Mathematical modeling of influenza and a secondary bacterial infection

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Abstract: In this work we model a pandemic where individuals are first infected with the influenza virus and later contract a secondary bacterial infection. The model uses a modified SIR approach with standard analytical and qualitative analysis. Theoretical questions are investigated concerning the proportion of the population to initially vaccinate for influenza, the proportion of the population to quarantine after being infected with influenza, and how improved treatments of bacterial infections all would play into reducing the net number of deaths.

Key–Words: SIR Model, Vaccinations, Quarantine

1 Introduction

A lot of research on the spread of the influenza virus had been done due to the widespread effects on the number of deaths it has caused in the modern world. This becomes especially evident during pandemic outbreaks, the most notable being the 1918 H1N1 influenza pandemic (Spanish flu) which killed an estimated 50-100 million people worldwide [1] and the most recent being the 2009 H1N1 pandemic. Other pandemic outbreaks of influenza include the 1957 H2N2 pandemic (Asian Flu) and the 1968 H3N2 pandemic (Hong Kong Flu) [2]. Since influenza pandemics and epidemics are a continuous threat, they are important to understand.

Generally, diseases transmitted by viral agents, such as influenza, confer immunity against reinfection [3]. Influenza A is the most severe and, in general, pandemics caused by this type of virus have large impacts on the human population such as missed work, hospital costs, and increased deaths. Annual influenza epidemics usually appear in the fall or winter and affect on average 10-20% of the global population each year. Epidemics are usually the result of frequent minor antigenic variations of the virus [4].

In the past, the main focus of study has been solely on the influenza virus. There have been numerous papers modeling the spread of multiple strains of the virus with partial immunity [5], [6], and [7]. There have also been some studies breaking down the population into different age classifications [8], [9], [10], and [11]. However, healthcare providers, medical experts, and published data from previous pandemics suggest that most deaths are largely caused by respiratory complications from a secondary bacterial infection, the most common being bacterial pneumonia [1], [12], [13], [14], [15], [16], [17], [18], [19], and [4]. In 2009 Handel et al. [20] derived a mathematical model for a bacterial infection following influenza. In their model they account for 4 subclasses of those infected with influenza and 4 subclasses for those infected with bacteria. Their model addresses this scientific problem very thoroughly, but the authors caveat their findings by stating that many of the parameters of interest are unknown to much detail. Most recently Chien et al. [21] proposed a model that takes both the influenza virus and bacterial aspects into account as well. This is an even more detailed model where they account for asymptomatic and symptomatic cases. Chien's model also considers co-infection with influenza and bacteria and allows an individual to first get infected with bacteria and then get influenza or vice-versa. Again, the complexity of this model limits its ability to be analyzed qualitatively.

At the time of submission, these are the only two mathematical models we are aware of that includes both the influenza virus and bacterial portions of an influenza pandemic. For this reason, we propose a simpler model that considers an individual contracting symptomatic influenza and then a possible sec-

ondary bacterial infection. We do this because theoretically it seems plausible that this is the main scenario that leads to an increased death rate. We also do not consider co-infection since studies by Ampofo et al. [22] and Grabowska et al. [14] suggest there exists a lag time between the two diseases. Further evidence in support of including this type of model is provided by [13] and [19]. Thus, we keep our proposed model simple enough to allow for qualitative analysis, eliminate many of the unknown parameters, yet still consider the dynamics between influenza and bacterial infection. Being able to perform a qualitative analysis has several benefits, which include being able to determine the maximum number of individuals with symptomatic influenza during the epidemic (a carry over from the basic SIR model [3]), being able to determine if an influenza epidemic will occur with only the parameter values for influenza and the initial number of susceptible individuals, and it allows us to determine the effects various parameter changes has on an epidemic. Despite being a much simpler model than Handel et al. [20] and Chien et al. [21] propose, we still get similar results to their more complicated models but with the advantage of some analytical formulas about the influenza pandemic.

By modifying the classic SIR (Susceptible, Infected, Recovered) model from epidemiology to include a secondary bacterial infection, we have developed a model which can be used to estimate the number of people who will become infected first with influenza and then a bacterial infection. With knowledge on how the disease will spread, the impact can be greatly lessened and ideally more deaths can be prevented. The model can be used to investigate how various levels of vaccinations in the population can be used to deter the spread of influenza, thus lessening the number of candidates in the pool to get a secondary bacterial infection in addition to influenza, and thereby reducing the number of deaths due to a secondary bacterial infection. The model can also be used to investigate how various levels of quarantine may also help prevent the spread of influenza and thus limit the pool for secondary bacterial complications and potential deaths.

2 Mathematical Model

For our proposed model, we split the population into five classes: S, I_1, T, I_2, and R. The class that has never been infected with the circulating strain of influenza is S and contains the individuals susceptible to influenza. Once an individual becomes infected with influenza, they leave S and enter I_1, the class infected with the influenza virus. After recovering from influenza, the individual moves from I_1 to T, the class recently recovered from influenza and temporarily susceptible to secondary bacterial pneumonia. These individuals can either move straight to R, the totally recovered class, after a certain amount of time has lapsed, in which their immune system has had time to restore to full strength, or they can contract the secondary bacterial pneumonia and move to I_2, the class infected with a secondary bacterial infection. Individuals in I_2 either die and are removed from the model, or recover from the bacterial infection and move to R. Once in R, individuals are considered fully recovered; they are unable to become re-infected with the circulating influenza strain and are therefore in no danger of the secondary bacterial infection. A brief description of each class can be found in Table 1 and the movement through the population classes described above is shown in Figure 1.

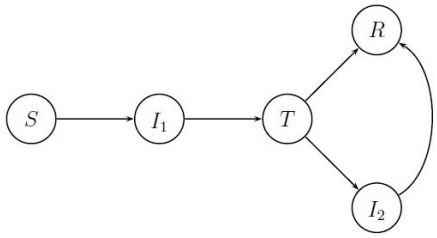

Figure 1: Schematic Diagram

Population Classes	Description
S	Susceptible to influenza
I_1	Infected with influenza
T	Recovered from influenza, temporarily susceptible to bacterial infection
I_2	Infected with secondary pneumonia
R	Completely recovered

Table 1: Population Classes

Individuals in I_1 are "infected" with influenza, by which we mean they have symptomatic influenza. It is important to note that, in a population, there will also be individuals with asymptomatic influenza, who will carry and transmit the influenza virus but show no symptoms. Both symptomatic and asymptomatic individuals are able to spread the influenza virus but, according to Chien [21], the increased risk of secondary bacterial pneumonia in individuals with asymptomatic influenza is negligible. Since we are concerned with the portion of the population that has an increased risk

to bacterial pneumonia, we are only concerned with individuals with symptomatic influenza. Therefore, these individuals are the only ones we consider in population class I_1.

As mentioned above, Grabowska et al. and Ampofo et al. have shown that there is a lag time between influenza and secondary bacterial pneumonia. Therefore, the population class T is necessary as it allows us to incorporate the lag time into the model. We interpret this time as the period in which individuals are no longer infected with influenza but their immune system is still compromised, leaving them susceptible to the deadly secondary bacterial pneumonia.

2.1 Governing Equations

The parameters of the model, along with a description of each, can be found in the following table:

Parameters	Description	Units
β_1	Transmission rate of influenza	1/time (time in months)
γ_1	Recovery rate of influenza	1/time (time in months)
σ	Rate at which an individual loses susceptibility to secondary infection	1/time (time in months)
β_2	Transmission rate of bacterial infection	1/time (time in months)
γ_2	Recovery rate of bacterial infection	1/time (time in months)
d_2	Excess death rate due to bacterial infection	1/time (time in months)

Table 2: Parameter Descriptions

The model we propose for the spread of influenza and a secondary bacterial infection consists of the following system of differential equations:

$$\frac{dS}{dt} = -\beta_1 I_1 S \tag{1}$$
$$\frac{dI_1}{dt} = \beta_1 I_1 S - \gamma_1 I_1 \tag{2}$$
$$\frac{dT}{dt} = \gamma_1 I_1 - (\sigma + \beta_2 I_2) T \tag{3}$$
$$\frac{dI_2}{dt} = \beta_2 I_2 T - (\gamma_2 + d_2) I_2 \tag{4}$$
$$\frac{dR}{dt} = \gamma_2 I_2 + \sigma T \tag{5}$$

Similar to the basic SIR model, the above model is based on the following assumptions:

1. An average infective in I_1 makes contact sufficient to transmit infection with $\beta_1 N$ others per unit time, where N represents the total population size. Similarly, an average infective in I_2 makes contact sufficient to transmit infection with $\beta_2 N$ others per unit time.

2. A fraction γ_1 (γ_2) of infectives leave I_1 (I_2) per unit time.

3. There is no entry into or departure from the population, except through the increased death rate from the secondary bacterial infection at a rate of d_2.

4. The natural birth and death rates are neglected in the model due to the fact that these time scales are typically much larger than it takes for the epidemic to sweep through a community.

Since N is the total population at time t, it can be represented as

$$N = S + I_1 + T + I_2 + R \tag{6}$$

2.2 Qualitative Analysis

Although we are unable to solve this system analytically, we can learn a great deal about the behavior of solutions by taking a qualitative approach.

By setting each of the equations 1 - 5 equal to zero and solving for S, I_1, T, I_2, and R simultaneously, a single equilibrium point, where $S = S_E$, $I_1 = 0$, $T = 0$, $I_2 = 0$, and $R = R_E$, is found (S_E and R_E are the number of susceptible and recovered individuals at equilibrium, respectively).

Knowing the limit of the population classes over time, one can perform a qualitative analysis of the system. Notice that

(i) $\frac{dS}{dt} < 0$ for all t as it approaches the value S_E.

This implies that S is decreasing to S_E for all t.

(ii) $\frac{dI_1}{dt} > 0$ if and only if $S > \frac{\gamma_1}{\beta_1}$.

Therefore, I_1 increases as long as $S > \frac{\gamma_1}{\beta_1}$. Let us consider three cases.

Case 1: Suppose $S_E > \frac{\gamma_1}{\beta_1}$. However, then I_1 would increase indefinitely since S decreases to S_E, and is thus greater than S_E for all t. This

cannot happen since $\lim_{t\to\infty} I_1 = 0$. Hence, $S_E < \frac{\gamma_1}{\beta_1}$.

Case 2: $\frac{\gamma_1}{\beta_1} > S_0 > S_E$.

Then, by (i), $S < \frac{\gamma_1}{\beta_1}$ for all t as S approaches S_E. This implies that $\frac{dI_1}{dt} < 0$ for all t. Hence, I_1 is decreasing for all t as it approaches its equilibrium point of zero and thus an epidemic does not occur.

Case 3: $S_0 > \frac{\gamma_1}{\beta_1} > S_E$. For $S > \frac{\gamma_1}{\beta_1}$, $\frac{dI_1}{dt} > 0$ so we know I_1 is increasing. However, since S is decreasing for all t as it approaches S_E, there exists t^* such that $S < \frac{\gamma_1}{\beta_1}$ for every $t > t^*$. This implies that I_1 decreases for $t > t^*$. Hence, I_1 increases to some maximum at $S = \frac{\gamma_1}{\beta_1}$ and then decrease to zero. In this case, an epidemic occurs.

The quantity $\frac{\beta_1}{\gamma_1}S(0)$ is a threshold quantity, known as the basic reproductive number. Similar to [3], we will denote this as R_1. The basic reproductive number of a disease determines if there is an epidemic or not. If $R_1 < 1$ the infection dies out so there is no epidemic. If $R_1 > 1$ there is an epidemic.

(iii) $\frac{dT}{dt} > 0$ if and only if $I_1 > \frac{(\sigma + \beta_2 I_2)T}{\gamma_1}$.
However, since ii) case 3 shows that I_1 decreases to 0, we know that T will eventually decay to it's equilibrium point of 0.

(iv) $\frac{dI_2}{dt} > 0$ if and only if $T > \frac{\gamma_2 + d_2}{\beta_2}$.
However, by the previous item, we know that at some time, T will decrease to 0, so I_2 will eventually decrease to it's equilibrium point of 0 as well.

(v) $\frac{dR}{dt} > 0$ for all t.
This clearly shows that R is increasing for all t.

This tells us that, given the initial conditions and parameters of the system, we are able to determine whether or not there will be an influenza epidemic.

Since the first 2 equations of our system can be decoupled and solved, we can follow methods outlined by [3] to get

$$I_1 = -S + \frac{\gamma_1}{\beta_1}\ln S + c_0 \tag{7}$$

where

$$c_0 = I_{1_0} + S_0 - \frac{\gamma_1}{\beta_1}\ln S_0. \tag{8}$$

Letting

$$V(S, I_1) = I_1 + S - \frac{\gamma_1}{\beta_1}\ln S \tag{9}$$

we see that the orbit is a curve given implicitly by $c_0 = V(S, I_1)$.

The maximum number of individuals infected with influenza at any given time occurs when the derivative of I_1 is zero; that is, when $S = \frac{\gamma_1}{\beta_1}$. Since $c_0 = V(S, I_1)$ for any t, it must be true that

$$V(S_0, I_0) = V\left(\frac{\gamma_1}{\beta_1}, I_{1_{max}}\right) \tag{10}$$

so by 9 we get

$$I_{1_0} + S_0 - \frac{\gamma_1}{\beta_1}\ln S_0 = I_{1_{max}} + \frac{\gamma_1}{\beta_1} - \frac{\gamma_1}{\beta_1}\ln\frac{\gamma_1}{\beta_1} \tag{11}$$

Thus,

$$I_{1_{max}} = I_{1_0} + S_0 - \frac{\gamma_1}{\beta_1}\ln S_0 - \frac{\gamma_1}{\beta_1} + \frac{\gamma_1}{\beta_1}\ln\frac{\gamma_1}{\beta_1}. \tag{12}$$

Therefore, we are able to find the maximum number of individuals infected with influenza during an epidemic by using equation (12). Note that if there does not exist an epidemic, then this equation does not hold since S will always be less than $\frac{\gamma_1}{\beta_1}$. In this case, the maximum number of infected individuals will simply be I_{1_0}.

We will now determine what the effect of varying S_0 will be on $I_{1_{max}}$ when we hold I_{1_0} and $\frac{\gamma_1}{\beta_1}$ constant. Since we are holding I_{1_0} and $\frac{\gamma_1}{\beta_1}$ constant, let $C = I_{1_0} - \frac{\gamma_1}{\beta_1} + \frac{\gamma_1}{\beta_1}\ln\frac{\gamma_1}{\beta_1}$. Then

$$I_{1_{max}} = S_0 - \frac{\gamma_1}{\beta_1}\ln S_0 + C. \tag{13}$$

Substituting the values for β_1, γ_1, and I_{1_0} found in Tables 3 and 4 listing parameters from the 1918 Influenza Pandemic, this equation becomes

$$I_{1_{max}} = S_0 - 0.847\ln S_0 - 0.984 \tag{14}$$

The graph of this equation is found in Figure 2. This graph shows that as we decrease the number of susceptible individuals to $S_0 = \gamma_1/\beta_1$ the maximum number of individuals infected with influenza also decreases. At $S_0 = \gamma_1/\beta_1$, a pandemic is no longer

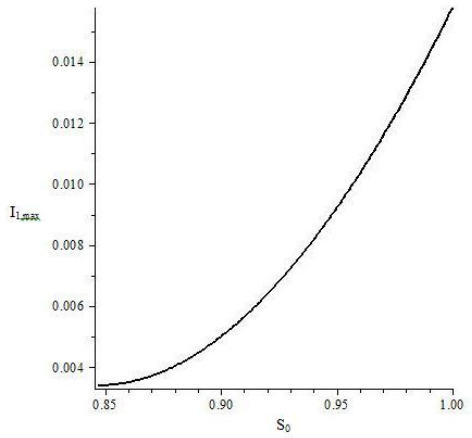

Figure 2: Maximum proportion of the population contracting the influenza virus for varying levels the initial population with $\beta_1 = 7.38$, $\gamma_1 = 6.25$, $\sigma = 2.14$, $\beta_2 = 20$, $\gamma_2 = 1.67$, $d_2 = 3$, $I_{10} = .0034$, $T_0 = 0$, $I_{20} = .0033$ and $R_0 = 0$.

a threat to the population. Using these same parameter values we see that at $\gamma_1/\beta_1 = .847$ we have $I_{1_{max}} = .0036$. This says that if we can vaccinate enough of the population so that $S_0 = .847$, we can prevent an influenza outbreak and the most people that would get the influenza virus would be .36% of the population. If we figure a vaccine to have a 70% effective rate [23], this suggests we need to vaccinate approximately 22% of the population to start with 15.3% of the population in the recovered population so that $S_0 = .847$ as desired.

Although by qualitative analysis we are still unable to gain insight into the behavior of I_2, other than end behavior, we are able to determine if there will be an influenza epidemic and the maximum number of individuals infected with influenza. Thus, given only $S(0)$, $I_1(0)$, β_1, and γ_1 during the beginning of a flu outbreak, we will be able to predict an epidemic and the severity of the epidemic. If an epidemic is predicted, further data should be obtained and numerical simulations will then help us determine how many individuals in a particular region may become infected with a secondary bacterial infection. To run this type of analysis, we need to choose parameter values. These values will vary for each pandemic.

3 Results and Discussion

In order to choose parameter values, we need to understand how these parameters will affect the system. Specifically, we are concerned with the number of deaths caused by the pandemic in order to determine policies that will save the most lives. First, notice that a higher death rate will cause I_2 to decrease to zero faster than it would otherwise and therefore the secondary bacterial pneumonia will die out. In reality, there will be healthy people also able to spread the bacteria that causes the secondary pneumonia; however, we can get a good idea of the number of resulting deaths without introducing this possibility into the model. Therefore, d_2 must be low enough so it does not drive I_2 to zero so fast that it wipes out the secondary bacterial pneumonia component of the pandemic. The death rate alone does not determine how many deaths there will be so we will keep d_2 constant and vary the other parameters to determine their affect on the number of deaths.

Consider N_0 to be the initial total population. Since I_1, T, and I_2 all tend to zero over time, the total population at equilibrium is $S_E + R_E$. Thus, $N_0 - (S_E + R_E)$ is the total number of deaths due to the pandemic. To increase the number of deaths due to the pandemic, S_E or R_E must be decreased and alternatively to decrease the number of deaths, S_E or R_E must be increased.

One can see from the governing equations 1 - 5 that the parameter values that affect S_E are β_1 and γ_1. In order to decrease S_E, β_1 must be increased or γ_1 must be decreased. When β_1 is increased, individuals in S are going to get influenza faster than they would have otherwise. When γ_1 is decreased, individuals stay in I_1 longer, which increases the number of people they come into contact with while infective and therefore increasing the number of people they ultimately infect. When more people are infected with influenza, more people are exposed to secondary bacterial pneumonia and therefore more people will be killed in the pandemic. By a similar argument, in order to increase S_E, β_1 must be decreased or γ_1 must be increased.

Similarly, the parameter values that have a direct effect on R_E are σ, β_2, and γ_2. We note that d_2 also has a direct affect on R_E, however, as discussed previously, we will be holding d_2 constant. In order to decrease R_E, σ must be decreased, β_2 must be increased, or γ_2 must be decreased. When σ is decreased, individuals stay in the population class T longer. This means they are susceptible to secondary bacterial pneumonia longer which increases their possibility of becoming infected. Therefore more people will enter I_2 and ultimately die; thus, decreasing R_E. Increasing β_2 and decreasing γ_2 has the same result as increasing β_1 and decreasing γ_1. Thus, both of these changes cause an increase in total deaths during the pandemic which decreases R_E. Similarly, in order to

increase R_E, σ must be increased, β_2 decreased, or γ_2 increased.

We are now able to use this information to determine the parameter values during a specific pandemic. Once the pandemic begins, we will assume that the parameter values will remain constant throughout the pandemic. This is a valid assumption for the most part, with the exception of interventions such as vaccinating more individuals before they get sick (altering S_0) and treatment after getting sick (altering γ_1 or γ_2). This will allow us to determine the parameter values of the disease and then we can make adjustments to reflect interventions. From this, we will be able to determine the best course of action to minimize the effect of the pandemic.

3.1 Numerical Simulation

In order to run a numerical simulation of the system, we must first decide on the parameter values. Thus, we must first decide on what pandemic we would like to model. The 1918 H1N1 influenza pandemic has been vastly studied, and represents a pandemic for which vaccines to prevent influenza virus infection and antibiotics to limit secondary bacterial complications were not largely available [24]. Therefore, we model this pandemic to ensure the accuracy of the model and fix known parameters.

3.1.1 1918 H1N1 Influenza Pandemic

The parameter values and initial conditions for the 1918 H1N1 influenza pandemic can be found in Table 3 and Table 4, respectively. For the initial conditions, we use the proportion of the population instead of the actual number of individuals in each class. Essentially, this is scaling our classes by the total population. Hence, 99.33% of the population is initially susceptible at the beginning of the pandemic.

Using these values, $S_E = 0.6964$ and $R_E = 0.2985$. Since only individuals who become infected with influenza leave S, the total proportion of the population becoming infected with influenza is $1 - S_E$. Thus, according to the model 30.36% of the population becomes infected with influenza. This is close to the estimated 28% of Americans having symptomatic influenza during the 1918 influenza pandemic [21]. Furthermore, as described in the previous section, we are able to determine the percentage of deaths during the pandemic to be 0.50%. The true percentage of deaths was 0.65% of the United States population; therefore, the model predicts over 75% of the deaths caused by secondary bacterial pneumonia during the 1918 influenza pandemic. We note that we could have increased β_2 until we obtained the desired 0.65%, but to do so would require a great increase to this value. The other option would be to lower either σ or γ_2; however, these values are fairly well known. Although not all of the deaths are predicted, the model is still able to give us a good idea of how many influenza vaccinations are needed in order to decrease the death toll to a significantly lower amount. Figure 3 shows the graphs of the different classes with these calculated parameters for the 1918 influenza pandemic.

Parameter	Value	Assumptions/References
β_1	7.38	Calculated from the model
γ_1	1/0.16	Infective period of influenza is 4.8 days [21], or 0.16 months
σ	1/.467	Susceptibility to secondary bacterial pneumonia lasts 14 days [14], 0.467 months
β_2	20	Calculated from the model
γ_2	1/0.6	Infective period of pneumonia is 18 days [25], or 0.6 months
d_2	1/0.33	Assume it takes an average of 10 days, or 0.33 months with secondary bacterial pneumonia to die

Table 3: 1918 H1N1 Influenza Pandemic Parameter Values

Initial Values
$S_0 = 0.9933$
$I_{1_0} = 0.0034$
$T_0 = 0$
$I_{2_0} = 0.0033$
$R_0 = 0$

Table 4: 1918 H1N1 Influenza Pandemic Initial Conditions

This is also visualized through phase planes, which map the trajectory of two of the population classes. Figure 4 shows two of the phase planes for this system. In graph A), we map R with respect to S. The trajectory starts at the initial points, S_0 and R_0, and moves up and to the left as time increases. This is because as time increases, S decreases and R increases, until we reach S_E and R_E. The phase portrait also shows that S_E is just under .7 and R_E is just under .3, as we noted earlier. In graph B), we created a similar map of I_1 with respect to S. Here we again see that as time increases, S decreases. We also see that as time increases, I_1 increases until it reaches about .85 and then decreases until it reaches its equilibrium point of 0. Hence, from Figures 3 and 4 we are able to conclude the same information about the pandemic while visualizing what is happening with the various

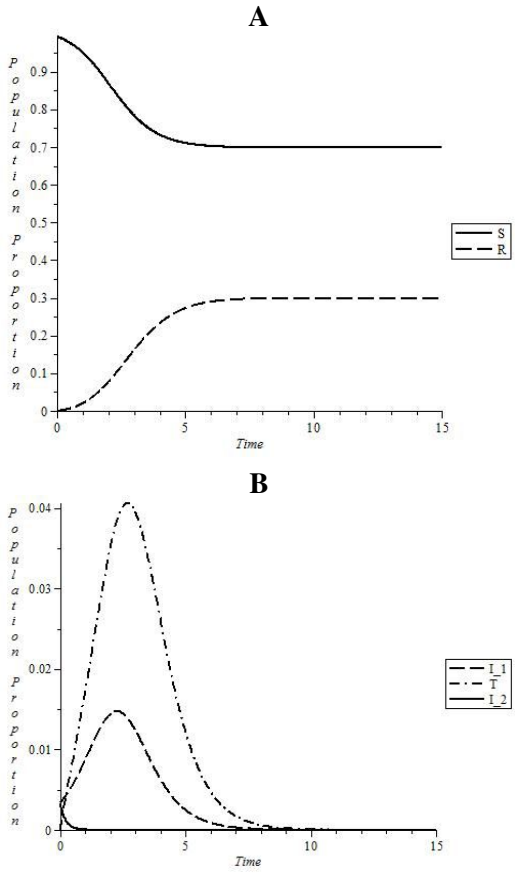

Figure 3: 1918 Influenza Pandemic population percentages of the (A) Susceptible and Recovered classes and (B) Influenza, Temporarily Recovered, and Secondary Bacteria classes in months for $\beta_1 = 7.38$, $\gamma_1 = 6.25$, $\sigma = 2.14$, $\beta_2 = 20$, $\gamma_2 = 1.67$, $d_2 = 3$, $S_0 = .9933$, $I_{1_0} = .0034$, $T_0 = 0$, $I_{2_0} = .0033$ and $R_0 = 0$.

classes against one another.

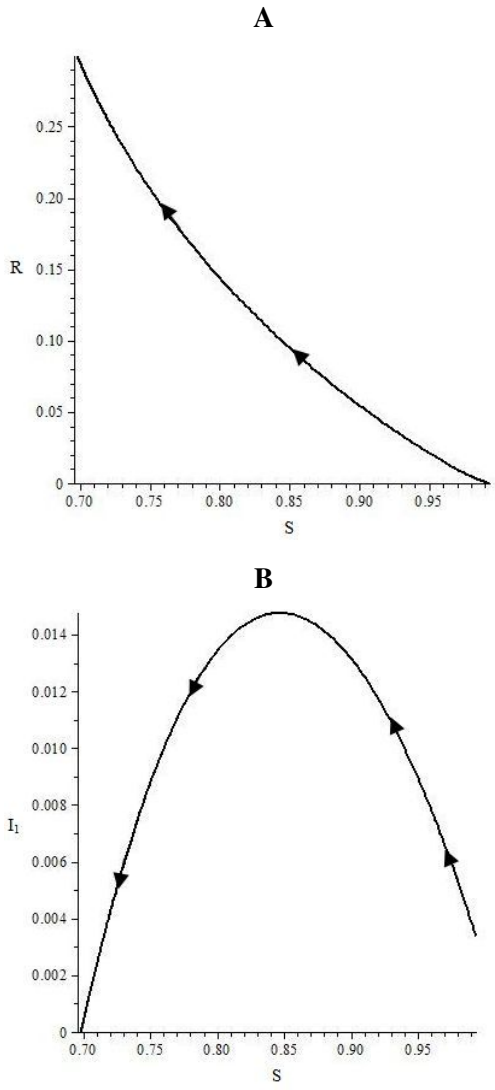

Figure 4: Phase Planes of the 1918 H1N1 Influenza Pandemic for $\beta_1 = 7.38$, $\gamma_1 = 6.25$, $\sigma = 2.14$, $\beta_2 = 20$, $\gamma_2 = 1.67$, $d_2 = 3$, $S_0 = .9933$, $I_{1_0} = .0034$, $T_0 = 0$, $I_{2_0} = .0033$ and $R_0 = 0$.

3.2 Vaccination Strategies

Now we consider 10% of the population being vaccinated for influenza before the pandemic begins. Recent randomized controlled trials of inactivated influenza vaccine among adults under 65 years of age have estimated 50%-70% vaccine efficacy during seasons in which the vaccines' influenza A components were well matched to circulating influenza A viruses [26]. Thus, if we consider a vaccine that is 70% effective against the circulating strain of influenza [23], then vaccinating 10% of the population is the equiva-

lent of taking 7% of the population from S and placing them in R. However, for simplicity, we will assume that the influenza vaccination is 100% effective. Thus, to represent vaccinating 10% of the population, we will take 10% of the population in S and place them into R. Making this change to our initial conditions and keeping the remaining initial conditions the same as when we ran the model previously, we now get the following result: $S_E = 0.75950$ and $R_E = 0.23605$, which is shown in Figure 5. Since 10% of the population who left S got vaccinated and was therefore not infected with influenza, the proportion of people becoming infected during the pandemic is $1-(S_E+0.1)$, which amounts to 14% of the population. We also see that only 0.45% of the population is killed in the pandemic. Thus, by vaccinating 10% of the population the number of deaths is lowered by 31%. Although vaccination was not an option during the 1918 influenza pandemic, we can see that if a similar pandemic broke out today we would be able to significantly lower the number of deaths by vaccinating a proportion of the population against influenza. We note that in Figure 3, $S_0 = .993$ and $I_{1_{max}} = .015$. Also, in Figure 3, $S_0 = .893$ and $I_{1_{max}} = .005$. This is exactly what we see in Figure 2 for these values of S_0, verifying our equation for $I_{1_{max}}$.

Assuming an effective rate of 100% and by moving the vaccinated population to the recovered class, R, we see in Figure 6 the effects of vaccination on the percentage of the population that dies from the secondary bacterial infection. As stated previously, when using parameters from Tables 3 and 4 we saw that with a vaccination that is 75% effective, when one vaccinates 22% of the population, a pandemic is prevented. For this reason we only show the portion of the graph that has up to 30% of the population being vaccinated. However, the graph seems to be linear so a direct proportion would seem appropriate when considering the relationship of vaccinations to deaths.

3.3 Quarantine Strategies

One can investigate the benefits from quarantining people that have contracted the influenza virus and the effects this would have on the proportions of deaths. Educating people on the importance of basic precautionary measures such as staying home when one potentially has the virus (quarantine) and the importance of basic hygiene practices such as washing hands, covering when coughing, and etc. could all have the effects of lowering β_1. One can see from Figure 7 that reducing β_1 by a factor of two will have virtually no effect on reducing the proportions of deaths. This type of information would prove beneficial to policy makers as they determine what strategies to involve and

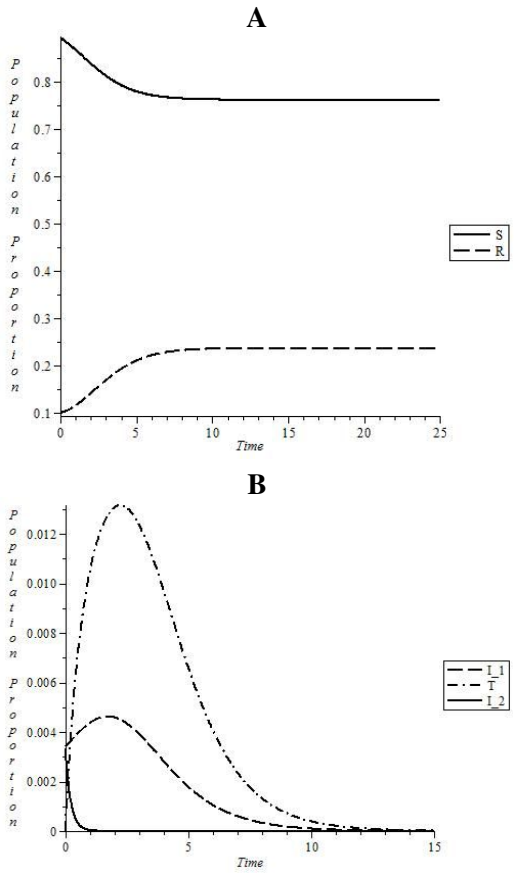

Figure 5: 1918 Population classes in months for the Influenza Pandemic parameters with 10% of the Population Vaccinated and $\beta_1 = 7.38$, $\gamma_1 = 6.25$, $\sigma = 2.14$, $\beta_2 = 20$, $\gamma_2 = 1.67$, $d_2 = 3$, $S_0 = .8933$, $I_{10} = .0034$, $T_0 = 0$, $I_{20} = .0033$ and $R_0 = 0.1$

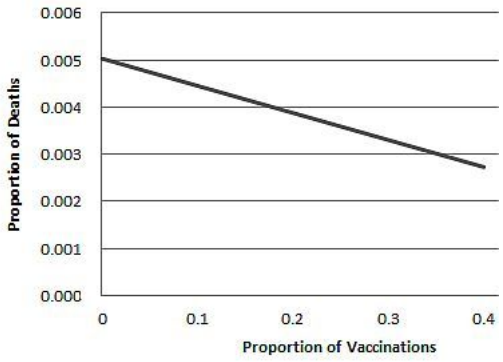

Figure 6: 1918 Influenza parameter values showing the proportions of Vaccinations vs. deaths for $\beta_1 = 7.38$, $\gamma_1 = 6.25$, $\sigma = 2.14$, $\beta_2 = 20$, $\gamma_2 = 1.67$, $d_2 = 3$, $I_{10} = .0034$, $T_0 = 0$, $I_{20} = .0033$.

where to invest money.

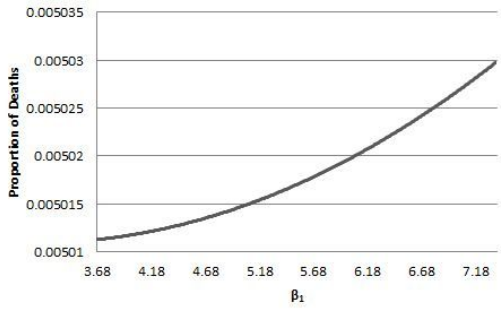

Figure 7: 1918 Influenza parameter values showing β_1 vs. deaths for $\gamma_1 = 6.25$, $\sigma = 2.14$, $\beta_2 = 20$, $\gamma_2 = 1.66$, $d_2 = 3$, $S_0 = .9933$, $I_{10} = .0034$, $T_0 = 0$, $I_{20} = .0033$,$R_0 = 0$.

3.4 Treatment of Bacterial Infection Strategies

Another investigation for reducing the proportions of deaths would be if our treatment of the secondary bacterial infection could be improved. We see in Figure 8 that it would require the parameter γ_2 to be doubled in order to reduce the proportions of deaths by approximately 10%. Feasibly, it may not be possible to increase the efficiency of our treatments by a factor of two at this time, but it does show large benefits from doing so and policy makers can now make decisions as to where to focus efforts and money. Currently, this is a very active area of research in the medical community as to the prevention and causes related to the secondary bacterial infection.

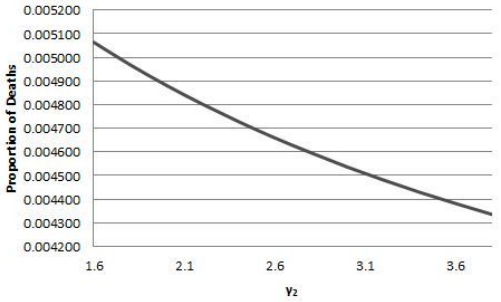

Figure 8: 1918 Influenza parameter values showing γ_2 vs. deaths for $\beta_1 = 7.38$, $\gamma_1 = 6.25$, $\sigma = 2.14$, $\beta_2 = 20$, $d_2 = 3$, $S_0 = .9933$, $I_{10} = .0034$, $T_0 = 0$, $I_{20} = .0033$,$R_0 = 0$.

4 Conclusion

By modifying the basic SIR model, we have gained useful insight on the effect of a secondary bacterial infection during an influenza pandemic. When we assume there is no entry into or departure from the population, except through death from the secondary bacterial infection, the system only has one equilibrium point with only S_E and R_E nonzero. Although a much more complicated model can be developed for influenza and secondary bacterial infection, as done by Chien et al. [21], this does not allow the qualitative analysis to be performed. Performing this qualitative analysis leads to a better understanding of the diseases and how they interact and also allows us to see how the parameter values affect the system which will in turn lead to more effective policies regarding influenza pandemics and therefore save more lives. By running the numerical simulation of the 1918 H1N1 influenza pandemic, the model accurately predicts the number of influenza cases and predicts 75% of the deaths during the 1918 influenza pandemic. In order to approximate the deaths more closely, parameter values would need to be changed quite substantially on the value of β_2. We were also able to determine the optimal percentage of vaccinations to prevent a pandemic using parameters from the 1918 influenza outbreak. Parameters β_1 and γ_2 were also investigated to show their influence upon the proportions of deaths to allow policy makers to make informed decisions as to where best to channel their efforts and funds.

Recent laboratory-based studies have demonstrated the contribution of the influenza virus virulence factor PB1-F2 toward increased susceptibility to secondary bacterial infections [27]. The math model that we propose in this manuscript could be used to bridge laboratory findings with clinical outcomes as we further define the contributions of PB1-F2 and other viral genes toward these deaths [28]. If we can determine the genetic signatures of viruses with increased potential to cause secondary bacterial infections, then our math model can be applied to determine the impact of these specific viruses on the human population. One can also include the sex (male or female), adult vs children, and elderly as important variables affecting the parameters of the model in these further studies. This modified SIR model can possibly allow decision makers to make a better informed decision on the impact of future pandemics and to determine the appropriate interventions for limiting these deadly complications. Calculations performed within this model assume a relatively healthy population at the time of influenza virus infection, and do not specifically consider populations that are known to be highly susceptible to primary influenza virus ill-

ness due to altered immune function. These at-risk populations include children, elderly individuals (65 years of age and older), pregnant females, immunocompromised hosts [29] and [30] , individuals with heart disease [31], or diabetes [32]. Within these specific populations, we would predict that vaccination against influenza virus would have additional benefits toward the prevention of secondary bacterial pneumonia, but full appreciation within this model would require statistics associated with the indicated medical condition.

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