The Transmission and Potential Outbreak of Disease X

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Abstract

Modeling of disease outbreaks is an efficient way to study the mechanisms of how diseases spread. In our study we wanted to explore the changes in dynamics of a hypothetical Disease X. This disease contains aspects from both the Measles virus and the Influenza virus. It has a high transmission like the measles, but reinfection is possible due to antigenic escape. We came up with a SIRV epidemic model that looks at the dynamics of this hypothetical Disease X in order to determine how much of the population needs to be vaccinated in order to prevent an epidemic from occurring. We ran multiple simulations with different vaccination rates to see how the dynamics changed. We also calculated the R0 and V critical values in order to determine the exact proportion of the population that needs to be vaccinated in order for no epidemic to occur. We found the R0 value to be 23 and the V critical value to be 96%. From our findings we can conclude that 96% of the population must be vaccinated in order to prevent an epidemic of Disease X. We can also conclude that Disease X has 23 infections per case, whereas measles only has 20 infections per case. This shows that Disease X is a highly transmissible disease and if a disease like the measles was able to cause reinfection it could be hard to control.

Introduction

For the past 30 years, the evolution and schematic system of childhood viral diseases like Measles, Chickenpox and Mumps have been well understood and resulted in vaccines that guarantee lifelong protection from such illness after administration. Our study chose to explore the changes in dynamics that a combination hypothetical viral Disease, X, would acquire from variation in its basic behavioral model. The two viral diseases used to model Disease X are Measles and Influenza A, both of which affect the host's respiratory system and are spread by direct contact or air transmission (Chertow & Kindrachuk, 2020). Although they have similar transmission or infection rate, Measles only requires one vaccination dose to be fully protected from reinfection, its symptoms or side effects. However, due to proper replication, Influenza undergoes antigenic escape by creating antigenic variants that are resistant to vaccination which results in the need for yearly vaccination to curb its effects (Fulton et al., 2015).

The Disease X builds on the basic "Susceptible - Infected - Recovered" archetype of Measles but reinfection is possible because of additional similarity to Influenza that minimizes error-prone replication and increases the production of antigenic variants (Fulton et al., 2015). This secondary skill leads to required re-vaccination dosages that, for this study, we assumed was every two years. As with most viruses, the potential of an Epidemic — the local, regional or global rapid spread of a disease or illness that affects a large number of people within a specific community, population, or geographic area — is an interesting avenue to explore in controlling disease transmission (Bedford et al., 2019). As a result, the essential question we hope to answer is **"How much of the population needs to be vaccinated against Disease X to prevent an epidemic, under the condition that vaccination only allows for 2 years of partial immunity?"** By answering this question, we also aspire to stipulate the Threshold Criterion as well as the Critical Vaccination Point ("VCrit") in order to properly discern the dynamics of this virus.

Model description

The programming language used to implement our Deterministic and Continuous time model was R, and we particularly used the package "deSolve" to develop and run simulations. The SIRV Epidemic model can be understood as a type of species interaction that categorizes populations into groups based on disease status, thereby creating divisions within the population. We began to construct our model on a basic SIR system with no vaccination classes, then they were incorporated sequentially to be certain that the model and its effects made logical and biological sense. To adequately describe the State variables and their interactions at work in this system, we decided to use an adapted form of this model that included specific Infection classes (Infected-Unvaccinated and Infected-Vaccinated), Vaccinated Classes (Maximum Vaccination, Minimum Vaccination and Null Vaccination) and Recovered Classes

(Recovered-Unvaccinated and Recovered-Vaccinated). Susceptible Individuals were classified as those who have had no significant interaction with Disease X, while the two infected classes represented the types of individuals with current infection and showed its symptoms. At the time of administration, those vaccinated were considered Maximum Vaccination and over the course of two years would transition into lower protected categories, Minimum and Null Vaccination, linearly until the need for bi-annual boosters. The Null Vaccination class was added to depict when the vaccine had no efficacy in individuals. Each of these categories has the ability to get infected and if applicable, would be considered Infected-Vaccinated or otherwise Infected-Unvaccinated (Schlickeiser & Kröger, 2021). Both Infected classes can progress into Recovery after the infection has died or waned off, and are categorized as either Recovered-Unvaccinated and Recovered-Vaccinated. The latter can loop into Maximum Vaccination class once they have gotten their booster, and the former can flow back to the Susceptible class to highlight how re-infection is possible in Disease X. The total number of individuals (N) in this population is the total of all state variables.

Figure 1: Model Diagram:

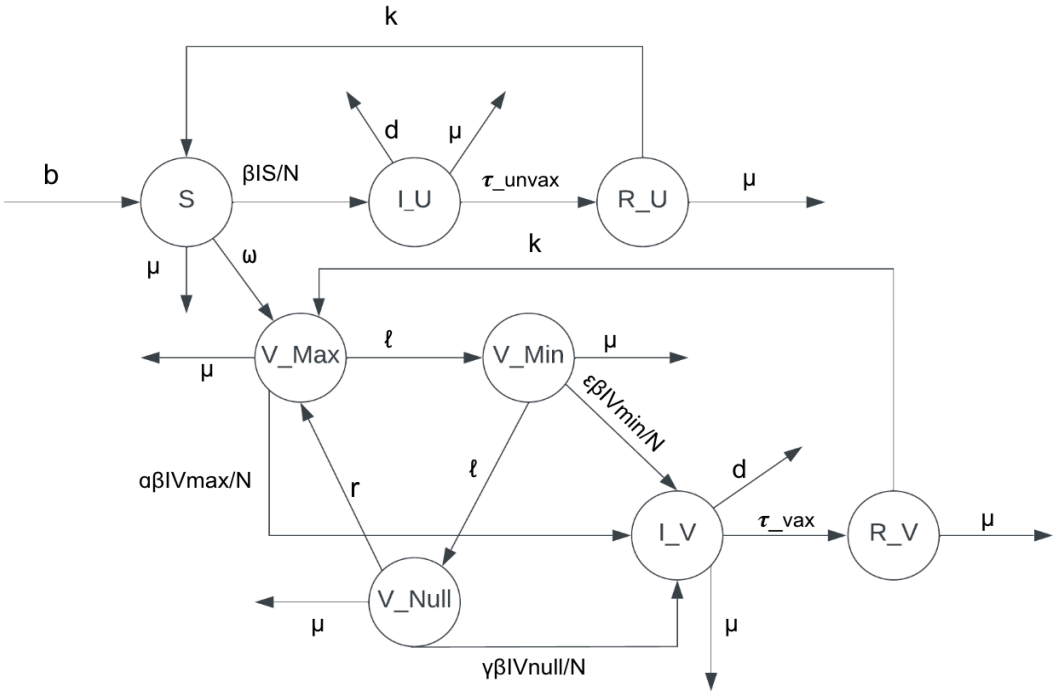

Figure 1 shows the flow diagram of our SIRV model where the 8 state variables are in circles and all flows in and out of the state variables are labeled with their corresponding parameters.

Figure 2: Model Equations:

$$\frac{dS}{dt} = bN + kR_{unvax} - \frac{\beta SI}{N} - \omega S - \mu S \quad (1)$$

$$\frac{dI_{unvax}}{dt} = \frac{\beta SI}{N} - dI_{unvax} - \mu I_{unvax} - \tau I_{unvax} \quad (2)$$

$$\frac{dR_{unvax}}{dt} = \tau I_{unvax} - \mu R_{unvax} - kR_{unvax} \quad (3)$$

$$\frac{dV_{max}}{dt} = \omega S + kR_{vax} + rV_{null} - lV_{max} - \frac{\alpha\beta IV_{max}}{N} \quad (4)$$

$$\frac{dV_{min}}{dt} = lV_{max} - lV_{min} - \frac{\varepsilon\beta IV_{min}}{N} \quad (5)$$

$$\frac{dV_{null}}{dt} = lV_{min} - rV_{null} - \frac{\gamma\beta IV_{null}}{N} \quad (6)$$

$$\frac{dI_{vax}}{dt} = \frac{\alpha\beta IV_{max}}{N} + \frac{\varepsilon\beta IV_{min}}{N} + \frac{\gamma\beta IV_{null}}{N} - \mu I_{vax} - dI_{vax} - \tau I_{vax} \quad (7)$$

$$\frac{dR_{vax}}{dt} = \tau I_{vax} - \mu R_{vax} - kR_{vax} \quad (8)$$

Figure 2 lists all of the Ordinary Differential Equations (O.D.E) corresponding to the model shown in Figure 1. There are 8 different equations that correspond to the 8 different state variables shown as circles in Figure 1. The parameters used in the equations are also labeled in the diagram model in Figure 1. The values that were used for the parameters and the definitions can be found in Figure 3.

The parameters that govern this model system characterize the several ways that each state variable can be influenced and affect its dynamics. β is the Transmission rate of Disease X and was stipulated to be "1" assuming that everyone who is infected passes it on to another person. Aside from Disease X, we assumed that this population is generally healthy and results in μ, the Natural Death rate, to be quite small at "0.01." Similarly, the birth rate, b, is also relatively small at "0.01" because we assumed that reproduction at such times is not suggested (Meherali et al., 2021). ω is the Vaccination rate and the main varying parameter we observed to notice the probability of an epidemic. Its values range from 0 to 1 to express no to complete vaccination. The Disease X induced death rate, d, is the proportion of people that die from infection and because Disease X is based on viral childhood diseases that have historically low death rates, its value in our model was assigned as "0.0195" which is about 95% more fatal than μ. The Recovery rate, τ, is denoted by either "un_vax" or "vax" is the rate at which infected people in either vaccinated class recovers into their respective Recovery classes. Its value is estimated at "0.015" suggesting that the residence time in the Infected classes is extensive and only about 1.5% can recover.

To indicate how the vaccine's efficacy decreases over time, l, is the parameter that describes how a vaccinated individual loses protection and transitions into a lower protected group and its value is "1" because we expect a total shift to lower levels over time. The booster parameter, r, is similar to l with a value of "1" because for simplicity, we assumed that all vaccinated people get boosted. The following parameters, $\alpha, \varepsilon,$ *and* γ, are rates that modify the transmission and potential infection rate of the Maximum Vaccinated, Minimum Vaccinated and Null Vaccinated populations respectively. Their values of "0.05", "0.075" and "0.095" when factored into the interaction with an infected person, illustrated how those with the least protection from the vaccine are at higher risk of infection (Thompson et al., 2018). However, these values are diminutive because the chance of infection once vaccinated is greatly reduced leading to a longer residence time under protected status. Lastly, k with a value of "1", is the transition rate back to Maximum Vaccination or Susceptible based on their vaccination status at the time of infection. To additionally clarify, k refers to post-infection booster rate while r refers to pre-infection booster rate.

Figure 3: Parameter Values and Definitions Table

Parameter	Definition	Value
β	Transmission Rate	1
μ	Natural Death Rate	0.01
b	Birth rate	0.01
k	Booster or Susceptibility Rate	0.3
r	Booster or Re-vaccination Rate	1
d	Disease X Induced Death Rate	0.0195
tau_vax	Recovery Rate of Vaccinated Individuals	0.015
tau_unvax	Recovery Rate of Unvaccinated Individuals	0.015
ω	Vaccination rate	0-1
l	Waning Vaccination Rate	1
ε	Infection Rate of Vmin	0.075
γ	Infection Rate of Vnull	0.095
α	Infection Rate of Vmax	0.05

Figure 3 is a table that includes the parameters used in the ODE and the model diagram. It has the definition of the parameter and the value that we used in the simulations.

Because this is an initial base model of a hypothetical disease that does not have an established and extensively studied history, we had to assume some features to ensure that its dynamics produced sensible results. For simplicity, we assumed that everyone who was initially vaccinated keeps up with their bi-annual boosters and we did not account for fluctuations in re-vaccination. We also assumed that the vaccine does not offer full protection and over 2 years, will decrease from its initial partial immunity to proportionately minute levels because it is a new virus and further studies and experiments were required for development of stronger vaccines (Dadras et. al., 2022). For the purposes of our study, we chose to describe an Epidemic as a condition where the total number of infected people increased significantly suggesting that Disease X has the potential to expand (Morens et al., 2009).. The project's aim is to prevent this event from happening in any capacity and consequently we identify any sudden rise as an epidemic implying that our model is very specific to change. Additionally, we presumed that vaccination and its boosters only affects the infection rate and its probability, but not the recovery rate (Puhach et al., 2022). This would mean that it helps reduce their risk of infection from contact with an infected individual, but once infected their recovery rate is similar to those of unvaccinated status. Due to the drastic differences in the chance of infection and assumed perfect booster rates, Recovered-Vaccinated individuals are looped back into Maximum Vaccination while Recovered-Unvaccinated are looped back into Susceptible. Lastly, we chose to exclude events of stochasticity in order to understand and discern the elementary processes at work without any complications from random occurrences.

Results

When running simulations for the SIRV model we changed the value of ω in order to see how the proportion of the vaccinated individuals changed the amount of infected individuals. When ω was set to 0.20, meaning 20% of the population was vaccinated the number of infected individuals increased, meaning that an outbreak would occur.

Figure 4: SIRV Model when 20% of the population is vaccinated

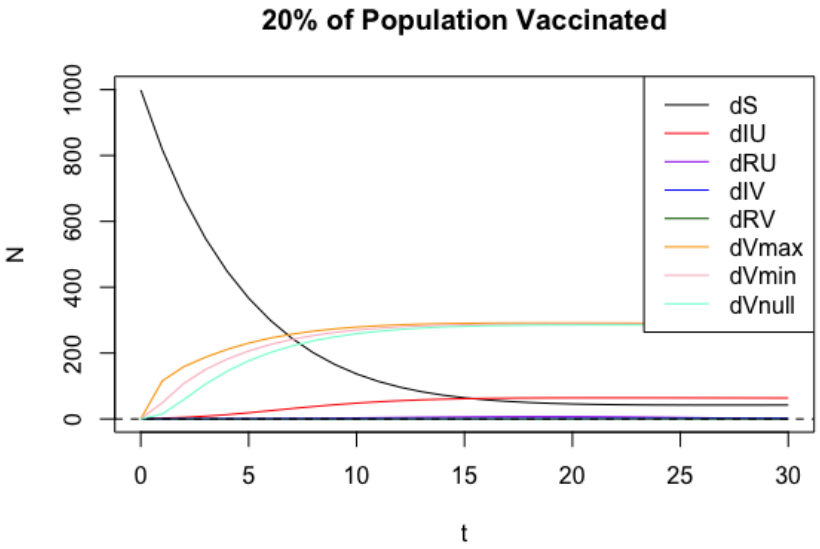

Figure 4 shows the dynamics of the population when only 20% of the population is vaccinated. The dashed line at zero is there to depict that the Recovered unvaccinated (shown in purple) and the infected vaccinated (shown in blue are not exactly at zero. The recovered vaccinated population (shown in green) does appear to also be above zero.

In Figure 4 we can see that the amount of infected individuals that are vaccinated are very low compared to the amount of infected individuals that are unvaccinated. This does show that the vaccination does work, but not enough of the population is vaccinated in order to prevent an epidemic. We can see that the number of infected unvaccinated is still growing meaning that there is an epidemic.

In Figure 5 we can see that when we ran the simulation with ω set to 0.5, indicating that half of the population has been vaccinated. Looking at the plot initially it looked like the population of infected individuals that were unvaccinated was not increasing. When decreasing the limit of the y-axis to zoom in, you can see that the number of infected individuals is still increasing, meaning that there is still an epidemic occurring in the population.

Figure 5: Plot of 50% of population vaccinated

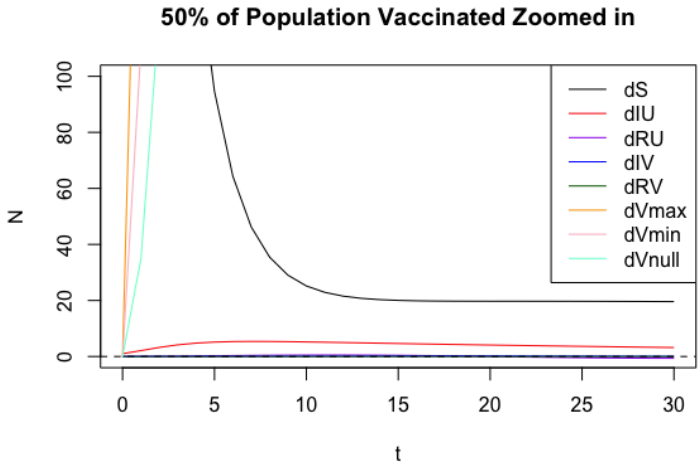

Figure 5 shows that the number of infected individuals that are unvaccinated are still increasing when 50% of the population has been vaccinated.

The last simulation that we ran can be seen in Figure 6, where ω was set to 0.96 indicating that the 96% of the population has been vaccinated. We can see that the infected population that is unvaccinated does increase at first, but then begins to decrease. Since the number of infected individuals begins to decrease there would not be an epidemic in the long term. The number of total infected individuals is very low and most of the population is in the vaccinated populations.

Figure 6: 96% of the population vaccinated

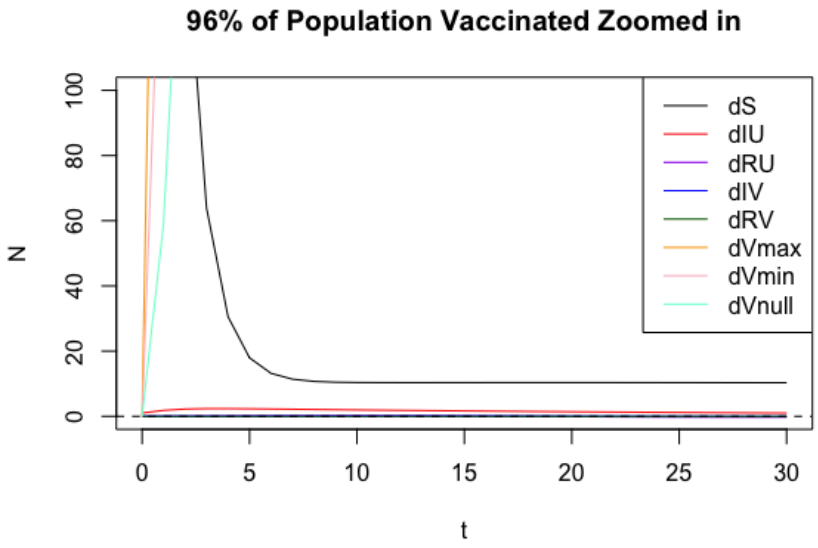

Figure 6 shows that the number of infected individuals that are unvaccinated increases at first then begins to decrease, depicting that there is not an epidemic in the long term.

In order to determine the exact proportion of the population needed to be vaccinated to prevent an outbreak, we calculated the R0 value using our equation for the infected individuals that are unvaccinated. We used the initial conditions of I(0) = 1 and S(0) = N. The equation that we ended up getting for R0 was $\frac{\beta}{\tau+\mu+d}$, when plugging in the values of the parameter we got, $\frac{1}{0.015+0.01+0.0195}$ = 23. We then solved for the V critical value using the equation $V\ crit\ =\ 1\ -\ \frac{1}{R0}$, when plugging in the value of R0 that we calculated, we got a V critical value of 96%. A V critical value of 96% means that 96% of the population needs to be vaccinated in order to prevent an epidemic. As we saw above in Figure 6 the model shows a slight increase in the infected individuals that are not vaccinated. In the long term there is not an epidemic, but since there is a slight increase at the beginning we can not say that there is not an epidemic at all.

Discussion

Our model did have some limitations as it did not take into account the possibility that the two different infected populations could infect one another as well as the susceptible and vaccinated populations (Fisman et al., 2022). We believe that this is the reason that our R0 value was not completely correct since including this in our model would change the equation used to calculate R0, potentially giving the exact value. This could cause great changes in our model since it would influence the number of infected individuals and how the susceptible individuals get infected. The model assumed that everyone keeps up with their boosters which if it were to change would influence the spread of the disease (Barnard & Davies, 2022). The categorization of when an epidemic in Disease X occurred was if the infected population was continuously growing. Potentially using a combination of what is labeled as a

Measles epidemic and an Influenza A epidemic could be used to make a more sound argument as to what benchmarks have to be met to classify Disease X as an epidemic.

Incorporating the waning vaccination of the disease proved to be a bit challenging because we wanted to model it over a 2-year span and doing so linearly increased the probability of our error. It also made us more aware of how many vaccination classes we needed and that to accurately measure the spread of the disease in vaccinated and unvaccinated individuals we had to create different recovered and infected classes. We also had many trial and error runs with the parameters of our model in order to get realistic results. Due to the variability in vaccination classes, at times our model did not run properly due to connections in those classes we had yet to realize.

Figure 7: Graph of R0 vs. V critical

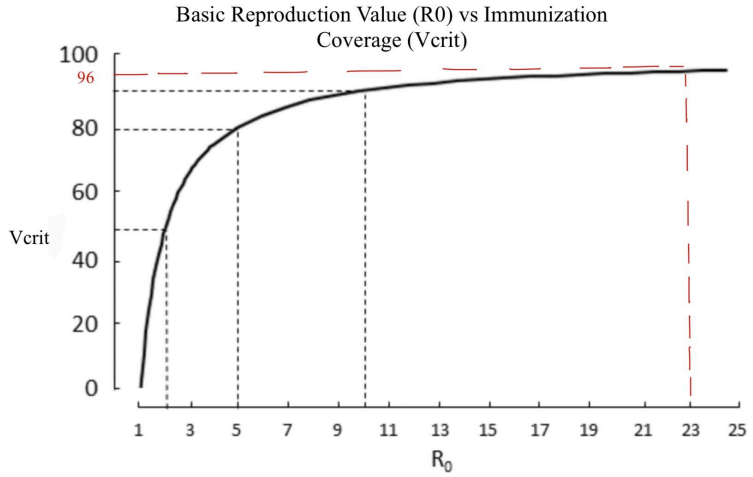

Figure 7 shows how the V critical value changes as the R0 value changes. As R0 increases so does the value of V critical.

Conclusion

Currently, Measles only requires one vaccination to no longer be susceptible for infection while Influenza A requires an annual vaccination due to antigenic variants. If Measles were to produce antigenic variants, it would require for more than one vaccination throughout a person's lifetime, similar to Influenza A. Studying this scenario appeared interesting which led to the creation of Disease X. Disease X is based on Measles but with the ability of reinfection.

Based on our model, 96% of the population needs to be inoculated in order to prevent an epidemic of Disease X. This is in contrast to Measles where 95% of the population needs to be inoculated. Overall, it appears that a greater number of the population has to be vaccinated to prevent an epidemic of Disease X in comparison to Measles. Our Disease X was more infectious than Measles as it produces roughly 23 infections per case which is higher than the average 20 infections per case Measles produces. Vaccination was helpful in reducing the number of infected individuals with the assumption that vaccinated individuals keep up to date with their boosters. In our model most of the population ends up being compromised of vaccinated individuals in different efficacy classes. Studying Disease X can give us insight into how the development of antigenic variants in the Measles virus can give rise to an epidemic and how to prevent the spread through vaccination.

Future Directions

Possible extensions to this model could include changing the model to be more age specific. The reasoning for this is that Measles is usually labeled as a childhood illness. The model being more age specific will allow for more accurate infected classes since young children are the ones who are more likely to spread and be impacted by the disease. Another factor to incorporate is to exclude the assumption that everyone gets boosted. In the real world, there is unpredictability as to whether a person will be on time in getting their boosters depending on accessibility and other socio-economic factors (Achrekar et al., 2022). Excluding this assumption will allow our model to be able to more accurately predict how Disease X would spread in a real world population. Increasing the efficacy of the vaccine can also prove to be an interesting extension of our model. This would have implications on the different vaccinated classes. For example, if the vaccine efficacy is 97% and it decreases by 50% every year then it would be 48.5% the next year. In contrast, if the vaccine efficacy was 50% and it decreased then it would be 25% the next year and thus could greatly impact the number of our infected class such as more instances where mutations of Disease X arise is also a possible extension of our model. Having more mutations of Disease X could have implications on how often an individual should receive a booster. Additionally, incorporating stochastic events would also prove to be an interesting extension as it would include events that could randomly impact our population such as a sudden lab outbreak, exposure or contamination (Allen, 2017). Integrating these possible extensions to our model would allow for it to be better able to accurately model the effect of Disease X in real world populations and situations.

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