Mathematical Modeling for the Eradication of Ebola

Team # 42047

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Abstract

In this paper, we create an epidemic model, a mathematical means of describing the transmission of communicable disease, of the Ebola Virus in the countries currently at risk of Ebola transmission: Liberia, Sierra Leone, and Guinea. We use a Susceptible-Exposed-Infected-Recovered (SEIR) model to find the spread of the Ebola Virus and vaccination efforts. With the critical vaccination fraction, we are able to find the proportion of each country's population that must be vaccinated. Given the lack of medical personnel in these countries, international aid is necessary to eradicate the Ebola Virus; we created a series of functions for arriving medical personnel, which we use to determine the rate of vaccination needed for the critical vaccination proportion. With this proportion, we find the minimum quantity of vaccines required for the eradication of the Ebola Virus in Liberia, Sierra Leone, and Guinea. Moreover, given the quantity of vaccines required, we calculated the minimum production rate of vaccines, the delivery locations, and the systems for delivery. Additionally, we constructed a computer simulation using *Gleamviz*, a global epidemic modeling software, to evaluate the effectiveness of our model. Based on these simulations, if our assumptions are met, the mathematical model and computerized model coincide to eradicate the Ebola Virus.

Contents

1 Introduction

The eradication of a deadly virus is a daunting task that has only been achieved once in human history with the elimination of smallpox. Thus, using the elimination of smallpox as a reference in conjunction with existing mathematical models for epidemics and vaccination, we have synthesized a mathematical model that accounts for the spread of disease, required medicine, delivery systems, delivery locations, production speed, and personnel needed to optimize the eradication of Ebola. Our model specifically focuses on the **required medical personnel to administer vaccinations** to the public in order to achieve the minimum critical vaccination fraction for the populations in the countries currently afflicted with Ebola in order to achieve its eradication.

1.1 Plan of Attack

Our objective is to create a mathematical representation of the critical vaccination fraction for the populations in the countries currently afflicted with Ebola to achieve its eradication. In order to achieve our aims, it is important to realistically represent the proportion of population receiving vaccination to the amount of doctors within that country in addition to the production and logistical variables of our mathematical model using the susceptible-encountered-infected-removed model (SEIR) for our vaccination regiment as imposed by the international community.

- **Develop The Ebola Epidemic Model** : Using information available on Ebola, we will synthesize an SEIR model for the Ebola epidemic while simultaneously modeling vaccination attempts to combat the epidemic.
- **Apply SEIR To At Risk Countries** : Once we have developed an SEIR model, we will apply relevant information on Ebola to obtain the minimum proportion of population that must be vaccinated to eradicate Ebola.
- **Find Logistic Requirements** : With the information from the SEIR model, we will find the logistic requirements our model needs to function correctly.
- **Apply Model To Simulator** : Using the functions for the SEIR model, we will simulate the epidemic using *Gleamviz*, a global epidemic and mobility model to test the effectiveness of our SEIR model.

1.2 Assumptions

Due to the nature of viral evolution and unpredictable human elements, several assumptions are necessary to construct an SEIR model for the Ebola epidemic. Below are the general assumptions we have made for our mathematical model:

- **New Medication is Vaccine** : Based on related viruses, there are no cures that have been found for the family Filoviridae or the order Mononegavirales; therefore, our model assumes the new medication is a highly effective vaccine that is unable to cure patients with advanced Ebola and only a possibility of curing the infected. Moreover, we have assumed the vaccine is in good condition and will not affect the health of the population.
- **Same Ebola Strand** : Since viruses have the capability to rapidly evolve, our model makes the assumption that the Ebola virus is identical in all locations and will not mutate to infect vaccinated-immunized population.
- **International Aid** : Since many of these countries do not have the funds or medical personnel available to effectively combat the Ebola epidemic, we have assumed the international community will provide aid in the form of medical personnel and funding.
- **No Travel** : When smallpox was eliminated, intensive surveillance and containment played a critical role in its elimination to stop the spread of smallpox. Our model assumes there is a high level of containment for each of the countries afflicted with Ebola, and that they are completely closed systems that will not infect other regions outside their respective borders.

2 Determine the Epidemic Model

An epidemic model is a simplified way to mathematically represent the transmission of disease through a population. There are several different types of epidemic models that exist to represent different forms of disease in a population and some models are better suited to some diseases than others. For the purposes of Ebola on the international level, we will implement a Susceptible-Encountered-Infected-Recovered model (SEIR) to mathematically represent the Ebola epidemic and vaccination efforts against it.

2.1 The SEIR model

An SEIR model is a deterministic model that divides the individuals in a population into different groups that correspond to different stages in an epidemic. In the deterministic model, differential equations are used to determine rates to express the transition from one group to another. The SEIR model groups the population into four groups: those susceptible to the epidemic, the amount of people encountered or exposed to the disease, the infected, and those who recover. In the SEIR model, the densities are deonted respectively by $S(t), E(t), I(t)$, and $R(t)$, such that $N = S(t) + E(t) + I(t) + R(t)$ [4]. Each of these densities are found with the equations below:

$$\frac{dS}{dT} = B - \beta SI - \mu S$$

$$\frac{dE}{dT} = \beta SI - (\varepsilon + \mu)E$$
$$\frac{dI}{dT} = \varepsilon E - (\gamma + \mu)I$$
$$\frac{dR}{dT} = \gamma I - \mu R$$

Where the variables are defined as: S: Susceptibles, E: Exposed, I: Infectives, R: Recovered with immunity, B: birth rate, β : contact rate, μ : death rate, ε : latent period, and γ : infectious period [4].

3 Doctors in Afflicted Countries

While we have assumed the international community will help the countries afflicted with Ebola by providing more medical personnel, we constructed **functions to quantify the amount of doctors required** to vaccinate the populations of the countries currently afflicted with Ebola.

3.1 Doctors in countries with Ebola

According to the World Health Organization, the recent outbreaks in Mali, Nigeria, Senegal, Spain, United States, and Congo have been declared free of Ebola transmission. Noticing that each of these countries has at least .1 doctors per 1000 people, it seems necessary to have medical personnel to combat Ebola and vaccinate the population. The three countries that are not free of Ebola transmission are Liberia, Sierra Leone, and Guinea, with .01, .02, and .09 doctors per 1000 people, respectively [5][6].

3.2 Functions for Afflicted Countries

We have constructed a set of piecewise equations for Liberia, Sierra Leone, and Guinea to bring them up to .1 doctors per 1000 people in order to have the medical personnel necessary to eradicate Ebola. With the general populations of each country, we find the following piecewise equations based on day x that runs from 0 to 365.

$$D_{Liberia}(x) = \begin{cases} 43 + 15x, & \text{if } 0 \leq x \leq 30 \\ 508 + 2x, & \text{if } 31 \leq x \leq 60 \\ 568 + x, & \text{if } 61 \leq x \leq 100 \\ 608, & \text{if } x > 100 \end{cases} \tag{1}$$

$$D_{Sierra\,Leone}(x) = \begin{cases} 120 + 18x, & \text{if } 0 \leq x \leq 30 \\ 678 + 2x, & \text{if } 31 \leq x \leq 60 \\ 738 + x, & \text{if } 61 \leq x \leq 100 \\ 778, & \text{if } x > 100 \end{cases} \tag{2}$$

$$D_{Guinea}(x) = \begin{cases} 1175 + 5x, & \text{if } 0 \leq x \leq 30 \\ 1330 + 2x, & \text{if } 31 \leq x \leq 60 \\ 1390 + x, & \text{if } 61 \leq x \leq 100 \\ 1430, & \text{if } x > 100 \end{cases} \tag{3}$$

These piecewise functions enable us to determine the amount of doctors at work in the three countries currently afflicted with Ebola. Later in this paper, these functions will be useful for determining the amount of population that has been vaccinated on day x.

4 Creating the SEIR Model

Using the SEIR model, we must find the critical vaccination fraction f for a closed, homogeneously mixing population. The critical vaccination fraction f is the minimum vaccination coverage that reduces the reproduction number to a value less than or equal to one. This ensures the reproduction rate slows and eventually stops to eradicate the infection.

4.1 Vaccine Efficacy

There are two areas of vaccine efficacy that need to be defined: susceptibility and infection [2].

- Vaccine efficacy for susceptibility is the vaccine's ability to reduce a person's susceptibility to the infection.
- Vaccine efficacy for infection is the vaccine's ability to reduce the infection in an infected person.

$$VE_S = 1(1 - \alpha)\theta \tag{4}$$

$$VE_I = 1 - \phi \tag{5}$$

4.2 The SEIR Matrix

From the law of total probability, we may define the exposed number of secondary infections for an unvaccinated and vaccinated person, $E(I_0)$ and $E(I_1)$, respectively [2].

$$E(I_0) = R_0(1 - f) + (1 - VE_I)R_0 f \tag{6}$$

$$E(I_1) = (1 - VE_S)R_0(1 - f) + (1 - VE_I)(1 - VE_S)R_0 f \tag{7}$$

From here, equations (6) and (7) can be translated into a linear system of difference equations. Suppose $y_v(g)$ is the number of infected people that are vaccinated and unvaccinated. If an someone is unvaccinated, v=0 and if they are vaccinated, then v=1 in generation g, the generated system is as follows [1],

$$y_0(g+1) = R_0(1-f)y_0(g) + (1-VE_I)R_0 f y_1(g)$$
$$y_1(g+1) = (1-VE_S)R_0(1-f)y_0(g) + (1-VE_I)(1-VE_S)R_0 f y_1(g). \quad (8)$$

Now, if we define the column vector $\mathbf{y}(g)$=$[y_0(g), y_1(g)]$' and a matrix $\mathbf{M}$ as

$$\mathbf{M} = R_0 \begin{bmatrix} 1-f & f(1-VE_I) \\ (1-f)(1-VE_S) & f(1-VE_I)(1-VE_S), \end{bmatrix} \quad (9)$$

Then we write the system (8) as

$$\mathbf{y}(g+1) = \mathbf{M}\mathbf{y}(g)$$

Next, we define R_f to be

$$R_f = (1 - f(VE_S + VE_I - VE_S VE_I))R_0 \quad (10)$$

If $R_f \leq 1$ then we arrive at the conclusion

$$y(g+1) - y(g) \leq \begin{bmatrix} 0 \\ 0 \end{bmatrix}, g = 0, 1, ...$$

This means that the epidemic cannot grow if $R_f \leq 1$ [1].

5 Applying the SEIR Model

Using Liberia, Sierra Leone, and Guinea since they are the three countries currently afflicted with Ebola according to the World Health Organization, we will apply the SEIR model to look at three separate, closed, homogeneously mixing populations.

First, the magnitude of our vaccination is dependent upon R_0, which is the basic reproduction number of the underlying epidemic process in the SEIR model. We define R_0 as

$$R_0 = \beta c d, \quad (11)$$

where β is the transmission probability of the infectious agent when contact occurs between an unvaccinated susceptible person and an unvaccinated infectious person, c is the rate of contacts per day that each person makes with anyone else in the population, and d is the average unit time an infected person is infectious from the confidence interval [2.1,3.6] that is 95% confident the true value of infected persons to how many they infect [4]. We have used 3.6 in our model to simulate the worst conditions over a ten day period at four contacts per day. From here,

$$\beta = 0.09$$

$$c = 4$$

$$d = 10.$$

Thus equation (11) becomes

$$R_0 = (0.18)(4)(5) = 3.6.$$

Recall equations (4) and (5), VE_S and VE_I, respectively. In equation (4), we must define α, θ, and ϕ.

α is the fraction of vaccinees that are fully protected by the vaccine. Earlier, we derived the number of doctors present in each of the countries from (1), (2), and (3) for Liberia, Sierra Leone, and Guinea, respectively. Using the number of doctors and the rate of vaccination τ, we calcualted the total number of vaccinations for the population in each country after thirty days to find α [2].

5.1 Afflicted Countries

For Guinea,

$$\alpha = \frac{\sum_{x=1}^{100}(\tau)D_{Guinea}(x)}{11750000}(0.995)$$

For Liberia,

$$\alpha = \frac{\sum_{x=1}^{100}(\tau)D_{Liberia}(x)}{4300000}(0.995)$$

For Sierra Leone,

$$\alpha = \frac{\sum_{x=1}^{100}(\tau)D_{SierraLeone}(x)}{6000000}(0.995)$$

θ is the proportionality factor that reduces the remaining fraction, $1-\alpha$, of vaccinee's susceptibility to infection. Due to the lack of conclusive evidence of Ebola's proportionality factor, we have set θ=.5.

ϕ is the proportionality factor that reduces the infectiousness of a vaccinated person that becomes infected. Since the person is already infected and our model supposes the use of a vaccine, the vaccine will not be too effective in assisting the infected persons. Therefore, using the data from the Center for Disease Control, we have set ϕ=.4 because with intervention the fatality rate of Ebola drops from 90% to 50%. Now, the susceptibility for Guinea, Liberia, and Sierra Leone, respectively, are as follows,

- $VE_{SG} = 0.6484$
- $VE_{SL} = 0.6511$
- $VE_{SSL} = 0.6408$

The vaccine efficacy for infection is

$$VE_I = 0.6$$

Recall matrix $\mathbf{M}(9)$ and its largest eigenvalue $R_f(10)$. From (10), we are able to find the critical vaccination fraction f by setting (10) equal to 1 since R_f is the largest eigenvalue of (6) and $R_F \leq 1$.

$$R_f = (1 - f(VE_S + VE_I - VE_S VE_I))R_0 = 1$$

Then,

$$f = \frac{R_0 - 1}{R_0(VE_S + VE_I - VE_S VE_I)}$$

5.2 Vaccinated Population Proportion

Finally, we are able to determine the minimum proportion of each country's population that must be vaccinated in order to eradicate the spread of Ebola.

$$f_G = \frac{3.6 - 1}{3.6(0.6484 + 0.6 - (0.6484)(0.6))} = 0.8404 \tag{12}$$

$$f_L = \frac{3.6 - 1}{3.6(0.6511 + 0.6 - (0.6511)(0.6))} = 0.8394 \tag{13}$$

$$f_{SL} = \frac{3.6 - 1}{3.6(0.6408 + 0.6 - (0.6408)(0.6))} = 0.8434 \tag{14}$$

Therefore, according to our model in order to eradicate Ebola from these three countries, we must vaccinate at least 84.04%, 83.94%, and 84.34% for Guinea, Liberia, and Sierra Leone, respectively.

6 The Logistics of Ebola Eradication

In order to implement an effective SEIR model, it is important to consider the production requirements necessary to find the optimal strategy to eradicate Ebola. For the purpose of this model, we have assumed funding has been supplied via international aid and now need to examine the production requirements needed to achieve Ebola's eradication.

6.1 Amount of Vaccines

Using (11), (12), and (13), we are able to calculate the minimum amount of vaccine necessary to eradicate Ebola in Guinea, Liberia, and Sierra Leone. With the values from the equations, we find that the minimum amount of vaccine required is $18,544,620$ doses of vaccines. For our model, we have not taken human error into consideration; therefore, the proposed amount of vaccines to produce is $20,000,000$.

6.2 Production Rate

There are fifteen major vaccine factories in Europe and North America that are able to each produce enough biomass to create one million vaccines per month, but these factories rarely work at full capacity and have other obligations aside from manufacturing an Ebola vaccine [7]. With this understanding in conjunction with the amount of vaccines needed, we find that the minimum rate of production is $1,666,667$ vaccines per month or 54795 production must be completed within one year. However, in order to meet the demand of our model, the minimum rate of production must be $71,725$ vaccines per day for the later stages of administering vaccinations. Since the factories together are able to produce $7,500,000$ vaccines per day together, it seems reasonable to assume the demand of $71,725$ vaccines per day can be met.

6.3 Delivery Locations

Liberia, Guinea, and Sierra Leone each have an international airport available, and they are all coastal countries. Therefore, the vaccines will be devilered to the airports and ports located in each of the respective countries.

For the delivery system of the vaccine to the general population, the model assumes doctors will actively find people to vaccinate. The model assumes that the population will be willing to be vaccinated and doctors will be able to meet the model's vaccination requirements to eradicate Ebola.

6.4 Delivery Systems

Using the fact that the minimum number of vaccines for our model is $71,725$, we know that as of day 0, there will be no vaccinations possible and vaccination will begin on day 1. Therefore, our model assumes that day 0 at least $71,725$ vaccines will be produced and at least $34,400$ make it to the afflicted countries by day 1. We find that the extra amount of vaccines per day from day 0 is:

$$y = 43426e^{-0.042x}$$

With this trendline, we find the optimal delivery system for the nations involved in terms of money. Since using a delivery system that relies on sea is far more inexpensive than air, we have found that air travel is only necessary for the first 13 days of the model. At the end of the third day, there is enough vaccine to completely cover the fourteenth and fifteenth days. From there, the airplanes will only need to carry the minimum amount of vaccines necessary per day for about two weeks, then shipping via sea travel will be the optimal route for transporting the vaccines.

7 Simulating the Model

Using the epidemic simulator *Gleamviz*, we applied our mathematical model to the spread of Ebola in Guinea, Sierra Leone, and Liberia.

7.1 Simulator Configuration

We took survey information from the World Health Organization, as per our model, and set day 0 to have that many cases of Ebola. The vaccination rate in the model has been altered for each country to reflect the vaccination schedule in the SEIR model. For the purposes of the simulator, there are four stages to Ebola: infected stage 1, infected, advanced, and dead. Once a person has been dead for a day, they are removed from the system. This is done intentionally to simulate the improper disposal of bodies and that bodies are still infectious for the Ebola Virus.

7.2 Simulator Results

If we assume a closed, homogeneous model in the simulation, we find that Ebola is eradicated within a year and no new cases occur after that point. In the simulator, we find the amount of infected is approximately 1.1 per $1,000$ people and the rate of death is approximately 50% for those who become infected.

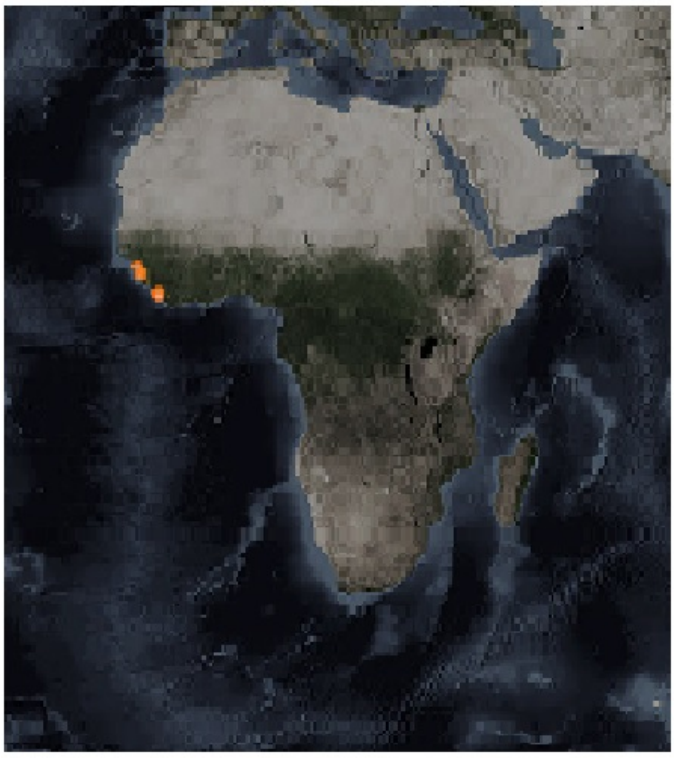

Figure 1: Simulator Results for Closed Model

8 Improving the Model

In our mathematical model, several assumptions have been made that are not entirely realistic. If we were to continue developing our model and account for more information, there are several avenues we would consider.

8.1 Allowing Travel

A serious flaw in our model is that it assumes there is no travel between the three countries that currently have Ebola because the SEIR model assumes it is closed. This is inaccurate and flawed. In a realistic model, there would be travel between countries and over borders. Using the *Gleamviz* simulator, we allowed travel and found Ebola spread throughout the entire world using our model.

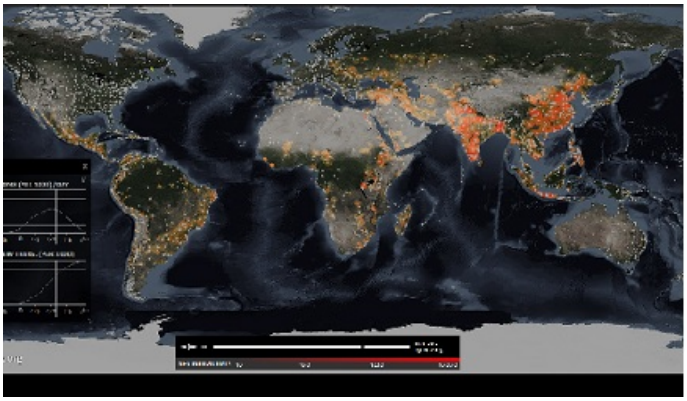

Figure 2: Simulator Results when Travel is Allowed

The data on the graph above displays where Ebola is present, and at the end of the year, 650 per $1,000$ people in the world are infected with Ebola and approximately 325 per $1,000$ die of Ebola in the simulations that allows people who have just contracted Ebola to travel via air and infected to travel via car.

8.2 Factor in Cost of Production

While the global eradication of Ebola is tempting, there are many members of the international community who may not want to participate in the humanitarian effort to eradicate Ebola. Moreover, this model supposes the use of vaccine factories that are currently producing other vaccines. Neither of these assumptions are overly realistic because money will play a crucial role in determining the production rate and ability to convince others of international participation.

8.3 Volunteers Required

Our SEIR model assumes the afflicted countries will receive volunteers to assist in the eradication of Ebola. A more specific idea of how many volunteers or medical personnel would be available could completely destroy this model, and the assumption that several hundred volunteers will assist is not overly realistic, nor does the model provide any alternatives if quotas are not met.

9 Sensitivity Analysis

In any mathematical model, it is important to evaluate one's results under a critical eye and determine where numbers might vary and how that might affect the results of the mathematical model. For epidemic model on Ebola, we have conduicted a sensitivity analysis on three variables: VE_I, VE_S, and ϕ.

9.1 VE_S Sensitivity Analysis

We have varied VE_S (4), the vaccine efficacy for susceptibles, from $[0, 1]$ for each country and superimposed the graphs onto each other. From these graphs, we see the lines are nearly identical, and we establish that there is little variation between countries. However, as VE_S decreases, f the minimum population required to eradicate Ebola increases. We can also intuitively understand that as the vaccine is more effective, that would make f able to be a smaller percentage of the population.

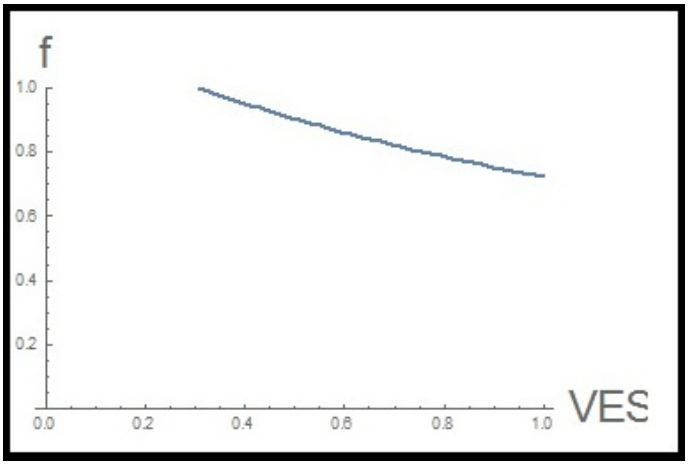

Figure 3: VE_S Sensitivity Graph

9.2 VE_I Sensitivity Analysis

As with VE_S, we have varied VE_I from (5) is vaccine's ability to treat the infected, and the sensitivity analysis varies the VE_I from $[0, 1]$ to calculate the proportion of each country's minimum population proportion that needs vaccination. As can be seen, as the VE_I increases, each country's f approaches the same point. As VE_I decreases, the f values begin to change and steadily becomes higher. Logically, this makes sense because VE_I is the measure of a vaccine's efficiency.

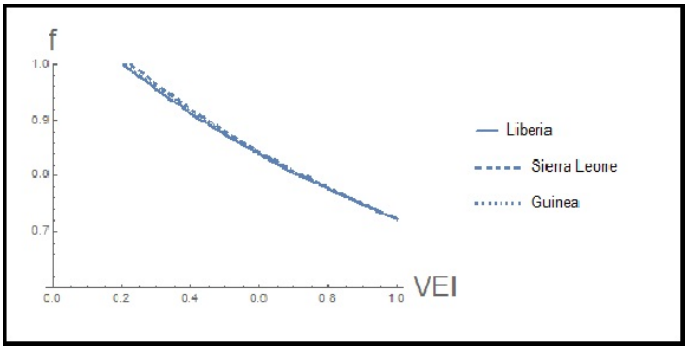

Figure 4: VE_I Sensitivity Graph ϕ

9.3 Drastically Varying VE_S and ϕ

As with the other graphs, we superimposed several different graphs onto one another. For our sensitivity analysis with a drastically varying VE_S (1) in conjunction with ϕ (2), we find that the sensitivity of VE_S and ϕ can be widely varied and drastically affect results.

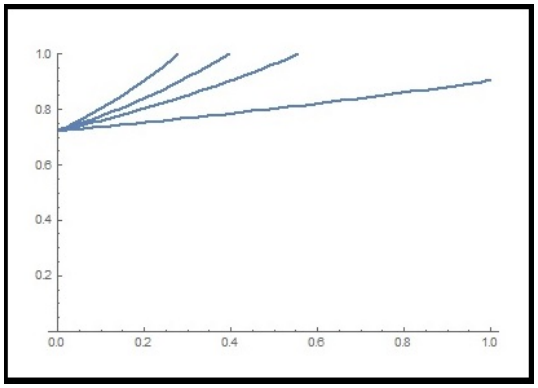

Figure 5: Drastically Varying VE_S and ϕ

10 Conclusion

Modeling the Ebola epidemic in West Africa for Liberia, Sierra Leone, and Guinea with limited information on the statistics of the Ebola Virus made calculating many of the conditions highly difficult, and in order to formulate a model, several difficult assumptions were made, such as the lack of travel outside country borders. While the mathematical model and computer simulation of the mathematical model were approximately identical in scope, fatality rate, and other relevant factors, they both use the same assumptions and calculations. If a strong method for containment with these nations proves impossible, there is little stopping the spread of Ebola to more at risk regions with lower rates of vaccination. Therefore, our model shows that the eradication of Ebola is possible only if the borders are closed, production times are met, and doctors volunteer to administer the vaccines, thus our model should be regarded with caution in a more realistic environment.

11 Letter to the World Medical Association

Knowing that the eradication of smallpox is one of humanity's crowning achievements, it is no small task to eliminate any disease. Since the recent development of the effective Ebola vaccine, it appears humanity once more stands at the precipice of human development. We have created a mathematical representation of the vaccination process that may carry out Ebola's eradication. There are several factors that must be taken into account before moving forward with our model to consider prior to its implementation.

First, there must be international cooperation between countries in the form of funding and sending the required medical personnel to assist the countries currently stricken with Ebola. At minimum, twenty million vaccines will be necessary to combat Ebola in these countries, and they do not possess the medical personnel necessary to carry out such a large regiment of vaccinations within our model's timeline. Moreover, funding the elimination of Ebola will likely be expensive due to delivery by air for the initial two weeks and the constant production of vaccines and their delivery.

Second, our model requires there is no travel from the occupants of these countries if they have contracted Ebola. Since Ebola does take some time for its symptoms to show, this will be difficult to simulate and intensive surveillance and containment will be vital to the success of eliminating Ebola. This is also a somewhat unrealistic expectation that must be regarded with caution and will be difficult to implement. However, when the world successfully rid itself of smallpox, it was carried out effectively. Therefore, it is entirely possible that containment will be maintained within the afflicted countries.

Third, our model assumes the vaccine is in good condition and does not pose any health risks. It also assumes that the current strand of Ebola will not mutate beyond the vaccine's capability before its elimination. If the Ebola virus were to evolve and develop a resistance or way to infect those who have been

vaccinated, it would devastate the results of our model. Moreover, we have also assumed that in all locations, the Ebola virus will behave identically and that it is all the same strand of Ebola at work.

Bearing these facts in mind, we urge the World Medical Association to make the decision it believes best. If the above conditions can be met, then our mathematical model may prove useful in implementing a vaccination regiment for the elimination of the Ebola Virus. However, all our results are very dependent on these assumptions and the model itself should be regarded with caution.

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