Parameterizing Ebola epidemiology

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1 Introduction

Our goal is to capture essential parameters for curbing theoretical Ebola endemics for application to actual outbreaks.

1.1 Background

Since its 1976 discovery in the country of Zaire (now the Democratic Republic of the Congo), four primary strains of the Ebola virus have been identified in Africa. At the time of this writing, the most recent outbreak of Ebola began in the Democratic Republic of the Congo in January of 2014 [4]. Since the Congo 2014 epidemic is ongoing, we developed and analyzed a model of the spread of the Ebola virus using population data obtained from the recent outbreak of a similar strain in Uganda in 2000. Because deceased individuals that died from Ebola remain infectious and traditional burial practices in Uganda involve high contact with the deceased, contact with the dead bodies is a means by which susceptible individuals contract the disease [10]. We base our model for this paper on the traditional $SEIR$ mathematical model for infectious diseases as well as the $SEIRv$ model, which added a prophylactic vaccine component to the $SEIR$ model [7].

1.2 History of Ebola Vaccine Development

Vaccination is a common control strategy for infectious diseases in humans [9, 14]. However, no licensed Ebola virus vaccines are currently available [15]. The first attempts to generate vaccines consisted of classical formulations of the inactivated virus with different adjuvants [8]. Some studies resulted in protective immunity in rodent models, but most of these strategies were not successful in protecting non-human primates, the "gold standard" animal model for Ebola. When classical vaccine methods failed, researchers began exploring new vaccine formulations, such as viral-vector-based vaccines, DNA vaccines, and virus-like particles [8].

In light of recent efforts to create an Ebola vaccine, we apply a prophylactic vaccination component to the traditional $SEIR$ mathematical model. Furthermore, we add two additional classifications, dead (and still infectious) and buried (and no longer infectious) [2, 7].

2 Mathematical Model

2.1 SEIRv Model

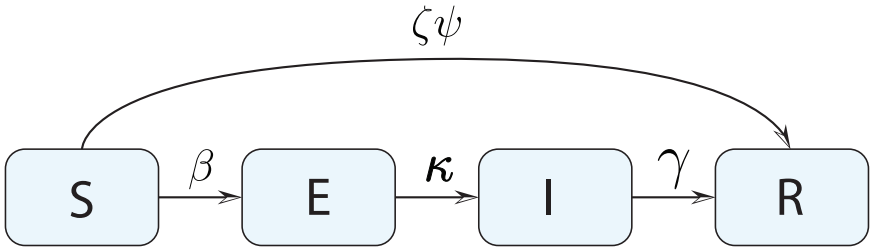


Figure 1: SEIRv Model Diagram

The $SEIR$ model in epidemiology simulates the dynamics of an infectious disease in a population. Previously, Cook, Magruder, and Poston modified this model by adding a prophylactic vaccine component to create the $SEIRv$ model [7]. In the $SEIRv$ model at time t, $S(t)$ represents the number of susceptible individuals, $E(t)$ represents the number of exposed individuals, $I(t)$ represents the number of infectious individuals, and $R(t)$ represents the number of removed individuals (recovered, deceased, and vaccinated). Dynamics of the system's state variables are unidirectional following the progression as shown in Figure 1. Parameter values are summarized in Table 1. The model is given

by the following equations:

$$\frac{dS}{dt} = -\beta\frac{SI}{N} - \zeta\psi S, \tag{1}$$
$$\frac{dE}{dt} = \beta\frac{SI}{N} - \kappa E, \tag{2}$$
$$\frac{dI}{dt} = \kappa E - \gamma I, \tag{3}$$
$$\frac{dR}{dt} = \gamma I + \zeta\psi S. \tag{4}$$

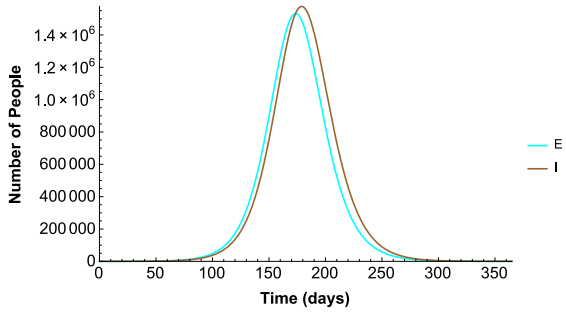
In this model, it is assumed that all individuals in the population are equally likely to become infected. Also, there are no migration, births, or deaths (not caused by Ebola) into or out of the population, because this number would be relatively small in the time of one year. Furthermore, it is assumed that the population is 100% susceptible to Ebola. Since there were no clinically proven prophylactic vaccines at the time of that writing, a simplifying assumption was made about the vaccine efficacy and waning, such that the vaccine is absolute: efficacy is 100% and there is no waning thereof. However, for comparisons between models, we ran the $SEIRv$ model again with an efficacy value of 80%. Although the term κE in Equations (2) and (3) models the disease progressing to infectiousness at a rate of $\frac{1}{\kappa}$, it is not necessarily the most reasonable assumption for progression because it assumes all exposed individuals fall ill. The removed class as the end state is also a conundrum because deceased individuals are still infectious, and susceptible individuals cannot be infected by removed individuals. A unidirectional $SEIRv$ model also lacks a mode of movement from the removed class back to the susceptible class [7].

After conducting uncertainty analysis, Cook, Magruder, and Poston found that the susceptible class always decreases as time elapses either due to infection or vaccination, the individuals eventually leave the susceptible class to go to the removed class. The model started with one hundred infected individuals and has an $\mathcal{R}_0$ value that is less than 1 (using the Next Generation method), which means that the infection should die out before starting an epidemic [20]. However, despite a small $\mathcal{R}_0$ there was an epidemic. Recalculating their $\mathcal{R}_0$ using the classical approach of Anderson & May we found a more accurate estimate of $\mathcal{R}_0$ as 1.8513 [18]. Sensitivity analysis determined that the vaccination rate is negatively correlated to the cumulative number of infectious individuals, so the higher the

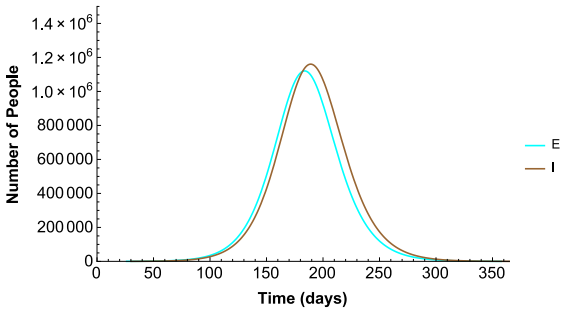
vaccination rate, the lower the number of cumulative infections. Therefore, the introduction of a prophylactic vaccination does result in decreasing the total number of infections during an outbreak of the Ebola virus.

Under the assumption that a prophylactic vaccine has 100% efficacy and is administered to a one hundred percent susceptible population during an Ebola outbreak, Cook, Magruder, and Poston concluded that vaccination would curb an endemic [7]. Because this assumption is unreasonable, we ran their model with 80% efficacy. Based on the new efficacy, the vaccine will keep the number of infections lower than if there were no vaccine present, but if the vaccine rate is too low then the number of infections will escalate as if no vaccines were administered. Without a vaccine, approximately 1.823×10^7 (75.1%) infections occur in the population (Figure 2a). When the prophylactic vaccine is added with a vaccination rate of $\psi = 0.0005$, only about 1.819×10^7 (74.9%) infections occur, $40,000$ individuals less than the no vaccine simulation (Figure 2b). The vaccine is able to reduce the number of infections by approximately $40,000$ [7]. It is important to note that these specific numbers are based on Uganda's population in the year 2000 [17].

Because the vaccine is prophylactic and not therapeutic, the $\mathcal{R}_0$ value is only slightly sensitive to the change in vaccination rates, showing that the vaccine does not prevent a non-vaccinated individual from infecting other susceptible individuals. With a large susceptible population and prophylactic vaccines introduced at the beginning of an outbreak, the vaccine is only effective when rapidly administered to the public. A similar effect is possible if the vaccine had been distributed to the susceptible population over a longer period of time prior to the outbreak. Hence, the vaccine's distribution prior to an outbreak may considerably vary the dynamics of the viral spread in the susceptible population's favor [7].



(a) No vaccination, $\psi = 0$.



(b) Vaccination rate of $\psi = 0.0005$.

Figure 2: SEIRv model of Ebola applied to Uganda (2000) with parameters: $\beta = 0.38$, $\kappa = \frac{1}{3.35}$, $\gamma = \frac{1}{3.5}$, $\zeta = 1$

Table 1: $SEIRvDB$ and $SEIRv$ model parameters derived from data from Uganda in 2000 [2, 6, 7, 12, 19]. Note the range of β_2 is assumed to be the same as β_1, and ψ is given a wide range to simulate different possible vaccination campaigns.

Parameter	**Units**	**Range**	**Description**
β_1	$\frac{1}{days}$	$0.14 - 0.62$	transmission rate of disease from infectious individuals
β_2	$\frac{1}{days}$	$0.14 - 0.62$	transmission rate of disease from dead individuals
$\frac{1}{\kappa}$	days	$2.86 - 3.84$	days before progressing to infectious class
$\frac{1}{\gamma}$	days	$2.83 - 4.17$	days before progressing to the removed, recovered, or deceased class
ρ	—	0.53	fatality rate (percentage)
ζ	—	0.80	vaccine efficacy (percentage)
ψ	$\frac{1}{days}$	$0.0001 - 0.01$	vaccination rate
$\frac{1}{\mu}$	days	$7 - 13$	number of days before a deceased body is buried

2.2 SEIRvDB Model

We have modified the $SEIR$ model by adding two additional classes and a prophylactic vaccine, and will refer to this model as $SEIRvDB$. At time t, let $S(t)$ represent the number of susceptible

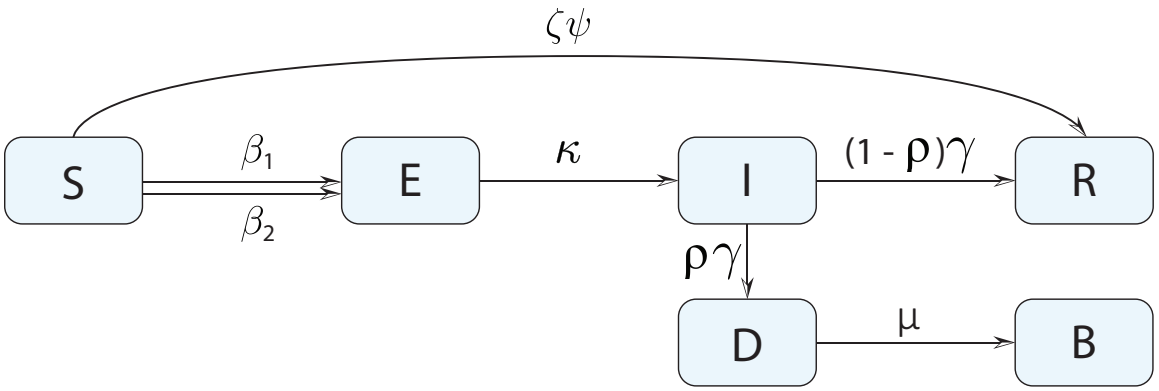


Figure 3: $SEIRvDB$ Model Diagram

individuals, $E(t)$ represent the number of exposed individuals, $I(t)$ be the number of infectious individuals, $R(t)$ be the number of recovered individuals, $D(t)$ represent the number of dead but not buried individuals, and $B(t)$ be the number of dead and buried individuals. Then, the model is given by:

$$\frac{dS}{dt} = -\beta_1 \frac{SI}{N} - \beta_2 \frac{SD}{N} - \zeta\psi S, \tag{5}$$

$$\frac{dE}{dt} = \beta_1 \frac{SI}{N} + \beta_2 \frac{SD}{N} - \kappa E, \tag{6}$$

$$\frac{dI}{dt} = \kappa E - \gamma I, \tag{7}$$

$$\frac{dR}{dt} = (1-\rho)\gamma I + \zeta\psi S, \tag{8}$$

$$\frac{dD}{dt} = \rho\gamma I - \mu D, \tag{9}$$

$$\frac{dB}{dt} = \mu D, \tag{10}$$

where $N = S + E + I + R + D + B$, and the parameter values can be found in Table 1. Figure 3 shows a flow diagram of the model. Note, we assume mass action for the mode of transmission, with the force of infection being $(\beta_1 I + \beta_2 D)S/N$. This is biologically reasonable because the disease can spread from both the infectious and the dead populations to the susceptible.

3 Methods

3.1 Determining Parameters

Our parameters (shown in Table 1) were obtained using data from previous models created to model the spread of the Ebola virus in Uganda in 2000 [6, 15]. We have an initial susceptible population equal to Uganda's population in 2000 ($24,276,000$) minus the number of initially infected individuals at the starting time [17]. We further assume that the Ebola virus may be equally likely to infect a susceptible individual who comes into contact with the infectious body whether the body is dead or alive; therefore, we assume that both β_1 and β_2 vary over the same range, but are not necessarily the same value (Table 1). This assumption is derived from the fact that regardless of the livelihood of the infected, close contact with its bodily fluids are the primary transfer of the disease. We varied the vaccination rate (ψ) between 0.0001 and 0.01 in order to assess the change in the results generated from the $SEIRvDB$ model, and their effects on the total number of infected and the duration of the outbreak (Table 1).

3.2 Threshold Condition

The basic reproductive ratio, $\mathcal{R}_0$, is a value that represents the average number of secondary infections that are caused by any one infected individual. The $\mathcal{R}_0$ value can be used to indicate if an infection will die out or cause an epidemic. Usually, if $\mathcal{R}_0 > 1$, then the infection will cause an epidemic, but if $\mathcal{R}_0 < 1$, then the infection dies out. While there are many different methods that can be used to determine an $\mathcal{R}_0$, we started with the Jacobian method, which takes into account movement across all classes.

In the Jacobian Method, $\mathcal{R}_0$ is the largest eigenvalue of a matrix constructed by taking the partial with regards to each state. This matrix was evaluated at the disease-free equilibrium, which we found to be $S = 0$, $E = 0$, $I = 0$, $R = N$, $D = 0$, and $B = 0$, where N is the total population. Evaluating for the eigenvalues of the Jacobian matrix at the disease-free equilibrium yields:

$$\mathcal{R}_0 = \begin{cases} -\gamma & \text{when } |\gamma| = \max\{|\gamma|, |\kappa|, |\mu|, |\zeta\psi|\} \\ -\kappa & \text{when } |\kappa| = \max\{|\gamma|, |\kappa|, |\mu|, |\zeta\psi|\} \\ -\mu & \text{when } |\mu| = \max\{|\gamma|, |\kappa|, |\mu|, |\zeta\psi|\} \\ -\zeta\psi & \text{when } |\zeta\psi| = \max\{|\gamma|, |\kappa|, |\mu|, |\zeta\psi|\} \end{cases}$$

Notice that the Jacobian Method returns only negative values regardless of our parameter choices. This is problematic because negative $\mathcal{R}_0$ values indicate that there would never be an endemic. However, our LHS simulations indicate that there are indeed parameter spaces resulting in a great outbreak (Figure 5). Therefore, as our Jacobian $\mathcal{R}_0$ (J $\mathcal{R}_0$) no longer accurately represents its physical interpretation, we must calculate $\mathcal{R}_0$ in another manner.

3.3 Anderson & May $\mathcal{R}_0$

The most classical definition of $\mathcal{R}_0$ is that given by Anderson & May (2001) as in [18]. Their definition is such that:

$$\mathcal{R}_0 = \beta c D \tag{11}$$

where β is the transmission probability, c is the number of contacts and D is the average time spent infectious (such that if the rate of infection is γ, then $D = \frac{1}{\gamma}$). It is important to note the assumptions under which Anderson & May $\mathcal{R}_0$ (A&M $\mathcal{R}_0$) is applicable, videlicet there is no background death rate. Furthermore, it should be noted that β values used here are such that they are the equivalent of A&M's βc.

However, calculation of the A&M $\mathcal{R}_0$ is not as straightforward with the $SEIRvDB$ model. As there exists two sources of infection, we must consider the $\mathcal{R}_0$ individually for each; namely, how many secondary infections are sprung by one infectious living individual or the number of secondary infections generated by one infectious deceased cadaver. As the source of a theoretical Ebola epidemic could arbitrarily start with either one, we can consider the A&M $\mathcal{R}_0$ for the $SEIRvDB$ model as the average of the A&M $\mathcal{R}_0$'s as calculated for each situation's A&M $\mathcal{R}_0$. That is to say:

$$\mathcal{R}_0 = \frac{\beta_1 + \beta_2}{2} \frac{1}{\gamma} \tag{12}$$

3.4 Latin Hypercube Sampling

We used Latin hypercube sampling (LHS) in performing uncertainty analysis to account for the ranges of each of our parameter values. In general, uncertainty analyses help explain the variance found in outcome values, given a range of parameters. The model is run using these unique parameter combinations and the initial susceptible population, $24,275,900$, which is the population of Uganda in 2000 minus 100 initially infected individuals [1, 17]. With uncertainty in the exact values of parameters, β_1, β_2, κ, γ, ψ, and μ, we used LHS to achieve random combinations from their probable ranges (Table 1). We then evaluated our model using $1,000$ different parameter combinations, and the graphs of these tests can be seen in Figure 5 of the results section.

3.5 Partial Rank Correlation Coefficients

Partial rank correlation coefficients (PRCC's) can be used in sensitivity analysis to compare the output of each parameter combination from the LHS across changes in the parameter values [16]. Sensitivity analysis reveals which parameter holds the most impact over the course of the model, and thus has the most influence on the output. These results can be seen in Figures 5 of the Results section.

4 Results

4.1 Solutions for a Single Parameter Set

Figures 4a and 4b display an Ebola epidemic modeled by the regular $SEIR$ model with the initial conditions of Uganda in 2000 and parameters (Table 1). Figures 4c and 4d demonstrate the effect of an added prophylactic vaccine as demonstrated in our previous paper [7]. Note that the number of exposed and infectious individuals decreases significantly with the presence of a vaccine. Figures 4e and 4f show the $SEIR$ model with the addition of the dead and buried classes. The number of exposed and infectious individuals dramatically increases, which is to be expected because this graph accounts for more ways that Ebola can be spread to susceptible individuals.

The final pair of graphs, Figures 4g and 4h illustrate the $SEIR$ model that accounts for the dead

and buried classes with a prophylactic vaccine. Note that the introduction of a vaccine decreases the number of exposed and infectious individuals compared to the previous set of graphs, but is still significantly more than those shown in Figures 4a and 4b. This is to be expected because the graph accounts for exposures and infections due to contact with deceased individuals, which makes the model more accurate but nonetheless shows a larger number of exposed and infectious individuals. Also, it is important to note that in Figure 4e there is a cumulative 1.28×10^7 buried individuals and 1.31×10^7 recovered individuals; however, in Figure 4g there is a cumulative 1.20×10^7 buried individuals and 1.23×10^7 recovered individuals, showing that a prophylactic vaccine decreases the total number of people who go through the infectious class.

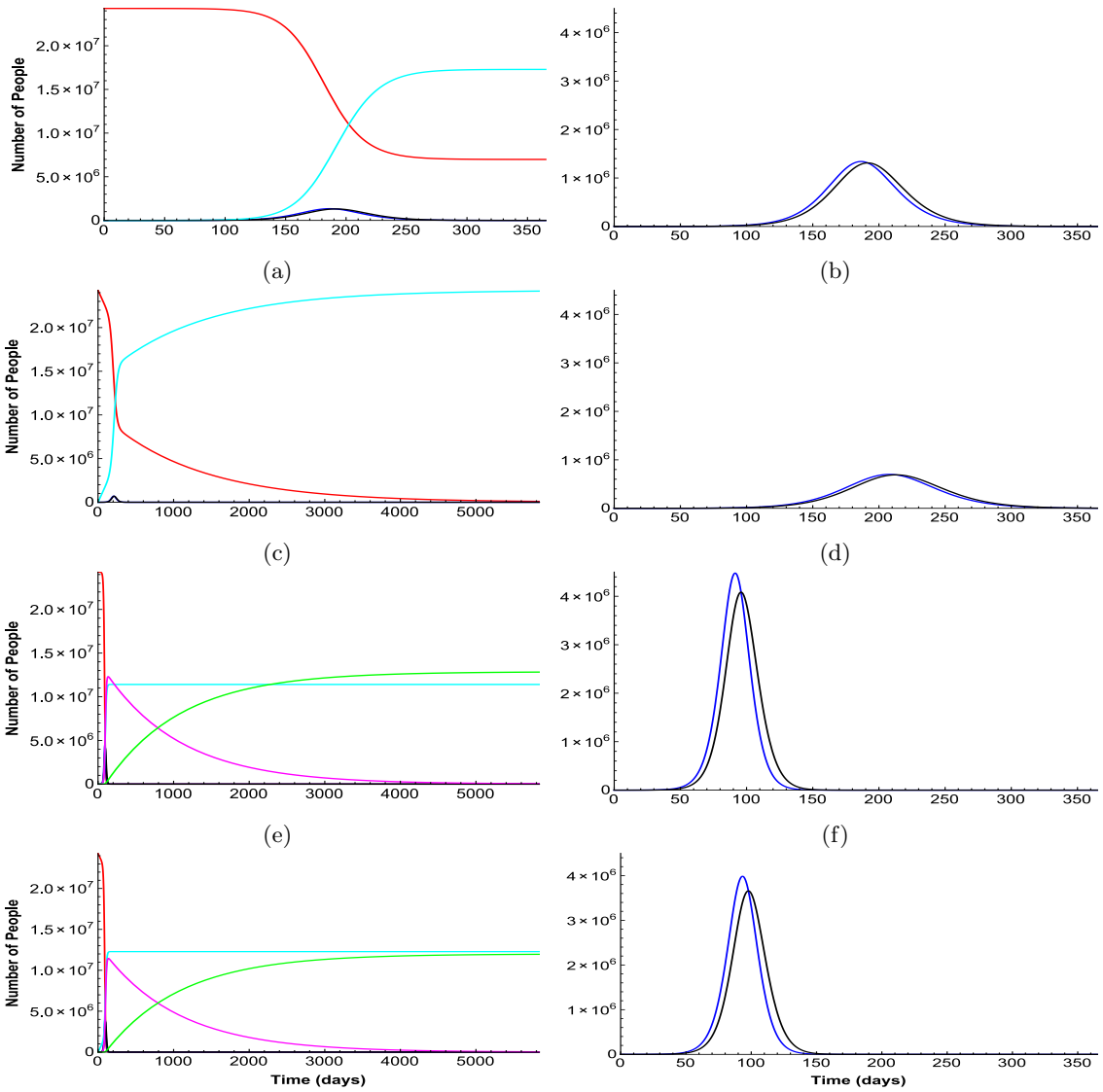


Figure 4: The colors in the graphs are represented as follows: S (red), E (dark blue), I (black), R (light blue), D (magenta), and B (green). The left column shows all classes and the right column shows a closer look at only the exposed and infected classes. The first row shows the traditional $SEIR$ model with no vaccination or infectiousness of dead individuals. The second row of graphs shows the $SEIRv$ model where there is prophylactic vaccination of the susceptible class but no infectiousness of dead individuals. The third row of graphs shows the $SEIR$ model without vaccination but with the addition of an infectious dead class and buried classes. The fourth row of graphs shows the $SEIRv$ model with the prophylactic vaccine for the susceptible class as well as an infectious dead class and buried class. The initial susceptible population is the population of Uganda in 2000 minus 100 initially infected individuals $(24,275,900)$ [17]. Note that the scale on Figures 4c, 4e, and 4g are on the order of 17 years, allowing the model to reach equilibrium; however, with such a long period of time, our model loses accuracy as our assumption of no migrations, births, or deaths into or out of the population becomes less likely.

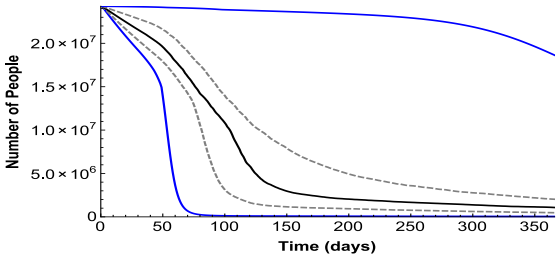
4.2 Uncertainty Analysis

The results of conducting uncertainty analysis on Equations (5)-(10) can be seen in Figure 5. We found that for all parameters sets, the susceptible class always decreases as time elapses, and this is because, either due to infection or vaccination, the individuals eventually leave the susceptible class. Consequently, the graph of the recovered class is an inverse of the graph of the susceptible class; people will always move into the recovered class either via vaccination or infection (Figures 5a and 5b). The second and first quartiles for the exposed and infected classes are both low compared to the third quartile and maximum (Figures 5c and 5e). This is due to the fact that our model starts with one hundred infected individuals and has a range for the $\mathcal{R}_0$ value that can be much less than 1, which means that the disease free equilibrium - the stable solution at which the disease is not present - is stable. However, the maximum and third quartile for both classes are very high in comparison to the second quartile range, as depending on the parameter set $\mathcal{R}_0$ may take on a magnitude greater than 1 (Figures 5d and 5f).

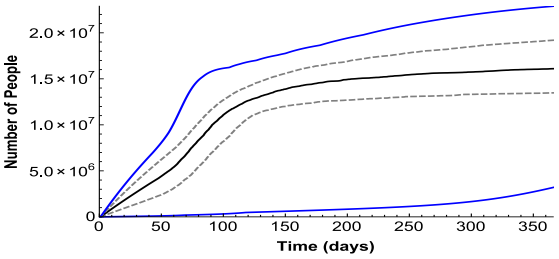
4.3 Sensitivity Analysis

We computed partial rank correlation coefficients (PRCCs) to measure the sensitivity of the cumulative number of infections by (t = 365 days) to the parameter uncertainty. The number of cumulative infected was most sensitive to small changes in the vaccination rate (ψ) because the lower the vaccination rate, the fewer individuals who could possibly be immune to Ebola, and the more individuals who can become infected. The number of cumulative infected was also sensitive to the rate of infection from infectious to susceptible individuals (β_1) (Table 2). The rate at which people are buried (μ) is only moderately correlated to the cumulative number of infected, which shows that while safe burial practices are important, they are not as important as a prophylactic vaccine. Furthermore the transmission rate of Ebola from dead individuals (β_2) the least correlated value to the cumulative number of infected.

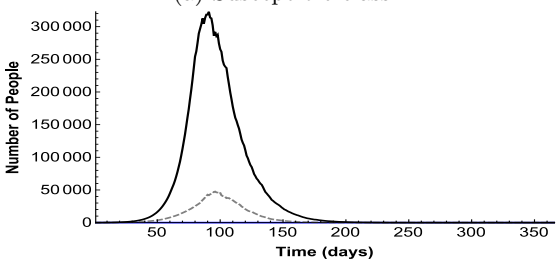
Next, we computed the PRCCs to measure the sensitivity of $\mathcal{R}_0$ by (t = 365 days) to our parameters uncertainty. The calculation of $\mathcal{R}_0$ is based on the theory that there is 1 infected individual in a 100% susceptible population. Thus, the vaccination rate, ψ, should not affect the



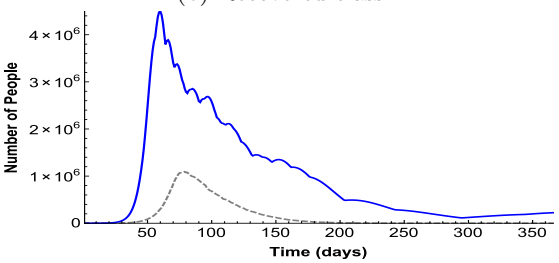
(a) Susceptible class.



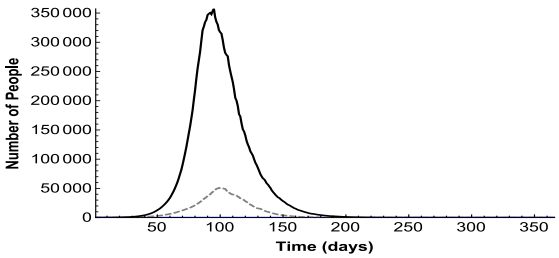
(b) Recovered class.



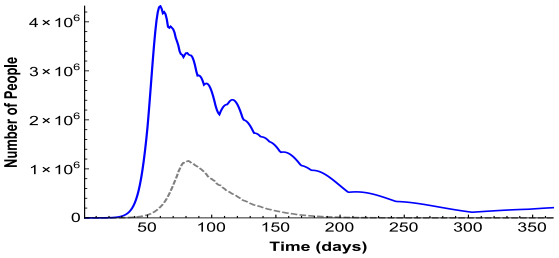
(c) Minimum, 1st quartile, and 2nd quartile (exposed class).



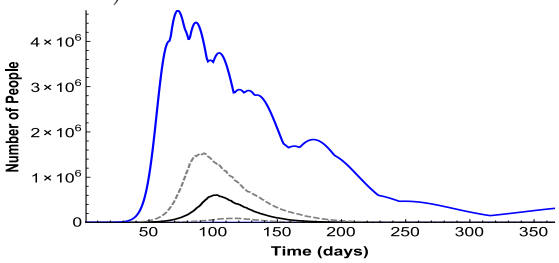
(d) Maximum and 3rd quartile (exposed classe).



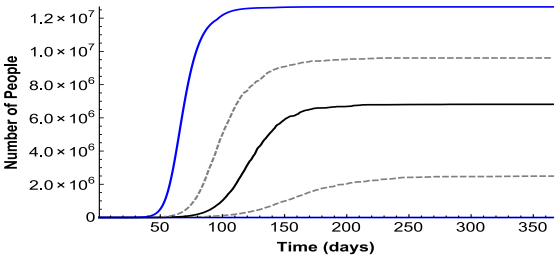
(e) Minimum, 1st quartile, and 2nd quartile (infectious class).



(f) Maximum and 3rd quartile (infectious class).



(g) Dead class.



(h) Buried class.

Figure 5: The colors in the graphs are represented as follows: minimum and maximum (blue), 3rd and 1st quartiles (grey dashed), and 2nd quartile (black). Note that there are scale differences between graphs.

calculation of $\mathcal{R}_0$. Furthermore, the Anderson and May calculation is only based on the values of β_1, β_2, and γ, and so the PRCC values are calculated excluding our other parameters (Equation (12)) [18]. $\mathcal{R}_0$ was very sensitive to the rate of disease transmission from infectious individuals (β_1) as the higher the transmission rate, the more infections occur (Table 2). Furthermore, our sensitivity analysis shows that β_1 is the most important overall factor to account for in curbing an Ebola epidemic, when evaluating $\beta 1$'s influence on both the cumulative number of infected and $\mathcal{R}_0$. Surprisingly, notice that β_2 has the greatest effect on the values of $\mathcal{R}_0$. Collectively, these β_2 findings are somewhat convoluted, as it indicates a large role for the infectious deceased on the secondary infections without much repercussion on the cumulative number of infections. Hence, infectious cadavers play a large role in the mass-action spread of Ebola, but not necessarily the cumulative number of infected. This seemingly contradictory statement is viable as the infectiousness of the deceased is dependent upon the lethality of the disease. Ergo, a weak Ebola strain, even though infectious, would not greatly increase the population of the infectious deceased, and allows β_2 to play a lesser correlated role with the cumulative infected.

Table 2: PRCC values for each parameter as it affects the cumulative number of infected individuals and $\mathcal{R}_0$ (as calculated by the Anderson & May method). All simulations started with one infectious individual. Color coding shows how correlated the magnitude of the PRCC is to the output (darker orange is most correlated). The most correlated values are closer to ± 1.

Output	Cum. I	$\mathcal{R}_0$
β_1	0.8491	0.9562
β_2	0.0950	0.9566
γ	-0.2913	0.8884
ψ	-0.9404	—
κ	0.0950	—
μ	-0.3867	—

4.4 Goal Revisited

The most essential parameters are the transmission rate between the infectious class and the susceptible class, β_1, the infectious deceased class and the susceptible class, β_2, the vaccination rate, ψ, and the extent to which one is infectious, γ. As the ability of Ebola to be transmitted amongst the living and duration of infection is not readily controllable, we can conclude that the controllable variables ψ and the burial rate, μ, are the most essential parameters in fighting an epidemic. As a result, the likelihood that susceptible individuals will contract the disease from the deceased depends on how long it takes to bury the deceased as well as how many susceptible individuals have yet to be vaccinated. In the case of an Ebola outbreak, greatest efforts should be made to vaccinate the population and bury the infectious deceased.

5 Conclusions

5.1 Comparison to $SEIRv$ Model

Our model is different from the $SEIRv$ model because there are two additional classes, dead and buried [7]. Individuals in the dead class remain infectious to susceptible individuals, which more accurately models the spread of the Ebola virus. Also, this model differentiates between individuals who recovered from the disease and those who died from it, which is not included in the $SEIRv$ model. Because this model more accurately represents the spread of Ebola, our infectious class is greater than in in the $SEIRv$ model. Like the $SEIRv$ paper, our results show that the addition of a prophylactic vaccine overall decreases the exposed and infectious classes, which in turn decreases the number of exposed individuals in an outbreak and thus leads to fewer deaths caused by Ebola.

In comparison to the initial $SEIRv$ model, the parameters with the greatest effect on $\mathcal{R}_0$ no longer remain strictly the same; whereas the rate of progression to the infectious class κ, the rate of progression to the removed $\zeta\psi$, and the recovered or deceased class γ contributed most dominantly to the $SEIRv$ model, here the transmission rate for the living infectious, β_1, and the infectious deceased, β_2, as well as γ influence $\mathcal{R}_0$ the most. In other words, the ease of which one becomes infected from another living or deceased individual and the rate of progression to becoming infectious themselves

have the greatest effect on the potential of a simulation becoming an epidemic. Further, unlike the $SEIRv$ model, ψ becomes the dominant parameter to which the cumulative number of infected is sensitive, rather than β_1, while all other parameters lost pull on the output. This suggests that the partitioning of the removed class to recovered and deceased, as well as the deceased progression to the buried class, causes the cumulative number of infections to depend most acutely on the primary source of infections β_1 and the means by which infections are avoided ψ, i.e. how fast susceptible individuals protect themselves from Ebola and just how easily they could catch the disease. This is true of both the $SEIRv$ and $SEIRvDB$ models [7].

5.2 Limitations and Improvements of the Model

Our model is limited by a few simplifying assumptions. A more accurate model would include separate health care professionals and high and low risk susceptible populations, because not all individuals are of equal susceptibility. For example, health care professionals with such close contact to the infected are at higher risk, whereas those in the immediate vicinity of the infected, such as family and friends, are at greater risk than those with no relations to the infected [3, 11]. Even those individuals who are already sick with another disease, pregnant, or have some other issue that can cause a lower immune system can be put in the high risk susceptible population for a duration of time [13]. Also, if individuals were allowed to enter and leave the population through birth, death (other than by Ebola), and migration between countries, then the model would better predict the spread of the virus. A further improvement to the analysis of the model would include evaluation of the cumulative number of deaths prevented via conducting the parameter sets with and without vaccination. Other models based upon the $SEIRvDB$ model would need to integrate these improvements in order to make the models as accurate as possible.

5.3 Recommendations

While safe burial practices should be followed and people instructed to properly dispose of infectious bodies, our model shows that it is more important to combat the spread of secondary infections amongst the living. Potential strategies include creating an effective vaccine, vaccinating as many susceptible people as possible, and properly expediting the burial of the deceased to contain the

epidemic. This being said, most efforts to prevent the outbreak of Ebola should be geared toward the development of a working prophylactic vaccine to diminish the susceptible population, which easily catches Ebola from the infectious living and deceased. However, future research should include the benefits of a prophylactic versus a therapeutic vaccine. Even though the burial rate is not as important of a factor as the development of a vaccine, research needs to be dedicated to burial practices in countries at risk of having an outbreak of Ebola. As our calculation of PRCCs for $\mathcal{R}_0$ is most sensitive to the transmission from the infectious deceased, in order to limit the exposure to infectious deceased individuals, proper burial and barrier nursing techniques need to be incorporated [5]. If proper burial precautions can be integrated into the traditional burial practices of a culture, then infectious, deceased individuals may eventually become a smaller contributing factor to the spread of Ebola, thus focusing efforts to protect the population on one front rather than two.

References

[1] Sally M. Blower, Erin N. Bodine, and Kathie Grovit-Ferbas. Predicting the potential public health impact of disease-modifying hiv vaccines in south africa: The problem of subtypes. *Current Drug Targets - Infectious Disorders*, 5(2):179–192, 2005.

[2] Brittany Bodine, Kayla Shorten, and Maraia Tremarelli. Gw12 alpha seirdb. *Proceedings of Rhodes College Math 315: Ebola Edition*, 3, 2014.

[3] Lisa Brosseau and Rachael Jones. Health workers need optimal respiratory protection for ebola.

[4] Sébastien Calvignac-Spencer, Jakob M. Schulze, Franziska Zickmann, and Bernhard Y. Renard. Clock rooting further demonstrates that guinea 2014 ebov is a member of the zaïre lineage. *Current Outbreaks*, 1, 2014.

[5] CDC. Cdc tightened guidance for u.s. healthcare workers on personal protective equipment for ebola.

[6] G Chowell, N.W. Hengartner, C. Castillo-Chavez, P.W. Fenimore, and J.M. Hyman. The basic reproductive number of ebola and the effects of public health measures: the cases of congo and uganda. *Journal of Theoretical Biology*, 229:119–126, 2004.

[7] Connor Cook, Elizabeth Poston, and Sumner Magruder. Gw12 squig ds seirv. *Proceedings of Rhodes College Math 315: Ebola Edition*, 3, 2014.

[8] Emmie de Wit, Heinz Feldmann, and Vincent J Munsters. Tackling ebola: new insights into prophylactic and therapeutic intervention strategies. *Genome Medicine*, 3(5), 2011.

[9] Timothy C. Germann, Kai Kadau, Jr. Ira M. Longini, and Catherine A. Macken. Mitigation strategies for pendemic influenza in the united states. *PNAS*, 2006.

[10] Barry S. Hewlett and Richard P. Amola. Cultural contexts of ebola in northern uganda. *Emerging Infectious Diseases*, 2003.

[11] Bonnie Hewlett and Barry Hewlett. Providing care and facing death: Nursing during ebola outbreaks in central africa. *Journal of Transcultural Nursing*, 2005.

[12] http://www.deathreference.com/A Bi/African-Religions.html.

[13] DJ Jamieson, Uyeki TM, WM Callaghan, D Meaney-Delman, and SA Rasmussen. What obstetrician-gynecologists should know about ebola: A perspective from the centers for disease control and prevention. *Obstet Gynecol.*, 2014.

[14] M. J. Keeling, M. E. J. Woolhouse, R. M. May, G. Davies, and B. T. Grenfell. Modelling vaccinatoin strategies against foot-and-mout disease. *Nature*, 2003.

[15] Natalya M. Kudoyarova-Zubavichene, Nikolai N. Sergeyev, Alexander A. Chepurnov, and Sergey V. Netesov. Preparation and use of hyperimmun serum for prophylaxis and therapy of ebola virus infections. *The Journal of Infectious Diseases*, 179:218–23, 1999.

[16] Simeone Marino, Ian B. Hogue, Christian J. Ray, and Denise E. Kirschner. A methodology for performing global uncertainty and sensitivity analysis in systems biology. *Journal of Theortical Biology*, 254, 2008.

[17] United Nations. Uganda population.

[18] Robert Smith? *Modelling DIsease Ecology with Mathematics*, volume 2 of *Differential Equations and Dynamical Systems*. American Institue of Mathematical Sciences, 2008.

[19] Ayato Takada, Hideki Ebihara, Steven Jones, Heinz Feldmann, and Yoshihiro Kawaoka. Protective efficacy of neutralizing antibodies against ebola virus infection. *Vaccine*, 25(6), 2007.

[20] P. van den Driessche and James Watmough. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 180:29–48, 2002.