EXPANDED SIR MODEL OF DRUG AND VACCINE DISTRIBUTION ON COVID-19*

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Abstract. Since the end of 2019, COVID-19 has threatened human life around the globe. As the death toll continues to rise, development of vaccines and antiviral treatments have progressed at unprecedented speeds. This paper uses an SIR model, extended to include asymptomatic carriers and deceased populations as a basis for expansions to the effects of a drug and vaccine. In our model, a drug is administered to infected individuals, decreasing recovery time and death rate. Alternatively, a vaccine is administered to susceptible individuals and, if effective, will move them into the recovered population. We observe final mortality outcomes of these countermeasures by running simulations across different release times with differing effectivenesses.

As expected, the earlier the drug or vaccine is released into the population, the smaller the death toll. We find that for earlier release dates, difference in the quality of either treatment has a large effect on total deaths. However as their release is delayed, these differences become smaller. Finally, we find that a vaccine is much more effective than a drug when released early in an epidemic. However, when released after the peak of infections, a drug is marginally more effective in total lives saved.

Key words. COVID-19, Coronavirus, SARS-CoV-2, Drug, Vaccine, SIR, Simulation

1. Introduction.

The world faces an unknown future due to SARS-CoV-2. In the U.S., discussion surrounds re-opening, social distancing measures, and a second wave. Researchers have made strides in the development of drugs and vaccines at unprecedented speeds, but the virus continues to spread with U.S. infections and deaths increasing every day [5].

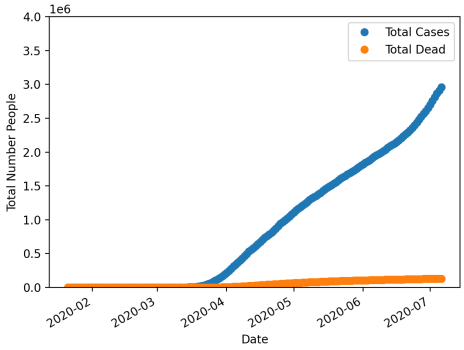

FIG. 1. *US Covid19 Outbreak [19]*

One of the United States' major responses to the pandemic has been Operation Warp Speed (OWS). The partnership between the CDC, FDA, NIH, DoD and others

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has committed to providing 300 million doses of a vaccine by the end of January 2021. OWS has provided more than $2 billion in funding for vaccines to Johnson & Johnson, Moderna, and AstraZeneca/Oxford [3]. As of September 26th, each of these trials are in phase 3 [8].

While OWS hasn't funded antiviral development, companies around the world are also racing to develop antivirals. Antivirals from Gilead Sciences (Remdesivir), AstraZeneca, and Merck & Co. (discovered at Emory University) are currently authorized, in phase 1, and in phase 2 respectively [8]. These treatments' mechanisms and deliveries vary but have all shown promise.

Because vaccines and drugs function in different ways and are administered to different populations, their effects on the pandemic will not be the same. Beyond their functional differences, outcomes will also depend on their pharmacological effectivenesses as well as the speed and date of their introduction.

In this work, we consider a mathematical model improved to provide insight into these outcomes. The model takes into account the different administrations of drugs and vaccines, their release speed and dates, and the outcomes of those treated (death or recovery rate). It can be expanded to fit any population or disease variable, but has been fit to those of the U.S. for the sake of this work.

Our model is based on a standard set of SIR equations for susceptible, infected and recovered populations. An SIR model is a system of ordinary differential equations which describes how an outbreak spreads through a population [18]. It is comprised of the following three equations:

$$\frac{dS}{dt} = -\frac{\beta IS}{N} \tag{1.1}$$

$$\frac{dI}{dt} = \frac{\beta IS}{N} - \gamma I \tag{1.2}$$

$$\frac{dR}{dt} = \gamma I \tag{1.3}$$

S, I, and R are the number of susceptible, infected, and recovered people at time t, respectively. The problem is completed by appropriate initial conditions S_i, I_i, R_i. At any time the size of the population, N, is defined as:

$$N = S + I + R$$

In this system, β is the expected number of people an infected person infects per day. It is closely related to the so-called R_0 or 'R naught' which is the total number of people that one infected person will infect in a population with no immunity. Therefore, β is R_0/L where L is the duration of the illness. The proportion of the infected group that will recover per day is defined as γ. It can also be expressed as $1/L$ because, for example, if it takes 5 days to recover then each day 20% of the infected group will recover.

While this basic model is indicative of important dynamics, it is too crude for our problems because it does not consider asymptomatic or deceased individuals that are important in the context of COVID-19. For this reason, we introduce an expanded SIR model as a Basis Model for further analysis.

The paper is organized as follows. Our basis equations are in section 2, our analysis for the inclusion of drug is in section 4, our analysis for the inclusion of vaccine is in **??**, and the discussion follows in section 5.

2. COVID-19 Basis Model.

2.1. Equations. Using the SIR model as a basis, the equations were expanded to include asymptomatic 'A' and deceased 'D' groups [11]. These will be critical when expanding the model for a drug and vaccine release. The total population therefore becomes:[1]

$$N = S + A + I + R + D$$

The flow chart representing the different compartments of our model and their interactions is shown in Fig. 2:

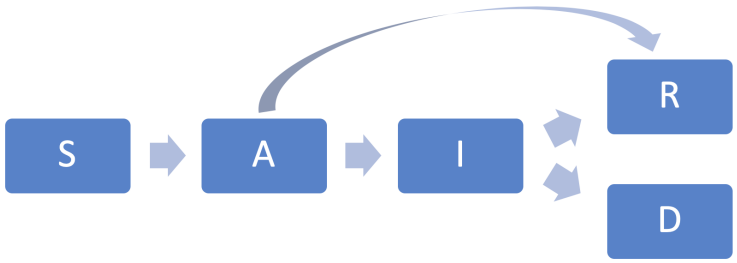

FIG. 2. *Compartmental Flow Chart for Base SAIRD Model*

With the inclusion of an asymptomatic population, there are two groups with different risks of infecting others. Therefore, different values of β are introduced for the infected and asymptomatic populations:

$$\frac{dS}{dt} = -\frac{\beta_i IS}{N} - \frac{\beta_a AS}{N} \tag{2.1}$$

Susceptible individuals will become asymptomatic before becoming infected, so the positive rate of change for the asymptomatic population will become:[2]

$$\left(\frac{dA}{dt}\right)^+ = \frac{\beta_i IS}{N} + \frac{\beta_a AS}{N}$$

Asymptomatic individuals will either become infected, or recover without showing symptoms. Let μ be the proportion of asymptomatic individuals who become infected. Therefore, the total change in the asymptomatic population can be defined as:

$$\frac{dA}{dt} = \frac{\beta_i IS}{N} + \frac{\beta_a AS}{N} - \mu A n_i - (1-\mu) A n_r \tag{2.2}$$

where n_i is the proportion of people transitioning from asymptomatic to infected in one day or 1/(days to transition to infected from asymptomatic). Further, n_r is the

[1] Note the distinction regarding our asymptomatic population 'A' and our infected population 'I'. Both groups have been infected with the virus, but the latter show symptoms and can die. It would make more sense to call these two groups 'symptomatic' and 'asymptomatic', but 'S' was already taken for Susceptible.

[2] Note that $\frac{dA}{dt} = \left(\frac{dA}{dt}\right)^+ + \left(\frac{dA}{dt}\right)^-$ where $\left(\frac{dA}{dt}\right)^-$ is the negative rate of change.

proportion of people transitioning from asymptomatic to recovered in a given day or 1/(days to transition to recovered from asymptomatic).

Increases in the infected population will result from asymptomatic individuals who begin to show symptoms. Once infected, individuals will either join the recovered or deceased populations. Let α represent the proportion of individuals who die from the virus. Moreover, let ρ be the proportion of people that die per day or 1/(days it takes to die if infected). Also, let γ be the proportion of people that recover per day, or 1/(days it takes to recover from infected). The change in infected individuals, I, will be:

$$\frac{dI}{dt} = \mu A n_i - \alpha\rho I - (1-\alpha)\gamma I \tag{2.3}$$

The change in the recovered population can be described using the components of the asymptomatic and infected populations who recover:

$$\frac{dR}{dt} = (1-\mu) A n_r + (1-\alpha)\gamma I \tag{2.4}$$

Similarly, the change in the deceased population can be described using the components of the infected population who die:

$$\frac{dD}{dt} = \alpha\rho I \tag{2.5}$$

In summary, the model can be written in matrix form where $\boldsymbol{u} = [S, A, I, R, D]^T$. With this, the model can be summarized as the vector $\boldsymbol{b}$, where each entry corresponds to each of the five equations:

$$\boldsymbol{b} = \boldsymbol{B}(\boldsymbol{u})\boldsymbol{u} \tag{2.6}$$

$$\boldsymbol{B}(\boldsymbol{u}) = \begin{bmatrix} 0 & -\frac{\beta_i S}{N} & -\frac{\beta_a S}{N} & 0 & 0 \\ 0 & \frac{\beta_a S}{N} - \mu n_i - (1-\mu) n_r & \frac{\beta_i S}{N} & 0 & 0 \\ 0 & \mu n_i & -\alpha\rho - (1-\alpha)\gamma & 0 & 0 \\ 0 & (1-\mu) n_r & (1-\alpha)\gamma & 0 & 0 \\ 0 & 0 & \alpha\rho & 0 & 0 \end{bmatrix} \tag{2.7}$$

The matrix format allows for analysis of the model in its equilibrium state to understand the potential of achieving a state where there is no change in the populations from the vaccine or drug.

2.2. Tuning Parameters. Values from current reports on SARS-CoV-2 provide potential values for the constants in these equations. However, due to the novelty of SARS-CoV-2, it is important to note that epidemiological parameters continue to change.

The proportion of infected patients that will show symptoms, μ, has been estimated to be 85% [9], [10]. The length of time before symptoms present themselves is approximately 5.1 days [13]. Therefore, n_i can be estimated at $\frac{1}{5.1} = 0.1961$. The number of days to transition to recovered from asymptomatic is estimated to be 9 days, therefore n_r is $\frac{1}{9} = 0.1111$ [17]. The proportion of individuals who die from the virus, α, can be estimated at the death rate, which is 0.64% [15]. The length of time it takes to die is estimated to be 17.8 days [20]. Therefore, ρ is estimated to be

$\frac{1}{17.8} = 0.0562$. The length of time it takes to recover is estimated to be between 10 - 13 days [4]. Therefore, γ is $\frac{1}{11.5} = 0.0870$.

β_a and β_i represent the number of people infected per day by asymptomatic and infected individuals respectively. Therefore, to calculate these values we would take the total number of people an asymptomatic or infected individual infects and divide by the duration of their disease. However, data about the infectivity of asymptomatic and infected people is not widely published or agreed upon. Because of this, as a heuristic, we use a single β for both the asymptomatic and infected population. It is calculated as $\frac{R_0}{\text{duration}}$.

R_0 is the total number of people that one individual will infect over the course of the disease. *Note that this is the 'base rate' infectivity of the virus and does not account for social distancing, masks, or other health precautions.* The estimated value of R_0 is widely disputed. However, the World Health Organization suggests that the value lies between 1.4 and 2.5, so we will approximate it as 2 [7].

Next we divide R_0 by a constant duration. However, depending on whether or not an individual is symptomatic this duration will change.

As a heuristic, we approximate the duration of the disease as $1/n_i + 1/\gamma$ because the majority of people will show symptoms and the vast majority of those will not die. Therefore, $\beta = R_0/(1/n_i + 1/\gamma)$. This gives us $2/(5.1 + 11.5) = 0.1205$.
To summarize, our estimates for these variables are as reported in Table 1:

$\beta = 0.1205$	$\mu = 0.85$	$\mathrm{n}_i = 0.1961$	$\mathrm{n}_r = 0.1111$
$\alpha = 0.0064$	$\rho = 0.0562$	$\gamma = 0.0870$	

TABLE 1
Base Parameter Summary

2.3. Equilibrium. We investigate the equilibrium and stability of our system of equations for a better assessment of our model. At the equilibrium in our model, each of the five differential equations equals zero under the assumption that the total population does not change. Therefore, the equilibrium is some $\boldsymbol{u^*}$ where $\boldsymbol{B}(\boldsymbol{u^*})\boldsymbol{u^*} = 0$. In our model, n_i, n_r, ρ, γ, and β are greater than zero. Further, μ and α are greater than zero and less than one. Given these constraints, $I(t)$ must equal zero to satisfy the equilibrium for equation (2.5). With this conclusion, $A(t)$ must also equal zero to satisfy the equilibrium for equation (2.3). By setting $I(t)$ and $A(t)$ equal to zero, all of the differential equations satisfy equilibrium. This is also visually apparent in (2.7). Therefore, the number of infected and asymptomatic individuals must equal zero for there to be no further change in the populations. $S(t)$, $R(t)$, and $D(t)$ can be any constants such that $S + R + D = N$. In summary, the equilibrium point $\boldsymbol{u^*}$ can be written as $[S^*, 0, 0, R^*, D^*]^T$ where S^*, R^* and D^* are constants.

Using the estimated values for the constants, the eigenvalues can be solved for using a Jacobian Matrix. Three eigenvalues equal zero. One eigenvalue is negative. The final eigenvalue is positive when $\frac{S}{N} > 0.52$. When this condition is satisfied, the equilibrium is not asymptotically stable but rather a saddle point. When $S(t)$ represents less than 52% of the total population, the fifth eigenvalue is negative and the equilibrium is asymptotically stable. This is an interesting result, and requires further analysis to understand the physical meaning and implication.

2.4. Results. As we would expect from an SIR model, the susceptible and recovered populations follow logistic curves as shown in Figure 3. The asymptomatic and infected curves peak and return to zero. The death curve is also logistic, but its

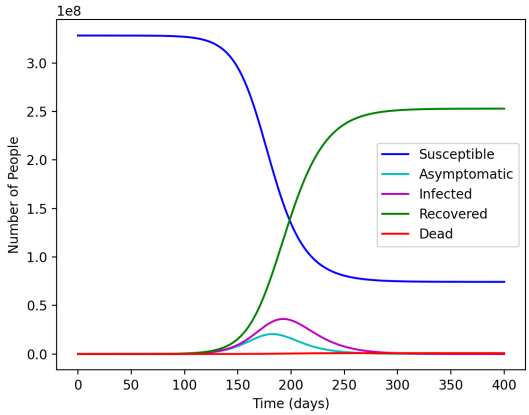

FIG. 3. *Base SAIRD Trajectory*

maximum is so small that it is hard to visualize with an asymptotic value of 956,155. The susceptible and recovered curves have inflection points close to the peak of the infected curve. This is what we would expect, because after the number of infections peaks, the growth of the recovered population will slow. Conversely, the susceptible curve also flattens because less people are being infected. These inflection points and peaks will be critical to the results of a drug or vaccine.

3. Inclusion of a Drug.

3.1. Modeling the Drug. The inclusion of a drug only changes the model's parameters, not the overall structure of the equations. Once a drug is available, more of the infected population will recover and less will die. Recovery of the infected also becomes faster. Therefore $\frac{dS}{dt}$ and $\frac{dA}{dt}$ remain the same from the Basis Model.

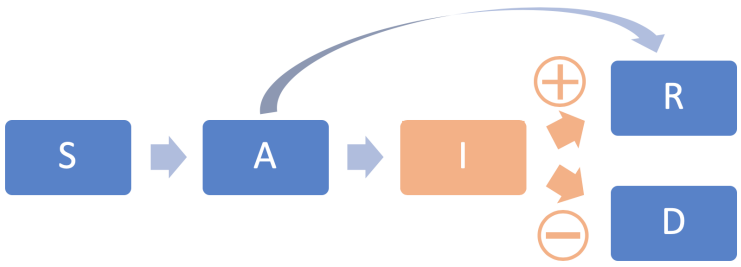

FIG. 4. *Compartmental Flow Chart With Inclusion of Drug*

Though the introduction of a drug will have an impact on the infected population, it can be assumed that not all individuals will receive the drug. Therefore, the population is separated where d is the proportion of individuals who receive the drug. The change in infected individuals, I, becomes:

(3.1)

$$\frac{dI}{dt} = \mu A n_i - \overbrace{(1-d)\alpha_1 \rho I}^{\text{no drug, deceased}} - \underbrace{(1-d)(1-\alpha_1)\gamma_1 I}_{\text{no drug, recover}} - \overbrace{d\alpha_2 \rho I}^{\text{drug, deceased}} - \underbrace{d(1-\alpha_2)\gamma_2 I}_{\text{drug, recover}}$$

where α_1 is the proportion of individuals who don't receive the drug and die while α_2 is the proportion of individuals who do receive the drug and die. Similarly, γ_1 is the proportion of people who recover without the drug while γ_2 is the proportion of people who recover with the drug. It is assumed that the time it takes to die does not depend on receiving the drug so ρ does not change.

With the addition of the drug, the change in the recovered population can be modeled as:

$$\frac{dR}{dt} = (1-\mu)An_r + (1-d)(1-\alpha_1)\gamma_1 I + d(1-\alpha_2)\gamma_2 I \tag{3.2}$$

Similarly, the change in the deceased population can be described as:

$$\frac{dD}{dt} = (1-d)\alpha_1\rho I + d\alpha_2\rho I \tag{3.3}$$

Overall, the equations (2.1), (2.2) and (3.1)-(3.3) describe the population change with the introduction of a drug.

3.2. Tuning Parameters. Because antiviral drug trials are still underway, data about their effectiveness is not available. Both influenza and COVID-19 are respiratory viruses, and share many symptoms and complications. Therefore, as a heuristic, we will begin by using data from influenza antivirals as baseline constants. We only use these data as baselines and run our model with different values through a sensitivity analysis.

The parameters β, μ, n_i, n_r, and ρ remain the same from the Basis Model. Similarly, α_1 and γ_1 correspond to α and γ in the Basis Model respectively. The proportion of individuals who do receive the drug and die, α_2, is estimated at 50% of the current death rate based on the effectivenesses of other antiviral drugs [12]. Therefore, α_2 is 0.32%.

Influenza antivirals can help sick people recover, on average, in 6.8 days. [14]. This is a 14.7% reduction in the diseases' duration. We use this fraction along with the previous duration of 11.5 days to estimate γ_2 as $\frac{1}{11.5\times(1-0.147)} = \frac{1}{9.810} = 0.102$.

To summarize, our estimates for these variables based on research of the current outbreak and data on antiviral drugs are as follows:

$\beta = 0.1205$	$\mathrm{n}_i = 0.1961$	$\mathrm{n}_r = 0.1111$
$\mu = 0.85$	$\alpha_1 = 0.0064$	$\alpha_2 = 0.0032$
$\gamma_1 = 0.0870$	$\gamma_2 = 0.102$	$\rho = 0.0562$

TABLE 2
Drug Parameter Summary

3.3. Drug Availability. For the distribution of the drug, we use a logistic curve to model the percentage of patients who are treated with the drug at time t. We feel logistic growth is reasonable because manufacturing will ramp up at the beginning, while towards the end, difficult access to rural communities or those with poor access to healthcare will slow growth.

$$d(t) = \frac{1}{1+e^{a(-t+b)}} \tag{3.4}$$

In Figure 5, $a = 0.1$ is the logistic growth rate of the curve and $b = 75$ (arbitrary) is the inflection point. For the purpose of this model, $a = 0.1$ has been chosen so

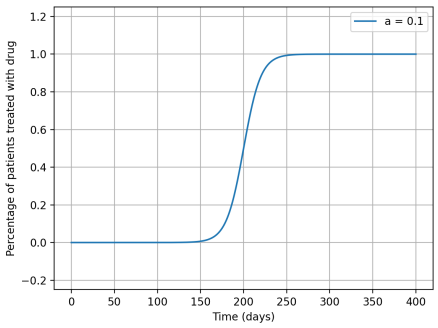

FIG. 5. *Drug Distribution d(t)*

that the majority of the change in drug distribution occurs over a span of 30 days. We feel this is a reasonable time span based on the COVID-19 response (see Figure 9 for further reference). In practice, small changes in the value of a do not have a significant impact on the final results of the model. *In the remainder of the paper when the term 'release date' of the drug or vaccine is used, we are referring to the inflection point of the curve.*

3.4. Equilibrium. As before, n_i, n_r, ρ, γ_1, γ_2 and β are greater than zero. Also, μ, α_1, and α_2 are greater than zero and less than one. Furthermore, $d(t)$ is a logistic curve bounded by 0 and 1 . Based on these constraints, the model follows the same structure as the Basis model. Thus, $I(t) = A(t) = 0$ at equilibrium. $S(t)$, $R(t)$, and $D(t)$ can be any constants such that $S + R + D = N$. In summary, similar to the Basis Model, the equilibrium point $\boldsymbol{u^*} = [S^*, 0, 0, R^*, D^*]^T$.

To understand the stability, $d(t)$ is set to its asymptotic value of 1 since it is assumed the drug would be fully distributed by the equilibrium where there are no infected individuals. In solving for the eigenvalues, three are found to equal zero. One eigenvalue is negative. The final eigenvalue is positive when $\frac{S}{N} > 0.48$. Stability is achieved when $S(t)$ represents less than 48% of the total population. Therefore, the drug does not change the nature of the equilibrium, merely the values.

3.5. Parameter Sensitivity Analysis. This section investigates how varying γ_2 and α_2 impacts the final death toll (i.e. $\lim_{t\to\infty} D(t)$). Figures 6 and 7 plot the release date of the drug against the final death toll. Each graph varies γ_2 and α_2 while the other remains constant at $\alpha_2 = \alpha_1$ or $\gamma_2 = \gamma_1$. The horizontal gray line at the top of each figure remains constant because neither γ or α have changed, so the drug has no effect. In both figures, each curve converges to the same final death toll because the drug has no effect if it is released after the pandemic has passed. In both figures, the inflection point of each curve aligns with the peak of infections.

In Figure 6, as we expect, the earlier that the drug is released, the lower the death toll. Each resulting curve is roughly sigmoidal, but the $\gamma_2 = 1/5$ curve tapers off as *release date* $\to 0$. For early release dates, the more effective (i.e. faster recovery time) drugs save many more lives than the less effective drugs. However, as the release date nears the peak of infections, this difference in outcome shrinks.

In Figure 7, if the drug is released on day 1, any change in α_2 is met with a proportional change in the death rate (see $\alpha_2 = 0.005, 0.004, 0.003$). Again, we see sigmoidal curves where earlier release dates save more lives.

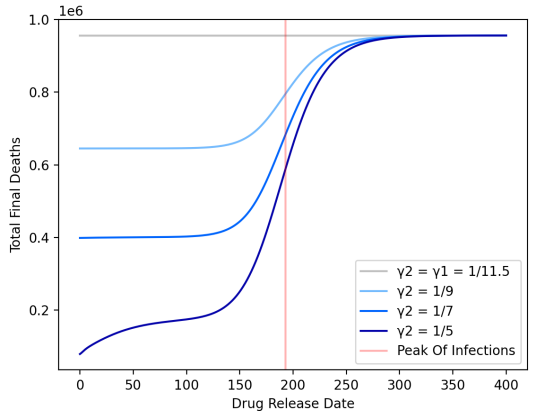

FIG. 6. *Final Death Toll vs. Release Date, Varying* γ_2

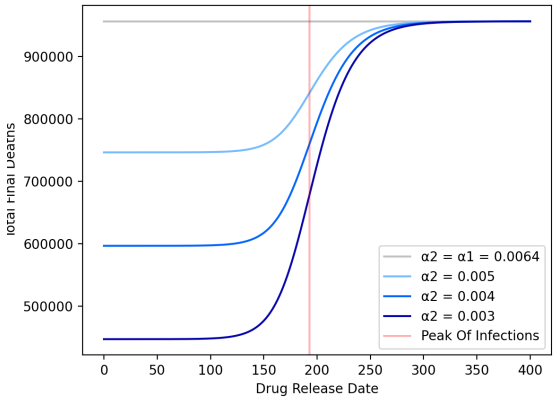

FIG. 7. *Final Death Toll vs. Release Date, Varying* α_2

Our model suggests that while substantial benefit can still be derived from releasing a drug after the peak of infections, the death toll will be reduced dramatically if the drug is released far before the peak. However, a 'good drug' can save more lives if released after the peak than a comparatively 'bad' drug available from the beginning.

4. Inclusion of a Vaccine.

4.1. Modeling the Vaccine. The inclusion of a vaccine impacts our susceptible population with a successful vaccination granting immunity to the virus, moving some patients directly to the recovered population [1]. However, vaccinations are not always successful and if a vaccine was unsuccessful, the recipient would not know and would *not become vaccinated again* [16]. Therefore, the susceptible population is split into two different groups: One with people who haven't been vaccinated (S), and one with those who have received an ineffective vaccination (S_{iv}). Now:

$$N = S + S_{iv} + A + I + R + D$$

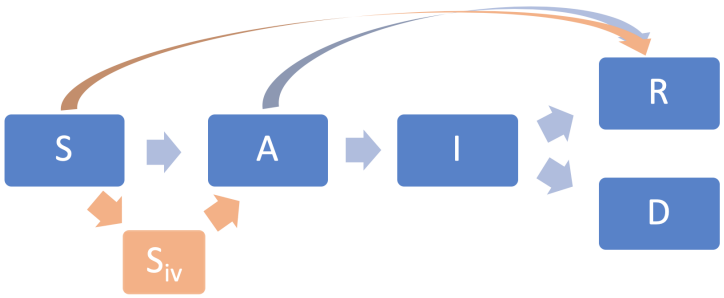

FIG. 8. *Compartmental Flow Chart With Inclusion of Vaccine*

As defined in Section 4.3, the number of vaccinations administered each day is $v(t)$. Each day, v vaccinations are distributed removing v people from the susceptible category. However, it could be the case that the susceptible category becomes so small that the number of vaccinations available, v, is larger than the remaining population minus those who would become infected. If this was the case, $|\frac{dS}{dt}| > S$, meaning that more people are removed from the susceptible population than were present to begin with. To resolve this problem, we use a modified Heaviside step function (4.1) to split each of the relevant equations ($\frac{dS}{dt}$, $\frac{dS_{iv}}{dt}$, $\frac{dA}{dt}$, $\frac{dR}{dt}$) into two cases; The first where $v < S - \textit{new infections}$ and the second where $v \geq S - \textit{new infections}$. In the first case, v is simply subtracted from the susceptible population. In the second, the entire remaining susceptible population is vaccinated. The second case assumes that each individual would become vaccinated that day before they could become infected.

$$H(v,S,A,I) = \begin{cases} 1 & \text{if } v < S - [BI(\frac{S}{N}) + BA(\frac{S}{N})] \\ 0 & \text{if } v \geq S - [BI(\frac{S}{N}) + BA(\frac{S}{N})] \end{cases} \tag{4.1}$$

With this function, the change in the population of susceptible individuals is modeled as:

$$\frac{dS}{dt} = -H(\frac{B_i IS}{N} + \frac{B_a AS}{N}) - H(v - S) - S \tag{4.2}$$

Notice that when $H = 1$, the equation becomes $\frac{dS}{dt} = -\frac{B_i IS}{N} - \frac{B_a AS}{N} - v$ (equation (2.1) minus v). When $H = 0$, the equation becomes $\frac{dS}{dt} = -S$ so that the remaining susceptible population is vaccinated and removed. After one day where the entire susceptible population is vaccinated, S and $\frac{dS}{dt}$ simply become zero.

The new compartment, susceptible ineffectively vaccinated is modeled by:

$$\frac{dS_{iv}}{dt} = H[(1-k)v - (1-k)S] + (1-k)S - [\beta_i I(\frac{S_{iv}}{N}) + \beta_a A(\frac{S_{iv}}{N})] \tag{4.3}$$

where k is the effectiveness of the vaccine and therefore $(1-k)$ is the percentage of ineffective vaccinations. The two positive terms (new ineffective vaccinations) are $(1-k)v$ and $(1-k)S$ for $H = 1$ and $H = 0$ respectively. Regardless of H, the negative term, $-[\beta_i I(\frac{S_{iv}}{N}) + \beta_a A(\frac{S_{iv}}{N})]$, remains the same. Again this is the same as equation (2.1).

The change in the asymptomatic population will now include a positive term for the part of the ineffectively vaccinated population that becomes infected. The first

term disappears when $H = 0$ because the entire susceptible population receives a vaccination and no one becomes infected.

$$\frac{dA}{dt} = H[B_i I(\frac{S}{N}) + B_a A(\frac{S}{N})] + [\beta_i I(\frac{S_{iv}}{N}) + \beta_a A(\frac{S_{iv}}{N})] - \mu A n_i - (1-\mu) A n_r \tag{4.4}$$

The infected population equation, $\frac{dI}{dt}$, remains the same as that of the Basis Model equation (2.3).

The change in the recovered population is very similar to equation (2.4) from the Basis Model, with the addition of those who receive a successful vaccination. This will either be kv or kS depending on the Heaviside function:

$$\frac{dR}{dt} = (1-\mu) A n_r + (1-\alpha)\gamma I + H[kv - kS] + kS \tag{4.5}$$

A vaccination does not affect the rate at which people die, so $\frac{dD}{dt}$ remains the same as that of the Basis Model equation (2.5).

Overall, the equations (2.3), (2.5) and (4.2) - (4.5) describe the population change with the introduction of a vaccine.

4.2. Tuning Parameters. For the sake of this model, we assume that the COVID-19 vaccine will consist of a single dose and will grant lasting immunity (i.e. the virus will not mutate significantly).

Therefore, κ, the effectiveness of the vaccine is estimated by averaging the effectiveness of viral vaccines with lasting immunity. We estimate the vaccine to be 91% effective averaging eight known effectivenesses of common viral vaccines [16].

Again, β, μ, n_i, n_r, α, γ and ρ can all be estimated based using the values from the Basis Model.

To summarize, our estimates for these variables are as follows:

$\beta = 0.2015$	$\mathrm{n}_i = 0.1961$	$\mathrm{n}_r = 0.1111$	$\mu = 0.85$
$\alpha = 0.0064$	$\rho = 0.0562$	$\gamma = 0.0870$	$\kappa = 0.91$

TABLE 3
Vaccine Parameter Summary

4.3. Vaccine Availability. For the release of the vaccine, a logistic distribution is used to model the number of new vaccinations available for susceptible individuals at time t:

$$v(t) = q\frac{ae^{(a(b-t))}}{(1+e^{(a(b-t))})^2} \tag{4.6}$$

Here, q is the total number of vaccines distributed, a is the logistic growth rate, and b is the date of maximum vaccine distribution growth.

The left graph in Figure 9, shows the total (blue) and daily (orange) number of vaccines distributed. The orange curve, $v(t)$, is the derivative of the blue curve. Note that the final number of vaccines distributed here is at an arbitrary value of 300,000,000. Our simulations uses different percentages of the total U.S. population as final distribution values. Like the drug, $a = 0.1$ has been chosen so that the majority (63%) of the vaccinations are distributed in a month-long span (shown in the right graph), a reasonable estimate considering the rate of response to COVID-19. Again from testing, the exact value of a has little effect on the outcome of the curves.

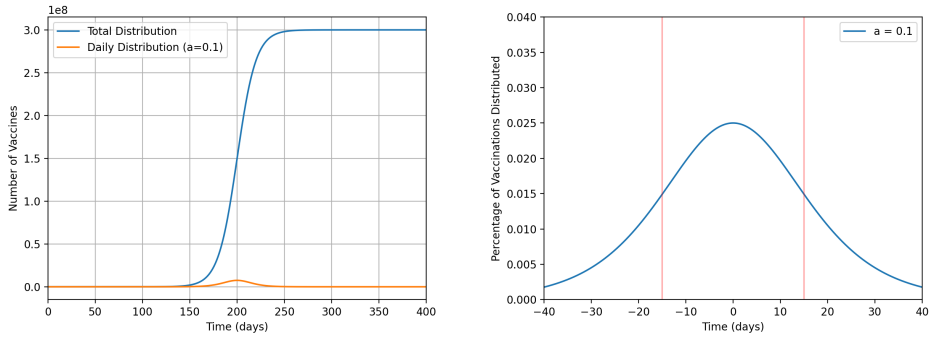

FIG. 9. *Total/Daily Vaccine Distribution (Left), and Daily Percentage Distribution (Right)*

4.4. Equilibrium. In this model, n_i, n_r, ρ, γ, and β are greater than zero. Similar to before, μ, α, and κ are also greater than zero and less than one. Furthermore, for $v(t)$, it can be assumed that a and q are greater than zero. Given these constraints, $I(t)$ must be zero so that $\frac{dD}{dt}$ is in equilibrium (equation (2.5)). Furthermore, $A(t)$ must also be zero so that $\frac{dI}{dt}$ is in equilibrium (equation (2.3)). With $I(t)$ and $A(t)$ set to zero, $\frac{dA}{dt} = \frac{dI}{dt} = \frac{dD}{dt} = 0$. To satisfy $\frac{dR}{dt} = 0$ (equation (4.5)), $v(t)$ and $S(t)$ must be zero. As t continues to infinity, $v(t)$ approaches zero. Therefore, there would be an equilibrium as t goes to infinity. However, for purposes of our analysis, we will focus on the second equilibrium, where $S(t)$ is zero. From the model, the day after $v(t)$ surpasses $S(t)$, $S(t)$ becomes zero. So, equilibrium is achieved when $S(t) > v(t)$ and $I(t)$ and $A(t)$ are zero. $S_{iv}(t)$, $R(t)$, and $D(t)$ can be any constants such that $S_{iv} + R + D = N$. Overall, the equilibrium point, $\boldsymbol{u^*}$, is achieved at $[0, S^*_{iv}, 0, 0, R^*, D^*]^T$.

Based on the estimated values for the constants, the first four of the the eigenvalues are -1, 0, 0, and 0. The fifth eigenvalue is negative. The sixth eigenvalue is positive when $\frac{S_i v}{N} > 0.52$. Similar to the Basis and Drug models, when $S_i v(t)$ represents less than 52% of the total population, the sixth eigenvalue is negative and the equilibrium is asymptotically stable.

4.5. Parameter Sensitivity Analysis. Figure 10 uses the same axes as Section 3's parameter analysis but with each curve modeling different values of q in equation (4.6) (i.e. total number of vaccines distributed). Remember that we refer to the inflection point of the distribution of vaccines as their 'release date'. Therefore each curve begins slightly after 0 so that for the earliest release date all of the vaccinations are still distributed. Like in the previous section, each curve is roughly sigmoidal. However, the left sides of the curves seem to fall off. Like we would expect, as the percent of the population that is vaccinated increases, the total deaths decrease. Also the earlier the vaccine is distributed, the better. At early distribution times, outcomes are *not* proportional to the difference in percentage of the population vaccinated. The curves tend to bend downward and to the left near time 0. This relates to what we know about the importance of herd immunity and tells us that a population derives an accelerating benefit (in saved lives) as a greater proportion of the population gains immunity.

Figure 11 shows how vaccine effectiveness rate, κ, impacts the death toll. As in

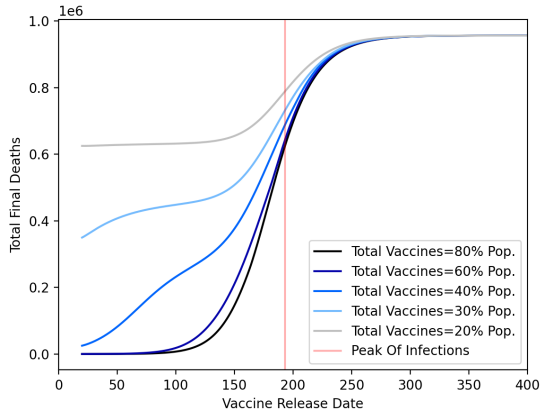

FIG. 10. *Final Death Toll vs. Vaccine Release Date, Varying Population Vaccination Rates*

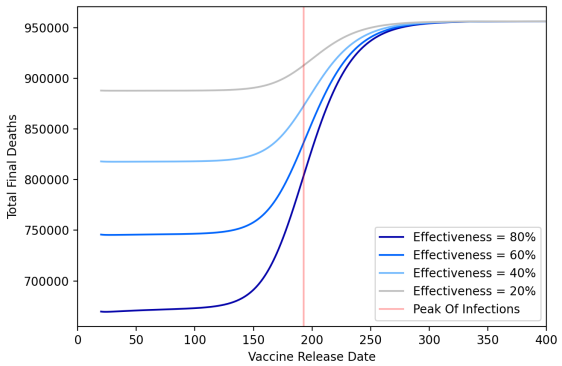

FIG. 11. *Final Death Toll vs. Vaccine Release Date, Varying Vaccine Effectiveness*

the other graphs, each result is a rough sigmoid curve. Unlike the previous graph, at early stages of the pandemic, the curves are linearly spaced. This implies that a proportional increase in vaccine effectiveness translates to an equi-proportional change in the death toll. Additionally, the curves do not converge as quickly as in the previous graph. This implies that even as the pandemic continues, the effectiveness of a vaccine maintains importance. An 80% effective vaccine released slightly after the peak of infections is more helpful than a 40% effective vaccine available from the beginning.

5. Discussion.

5.1. Antiviral Drugs and Vaccines. Based on our previous analysis, the best time to release a drug or vaccine is far before the peak of the pandemic itself. At and after the peak of infections, the outcome quickly worsens. Many times a relatively 'good' countermeasure saves more lives if released at the peak of infections compared to a 'bad' countermeasure released long before. This section directly compares the effects of a drug and vaccine.

Figure 12 compares a perfect drug and a perfect vaccine while Figure 13 compares

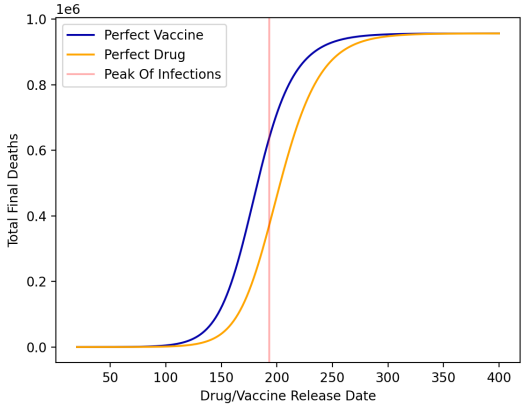

FIG. 12. *Final Death Toll vs. Perfect Drug/Vaccine Release Date*

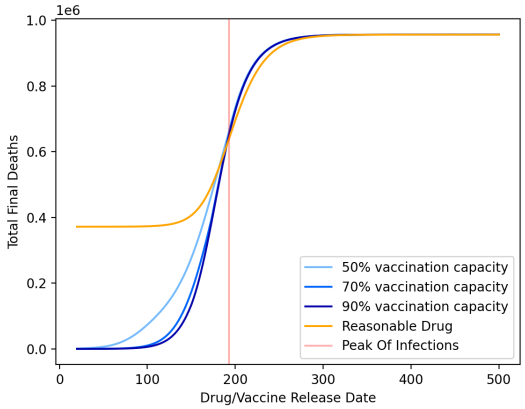

FIG. 13. *Final Death Toll vs. Reasonable Drug/Vaccine Release Date*

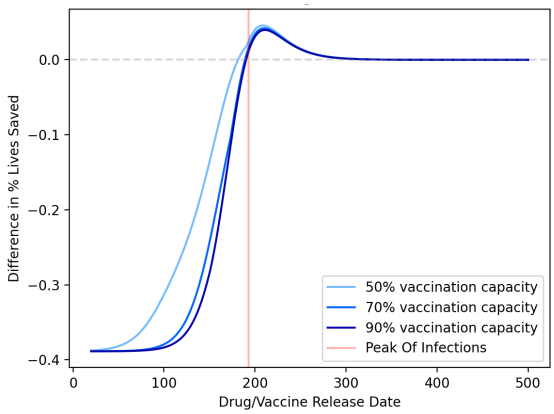

FIG. 14. *Difference in % of Lives Saved (Drug - Vaccines)*

a reasonable drug and reasonable vaccine (with added variation in proportion of people vaccinated). The perfect drug reduces the death rate to 0%, the recovery time becomes instant, and every infected patient receives it. The perfect vaccine is 100% effective and is distributed to the entire susceptible population. The reasonable drug and vaccine use the variables and values that were researched and discussed in previous sections. About 50% of the US population receives the flu vaccine each year [2]. Therefore we have chosen 50%, 70% and 90% as capacity values.

In Figure 12, the perfect drug has fewer total deaths compared to the perfect vaccine over the entire span of potential release dates. This makes sense intuitively. A vaccine can not save people who are already infected. If the vaccine were released during the peak of the pandemic, fewer people would benefit. However, the drug can help those already in the infected category. Additionally, with every infected person receiving it and immediately recovering, the ability for the virus to spread is severely diminished.

In Figure 13, every reasonable vaccine vastly outperforms the reasonable drug when released before the peak of infections, while the reasonable drug slightly outperforms each vaccine following the peak of infections. This follows similar logic to the first graph. The vaccine is much more effective when released early because it grants the population herd immunity, but it is not as helpful after many are infected whereas a drug is.

Figure 14 presents the same information as Figure 13, but directly compares the percentage of lives saved by the drug and the vaccines. To construct this graph, first we find how effective each countermeasure is in terms of percentage of total deaths reduced. Total deaths without any intervention is 956,222. To calculate percentage of total deaths reduced for each countermeasure we use the equation $1 - (deaths/956,222)$, where deaths is the total final deaths for that countermeasure if it is released at the given time. Finally, we subtract the percentage of lives saved by each vaccine from that of the drug to give us the y-axis. Interpreting this graph, a y-axis value of 0 means that the countermeasures are equally as effective, whereas a positive value of 0.1 means that the drug saved 10% more lives than the vaccine.

Analysis of Figure 14 finds that at time zero (i.e. the drug and vaccine are available since the beginning), each vaccine saves ∼39% more lives than the drug. However shortly after the peak of infections, each curve reaches a maximum at 0.0457%, 0.0421%, and 0.0398% for the 50%, 70%, and 90% distribution brackets respectively. This means that at its best, the drug saves ∼4%−4.6% more lives if released at that time. If each countermeasure is released directly at the peak of infections, the drug only performs slightly better than the vaccine, saving 2.53%, 1.64%, and 1.17%, more lives than the 50%, 70%, and 90% distribution brackets.

5.2. Equilibrium Analysis. In general, all of the equilibrium points are asymptotically stable when S or S_{iv} is small enough. For the Basis and Vaccine Models, S and S_{iv} must be less than 52% of the population. For the drug, this is slightly lower, at 48%. The introduction of a drug does not change the equilibrium, as both the basis and the drug models are in equilibrium when $A(t)$ and $I(t)$ are zero. However, with the introduction of a vaccine, equilibrium is only reached when $S(t)$ or $v(t)$ as well as $A(t)$ and $I(t)$ are zero. Based on this result, it is critical that every person receives the vaccine so that $v(t)$ surpasses $S(t)$ and $S(t)$ becomes zero. The population benefits from each person receiving a vaccine because each susceptible person must either become infected or receive the vaccine, and the latter is preferred. In

general, the three models are similar, and the introduction of a drug or vaccine does not significantly change the equilibrium and its stability.

5.3. Limitations. The model's basis as an SIR model is one limitation. While we would expect, and do observe, real world pandemic infection data to grow logistically, it is never a perfect fit. There are many more factors at play in a pandemic that cannot be fully explained by a simple system of equations. Unpredictable, exogenous factors include the availability of medical supplies, hospital capacity, social distancing, and municipal lock-downs, among others. Our model also treats every person the same, as it neglects risk factors (e.g. age, obesity), geography (urban vs. rural), gender, and many other personal characteristics. Therefore, the actual value for the total number of deaths can not be extrapolated due to the rapid changes of the current pandemic. In spite of this, we argue that general trends and relationships are captured by our model.

Other limitations arise from our heuristics. These include using a constant R_0, using uniform disease duration to calculate β, assuming asymptomatic people are equally contagious to those who are symptomatic, approximating drug values based on influenza data, and assuming a vaccine's effectiveness is black and white.

5.4. Possible Next Steps. First potential next steps would include fixing and adding elements from the limitations section. It may be possible to forecast and use historical R_t data to make β_a and β_i time dependent variables. This would require more data about differences in infectivity between asymptomatic and infected populations as well as some idea about future social distancing and its impacts on R_t. Further, subdividing the infected and symptomatic populations into at risk groups would also bring the model closer to reality. These risk groups could include the elderly, the immunocompromised, and the obese among others [6].

Another possible next step would have to do with increasing case counts in the U.S. and a potential second wave. The projected release dates for many vaccines and Operation Warp Speed come around January 2021. This could coincide with a second wave after people return to school and work in the fall. While the details would be much more complex, a second wave is on many Americans' minds right now and is as important as ever.

Furthermore, additional analysis on the physical meaning of the equilibrium stability is required. We found that a certain percent of the population must no longer be susceptible to reach a stable equilibrium. By further examining these results, we can begin to understand the population dynamics and adjustments which are necessary to slow and stop the spread of COVID-19.

Finally, as new vaccines and drugs are developed, more data about their specific effectivenesses will be available. It will be interesting to plug those values directly into the model to compare each vaccine and drug along with each of their projected release dates to observe different outcomes.

6. Conclusion and Perspectives. From analysis of our model, the best time to release a drug or vaccine is long before a pandemic begins. Each day that a countermeasure's release is delayed many more lives are lost. A change in death rate of a drug will result in an equi-proportional change in the final death toll. However for early release dates of a vaccine, this is not the case. The rate of return on the number on increased vaccines distributed actually accelerates, pointing towards the importance of herd immunity.

In comparing the outcome of different drug and vaccine releases, we find that long

before the peak of infections, vaccines are more effective. At and after the peak of infections, the release of a drug will save marginally more lives. If a vaccine or drug were available for the entire duration of the disease, about 40% more lives would be saved with a vaccine. However, after the peak of infections, a drug can save, at most, $\sim$4%$-$4.6% more lives depending on how many vaccines are distributed.

It is critical that a response to COVID-19 focuses on slowing infections until a drug or vaccine can be introduced to the public. The U.S. has already seen its first spike of infections, so vaccines have already lost their comparative advantage. The release of a drug will have an equal, if not slightly greater, reduction on the final death toll of the pandemic. These results are not to suggest that development of vaccinations should be abandoned, or even that a drug should be prioritized. It remains that slowing down the virus and buying time for the development of these countermeasures is most important.

REFERENCES

[1] *Vaccines (immunizations)*, 2018, https://medlineplus.gov/ency/article/002024.htm.

[2] *Seasonal Influenza Vaccine Supply for the U.S. 2019-2020 Influenza Season*, 2019, https://www.cdc.gov/flu/prevent/vaxsupply.htm.

[3] *Fact Sheet: Explaining Operation Warp Speed*, 2020, https://www.hhs.gov/about/news/2020/06/16/fact-sheet-explaining-operation-warp-speed.html.

[4] *Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)*, 2020, https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html.

[5] *Novel coronavirus (covid-19) cases data*, July 2020, https://data.humdata.org/dataset/novel-coronavirus-2019-ncov-cases.

[6] *People with Certain Medical Conditions*, 2020, https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.

[7] *Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (Covid-19)*. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf, 2020.

[8] D. Armstrong and E. Pfanner, *Coronavirus Vaccine Tracker: Race for a Covid-19 Cure*. https://www.bloomberg.com/features/2020-coronavirus-drug-vaccine-status/, 2020.

[9] D. C. Buitrago-Garcia, D. Egli-Gany, M. J. Counotte, S. Hossmann, H. Imeri, A. M. Ipekci, G. Salanti, and N. Low, *The role of asymptomatic SARS-CoV-2 infections: rapid living systematic review and meta-analysis*, medRxiv, (2020), https://doi.org/10.1101/2020.04.25.20079103, https://www.medrxiv.org/content/early/2020/05/24/2020.04.25.20079103.

[10] O. Byambasuren, M. Cardona, K. Bell, J. Clark, M.-L. McLaws, and P. Glasziou, *Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis*, medRxiv, (2020), https://doi.org/10.1101/2020.05.10.20097543, https://www.medrxiv.org/content/early/2020/06/04/2020.05.10.20097543.

[11] H. Froese, *Infectious Disease Modelling: Beyond the Basic SIR Model*. https://www.towardsdatascience.com/infectious-disease-modelling-beyond-the-basic-sir-model-216369c584c4, 2020.

[12] R. Gani, H. Hughes, D. Fleming, T. Griffin, J. Medlock, and S. Leach, *Potential impact of antiviral drug use during influenza pandemic*, Emerging infectious diseases, 11 (2005), p. 1355.

[13] S. A. Lauer, K. H. Grantz, Q. Bi, F. K. Jones, Q. Zheng, H. R. Meredith, A. S. Azman, N. G. Reich, and J. Lessler, *The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application*, Annals of internal medicine, 172 (2020), pp. 577–582.

[14] R. Lehnert, M. Pletz, A. Reuss, and T. Schaberg, *Antiviral Medications in Seasonal and Pandemic Influenza: A Systematic Review*, Deutsches Ärzteblatt International, 113 (2016), p. 799.

[15] G. Meyerowitz-Katz and L. Merone, *A systematic review and meta-analysis of published research data on covid-19 infection-fatality rates*, medRxiv, (2020),

https://doi.org/10.1101/2020.05.03.20089854,
https://www.medrxiv.org/content/early/2020/07/07/2020.05.03.20089854.
[16] R. Reiss, *Childhood vaccine effectiveness easy to use table*, 2016,
https://www.skepticalraptor.com/skepticalraptorblog.php/
childhood-vaccine-effectiveness-easy-use-table/.
[17] A. Sakurai, T. Sasaki, S. Kato, M. Hayashi, S.-i. Tsuzuki, T. Ishihara, M. Iwata,
Z. Morise, and Y. Doi, *Natural History of Asymptomatic SARS-CoV-2 Infection*, New
England Journal of Medicine, (2020), https://doi.org/10.1056/NEJMc2013020,
https://arxiv.org/abs/https://doi.org/10.1056/NEJMc2013020.
[18] D. Smith and L. Moore, *The SIR Model for Spread of Disease - The Differential Equation
Model*, 2020, https://www.maa.org/press/periodicals/loci/joma/
the-sir-model-for-spread-of-disease-the-differential-equation-model.
[19] M. Smith, K. Yourish, S. Almukhtar, K. Collins, D. Ivory, and A. Harmon,
Coronavirus (Covid-19) Data in the United States, 2020,
https://github.com/nytimes/covid-19-data.
[20] R. Verity, L. C. Okell, I. Dorigatti, P. Winskill, C. Whittaker, N. Imai,
G. Cuomo-Dannenburg, H. Thompson, P. G. Walker, H. Fu, et al., *Estimates of the
severity of coronavirus disease 2019: a model-based analysis*, The Lancet infectious
diseases, (2020), https://doi.org/10.1016/S1473-3099(20)30243-7,
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30243-7.