An Optimal Intervention Experiment with Multiple Controls

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Abstract

This work studies an optimal control problem for a discrete-time Susceptible/Infective/Removed (SIR) deterministic epidemic model with a finite time horizon and multiple controls. The model used in our paper is inspired from [Iacoviello and Liuzzi, 2008], but our approach is new and different from classical population models based on differential equations. We seek first to show that the problem can be modeled and solved discretely using dynamic programming, eschewing all discussions of convergence and existence of solutions. Moreover, the discrete approach is more closely aligned to the real situation as patients and controls are discrete entities. To further justify the results, we also explore a case study with real data on the measles outbreak in Africa from 1980 to 2005 and show that a multi-level, multi-control approach would have been less costly and more effective in reducing the effect of measles.

1 Introduction

There are numerous epidemiological models with various epidemiological classes, often abbreviated by M, S, E, I, and R, used in epidemic intervention and modeling techniques. M represents the class of infants who have passive immunity, S represents the susceptible class (those capable of becoming infected), E represents the exposed class (a latent period, in which the individual is infected, but not yet infectious), I represents the infected class (those who have the infection), and R represents the recovered/removed class (consisting of those with permanent infectious-acquired immunity, temporary immunity, or those who have been removed from a population due to recovery, isolation, or death) [Hethcote, 2000]. Figure 1 shows the general transfer diagram for a MSEIR model [Hethcote, 2000, Iacoviello and Liuzzi, 2008].

This paper seeks to explore a Susceptible/Infective/Removed (SIR) model with multiple controls over a fixed time horizon, such as those explored in [Iacoviello and Liuzzi, 2008, Joshi, 2002, Jung et al., 2002]. The optimal control problem for an SIR-epidemic model presented in [Iacoviello and Liuzzi, 2008] is considered, in which control efforts are applied to both the susceptible population

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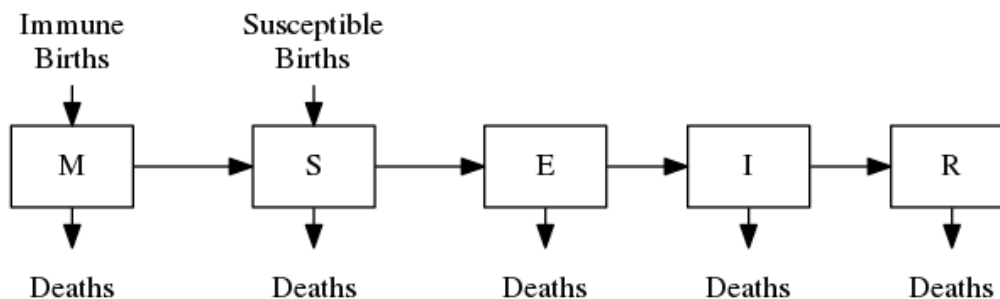*rnierman@oakland.edu

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Figure 1: A General Transfer Diagram for the MSEIR Model

(vaccination) as well as the infectives (isolation). Many models rely on the use of continuous mathematics, i.e., ordinary or partial differential equations to entirely, or in part, model the spread of a disease and/or discuss various optimization questions. Our paper, however, seeks to find the optimal solution to a minimization problem using discrete mathematics (dynamic programming) [Hansen and Day, 2011, Hethcote, 2000, Ögren and Martin, 2002, Sanders, 1971, Siegal and Kunze, 1994]. A comparison is presented demonstrating the effect of applying only one control (i.e., vaccination only or isolation only) versus applying both controls simultaneously. Finally, a case study of the African measles outbreak from 1980-2005 is presented and analyzed.

2   The Epidemic Optimal Control Problem Statement

To briefly review the model described in [Iacoviello and Liuzzi, 2008], let $s(t)$ represent the susceptibles in a population, $i(t)$ represent the infectives, and $r(t)$ represent those removed. The dynamics of the epidemic, with the interaction function f between the susceptibles and the infectives, can be written as,

$$\dot{s}(t) = -f(s,i)$$
$$\dot{i}(t) = f(s,i) - \gamma i$$
$$\dot{r}(t) = \gamma i,$$

where

$$f(s,i) = \frac{\beta s i}{s+i}, \quad \beta > 0,$$

and

$$s(0) = s_0$$
$$i(0) = i_0.$$

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In this model, $\gamma > 0$ denotes the rate of removal of the infectives. Introducing vaccination and isolation results in the following:

$$\dot{s}(t) = -f(s, i) - su_v$$
$$\dot{i}(t) = f(s, i) - \gamma i - iu_q$$
$$\dot{r}(t) = \gamma i,$$

where $0 \leq a_1 \leq u_v \leq b_1 \leq 1$ and $0 \leq a_2 \leq u_q \leq b_2 \leq 1$. Therefore, the controls represent box constraints. The model seeks to minimize the resulting cost function considered is:

$$J(u_v, u_q) = \int_0^T \left[i(t) + c_v u_v^2 + c_q u_q^2 \right] dt,$$

where $T < 0$, c_v is the cost of applying the vaccination control and c_q is the cost associated with controlling via isolation/quarantine [Iacoviello and Liuzzi, 2008, Nowzari et al., 2016].

We seek to branch out from the work done in [Iacoviello and Liuzzi, 2008], and instead of solving the model continuously using differential equations, we solve the problem discretely. Let N_t represent the total population at time t, S_t be the number of susceptibles at time t, I_t be the number of infectives at time t, and R_t represent those removed at time t [Blount et al., 1997, Iacoviello and Liuzzi, 2008, Sethi, 1974]. The model assumes that the total population is held constant while the boundary between the sub-populations is left to vary with time. Therefore, the model studied is an epidemic model, since it does not allow for natural births nor deaths (or immigration nor emigration), which would alter the size of the total population [Hethcote, 2000]. All changes to N are therefore due to deaths from the disease or from vaccination or isolation controls. Therefore,

$$N_t = I_t + S_t + R_t. \tag{2.1}$$

The transmission of the disease is predicated on contact between an infective and a susceptible according to homogeneous mixing with no chance of spontaneous infection. Homogeneous mixing assumes that each individual randomly comes in contact with exactly one other individual during each time period $(t, t + 1)$ [Blount et al., 1997, Hethcote, 2000, Daley et al., 2000]. For the total population, N, and sub-populations S_t and I_t, the probability of infection is represented by β, the rate of death is represented by γ, and u_v and u_q represent the two possible controls, vaccination and isolation/quarantine, respectively. The sub-populations at time $t + 1$ are given by:

$$S_{t+1} = S_t - \frac{\beta(1 - u_v)(1 - u_q)I_t S_t}{I_t + S_t} - S_t u_v \tag{2.2}$$

$$I_{t+1} = I_t + \frac{\beta(1 - u_v)(1 - u_q)I_t S_t}{I_t + S_t} - \gamma I_t - I_t u_q. \tag{2.3}$$

The term

$$\frac{\beta(1 - u_v)(1 - u_q)I_t S_t}{I_t + S_t} \tag{2.4}$$

represents the interaction between a susceptible and an infective (the interaction term), where u_v and u_q represent the rate of control (control effort) according to $0 \leq a_1 \leq u_v \leq b_1 \leq 1$ and $0 \leq a_2 \leq u_q \leq b_2 \leq 1$. Therefore, the two controls represent box constraints [Iacoviello and

Liuzzi, 2008]. The vaccination control, u_v, is applied only to the population of susceptibles, since vaccinating infectives would do nothing. Similarly, the isolation/quarantine control, u_q, is only applied to the infectives, with the goal being to isolate some of the individuals currently infected with the disease together and away from those currently susceptible. Recall (2.1). At time $t = 0$, $R_0 = 0$. At $t > 0$, R_t does not influence S_{t+1} or I_{t+1}, since individuals removed from the population via vaccination or isolation do not effect the interaction term (2.4). The cost function considered in our redefinition of the model is

$$J(u_v, u_q) = \sum_0^T [I_t + c_v u_v^2 + c_q u_q^2],$$

where c_v is the cost of applying the vaccination control and c_q is the cost associated with controlling via isolation/quarantine. We replace the integral with a sum from time $t = 0$ to $t = T$, where $T < 0$. Minimizing the cost function amounts to decreasing the number of infected individuals at minimal effort (represented in quadratic form) [Iacoviello and Liuzzi, 2008].

Figure 2 is a visual representation of the dynamics of the various sub-populations under consideration. The arrows indicate how individuals move between the various conditions. Susceptibles can transition to the infective state by becoming infected with the disease, infectives can transition to the removed state either by death or isolation, and susceptibles can transition to the removed state by becoming vaccinated. Therefore, the model assumes that the vaccination and isolation are 100% effective.
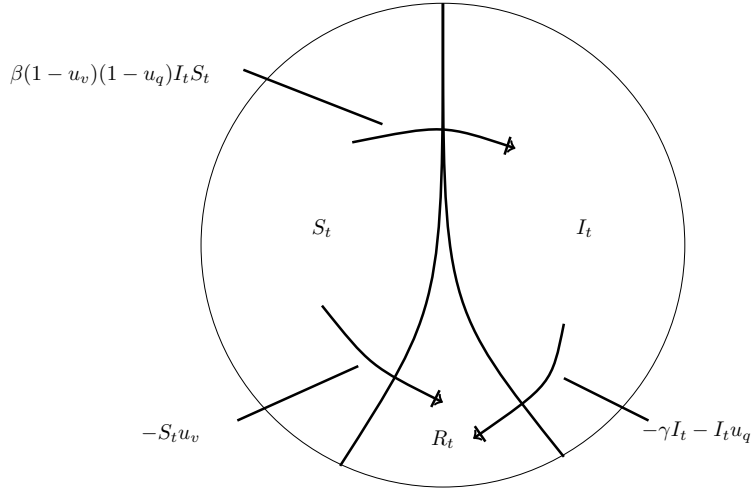

Figure 2: Population Dynamics

We will seek to solve the optimization problem discretely using dynamic programming. To develop the model, define $J(0)$ to be the cumulative cost at time $t = 0$. At $t = 0$, the cumulative cost is equal to the number of initially infected individuals, so $J(0) = I_0$. Additionally, at $t = 0$, $S_0 = N - I_0$, since no one has been removed from the population due to vaccination or isolation yet. The cumulative cost at $t = 1$, is given by $J(1)$. $J(1) = I_1 + c_v u_v^2 + c_q u_q^2$. So, now the goal will be to minimize $\{I_1 + c_v u_v^2 + c_q u_q^2 \mid I_1 = \beta(1 - u_v)(1 - u_q)I_0 S_0 - \gamma I_0 - I_0 u_q\}$, where $0 \leq u_v \leq 1$

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and $0 \leq u_q \leq 1$. The dynamic program can be modeled as follows:

$$J_0 = I_0$$
$$S_0 = N - I_0$$
$$J_t = J_{t-1} + \text{opt}_t,$$

where opt_t is

$$\min\{(\beta(1 - u_v)(1 - u_q)S_t - u_q)I_{t-1} + c_v u_v^2 + c_q u_q^2 \mid 0 \leq a_1 \leq u_v \leq b_1 \leq 1; 0 \leq a_2 \leq u_q \leq b_2 \leq 1\}.$$

Therefore, J_t keeps track of the cumulative cost at each optimal step.

3   Numerical Results

This section focuses on the numerical results obtained from solving the dynamic problem presented in Section 2 with parameters: $\beta = 0.044$, $a_1 = 0$, $b_1 = 0.2$, $a_2 = 0$, $b_2 = 0.1$, $c_v = 1$, and $c_q = 10$, initial conditions $I_0 = 50$ and $S_0 = 200$, and a final fixed time of $T = 80$. Therefore, the total population given by N is the sum of I_0 and S_0, or 250. These parameters are based on those used in [Iacoviello and Liuzzi, 2008] and referenced in the HIV immunology model in [Joshi, 2002] and the Tuberculosis model in [Jung et al., 2002].

Figure 3a and Figure 3b model the applications of each control given the specified parameters. Figure 3a displays the optimal control pattern when only the vaccination control is applied to the population and Figure 3b displays the optimal control graph resulting from applying only the isolation control to the population. Recall, the vaccination control is only applied to those in the susceptible sub-population and the isolation control is only applied to those in the infectives sub-population. In the case of the vaccination only control, the range is $a_1 = 0 \leq u_1 \leq b_1 = 0.2$ and in the case of the isolation only control, the range is $a_2 = 0 \leq u_2 \leq b_2 = 0.1$. Since we are solving the problem discretely, we have to specify a set number of partitions to our control ranges to allow for partial control efforts. This will prevent the model from simply being an "on-off" or "bang-bang control" problem, in which either no control or full control is applied. Let $n_b u_v$ be the number of partitions of the range of control for vaccination control and $n_b u_q$ be the number of partitions of the range of control for the isolation only control. Figure 3a and figure 3b represent the cases in which we let $n_b u_v = n_b u_q = 3$, resulting in four levels of possible control. In both cases, we see that the optimal control pattern is to continue maximally, and then the control decreases over time until no control is necessary.

(a) Vaccination Control Only $n_b u_v = 3$

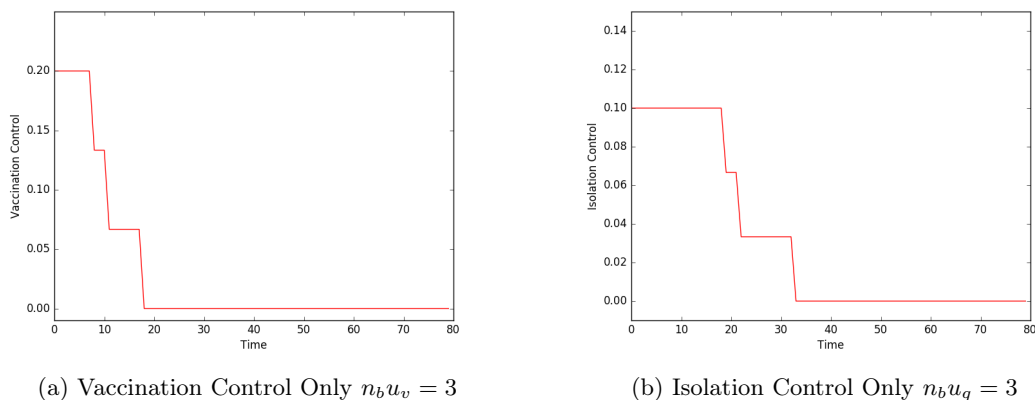(b) Isolation Control Only $n_b u_q = 3$

Figure 3: Vaccination or Isolation Control Only

Figure 4a and Figure 4b show the numerical results for the susceptibles and the infectives over the finite time horizon when when optimal control patterns are applied. Applying both controls at the specified parameter values results in two very quick, monotonically decreasing graphs. The graphs make sense, since if we apply the optimal vaccination pattern to those who are susceptible, the number of susceptible individuals is going to decreases very quickly. Similarly, if we work optimally to isolate/quarantine those who are infected with the disease, then we are going to isolate/quarantine as many people as possible very quickly, so that they are removed from the population and are no longer able to come into contact with a susceptible.

(a) Susceptibles at Optimum for $n_b u_v = 3$
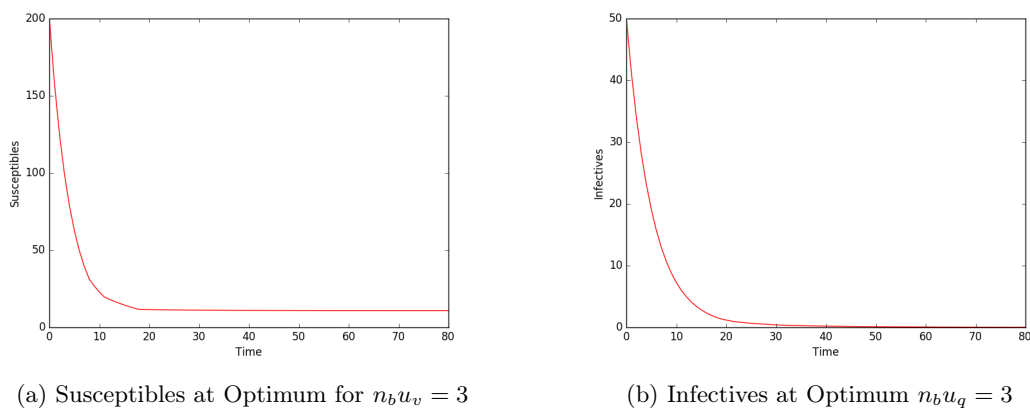

(b) Infectives at Optimum $n_b u_q = 3$

Figure 4: Susceptibles and Infectives at Optimum

Figure 5a and Figure 5b represents the optimal control graphs for vaccination only and isolation only control when $n_b u_v = n_b u_q = 20$, allowing for increased levels of partial control. The overall appearance of the graph looks the same; the optimal control patterns starts out maximally and then decreases quickly over time until no control is necessary, but the overall graph is much more

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smooth than in the case when $n_b u_v = n_b u_q = 3$.

(a) Vaccination Control Only for $n_b u_v = 20$ (b) Isolation Control Only for $n_b u_q = 20$
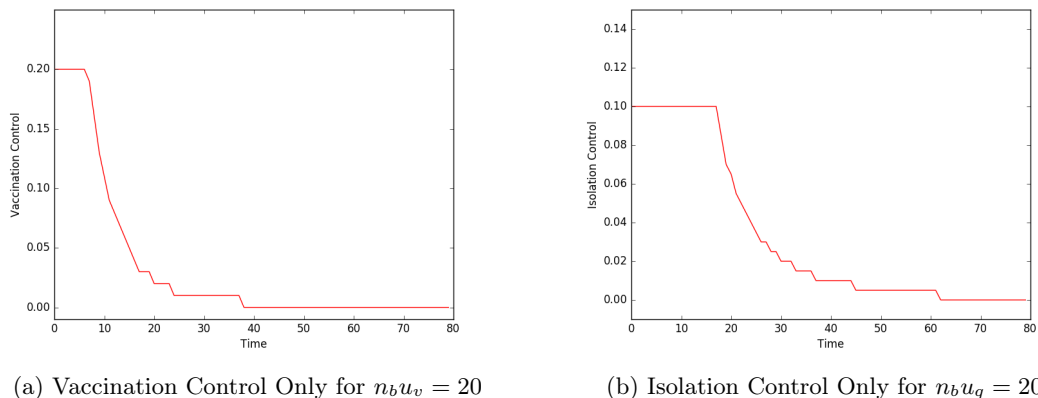
Figure 5: Vaccination or Isolation Control Only

Figure 6a and Figure 6b shows the optimal solution to the susceptibles and infectives over time for the optimal control patterns when $n_b u_v = n_b u_q = 20$. As one can observe in both cases, applying both controls at the specified parameter values results in a very quick, monotonically decreasing graph. The graphs appear very similar in shape to the ones with only three partitions, but increase in smoothness, especially around time $t = 10$.

(a) Susceptibles at Optimum $n_b u_v = 20$ (b) Infectives at Optimum $n_b u_q = 20$
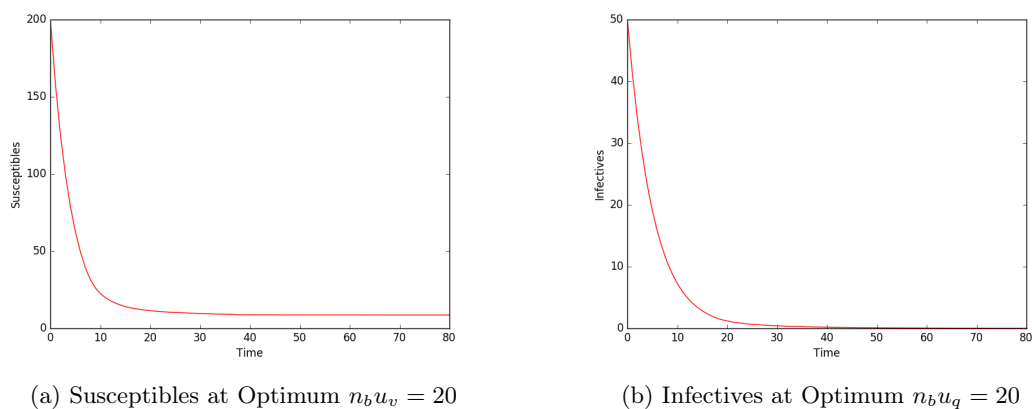
Figure 6: Susceptibles and Infectives at Optimum

Finally, we studied what happens to the optimal control patterns if we let $n_b u_v = n_b u_q = 100$. As one can observe, the optimal control graphs both become quite smooth and begin to resemble what one would expect to see in a continuous case.
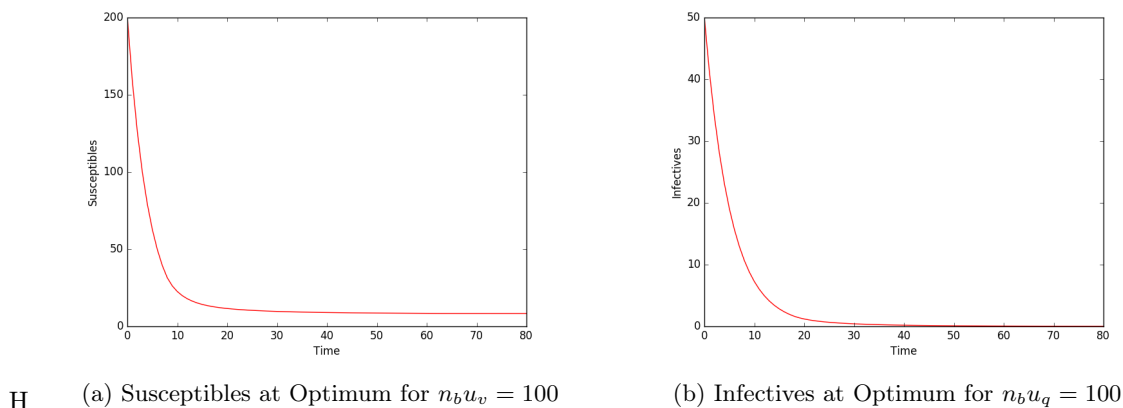
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H   (a) Susceptibles at Optimum for $n_b u_v = 100$ (b) Infectives at Optimum for $n_b u_q = 100$

Figure 8: Susceptibles and Infectives at Optimum

(a) Vaccination Control Only $n_b u_v = 100$ (b) Isolation Control Only for $n_b u_q = 100$
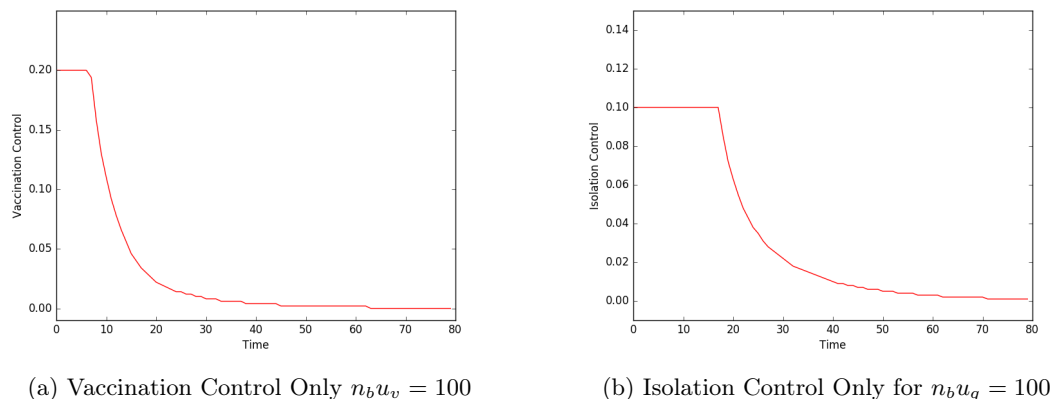
Figure 7: Vaccination or Isolation Control Only

Figure 8a and Figure 8b show what happens to the susceptibles and infectives over time when the optimal control pattern is applied for both controls. Once again, the graphs have the same overall appearance, but appear very smooth. Therefore, our discrete formulation of the problem appears to be very good at finding the optimal solution, especially for relatively small number of partitions. The results also show that it is not necessary to let n grow too large, because the approximation, even at $n = 20$ is very good. Figure 9a models the behavior of the susceptible population when only the vaccination control is applied versus the behavior of the susceptible population when only the infectives are controlled. When no vaccine is administered, the number of susceptibles stays pretty close to $S_0 = 200$, since the isolation control is applied only to those in the infectives category. When only the vaccination control is applied, then number of susceptibles decreases monotonically and very quickly, since more and more people are being vaccinated at each time step, and hence, are incapable of getting the disease.

Analogously, Figure 9b models the behavior of the infectives when only the susceptibles are

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controlled versus the behavior of the infectives when only the infectives are controlled. When no vaccination is administered and only isolation is used, the number of infectives decreases quickly, since they are being isolated and removed from the population with each time step. When only vaccination is applied, the number of infectives still decreases monotonically, but not as quickly as in the case of isolation, since there is an indirect effect. Vaccinating individuals prevents them from getting the disease and therefore becoming an infective, but this process is less direct than isolating those who already have the infection, which prevents them from spreading the disease to a susceptible in the first place.

(a) Behavior of Susceptibles
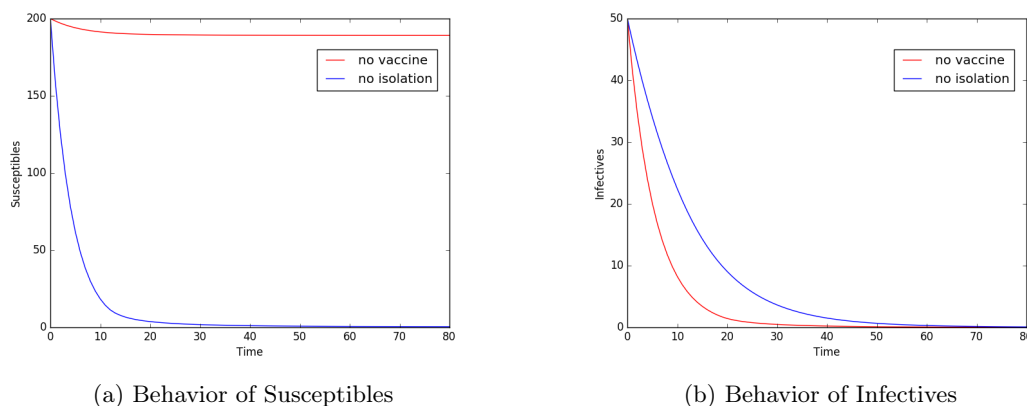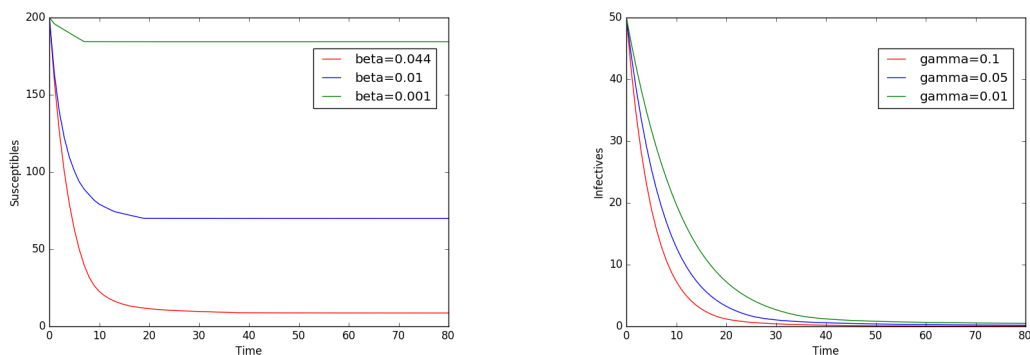

(b) Behavior of Infectives

Figure 9: Behavior of Susceptibles and Infectives Using Only One Control

Figure 10a shows the effect of changing the probability of infection parameter, the value of β, while holding the death parameter, γ, constant at 0.1. Figure 10a reports the behavior of the susceptibles for $\beta = 0.001, 0.01, 0.044$, as chosen in [Iacoviello and Liuzzi, 2008]. When the value of β is higher, the number of susceptibles decreases quicker, since the probability of infection is greater. Therefore, more susceptibles are becoming infected with the disease and entering the infectives class. When β is small, the probability of a susceptible becoming infected with the disease is really small, so the rate at which individuals from the susceptibles class are moving to the infectives class is very small.

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(a) Behavior of Susceptibles: Varying Betas and Gamma = 0.1

(b) Behavior of Infectives With Changing Gamma and Beta = 0.044

Figure 10: Analysis of Model Parameters

Figure 10b shows the effect of changing the death parameter, the value of γ, on the number of infectives when $\beta = 0.044$. Figure 10b reports the behavior of the susceptibles for $\gamma = 0.1, 0.05, 0.01$, in [Iacoviello and Liuzzi, 2008]. As γ increases, the rate at which the number of infectives decreases monotonically increases, resulting in more people are dying off.

3.1   Case Study Analysis

In order to test the effectiveness of the multiple control approach (i.e., using both vaccination and isolation), we have considered an actual epidemic control problem to compare our results with. The case study focuses on the measles outbreak in Africa between 1980 and 2005. The data is based on the data used in [Iacoviello and Liuzzi, 2008], which was acquired from the World Health Organization's website[1]. The number of infectives by each year during the outbreak is shown in Table 1.

Year	Infectives	Year	Infectives	Year	Infectives	Year	Infectives
1980	1240993	1987	641057	1994	420193	2001	491989
1981	1413184	1988	604244	1995	362925	2002	288340
1982	1342685	1989	561896	1996	484914	2003	403016
1983	1346883	1990	481204	1997	299623	2004	220180
1984	1076106	1991	446517	1998	373149	2005	316219
1985	1142002	1992	581125	1999	486660		
1986	676757	1993	395025	2000	520102		

Table 1: Number of People Infected by Measles in Africa $1980 - 2005$

During the time period from 1980 to 2005, substantial effort was put into vaccinating susceptibles, but there was very little (if any) effort placed on quarantining or isolating those already

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[1] http://apps.who.int/gho/indicatorregistry/App_Main/view_indicator.aspx?iid=60

infected. Therefore, the data presented is representative of a model in which only one form of control was applied. This implies that $u_q = 0$. Figure 11a shows a graph of the true data, modeling the infectives during the vaccination efforts between 1980 and 2005. The solid line through the data shows that our model is a good approximation for what truly occurred using $n_b u_v = 20$ for the number of partitions. The model uses the following parameter values: $c_v = 1$, $c_q = 10$, $a_1 = a_2 = 0$, $b_1 = 0.2$, $b_2 = 0$, $\beta = 0.0044$, and $\gamma = 0.07$ over the same 26 year time period. The initial number of susceptibles is approximated at $14,000,000$ and the initial number of infectives is approximated at $1,400,000$.

(a) Infectives in Africa Between 1980 and 2005
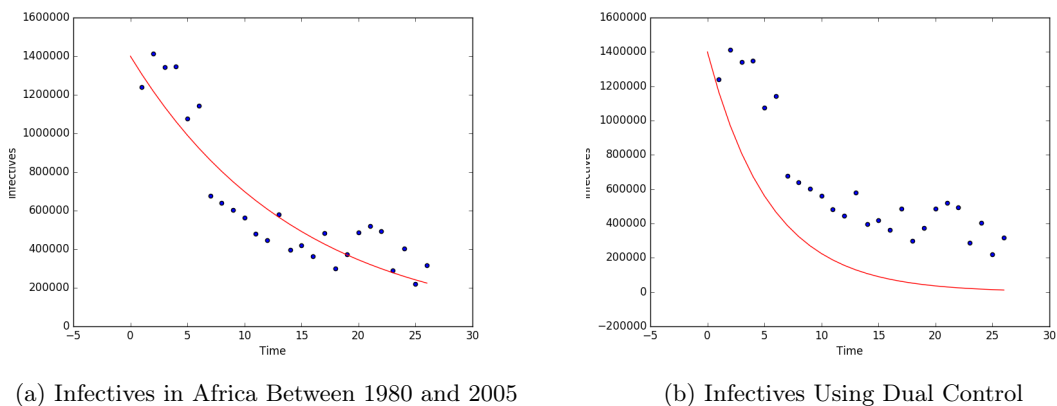
(b) Infectives Using Dual Control

Figure 11: Analysis of Real Data - Measles Case Study

Figure 11b shows the behavior of the susceptibles over the same time horizon and parameters previously listed, except this time, we allow $b_2 = 0.1$, so that we can also apply an isolation/quarantine control effort in addition to the vaccination control. As the graph demonstrates and our model confirms, if both isolation and vaccination had been used, rather than just vaccination, the disease could have been better controlled and the number of infectives would have decreased more quickly. Interestingly, according to our model, the total cost after 26 years of using only vaccination control in Africa is more than twice as costly as controlling using both forms of control. Therefore, had both vaccination and quarantine/isolation controls been applied during the 1980-2005 measles outbreak in Africa, then, not only would the epidemic been better controlled, it would have been controlled at a much lower cost.

4 Conclusion

An analysis of an SIR model in the presence of multiple controls is studied. Vaccination only and isolation only have been studied with varying number of partitions. The results showed that dual controlling served to minimize the cost and the number of infectives over a specified finite time horizon better than relying on only one control. Numerical results and a case study on the measles outbreak in Africa was presented and analyzed.

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