What Role has Mathematics Played in the Understanding of the COVID-19 Pandemic?

On March 11, the World Health Organisation (WHO) declared the outbreak of SARS-CoV-2 to be a pandemic – one that has since triggered unprecedented health and economic hardships worldwide. Mathematical models have played a crucial role in this ongoing crisis, providing insights and predictions about the pandemic's trajectory and informing public policies on how best to "flatten the curve". More recently, mathematics has been fundamental for testing the reliability of vaccinations and ensuring their optimal roll-out. This report will delve into mathematical models, designed in response to COVID-19, and discuss their importance in helping us understand the behaviour, transmission and prognosis of the virus.

Background to Mathematical Modelling

In general, a mathematical (or epidemiological) model is a representation of a system that can be used to explore its behaviour. Mathematical modelling works on the basis that, using simple assumptions or collected statistics, a set of mathematical equations can be carefully chosen that mimics the underlying epidemiology of an infectious disease. From here, simulations of the model can be trialled and parameters within the equations can be solved to foresee how different interventions would impact health, society and the economy.

A Simple Model

One of the most basic compartmental models for the monitoring of infectious diseases is the SIR model, whereby a total population, N, is divided into three subsets: susceptible individuals, infected individuals, and removed individuals, each represented as functions of time. Movement between these compartments is characterised by the following differential equations:

$$\frac{dS}{dt} = -\beta SI, \quad (1.1)$$

$$\frac{dI}{dt} = \beta SI - \gamma I, \quad (1.2)$$

$$\frac{dR}{dt} = \gamma I, \quad (1.3)$$

where $N = S(t) + I(t) + R(t)$ represents the total population.

The infection rate is denoted by β and the remaining parameter, γ, represents the recovery rate. These two rates can be improved by non-pharmaceutical interventions (NPIs), such as social distancing, wearing masks and hand-washing, and improved health resources, such as antibiotics, respectively.

By computing the above differential equations into programming software, with appropriate initial conditions and values for beta and gamma, we can generate a curve that represents the number of cases that occur over time [see Figure 1].

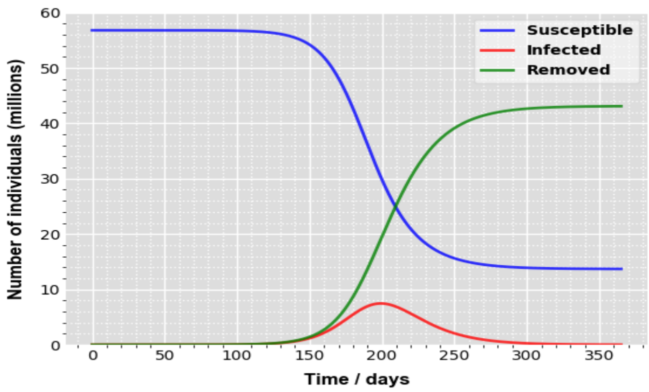

Figure 1: SIR curve programmed in Python, based on data from https://github.com/CSSEGISandData/COVID-19/tree/master/csse_covid_19_data/csse_covid_19_ daily_reports

From such a curve, we can observe that:

i. During the early phases of the epidemic, the number of cases increases exponentially.

ii. In the long-run, $S_\infty > 0$ and $R_\infty < 1$, so not everybody will become infected.[1]

iii. The herd immunity threshold coincides with the peak of the infected curve – once the susceptible curve has been sufficiently depleted.[2]

These are foundational concepts, but have shaped how we have responded to COVID-19. For instance, recognising that cases originally increase exponentially places an emphasise on implementing social policies quickly and efficiently, in order to avoid overwhelming the NHS.

Over the course of this essay, we will expand on points (ii) and (iii).

The Importance of R_0

Arguably the most fundamental threshold value in epidemiology is the basic reproduction ratio R_0, defined as the expected number of secondary cases caused by a single infected individual, when an epidemic begins in a completely susceptible population.[3] For instance, if a virus has an R_0 of 3, this means that an infected person will pass on the disease to three susceptible individuals if no preventative measures are taken.

Beyond giving us an indication of how many people COVID-19 is likely to infect, R_0 also highlights the proportion of new infections that need to be prevented to reduce the growth of the pandemic. For this reason, R_0 is generally used to gauge whether pandemic mitigation is working successfully.

Determining Whether an Epidemic Will Emerge

A primary use of R_0 is to inform of whether an epidemic is likely to take off within a population. In order for an epidemic to occur[4], the number of infected individuals must increase, i.e.,

$$\beta SI - \gamma I > 0 \quad (2.1)$$

At t = 0, we can approximate S to be 1, as everyone within the population (bar the index case) is susceptible. Therefore

$$\beta I - \gamma I > 0 \quad (2.2)$$

If we add γI to the RHS and divide by γ, we achieve

$$\frac{\beta I}{\gamma} > I \quad (2.3)$$

Dividing both sides by I

$$\frac{\beta}{\gamma} > 1, \quad (2.4)$$

where $\frac{\beta}{\gamma}$ is termed as R_0.

Conversely, were $R_0 < 1$, any chance of an epidemic occurring peters out, as, on average, each infected individual would pass the disease to less than one other person, so the outbreak can not be sustained.

As epidemic incidence curves decline in response to changes in a population's policy and behaviour, much weight is placed upon developing a robust exit strategy, by keeping an eye on the value of R_0. It can take over a month for the effects of policy changes to manifest in SARS-CoV-2 data and if restrictions are lifted prematurely, whilst the virus is still widely spreading, this can result in second waves and an exponential surge of cases.

Calculating the Final Susceptible Population Size

Perhaps a more significant use of R_0 is that is allows us to estimate the size of the population that remains uninfected after the end of the epidemic.[5]

Adding equations (1.1) and (1.2)

$$\frac{dS}{dt} + \frac{dI}{dt} = -\gamma I \quad (3.1)$$

Integrating from t = 0 to t → ∞

$$\int_0^\infty \left(\frac{dS}{dt} + \frac{dI}{dt} \right) dt = -\int_0^\infty \gamma I \, dt \quad (3.2)$$

Acquire

$$(S_\infty + I_\infty) - (S_0 + I_0) = -\int_0^\infty \gamma I \, dt \quad (3.3)$$

This simplifies to

$$S_\infty - N = -\int_0^\infty \gamma I \, dt \quad (3.4)$$

Rearranging equation (1.1)

$$I = \frac{dS}{dt} \frac{1}{-\beta S} \quad (3.5)$$

So

$$S_\infty - N = \frac{\gamma}{\beta} \int_0^\infty \gamma \frac{dS}{dt} \frac{1}{S} dt \quad (3.6)$$

Yielding

$$S_\infty - N = \frac{1}{R_0} \log(S) \Big|_0^\infty \quad (3.7)$$

As $t \to \infty$, $I \to 0$ and the proportion of N that was initially susceptible or infected = 1, we arrive at

$$\log(s_\infty) = R_0(S_\infty - 1) \quad (3.8)$$

This is an implicit equation for S_∞, identified as the number of susceptibles left at the end of the epidemic. Essentially, it represents where the curve crosses the x-axis. If $R_0 > 1$, this equation must have two roots: one when $S_\infty = 1$ (corresponding to the start of the pandemic), and another when $0 < S_\infty < 1$ (corresponding to the end of the pandemic). This second root is the value we are interested it.

Case Study

To put all this theory into practice, let us consider the early 2020 study conducted by the London School of Hygiene and Tropical Medicine, which discusses the effects of non-pharmaceutical interventions (NPIs) on COVID-19 cases in the UK.[6] Their model is based on an extension of the SIR model, known as the SEIR model, which also accounts for exposed individuals (those who have been infected, but are not yet infectious). On top of being divided into their disease state, the UK population was aggregated into 186 counties and 5-year age groups. Another notable feature of their model is its stochasticity, meaning it accounts for inherent randomness in the real world.

The authors calculated R_0 to be approximately 2.7, indicating epidemic growth, and using this value, they foresaw that if the epidemic remained unmitigated, 85% of the population would eventually become infected, which would result in an ICU demand that would be 25–80 times greater than the NHS capacity. By running twelve-week simulations of their model, with different interventions in place, they noted that a combination of control measures, including school closures, social distancing, shielding of the elderly and self-isolation of symptomatic individuals would reduce the total number of cases by 70-75%.

Davies et al. estimated that if these interventions were implemented alone, R_0 would not be reduced enough to substantially decline the total number of cases. They then went on to demonstrate that a series of intermittent lockdowns could manage the number of patients requiring ICU beds and delay the peak of the epidemic by3-8 weeks.

These results were presented to the Scientific Advisory Group for Emergences (SAGE), which provide evidence-based scientific advice to leading UK government officials. It comes as no surprise, given these figures, that a twelve-week lockdown was implemented in the UK on 23 March 2020, which significantly reduced transmission, and as R_0 fell to 0.8,[7] indicating epidemic decline, restrictions began to be eased.

Herd Immunity (and the end of COVID-19?)

With many vaccines for COVID-19 now being produced, it becomes relatively clear that herd immunity – when a large proportion of a population becomes immune to a specific disease – will play a large role in bringing the pandemic to an end. The threshold for herd immunity involves R_e, the effective reproduction ratio, which represents the expected number of secondary cases caused by a single infected individual, at any specific time.[8] The value of R_e changes as a population becomes increasingly immunised and is found by multiplying R_0 by the fraction S of susceptible individuals within the population.

The proportion of the population that needs to be vaccinated is calculated by setting R_e equal to 1. Therefore

$$R_0 \cdot S = 1 \quad (4.1)$$

S can be rewritten as (1 – p), where p is the proportion of the population that is immune and p + S = 1. So acquire

$$R_0 \cdot (1 - p) = 1 \quad (4.2)$$

Rearranging this for p

$$1 - p = \frac{1}{R_0} \quad (4.3)$$

$$p_c = 1 - \frac{1}{R_0}, \quad (4.4)$$

where p_c represents the herd immunity threshold.

Given that the value for R_0, is approximately 3 worldwide[9], if we plug this figure into the formula, we get that 67% of the world's population would need to be vaccinated to reach herd immunity.

An SEIR-type model[10] developed by Hogan et al. at Imperial College London predicts that, with some control policies in place, a vaccine with 90% efficacy would achieve herd immunity once a minimum of 55% of the population has been vaccinated. This percentage would increase to 67% coverage if all social distancing measures were lifted. Though there is much uncertainty around being able to calculate an accurate value of p_c, these estimates are still of great significance, as they inform us of how we must control the pandemic and potentially when it will stop spreading through the population.

Figuring out how to allocate vaccines to the right groups at the right time – and thus eradicate SARS-CoV-2 – is another complex problem, for which mathematics plays a large role. Most modellers agree that, if we are to reduce mortality rates, the elderly must be vaccinated first. If transmission is to be slowed, younger adults must be targetted first.[11] As of now, the approach of the NHS is to reduce mortality, by vaccinating the older generations and front-line NHS workers. With 22 million people having already received their first vaccination dose,[12] predictions for herd immunity fluctuate around as early as mid-May 2021.[13]

Discussion

The outbreak of COVID-19 has led to a resurgence of interest in mathematical modelling and its applications in understanding and shaping how to respond to the pandemic. In real life, we can only see one version of the pandemic, but mathematical modelling has allowed for the visualisation of infinitely many. Their use has varied as the virus has progressed, but their purpose has ultimately remained the same – to best comprehend the trajectory that the virus follows and to recommend the implementation of control measures as a result.

Mathematicians, epidemiologists and data scientists have been the unsung heroes during the course of this crisis, improving our understanding of how best to suppress and mitigate SARS-CoV-2, saving millions of lives in the process.

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