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# On Basic Reproduction Number $R_0$: Derivation and Application

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**ABSTRACT**

The basic reproductive number ($R_0$) is a threshold parameter for a population-level model of infectious disease control. The basic reproduction number is derived by epidemiologists using different techniques. It is used to estimate the basic reproductive rates of infected and susceptible hosts and to guide intervention strategies. In this paper, we give an overview of the methods used in the derivation of $R_0$ and assess the use of $R_0$ in the literature. Finally, we discuss some of the limitations and alternatives to the basic reproduction number that have been identified in the literature. The main contribution of this paper is to provide a guideline and shed light on the basic reproduction number to mathematical modellers and policy makers in order to prevent the possible blown out of the epidemic in the susceptible population.

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## Introduction

The basic reproductive number,($R_0$), is the expected number of secondary infections produced by a single individual during his or her entire infectious period, in a completely susceptible population. This concept is fundamental to the study of epidemiology, within-host pathogen dynamics and host-pest interaction (Rong et al., 2020) [1]. It is the most important idea that mathematical thinking has brought to the theory of epidemic and a key concept in bio-mathematics and epidemiology (Rong et al., 2020) [2-3]. The basic reproduction number is also a threshold condition used to determine whether an infectious disease will spread or not in a completely susceptible population when the disease is introduced into the population [3]. The zero in "R zero" means that the basic reproduction number is estimated when there is zero immunity in the population, even though not everyone will necessarily be susceptible to infection, which is the usual assumption. Therefore, in an epidemic with a completely new virus, the earlier the measurements are made the nearer the calculated value is likely to be to the true value of $R_0$, assuming high-quality data are available [4-5].

In demography, $R_0$ denotes the proportion of the total population from the beginning to the end of a generation. Thus, in epidemic models, generation refers to the subsequent infection waves that result from each initial infection. In other words, the first generation of an epidemic is comprised of all secondary illnesses that occur from infectious contact with the index case [6]. Thus, if $R_i$ represents the reproduction number of the ith generation, $R_0$ is the number of infections created by the index instance (zero generation). Thus, $R_0$ may alternatively be defined as the anticipated number of secondary cases generated by generation zero [6]. As a broad definition, $R_0$ is the predicted number of secondary people created throughout the lifespan of a given person. In the fields of demography and ecology, $R_0$ refers to the lifetime reproductive success of a typical member of the species [1]. In epidemiology, $R_0$ is used to indicate the number of susceptible persons infected by a single sick individual for the duration of the infectious period in a population that is completely susceptible. For in-host dynamics, $R_0$ is the amount of fresh infected cells created by a single infected cell over the course of its lifespan, supposing that all other cells are susceptible [2].

The basic reproduction number is an important indication for transmission hazards and illness prevention (Rong et al., 2020) [7]. Given that the magnitude of $R_0$ may be used to assess the amount of effort necessary to avoid an epidemic or eradicate an illness from a community, it is crucial to estimate $R_0$ for a specific disease in a given population. Thus, if one person contracts the virus and transmits it to two others, the $R_0$ equals two. If the population's average $R_0$ is larger than 1, the virus will spread exponentially; however, if $R_0$ is less than 1, the virus will spread slowly and finally die out. Consequently, the greater the value of $R_0$, the quicker an epidemic will spread [4,8]. Consequently, it is evident from the definition of $R_0$ that when $R_0<1$, each infected person generates, on average, fewer than one new infected individual, and it is possible to anticipate that the infection will be eradicated from the population over time. If $R_0>1$, it is possible for the disease to infect the vulnerable population.

The basic reproduction number is influenced by the size of the population and the proportion of susceptible individuals at the onset, the infectiousness of the organism, and the rate of disappearance of cases through recovery or death, the former of which is dependent on the length of time an individual is infectious. The bigger the population, the greater the number of susceptible individuals, the more infectious the virus, and the greater the $R_0$ for a specific virus. The $R_0$ value for a specific virus

will decrease when the rate of elimination of infected people from the population increases [4].

To stop endemic equilibrium from being attained, it is crucial to establish which control measures and at what magnitude would be most successful in decreasing $R_0$ below 1, based on the preceding definition, this can be achieved by performing optimal control on the model in order to identify the most efficient and cost effective way of controlling the disease. This will serve as a crucial guideline for public health activities aimed at preventing the epidemic's likely spread among the vulnerable population. The size of $R_0$ is also used to assess the likelihood of an epidemic or pandemic in emerging infectious diseases (Hoffmenn et al., 2005).

The basic reproduction number should not be confused with the effective reproduction number ($R_e$), sometimes referred to as ($R_t$), which is the number of persons in a population that may be infected at any given moment by a single individual. It varies as the community gets more immunised, either via individual immunity after illness or through vaccination, and as individuals die. effective reproduction number is modified by the number of infected persons, the number of susceptibles with whom infected people come into touch, and people's behaviour, such as social distance [4-5].

The trend of $R_0$ over time is a measure of the success of control and preventive efforts in a community, and the objective of controlling an epidemic is to lower and maintain reproduction numbers below 1 (Khosravi et al., 2020). The biological potential of an agent influences $R_0$, but also depends on the rate of population contact and the duration of infectiousness. It may be used to predict and model infectious disease propagation in populations (Khosravi et al., 2020). This work aims to provide an overview of the techniques used to calculate the basic reproduction number and evaluate the applications of $R_0$ in epidemiology. Finally, we discuss some of the limitations and alternatives to $R_0$ that have been identified in the literature.

**Methods of Deriving Basic Reproduction Number ($R_0$)**

There are several different methods in which $R_0$ can be derived. These procedures vary depending on the kind of model and their intended use. Many approaches provide different $R_0$ values for the same model, and many of the ways produce different $R_0$ values depending on what the modeler deems suitable. Each approach takes its criteria from the threshold nature of $R_0$; yet, several of these ways provide a value that is inconsistent with the biological definition. It is crucial to recognise that utilising one of the procedures at random does not guarantee a certain number of secondary infections resulting from a single affected person.

**Calculating $R_0$ form a Deterministic Model**

The derivation of $R_0$ from a deterministic model is fairly straightforward from first principles. The survival function method is applicable even when non-constant transmission probabilities between classes are assumed. For compartmental models of infected individuals, the next-generation operator can be used. However, we note that the definition of $R_0$ may have more than one possible interpretation in the multi-class system.

**The Survival Function Method**

Heesterbeck and Dietz, (1996) derived the $R_0$ using the survival function approach from the first principle [9]. The derivation was further summarized by Hoffmenn et al.. (2005). They proceeded as follows: Let F(a) be the probability that a newly infected individual remain infectious for at least time (a) and b(a) be the average number of newly infected individuals that an infectious individual will produce per unit time when infected for total time a, then $R_0$ is given by:

$$R_0 = \int_0^\infty b(a)F(a)da \qquad (1)$$

This method makes it easy to handle circumstances in which the infectivity is time-dependent or other transmission probabilities across states vary over time. Not only systems characterised by ordinary differential equations may benefit from this $R_0$ derivation. Additionally, the approach can be used to explain models in which a number of stages are involved in the reproduction of infected people. Nevertheless, it may be challenging to compute the individual probabilities, especially when several states are involved.

Although the survival function approach reliably produces the correct $R_0$, it is difficult to implement in practice. This is particularly true for sufficiently complicated models, which are often the most used. In addition, expanding the survival function approach to infection cycles spanning three or more generations makes its derivation more challenging (Hethcote Tudor, 1980; Lloyd, 2001b; Huang, 2003). Numerous writers, like Luz et al. have used this technique to calculate the basic reproduction number [10]. They used $R_0$ to quantify the likelihood of dengue fever outbreaks in Rio de Janeiro and to evaluate potential control methods.

**The Next-Generation Method**

In circumstances when the population is separated into discrete classes or discontinuous classes, Van den Driessche and Watmough (2002) presented a more rigorous next-generation method to derive $R_0$. Thus, among other things, the next-generation operator can be applied to models with underlying age structures or spatial structures. The next generation matrix's spectral radius is described in this way as the $R_0$. In order to create the matrix, two compartments from the model infected and non-infected must be identified. Van den Driessche and Watmough (2002)'s next-generation matrix method follows the following steps: Let n be the compartments in which m compartment are infected, such that the vector $\bar{x} = x_i$, $i$=1,…$n$ where $x_i$ denotes the number of individuals in the ith compartment. Also, let $F_i(x)$ be rate of appearance of new infections in compartment $i$ and

$V_i(x) = V_i^-(x) - V_i^+(x)$, where $V_i^+$is the rate of transfer of individuals into compartment $i$ by all other means and $V_i^-$ is the rate of transfer of individuals put of the ith compartment. Then, the next generation matrix $G$ is given by

$FV^{-1}$ where $F = \left[\frac{\partial F_i(x_0)}{\partial x_j}\right]$ and $V = \left[\frac{\partial V_i(x_0)}{\partial x_j}\right]$ Where $x_0$ is the disease-free equilibrium state. Then, the $R_0$ is the disease-free equilibrium state. Then, the $R_0$ is dominant eigenvalue of matrix G = $FV^{-1}$. such that:

$$R_0 = \rho(FV^{-1}) \qquad (2)$$

where $\rho$ denotes the spectral radius.

Since just the infection states are required and all other states that are not disease compartments are disregarded, the next-generation matrix is far easier to employ than Jacobian-based methods.

Consequently, the size of the matrices remains manageable. However, the approach of the following generation lacks creativity. To identify which terms are new infections and which terms are transfer terms in order to calculate the matrices F and V, clear biological understanding is necessary.

Van den Bosch *et al*. described a systematic method to calculate the basic reproduction number from knowledge of a pathogen's life cycle and its interactions with the host plant [11]. They developed a system of linear difference equations and rearranged the dominant eigenvalue to find $R_0$.A fraction $\eta$ of infected spores are deposited in location 1, while a fraction 1-$\eta$ are deposited in location 2. This yield:

$$R_0 = \eta(\gamma_1\alpha_1\tau_1\rho H) + (1-\eta)(\gamma_2\alpha_2\tau_2\rho H) \qquad (3)$$

wherein the first term indicates the number of spores that germinate successfully in location 1, and the second term represents the number of spores that germinate successfully in location 2. $\eta$, is the probability that a deposited spore on location i will germinate, $\alpha$1 is the number of spores produced per time unit on location I $\tau$ is the infectious period of a spore-producing lesion on location I $\rho$ is the probability that a spore is deposited on a susceptible site, and H is the density of susceptible sites in a host population. They calculated two independent values for $R_0$ and underlined its nonuniqueness in a separate box describing the hazards of estimating the fundamental reproductive ratio from nonlinear models. However, they were unable to determine the proper value of $R_0$. Although nonlinear differential equations are essential tools for understanding epidemics, they should not serve as the sole foundation for determining $R_0$, conclude the authors.

Gaff et al., modelled Rift Valley fever, a mosquito-borne sickness that affects both humans and animals and is now found exclusively in underdeveloped countries but has the potential to spread to the western world [12]. The model assumed that illness may spread both horizontally and vertically. Using the next-generation matrix approach, the basic reproductive number was determined as follows: $R_0$=$R_{0,v}$ + $R_{0,H}$, where $R_{0,v}$ is the basic reproductive ratio for vertical transmission and $R_{0,H}$ is the basic reproductive ratio for horizontal transmission. Their investigation revealed that $R_0$=1.19, with a range from 0.037 to 3.743.

Jones (2007) described the next-generation matrix technique for determining the $R_0$ using an obvious approach: assuming a system has numerous distinct categories of infected people. Then, the next generation matrix may be described as the square matrix textbfG, where the *i*, *j*th element of Gis the estimated number of secondary infections of type *i* generated by a single infected person of type j, assuming the whole susceptible population of type *i*. Therefore, each entry in the matrix **G** represents a production number. The spectral radius of **G**, which is the dominating eigenvalue of **G**, may then be used to get the fundamental reproduction number $R_0$. The generation matrix was obtained as:

$$\mathbf{G} = \begin{bmatrix} a & b \\ c & d \end{bmatrix} \qquad (4)$$

and the eigenvalues of **G** is given as:

$$\lambda_{\pm} = \frac{T}{2} \pm \sqrt{\left(\frac{T}{2}\right)^2 - (D)} \qquad (5)$$

where $T$=$a$+$d$ represents the trace of the matrix G and D = $ad$-$bc$ represents the matrix's determinant. Consider the introduction of a sexually transmitted illness into a purely heterosexual community. In a totally susceptible population, $f$ is the anticipated number of infected women, and $m$ is the expected number of infected males, given interaction with a single diseased member of the opposite sex. The subsequent generation matrix appears as follows:

$$\mathbf{G} = \begin{bmatrix} 0 & f \\ m & 0 \end{bmatrix} \qquad (6)$$

and $R_0$ would thus be $\sqrt{mf}$.

For models with many strains, the basic reproduction number is often the greater of the reproduction numbers for each strain individually. The capacity of one strain to invade and outcompete another has a threshold comparable to the basic reproduction number; however, many of these models also include many endemic equilibria. The n-strain SIR model developed by Andreasen [13]. was characterised by the following set of equations in combination with beginning conditions that were not negative:

$$\begin{aligned}
\frac{ds}{dt} &= \Pi - \mu S - \beta_1(I_2 + I_{12})S - \beta_1(I_1 + I_{21})S \\
\frac{dI_1}{dt} &= \beta_1(I_1 + I_{21})S - (\mu + \gamma_1)I_1 \\
\frac{dI_2}{dt} &= \beta_1(I_2 + I_{12})S - (\mu + \gamma_2)I_2 \\
\frac{dS_1}{dt} &= \gamma_1 I_1 - \beta_2\alpha_1(I_2 + I_{12})S_1 - \mu S_1 \\
\frac{dS_2}{dt} &= \gamma_2 I_2 - \beta_1\alpha_2(I_1 + I_{21})S_2 - \mu S_2 \\
\frac{dI_{21}}{dt} &= \beta_1\alpha_2(I_1 + I_{21})S_2 - (\mu + \gamma_1)I_{21} \\
\frac{dI_{12}}{dt} &= \beta_2\alpha_1(I_1 + I_{21})S_1 - (\mu + \gamma_2)I_{12}
\end{aligned} \qquad (7)$$

Strain one infects naive individuals (S) at a rate of $\beta_1$ ($I_1$+$I_{21}$)$S$ while strain two infects at a rate of $\beta_2$ ($I_2$+$I_{12}$)$S$. Individuals in compartment $S_1$ have recovered from an infection with strain one at a rate of $\gamma_1$, with complete immunity to reinfection with strain one and partial immunity to infection with strain two, as modelled by the factor $\alpha_1$. They enter compartment $I_{12}$ upon infection with strain two, which happens at a rate of $\alpha_1\beta_2$ ($I_2$+$I_{12}$)$S_1$. Consequently, $I_{12}$ represents the number of persons who are now infected with strain two and have previously been infected with strain one. There are four equilibria in the model. Linearizing the disease-free equilibrium model equations, S = $S_o$=$\Pi$/$mu$, $I_1$=$S_1$= $I_2$=$S_2$= $I_{21}$= $I_{12}$=0, yields the following formulations for F and V:

$$F = \begin{pmatrix} \beta_1 S_o & 0 & \beta_1 S_o & 0 \\ 0 & \beta_2 S_o & 0 & \beta_2 S_o \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} \mu + \gamma_1 & 0 & 0 & 0 \\ 0 & \mu + \gamma_2 & 0 & 0 \\ 0 & 0 & \mu + \gamma_1 & 0 \\ 0 & 0 & 0 & \mu + \gamma_2 \end{pmatrix}$$

The next generation matrix, $G=FV^{-1}$, and the Jacobian matrix, $(FV^{-1})$, are reducible. The equations for the infected subpopulations decouple near the disease-free equilibrium, and G has two positive eigenvalues corresponding to the reproduction numbers of each strain.

$$R_1 = \frac{\beta_1 S_0}{\mu + \gamma_i} \tag{8}$$

where $i = 1, 2$ There is also a reproduction number associated with the strain one equilibrium, $S = \overline{S}, I_1 = \overline{I}_1, S_1 = \overline{S}_1, I_2 = S_2 = I_{21} = I_{12} = 0$. The basic reproduction number for the two strains was found to be

$$R_0 = \frac{R_2}{R_1} + \frac{\alpha_1\gamma_1 R_2}{\mu + \gamma_1}\left(1 - \frac{1}{R_1}\right) \tag{9}$$

Ochwach developed host-pest interaction model and determined the basic offspring number of false codling moth (FCM) [1]. In their study, considered FCM compartments that are in charge of offspring reproduction and classify them as infectious and non-infectious classes, they developed a system of differential equations:

$$\begin{aligned}
\frac{dL_f(t)}{dt} &= \lambda_1 E_f(t) + \frac{a\xi S_h(t) L_f(t)}{m + S_h(t)} - (\lambda_2 + \tau_2\omega_2) L_f(t)\\
\frac{dP_f(t)}{dt} &= \lambda_2 L_f(t) - (\lambda_3 + \tau_3\omega_3) P_f(t)\\
\frac{dF_f(t)}{dt} &= \kappa\lambda_3 P_f(t) + \delta_1 F_{ff}(t) - [\lambda_4 + \tau_4\omega_4] F_f(t)\\
\frac{dM_f(t)}{dt} &= (1-\kappa)\lambda_3 P_f(t) - \left[\left(\frac{F_P}{F_f + F_p}\right) + \tau_5\omega_5\right] M_f(t)\\
\frac{dF_{ff}(t)}{dt} &= \lambda_4 F_f(t) - (\delta_1 + \tau_6\omega_6(t)) F_{ff}(t)\\
\frac{dE_f(t)}{dt} &= rF_{ff}(t)\left(1 - \frac{E_f(t)}{A}\right)\phi S_h(t) - (\lambda_1 + \tau_1\omega_1) E_f(t)\\
\frac{dF_p(t)}{dt} &= v - \mu F_p(t)
\end{aligned} \tag{10}$$

Let $F_i(y)$ be the recruitment rate of new individuals in compartment i, $V_i^-(y)$ the transfer of individuals out of the compartment i and $V_i^+(y)$ the transfer of individuals into the compartment

$i.\ \frac{dy}{dt} = \mathcal{F}_i(y) - \mathcal{V}_i(y)$.Where $i = 1, ....6$ and $V_i(y) = V^-_i(y) - V^+_i(y)$.

To obtain the next generation operator, They computed the Jacobian Matrices of $F_i$ and $V_i$ and solve it at the pest-free equilibrium (PFE). Consequently, the basic offspring number of their system model was obtained by determining the spectral radius of the matrix $FV^{-1}$ as:

$$\mathcal{R}_0 = \frac{a\xi K_h(\alpha - \mu_1)}{(m + K_h(\alpha - \mu_1))(\lambda_2 + \tau_2\omega_2)} \tag{11}$$

Feng and Velasco-Hern´andez developed a simple vector-host model couples a simple SIS model for the hosts with an SI model for the vectors [14]. Susceptible hosts ($S_h$) become infectious hosts ($I_h$) at a rate $\beta_h S_h I_v$ through contact with infected vectors ($I_v$). Similarly, susceptible vectors ($S_v$) become infectious vectors ($I_h$) at a rate $\beta_v S_v I_h$ by contacts with infected hosts. The model is given by the following equations together with nonnegative initial conditions

$$\begin{aligned}
\frac{dI_h}{dt} &= \beta_h S_h I_v - (\mu_h + \gamma) I_h\\
\frac{dI_v}{dt} &= \beta_v S_v I_h - \mu_v I_v\\
\frac{dS_h}{dt} &= \Pi_h - \mu_h S_h - \beta_h S_h I_v + \gamma I_h\\
\frac{dS_h}{dt} &= \Pi_v - \mu_v S_v - \beta_v S_v I_h
\end{aligned} \tag{12}$$

where $\mu_h$ and $\mu_v$ represent removal rates and $\Pi_h$ and $\Pi_v$ recruitment rates. The parameter γ is the recovery rate for infected hosts. Vectors are assumed to remain infected for life. This simple model forms the core of many vector-host models. The two disease compartments are $I_h$ and $I_v$. The disease-free equilibrium has a host and vector populations of $S_{ho} = \Pi_h/\mu_h$ and $Svo = \Pi v/\mu v$ respectively. The value of F and V was found to be

$F = \begin{pmatrix} 0 & \beta_h S_{h_0} \\ \beta_v S_{v0} & 0 \end{pmatrix}$, and $V = \begin{pmatrix} \mu_h + \gamma & 0 \\ 0 & \mu_v \end{pmatrix}$ The next generation matrix was found to $G = \begin{pmatrix} 0 & \frac{\beta_h S_{h0}}{\mu_v} \\ \frac{\beta_v S_{v0}}{\mu_h + \gamma} & 0 \end{pmatrix}$ The basic reproduction number was found to be

$$R_0 = \sqrt{\frac{\beta_h S_{h0}\beta_v S_{v0}}{(\mu_h + \gamma)\mu_v}} \tag{13}$$

## Calculating $R_0$ using Threshold Criteria

### The Jacobian Method

The predictive threshold parameter was discovered using the Jacobian technique by Diekmann and Heesterbeek in 2005. The Routh- Hurwitz stability conditions, along with the characteristic polynomials, are used to derive the predictive parameter from the requirement that all of the Jacobian's eigenvalues have negative real parts. The Jacobian method is widely used in the majority of systems of ordinary differential equations. A parameter that reflects the stability of the disease-free equilibrium can be derived using the Jacobian approach. The predictive parameter derived using this technique could not, however, represent a medically significant value for R_0. They proposed that the threshold parameter should not be referred to as the basic reproductive number or abbreviated as R_0 if it does not have the same biological interpretation as the dominating eigenvalue of the next-generation matrix.

A nonlinear system of differential equations was linearized by Jing Li using a Jacobian matrix [7]. If the linear system is hyperbolic, that is, if no eigenvalues have zero real component, it will have the same stability qualities as the nonlinear system around the disease-free equilibrium. In specifically, the equilibrium is stable if all of the eigenvalues have a negative real part, whereas the equilibrium is unstable if there is an eigenvalue with a positive real part. As a result, a threshold ($\lambda_{max}=0$) is determined by the Jacobian matrix's biggest eigenvalue, (or the largest real part if the eigenvalues are complex). However, this calls for solving an nth-order polynomial, which may be impossible for a system of n differential equations. The threshold $R_{0,J}=1$ is created by rearranging the requirement $lambda_{max}=0$, although this is not a special method, and it does not always result in the typical amount of secondary infections.

### Existence of the Endemic Equilibrium

The basic reproduction number as a threshold criterion can also be derived from a condition based on parameter values such that, when the condition holds, the endemic equilibrium exists, but only when the condition is false, the disease-free equilibrium exists, according to Hofferman et al (2005). This phenomenon, known technically as the transcritical bifurcation, causes the condition to change from being false to true at parameter values that result in $R_0=1$. Virus outbreaks are transient but persistent throughout the patient's lifespan, with the virus dormant at other times.

This makes determining $R_0=1$ using other techniques challenging.

**Estimating $R_0$ from the Initial rate of growth of the Epidemic**

Dietz [9] derived relationships between the initial growth of disease and $R_0$ of the AIDS epidemic from a very simple model which yields a value of $R_0$ of 19.7 for the San Francisco gay community based on the formula:

$$R_0 = 1 + \frac{Dln2}{\tau_d} \tag{14}$$

Here D is the duration of the infectious period and $\tau_d$ is the initial doubling time. In order to create a link between the initial rate of growth and $R_0$, which must now be computed as the eigenvalue of a specific matrix, taking into account the heterogeneity in the contact rates and variable infectivity.

**Constant Term of the Characteristic Polynomial Method**

The characteristic polynomials constant term, $\lambda_{max} = 0$, will be zero. Contrary to popular belief, the polynomial can have both zero and positive roots. More generally, the Routh-Hurwitz condition permits the coefficients to take on various signs, subject to specific limits, although having all positive nonconstant coefficients is a sufficient requirement. Another need is that $a_j$>0 with the restriction $a_0$=0. Although confirming that a_0=0 necessarily corresponds to the biggest eigenvalue might be challenging for some models, using this technique is substantially simpler than determining the largest eigenvalue. Similar to the previous example, the procedure of rearranging $a_0$=0 to generate $R_{0,C}$=1 is not unique and does not always result in the usual amount of secondary infections.

A mathematical model of the COVID-19 epidemic with multiple populations and control strategies was put forth by Sun [15]. It included groups for those who were susceptible (S), asymptomatic and undiagnosed (A), symptomatic and diagnosed (AD), symptomatic and infected (I), recovered (R), and dead (D):

$$\begin{aligned}
\frac{ds}{dt} &= -r_1 S(t)A(t) - r_2 S(t)AD(t) - r_3 S(t)I(t) \\
\frac{dA}{dt} &= r_1 S(t)A(t) + r_2 S(t)AD(t) + r_3 S(t)I(t) - aA(t) - bA(t) - cA(t) \\
\frac{dA_D}{dt} &= aA(t) + dA_D(t) + gA_D(t) \\
\frac{dI}{dt} &= bA(t) + dA_D(t) - (f_1 + f_2)I(t) \\
\frac{dR}{dt} &= cA(t) + gA_D(t) + f_1 I(t) \\
\frac{dR}{dt} &= f_2 I(t).
\end{aligned} \tag{15}$$

Based on equation, the equilibrium ($S$*, 0, 0, 0, $R$*,$D$*) was calculated firstly, and the Jacobian matrix around the equilibrium.

$$\mathcal{J} = \begin{bmatrix}
\lambda + r_1 A^* + r_2 A_D^* + r_3 I^* & r_1 S^* & r_2 S^* & r_3 S^* & 0 & 0 \\
r_1 A_D^* + r_2 A_D^* - r_3 I^* & \lambda - r_1 S^* + a + b + c & -r_2 S^* & -r_3 S^* & 0 & 0 \\
0 & -a & \lambda + d + g & 0 & 0 & 0 \\
0 & -b & -d & \lambda + f_1 + f_2 & 0 & 0 \\
0 & -c & -g & -f_1 & \lambda & 0 \\
0 & 0 & 0 & -f_2 & 0 & \lambda
\end{bmatrix} \tag{16}$$

The characteristics polynomial was found to be $p(\lambda)=D(\lambda)$-$S$* $N(\lambda)$. Where $D(\lambda)=(\lambda+f_1+f_2)(\lambda+a+b+c)(\lambda+d+g)$ and $N(\lambda)=r_1\ (\lambda+f_1+f_2)(\lambda+d+g)+ar_2\ (\lambda+f_1+f_2)+br_3\ (\lambda+d+g)$. The basic reproduction number was calculated based on Hurwitz criterion Therefore, the basic reproduction number is:

$$R_0 = \frac{r_1(f_1+f_2)(d+g) + adr_3 + ar_2(f_1+f_2) + br_3(d+g)}{(f_1+f_2)(a+b+c)(d+g)}$$

The Jacobian matrix was created by them. The fundamental reproduction rate gives an idea of how much a virus may spread. The basic reproduction number determines how well a virus may spread; the bigger the basic reproduction number, the more effective the transmission capacity. Consequently, it is imperative to do research on basic reproduction numbers.

**Estimating $R_0$ from Epidemiological data**

**Average age at infection**

Cross-sectional population surveys are a common data source used in the epidemiology of infectious illnesses to evaluate the age-specific prevalence of antibodies with reference to a certain illness suggesting past infection. Therefore, one can only determine if antibodies are present or not for a certain age of a person to determine whether the age of infection is lower or greater than the current age. This translates to the fact that one only has censored data in a statistical sense. These age-specific prevalence statistics show a typical increase known as a catalytic climb [9]. Dietz [9] research found that the following relationships exist between the basic reproduction number and this hazard rate:

$$\lambda = \mu(R_0 - 1) \tag{17}$$

where λ denotes the intensity of the illness and μ the death rate of the population. The death rate is assumed to be constant in this model, and the force of infection is assumed to be age-independent. The following equation is produced when the average A age at infection is calculated:

$$A = (\lambda + \mu)^{-1} \tag{18}$$

The force of infection formula yields the following simple expression for $R_0$ when the life expectancy of a human host is represented as $e_o = \mu^{-1}$:

$$R_0 = e_o / A \tag{19}$$

This means that the ratio of life expectancy to average age at infection may be used to estimate the fundamental reproduction number $R_0$.

Another similar method is to estimate $R_0$ as $L/A$, where L is the mean lifetime and A is the mean age of illness onset a method provided by Hethcote [16]. This method is based on the endemic equilibrium Dietz [9]. In this method, it is assumed that there is homogeneous mixing throughout age groups, that all individuals are born susceptible, that once they contract the illness they are no longer susceptible, and that the population is at the endemic equilibrium. The application of this technique is obvious because both L and A are easily measurable, despite the fact that both assumptions might never be fully met in an actual context.

**Age-Independent Prevalence Data**

The initial estimate of $R_0$, or rather $R_0$ as mentioned above, was derived from statistics on equilibrium prevalence by Macdonald in 1955 [17]. The single controlling component in Macdonald's model was the mosquito's ability to avoid super infections, meaning that only vulnerable mosquitoes could get the disease. He permitted superinfections in humans, and the mosquito's risk of infection was related to the mean number of infections per human host rather than the prevalence of human infections. The Macdonald's formula for $R_0$ in the current study is written as follows:

$$R_0 = [1 - y_2 e^{(}\mu_2 I_2)]^{-1} \quad (20)$$

where $\mu_2$ and $I_2$ have the same meanings as earlier and $y_2$ is the equilibrium prevalence of mosquitoes carrying sporozoites in their salivary glands or the percentage of infectious mosquitoes. He discovered a value of $R_0^2$ of 1.15 using Tanganyika data, which is based on a survival probability for the extrinsic cycle of 0.39 and a fraction of sporozoite-positive mosquitoes of 5

**Final Size of an Epidemic**

The basic reproduction number for closed populations, where infection results in either immunity or death, was computed by Diekmann, Houben, and Hethcote (2000) [16,18-19]. In this situation, the sensitive population can only get smaller, and the R_0 may be calculated as:

$$R_0 = \frac{inS_\infty}{S^\infty - 1} \quad (21)$$

If the disease itself does not impede the contact process or if contact intensity is inversely correlated with population density, this estimate is valid.

Smith suggested calculating $R_0$ by the inverse of the fraction of susceptibles remaining after an epidemic had ended [20]. He uses urban yellow fever outbreaks as an illustration, which ended after 48–65% of the population had immunity. As a result, $R_0$ would be estimated to be between 2 and 3. The fraction of susceptibles after an epidemic has ended and $R_0$ may be calculated using the following straightforward formula, according to the theory of the deterministic global epidemic:

$$R_0 = (1 - u_\infty)^{-1} lnu_\infty^{-1} \quad (22)$$

Accordingly, the estimates of $R_0$ for the values given by Smith would range from 1.4 to 1.6, meaning that immunising around 38 percent of the population would have been sufficient to stop the epidemic [20]. However, it should be noted that the calculation stated above makes the assumption that the whole population was vulnerable at the start of the pandemic.

**Using Intrinsic Growth Rate**

In their work, Nowak *et al*. (1997) and Lloyd (2001a) calculated $R_0$ using the intrinsic growth rate of the infected population, commonly denoted as $r_0$. The typical connection between $R_0$ and $r_0$ derived from the classic models of viral dynamics is as follows:

$$R_0 = 1 + \frac{r_0(r_0 + a + \nu)}{au} \quad (23)$$

Where ν is the clearance rate of the virions and a is the mortality rate of the infected cells. In the event when $r_0$+$a$<<$v$, the relation approaches:

$$R_0 = 1 + \frac{r_0}{a} \quad (24)$$

Since $r_0$ can be easily determined from viral load data for in-host models and from incidence data in epidemiology, this technique is advantageous. Finally, the intrinsic growth rate of the infected population may be used to calculate $R_0$. This growth rate, which is sometimes designated as $R_0$, is the rate at which an infected population, I, expands such that $dI/dtZr_0 I$. Since there is an implied definition of $r_0$, utilising $R_0$ is seldom elegant from a modelling standpoint. However, using incidence statistics, $r_0$ may frequently be roughly predicted from the infection class's growth rate, and $R_0$ can then be calculated from r0. There might be a number of issues with this strategy: The measure of $r_0$ can be obscured by random fluctuations in the early stages of an epidemic, and reporting errors are extremely likely to skew incidence statistics. Finally, the link between $R_0$ and $r_0$ is very model dependent, even when $r_0$ can be observed with some degree of certainty.

**Calculation of $R_0$ for discrete time systems**

According to Pauline van den Driessche, care must be given while creating these discrete temporal models to prevent the population of each compartment from declining [21]. Discrete-time epidemic models may also be employed using the next-generation matrix method. In order to briefly explain this, let's assume that the epidemic model's equations are provided by:

$$x(t+1) = G(x(t)) \quad (25)$$

where $x(t)$ represents the population states at time t, with the states $x_1,\ldots,xm$ being infected and the rest being unaffected. If a single DFE exists, then linearizing the equations describing the infected state around this DFE results in $y(t+1)=(F+T)y(t)$, where F and T are nonnegative matrices evaluated at the DFE. Here, F is the transition matrix with ρ(T)<1 and F is the matrix of new infections that endure the time interval.

The matrix $Q=F(I\delta-T)$ is the next-generation matrix for this discrete system and the basic reproduction number. Allen and van den Driessche give details of the assumptions and show that the DFE is locally asymptotically stable if $R_0$<1 but unstable if $R_0$>1 [22]. The assumed order of events within each time step is important since different assumptions can yield different $R_0$ values (van den Driessche, and Wonham, 2006).

Jiru performed a mathematical analysis to explain the effects of isolating infected populations on the dynamics of an epidemic of diarrhoea [23]. To model the effects of isolating infected population in the dynamics of diarrhoea epidemic, a system of non-linear differential equations was used to determine a specific threshold value as the fundamental reproductive number $R_0$ that represents the epidemic indicator obtained from the Eigenvalue of the next-generation matrix.

$$R_0 = \frac{\alpha\beta\theta\Lambda}{\mu(\alpha+\mu)(\theta+\mu+\delta)(\mu+\delta+\omega)} \quad (26)$$

where Human recruitment rate Λ Effective contact rate $\beta$ Treatment rates for contagious people are in $\omega$ Natural mortality rate for the human population is mu $\alpha$ The prevalence of diarrheal illness in humans Isolation rate from the diseased population of humans, $\theta$, $\delta$ Virus prevalence. The study demonstrated that the fundamental reproduction ratio, $R_0$, controls the stability of the disease-free and endemic equilibrium points.

**$R_0$ in a periodic environment**

Many methods of calculating $R_0$ assumes that the environmental factors are constant, but in reality, environmental factors such as humidity and temperature are constantly changing. The models then become non-autonomous dynamical systems. In line with this, many authors have extended the definition of $R_0$ to include the periodic environmental changes. Wang and Zhao (2017) proposed a time-delay lyme disease model that takes climate into account. In

their study, $R_0$ was calculated from a disease-free periodic solution. Inaba also introduced a new definition of in a heterogeneous environment" based on the generation evolution operator as a generalization of previous definitions [24].

**Calculating $R_0$ for Stochastic Models**

When stochastic influences, such as those unavoidably present in nature, are accounted for, the $R_0$=1 threshold may be disrupted. This consists of assumptions on the distribution of transition times and variances in specific parameters. A stochastic epidemic model may be seen as a discrete spatial, continuous time Markov chain with exponential distribution parameters for all rates.

In a stochastic context, it is evident that $R_0$ is a dimensionless number and not a dimensionless quantity. When N→∞ is sufficiently big, the memory-less characteristic of exponential distributions allows one to approximate the epidemic process with a Galton-Watson process in which one infectious person may create zero or two people at each generation. The number of infected individuals induced by the first infected individual is a geometric random variable with a mean of $R_0$.

$$P(X = k) = (1 - p)^k p \tag{27}$$

where $k$ = 0,1,2…, and $R_0$=(1-$p$)$p$. In terms of $R_0$, the probability mass function of the number of infected can be written a

$$P(X = k) = \left(\frac{R_0}{1 + R_0}\right)^k (1 + R_0)^{-1} \tag{28}$$

where $k$ = 0, 1, 2 . . .. The probability of eventual extinction, $P_E$, can be found using first step analysis

$$P_E = p + (1 - p)P_E^2 \tag{29}$$

The importance of calculating $R_0$ in a stochastic epidemic model is then that it can be used to approximate the probability of extinction of an epidemic when N→∞, by approximating the epidemic process with a branching process.

Allen (2010) provided an outstanding introduction to stochastic epidemic models expressed as discrete-time Markov chains, continuous-time Markov chains, and stochastic differential equations. Several numerical examples of stochastic sample pathways and their related deterministic solutions are shown in the paper. Allen (2010) demonstrated that stochastic sample routes may converge to a disease-free state, while the comparable deterministic solution converges to an endemic equilibrium. In a vaccination campaign, stochasticity may result in the eradication of a disease prior to the attainment of herd immunity to vaccination. When stochastic effects, such as those present in nature, are incorporated, the $R_0$=1 threshold may be perturbed.

Heffernan and Wahl (2006) generated better estimates of $R_0$ for clinical or epidemiological practitioners who have access to information on the dispersion of transition periods. In their work, they developed the ϕ correction factor, which is the ratio of $R_0$ when the lives are not exponentially distributed to $R_0$ computed assuming exponential lifetimes. They found that when two or more processes "compete" to terminate the infectious period and their mean times are of the same order of magnitude, the effective infectious period, and hence $R_0$, is sensitive not only to the distribution means but also to the distribution shapes. Methods for determining $R_0$ from incidence or clinical data often assume that all underlying processes follow an exponential distribution, as mentioned above (Heffernan and Wahl, 2006). They further, found a more precise estimates for R_0 under the assumption that one or both of the contending processes are not exponentially distributed. They were able to compute the limiting values of ϕ and use them to evaluate R_0's sensitivity to the dispersion of the underlying distributions. Incorporating the mobility of hosts, transmission within groups, recovery after infection, and recruitment of new susceptibles.

Keeling and Rohani (2008) give three methods for approximating stochasticity in disease transmission and recovery. The likelihood of an outbreak is determined by the value of $R_0$ as well as the initial number of infected individuals, i0. If the population size is large, this probability is close to zero if $R_0 \leq 1$ and $1 - (\frac{1}{R_0})i_0$ if $R_0 > 1$.

This estimate only applies to the stochastic SIS and SIR models for a finite time range, because the probability of an outbreak is zero as $t \rightarrow infty$. Consequently, one distinction between stochastic and deterministic models is that stochastic sample routes may converge to a disease-free state whereas the equivalent deterministic solution converges to an endemic equilibrium. So, in a vaccination campaign, randomness might cause a disease to disappear before the vaccination rate required for herd immunity is obtanined.

Hasan et al. (2022) provided a new technique to estimate the time-varying effective reproduction number of the novel coronavirus illness (COVID-19) based on a discrete-time stochastic augmented compartmental model that represents the transmission of the virus. They considered a compartmental SIRD model composed of the following nonlinear first-order differential equations:

$$\begin{aligned}
\frac{S(t)}{dt} &= -\frac{\beta I(t)S(t)}{N} \\
\frac{I(t)}{dt} &= \frac{\beta I(t)S(t)}{N} - (\gamma + \kappa)I(t) \\
\frac{R(t)}{dt} &= \gamma I(t) \\
\frac{D(t)}{dt} &= \kappa I(t)
\end{aligned} \tag{30}$$

where S, I, R, and D denote the number of susceptible cases, the number of active cases, the number of recovered cases, and the number of deceased cases, respectively. N is the total number of population, $\beta$ is the average number of contacts per person per time, while $\gamma$ and $\kappa$ are the recovery and death rate. Remark that the value of $\beta$ is time-varying due to intervention, $\beta = \beta(t)$. To use the model, we require information on the average infectious time $T_i$ and the Case Fatality Rate (CFR), so that $\gamma = \frac{1-CFR}{T_i}$, $\kappa = \frac{CFR}{T_i}$. For COVID-19, they took $T_i = 9$ as the infectious period on average lasts for 9 days (7–11 days with 95% CI)15, while the CFR is assumed around 1%. The time-varying effective reproduction number is then given by: $\mathcal{R}_t(t) = \frac{S(t)}{t}(\frac{\beta(t)}{\gamma+\kappa}) \approx \frac{\beta(t)}{\gamma+\kappa}$. The approximation is under the assumption that government intervention is taken at an early stage so that the susceptible is relatively the same over time as the total population. This is the case, especially for emerging diseases. We modify the SIRD model by augmenting the following two equations into the system: $\frac{dE(t)}{dt} = (\gamma + \kappa)I(t) - E(t), \mathcal{R}_t(t) = 0$.

The equation takes into account the daily number of new reported

cases E, while the latter one says that the effective reproduction number $R_t$ is assumed to be a piece-wise constant function with jump every 1 day time interval. Discretizing the model using the forward Euler method, they obtain the following discrete-time augmented SIRD model:

$$\begin{aligned} S(k+1) &= \left(1-\tfrac{(\gamma+\kappa)\Delta t}{N}\mathcal{R}_t(k)I(k)\right)S(k) \\ I(k+1) &= (1-(\gamma+\kappa)\Delta t)I(k)+\tfrac{(\gamma+\kappa)\Delta t}{N}\mathcal{R}_t(k)I(k)S(k) \\ R(k+1) &= R(k)+\kappa\Delta t I(k) \\ D(k+1) &= D(k)+\kappa\Delta t I(k) \\ E(k+1) &= (\gamma+\kappa)\Delta t)I(k)+(1-\Delta t)E(k) \\ \mathcal{R}_t(k+1) &= \mathcal{R}_t \end{aligned} \quad (31)$$

The technique generates an updated estimate of $R_t$ based on newly reported examples. Due to their low frequency, the reported data may be interpolated using a technique such as a modified Akima cubic Hermite interpolation in order to accommodate the time step Δt. In our simulation, the time step Δt is selected to be 0.01 seconds, which corresponds to 100 discretizations of time every day. The confidence range of our predicted $R_t$ is calculated by calculating the reproduction number for various values of the infectious period Ti within a certain interval. Using the Extended Kalman Filter (EKF) to estimate the reported state variables (active and removed cases) and a low pass filter based on a rational transfer function to remove short-term fluctuations of the reported cases, a two-stage estimation technique is employed with the assumption that case uncertainties are Gaussian. As advised by WHO, they used the model to COVID-19 cases in Scandinavian nations with positive rates less than 5

### $R_0$ in Spatial Contexts

When $R_0$ is viewed in a spatial context, a number of its characteristics break down. Depending on the nature of spatial transmission, illnesses with $R_0$>1 may not be able to survive if $R_0$>1. As a result of the geographical dependence of several illnesses, the usefulness of $R_0$ is significantly diminished. As $R_0$ climbs beyond 1, the likelihood of illness infiltrating the first infected host group rises; however, additional criteria are required to determine the probability of the disease spreading to other groups.

### Networks Models

The derivation of $R_0$ has been extended to the scenario when contact network information is provided. In this situation, the derivation is often limited to the case of normal networks, in which all nodes have the same degree. Occasionally, individuals utilise definitions of $R_0$ that are not identical to the original. In actuality, the assumption that two persons interact at the same pace across time does not hold true. For instance, interaction is more likely to occur when the majority of individuals are awake. This is one reason for the growing interest in temporal networks as a depiction of the interactions underpinning the transmission of epidemics, which emphasise the time dependency of networks. A second factor is the rising availability of data sets of temporal networks, which are often lists of the anonymized id numbers of two persons and the times when they have interacted. The research on temporal networks has concentrated on spreading mechanisms and how the structure affects them. In this context, structure refers to the manner in which the network varies from a random temporal network. According to studies of epidemic models on temporal networks, a large distribution of interevent periods, for instance, inhibits the spread.

Green et al., connected deterministic meanfield models to network models, taking into account how contact rate and infectiousness fluctuate over time [26]. The predicted number of secondary infections at infection age u for a node with precisely

m connections is provided by $R(m,u)=m(1-e^{\beta u/k})$, where $\beta$ is the transmissibility and $k$ is the average number of connections per node. When the rate of infectious contact is independent of k, this model applies. If there is a constant rate of generation of new cases, the expected number of secondary infections during an infectious period of length u is given implicitly by

$R(m,u)=\int_0^{\mu}(mR)C_{IS}(t)\psi(t)dt$,, where $C_{IS}(t)$ represents the contact per susceptible neighbour and $\psi(t)$ represents the infectiousness at time $t$ after infection.

Kao demonstrated that new infections may develop toward a lower $R_0$, even if pathogen extinction occurs [27]. Because the existence of exploitable heterogeneities, such as a large variation in the number of potentially infected contacts, raises $R_0$, pathogens that can exploit heterogeneities in the contact structure have a competitive advantage over those that cannot. The exploitation of heterogeneities leads in a more faster depletion of an infected host's potentially vulnerable neighbourhood. Despite the fact that the low- $R_0$ strategy is never evolutionary stable, invading strains with greater $R_0$ will converge to it if they are not sufficiently distinct from the resident strain. In contrary to the commonly held idea that the development of new diseases is driven by the maximisation of $R_0$, this is not the case. In a randomly mixed epidemiological network, $R_0$ may be approximated by

$R_0=l_{in}l_{out}/l_{out}$, where $l_in$ and $l_{out}$ indicate, respectively, the number of inward and outward "really infectious" linkages per node, and the angle brackets reflect the predicted value of the relevant quantity.

Meyers demonstrated that in a contact network architecture,

$R_0=T(\frac{(k^2)-(k)}{(k)})$, where T is the mean probability of transmission between individuals and $k$ and $k^2$ are the mean degree and mean square degree of the network, respectively [28]. Here, $R_0$ is directly dependent on the network's topology. Therefore, the transmissiodynamics of a single disease may vary greatly depending on the community through which it travels. If two networks have the same mean degree, k, then the network with the greater variation in degree, $(k^2)-(k)$, will be more susceptible to disease transmission. In compartment models, it is believed that infected hosts have potentially disease-causing encounters with random population members according to a Poisson process that generates an average contact rate of β per unit time. Compartmental models' mass-action assumption is equivalent to assuming the underlying contact patterns form a random graph with a Poisson degree distribution. Estimates of $R_0$ based on a mass-action model may thus be incorrect for populations with non-Poisson interaction patterns, and may notably underestimate the actual development rate of the illness in highly diverse networks.

Schimit and Monteiro demonstrated that in an individual-level model, $R_0$ cannot be uniquely inferred from transitory group behaviour characteristics [29]. The value of $R_0$ can be established clearly from the asymptotically stable stationary concentrations, but this requires the system to enter its permanent regime, which

is impractical in reality. Networks with unique values of clustering coefficients and average shortest route length may have the same value of $R_0$. This conclusion may influence the assessment of the efficacy of various measures adopted to control a disease. Due to the fact that different topological property values might give the same value of $R_0$ in a model that takes into account the spatial structure of the contact network, it is challenging to assess the contribution of each control measure. This is because there is no one-to-one correlation between $R_0$ and the topological features of the contact network.

**Metapopulation Models**

Metapopulation is a collection of populations of the same species that interact. Cross et al. (2005) demonstrated that when $R_0$ is derived from data gathered from simulated epidemics that mirror epidemiological contact-tracing data, $R_0$ may be much bigger than one without causing a pandemic. In populations with social or geographical structure, a chronic illness with the same $R_0$ is more likely to invade than an acute disease with the same $R_0$ because it lingers longer within each group and permits more host migration across groups. Under conditions where the rate of host population turnover was negligible in comparison to the rate of disease processes of infection and recovery, they demonstrated that $R_0$>11 was insufficient for disease invasion when the product of the average group size and the expected number of between-group movements made by each infectious individual was less than 1.

Classification tree analysis of model findings demonstrates the hierarchical structure of disease invasion in host metapopulations. First, the pathogen must travel efficiently inside a group ($R_0$ > 1), and then it must remain long enough within a group to permit migration across groups. In order to anticipate the spread of infections throughout a metapopulation, the infectious duration, group size, and recruitment of new susceptibles are as critical as the local transmission rates. Smith? et al. (2009) investigated a metapopulation model involving travel between two areas, with reproduction ratios of $R_{0,1}^{(0)}$ and $R_{0,2}^{(0)}$ for each region in the absence of travel, and $R_{0,1}^{(0)}$ and $R_{0,2}^{(0)}$ when only susceptibles travel, but not infectives [30].They demonstrated that if $R_{0,1}^{(0)} < 1$ and $R_{0,2}^{(0)} < 1$, then there are circumstances on the path of the vulnerable such that $R_0^1 > 1$ and $R_0^2 < 1$. Thus, a disease that would normally be eliminated in both zones may persist in one region if sufficient vulnerable individuals travelled between the regions. Moreover, if $R_{0,1}^{(0)} < 1$ and $R_{0,2}^{(0)} < 1$, then there exist travel circumstances under which $R_{0,1}^{(0)} < 1$ and $R_{0,2}^{(0)} < 1$, Consequently, if one area supports the illness on its own and the other does not, sufficient travel by susceptible individuals might perpetuate the sickness in both locations.

**$R_0$ from Partial Differential Equation Models**

Althaus et al., examined an age-dependent partial differential equation model of human immunodeficiency virus type 1 life cycle [31]. In their study, they showed that the basic reproduction number can given by the equation $R_0 = \frac{1}{\int_0^\infty e^{-ra} g(a) da}$, where the denominator is the Laplace transform of the generation time distribution $g(a)$ and $r$ is the growth rate. They found that estimates for $R_0$ were generally smaller than those derived from the standard model when the generation time was taken into account.

**Application of $R_0$ in the Epidemiology**

**Elimination or Eradication**

According to Dietz, the terms elimination and eradication are often used interchangeably in the epidemiology literature [9]. Both terms allude to a condition in which the infection is not present. A frequency of zero, however, may indicate a stable or unstable equilibrium. Stability refers to the consequence of an infectious case being introduced into a community. If the zero equilibrium is stable, the introduction of a single instance will produce no more than a few generations of secondary cases, resulting in a return to zero's initial predominance. This can occur either naturally, without special interventions, as a result of low local contact rates and infection probabilities per contact, or as a result of permanent interventions, such as vaccination programmes, which reduce the proportion of susceptibles to the point where $R_0X/N$ is less than one. Elimination refers to the constant predominance of zero. If, however, the zero equilibrium is unstable, the introduction of one infected case will result in a significant epidemic and perhaps an endemic state, depending on the population size and the pace of introduction of susceptibles. A time-limited intervention that allows $R_0$ to return to its initial level would result in a predominance of zero.

**Reduction of the Contact Rate**

If we consider a control programme which reduces either the duration of the infectious period by chemotherapy or the contact rate by changes in behaviour then the reproduction number $R^*$ is given by the following formula $R^* = \frac{R_0}{r_K r_D}$, where rk and rD denote the reductions for the corresponding parameters indicated in the index. For elimination or eradication $R^*$ has to be less than one [32-33]. Therefore the $r_K r_D$ has to be greater than $R_0$. This inequality clearly shows that $R_0$ can be interpreted as the minimum absolute elimination or eradication effort, if we are dealing with a homogeneous population, and a control method which effects everybody in a non selective way. This means that the minimum proportional reduction of the susceptible fraction is given by $1-R_0^{-1}$ which is a highly non-linear function of $R_0$. For $R_0 > 10$, control programmes have to be nearly perfect requiring a reduction of the parameters by more than 90%; whereas for values of $R_0$ between 1 and 2 a reduction of the parameters by less than 50% will already be successful. This non-linear relationship between the minimum proportional reduction in the transmission factors K and D, and the basic reproduction number $R_0$, is the key to understanding the puzzle that apparently the same control programme may be successful in one situation and not at all in other situations.

**Bifurcations Analysis**

Hadeler reported that multiple stable equilibria coexist when $R_0$<1, indicating a backward bifurcation [34]. When a disease is already endemic, this offers a severe difficulty, since reducing the basic reproduction number below 1 may no longer be a feasible control method; hence, other preventative and control approaches may need to be explored. Specifically, a backward bifurcation complicates the system since the behaviour is now dependent on the beginning circumstances. A backward bifurcation at $R_0 = 1$ might lead to illness persistence when $R_0 < 1$. In this situation, the sickness will continue to exist as long as $R_0 > 1$. Nevertheless, there exists a point $R_a < 1$ where the endemic equilibrium occurs for $R_a$

$< 1$ $R_0 < 1$ and a third, unstable equilibrium exists between the two stable equilibria. Consequently, an endemic illness is eliminated only if $0 < R_0 < R_a$. The result relies on beginning circumstances when $R_a < R_0 < 1$. If the illness is still in its early stages, i.e., if beginning circumstances are modest enough, then the system will approach the disease-free equilibrium and the disease will be eliminated. Nevertheless, if beginning circumstances are extreme, the system will reach endemic equilibrium and the sickness will persist. Consequently, a backward bifurcation prevents the system from moving to the disease-free equilibrium once $R_0 < 1$ is attained.

Safan et al., investigated an epidemiological model based on the hypothesis that the susceptibility after a main infection is r times the susceptibility before a primary infection [9]. They provide a technique for calculating the control effort necessary to eradicate an infection from a host population when subcritical persistence is possible. This effort may be read as a reproduction number, however it is not necessarily the fundamental reproduction number. This model displays backward bifurcations when $r > 1 + \mu/\alpha$, where $\mu$ is the death rate and *alpha* is the recovery rate. For such models, the authors proposed a technique for finding the minimal effort necessary to eliminate the virus from the endemic steady state if one focuses on control strategies that impact the constant transmission rate. Garba et al., proposed a deterministic model for the transmission dynamics of a single dengue strain by using a realistic incidence formulation and permitting dengue transmission by exposed people and vectors [35]. The model was expanded to accommodate a flawed dengue vaccine. In both models, a backward bifurcation was seen. This renders $R_0$<1 insufficient for successful dengue control in a community. However, this issue may be eliminated by substituting a mass-action formulation for the usual incidence function in the model.

Gomez-Acevedo and Li examined a mathematical model for human T-cell lymphotropic virus type I (HTLV-I) infection of $CD^{4+}$ T cells that encompasses both horizontal transmission through cell-to-cell contact and vertical transmission via mitotic division of infected T cells [36]. After error-prone viral replication, they hypothesised that a portion of infected cells would escape the immune system's onslaught. Under the physiologically plausible assumptions that α should be extremely small and the rate of mitotic division should be high, their model contains a bifurcation that predicts ongoing infection throughout a broad range of the basic reproduction $R_0$>$R_0$ ($\alpha$0), where $R_0$ ($\alpha$0)<1. As α rises, this model experiences a backward bifurcation: several stable equilibria exist for an open range of parameter values when the fundamental reproduction number is less than one.

**To Determine the Sensitivity of a Parameter**

To select the most effective control strategies, it is helpful to understand the relative significance of the many components involved for transmission [37]. Initial disease transmission is associated with $R_0$, and sensitivity predicts which characteristics have a significant influence on $R_0$. The equation: $\frac{\partial R_0}{\partial \omega}$ is the sensitivity index of $R_0$ with regard to a parameter. The elasticity index quantifies the relative change of $R_0$ with regard to $u$ It is represented by $\gamma_{omega}^{R_0}$, and defined as $\gamma_{omega}^{R_0} = \frac{\partial R_0}{\partial \omega} \times \frac{\omega}{R_0}$. For the assessment of control techniques, it is crucial not only to estimate by how much $R_0$ exceeds 1, but also to evaluate $R_0$'s sensitivity to changes in the individual factors that enter its formula. The following basic method makes this clear. However, if individual factors enter in a nonlinear fashion, then significant inferences may be derived on the relative effectiveness of various control systems. Other studies such as Chowel et al., [38-39].

**To Determine of Elasticity a Parameter**

The sign of the elasticity index indicates whether $R_0$ rises (positive sign) or lowers (negative sign) with the parameter, whilst the value of the parameter indicates its relative significance. Although feasibility and cost play a part in practical control strategy, these indices may assist control by highlighting the most crucial characteristics to target. If $R_0$ is explicitly known, then the elasticity index for each parameter may be directly calculated and assessed for a particular set of parameters. The magnitude of the elasticity indices is dependent on these potentially approximative parameter values. Latin Hypercube Sampling maximin criteria may be used to detect the robustness of $R_0$ to the parameters. Compute $R_0$ across the feasible area of a particular parameter while retaining the other parameters at their initial values as computed in Manore et al., [40].

**Limitation of $R_0$**

The majority of biologists assert that there is only one value of $R_0$ for each given model. While this may be the case, several indices demonstrate the same threshold behaviour [41]. The Next Generation approach merely ensures that $R_0$ retains its threshold character, not that it properly reflects the number of secondary infections. Suppose $R_0$=2 for the Next Generation. Because $R_0$>1, it is assured that the infection will remain in the population, but it is not guaranteed that a single infected person would spawn two secondary infections; it may be three or one thousand. Similarly, if $R_0$=0.5, it is certain that the infection will die out, but it is not always true that a single infected person would create an average of 0.5 secondary infections. Checking if the in question $R_0$ shows the threshold behaviour is not a thorough evaluation for assessing $R_0$ validity. It is simple to create a model with two indices that demonstrate the same threshold, even when one of them has nothing to do with the average number of secondary instances resulting from a single main case. Despite the fact that both indices are threshold-based, they cannot concurrently indicate the number of secondary infections caused by a single sick person. In several experiments, two models with identical solution trajectories but distinct $R_0$ values have been observed.

The use of $R_0$ is not fully problem-free. First, it is difficult to quantify using models and outbreak data. Second, the conclusion that $R_0$=1 determines an epidemic threshold is predicated on quite rudimentary assumptions. For instance, it is necessary to assume that each pair of persons has the same probability of interacting at any given moment. In reality, interaction rates vary amongst individuals, with those residing in the same city being more likely to interact than those residing in other cities [42]. Adding to the complications of $R_0$, a whole class of models is incompatible with Next Generation building. In Section 9.2, instances of this model type in which the Next Generation $R_0$ is invalid are provided. The examples are based on current and relevant research, and the assumptions that invalidate the Next Generation $R_0$ are reasonable. In Section 9.3, an example is shown in which the Next Generation $R_0$ seems to fail the threshold criteria while satisfying the mathematical theorems' prerequisites. If a disturbance of limited amplitude rather than a single infected person is introduced into the population, $R_0$ may be less than one if the illness persists in the population. The theory on $R_0$ only assures the persistence of infection under tiny disturbances and provides no information on disturbances of finite amplitude, despite the fact that an increase of a single infected person is itself a disturbance of finite amplitude.

Breban et al., claimed that in order to correlate a $R_0$ with an ODE model, a corresponding individual-level model must be constructed; only then can the $R_0$ of the individual-level model be determined clearly [43]. In these individual-level models, individuals are added to a network of who infected whom based on global or local network rules. Then, $R_0$ is determined as the upper bound of the average number of outgoing connections of persons in a node that no longer accepts new links as time approaches infinity. They demonstrated that a wide variety of $R_0$ values were consistent with a particular ODE model. Roberts identified three essential features often ascribed to $R_0$: An endemic infection can only survive if $R_0$>1, R_0 is a direct measure of the control effort necessary to eradicate the illness, and pathogens evolve to maximise their $R_0$ value. He proved that each of the three assertions might be untrue [44]. As previously mentioned, the first might fail owing to the existence of backward bifurcations. The second may fail when control efforts are performed inconsistently across various host types, since $R_0$ is obtained by averaging all host types and does not directly predict the control effort necessary to remove infection. The third condition may fail if two pathogens coexist in a steady state that exists and is stable, yet both single-pathogen steady states exist and are unstable. In this instance, the sequence in which infections establish themselves in the host population is significant. The established parasite plays a role in determining the modified carrying capacity, and the pathogen with the highest basic reproductive ratio does not necessitate the exclusion of the other.

Breban et al., demonstrated that two individual-level models with identical expectations for the relevant population-level variables may produce distinct $R_0$ values [45]. They demonstrated that obtaining $R_0$ from empirical contact-tracing data collected by epidemiologists and using this $R_0$ as a threshold parameter for a population-level model could lead to erroneous estimates of the infectiousness of the pathogen, the severity of an outbreak, and the medical and/or behavioural interventions required for control. Therefore, evaluating $R_0$ via contact tracing (as is often done during an epidemic investigation) may not be an effective method for establishing the efficacy of critical control strategies. Similar incidence and prevalence patterns may be generated by several distinct individual-level mechanisms. Consequently, it may be hard to provide a meaningful $R_0$ value to an ODE model without knowledge about the underlying disease transmission network. Only a threshold parameter for an epidemic may be utilised to create control tactics. Since $R_0$ lacks this criterion characteristic, its usefulness may be grossly exaggerated.

Meyers contrasted the theoretical computation of $R_0$ with real SARS data from China to demonstrate that $R_0$ estimations seemed incongruous [28]. The basic reproduction rate is determined by two factors: (1) the intrinsic features of the pathogen, which influence the transmission efficiency per contact and the length of the infectious phase; and (2) the contact patterns between infected and susceptible hosts in the population. While the first element may be somewhat consistent throughout outbreaks, the second may be very context-dependent and vary greatly within and across communities. The issue with the SARS estimations derives from the mass-action assumption of compartmental models, which states that all susceptible persons have an identical chance of being infected. When this assumption is violated, the models may provide estimates that are erroneous or may not apply to all populations. The majority of the $R_0$ estimates for SARS in the field were derived from outbreak data from a hospital and a densely populated apartment complex with atypically high rates of close contact between persons. The author noted that extrapolating estimates for $R_0$ from specialised circumstances such as these to the general population may be problematic. Since the general population is unlikely to meet mass-action criteria, it is also possible to argue that $R_0$ is not a reliable estimate of disease transmission.

**Alternatives to $R_0$**

Jing Li highlighted numerous alternatives to $R_0$, such as: The real reproduction number, $R_a$, is defined as the product of the average infectiousness duration and the incidence to prevalence ratio [7]. $R_0$ corresponds with $R_a$ when the transmission probability is constant; however, it compensates for the more typical condition in which the transmission probability fluctuates as a function of infection age. Once an epidemic has begun, the effective reproduction number $R(t)$ estimates the number of secondary cases created by each infectious case. $R(t)=R_0\ S(t)/N$ in the absence of control measures, where S(t)/N represents the fraction of the population that is vulnerable. The determination of reproductive numbers is often an indirect procedure due to the difficulty or impossibility of precisely quantifying some of the characteristics on which these numbers rely. The effective reproductive number meets the condition $R(t)\leq R_0$ only when the whole population is susceptible. The effective reproduction number is of practical importance since it is time-dependent and may explain the degree of cross-immunity from previous outbreaks. However, since it is derived from $R_0$, the effective reproduction number inherits a number of its shortcomings.

According to Breban et al., the average number of secondary infections among infected individuals [43]. $Q_0\ (t)$ is the average number of outgoing connections of a node inside the infected compartment at time t. When the limits exist, $R_0=\lim_{t\to\infty} R_0\ (t)$ $Q_0=\lim_{t\to\infty} Q_0\ (t)$ are calculated. Sadly, $R_0\ (t)$ is never specified in the study, restricting the applicability of this definition of R0. By similarity with $Q_0\ (t)$, however, $R_0\ (t)$ represents the average number of outgoing connections of a deleted compartment at a given moment. Under the premise that every infection is uniquely designated as a secondary infection for either a removed or an infected individual, $Ni(t)=I(t)Q_0\ (t)+Nr(t)R_0$ (t), where $Ni(t) = \int_0^t \beta I(\mu)d\mu$ is the cumulative number of infected people in the time range (0,t and $Ni(t) = \int_0^t \nu I(\mu)d\mu.$ As the distribution of secondary cases becomes stable, their definition of $R_0$ compares the average number of secondary cases to the number of eliminated persons. This definition does not imply a specific model at the level of the person; it is only dependent on the topology of the disease-transmission network. However, $R_0$ is not measured at the onset of an epidemic, limiting its use during the first outbreak. When infectious illnesses are impacted by seasonal fluctuations, typical epidemiological theory and notions such as R0 do not apply, ꝺ $\int_0^0 \beta(t)dt$.ed by Grassly and Fraser (2006). They define $R_0$ as D_0^0, where β(t) is the transmission parameter at time t and $D$ is the mean duration of infection. Consequently, $R_0$ may be read as the average number of secondary cases resulting from the introduction of a single infectious agent into an entirely susceptible population at a random time of year. They discovered that $R_0$<1 is insufficient to prevent an epidemic, since transmission chains may be built during highly infectious seasons if $D\beta(t)$>1. However, $R_0$<1 is essential and sufficient for the long-term elimination of illness.

Kao constructed an epidemiological network contact matrix M with entries $m_{ij}$ that are either 1 or 0 based on the possibility of an infectious contact between nodes I and j [27]. The spectral radius of M is an alternative estimate for $R_0$, which may be computed with a weighted version of ( Heffernan and L. M. Wahl, 2006). This explicitly accounts for the complete contact structure of the network, but the evaluation of extremely large, reasonably dense matrices is challenging and time-consuming, especially when this evaluation process must be repeated multiple times.

Comparing the two estimates for portions of a sheep network with several thousand nodes, however, reveals a negligible discrepancy between $R_0$ and the spectral radius of M. $T_0$, an analytical threshold condition, was defined by Kamgang and Sallet using the unique structure of Metzler matrices [46]. If $T_0<1$, the disease-free equilibrium is locally asymptotically stable, but if $T_0>1$, the disease-free equilibrium is unstable. They reported that, $T_0$ has a correlation with $R_0$, albeit a greater one; yet, it has no clear biological significance. Despite its highly mathematical character, the technique for deriving $T_0$ permits the derivation of a threshold for high-dimensional epidemic models.

Huang identified four reproductive numbers linked with four kinds of transmission patterns, each dependent on z, the mean infectious period to mean latent period ratio [47]. These are the reproduction numbers for these four items: i) the reproductive number associated with the slowest latency process and the quickest recovery process, ii) the reproductive number associated with the average latency and recovery processes, iii) the greatest reproductive number associated with the quickest latency process and the slowest recovery process, and iv) the greatest reproductive number associated with the quickest latency process and the slowest recovery process. These numbers allow for the classification of diseases as mild or severe.

Hosack et al., emphasised that R_0 does not always account for the dynamics of epidemics in endemic equilibrium models [48]. Using the idea of reactivity, they deduced a threshold index for epidemicity, E_0, which represents the maximum number of new infections created by an infective person in a disease-free equilibrium. If the threshold for epidemicity is exceeded, then the illness prevalence might grow even if it is not endemic. They showed that epidemics may develop even in regions where transmission cannot be sustained over the long run.

Reluga et al., defined R_d, the discounted reproductive number [49]. The discounted reproductive number is a measure of reproductive success that is calculated by discounting an individual's predicted lifetime offspring production by the background population growth rate. The R_d incorporates characteristics of both the basic reproductive number and the final proliferation rate, while inheriting the non-uniqueness issues of the next-generation approach.

Nishiura devised a likelihood-based technique for calculating R_0 without assuming exponential case growth and provides a corrected estimate for the real reproduction number [50]. The author observed that R_0 is particularly sensitive to the spread of a disease's development or modifications in the underlying epidemiological assumptions [51-57].

## Conclusion

The nature of $R_0$ is used to monitor and control severe real-time epidemics; control tactics are frequently abandoned if $R_0<1$. This means that it is impossible to compare various disorders. Some techniques use an equilibrium value that might not be reached for a very long period to determine an eradication threshold. This implies that in order to characterise transmissibility and direct intervention methods, various metrics are required at different phases of an epidemic. The next-generation method is probably the most popular, yet it suffers from uniqueness problems and does not cope well with more than one disease state. Only the survival function reliably calculates the average number of secondary infections; this method is too cumbersome to use in most practical settings. $R_0$ is a quantity that relates to the initial phase of an epidemic. It is used to guide eradication efforts when a disease is endemic. When a new pathogen emerges, a quantity describing the initial spread is useful.

The contact structure of the population, the variation of risk factors and the order of establishing a disease should accompany the identification of a meaningful $R_0$ quantity. What is urgently needed is a simple, but accurate, measure of disease spread that has a consistent threshold property and which can be understood by non mathematicians.In addition to never being consistently computed, $R_0$ fails to satisfy the threshold property and does not quantify the number of secondary infections. No other concept has ever outperformed biology, mathematics, epidemiology, and immunology in this way. No other idea is so broad that it can be explained using partial differential equations, compartment models, network models, metapopulation models and stochastic models. Rarely has an erroneous idea gained such widespread support. Therefore, if $R_0$ is to be used, it must be accompanied by a declaration of which method was used, which assumptions are underlying the model and evidence that it is actually a threshold, with no backward bifurcation.

## Conflicts of interest

There are no conflicts to declare.

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