Modeling the Effect of Vaccines on the Spread of COVID-19

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https://github.com/dukenorton/Group_3_MATH_485

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Abstract

This study is aimed to understand the effects of changing the SIDARTHE-V model so that it assumes vaccinated, recovered vaccinated, and recovered non-vaccinated populations may return to the susceptible compartment of the model, possibly becoming reinfected by the COVID-19 virus. This was achieved by using the SIDARTHE model simulation and adding the compartment for the vaccinated population so that the model is termed SIDARTHE-V, then creating two reinfection parameters. This is done by updating a matrix which represents the 8 coupled differential equations in the SIDARTHE simulation and adding a row for the vaccinated compartment, and adding the terms proportional to ϕ, 'rein' and 'rein_vacc' . One reinfection parameter ('rein_vacc') allows members from the vaccinated compartment to return to the susceptible compartment, while the other ('rein') allows healed compartment members. This is because it is assumed that vaccination is effective against the virus, thus persons from the vaccinated population are less likely to become susceptible to the virus again. Incorporating and defining these parameters in the model, the forecast of daily new cases for vaccination occurring at a constant rate is then compared with the forecast for vaccination occurring piecewise-constant. Piecewise-constant vaccination is implemented into the model simulation by the addition of an if-else block of code, which adjusts the rate of vaccination at specific time-steps. The epidemic forecasts for these vaccination scenarios (piecewise-constant and constant) are compared with the inclusion of reinfection, then without reinfection included. Through this research we find that quick vaccination reduces the number of new positive COVID-19 cases.

1 Introduction

The COVID-19 pandemic is an ongoing global health and economic crisis, where Italy is one of the first European countries to be affected most. As the world grapples with the ongoing impact of the pandemic, forecasting the spread of COVID-19 and the effectiveness of different countermeasures has become a critical area of research. Among these pandemic countermeasures are lockdown procedures and vaccines, which vary in implementation and are the main concern for this paper in confirming favorable implementation scenarios found by researchers Giordano et al [6]. using their model, SIDARTHE-V, and Italian epidemiological data up to March 12, 2021.

Currently, many epidemiological models committed to understanding immunity response and the impact of new variants throughout the pandemic find their framework from the famous SIR model and its derivatives [15]. The SIDARTHE-V mean-field compartmental model extends the SIDARTHE model introduced by Giordano et al [5]., by including the effect of vaccination. These models provide a prediction evolution of new positive COVID-19 cases and capture the dynamic interactions between populations: S, Susceptible (uninfected); I, Infected (asymptomatic infected, undetected); D, Diagnosed (asymptomatic infected, detected); A, Ailing (symptomatic infected, undetected); R, Recognized (symptomatic infected, detected); T, Threatened (infected with life-threatening symptoms, detected); H, Healed (recovered); E, Extinct (dead); and V[for SIDARTHE-V only], Vaccinated (successfully immunized).

Using the SIDARTHE-V model for predicting the evolution of new positive cases, the model is tested against different multi-pronged countermeasures for vaccine roll-out and lockdown intervention scenarios, as well as their independent scenarios to determine favorable results for mitigating the progression of the pandemic under the scenario condition. Researchers [6] found that a combination of quick vaccine roll-outs and heavier lockdown interventions is optimal for mitigating spread by simulating the dynamics of SIDARTHE-V. populations over time.

The goal of our team is to reproduce the findings for the effectiveness of pandemic countermeasures such that the best scenario for mitigating spread is the implementation of strict lockdowns and quick vaccine roll-outs, using our own model to simulate the evolution of new positive cases.

To do this, our team utilizes the model and simulation from the SIDARTHE model and extends this work by including the effect of vaccination. The simulation for the SIDARTHE-V model from [6] produces no figures for the pandemic evolution but instead creates its forecast for new daily cases, then feeds this data into their health-cost model for predicting the impact of the pandemic on hospital occupancy and costs. Since this was the case, our team chose to use the SIDARTHE model simulation to construct our own model from. Extending the simulation and model for SIDARTHE so that it is termed SIDARTHE-V has allowed our team to view the pandemic evolution directly rather than through the health-cost model.

Additionally, the original SIDARTHE-V model assumes that vaccination reduces viral transmission as well as disease severity and risk of death, and that the number of reinfections occurring within the considered horizon is negligible. Our model differs from the assumption that persons are not able to return to the susceptible population after recovery and/or vaccination and introduces reinfection parameters which allow such; however, our model still follows the assumption that vaccination is effective against SARS-CoV-2 variants. In fact, our model assumes that recovered populations and vaccinated populations can return back to the susceptible compartment of the model, and that the vaccinated population returns at a rate lesser than that of the non-vaccinated population.

After adding reinfection parameters to account for the different rates at which vaccinated and non-vaccinated populations return back to the susceptible compartment of our model, we expect that the results should still agree with the authors from the observed model in that a combination of strict non-pharmaceutical interventions and vaccination should minimize the resurgence of cases. Through the amended simulation describing our model, we confirm this hypothesis and reproduce the findings from the original model and research through various methods explained in the rest of this paper.

2 Methods

In this project, we simulated the spread of COVID-19 using a discrete dynamical model called SIDARTHE-V. The SIDARTHE-V model is an epidemic model that is more complicated than the SIS or MISNER model that was discussed in class. The original SIDARTHE model was used to predict the spread of COVID-19 in Italy during the earliest phases of the pandemic. This model attempted to mitigate the spread of the pandemic by implementing lockdowns but with no vaccines. The SIDARTHE-V model adds vaccines as a component of the model. It is assumed in the model that the COVID desiese evolves on the time scale of days. This way the model updates every day and not on an even shorter timescale.

THE SIDARTHE-V model is a discrete dynamical model. In this type of model, there are a series of compartments. In each time step the system evolves by changing the number of people in each compartment. For each time there is a state vector representing the population in each compartment. The system of differential equations is represented by a matrix that multiplies the state vector to update it. The compartments in the SIDARTHE-V model are the following. 'S' is the susceptible category; 'I' is the population that can potentially contract the disease. 'I' is the infected category which is people that are infected, asymptomatic and un-diagnosed. 'D' is the diagnosed category representing people whose infection is diagnosed but asymptomatic. 'A' is the population of symptomatic but unrecognized people. 'R' is the category of recognized symptomatic cases. 'T' is the category of people that develop acute, life-threatening symptoms. H is the population of people that survived and gained immunity to the infection. E is the number of people that have died from the infection. V is the number of people that gained immunity from the infection by vaccination without actually getting the disease.

A set of nine differential equations describe the evolution of the epidemic. These equations are [5]:

$$\dot{S}(t) = -S(t)(\alpha I(t) + \beta D(t) + \gamma A(t) + \delta R(t)) - \phi(S(t)) \tag{1}$$

$$\dot{I}(t) = S(t)(\alpha I(t) + \beta D(t) + \gamma A(t) + \delta R(t)) - (\epsilon + \zeta + \lambda)I(t) \tag{2}$$

$$\dot{D}(t) = \epsilon I(t) - (\eta + \rho)D(t) \tag{3}$$

$$\dot{A}(t) = \zeta I(t) - (\theta + \mu + \kappa)A(t) \tag{4}$$

$$\dot{R}(t) = \eta D(t) + \theta A(t) - (\nu + \xi + \tau_1)R(t) \tag{5}$$

$$\dot{T}(t) = \mu A(t) + \nu R(t) - (\sigma - \tau_2)T(t) \tag{6}$$

$$\dot{H}(t) = \lambda I(t) + \rho D(t) + \kappa A(t) + \xi R(t) + \sigma T(t) \tag{7}$$

$$\dot{E}(t) = \tau_1 R(t) + \tau_2 T(t) \tag{8}$$

$$\dot{V}(t) = \phi(S(t)) \tag{9}$$

Each variable is related by a series of parameters that quantify how individuals move from one compartment to another in the model. The coefficients are the Greek letters seen in the modeling equations below. The parameters α, β, γ, and δ describe infection rates of an infected, diagnosed, ailing, or recognized individual.

ϵ and θ denote the probability rate of detecting that an individual is infected. ζ and η represent the chance an infected individual develops clinically relevant symptoms. μ and ν denote the rate at which infected symptomatic individuals develop life-threatening symptoms.τ_1 and τ_2 denote the mortality rate for infected and symptomatic individuals and of those with acute symptoms, both of which can be reduced by means of improved therapies. λ, κ, ξ, ρ, and σ denote the recovery rate for the five classes of infected individuals [5]. The parameters are chosen to quantify real phenomena such as person-to-person transmission of the disease and should be estimated using real epidemic data. In this study, we take the authors of the paper's values.

There is a conservation property associated with this system of equations. The conserved quantity is the total number of people in the population. This conservation is enforced by adding all of the differential equations together and finding zero.

$$\dot{S}(t) + \dot{I}(t) + \dot{D}(t) + \dot{A}(t) + \dot{R}(t) + \dot{T}(t) + \dot{H}(t) + \dot{E}(t) + \dot{V}(t) = 0 \tag{10}$$

As a control, this group ran a version of the simulation with lock-downs and no vaccines, which is achieved by setting the function of describing the vaccination to zero. Vaccines could be implemented in many different ways by choosing different functions for $\dot{V}(t) = \phi(S(t))$. The first choice was setting the function to a constant multiplying the susceptible population. Another choice is a piece-wise constant function for the vaccination function. This could represent an increase in the supply of vaccines over time or greater awareness and pressure for the population to get vaccinated. Finally as an experiment, a variable vaccination rate was tried. This involved trying Gaussian and sinusoidal functions to determine the vaccination rate. These could represent either hesitancy, disruptions in the vaccine supply, or changing attitudes to the vaccines.

3 Results

In this section, the codes and graphs of the model are presented.

A change to the model was implementing the possibility of reinfection. This involves adding extra terms to the model to move people from either the healed or vaccinated compartments back into the infected compartment. With these changes, the model becomes:

$$\dot{S}(t) = -S(t)(\alpha I(t) + \beta D(t) + \gamma A(t) + \delta R(t)) - \phi(S(t)) + \psi_1 H(t) + \psi_2 V(t) \tag{11}$$

$$\dot{I}(t) = S(t)(\alpha I(t) + \beta D(t) + \gamma A(t) + \delta R(t)) - (\epsilon + \zeta + \lambda) I(t) \tag{12}$$

$$\dot{D}(t) = \epsilon I(t) - (\eta + \rho) D(t) \tag{13}$$

$$\dot{A}(t) = \zeta I(t) - (\theta + \mu + \kappa) A(t) \tag{14}$$

$$\dot{R}(t) = \eta D(t) + \theta A(t) - (\nu + \xi + \tau_1) R(t) \tag{15}$$

$$\dot{T}(t) = \mu A(t) + \nu R(t) - (\sigma - \tau_2) T(t) \tag{16}$$

$$\dot{H}(t) = \lambda I(t) + \rho D(t) + \kappa A(t) + \xi R(t) + \sigma T(t) - \psi_1 H(t) \tag{17}$$

$$\dot{E}(t) = \tau_1 R(t) + \tau_2 T(t) \tag{18}$$

$$\dot{V}(t) = \phi(S(t)) - \psi_2 V(t) \tag{19}$$

Each different vaccination model was repeated with the addition of a re-infection term. Introducing the re-infection term adds a new parameter to the model called ψ. Using the data presented in the article by Guedes et. al., we decided to use a value of 0.05 for the unvaccinated and 0.01 for the vaccinated[7]. This means in our models that the vaccines are not completely effective at conferring immunity. However, we did assume that being vaccinated does give a person an advantage of not being as likely to contract COVID.

Presented below is the original matrix that evolves the system[5]. The number of people in each category of SIDARTHE is represented by a state vector. Since this is a discrete dynamical system, the state is evolved by multiplying by the matrix 'B' to get the state at time 't+1'. Each row of the matrix corresponds to one of the categories. Since the system has a conserved quantity, the total number of people is constant.

```
%This is the matrix that evolves the system
    % Compute the system evolution
    %ADDED A NEW zero to the end of each row and added a tenth row with vaccination
```

```
    B=[-alfa*x(2)-beta*x(3)-gamma*x(4)-delta*x(5)-phi*x(1) 0 0 0 0 0 0 0 0 0 0;
        alfa*x(2)+beta*x(3)+gamma*x(4)+delta*x(5) -(epsilon+zeta+lambda) 0 0 0 0 0 0 0 0 0;
        0 epsilon  -(eta+rho) 0 0 0 0 0 0 0;
        0 zeta 0 -(theta+mu+kappa) 0 0 0 0 0 0;
        0 0 eta theta -(nu+xi) 0 0 0 0 0;
        0 0 0 mu nu  -(sigma+tau) 0 0 0 0;
        0 lambda rho kappa xi sigma 0 0 0 0;
        0 0 0 0 0 tau 0 0 0 0;
        phi*x(1) 0 0 0 0 0 0 0 0 0;
        0 0 rho 0 xi sigma 0 0 0 0;
        alfa*x(2)+beta*x(3)+gamma*x(4)+delta*x(5) 0 0 0 0 0 0 0 0 0];
    x=x+B*x*step;
```

As a team in this project, we added the vaccines to the model to make it SIDARTHE-V [5]. This involved adding the terms proportional to ϕ in lines 250 and 258. Line 258 in the matrix is the new 'V' compartment that represents vaccinated people. We also added new terms to represent the possibility of reinfection. These are the 'rein' and 'rein_vacc' terms that are in lines 250, 254, and 258 of the matrix. These terms represent a constant rate of reinfection proportional to the categories 'H' and 'V'. People in the healed and vaccinated categories are placed back into the susceptible category.

```
    % Compute the system evolution
    %ADDED new terms in the first, seventh and ninth equations to represent
    %reinfections
    B=[-alfa*x(2)-beta*x(3)-gamma*x(4)-delta*x(5)-phi*x(1) 0 0 0 0 0 rein 0 rein_vacc 0 0;
        alfa*x(2)+beta*x(3)+gamma*x(4)+delta*x(5) -(epsilon+zeta+lambda) 0 0 0 0 0 0 0 0 0;
        0 epsilon  -(eta+rho) 0 0 0 0 0 0 0;
        0 zeta 0 -(theta+mu+kappa) 0 0 0 0 0 0;
        0 0 eta theta -(nu+xi) 0 0 0 0 0;
        0 0 0 mu nu  -(sigma+tau) 0 0 0 0;
        0 lambda rho kappa xi sigma -rein 0 0 0;
        0 0 0 0 0 tau 0 0 0 0;
        phi*x(1) 0 0 0 0 0 0 0 -rein_vacc 0 0;
        0 0 rho 0 xi sigma 0 0 0 0;
        alfa*x(2)+beta*x(3)+gamma*x(4)+delta*x(5) 0 0 0 0 0 0 0 0 0 0];
    x=x+B*x*step;
```

Versions of the simulation were run with a constant rate of vaccination starting at day 100 of the simulation and reinfection starting at day 200, and lasting to the end of the simulation at day 350. In addition, a version was run with a piece-wise constant rate as well. In these versions of the simulation, an additional if-else block of code, seen below, was added to change the vaccination and reinfection coefficients at the appointed time steps.

```
%Add a ramping up vacc campaign
    %Do this by changing the vaccination rate phi and reinfection rate
    %rein.
    if (i>5/step)
        phi=0.00001;
        rein=0.000001;
        rein_vacc=0.000001;
    elseif (i>50/step)
        phi=0.00005;
        %phi=0.001;
        rein=0.0001;
        rein_vacc=0.0001;
    elseif (i>100/step)
        phi=0.0001;
        rein=0.01;
        rein_vacc=0.001;
    elseif (i>200/step)
        phi=0.0005;
    end
```

The graphs produced from the simulations are found in the appendix of this report. In figure 1 is an example of the simulation run with the original authors' code without any changes. This is the situation with no vaccinations or reinfection and the pandemic is mitigated only with lockdowns. Figure 2, is the

result of the simulation with constant vaccination starting at day 100 but not reinfection. Figure 3 is from a simulation with piece-wise vaccination and no reinfection. Figure 4 is the result of the simulation with constant vaccination starting at day 100 and reinfection, and figure 5 is the result of the piece-wise vaccination with reinfection.

Type of simulation	**Cumulative Fraction of Population Infected**
Only Lockdowns	0.0060
Constant Vaccination	0.0058
Constant Vaccination with Reinfection	0.0061
Piece-wise Vaccination	0.0060
Piece-wise Vaccination with Reinfection	0.0062

Table 1: This Table summarizes the total fraction of the population that was infected at day 350 of each simulation.

In each simulation, we recorded the fraction of the population that was infected at day 350. At the end of the day, 350 the cumulative fraction of the population that was infected was recorded and placed in table 1. It is seen from these values if reinfection is present a higher portion of the population becomes infected and if the vaccination is slower the same is true. Having the population vaccinated can lower the fraction that gets infected.

4 Discussion

At the time of the original paper, evidence suggested that the chance of reinfection was negligible [6]. However, as we have seen in the time since then, reinfection is a significant consideration that we looked to model by extending SIDARTHE-V [14]. This also seemed the natural progression of disease modeling, and previous work leading up to the SIDARTHE model shows that we have come a long way [3] [4] [20] [21]. After some initial difficulty, we were able to adjust the model so that there would be an infection parameter ϕ_1 and ϕ_2 which correspond to the reinfection rate of unvaccinated and vaccinated populations respectively and according to data from Guedes et al [7].

Running our model we found that vaccinations are effective in reducing the impact of COVID. Figure 1 shows NPIs as the sole countermeasure against the spread of COVID. However, figure 2 shows that with constant vaccination of the population starting even at day 100, the population would experience fewer cases. By increasing this vaccination rate, of course, you have better outcomes the faster that vaccines are rolled out. With our piece-wise constant model which aims to represent greater awareness of COVID and increasing pressure to get vaccinated, as seen in Figure 3, we see that cases plateau at a higher fraction of the population. From this, one may argue that campaigns to increase awareness and faster roll-out of vaccinations are beneficial to reducing the impact of the epidemic. Figure 4 shows us that the cases may seem to level off, which is similar to what we had seen in previous simulations. The particular values can be referenced in Table 1 with the rows

These findings can be supported by much of the research and observations were done during the pandemic emphasizing the value of vaccination schemes and mathematical modeling, especially those that incorporate reinfection into their models. A study by Challen et al. demonstrated that the mass vaccination campaign in the UK led to a significant reduction in hospitalizations and deaths, particularly among the elderly and vulnerable populations [2]. A study by Lavine et al. found that because of reinfection and the absence of adequate vaccination distribution (e.g. absence of constant or increasing vaccination rate), it could lead to recurrent COVID-19 outbreaks [10]. Additionally, a study by Guedes et al. showed that even with relatively low rates of reinfection, accounting for reinfection in COVID-19 models is essential to accurately predict the dynamics of the pandemic [7].

Additionally, our model underscores the importance of implementing targeted vaccination strategies, particularly during the early stages of vaccination campaigns when supply may be limited. A study by Matrajt et al. found that prioritizing high-risk populations, such as the elderly and individuals with pre-existing conditions, can significantly reduce COVID-19 mortality [13]. This is consistent with our simulations,

which showed that different vaccination strategies can impact the overall trajectory of the pandemic.

5 Conclusion

Our group extended the SIDARTHE-V model to account for the possibility of reinfection. By modifying the model and introducing reinfection parameters, we were able to analyze the effects of different vaccination and lockdown scenarios on the daily new COVID-19 cases. The results of our simulations confirmed the findings of the original SIDARTHE-V model, suggesting that a combination of strict NPIs and strong vaccine roll-outs is the most effective strategy for minimizing the resurgence of cases. While the model assumes that vaccination is effective against SARS-CoV-2 variants, we based the possibility of reinfection on prior research by Guedes et al. Possible extensions to this work include a model that incorporates a true second variant. Instead of being reinfected with the same variant that the population had, they could be infected with a new one that has different transmissibility, and mortality rates. This would be more reflective of the true situation experienced in the COVID epidemic.

The findings of this study contribute to the ongoing research on effective countermeasures against the COVID-19 pandemic and provide valuable insights for policymakers and health authorities in their efforts to mitigate the spread of the virus. These results underscore the value of mathematical modeling, especially those that incorporate reinfection, in understanding the dynamics of the pandemic and informing effective public health policies.

6 Acknowledgements and Statement of Roles

6.1 Acknowledgements

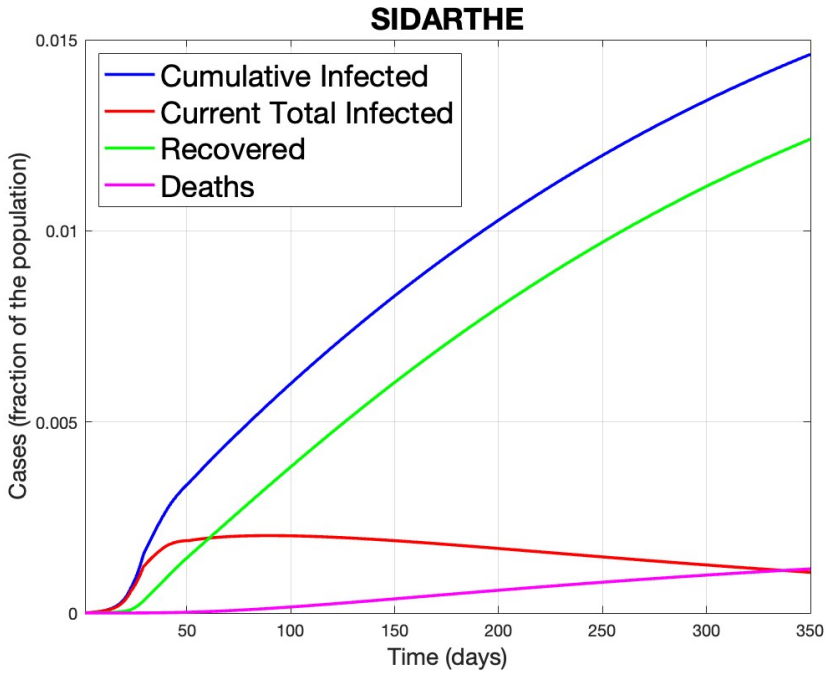
Thank you to Gaurish Korpal and Prof. Lega for their help and mentorship during this project.

6.2 Statement of Roles

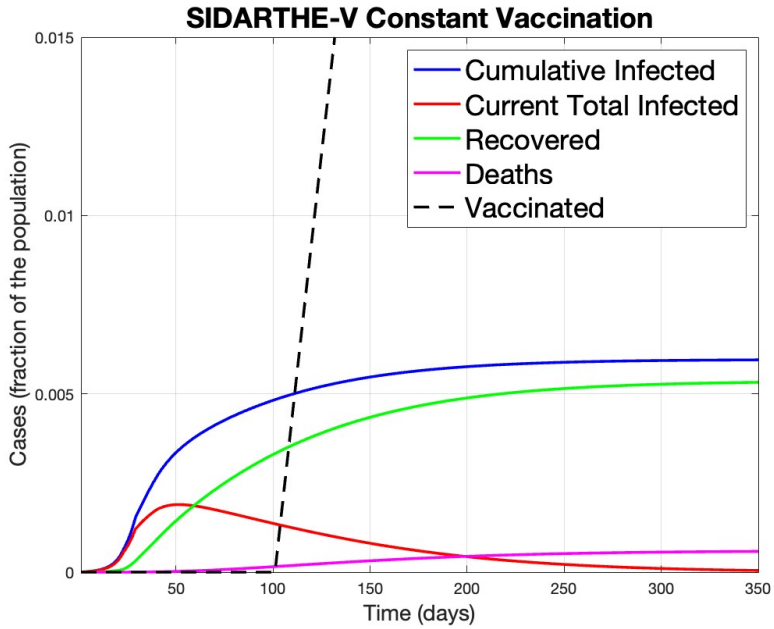
Carl Ingebretsen had the idea to try introducing reinfection to the model, modified the code, and contributed to writing sections of the midterm and final reports. Duke Norton worked on the code, managed the GitHub repository and wrote portions of the reports. Andrew Olson helped create and format the graphs and created the PowerPoint presentations. John Richie Quillopo gathered references, wrote portions of the the reports and edited the videos of the presentations.

All members of the group contributed equally in effort for this project.

A Figures

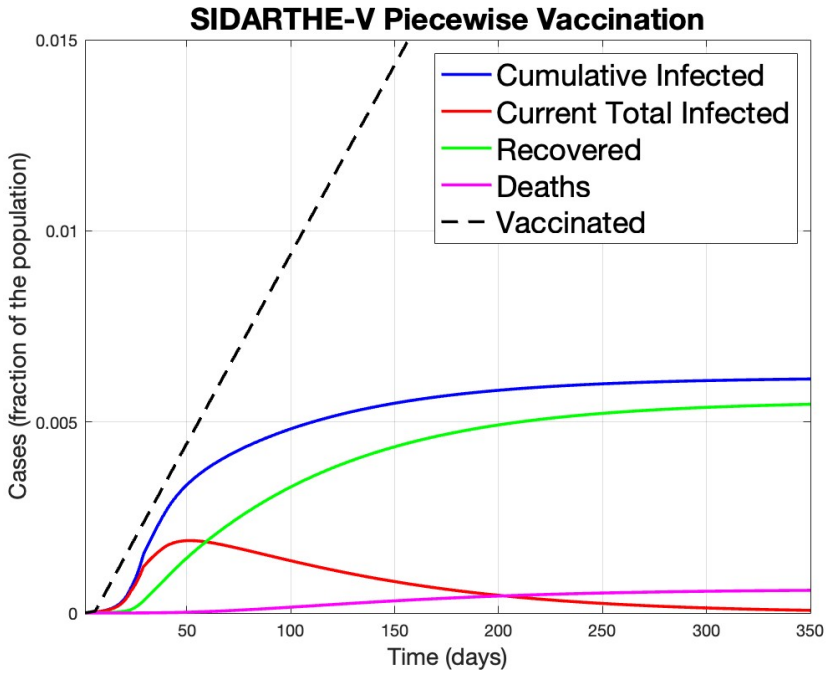


(a) Figure 1: This graph shows the different sections of the population in the simulation with no vaccinations or reinfection. The pandemic is mitigated only using lockdowns that change the infection parameters. This graph was produced using the authors' code and kept as a control.

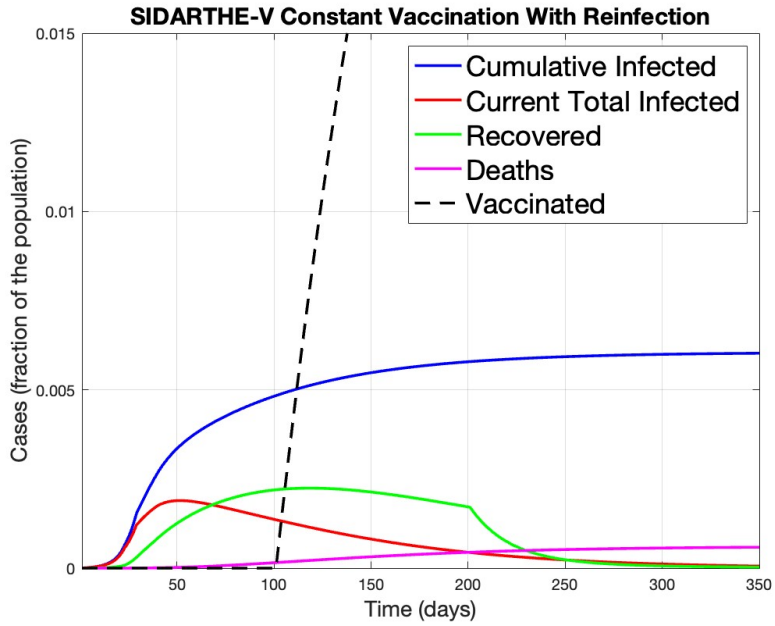


(b) Figure 2: This graph represents a constant vaccination rate in the epidemic starting at day 100. This figure shows that the epidemic plateaus at a lower fraction of the population than in the non-vaccinated case.

Figure 1

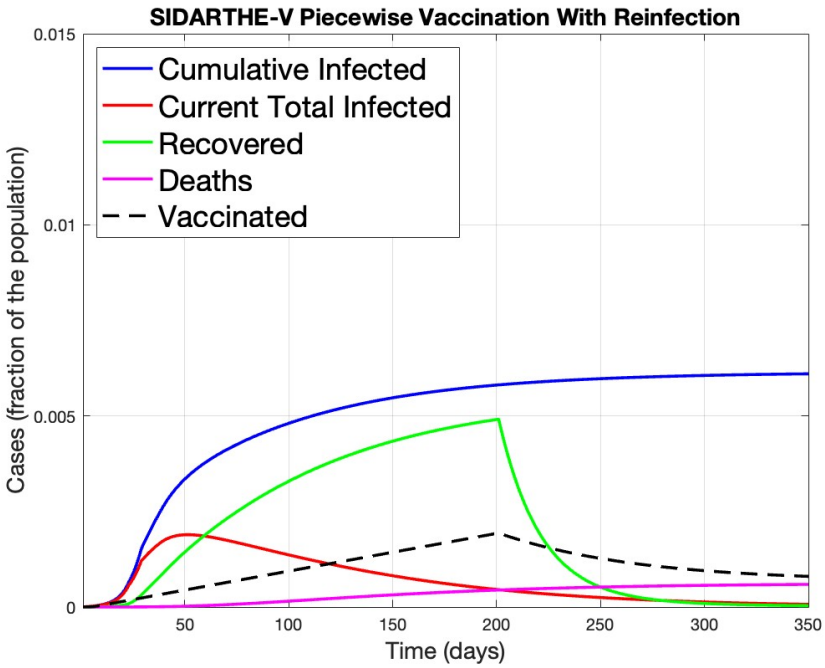


(a) Figure 3: This figure shows the result of the simulation with piece-wise vaccination that starts early in the simulation. The epidemic plateaus at a higher fraction of the population than in the constant vaccination case.



(b) Figure 4: This figure shows the result of the simulation with piece-wise vaccination that starts early in the simulation, along with the possibility of reinfection. The epidemic plateaus at a much higher fraction of the population than the simulation without reinfection.

Figure 2



(a) Figure 5: This graph represents a constant vaccination rate in the epidemic starting at day 100 as well as reinfection. The epidemic seems to start to level off near day 100 before increasing again, representing a second round of infections.

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