 - G_i(t)) \\ I_i(t+1) &= S_i(t)G_i(t) + (1 - \tau_i(t))\,(1 - \sigma_i)\,I_i(t) \\ T_i(t+1) &= (1 - \sigma)\,T_i(t) + \tau_i(t)\,(1 - \sigma_i)\,I_i(t) \\ R_i(t+1) &= R_i(t) + \sigma_i I_i(t) + \sigma T_i(t). \end{aligned} \tag{2}$$

In the absence of control, the model is reduced to an SIR model, the basic reproductive number R_0 is given by [8] $R_0 = \sum_{i=1}^{2} \frac{\rho_i q_i}{1-(1-\sigma_i)}$. Now we introduce the optimal control problem associated with the group-structured model (2). Our goal is to minimize the number of infected individuals in each group over a

finite interval $[0, n]$, by using the least amount of treatment. The optimal control problem can be written as:

$$\min \frac{1}{2} \sum_{i=1}^{2} \left(\sum_{t=0}^{n-1} \left(B_{I_i} I_i(t)^2 + B_{\tau_i} \tau_i(t)^2 \right) \right), \text{subject to Model (2)}, \tag{3}$$

where n denote the final time. The weight constants B_j, $(j = I_i, \tau_i)$ are a measure of the *relative* cost of interventions over $[0, n]$. In particular, B_{τ_i} denote the relative costs associated with the implementation of antiviral treatment in group i, respectively.

3 Methodology

The problem is solved by using the primal-dual interior-point method [6,8,14]. Interior-Point Methods (IPM) are algorithms used to solve linear and nonlinear optimization problems. Contrary to the simplex method, which finds an optimal solution by testing the adjacent vertices of a feasible set, IPM find optimal solutions by crossing the interior of a feasible region. Computationally, IPM are more efficient than the simplex method because they have polynomial complexity. In addition, the simplex method finds solutions at the corner points only, while IPM may find solutions in the interior as well.

We rewrite Problem (3) as a nonlinear programming problem:

$$\min f(y), \text{ s.t. } E(y) = 0, \ 0 \leq y \leq y_{\max}, \tag{4}$$

where $\mathbf{y} = \begin{bmatrix} y_1 \\ y_2 \end{bmatrix}$, $\mathbf{y}_i = [S_i(1), I_i(1), T_i(1), \tau_i(0), \ldots, S_i(n), I_i(n), T_i(n), \tau_i(n-1)]^T$, for $i = 1, 2$ and the final time n. The objective functional is given by:

$$f(y) = \frac{1}{2} \sum_{i=1}^{2} \left(B_{I_i} \|\tilde{I}_i\|^2 + B_{\tau_i} \|\tau_i\|^2 \right),$$

$f : \mathbb{R}^{8 \cdot n} \to \mathbb{R}$, with $\tilde{I}_i = (I_i(0), I_i(1), \ldots, I_i(n-1))^T$ and $\tau_i = (\tau_i(0), \tau_i(1), \ldots, \tau_i(n-1))^T$, for $i = 1, 2$. From Model (2), we get the equality constraint $E : \mathbb{R}^{8 \cdot n} \to \mathbb{R}^{6 \cdot n}$, $E(y) = \begin{pmatrix} E_1(y) \\ E_2(y) \end{pmatrix}$, where $E_i(y)$, for $i = 1, 2$ is defined from (2) [8]. Now we consider a more realistic scenario when treatment supplies are limited. We modify Problem (3) by including the "isoperimetric" constraint [12,13]

$$\sum_{i=1}^{2} \left(\sum_{t=0}^{n-1} (\tau_i(t) I_i(t)) \right) = k, \tag{5}$$

where k represents the available number of treatment doses and n the final time. Notice that (5) can be written as $\sum_{i=1}^{2} \boldsymbol{\tau}_i^T \tilde{\mathbf{I}}_i - k = 0$. A similar problem has been solved in [12] by considering limited vaccine in a continuous time influenza

model. The problem was solved by including a new state variable related to the isoperimetric constraint, which requires boundary conditions at $t = 0$ and $t = n$; The authors of [12] remark that convergence issues have to be addressed. We solve the new problem by using the primal-dual interior-point method, which allows the inclusion of the new constraint more efficiently. The optimal control problem can be written as (4) where the previous equality constraint is modify as $E : \mathbb{R}^{4\cdot n\cdot m} \to \mathbb{R}^{3\cdot n\cdot m+1}$, $E(y) = \left(E_1(y), E_2(y), \boldsymbol{\tau}_1^T\tilde{\mathbf{I}}_1 + \boldsymbol{\tau}_2^T\tilde{\mathbf{I}}_2 - k\right)^T$.

The Lagrangian function associated with Problem (4) is defined by:

$$L(y, w, z_1, z_2) = f(y) + E(y)^T w - y^T z_1 - (y_{\max} - y)^T z_2,$$

where w, z_1, and z_2 are the Lagrange multipliers associated with the equality and inequality constraints, respectively. Therefore the perturbed KKT conditions [8,14] are given by:

$$F_\mu(y, w, z_1, z_2) = [\nabla_y L, E(y), YZ_1 - \mu e, (Y_{\max} - Y)Z_2 - \mu e]^T = 0, \qquad (6)$$

where $Y = \text{diag}(y)$, $Y_{\max} = \text{diag}(y_{\max})$, $Z_1 = \text{diag}(z_1)$, $Z_2 = \text{diag}(z_2)$, and $e = (1, \ldots, 1)^T \in \mathbb{R}^{8n}$. The primal-dual interior-point algorithm for the nonlinear programming problem (4) is presented in [8]. The results of some numerical simulations both in the case of limited and unlimited supplies for different scenarios are presented in the next section.

4 Numerical Results

In this section, we present some results of selected simulations under various scenarios. For each case, we compare the proportion of infected individuals generated in the absence or in the presence of control. The baseline parameter values are given in [8]. For scenario 1, we consider the case of seasonal influenza. We divide the total population into two groups with different population sizes. Group

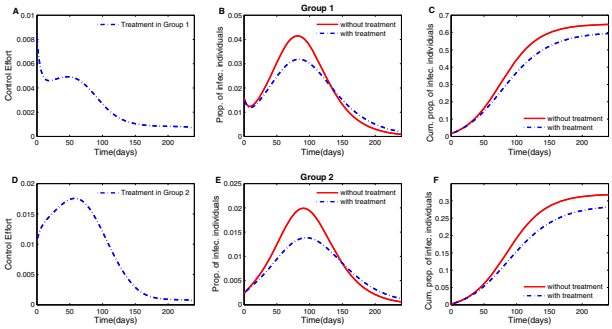

Fig. 1. In scenario 1, Group 1 (12.5 % of the population) is more susceptible but less active than Group 1. Since Group 2 is more active, more effort has to be applied in this group.

1 is given by 12.5% of the population aged 65 or more, and Group 2 is 87.5% of the population aged less than 65 [1]. We assume that $R_0 = 1.27$ and that Group 1 is the high risk population ($\rho_1 > \rho_2$). The final time is 240 days. Figure 1 shows the results for Scenario 1. Since we have Group 2 as the more active one, the optimal control requires more resources for this group than for Group 1; Figure 1D shows that we need to apply twice the treatment for Group 2 than for Group 1 (Figure 1A). The reduction on the final epidemic size is given by 8% and 12% in Groups 1 and 2, respectively.

The case of limited resources is considered in Scenario 2 and 3. We assume that both groups have the same population size. In Scenario 2 we assume same activity level but Group 1 is more susceptible than Group 2, $\rho_1 > \rho_2$. For Scenario 3, we consider same susceptibility but Group 1 is more active than Group 2, $C_1 > C_2$. Figures 2 and 3 show the optimal control function, the proportion of infected individuals, and the cumulative proportion of infected individuals in both groups under each scenario for different values of treatment doses k.

Figure 2 shows the results for Scenario 2. The optimal control solution shows that more resources should be used for Group 1 (Figure 2A and 2C), since this is the high risk group; however the proportion of infected individuals is higher in Group 1 (Figures 2B and 2D). By using different values of k, 3%, 6%, and 13%, the final epidemic size in Group 1 is reduced by 2.4%, 6%, and 16% for each case; for Group 2, it is reduced by 3%, 7%, and 19%. Although the optimal solution allows the use of more resources towards Group 1, the reduction on the final epidemic size is a little higher in Group 2. For small values of k, (3% and 6%), Figures 2A and 2D show that in both groups, the resources should be used at the beginning of the epidemic, 55 and 75 days respectively.

In the case of Scenario 3, Group 1 has a higher activity level than Group 2 but the same susceptibility. Figure 3 shows that the optimal control solution requires the application of more treatment doses in Group 1 (Figures 3A and 3D); however, the proportion of infected individuals is the same in both groups

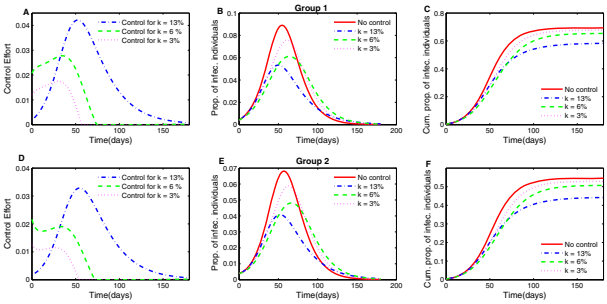

Fig. 2. For Scenario 2, since Group 1 has higher activity level, more resources need to be used towards this group (Figure A and D) however for each value of k the reduction on the final epidemic size is higher in Group 2.

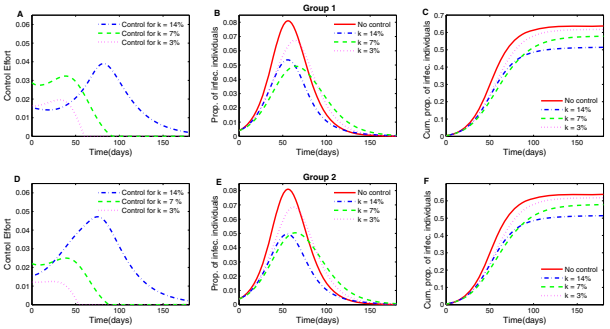

Fig. 3. For Scenario 3, since Group 2 is at higher risk, more resources need to be used for this group. However, since the activity level is the same for both groups, the number of infected individuals is similar for Group 1 and Group 2.

(Figures 3B and 3E). For different values of k (4%, 7%, and 14%), Figures 3C and 3E shows that the final epidemic size is reduced by 5%, 8%, and 15% respectively.

In all scenarios, we find that the use of treatment reduces the number of infected individuals. If one of the groups is more susceptible, more effort has to be implemented in that group, but the reduction in the final epidemic size will be larger in the less susceptible group. In addition, if we consider limited resources, we found that the resources should be used at the beginning of the epidemic until all the resources are used.

5 Conclusions

We formulated a discrete group-structured model under the assumption that people mix more with individuals in the same group and groups are mixing randomly. We introduced an optimal control problem (3) in order to study how treatment should be implemented in each group in order to minimize the number of infected individuals at the end of the epidemic. In all scenarios, we found that the implementation of treatment reduces the number of infected individuals at a minimal cost. If one of the groups is more susceptible, more effort has to be implemented in that group but the reduction in the 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. Most of the optimal control problems in this area are solved by using Pontryagins Maximum Principle [7,12,13] We proposed to solve it by using the primal-dual interior-point method. This methodology allows the inclusion of constraints in a simpler way, specially in the case of isoperimetric constraint.

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