Vaccination during an endemic outbreak: an analysis of transmission dynamics

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1. Introduction

Human disease and its spread have always been a subject of interest of both scientists and policymakers. If on the one hand knowledge of the etiology and evolution of human diseases is fundamental, so is the demographic work of modelling their spread as well as the communication and application of scientific knowledge to the administration of public health and hygiene. Thus, the study of epidemics encompasses various disciplines such as microbiology, medical sciences, demography, public health. While we do have records of epidemics that date back to the 5th century BC, such as the plague of Athens or the Black Death in the 14th century AD, it wasn't until mid-19th century that germ theory gained recognition, which stated that the causes of infectious diseases are pathogens such as viruses, bacteria or fungi (Augustyn, n.d.) . This allowed the scientific community to conceive the spread of infectious diseases as local outbreaks.

Improvement in the mathematical modelling of epidemics, alongside the advancement of microbiological knowledge and techniques, allowed for a better understanding of the spread of infectious disease. Physicist and mathematician Bernoulli published the first mathematical model of the spread of smallpox in 1760 (Kiser, 2019), however the single model that nowadays is still widely accepted and used is the Kermack and McKendrick S I R model (1927), which is a basic compartmental model that divides the studied population into three subsets: susceptible, infected and removed (meaning recovered or dead). This model can be extended and altered with the inclusion of additional parameters such as immunity loss, vaccination, treatment and so on in order to achieve further specification.

Following the start of the Covid-19 pandemic in December 2019, efforts of modelling the spread of the coronavirus have been made in order to identify the best strategies for attenuating the effects of the epidemic, however recent developments of the pandemic such as the start of vaccination programs in European countries as well as the detection of a mutated B.1.1.7 variant of the virus in the UK highlight the need to understand how increased transmission may require higher vaccination rates. Similar to Dhar et al.

(2014), Han Kang et al. (2008), and Feng (2009), in this paper we will present an SIR-type epidemiological model to determine if a higher vaccination rate is needed to curb viral transmission.

1.1 The B.1.1.7 variant

The newly emerging variant of the SARS-CoV-2 virus, the B.1.1.7 lineage, was estimated to have originated in September 2020 in the UK and has been under surveillance because of its possible implication for individual and public health. The B.1.1.7 variant presents a number of mutations that appear to increase the rate of viral transmission, among other things (CDC, 2021). Given the timing of the newly available SARS-COV-2 vaccines, it is important to be able to understand the effect of increased rates of transmission during periods of vaccination.

2. The SIRV Model: parameters and assumptions

To determine the transmission dynamics of an endemic outbreak with vaccination, we construct a nonlinear dynamical system with four distinct classes: Susceptible **(S)**, Infected with SARS-COV-2 **(I)**, Recovered **(R),** Vaccinated **(V)**.

Parameter	Definition	Value
μ	recruitment rate = death rate	0.000035
β	transmission coefficient for wild-type	0.1
β_v	transmission coefficient for B.1.1.7 variant	0.15
$1/\gamma$	mean duration of infection	16 days
ψ	proportion of population vaccinated per time	0.003

A key assumption in this model is the constant renewal of individuals into the susceptible class as a result of births and deaths, which gives the opportunity for the infection to persist through generations, namely to become endemic. The influx of individuals to the susceptible class is denoted by the parameter μ. At the same time, there is a constant efflux of individuals from all classes due to deaths. Doing this allows an infection to persist in the population, which we simplify as a constant N. Thus, the total population at time t is the sum of all epidemiological classes, $S(t) + I(t) + R(t) + V(t) = N(t)$. For simplicity, we set the growth rate and death rate to be equal, so population influx is equal to efflux: $\mu N = \mu S + \mu I + \mu R + \mu V$.

In addition, we assume that individuals interact to produce infections via the law of mass action. This is represented by the term $\beta IS/N$, where β is the transmission coefficient for a wild-type virus variant. For a more infective viral variant, such as SARS-COV-2 B.1.1.7, we would assign a higher parameter value of β_v . However, unlike Feng (2009), we will use a single infected class without differentiating between the two variants and simply demonstrate the result of higher transmission rates.

We then assume that the duration of all infections is $(1/\gamma) = 16$, after which infected individuals are moved to the recovered class.

Finally, we consider a vaccination rate ψ that represents the number of people in the whole population being vaccinated per unit time. In the UK, the vaccination rate is currently around 0.003 (Our World in Data). These individuals are then assumed to acquire protective immunity. The unvaccinated proportion of the population is then represented by (1-ψ), and is used to adjust population influx into the susceptible class. These are greatly simplifying assumptions, as we would not expect the vaccination rate to remain constant due to staggered vaccination schedules.

As a side note, the symbol ψ is also used in the genomics community to represent chemically modified uracil, which is utilised in the SARS-COV-2 mRNA vaccine to prevent an unwanted overactive immune response.

We can then construct the following differential equations which describe the dynamics of the system:

$$\begin{aligned}
\frac{dS}{dt} &= (1-\psi)\mu N - \mu S - \frac{\beta IS}{N} \\
\frac{dI}{dt} &= \frac{\beta IS}{N} - (\gamma+\mu)I \\
\frac{dR}{dt} &= \gamma I - \mu R \\
\frac{dV}{dt} &= \psi\mu N - \mu V
\end{aligned} \tag{1}$$

Since our population N remains constant, the proportion of the population in each epidemiological class adds up to 1: $(s = S/N) + (i = I/N) + (r = R/N) + (v = V/N) = 1$. We can simplify the system in **(1)** by dividing our class variables by N to show the population density of each. Doing this yields the following:

$$\begin{aligned}
\frac{ds}{dt} &= (1-\psi)\mu - \mu s - \beta is \\
\frac{di}{dt} &= \beta is - (\gamma+\mu)i \\
\frac{dr}{dt} &= \gamma i - \mu r \\
\frac{dv}{dt} &= \psi\mu - \mu v
\end{aligned} \tag{2}$$

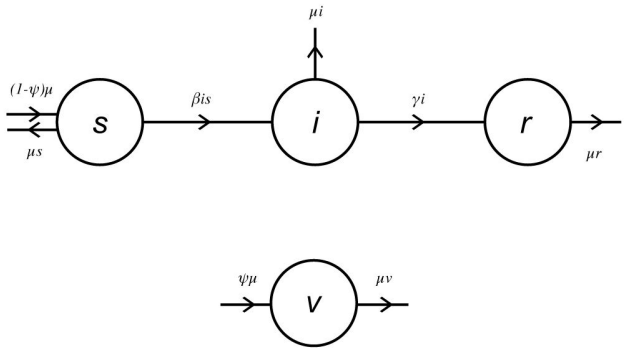


Figure 1. classes of the SIRV model

2.1 Endemicity

Given the influx of population in the susceptible class, a disease has the chance of becoming endemic, meaning persisting within the population across time. This can be proved by studying the equilibrium points of the S I R system and assessing their stability. This will also show the relevance of the reproduction number R_0 in epidemiology.

Given that at any given time $s_{(t)} + i_{(t)} + r_{(t)} + v_{(t)} = 1$, it follows that $r_{(t)} = 1 - s_{(t)} - i_{(t)} - v_{(t)}$, so we can reduce our system in (2) to the following:

$$\begin{aligned}
\frac{ds}{dt} &= (1-\psi)\mu - \beta is - \mu s \\
\frac{di}{dt} &= \beta is - (\gamma+\mu)i \\
\frac{dv}{dt} &= \psi\mu - \mu v
\end{aligned} \tag{3}$$

Which should make the task of finding the equilibria of the system more manageable. By using nullclines and finding their intersections, we can deduce the equilibrium points of the system (Strogatz 2018). These are given by the solutions to the following system:

$$\begin{cases} \frac{ds}{dt} = (1-\psi)\mu - \beta is - \mu s = 0 \\ \frac{di}{dt} = \beta is - (\gamma+\mu)i = 0 \\ \frac{dv}{dt} = \psi\mu - \mu v = 0 \end{cases} \quad (4)$$

We define two distinct cases. The first case is the **disease-free equilibrium** where $i = 0$, meaning that there are no infected cases. Fixing these values into eq. 1 and eq.4 from **(4)** yields:

$$(1-\psi)\mu - \mu s = 0$$

$$s* = (1-\psi)$$

$$v* = \psi$$

Thus, the disease-free equilibrium $(s^*, i^*, v^*) = ((1 - \psi), 0, \psi)$. Recall that $s + i + r + v = 1$. So if $s = (1 - \psi)$, $i = 0$, and $v = \psi$, it then follows that $r = 0$.

The second case is the **endemic equilibrium** where $i > 0$, meaning that there is always a portion of the population which is infected and therefore, the epidemic persists through time. Once again, $v^* = \psi$. To determine the other values in at the equilibrium we solve for s in eq. 2 of **(4)**:

$$s* = \frac{(\gamma+\mu)}{\beta}$$

Substituting s in eq. 1 of **(4)** yields:

$$i* = \frac{(1-\psi)\beta\mu - \mu(\gamma+\mu)}{\beta(\gamma+\mu)}$$

Thus, the endemic equilibrium $(s_e, i_e, v_e) = \left(\frac{(\gamma+\mu)}{\beta}, \frac{(1-\psi)\beta\mu - \mu(\gamma+\mu)}{\beta(\gamma+\mu)}, \psi\right)$. Once again, $r = 1 - s - i - v$.

3. Analysis of equilibria

Now that we have found the two equilibria of the system, we can linearize about these points to determine the local stability of each equilibrium (Strogatz 2018). We first compute the Jacobian matrix of the system:

$$J = \begin{pmatrix} \beta i - \mu & -\beta s & 0 \\ \beta i & \beta s - \gamma - \mu & 0 \\ 0 & 0 & -\mu \end{pmatrix} \quad (5)$$

Now, we evaluate each equilibrium point: firstly the **disease-free equilibrium**. The Jacobian of the disease-free equilibrium is as follows:

$$J_{(s^*,i^*,v^*)} = \begin{pmatrix} -\mu & -\beta(1-\psi) & 0 \\ 0 & \beta(1-\psi) - \gamma - \mu & 0 \\ 0 & 0 & -\mu \end{pmatrix} \quad (6)$$

Since the matrix is diagonal, the eigenvalues for the matrix are relatively easy to find:

$$\begin{aligned} \lambda_1 &= -\mu \\ \lambda_2 &= \beta(1-\psi) - \gamma - \mu \\ \lambda_3 &= -\mu \end{aligned} \quad (7)$$

For the equilibrium to be asymptotically stable, all three eigenvalues must be negative real parts (ref). λ_1 and λ_3 are always negative, because μ must be a non-negative parameter. However, λ_2 is positive when $\beta > (\gamma + \mu)/(1-\psi)$, and only negative when $\beta < (\gamma + \mu)/(1-\psi)$. It follows that the disease-free equilibrium is unstable when $\beta > (\gamma + \mu)/(1-\psi)$. When $\beta < (\gamma + \mu)/(1-\psi)$ the equilibrium becomes stable.

Moving onto the endemic equilibrium and its Jacobian matrix:

$$J_{(s^*,i^*,v^*)} = \begin{pmatrix} \frac{(1-\psi)\beta\mu - \mu(\gamma+\mu)}{(\gamma+\mu)} - \mu & -(\gamma+\mu) & 0 \\ \frac{(1-\psi)\beta\mu - \mu(\gamma+\mu)}{(\gamma+\mu)} & 0 & 0 \\ 0 & 0 & -\mu \end{pmatrix} \quad (7)$$

Unlike the approach taken by Dhar et al, we find that the full generalized eigenvalues for this matrix are unhelpful for later calculations, so we will first substitute all parameter values except for β, the transmission coefficient. Then, considering $(\gamma + \mu)/(1 - \psi) = 0.06272$, we obtain the parameterized eigenvalues for $\beta < 0.06272$ and $\beta > 0.06272$ using the numerical Eigenvalues method from Wolfram Mathematica (2020). Although not a rigorous determination, this will allow us to sample local stability of the endemic equilibrium around this value of β.

For $\beta = 0.06 < 0.06272$:

$$\begin{aligned} \lambda_1 &= -0.0003271 \\ \lambda_2 &= 0.0002905 \\ \lambda_3 &= -0.000035 \end{aligned} \tag{8}$$

As λ_2 is positive, we can infer that the endemic equilibrium is unstable for this value of β, for which we know the disease-free equilibrium is stable.

For $\beta = 0.065 > 0.06272$, the eigenvalues have the following real parts :

$$\begin{aligned} \lambda_1 &= -0.00001686 \\ \lambda_2 &= -0.00001686 \\ \lambda_3 &= -0.0002814 \end{aligned} \tag{9}$$

All eigenvalues have negative real parts, thus we can infer that the endemic equilibrium is stable for this value of β, for which we know the disease-free equilibrium is unstable.

With these findings, we may tentatively conclude that $\beta = (\gamma + \mu)/(1 - \psi)$ appears to be the point of a transcritical bifurcation, as there is an exchange of stabilities between the two equilibria.

3.1 The reproduction number R

In epidemiological modelling, the average number of secondary cases produced by one infected case is denoted as R and in SIR models that do not take into account vaccination R is set to be equal to $\beta/(\gamma + \mu)$, namely the contacts per unit of time multiplied by the infectious period in units of time. However we do take into account vaccination in our

SIRV model, which has an inhibiting effect on beta, therefore, having set a vaccination rate ψ, R must be adjusted as follows: $R_{vac} = \beta(1-\psi)/(\gamma+\mu)$. Intuitively, we can grasp how if R is bigger than 1, as in one sick person infects one or more susceptible people, then the number of infected individuals will rise. While if it is smaller than 1, i.e. on average one sick person infects less than one susceptible person, then the disease will die out.

Our stability analysis confirmed the critical value of R_{vac} to be 1, around which the stability of the disease free equilibrium change. Readjusting $\beta > (\gamma+\mu)/(1-\psi)$ and $\beta < (\gamma+\mu)/(1-\psi)$, we get $R_{vac} = \beta(1-\psi)/(\gamma+\mu) > 1$ and $R_{vac} = \beta(1-\psi)/(\gamma+\mu) < 1$

Therefore, based on our analysis, at $R_{vac} = 1$ a transcritical bifurcation happens, such that for $R_{vac} < 1$, the disease free equilibrium is stable and the endemic equilibrium is unstable, while for $R_{vac} > 1$ the disease free equilibrium is unstable and the endemic equilibrium is stable.

The relevance of this in tackling epidemics comes down to the need to lower R below 1 in order to let the disease die out. However, because R is the result of $\beta(1-\psi)/(\gamma+\mu)$, Action can be taken upon different parameters: for instance measures such as a strict lockdown will reduce β to some extent because it will limit physical contact among the population, while a higher vaccination rate will also reduce β, because $(1-\psi)$ will always be a number included between 0 and 1. This means that a higher transmission coefficient can be offset with a higher vaccination rate.

4. Numerical simulation: varying β

To demonstrate how the emergence of a new viral variant that is 50% more transmissible than wild-type might affect the efficacy of a vaccination programme, we plot a series of three-dimensional (s, i, v) and two-dimensional (s, i) phase portraits with a constant vaccination rate, while varying the transmission coefficient. Note that some of the parameters used here are not realistic, but are chosen for visual demonstration. Initial values are illustrated by dots, and the trajectories were solved using the Runge-Kutta 4th order method in Python.

We consider three transmission coefficients that represent three different viral variants: one wild-type, one variant that is 50% more transmissible (like B.1.1.7), and one that is many times more transmissible. Keeping $\gamma = 1/10$, $\mu = 1/50$, and $\psi = 0.05$ constant, we expect that $R_{vac} = 7.917\beta$. The disease-free and endemic equilibria *(s, i, v)* will then be (0.95, 0, 0.05) and ($\frac{0.12}{\beta}$, $\frac{0.019\beta - 0.0024}{0.12\beta}$, 0.05) respectively.

Figure 2. $\beta = 0.1$, $R_{vac} < 1$

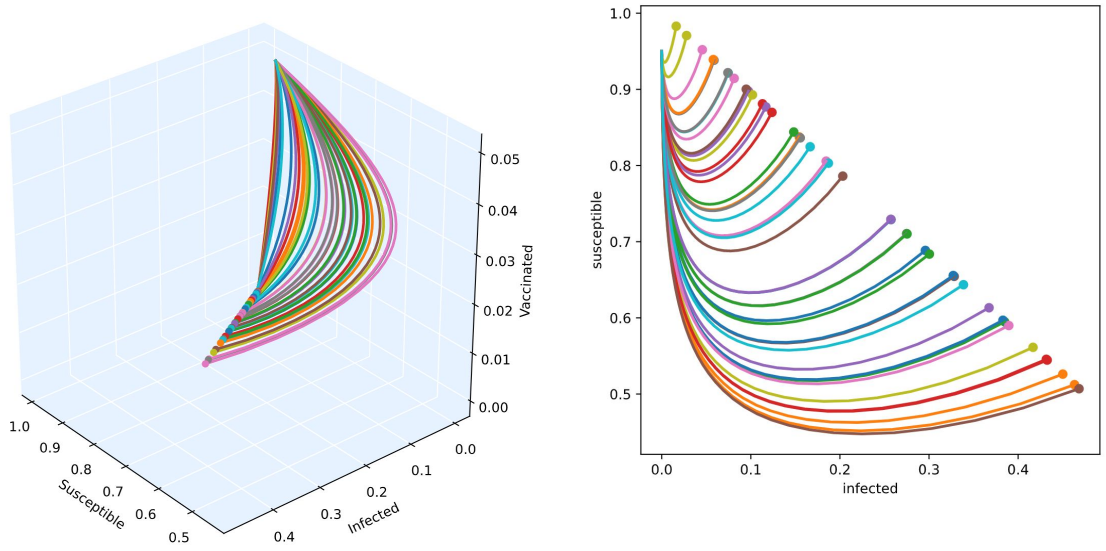


Figure 3. $\beta = 0.15$, $R_{vac} > 1$, endemic equilibrium $= (0.8,\ 0.025,\ 0.05)$

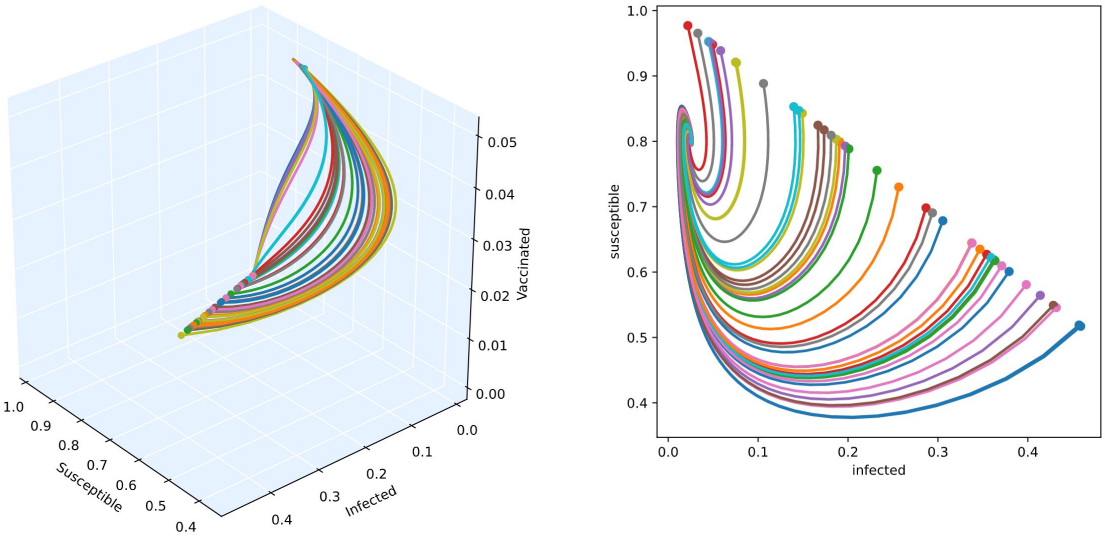
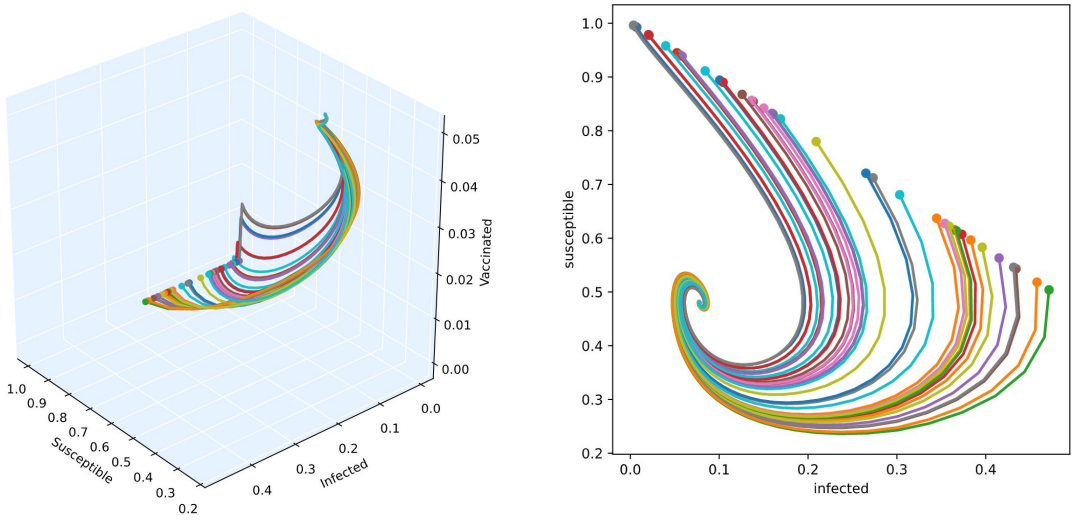


Figure 4. $\beta = 0.25$, $R_{vac} >> 1$, endemic equilibrium $= (0.48,\ 0.07833,\ 0.05)$



In our first scenario, as $R_{vac} < 1$, we note that all trajectories tend towards the disease-free equilibrium at (0.95, 0, 0.05). We expect that a vaccine programme would indeed be an effective intervention that would cause an outbreak to run out of susceptibles quickly. However, if a new variant emerges with mutations that confer a 50% higher person-to-person transmissibility, then it becomes clear that a previously planned vaccination rate is no longer sufficient. This is quantified by $R_{vac} > 1$, leading to an exchange of stabilities between the equilibria as any trajectories near the disease-free equilibrium now move towards the endemic equilibrium. For our third case, where a new variant is much more transmissible, we note that the endemic equilibrium now has a higher fraction of infected individuals and a lower fraction of healthy susceptibles.

5. Discussion

On a concluding note, the appearance of the mutant B.1.1.7 variant of the coronavirus along with the implementation of several vaccination strategies across the world, particularly in Europe, have changed the situation of the Covid-19 pandemic. If at first glance the approval of various vaccines seems like positive news, the repeated mutations of the genetic material of SARS-CoV-2 and thus creation of a new variant suggests otherwise, for it seems to have increased its transmissibility, and therefore its severity on public health and pressure on hospitals and their staff. In this paper we argued how these two elements can affect each other; whereas our model was a gross simplification of the epidemic and although it may be overlooking some real world elements, it still emphasizes the relevance and importance of vaccination strategies in relation to the transmissibility of the pathogen. We have attempted to show how, if the vaccination strategy remains the same, a higher transmissibility could make the difference between a disease free population and endemicity. It is also important to note

how vaccination and antiviral treatment can represent an evolutionary advantage for mutant versions of the virus that have developed drug resistance and to which antibodies created by the vaccine or previous infections are ineffective. This once again emphasizes the relevance of well-performed vaccination strategies and meticulous public health administration in order to keep this phenomenon under control.

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