Scientific Research Publishing

Open Journal of Epidemiology, 2025, 15(2), 272-295
https://www.scirp.org/journal/ojepi
ISSN Online: 2165-7467
ISSN Print: 2165-7459

Understanding the Basic Reproduction Number (R_0): Calculation, Applications, and Limitations in Epidemiology

Hamid H. Hussien[1,2*], Khalid Rhamtallah Genawi[1], Nuha Hassan Hagabdulla[3], Khalda M.Y. Ahmed[4]

[1]Department of Statistics, College of Science, Sudan University of Science and Technology, Khartoum, Sudan
[2]Department of Mathematics, College of Science and Arts, King Abdulaziz University, Rabigh, Saudi Arabia
[3]Department of Mathematics, College of Science, Qassim University, Buraid, Saudi Arabia
[4]Department of Business Administration, College of Business and Economics, Qassim University, Buraid, Saudi Arabia
Email: *hamid128@yahoo.com

How to cite this paper: Hussien, H.H., Genawi, K.R., Hagabdulla, N.H. and Ahmed, K.M.Y. (2025) Understanding the Basic Reproduction Number (R_0): Calculation, Applications, and Limitations in Epidemiology. *Open Journal of Epidemiology*, **15**, 272-295.
https://doi.org/10.4236/ojepi.2025.152018

Received: March 8, 2025
Accepted: April 8, 2025
Published: April 11, 2025

Abstract

Background: The basic reproduction number (R_0) is a key metric in epidemiology, representing the expected number of secondary infections from a single case in a fully susceptible population. Despite its widespread application, R_0 is often misinterpreted due to its dependence on model assumptions and population dynamics. Understanding its calculation, applications, and limitations is crucial for refining epidemic models and enhancing disease control measures. **Objectives:** This study examines the mathematical foundations of R_0, its estimation methods, applications in disease modeling, and limitations. Additionally, it explores the effective reproduction number (R_0) and its role in assessing intervention impacts. **Methods:** A systematic review of mathematical models, including the SIR, SIRD, and modified SIRD models, was conducted to evaluate various approaches for estimating R_0. The study also highlights variations in R_0 and the effective reproduction number (R_0) across different infectious diseases, such as measles, influenza, and COVID-19. **Results:** Findings indicate that R_0 is highly dependent on disease-specific factors, population dynamics, and intervention strategies. While R_0 serves as a useful threshold indicator for disease outbreak potential, R_0 provides a more practical assessment of ongoing transmission dynamics. The study highlights that interventions such as vaccination can significantly reduce R_0 and achieve herd immunity thresholds, but their effectiveness varies depending on vaccine coverage and pathogen characteristics. Additionally, limitations of R_0, such as its assumptions of homogeneous mixing and static pop-

ulation structures, necessitate the integration of advanced epidemiological models for more accurate predictions. **Conclusion:** R_0 remains a cornerstone in infectious disease modeling, offering valuable insights into pathogen transmissibility and outbreak control. However, its utility is constrained by simplifying assumptions, including homogeneous mixing and static population structures. To enhance the accuracy of epidemic forecasts, future research should focus on refining predictive models that incorporate variability in host susceptibility, behavioral adaptations, and environmental influences. A nuanced understanding of R_0 and its limitations is essential for developing effective public health policies and improving epidemic preparedness.

Keywords

R_0, Effective Reproduction Number, Epidemic Modeling, Herd Immunity, Vaccination Strategies, SIR Model

1. Introduction

Epidemics have long influenced public health policies and research priorities, shaping global efforts to mitigate disease spread. In modern epidemiology, mathematical modeling has emerged as an essential tool for understanding disease dynamics and guiding intervention strategies [1]. At the core of these models lies the basic reproduction number (R_0), a fundamental metric in infectious disease modeling [2]. While its significance is well established, perspectives on its utility vary. Some critics argue that R_0 relies on overly simplified assumptions—such as homogeneous mixing, stable populations, and permanent immunity—that may not hold true in real-world scenarios, thereby limiting its accuracy and practical relevance [3]. Despite these critiques, R_0 remains a crucial measure of a pathogen's transmissibility and outbreak potential, making it one of the most frequently utilized metrics in the study of infectious disease dynamics [4]-[8].

The ability of a pathogen to establish and sustain transmission is directly linked to R_0, making it a cornerstone for understanding transmission dynamics. By quantifying the expected number of secondary infections caused by a single infected individual in a fully susceptible population, R_0 provides crucial insights into epidemic potential. This enables public health officials to design targeted interventions, such as vaccination campaigns, social distancing measures, and quarantine protocols [5]. Understanding the interplay between pathogen characteristics, host susceptibility, and environmental factors is vital for accurately estimating R_0 and developing effective control strategies. Integrating biological, environmental, and social factors into epidemiological models enhances the ability to predict and contain infectious disease outbreaks.

While R_0 is a valuable epidemiological metric, its definition, calculation, and interpretation are complex and often misunderstood. Although R_0 reflects a biological reality, it is typically estimated using mathematical models that rely on

various assumptions. Proper interpretation requires a deep understanding of model structures, inputs, and limitations. Misrepresentation and misinterpretation are common, particularly regarding vaccination effects and disease dynamics [6]. Given the increasing focus on R_0 in academic literature, this review aims to provide a comprehensive analysis of R_0 by clarifying its calculation, interpretation, and application in epidemiology, particularly regarding its role in herd immunity, vaccination strategies, and disease dynamics. By examining its mathematical foundations, appropriate usage, and potential pitfalls, this review aims to improve epidemic modeling, policy decisions, and communication in combating infectious diseases.

The remainder of this paper is structured as follows: Section 2 provides a comprehensive overview of the SIR, SIRD, and modified SIRD models, highlighting their mathematical properties and epidemiological significance. Section 3 explores R_0, detailing its derivation, interpretation, and role in disease modeling. Additionally, this section examines the practical applications of R_0, particularly in the context of herd immunity and vaccination strategies, while discussing its implications for public health policies and its inherent limitations. Finally, Section 4 presents the conclusion, summarizing key findings, addressing study limitations, and proposing directions for future research.

2. Mathematical Models

Mathematical models, such as the Susceptible-Infectious-Recovered (SIR) and Susceptible-Exposed-Infectious-Recovered (SEIR) models, play a crucial role in estimating R_0 and evaluating the effectiveness of various intervention strategies [2]. These models integrate real-world epidemiological data to simulate diverse outbreak scenarios and assess the impact of public health measures, including vaccination programs, quarantine protocols, and social distancing policies [9]. By incorporating key transmission parameters—such as the rate of contact (C), total infectious period (D), and transmission probability (β)—these models offer a quantitative framework for understanding disease spread. They help identify critical thresholds for disease control, optimize resource allocation, and predict potential epidemic trajectories under different intervention strategies.

2.1. SIR Model

The Susceptible-Infectious-Recovered (SIR) model, introduced by Kermack and McKendrick in 1927, provides a fundamental framework for studying infectious disease dynamics [10]. It categorizes the population into three compartments:

- Susceptible (S): Individuals at risk of contracting the disease.
- Infected (I): Individuals actively infected and capable of transmitting the disease.
- Recovered (R): Individuals who have either recovered with immunity or been removed due to death.

The model is described by the following set of differential equations:

$$\begin{aligned}\frac{\mathrm{d}S}{\mathrm{d}t} &= -\beta IS/N \\ \frac{\mathrm{d}I}{\mathrm{d}t} &= \frac{\beta IS}{N} - \lambda I \\ \frac{\mathrm{d}R}{\mathrm{d}t} &= \lambda I\end{aligned} \tag{1}$$

where β represents the transmission rate and λ is the recovery rate (see **Figure 1**). The SIR model assumes a closed population with homogeneous mixing, lifetime immunity, and no demographic changes. However, real-world epidemics often involve mortality, prompting modifications such as the SIRD model. Equation (1) is subject to the initial conditions, $S(t_0) > 0$, $I(t_0) \geq 0$, and $R(t_0) \geq 0$ at the initial time t_0.

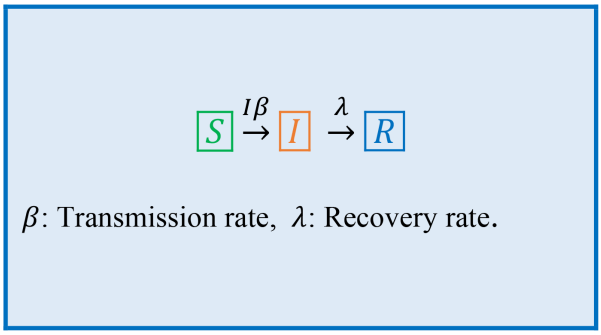

Figure 1. Schematic illustration of the interactions between the compartments in the SIR model.

The model is based on a large, closed population, a short-lived outbreak, immediate infectiousness, lifetime immunity, and mass-action mixing. It also assumes that all people who recover from the disease are either fully immune or no longer able to help it spread. However, real-world epidemics often involve significant mortality, which the SIR model does not explicitly address [11]. The model is expanded into the susceptible-infected-recovered-deceased (SIRD) model.

2.2. SIRD Model

The model adds a fourth compartment to SIR model called "deceased" (D) to account for people who died from the disease. This makes the model more useful and accurate. The deceased (D) component represents individuals who have died as a direct result of the infection. This compartment differentiates between those who recover and those who do not survive the disease.

A key assumption in the SIRD model is that the total population, represented by the sum of $S(t), I(t), R(t)$, and $D(t)$, remains constant over time. Additionally, the model assumes immediate infection upon exposure, with no latent period between exposure and the onset of infection. Factors such as quarantine measures or confinement are not incorporated into this model [12].

The SIRD model is a widely utilized framework for characterizing epidemiology and classifying diseases within a community [13]. The model extends the SIR model by incorporating a variable for the deceased population as a function of time. This model has been widely used in epidemiological studies to analyze the spread and control of infectious diseases, including COVID-19, AIDS, and Ebola. Researchers have applied it to understand transmission dynamics, estimate key epidemiological parameters, and evaluate the effectiveness of intervention strategies such as vaccination, social distancing, and quarantine measures [13]-[17].

The model is governed by a set of differential equations that describe the rate of change in each compartment over time:

$$\begin{aligned} I + S &\xrightarrow{\beta} I \\ \frac{\mathrm{d}S(t)}{\mathrm{d}t} &= -\beta S(t) I(t)/N \\ I &\xrightarrow{\lambda} R \\ \frac{\mathrm{d}I(t)}{\mathrm{d}t} &= \beta S(t) I(t)/N - \lambda I(t) - k_d I(t) \\ I &\xrightarrow{k_d} D \\ \frac{\mathrm{d}R(t)}{\mathrm{d}t} &= \lambda I(t) \\ \frac{\mathrm{d}D(t)}{\mathrm{d}t} &= k_d I(t) \end{aligned} \tag{2}$$

where: β is a transmission rate, representing the likelihood of disease spread through contact between Susceptible and Infected individuals. λ is a recovery rate, representing the fraction of infected individuals who recover per unit time, and k_d is a mortality rate, representing the fraction of infected individuals who die per unit time.

While the SIRD model is an improvement over the SIR model, it still has limitations. These limitations are: 1) No Latent Period: Diseases with significant incubation periods, such as COVID-19, may require the inclusion of an exposed compartment, 2) Simplistic Assumptions: The SIRD model assumes homogeneity in the population, ignoring variations in age, behavior, or geography. The transition from the SIR to the SIRD model marks an important step in improving the realism of epidemic modeling by incorporating disease-related mortality. This modification provides a clearer picture of the epidemic's toll, helping researchers and policymakers design better interventions to manage and mitigate outbreaks. However, further extensions and refinements are needed to adapt the model to specific diseases and real-world complexities.

2.3. Modified SIRD Model

Sen and Sen (2021), introduced a significant enhancement to the standard SIRD model to better analyze and predict the spread of COVID-19 by accounting for real-world complexities that the original model does not address [14]. Their modified

model incorporates the effects of exposure, quarantine, confinement, and asymptomatic populations [15] [18] [19], reflecting the unique dynamics of COVID-19 transmission and control measures. These additions make the model more aligned with the realities of managing a global pandemic. The governing equations of the modified model are as follows (See Table 1 for description of parameter):

$$\frac{\mathrm{d}S(t)}{\mathrm{d}t} = -\alpha S(t) - \frac{\beta S(t) I(t)}{N} - \frac{\sigma S(t) A(t)}{N} - \eta S(t) \tag{3}$$

$$\frac{\mathrm{d}A(t)}{\mathrm{d}t} = -\tau A(t) + \xi E(t) \tag{4}$$

$$\frac{\mathrm{d}C(t)}{\mathrm{d}t} = \alpha S(t) - \mu C(t) \tag{5}$$

$$\frac{\mathrm{d}E(t)}{\mathrm{d}t} = -\gamma E(t) + \beta S(t) I(t) N + \mu C(t) + \eta S(t) + \sigma S(t) A(t) N - \xi E(t) \tag{6}$$

$$\frac{\mathrm{d}I(t)}{\mathrm{d}t} = \tau A(t) + \gamma E(t) - \delta I(t) \tag{7}$$

$$\frac{\mathrm{d}R(t)}{\mathrm{d}t} = \lambda(t) \varrho(t) \tag{8}$$

$$\frac{\mathrm{d}\varrho(t)}{\mathrm{d}t} = \delta I(t) - \lambda(t) \varrho(t) - k_d(t) \varrho(t) \tag{9}$$

$$\frac{\mathrm{d}D(t)}{\mathrm{d}t} = k_d(t) \varrho(t) \tag{10}$$

$$S(t) + C(t) + E(t) + A(t) + I(t) + Q(t) + R(t) + D(t) = N \tag{11}$$

Table 1. The model definition of parameters.

S. No.	Parameter	Definition
1	β	Transmission rate of the virus from infected individuals to susceptible individuals.
2	α	Transmission rate from asymptomatic individuals to susceptible individuals.
3	η	Rate at which susceptible individuals are exposed due to external factors.
4	μ	Transition rate from confinement to the exposed compartment.
5	ξ	Rate at which exposed individuals become asymptomatic.
6	τ	Transition rate from asymptomatic to symptomatic (infected) individuals
7	γ	Rate at which exposed individuals develop symptoms and move to the infected class.
8	δ	Recovery or removal rate of symptomatic infected individuals.
9	$\lambda(t)$	Recovery rate of quarantined individuals.
10	$k_d(t)$	Death rate of quarantined individuals.

In this model, N represents the total population, while different compartments describe the progression of individuals through various stages of infection and

containment.

- $C(t)$: Confined Population—Individuals who adhere to preventive measures such as social distancing, wearing face masks, and following lockdown protocols to reduce transmission risk.
- $E(t)$: Exposed Population—Individuals who have encountered the virus but are in a latent phase, meaning they have not yet tested positive or become infectious. During this stage, they do not contribute to disease transmission.
- $A(t)$: Asymptomatic Population—Individuals who have been exposed and carry the virus but remain symptom-free. Unlike the $E(t)$ group, $A(t)$ individuals are infectious and contribute to the spread of the virus.
- $Q(t)$: Quarantined Population—Infected individuals who have been identified and isolated to prevent further spread. Effective quarantine measures help reduce transmission by limiting interactions between infected and susceptible individuals.

The interaction between $A(t)$ (asymptomatic carriers) and $Q(t)$ (quarantined individuals) is critical in shaping the disease's trajectory. Since asymptomatic individuals unknowingly spread the virus, early detection, contact tracing, and isolation strategies are essential in breaking transmission chains [20]. Efficient public health interventions—such as rapid testing, timely quarantine, and community awareness campaigns—play a crucial role in reducing the overall infection rate and preventing healthcare system overload. By swiftly identifying and isolating infected individuals, health authorities can protect high-risk populations, minimize socio-economic disruptions, and effectively manage disease outbreaks.

3. The Basic Reproduction Number (R_0): Concept, Calculation, and Implications

R_0 is a fundamental concept in epidemiology that quantifies the potential spread of an infectious disease within a fully susceptible population. It is defined as the expected number of secondary infections generated by a single infected individual in the absence of immunity or intervention measures [3] [21]. Understanding R_0 is crucial for assessing disease transmissibility, predicting outbreaks, and informing public health strategies [22]. Mathematically, R_0 can be expressed as:

$$R_0 = \beta \times D \times C$$

where:

- β (Transmission Rate): The probability of disease transmission per contact between an infected and a susceptible individual.
- D (Infectious Period): The average duration an individual remains contagious.
- C (Contact Rate): The average number of susceptible individuals an infected person interacts with per unit time, which can be represented mathematically as:

$$C = \frac{\text{Total number of contacts per unit time}}{\text{Total population size}}$$

This equation highlights the key determinants of disease spread—higher transmission efficiency, prolonged infectious periods, and frequent interactions within a population all contribute to increasing R_0. Consequently, public health interventions, such as reducing contact rates (social distancing), shortening the infectious period (early treatment), and lowering transmission probability (vaccination), aim to decrease R_0 and control disease outbreaks.

3.1. Methods of Calculating R_0

Several methods exist for estimating the basic reproduction number (R_0), each suited to different types of data and levels of disease model complexity. The choice of method depends on factors such as available epidemiological data, assumptions about disease transmission, and the structure of the underlying mathematical model. Below are some of the most used approaches:

3.1.1. Next-Generation Matrix Method

The next-generation matrix method is widely used in deterministic compartmental models to estimate R_0. It calculates the expected number of secondary infections by examining the dominant eigenvalue of the next-generation matrix, which describes disease transmission within a structured population [23]. Mathematically, R_0 is derived from the spectral radius of the next-generation matrix G, given by:

$$R_0 = \rho(G) \tag{12}$$

Here, $\rho(G)$ represents the dominant eigenvalue (i.e., the largest absolute eigenvalue) of the next-generation matrix G, which is constructed from the new infection terms and transition terms of the model. The next-generation matrix method decomposes the infection process into two key components: (1) the New Infections Matrix F, which represents the rate at which new infections arise in each compartment, and (2) the Transition Matrix V, which describes the movement of infected individuals between compartments, including recovery and death. Mathematically:

$$G = FV^{-1} \tag{13}$$

where: F is a non-negative matrix describing new infections and V is an invertible matrix describing the movement of infected individuals. Consider an SEIR (Susceptible-Exposed-Infected-Recovered) model with:

$$\frac{\mathrm{d}t}{\mathrm{d}E} = \beta SI - \sigma E \tag{14}$$

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \sigma E - \gamma I \tag{15}$$

where: β represents the transmission rate, σ represents the rate of progression from exposed to infected, and γ represents the recovery rate. From eq. 14 – 15, the matrices F and V are:

$$F = \begin{bmatrix} 0 & \beta \\ 0 & 0 \end{bmatrix} \tag{16}$$

$$V = \begin{bmatrix} \sigma & 0 \\ -\sigma & \gamma \end{bmatrix} \tag{17}$$

Computing $G = FV^{-1}$:

$$V^{-1} = \begin{bmatrix} \frac{1}{\sigma} & 0 \\ \sigma/(\gamma\sigma) & \frac{1}{\gamma} \end{bmatrix} \tag{18}$$

$$G = FV^{-1} = \begin{bmatrix} 0 & \frac{\beta}{\gamma} \\ 0 & 0 \end{bmatrix} \tag{19}$$

The eigenvalue G are $\lambda = 0$ and $\lambda = \frac{\beta}{\gamma}$, that is: $R_0 = \frac{\beta}{\gamma}$.

3.1.2. Euler-Lotka Equation

For diseases with an explicit generation time distribution, the Euler-Lotka equation provides an alternative way to estimate R_0 using epidemiological data. To derive Euler-Lotka equation, assume the epidemic is growing exponentially with rate r. Then the incidence (number of new cases) at time t is given by:

$$n(t) = n(0)\mathrm{e}^{rt} \tag{20}$$

where $n(0)$ represents the incidence at time $t = 0$.

Following a renewal equation for incidence, the number of new infections at time t is the sum of contributions from all previous infections. Each infected individual generates new cases according to the generation time distribution $b(\tau)$, where τ is the time since infection. Thus, we can write [24]:

$$n(t) = \int_0^\infty b(\tau)n(t-\tau)\mathrm{d}\tau \tag{21}$$

Replace $n(t-\boldsymbol{\tau})$ by the exponential form: $n(t-\tau) = n(0)\mathrm{e}^{r(t-\tau)}$, eq. (21) can be rewritten as:

$$n(t) = n(0)\mathrm{e}^{rt}\int_0^\infty b(\boldsymbol{\tau})\mathrm{e}^{r\tau}\mathrm{d}\boldsymbol{\tau} \tag{22}$$

Consider eq. (20), we can write:

$$n(0)\mathrm{e}^{rt} = n(0)\mathrm{e}^{rt}\int_0^\infty b(\boldsymbol{\tau})\mathrm{e}^{r\tau}\mathrm{d}\boldsymbol{\tau} \tag{23}$$

Hence, the Euler–Lotka equation follows.

$$1 = n(0)\mathrm{e}^{rt}\int_0^\infty b(\boldsymbol{\tau})\mathrm{e}^{r\tau}\mathrm{d}\boldsymbol{\tau} \tag{24}$$

where: $b(\tau)$ represents the generation time distribution (or infectivity profile), describing the probability that an infected individual generates a new case at time τ infection, and $\mathrm{e}^{r\tau}$: Acts as a discount factor, accounting for the fact that secondary cases occurring later contribute less to the current growth of the epidemic.

This derivation shows how the Euler–Lotka equation links the epidemic growth rate r with the generation time distribution $b(t)$ and provides a framework for estimating the basic reproduction number R0 when the total reproduction can be related as:

$$R_0 = \int_0^\infty b(\tau)\mathrm{d}\tau \tag{25}$$

Thus, by knowing r and $b(t)$, one can assess the transmission dynamics of an infectious disease.

3.1.3. Maximum Likelihood Estimation (MLE)

MLE is a statistical approach for estimating R_0 using case incidence data. It fits a likelihood function to observed epidemic data and derives R_0 by optimizing parameters [25]. The likelihood function can be expressed as:

$$L(R_0) = \prod_{t=1}^{T} P(I_t \mid R_0, I_{t-1}, \cdots) \tag{26}$$

where I_t represents the number of new infections at time t. This method is particularly useful for real-time epidemic assessments.

3.1.4. Stochastic Models

Stochastic models incorporate random variation in disease transmission, making them suitable for small population settings or emerging outbreaks where deterministic models may not fully capture transmission dynamics [3]. The branching process approximation is a common approach, defining R_0 as:

$$R_0 = \sum_{k=0}^{\infty} kP(k) \tag{27}$$

where $P(k)$ represents the probability of an infected individual generating k secondary cases. Stochastic models can also use Markov chains or agent-based simulations to model individual-level transmission.

The probability $P(k)$ represents the likelihood that an infected individual transmits the infection to exactly k secondary cases. This probability distribution is typically derived from empirical outbreak data or assumed based on known epidemiological characteristics of the disease, such as transmission modes, contact structure, and variability in infectiousness. Common choices for $P(k)$ include the Poisson, negative binomial, or geometric distributions, depending on whether transmission exhibits homogeneity or overdispersion. Let us consider the choice of Poisson distribution, if each infected individual has independent and identical probabilities of transmitting the infection to others, and contacts occur randomly in a large, well-mixed population, the number of secondary infections follows a Poisson distribution:

$$P(k) = \frac{\mathrm{e}^{-\lambda}\lambda^k}{k!} \tag{28}$$

where: $\lambda = R_0$ represent the average number of secondary infections per case. This assumption is valid when transmission is relatively uniform across individuals.

In real-world outbreaks, $P(k)$ plays a crucial role in determining the likelihood of disease extinction or persistence. If most infected individuals generate few or no secondary infections (high probability for small k), the outbreak is likely to die out early. Conversely, if $P(k)$ has a heavy tail (e.g., due to superspreading events), even a small fraction of highly infectious individuals can sustain an epidemic. This branching process framework is particularly useful in modeling early outbreak dynamics, where stochastic effects dominate and deterministic models may overestimate transmission potential [26].

3.1.5. Time-Series-Based Approaches

Time-series models, such as the Wallinga-Teunis method, estimate R_0 from epidemic curves by analyzing serial intervals and transmission patterns over time [27]. These approaches are particularly useful when estimating R_0 dynamically during outbreaks. Each method for estimating R_0 has distinct strengths and limitations, influenced by the quality and type of available data. Deterministic approaches, such as the next-generation matrix method, are well-suited for structured population models, while the Euler-Lotka equation is particularly effective in estimating R_0 during early outbreak stages. Stochastic and likelihood-based methods, including MLE, provide robust estimates using incidence data, whereas time-series methods enable dynamic, real-time monitoring of disease transmission. By integrating multiple estimation techniques, researchers can enhance the accuracy and reliability of R_0 estimates, ultimately improving public health responses and intervention strategies [28].

3.2. Interpretation of R_0

The interpretation of R_0 follows a clear epidemiological framework:

- If $R_0 > 1$ → The disease is likely to spread exponentially, leading to an outbreak or epidemic.
- If $R_0 = 1$ → The disease remains stable within the population, meaning each infected individual replaces themselves with exactly one new case.
- If $R_0 < 1$ → The disease will gradually decline and eventually disappear, as each infected individual transmits the infection to fewer than one person on average.

By understanding R_0, public health authorities can implement timely interventions such as vaccination programs, quarantine measures, and hygiene campaigns to control disease spread effectively.

3.3. Variability of R_0 across Diseases

The basic reproduction number (R_0) varies significantly across infectious diseases, reflecting differences in their transmissibility and outbreak potential. For COVID-19, early pandemic variants the R_0 range between 2 - 3 [29], and Omicron variant with R_0 of around 8.2 [30]. This variation demonstrates how viral mutations can dramatically change transmission potential.

Seasonal influenza, for instance, has an estimated R_0 ranging from 0.9 to 2.1, indicating moderate transmission rates. The 1918 flu pandemic had a slightly higher R_0 of 1.4 to 2.8, contributing to its widespread impact. In contrast, measles, one of the most highly contagious diseases, has an R_0 between 12 and 18, meaning a single infected person can spread the virus to a large number of susceptible individuals [31]. Monkeypox (MPXV) presents a more variable transmission pattern. Earlier studies estimated an R_0 of 0.83, suggesting self-limiting outbreaks [32] [33]. However, recent modeling in non-endemic regions found R_0 values between 1.10 and 2.40, raising concerns about its potential for sustained transmission [34]. The 2014 Ebola virus outbreak in West Africa is the largest outbreak of the genus Ebolavirus to date. The maximum likelihood estimates of the basic reproduction number are 1.51 for Guinea, 2.53 for Sierra Leone and 1.59 for Liberia [35].

These variations highlight the necessity for disease-specific control measures, emphasizing the importance of tailored public health strategies to mitigate transmission risks effectively. Estimating R_0 comes with inherent uncertainties, particularly during the early stages of an outbreak. Most modeling simulations produce a range of R_0 values, reflecting difficulties in accurately determining key parameters. One major challenge is identifying the true number of cases, as many mild or asymptomatic infections may go undetected, contributing to unobserved transmission [36]. These uncertainties underscore the importance of continuous epidemiological surveillance and refinement of disease models to improve public health response strategies.

3.4. Factors Influencing R_0

Several factors influence R_0, extending beyond the intrinsic properties of a pathogen to include environmental and social determinants. Pathogen characteristics such as virulence, which affects disease severity and infectious duration, play a crucial role—higher virulence often leads to increased R_0. The mode of transmission also impacts R_0, with airborne diseases like measles exhibiting higher values compared to contact-based infections. Additionally, the incubation period influences transmission dynamics, as shorter incubation times accelerate infection cycles [3]. Antigenic variation, observed in viruses like influenza, allows pathogens to evade host immunity, prolonging outbreaks and sustaining transmission [37]. Beyond pathogen biology, environmental and social factors significantly affect R_0. Population density facilitates frequent interactions, increasing disease spread, whereas behavioral practices such as improved hygiene, sanitation, and social distancing can effectively reduce contact rates and lower R_0 [38]. The efficiency of the healthcare system further modulates R_0, as rapid diagnosis, effective treatment, and robust containment strategies help suppress transmission and mitigate outbreak severity [23]. Together, these factors shape disease dynamics, highlighting the complexity of controlling infectious disease spread and the necessity of integrated public health strategies.

3.5. Public Health Implications of R_0

R_0 serves as a critical metric in public health decision-making, helping to predict whether an infectious disease will spread or decline. It provides essential insights into the severity of an outbreak, the level of intervention required (such as vaccination coverage or quarantine duration), and the effectiveness of control measures. Reducing R_0 below 1 is fundamental to epidemic prevention, achievable through widespread immunization, improved healthcare access, and public awareness campaigns [39]. However, while R_0 is a valuable tool for assessing disease spread, its interpretation must account for pathogen properties, population behavior, and healthcare system efficiency, as these factors significantly influence transmission dynamics. Integrating epidemiological models with real-world data allows public health officials to refine outbreak response strategies, ensuring timely and effective interventions [40].

3.6. Threshold for Disease Control: R_0 and Its Role in Herd Immunity and Vaccination Strategies

The basic reproduction number, R_0, is a fundamental metric in epidemiology that determines the potential spread of an infectious disease in a fully susceptible population. It is a critical parameter for informing public health interventions such as vaccination strategies. The concept is widely used in the literature concerning infectious disease models, exhibiting varying degrees of affection [41]. When applied to control measures, it establishes a threshold for the proportion of the population that must be immunized to halt the spread of the disease, a concept known as herd immunity.

3.6.1. Herd Immunity Threshold

Herd immunity occurs when a sufficient proportion of the population becomes immune—either through vaccination or natural infection—thereby reducing disease transmission. This protects both immunized individuals and those who cannot be vaccinated, such as people with contraindications or compromised immune systems. Public health measures, such as vaccination, social distancing, and improved hygiene, are essential for reducing R_0. Vaccination directly lowers R_0 by decreasing the proportion of susceptible individuals. The critical vaccination threshold required to achieve herd immunity is calculated using:

$$\text{Herd Immunity Threshold } (HIT) = 1 - 1/R_0 \tag{29}$$

For example, diseases with higher R_0 values require a larger proportion of the population to be immunized. Measles, with an R_0 of approximately 12 - 18, necessitates immunizing 92% - 95% of the population, whereas seasonal influenza, with an R_0 of about 1.3, requires only around 23% immunity to prevent outbreaks. This relationship follows from the idea that if ($R_0 - 1$) out of the R_0 individuals an infected person might have transmitted the disease to are vaccinated, each infected individual will generate fewer than one secondary infection. Thus,

in general, *HIT* can be expressed as:

$$HIT = \left(R_0 - 1\right)/R_0 \text{ , as stated in eq.} \quad (29)$$

Vaccination strategies aim to lower R_0 by reducing susceptibility through immunization or by minimizing contact rates via social distancing and other public health interventions. For highly contagious diseases, targeted vaccination of high-transmission groups (e.g., healthcare workers and essential personnel) can be especially effective [42].

3.6.2. Vaccine Efficacy

When designing vaccination programs, the effectiveness of the vaccine is a pivotal factor in determining the coverage needed to achieve herd immunity and effectively control the spread of infectious diseases. Vaccine efficacy refers to the percentage reduction in disease incidence among vaccinated individuals compared to those who are unvaccinated, typically measured under controlled conditions such as clinical trials. The success of a vaccination program hinges not only on achieving the herd immunity threshold (*HIT*) but also on accounting for the effectiveness of the vaccine. This adjustment ensures that enough individuals in the population are protected to reduce transmission. The relationship between vaccine efficacy (Ev) and the actual proportion of the population that must be vaccinated (Vc) can be expressed as:

$$Vc = HIT/Ev \quad (30)$$

3.6.3. Example Calculation

If *HIT* is 80% (0.8) and the vaccine efficacy is 90% (0.9), then:

$$Vc = 0.8/0.9 \approx 89\%$$

This means nearly 89% of the population must be vaccinated to achieve herd immunity. If vaccine efficacy is lower—say 70%—the required coverage rises to approximately 114%, indicating that additional interventions or booster doses would be necessary.

Vaccine efficacy plays a crucial role in shaping vaccination programs and determining the required coverage to achieve herd immunity. When vaccines have high efficacy, a smaller proportion of the population needs to be immunized, making it easier to control disease spread. Conversely, for vaccines with moderate efficacy, a larger portion of the population must be vaccinated, which can present logistical and resource challenges. Additionally, the efficacy observed in clinical trials may not always translate directly to real-world effectiveness due to factors such as improper storage, delays in dosing, or individual variations in immune response. To account for these discrepancies, vaccination programs must incorporate a buffer in coverage calculations to maintain adequate protection. Furthermore, population heterogeneity—including differences in susceptibility, contact patterns, and vaccine access—necessitates tailored strategies to ensure that adjusted coverage goals are met across diverse demographics and regions.

3.6.4. Limitations of the Herd Immunity Threshold in Real-World Epidemics

Herd immunity is often perceived as a definitive threshold beyond which disease transmission ceases, but this oversimplified view does not align with real-world epidemiology [3]. The commonly used formula for the herd immunity threshold, $1-1/R_0$, assumes homogeneous mixing, stable population dynamics, and lifelong immunity. For instance, if R_0 is 3, the threshold is estimated at 66%. However, real-world populations exhibit heterogeneous mixing, where individuals with high contact rates acquiring immunity may reduce transmission, but susceptible subgroups can sustain localized outbreaks. Additionally, population turnover through births and migration continuously replenishes the susceptible pool, explaining why diseases like measles persist despite strong lifelong immunity and high vaccination coverage [43]. Moreover, waning immunity and viral evolution further complicate herd immunity dynamics. Many respiratory viruses, including influenza, RSV, and coronaviruses, allow reinfections due to immune waning or antigenic drift. The COVID-19 pandemic demonstrated that vaccines, while effective in reducing severe illness, provide only temporary protection and do not entirely block transmission [44]. The emergence of immune-evasive variants, such as Omicron, has raised the effective reproduction number (R_t), increased herd immunity thresholds, and contributed to breakthrough infections [45]. Furthermore, vaccine hesitancy remains a critical challenge, as misinformation, distrust in healthcare systems, and logistical barriers hinder widespread uptake, preventing communities from reaching theoretical immunity levels [46]. These complexities highlight that herd immunity is not a fixed endpoint but a dynamic process influenced by epidemiological, immunological, and behavioral factors. As a result, infectious diseases rarely disappear entirely but often establish endemicity, necessitating ongoing public health interventions to manage their impact.

3.7. Limitations of R_0

While R_0 is a powerful metric in epidemiology, it has several limitations that must be considered when interpreting disease dynamics and public health strategies. The following details illustrate how these limitations impact R_0's estimate:

3.7.1. The Influence of Population Heterogeneity

Traditionally, R_0 is calculated under the assumption of an infinitely large, homogeneously mixed population. However, real-world populations exhibit heterogeneity in various forms—demographic structure, spatial distribution, and individual contact patterns—all of which can significantly impact R_0 estimates and disease dynamics [24].

Demographic factors such as age, immunity levels, and susceptibility create variations in R_0. Different age groups have varying levels of susceptibility and contact rates. For instance, children often have higher contact rates, increasing transmission potential, while the elderly may have weaker immune responses, prolonging infectious periods [47]. Age-structured contact matrices reveal that certain

groups interact more frequently, influencing transmission dynamics and leading to heterogeneous R_0 values [48]. Additionally, birth and death rates affect R_0; high birth rates continuously introduce new susceptible individuals, maintaining disease transmission and increasing R_0 over time [3].

Geographical factors also shape disease spread and R_0 estimates. Densely populated urban areas facilitate higher contact rates, increasing R_0, whereas rural areas experience slower transmission due to lower population density [49]. Movement between regions, such as commuting and migration, can introduce infections to new populations, modifying local R_0 values and influencing regional outbreaks [50]. Additionally, natural barriers (e.g., mountains, rivers) and artificial interventions (e.g., lockdowns, travel restrictions) alter contact networks and may lower R_0 by limiting transmission pathways [51].

Variability in individual interactions plays a crucial role in shaping R_0. Some individuals, known as super-spreaders, may have disproportionately high contact rates, leading to localized outbreaks with much higher R_0 values [52]. Social and professional networks create household and workplace transmission clusters, causing local variations in R_0 and influencing epidemic wave patterns [53]. Furthermore, public health measures such as mask-wearing, social distancing, and vaccination uptake impact transmission rates and the effective R_0 [54].

The effect of heterogeneity on R_0 differs between infinite and finite populations. In infinite populations, heterogeneity generally increases R_0 because high-contact individuals spread the disease more effectively, making eradication more difficult [55]. In finite populations, the effects become more complex. When R_0 is small relative to the population size, heterogeneity increases R_0 by enhancing transmission efficiency. However, when R_0 is large relative to the population size, heterogeneity can reduce R_0, making disease control easier than predicted by classical models [56].

Heterogeneity in population structure and behavior influences epidemic dynamics and intervention strategies. Simplistic models that assume homogeneous mixing may misestimate R_0, leading to inaccurate predictions of disease spread [57]. Population heterogeneity can also cause staggered outbreaks as different subpopulations experience transmission at different times [58]. Additionally, vaccination strategies prioritizing high-contact individuals can lower R_0 more effectively than uniform approaches [59].

Population heterogeneity plays a crucial role in determining R_0 and shaping disease dynamics. Epidemiological models must account for variations in demographic structure, spatial distribution, and individual contact patterns to improve predictive accuracy and optimize intervention strategies. Network-based, spatially explicit, and age-structured models provide more realistic estimates of R_0, aiding in more effective disease control and prevention measures.

3.7.2. Homogeneity Assumptions

Many R_0 calculations assume that individuals in a population mix homogeneously, meaning that everyone has an equal chance of coming into contact with an

infected individual. Populations have structured interactions influenced by factors such as age, geography, and social behavior. For example, diseases spread differently in urban areas versus rural communities due to variations in population density and movement patterns [60].

3.7.3. Static Nature

R_0 is a theoretical measure based on an entirely susceptible population, meaning it does not account for dynamic changes over time. Factors such as acquired immunity, vaccination campaigns, behavioral adaptations (e.g., social distancing), and government interventions all influence disease transmission. The effective reproduction number (R_t) is often used instead to measure real-time disease spread, as it evolves based on current population immunity and control measures [43].

3.7.4. Dependence on Model Structure

The estimated value of R_0 depends on the underlying epidemiological model used, including assumptions about transmission pathways, incubation periods, and intervention effectiveness. This variability makes it difficult to compare R_0 values across studies and diseases. For instance, different studies on COVID-19 reported varying R_0 estimates due to differences in data sources, population settings, and modeling techniques [60].

Examples: The following examples illustrate how R_0 and the corresponding herd immunity thresholds vary across diseases, and they highlight the importance of tailored public health strategies that consider real-world complexities such as vaccine efficacy, population behavior, and viral evolution.

1) Measles: Measles is one of the most contagious diseases, with an R_0 estimated between 12 and 18. This high R_0 means that, in a completely susceptible population, one individual could infect 12 to 18 others. To achieve herd immunity against measles, approximately 92% - 95% of the population must be immunized. This example underscores why even small declines in vaccination rates can lead to significant outbreaks [61]. 2) Influenza: Seasonal influenza typically has a lower R_0, around 1.3. The herd immunity threshold in theory would be about 23% of the population needing immunity. However, due to antigenic drift (changes in the virus) and waning immunity, annual vaccination is necessary to manage and control influenza outbreaks effectively. 3) COVID-19: At the start of the COVID-19 pandemic, early estimates of SARS-CoV-2's R_0 were around 2 to 3, indicating moderate transmissibility. With the emergence of more contagious variants, such as Omicron—where R_0 was estimated to be as high as 8—the challenge of controlling the spread increased dramatically. Despite high vaccination rates, factors like waning immunity and variant evolution necessitated booster programs and reinstated non-pharmaceutical interventions (e.g., mask mandates, social distancing) to keep the effective reproduction number (R_t) below 1 [1].

These limitations do not diminish the utility of R_0; rather, they define how it should be applied in public health interventions. Instead of viewing R_0 as a fixed threshold for disease control, it should be used alongside other metrics, such as

the effective reproduction number (R_t), to guide dynamic response strategies. For instance, while R_0 helps estimate the herd immunity threshold for vaccination planning, real-world factors like vaccine efficacy, population heterogeneity, and waning immunity must also be considered. Similarly, outbreak containment relies on continuous monitoring of R_t rather than a static R_0 value. By integrating multiple data sources and adapting strategies based on real-time surveillance, public health officials can make informed decisions that effectively mitigate disease spread.

While R_0 provides insight into a pathogen's theoretical transmission potential in a fully susceptible population, real-world disease spread is far more complex. This is where another crucial metric, the effective reproduction number (R_t), becomes essential. Unlike R_0, which remains constant under idealized conditions, R_t fluctuates over time as immunity builds, public health measures are implemented, and behavioral adaptations occur, making it a vital metric for real-time epidemic monitoring.

3.8. The Effective Reproduction Number (R_t)

The growth and decline of an epidemic depend on changes in disease transmission over time. At the beginning of an outbreak, when the entire population is susceptible, transmission rates are typically high. As the epidemic progresses, transmission decreases due to behavioral changes, acquired immunity through infection, or immunization efforts. The epidemic reaches its peak when transmission drops below a critical threshold, meaning each infected individual no longer spreads the disease to more than one person on average. The effective reproduction number (R_t) quantifies this dynamic by measuring the average number of new infections generated by each case at a given time within a population, considering the impact of immunity, interventions, and behavioral changes [61]. It measures the actual transmission of a disease in a population where some people may be immune and control measures are in place. R_t is derived from R_0 but adjusts for factors such as vaccination, acquired immunity, social distancing, and public health interventions. It provides a real-time assessment of disease transmission. When $R_t > 1$, an outbreak continues to grow; when $R_t < 1$, the outbreak declines and eventually dies out.

Several factors influence the effective reproduction number (R_t), determining how a disease spreads within a population over time. Immunity and vaccination play a significant role, as increasing immunity—either through natural infection or vaccination—reduces the proportion of susceptible individuals, thereby lowering R_t [61]. However, if immunity wanes over time or new variants emerge that evade prior immunity, R_t may rise again, leading to renewed outbreaks. Public health measures, such as mask mandates, lockdowns, and social distancing, directly impact R_t by limiting transmission opportunities and reducing contact between infected and susceptible individuals. Additionally, behavioral changes at the individual level, such as avoiding crowded places, practicing good hygiene,

and adhering to health recommendations, can further decrease R_t, slowing disease spread even in the absence of formal interventions [29]. Understanding these factors is crucial for implementing effective, adaptive public health strategies.

At the onset of the COVID-19 pandemic, R_0 for SARS-CoV-2 was estimated to be between 2 and 3, indicating that each infected individual could transmit the virus to two or three others in a completely susceptible population. However, as governments implemented various public health measures—including lockdowns, mask mandates, and vaccination programs—the effective reproduction number (R_t) fluctuated. During periods of strict restrictions, R_t dropped below 1, leading to a decline in case numbers. Conversely, when these measures were relaxed, R_t increased again, triggering new waves of infections.

Compared to R_0, R_t provides a more practical and real-time assessment of disease transmission under prevailing conditions. While R_0 is useful for estimating the initial risk and informing control strategies, tracking R_t allows for ongoing evaluation of an outbreak's trajectory. By continuously monitoring R_t, public health officials can determine whether infections are increasing, decreasing, or stabilizing, enabling them to adapt interventions and optimize response strategies accordingly.

4. Conclusions

The concept of R_0 is critical for understanding the potential impact of a pathogen on a population and for informing the design of control strategies. It serves as a foundational tool for predicting outbreak dynamics, shaping vaccination policies, and assessing the effectiveness of public health interventions. R_0 is especially significant in the context of emerging infectious diseases, where its value in new host populations can determine whether a pathogen causes limited outbreaks or triggers widespread epidemics. However, while R_0 offers valuable insights, its limitations must be carefully considered. Real-world epidemiological scenarios rarely align with the idealized assumptions of homogeneous mixing, population stability, and permanent immunity, making the effective reproduction number (R_t) a more practical and dynamic metric for monitoring ongoing epidemics [40].

Moreover, disease control strategies based on R_0 alone can be misleading if they fail to account for factors like transient immunity, reinfection risks, and population heterogeneity. For example, the COVID-19 pandemic underscored how interventions such as vaccination, social distancing, and changes in behavior can continuously influence R_t, often in ways not captured by static R_0 estimates. Thus, while R_0 remains an essential epidemiological tool, it should be used in conjunction with other metrics and real-world data to guide public health decision-making effectively. A comprehensive approach—incorporating diverse modeling techniques, surveillance data, and adaptive interventions—is key for optimal epidemic control and preparedness.

In conclusion, while R_0 is indispensable for understanding disease transmission dynamics, it must be interpreted within the context of pathogen characteris-

tics, population behaviors, and healthcare system capacities. Integrating R_0 estimates with real-time data improves the accuracy of predictions, enabling more effective decision-making [40]. As pathogen dynamics continue to evolve, future research should focus on refining R_0 estimation methods across various populations and environmental conditions to strengthen global disease control strategies and preparedness.

Authorship Contribution Statement

Hamid H. Hussien contributed to the conceptualization, methodology, investigation, formal analysis, and supervision, as well as drafting the original manuscript. Khalid Rhamtallah Genawi played a key role in conceptualization, methodology, formal analysis, data curation, validation, and supervision, while also contributing to the review and editing of the manuscript. Nuha Hassan Hagabdulla was involved in methodology, formal analysis, validation, and resource management, along with reviewing and editing the manuscript. Khalda M. Y. Ahmed provided critical revisions, ensuring clarity, grammatical accuracy, and intellectual coherence. All authors actively participated in discussing the results and refining the manuscript.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

[1] Patil, V.C., Ali, G.S., Nashte, A., Rautdesai, R., Garud, S.K. and Sable, N.P. (2023) Public Health Policy and Infectious Disease Control: Lessons from Recent Outbreaks. *South East European Journal of Public Health*, **XXI**, 162-170. https://www.seejph.com/index.php/seejph/article/view/449

[2] Peddinti, S. and Sabbani, Y. (2024) Mathematical Modeling of Infectious Disease Spread Using Differential Equations and Epidemiological Insights. *Journal of Nonlinear Analysis and Optimization*, **15**, 114-122.

[3] Anderson, R.M. and May, R.M. (1991) Infectious Diseases of Humans: Dynamics and Control. Oxford University Press.

[4] Amburi, S., Jalan, V. and Saravanan, S. (2021) Transforming Native Epidemic Models by Using the Machine Learning Approach. *Annals of the Romanian Society for Cell Biology*, **25**, 2891-2899.

[5] Delamater, P.L., Street, E.J., Leslie, T.F., Yang, Y.T. and Jacobsen, K.H. (2019) Complexity of the Basic Reproduction Number (R_0). *Emerging Infectious Diseases*, **25**, 1-4. https://doi.org/10.3201/eid2501.171901

[6] Heffernan, J.M., Smith, R.J. and Wahl, L.M. (2005) Perspectives on the Basic Reproductive Ratio. *Journal of The Royal Society Interface*, **2**, 281-293. https://doi.org/10.1098/rsif.2005.0042

[7] Roberts, M.G. (2007) The Pluses and Minuses of $_0$. *Journal of The Royal Society Interface*, **4**, 949-961. https://doi.org/10.1098/rsif.2007.1031

[8] Pellis, L., Ball, F. and Trapman, P. (2012) Reproduction Numbers for Epidemic Models with Households and Other Social Structures. I. Definition and Calculation of R_0. *Mathematical Biosciences*, **235**, 85-97. https://doi.org/10.1016/j.mbs.2011.10.009

[9] Dembek, Z.F., Chekol, T. and Wu, A. (2018) Best Practice Assessment of Disease Modelling for Infectious Disease Outbreaks. *Epidemiology and Infection*, **146**, 1207-1215. https://doi.org/10.1017/s095026881800119x

[10] Corteel, M. (2025) Shaping Epidemic Dynamics: An Historical Epistemology Study of the SIR Model. *History of the Human Sciences*. https://doi.org/10.1177/09526951251317104

[11] AlQadi, H. and Bani-Yaghoub, M. (2022) Incorporating Global Dynamics to Improve the Accuracy of Disease Models: Example of a COVID-19 SIR Model. *PLOS ONE*, **17**, e0265815. https://doi.org/10.1371/journal.pone.0265815

[12] Amiri Babaei, N., Kröger, M. and Özer, T. (2024) Theoretical Analysis of a SIRD Model with Constant Amount of Alive Population and COVID-19 Applications. *Applied Mathematical Modelling*, **127**, 237-258. https://doi.org/10.1016/j.apm.2023.12.006

[13] Giordano, G., Blanchini, F., Bruno, R., Colaneri, P., Di Filippo, A., Di Matteo, A., *et al.* (2020) Modelling the COVID-19 Epidemic and Implementation of Population-Wide Interventions in Italy. *Nature Medicine*, **26**, 855-860. https://doi.org/10.1038/s41591-020-0883-7

[14] Sen, D. and Sen, D. (2021) Use of a Modified SIRD Model to Analyze COVID-19 Data. *Industrial & Engineering Chemistry Research*, **60**, 4251-4260. https://doi.org/10.1021/acs.iecr.0c04754

[15] Chen, Y., Liu, F., Yu, Q. and Li, T. (2021) Review of Fractional Epidemic Models. *Applied Mathematical Modelling*, **97**, 281-307. https://doi.org/10.1016/j.apm.2021.03.044

[16] Wang, P. and Jia, J. (2019) Stationary Distribution of a Stochastic SIRD Epidemic Model of Ebola with Double Saturated Incidence Rates and Vaccination. *Advances in Difference Equations*, **2019**, Article No. 433. https://doi.org/10.1186/s13662-019-2352-5

[17] Zafar, Z.U.A., Rehan, K. and Mushtaq, M. (2017) HIV/AIDS Epidemic Fractional-Order Model. *Journal of Difference Equations and Applications*, **23**, 1298-1315. https://doi.org/10.1080/10236198.2017.1321640

[18] Miniguano-Trujillo, A., Pearson, J.W. and Goddard, B.D. (2025) A Constrained Optimisation Framework for Parameter Identification of the SIRD Model. *Mathematical Biosciences*, **380**, Article ID: 109379. https://doi.org/10.1016/j.mbs.2025.109379

[19] Tsay, C., Lejarza, F., Stadtherr, M.A. and Baldea, M. (2020) Modeling, State Estimation, and Optimal Control for the US COVID-19 Outbreak. *Scientific Reports*, **10**, Article No. 10711. https://doi.org/10.1038/s41598-020-67459-8

[20] Afful, B.A., Safo, G.A., Marri, D., Okyere, E., Ohemeng, M.O. and Kessie, J.A. (2025) Deterministic Optimal Control Compartmental Model for COVID-19 Infection. *Modeling Earth Systems and Environment*, **11**, Article No. 87. https://doi.org/10.1007/s40808-024-02183-0

[21] Diekmann, O. and Heesterbeek, J.A.P. (2000) Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation (Vol. 5). John Wiley & Sons.

[22] Anastassopoulou, C., Russo, L., Tsakris, A. and Siettos, C. (2020) Data-Based Analysis, Modelling and Forecasting of the COVID-19 Outbreak. *PLOS ONE*, **15**, e0230405. https://doi.org/10.1371/journal.pone.0230405

[23] Boonpatcharanon, S., Heffernan, J.M. and Jankowski, H. (2022) Estimating the Basic Reproduction Number at the Beginning of an Outbreak. *PLOS ONE*, **17**, e0269306. https://doi.org/10.1371/journal.pone.0269306

[24] Diekmann, O., Heesterbeek, J.A.P. and Roberts, M.G. (2013) The Construction of Next-Generation Matrices for Compartmental Epidemic Models. *Journal of the Royal Society Interface*, **10**, Article ID: 20120656.

[25] Ferguson, N.M., Laydon, D., Nedjati-Gilani, G., Imai, N., Ainslie, K., Baguelin, M., Ghani, A.C., *et al.* (2020) Impact of Non-Pharmaceutical Interventions (NPIs) to Reduce COVID-19 Mortality and Healthcare Demand. Imperial College London. https://doi.org/10.25561/77482

[26] Southall, E., Ogi-Gittins, Z., Kaye, A.R., Hart, W.S., Lovell-Read, F.A. and Thompson, R.N. (2023) A Practical Guide to Mathematical Methods for Estimating Infectious Disease Outbreak Risks. *Journal of Theoretical Biology*, **562**, Article ID: 111417. https://doi.org/10.1016/j.jtbi.2023.111417

[27] Fox, J.P., Elveback, L., Scott, W., Gatewood, L. and Ackerman, E. (1995) Herd Immunity: Basic Concept and Relevance to Public Health Immunization Practices1 *American Journal of Epidemiology*, **141**, 187-197. https://doi.org/10.1093/oxfordjournals.aje.a117420

[28] Greenhalgh, T., Alwan, N., Bogaert, D., Burns, S.H., Cheng, K.K., Colbourn, T., Tannock, C., *et al.* (2020) COVID-19: An Open Letter to the UK's Chief Medical Officers. https://blogs.bmj.com/bmj/2020/09/21/covid-19-an-open-letter-to-the-uks-chief-medical-officers

[29] Sanche, S., Lin, Y.T., Xu, C., Romero-Severson, E., Hengartner, N. and Ke, R. (2020) High Contagiousness and Rapid Spread of Severe Acute Respiratory Syndrome Coronavirus 2. *Emerging Infectious Diseases*, **26**, 1470-1477. https://doi.org/10.3201/eid2607.200282

[30] Liu, Y. and Rocklöv, J. (2022) The Effective Reproductive Number of the Omicron Variant of SARS-CoV-2 Is Several Times Relative to Delta. *Journal of Travel Medicine*, **29**, taac037. https://doi.org/10.1093/jtm/taac037

[31] Biggerstaff, M., Cauchemez, S., Reed, C., Gambhir, M. and Finelli, L. (2014) Estimates of the Reproduction Number for Seasonal, Pandemic, and Zoonotic Influenza: A Systematic Review of the Literature. *BMC Infectious Diseases*, **14**, Article No. 480. https://doi.org/10.1186/1471-2334-14-480

[32] Nguyen, P., Ajisegiri, W.S., Costantino, V., Chughtai, A.A. and MacIntyre, C.R. (2021) Reemergence of Human Monkeypox and Declining Population Immunity in the Context of Urbanization, Nigeria, 2017-2020. *Emerging Infectious Diseases*, **27**, 1007-1014. https://doi.org/10.3201/eid2704.203569

[33] Fine, P.E.M., Jezek, Z., Grab, B. and Dixon, H. (1988) The Transmission Potential of Monkeypox Virus in Human Populations. *International Journal of Epidemiology*, **17**, 643-650. https://doi.org/10.1093/ije/17.3.643

[34] Grant, R., Nguyen, L.L. and Breban, R. (2020) Modelling Human-to-Human Transmission of Monkeypox. *Bulletin of the World Health Organization*, **98**, 638-640. https://doi.org/10.2471/blt.19.242347

[35] Althaus, C.L. (2014) Estimating the Reproduction Number of Ebola Virus (EBOV) during the 2014 Outbreak in West Africa. *PLOS Currents*, **6**, 5 p. https://doi.org/10.1371/currents.outbreaks.91afb5e0f279e7f29e7056095255b288

[36] Heesterbeek, J.A.P. (2002) A Brief History of R_0 and a Recipe for Its Calculation. *Acta Biotheoretica*, **50**, 189-204. https://doi.org/10.1023/a:1016599411804

[37] Adegoke, B.O., Odugbose, T. and Adeyemi, C. (2024) Data Analytics for Predicting Disease Outbreaks: A Review of Models and Tools. *International Journal of Life Science Research Updates*, **2**, 1-9. https://doi.org/10.53430/ijlsru.2024.2.2.0023

[38] Alimohamadi, Y., Taghdir, M. and Sepandi, M. (2020) Estimate of the Basic Reproduction Number for COVID-19: A Systematic Review and Meta-Analysis. *Journal of Preventive Medicine and Public Health*, **53**, 151-157. https://doi.org/10.3961/jpmph.20.076

[39] Breban, R., Vardavas, R. and Blower, S. (2007) Theory versus Data: How to Calculate R_0? *PLoS ONE*, **2**, e282. https://doi.org/10.1371/journal.pone.0000282

[40] Cori, A., Ferguson, N.M., Fraser, C. and Cauchemez, S. (2013) A New Framework and Software to Estimate Time-Varying Reproduction Numbers during Epidemics. *American Journal of Epidemiology*, **178**, 1505-1512. https://doi.org/10.1093/aje/kwt133

[41] Grenfell, B.T., Pybus, O.G., Gog, J.R., Wood, J.L.N., Daly, J.M., Mumford, J.A., *et al.* (2004) Unifying the Epidemiological and Evolutionary Dynamics of Pathogens. *Science*, **303**, 327-332. https://doi.org/10.1126/science.1090727

[42] Hall, V., Foulkes, S., Insalata, F., Kirwan, P., Saei, A., Atti, A., *et al.* (2022) Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection. *New England Journal of Medicine*, **386**, 1207-1220. https://doi.org/10.1056/nejmoa2118691

[43] Grenfell, B.T. and Anderson, R.M. (1989) Pertussis in England and Wales: An Investigation of Transmission Dynamics and Control by Mass Vaccination. *Proceedings of the Royal Society B*: *Biological Sciences*, **236**, 213-252.

[44] Chemaitelly, H., Tang, P., Hasan, M.R., AlMukdad, S., Yassine, H.M., Benslimane, F.M., *et al.* (2021) Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar. *New England Journal of Medicine*, **385**, e83. https://doi.org/10.1056/nejmoa2114114

[45] Burki, T.K. (2022) Omicron Variant and Booster COVID-19 Vaccines. *The Lancet Respiratory Medicine*, **10**, e17. https://doi.org/10.1016/s2213-2600(21)00559-2

[46] Troiano, G. and Nardi, A. (2021) Vaccine Hesitancy in the Era of Covid-19. *Public Health*, **194**, 245-251. https://doi.org/10.1016/j.puhe.2021.02.025

[47] Mossong, J., Hens, N., Jit, M., Beutels, P., Auranen, K., Mikolajczyk, R., *et al.* (2008) Social Contacts and Mixing Patterns Relevant to the Spread of Infectious Diseases. *PLOS Medicine*, **5**, e74. https://doi.org/10.1371/journal.pmed.0050074

[48] Robertson, D., Heriot, G. and Jamrozik, E. (2024) Herd Immunity to Endemic Diseases: Historical Concepts and Implications for Public Health Policy. *Journal of Evaluation in Clinical Practice*, **30**, 625-631. https://doi.org/10.1111/jep.13983

[49] Rocklöv, J. and Sjödin, H. (2020) High Population Densities Catalyse the Spread of Covid-19. *Journal of Travel Medicine*, **27**, taaa038. https://doi.org/10.1093/jtm/taaa038

[50] Colizza, V., Barrat, A., Barthélemy, M. and Vespignani, A. (2007) Predictability and Epidemic Pathways in Global Outbreaks of Infectious Diseases: The SARS Case Study. *BMC Medicine*, **5**, Article No. 34. https://doi.org/10.1186/1741-7015-5-34

[51] Kraemer, M.U.G., Yang, C., Gutierrez, B., Wu, C., Klein, B., Pigott, D.M., *et al.* (2020) The Effect of Human Mobility and Control Measures on the COVID-19 Epidemic in China. *Science*, **368**, 493-497. https://doi.org/10.1126/science.abb4218

[52] Lloyd-Smith, J.O., Schreiber, S.J., Kopp, P.E. and Getz, W.M. (2005) Superspreading and the Effect of Individual Variation on Disease Emergence. *Nature*, **438**, 355-359. https://doi.org/10.1038/nature04153

[53] Danon, L., Ford, A.P., House, T., Jewell, C.P., Keeling, M.J., Roberts, G.O., *et al.* (2011) Networks and the Epidemiology of Infectious Disease. *Interdisciplinary Perspectives on Infectious Diseases*, **2011**, Article ID: 284909. https://doi.org/10.1155/2011/284909

[54] Brauner, J.M., Mindermann, S., Sharma, M., Johnston, D., Salvatier, J., Gavenčiak, T., *et al.* (2021) Inferring the Effectiveness of Government Interventions against Covid-19. *Science*, **371**, eabd9338. https://doi.org/10.1126/science.abd9338

[55] Pastor-Satorras, R., Castellano, C., Van Mieghem, P. and Vespignani, A. (2015) Epidemic Processes in Complex Networks. *Reviews of Modern Physics*, **87**, 925-979. https://doi.org/10.1103/revmodphys.87.925

[56] Ball, F. and Neal, P. (2002) A General Model for Stochastic SIR Epidemics with Two Levels of Mixing. *Mathematical Biosciences*, **180**, 73-102. https://doi.org/10.1016/s0025-5564(02)00125-6

[57] Keeling, M.J. and Rohani, P. (2008) Modeling Infectious Diseases in Humans and Animals. Princeton University Press.

[58] Kiss, I.Z., Miller, J.C. and Simon, P.L. (2017) Mathematics of Epidemics on Networks: From Exact to Approximate Models. Springer. https://doi.org/10.1007/978-3-319-50806-1_1

[59] Bansal, S., Grenfell, B.T. and Meyers, L.A. (2007) When Individual Behaviour Matters: Homogeneous and Network Models in Epidemiology. *Journal of The Royal Society Interface*, **4**, 879-891. https://doi.org/10.1098/rsif.2007.1100

[60] Wallinga, J. and Lipsitch, M. (2006) How Generation Intervals Shape the Relationship between Growth Rates and Reproductive Numbers. *Proceedings of the Royal Society B: Biological Sciences*, **274**, 599-604. https://doi.org/10.1098/rspb.2006.3754

[61] Wallinga, J. (2004) Different Epidemic Curves for Severe Acute Respiratory Syndrome Reveal Similar Impacts of Control Measures. *American Journal of Epidemiology*, **160**, 509-516. https://doi.org/10.1093/aje/kwh255