Modeling the Eradication of Ebola

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Abstract

We construct a modified SEIR epidemic model to track the spread of a disease through a population while also looking at the influence of vaccination, treatment, and other medical care options. Applying this model to Ebola reveals not only how many people may become infected and die as a result of this fatal disease in the event of an outbreak, but also how many people can be saved as a result of preventative and reactive measures given that they are executed in a timely manner.

We use our SEIR model to estimate how quickly drugs and vaccines need to be manufactured and distributed in order to best respond to an outbreak. We find that the introduction of a cure is significantly more effective in accelerating the eradication of Ebola than the introduction of a vaccine. We then test our model against real data from the most recent Ebola outbreak in West Africa to determine what further refinements are needed. We find that our model predicts the previous outbreak's progression to a reasonable degree.

Introduction

Ebola is an infectious and fatal disease that has plagued much of West Africa. The symptoms include fever, fatigue, tachycardia, and dehydration from excessive diarrhea and vomiting. Infectious victims of Ebola are expected to die within weeks if they do not receive treatment [1]. To understand the effects of a disease on a population, we apply an SIR (Susceptible, Infectious, and Removed) Model. With no intervention individuals in a population will move, in order, from Susceptible to Infectious to Removed.

By its nature, Ebola calls for a modified version of the SIR model. The original model assumes that an individual becomes infectious upon contraction of the disease, however, Ebola may exist in a person's body without becoming active for a period of 2-21 days [5]. The SEIR model accounts for this time delay by considering individuals who are exposed but not infectious. We aim to modify this existing model to account for the manufacturing, delivery, and distribution of a vaccine and/or a cure to the population. In doing so, we hope to create a model that will aid in the optimization of Ebola eradication given disease/population characteristics and limited resources.

Assumptions

- Individuals mix freely at all times (i.e disease or knowledge thereof do not affect human behavior).
- Every susceptible individual has an equal chance of contracting Ebola when they come into contact with an infectious individual.
- When individuals are exposed but not showing symptoms, they do not seek a cure.
- Each infected individual has the same chance of infecting someone else if they are infectious.
- A previously infected individual is no longer infectious after death.
- Vaccines are not effective for individuals that are already exposed to the disease.
- The vaccine available for Ebola is 100% effective meaning individuals that have been vaccinated are no longer susceptible to the disease.
- The treatment for Ebola is 100% effective meaning individuals that have been treated no longer have the disease.
- Individuals cannot become infected again once the disease has run its course or they have been cured.

Variables

Table 1 lists all of the variables used in our model and throughout this paper.

Notation	Property
D	Number of outbreak fatalities
D'	Rate of change in number of outbreak fatalities per day
E	Number of exposed individuals
E'	Rate of change in number of exposed per day
I	Number of infectious individuals
I'	Rate of change in number of infectious individuals per day
R	Number of removed individuals
R'	Rate of change in number of removed individuals per day
S	Number of susceptible individuals
S'	Rate of change in number of susceptible individuals per day
c_0	Cure rate
c	Cure rate function
t	Time in days
t_c	Time at which cure distribution to population begins
t_d	Delivery time
t_m	Manufacturing time
t_v	Time at which vaccine distribution to population begins
v_0	Vaccination rate
v	Vaccination rate function
α	Average length of infectious period
β	Average length of latency period
γ	Estimated daily recovery rate
λ	Estimated daily infection rate

Table 1: Nomenclature

Model Development

Base Model

During the outbreak of an infectious disease we can classify all individuals in the population as one of four types: Susceptible (S), Exposed (E), Infectious (I), or Removed (R), where $S(t)$ is the number of individuals at time t that have yet to come in contact with the disease and are therefore currently susceptible to it, $E(t)$ is the number of individuals at time t that have been exposed to the disease by an infectious individual but have yet to develop symptoms and cannot yet spread the disease, $I(t)$ is the number of individuals at time t that are infectious (i.e. they can spread the disease), and $R(t)$ is the number of individuals at time t that have recovered or died from the disease and thus have been removed from the more dynamic parts of the system. As an outbreak progresses, we model the rates of change of $S(t)$, $E(t)$, $I(t)$, and $R(t)$ using a slight variation of a simple SEIR model [4].

$$S'(t) = -\lambda S(t) I(t) \tag{1}$$

$$E'(t) = \lambda S(t)I(t) - \frac{1}{\beta}E(t) \tag{2}$$

$$I'(t) = \frac{1}{\beta}E(t) - \gamma I(t) \tag{3}$$

$$R'(t) = \gamma I(t) \tag{4}$$

Where λ, β, and γ are parameters specific to the current Ebola strain. λ represents the estimated daily infection rate, γ represents the estimated daily recovery rate, and β represents the average time elapsed from when an individual is exposed to the disease to when the individual becomes capable of infecting others. In our model we set the values of λ and γ to 0.2 and 0.1, respectively, in order to achieve the desired ratio of $\lambda/\gamma = 2$ [3]. We set β to be 10.1 days [2].

Taking into Account the Length of the Infectious Period

This SEIR model is useful in showing how a disease spreads under the assumption that once an individual becomes infectious, they remain infectious until the disease leaves their body naturally. However, Ebola is very deadly and often kills off its host in a matter of weeks. Per our assumption that infectious individuals are no longer infectious after death, we can take the death of an individual into account by taking him or her out of the infectious group (I) and placing him or her into the removed group (R) . This alters Equations 3 and 4 in the following way:

$$I'(t) = \frac{1}{\beta}E(t) - \gamma I(t) - \frac{1}{\alpha}I(t) \tag{5}$$

$$R'(t) = \gamma I(t) + \frac{1}{\alpha}I(t) \tag{6}$$

Where α is the average time elapsed from when an individual first becomes infectious to when they are killed by the disease. This parameter is specific to individual Ebola strains, and we estimate α for the current strain to be 6.5 days [2]. This revision to the SEIR model now takes into account the relatively high fatality rate of Ebola.

The Effects of a Vaccine/Drug

Now that we have an idea of how Ebola spreads throughout a population, we examine the effects of preventative and reactive measures to this spread. If we consider the potential for distribution of a vaccine to the susceptible population and/or of a cure to the infectious population, our model becomes:

$$S'(t) = -\lambda S(t)I(t) - v(t)S(t) \tag{7}$$

$$E'(t) = \lambda S(t)I(t) - \frac{1}{\beta}E(t) \tag{8}$$

$$I'(t) = \frac{1}{\beta}E(t) - \gamma I(t) - \frac{1}{\alpha}I(t) + c(t)I(t) \tag{9}$$

$$R'(t) = \gamma I(t) + \frac{1}{\alpha}I(t) + v(t)S(t) + c(t)I(t) \tag{10}$$

The term $v(t)S(t)$ represents the rate at which susceptible individuals are being vaccinated at time t, and the term $c(t)I(t)$ represents the rate at which infectious individuals are being cured at time t. Per our assumptions, vaccinated individuals are no longer able to contract the disease and cured individuals are no longer able to spread the disease or contract the disease a second time. Thus both are sent to group R.

Factoring in Response Time Delay

The functions $v(t) = v_0 u(t - t_v)$ and $c(t) = c_0 u(t - t_c)$, where v_0 is the daily vaccination rate and c_0 is the daily cure rate (both with units of $days^{-1}$), account for the fact that response time to an outbreak is not immediate. For example, a vaccine/drug may not be developed at the time of the first disease transfer or it may take a while for people to realize that an outbreak is occurring. Thus, we apply the unit step function, $u(t)$, to these constants in our vaccination and cure functions, $v(t)$ and $c(t)$, to account for the inevitable response time delay. These functions only apply v_0 after vaccination distribution begins at time t_v and c_0 after the distribution of a cure begins at time t_c.

But what factors determine t_v and t_c? As mentioned above, a vaccine/drug may not even exist at first. In order to vaccinate and/or cure the population, we must first develop and produce the means to do so. We define manufacturing time, t_m, to be the elapsed time between the introduction of the disease to the population and when the vaccine/drug has been successfully manufactured. Once the means exist, the vaccine/drug must then be distributed among the population. We define delivery time, t_d, to be the elapsed time between when the vaccine/drug has been manufactured and when the vaccine/drug has been distributed to the target population. Both of these processes make up the time delays t_v and t_c. Therefore we can represent t_v and t_c as follows.

$$t_v = t_{m_v} + t_{d_v} \tag{11}$$

$$t_c = t_{m_c} + t_{d_c} \tag{12}$$

Model Testing

What does our model predict?

The simple SEIR model predicts that, in all populations with an initial infectious population (I_0), Ebola (defined by the parameters α β γ λ) will eventually die out and the end population will consist entirely of either susceptible (S) or removed (R) individuals (this is true even in cases where I_0 is as large as 90% of the population). However, just because a disease will not become endemic does not mean a response to its outbreak is not needed; many of those in population R are actually dead, as Ebola has a very high fatality rate. To prevent these deaths, we must first keep track of them. To do this we introduce the category D, where $D(t)$ is the number of fatalities caused by the disease at time t, and $D'(t)$, the rate of change in the number of fatalities at time t. In Equation 10, we have already taken into account the rate of change in the number of fatalities as part of our removed (R) population, therefore we move this term to our new $D'(t)$ equation:

$$D'(t) = \frac{1}{\alpha} I(t) \tag{13}$$

Vaccination or treatment: which is more effective?

As we run our model, we can vary the amount of vaccines and drugs we introduce to our population per day, and monitor how effective they are at preventing fatalities. We found that, for equal values of c and v introduced at the same time, c had a significantly greater effect on the number of fatalities than did v (see Figure 1 below), on the scale of about one order of magnitude. This means that a cure has a greater effect on eradicating Ebola than a vaccine does.

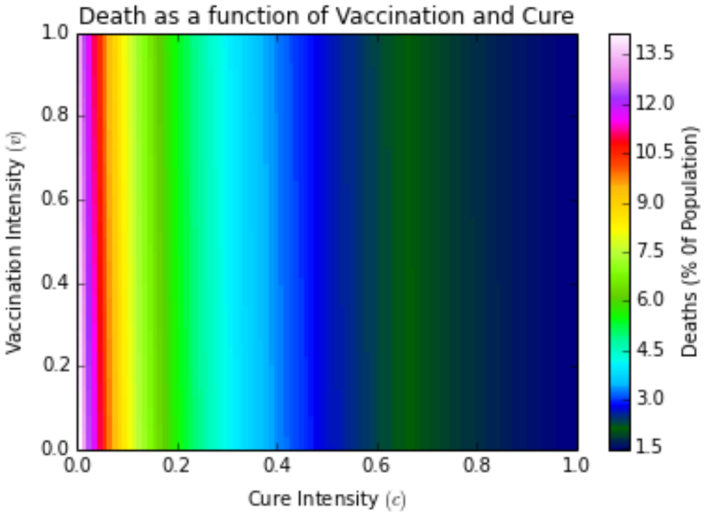

Figure 1: Death as a function of v and c

To what extent does response time delay effect disease spread?

As noted previously in the model development section, it is impossible to immediately deliver vaccines and cures to the population in which the outbreak occurs, and we accounted for this delay in our $v(t)$ and $c(t)$ functions. As v has been shown to have minimal impact, we only consider the introduction of a cure into our population when we model the effect of various time delays.

Our results (Figures 2 through 4), show that, given $c = 0.5$, the number of fatalities levels off quite quickly once a cure is introduced to the epidemic population.

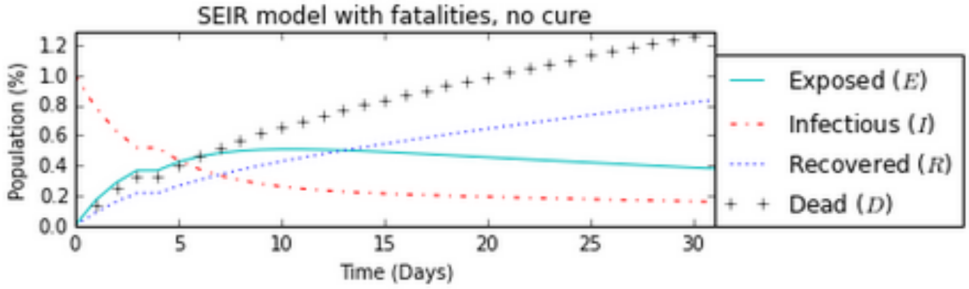

Figure 2: Population dynamics with no cure

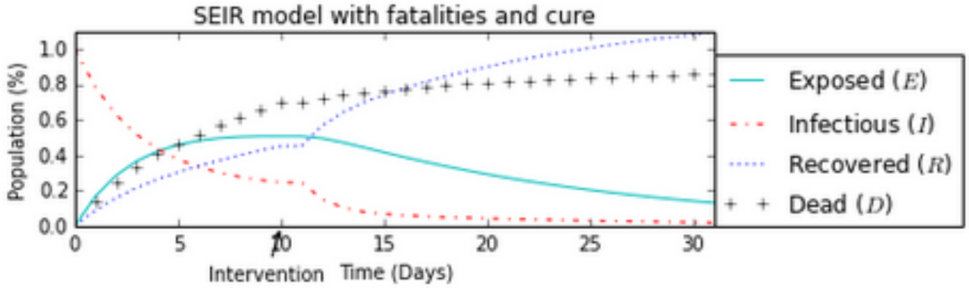

Figure 3: Population dynamics with a cure introduced on day 10

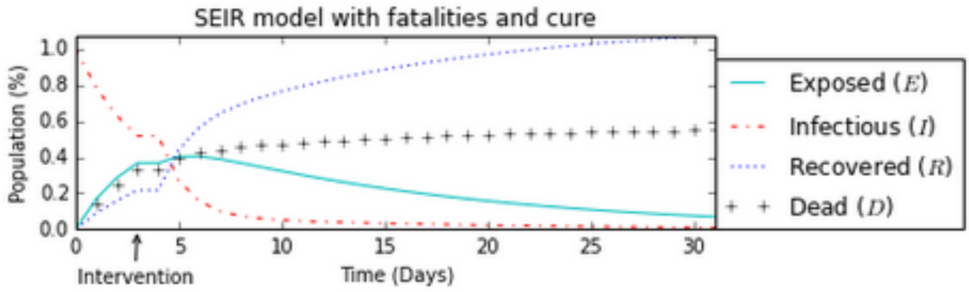

Figure 4: Population dynamics with a cure introduced on day 3

We then varied the value of c around a fixed time delay (compare Figures 4 and 5) and found results similar to those in Figure 1: death rate drops off rapidly as c increases.

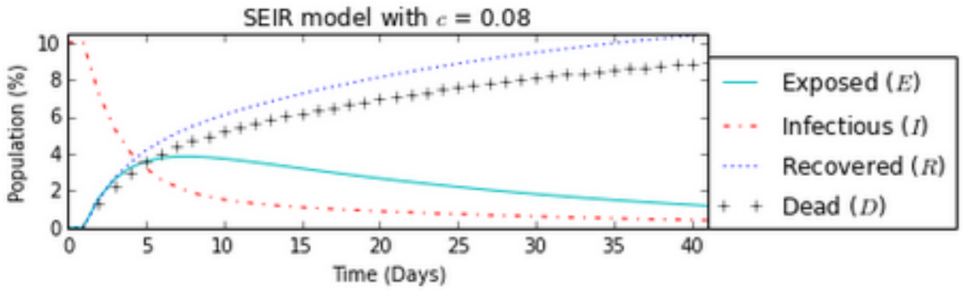

Figure 5: Population dynamics with $c = 0.08$ introduced on day 3

How well does our model fit real world data?

Finally, we tested our model's predictions against real data from the recent Ebola outbreak[6]. We looked at the number of fatalities in Guinea from August 7^{th} to October 31^{st}, and compared them to our model's predictions. Two results are shown against the real data in Figure 6.

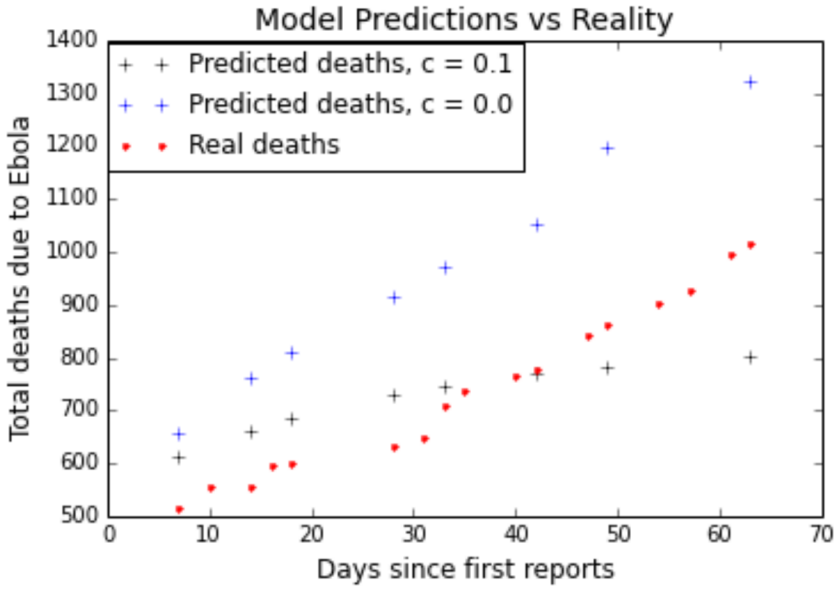

Figure 6: Predicted vs. Actual Deaths in Guinea (Aug. 7^{th} through Oct. 31^{st})

The case where $c = 0.1$ does not at all match what actually happened in Guinea. However, our predictions for $c = 0.0$ are more promising. Both our model and the data appear to fit a linear trend, and the discrepancy between numbers could be significantly reduced with a more rigorous method for determining I_0; our method for determining the initial infectious population was an arbitrary estimate. We set the infectious population in Guinea on August 7^{th} to be 60% of those who have contracted the disease. Our reasoning was that those identified as being infectious would have been quarantined after their I status was known. However, some portion of them most likely had an effect on the susceptible population before they were identified.

Results

Model Analysis

In the event of an Ebola outbreak, we would ideally want to vaccinate all susceptible individuals and treat all infectious individuals immediately after the initial outbreak. However, this is unfeasible in the real world, and much greater effort is needed to contain the current outbreak. We created a model of the disease to help us predict the dynamics of a susceptible population, and to estimate the quantity of vaccine/drug needed in order to eliminate this virus from a population. We found that, of the two options, a vaccine is almost inconsequential in comparison to a direct cure, and so a realistic approach to outbreak prevention is to focus on curing those already in disease hotspots.

In the case of Guinea, we see that introducing a c of as low as .1 would be enough to curtail the current spread of Ebola and prevent the possible deaths of thousands. On October 31^{st}, this would mean distributing our cure to 2526 infected individuals per day. Or, alternatively, this could also be the number of infected individuals that need to be quarantined each day in order to stop Ebola's spread.

The success of the resulting plan of action is heavily dependent upon both targeted delivery and a reliable delivery system. That is, we must ensure that vaccines/cures are distributed to their respective targeted populations in a timely manner. So far we have assumed that production and delivery lines will not be hampered, and that medication will flow freely into a population once first introduced. This may not always be the case, and further refinement of our model would take into account a more dynamic value of c, as well as factors like infectiousness after death and population density.

Strengths

- In using the SEIR model, which takes into account the latency period of Ebola, as our model foundation, our final model better predicts the spread of the disease than the standard SIR model.
- Our model accounts for the influence of vaccines and cures on the spread of the disease and allows us to adjust how much we put into the system. This allows us to not only model the spread of Ebola but also the eradication of Ebola with the influence of vaccines and cures.
- Our model accounts for a realistic response time (production and distribution time of vaccine/cure) to the outbreak.
- By simply adjusting the parameters, our model can be used to predict the spread of many other diseases.

Weaknesses

A major assumption we make is that all vaccines and cures received by targeted individuals are 100% effective. This is difficult to address realistically right now as there is not a significant amount of real world data for Ebola and there is no current, reliable vaccine or treatment to collect data on. However, it would not be difficult to fold this into our current model given data. For example, to incorporate into our model a cure that is only effective 80% of the time we would simply multiply our daily cure rate, c_0, by .8.

The second major issue is that our model assumes that human behavior is homogeneous across the groups S and I. However, these shortcoming in our model are difficult to account for as human behavior is not consistent, nor is it easily predictable. For example:

- In some real world scenarios people may seek a screening or test after they have travelled internationally, challenging our assumption that people in the exposed category do not seek medical attention.
- Once people are aware that they have Ebola, it is likely that they will isolate themselves, at least to some extent, to avoid infecting others.
- Considering the debilitating nature of Ebola, it is unlikely that a person exhibiting symptoms would be able to maintain the rate at which they infect others.

Another assumption we made was that every susceptible individual has an equal chance of contracting the disease. However, the most at-risk individuals are those in the health care industry and the relatives of those that are infected [5].

We also assumed that previously infected individuals are no longer infectious after they die. However, in some cultures there are burial rituals that may result in infection transmission [5].

Conclusions

From our results, we know that our model is useful in predicting the spread and eradication of Ebola to a reasonable degree. The foundation of our model is robust. However, further research is required in order to obtain more precise parameter estimates for the current Ebola strain, and understand the extent to which human behavior affects the spread of the disease.

References

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