IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

"Mathematical Modeling of Infectious Diseases: Insights, Challenges, and Strategies for Epidemic Control"

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ABSTRACT

Mathematical modelling plays a crucial role in understanding and controlling infectious diseases. The abstract provides an overview of the insights, challenges, and strategies associated with this field, shedding light on its significance in epidemic control.

In the realm of infectious diseases, mathematical modelling serves as a powerful tool for gaining insights into the dynamics of disease transmission. Through the use of mathematical equations and computational simulations, researchers can analyse patterns of spread, estimate key parameters such as transmission rates and immunity levels, and assess the potential impact of interventions. These insights are instrumental in formulating effective strategies for disease control and prevention.

However, the field of mathematical modelling of infectious diseases is not without its challenges. One of the primary hurdles is the inherent complexity of disease dynamics, which can be influenced by various factors such as population movement, immunity levels, and pathogen evolution. Additionally, obtaining accurate data for model inputs and validating model outputs against real-world observations pose significant challenges. Furthermore, the dynamic nature of infectious diseases demands continuous model refinement to keep pace with changing epidemiological trends.

Despite these challenges, researchers and public health professionals have developed innovative strategies for epidemic control based on mathematical Modeling. These strategies encompass a wide range of interventions, including vaccination campaigns, targeted treatment programs, and non-pharmaceutical interventions such as social distancing measures. Mathematical models have been instrumental in guiding policy decisions and assessing the potential impact of different control measures, thereby aiding in the development of robust epidemic control strategies.

In summary, the abstract provides a glimpse into the world of mathematical Modeling of infectious diseases, outlining the valuable insights it offers, the challenges it poses, and the strategies it facilitates for epidemic control. This comprehensive overview sets the stage for further exploration and development in this critical area of public health.

Key words: Mathematical modelling, Infectious diseases, Insights, Challenges, Epidemic control

Introduction

It is a long-standing belief that infectious illness transmission and dissemination are governed by mathematically explicable principles. Daniel Bernoulli wrote a paper in 1766 on the consequences of smallpox variolation, a predecessor using mathematical life table analysis to examine the impact of immunization on

life expectancy (Dietz and Heesterbeek 2000). But the true understanding of the nonlinear dynamics of infectious illness spread did not emerge until the 20th century. There was a lot of debate at the start of that century on why an epidemic terminated before all vulnerable individuals were sick, with theories ranging from the pathogen's fluctuating severity throughout the epidemic to this. One of the first to realize that the pandemic may be stopped by the decreasing density of vulnerable individuals alone was Hamer (1906). Sir Ronald Ross, who won the Nobel Prize in 1902 for deciphering the malaria parasite's life cycle, using mathematical modelling to assess the efficacy of different malaria intervention techniques.

A set of differential equations was used by Kermack and McKendrick to explain the dynamics of disease transmission in a series of publications they released in 1927 (Kermack and McKendrick 1991a; Kermack and McKendrick 1991b; Kermack and McKendrick 1991c). The idea of a threshold quantity dividing several dynamic regimes was invented by them. An infectious illness can only spread in a vulnerable population if the so-called fundamental reproduction number is higher than a certain value. This gives rise to the idea of "herd immunity" in the context of vaccination, which holds that an infectious illness may be eradicated without vaccinating the whole population. The usefulness of this hypothesis was shown in the 1970s smallpox eradication effort. The virus was eradicated by a combination of ring vaccination and immunization coverage of around 80% throughout the globe.

Only toward the close of the 20th century did mathematical modelling become more widely used in the formulation of public health policy. During the first two decades of the AIDS pandemic, modelling techniques were employed more often to forecast the epidemic's future trajectory and to attempt to pinpoint the best preventative measures. But the need to assess intervention tactics for recently emerging and re-emerging infections was the true mathematical modelling influence on public health. First, the application of mathematical modelling to integrate historical data from smallpox outbreaks with concerns about vaccination in contemporary countries was spurred by the prospect of a bioterrorist strike using smallpox virus (Ferguson et al. 2003). The application of mathematical modelling for real-time analysis of infectious disease outbreak data to evaluate the efficacy of intervention strategies was later spurred by the SARS virus epidemic, which was a newly developing pathogen (Wallinga and Teunis 2004).

The key finding from the analysis of historical data about influenza A pandemic outbreaks is that, while the serial interval is short, the fundamental reproduction number of influenzas has historically been low (Mills et al. 2004). This suggests that, in theory, low levels of intervention may end an influenza epidemic, but that successful intervention requires quick action. In contrast, extremely high vaccination coverage is required for the eradication of an illness with a high basic reproduction number, like the measles. The assessment of current interventions and the establishment of suitable intervention policies both greatly benefit from such mathematically derived insights.

Basic Concepts in Mathematical Modeling

Unlike statistical models, the fundamental concept of transmission models is a mechanical account of the spread of illness between two people.

By connecting the individual level mechanism of transmission with a population level description of the incidence and prevalence of an infectious illness, this mechanistic explanation enables the mathematical description of the temporal evolution of an epidemic. Because of the exacting mathematical method used to express these connections, a thorough analysis of every dynamic process involved in the spread of illness is required. Consequently, creating a mathematical model aids in concentrating attention on the crucial mechanisms influencing the epidemiology of an infectious illness and identifies the factors that have the most influence and are most controllable. Consequently, the integration of information from several disciplines such as microbiology, social sciences, and clinical sciences is made possible by mathematical modelling. People may be classified as "susceptible," "infected," or "recovered and immune" for a variety of illnesses, including smallpox and influenza. These phases of infection are experienced by the susceptible impacted by an epidemic.

The reproduction number (represented by the symbol R) is a crucial parameter in the epidemiology of infectious diseases. It represents the total number of secondary cases that are contaminated by a single infectious person. For instance, if the reproduction number R = 3 (where the generation time equals the infectivity duration) is met, we may illustrate the usual evolution of an epidemic.

In the first generation, the number of new infections rises by a factor equal to the reproduction number R. Throughout the duration of the pandemic, the pool of vulnerable people becomes smaller. The pandemic ends when the last afflicted individual doesn't get in touch with anybody who may be at risk.

The whole percentage of the population that becomes infected at some point throughout the epidemic is known as the infection attack rate, and it is represented by the letter A. The reproduction number R and the contact method, which outlines who contacts whom, are the only factors that affect this infectious attack rate. Assuming that infected contacts occur at random, we can show the general form of the relationship between the reproduction number R and the infection attack rate A.
With a reproduction number of roughly R = 1.5 for influenza and a reproduction number of roughly R = 5 for smallpox, respectively, we expect that over half of the population will contract the new infection during an epidemic without treatment. This gives us a straightforward and reliable relationship that illustrates what would happen if a new infection were to strike a population that was completely susceptible to it.
We must consider the normal course of an individual host's infection in order to fully depict the dynamics of an epidemic over time. An infected host progresses through the prodromal phase, infectious period, recuperation phase, and immune phase throughout time (Fig. 12.4). Such timings for smallpox and influenza are shown in Fig. 12.4. The length of the incubation period and the degree of infectiousness in the prodromal phase, which comes before symptoms appear, and the symptomatic stage are critical factors in determining how well control measures like contact tracing and isolating symptomatic patients work.
The generation time T, another important epidemiological variable, is determined by the timeframes. The normal amount of time that passes between a source's infection and the infection of its secondary case or cases is known as this generation period. The generation time for influenza is around T = 3 days.
The generation period for smallpox is around T = 20 days.
When enough people are infected to prevent random occurrences that may cause the epidemic to stop too soon, the chain reaction nature of the epidemic process causes exponential growth in actual (calendar) time during the early phase of the epidemic. The exact timing of infection dictates the exponential growth rate, or r. The reproduction number R and the generation time T both have an upper bound on the growth rate r, that is, r > ln (R)/T.
We evaluate the effect of border closure on epidemic transmission to highlight the potency of this fundamental method of epidemic modelling.
Exponentially growing at a growth rate of r, the number of infected individuals who attempt to enter an uninfected nation across borders will rise. The majority of sick people will be stopped by border closures, but some may still manage to get through. Consequently, the number of imported cases will decrease exponentially by a factor of p when the borders are closed. This decrease is equivalent to a delay of at most (–ln p /ln R) T in the exponential rise of the number of imported cases. Closing borders will thus only prevent the import of cases for a limited number of infectious generations. For example, the arrival of an influenza pandemic and the introduction of a smallpox epidemic may be delayed by about one and two months, respectively, if closure was to decrease all infected passengers who would have otherwise crossed the border to 1%.
The reproduction number R and the generation time T are the two main epidemiological factors that define the transmission of illness. When a new virus spreads, as SARS did in 2003, these critical factors are not recognized. However, even in the event of an epidemic of a more well-known sickness, like norovirus, we may be unsure of the exact values of these crucial elements. However, the best estimates for the generation time and reproduction number—as well as other characteristics like the incubation time and hospitalization rate—are essential if modelling is to be useful in the management of infectious diseases. If we knew every detail regarding the epidemic, estimation would be simple. We could easily measure the length of each time interval from the infection of a case back to the time of infection of its source if we knew exactly who had infected whom and when.
The distribution of the length of these time intervals would tell us about the generation interval. In a similar vein, we could just count the number of people that each diseased person infected, and the dispersion of these counts would tell us the number of reproductions. Of course, fragmentary observations, proxy measurements, and reporting delays are commonplace in the actual world when such information is unavailable. However, real-time estimating procedures have been put forth that make use of standard statistical techniques for handling missing data and censoring in an effort to reconstruct the likely patterns of who infected whom and when from the incomplete data and proxy measures (Wallinga and Teunis 2004; Cauchemez et al. 2006). The key takeaway is that data collection on cases (including the timing of symptom start) and the relationship between cases (including the presence of an epidemiological connection) is crucial during an epidemic. The more accurate the data, the more helpful it is to estimate the reproduction number R and the generation time

T, which are the two essential model ingredients. It can also be used to predict the likely future course of the epidemic in the absence of intervention and the amount of control effort needed to stop it.
Numerous concepts mentioned above may be expressed quantitatively in the so-called SIR model, which uses a set of ordinary differential equations to explain the dynamics of various individual states within the population. The compartments mentioned above represent the variables of the system: the group of susceptible individuals (denoted by S), the group of infected individuals (denoted by I), and the group of removed individuals (denoted by R) who have been immune-checked out of the process of transmission. The motions into and out of the three compartments are precisely described by the mathematical model. Birth is the movement into the compartment containing susceptible people; death is the migration out of all compartments; transmission of infection is the movement from S into I; and recovery is the movement from I into R.
Rates control transitions between compartments, and in the most basic form of the model, these rates are assumed to remain constant across time. The birth rate (ν) represents the influx of new vulnerable individuals into the population, the death rate (μ) the people lost to background mortality unrelated to the illness, and the recovery rate (γ) the percentage of diseased persons that recover into immunity. The phrase that uses a mass action word to describe the spread of infection at a rate β is the main component of the model. The concept of a mass action term for transmission is based on the premise that members of the population randomly collide and have an equal chance of doing so in a certain amount of time. Thus, for an individual who is susceptible, the likelihood of coming into contact with infected individuals is determined by their density or prevalence among the community. This may be expressed mathematically as $\lambda = \beta I$, where λ represents the so-called force of infection. The likelihood that a vulnerable individual may get an infection per unit of time is measured by the force of infection. It is dependent on prevalence, which may be defined as the proportion of infected individuals in the population or as the total number of infected individuals in the population. In the latter scenario, the population size N would be represented by the formula $\lambda = \beta I / N$. Beta is a composite quantity that measures both the likelihood of transmission upon contact (q) and the contact rate (κ), therefore $\beta = \kappa q$.
The starting state of the system, or the numbers or fractions of the population in the states S, I, and R at time t = 0, must be provided in order for the model to be fully defined. It is necessary to choose values for the parameters ν, μ, η, and β using either data estimations or conjecture.
The system's temporal evolution may then be calculated using conventional numerical techniques, beginning with the initial state.
The model currently explains the spread of illness in the absence of any potential interventions. Now that we've included neonatal immunization in this straightforward method, we can get some crucial insights into the impact of universal infant vaccination.
We use the letter p to represent the percentage of neonates that get their vaccinations right away. Consequently, the recruitment rate is now (1-p)ν into the susceptible compartment rather than ν, and pν is recruited straight into the immune compartment.

Basic Concepts: Reproduction Number, Final Size, Endemic Steady State, and Critical Vaccination Coverage

The SIR model may be used to illustrate the key ideas of epidemic models. First, let's look at an infectious illness, which spreads much more quickly than the population process. The birth rate (ν) and mortality rate (μ) may thus be seen as being very near to zero on the disease transmission scale.
When will the population's prevalence start to rise? When $dI/dt > 0$, an increase in prevalence indicates that $\beta SI/N > \gamma I$. As a result, $\beta S/N > \gamma$, or $\beta S/(\gamma N) > 1$, is obtained. When every member of the community is vulnerable, we get S = N, which indicates that if $\beta/\gamma > 1$, an infectious illness may spread across the whole susceptible population. Alternatively referred to as the fundamental reproduction number, the value $R0 = \beta/\gamma$ may be computed and determined for Any infectious disease model in theory. According to Diekmann et al. (1990) and Diekmann and Heesterbeek (2000), the fundamental reproduction number in biology refers to the total number of secondary infections that an index case causes in a population that is fully susceptible to him for the course of his infectious phase. When intervention measures are implemented or a portion of the population has previously been infected and is now immune, the number of secondary cases per index case is known as the effective reproduction number R, as discussed in Section 12.2.

Since each sick person often is replaced by several new infected individuals, the virus may spread across the population if R0 > 1. But this process can only go on for as long as there are enough people who are sensitive to it. The likelihood that an infected individual will come into contact with a susceptible person declines when a greater proportion of the population has recovered from the illness and developed immunity, and along with it does the average number of secondary cases that are generated. If there are no additional vulnerable people entering the community, as we previously anticipated, the pandemic breakout will inevitably come to an end. However, model analysis reveals that there will always be a subset of vulnerable people remaining after the epidemic has abated and that the outbreak's ultimate extent will never include the whole population. The implicit formula A = 1 – exp(–R0 A) may be used to demonstrate the relationship between the basic reproduction number and the ultimate size A, or attack rate in epidemiological terms. Put another way, the attack rate in a population that is fully susceptible to an infectious illness may be calculated if the basic reproduction number of the disease is known.

When we examine the system on a demographic time scale, when births and deaths are factors, the picture is different. With the same reasons as earlier and the assumption that ν and μ are positive, we get $R0 = \beta/(\gamma+\mu)$. Now, if R0 > 1, the system may reach an equilibrium state in which the transmission mechanism balances the birth rate of new susceptible individuals and each sick person typically spreads the illness to one new person. By setting the left-hand sides to zero and solving for the variables S, I, and R in terms of the model parameters, it is possible to calculate this so-called endemic equilibrium from the model equations. $N* = \nu/\mu$ is the first method used to get the steady state population size.

It should be noted that in the endemic steady state, the proportion of susceptible people $S*/N*$ is independent of the vaccination coverage p. Conversely, the frequency of infection $I*/N*$ is dependent on p; that is, until the point of elimination, the frequency falls linearly with increasing vaccination coverage. This implies that we may use pc = 1 – 1 / R0 to calculate the essential vaccination coverage, or the threshold coverage required for elimination, from 0 = 1–1 / R0 – pc. Naturally, the percentage of the population that must get vaccinations in order to eradicate an illness from the population rises with the fundamental reproduction number. It also implies, nevertheless, that eradication is possible even in cases when vaccination of the whole population is not possible.

The rationale is that the likelihood that someone who has not had vaccinations may be exposed decreases as the population's immune cell density rises. Herd immunity is the term used to describe this phenomenon, which protects vulnerable people indirectly by raising immunity levels in the community. Herd immunity may occasionally have a negative impact on a population's mean age at first infection, in addition to its beneficial effect of lowering the risk of infection for those who have not received vaccinations. If vaccination rates are not high enough, this might result in a higher frequency of unfavorable consequences that follow infection.

A minimum coverage of 96% is required for the eradication of measles, whose estimated basic reproduction number is approximately 20, but an illness like smallpox, with an estimated reproduction number of around 5, requires a coverage of 80%. This is one reason for why it was able to completely eliminate smallpox in the 1970s while eliminating measles remains a distant goal. On the other hand, several nations have been able to completely eradicate the measles because of a continuously high vaccination rate (Peltola et al. 1997).

Advanced Models

Based on the fundamental concepts of the SIR framework, a variety of mathematical models have been created in the interim, each adding more structure and information on the dynamics of infectious disease transmission.

More Complex Compartmental Models

Adding extra disease-specific information to a model is an obvious initial expansion. The literature has defined compartments that characterize a latent period, the vaccinated population, chronic and acute phases of infection, and many other things (Anderson and May 1991). Adding population heterogeneity to the model—for example, by differentiating between population subgroups with distinct behaviors, population subgroups with varying susceptibilities, or geographically distinct populations—is another crucial improvement to compartmental models.

Hethcote and Yorke's (1994) models of the transmission of sexually transmitted illnesses were the first to include heterogeneity in behavior.

Later, models that may explain population variability in sexual activity and mixing patterns between population subgroups of different degrees of sexual activity were put out during the first ten years of the HIV/AIDS epidemic (Koopman et al. 1988). These kinds of models are often used to evaluate how an intervention affects the transmission of STDs. Another way to describe age structure is as a set of compartments, where people move from one to the next based on how quickly they age. However, this approach necessitates adding a significant number of new compartments to the model structure. This further demonstrates the drawbacks of compartmental models: as population structure rises, so do the number of compartments and the need to characterize and parameterize the mixing between each population subgroup in the model.

Diekmann et al. (1990) created the notion of how to define and calculate the fundamental reproduction number in diverse populations. The concept of meta-populations has been used to study geographically separated population groups interacting with one another in order to analyze the dynamics of pediatric illnesses (Rohani et al. 1999).

Models with Continuous Age Structure

The ideal way to characterize age structure is as a continuous variable in which age increases with time. From a mathematical perspective, this results in partial differential equation models, in which time and age determine all of the model's variables (Diekmann and Heesterbeek 2000). Partial differential equations are more challenging to solve analytically than ordinary differential equations, but it is simple to solve an age-structured system of model equations numerically.

Stochastic Transmission Models

It is implicitly assumed that the numbers in the different compartments of a deterministic model based on a system of differential equations are big enough to allow for the disregard of stochastic effects. This isn't always the case, however. For instance, typical stochastic occurrences like the infection's extinction from the population or significant stochastic changes in the epidemic's ultimate size might occur when evaluating epidemic breakouts in tiny populations, like schools or small towns. Stochastic models, in contrast to deterministic models, are expressed in terms of integers, where the probabilities associated with state transitions are described. This indicates that results, like the ultimate size distribution, are expressed in terms of probability distributions. Numerous approaches have been used to investigate questions of stochastic impacts on infectious disease dynamics, ranging from the Reed–Frost model for a discrete temporal transmission of infection to a stochastic variant of the SIR model previously mentioned (Bailey 1975; Becker 1989). Lastly, Monte Carlo simulations, a kind of simulation method, have been used to study stochastic models.
The difference between minor and big outbreaks for infectious illnesses with R0 >1 is a significant theoretical finding from the study of stochastic models.In a stochastic model, a certain percentage of introductions remain tiny outbreaks with just a few secondary infections, but in a deterministic model, a R0 bigger than unity always results in an epidemic if the pathogen is introduced into a completely susceptible population. As a result, after one infectious index case is introduced, the ultimate epidemic size has a bimodal probability distribution. The scenario where the illness ends after just a few secondary infections is described by the peak for small outbreak sizes; the scenario where the epidemic takes off and affects a sizable portion of the population is described by the peak for big outbreak sizes. The greater the fundamental number of reproduction.

Network Models

It is difficult to accurately represent several elements of interpersonal interaction in compartmental models. The term "pair formation models" refers to models that were created in the context of the transmission of STDs that consider the length of relationships (Hadeler et al. 1988). The class of network models, where the network of connections is characterized by a graph with nodes representing persons and links reflecting their relationships, is produced by extending existing models to incorporate simultaneous long-term partnerships (Keeling and Eames 2005). The rate of an epidemic's population-wide spread has been linked to several network structure features. The majority of human interactions in the so-called small world networks are local, but certain long-distance connections guarantee an epidemic's quick worldwide spread (Watts and Strogatz 1998). As the 2003 SARS outbreak showed, long-distance illness propagation is becoming more and more significant in a globalizing society where people are moving around more. A recent discussion on the transmission of diseases brought up the idea of scale-free networks, in which the number of connections per node follows a power law distribution (that is, the chance that a node has k links is proportional to $k^{-\gamma}$ with a positive constant γ). When it comes to the transmission of STDs, a network structure in which some persons have a large number of partners while the majority have few might make it exceedingly difficult to intervene to manage the illness (Liljeros et al. 2001). The study of respiratory illness transmission has also made use of network principles (Meyers et al. 2003).

Use of Modeling for Public Health Policy

The efficacy of immunization programs, the ideal vaccination ages and target populations, and the amount of work required to eradicate an illness from the community have all been evaluated using mathematical models. More recently, mathematical modeling has helped in contingency planning for potential smallpox virus attacks (Ferguson et al. 2003) as well as planning public health responses to pandemic strains of influenza A outbreaks (Ferguson et al. 2006). A variety of other intervention strategies have also been tested, including contact tracing (Eames and Keeling 2003), antiviral therapy for HIV, and screening for asymptomatic Chlamydia trachomatis infection (Kretzschmar et al. 2001). Modeling has been used to examine hospital-specific treatments including health staff cohorting, improved cleanliness, and patient isolation in the context of nosocomial infections and the spread of antibiotic-resistant organisms (Grundmann and Hellriegel 2006). Dynamic transmission models have been identified in health economic assessments as a prerequisite for doing high-quality cost-effectiveness studies for the control of infectious diseases (Edmunds et al. 1999). From the development of mathematical theory for the dynamics of infectious illnesses to practical application in a setting important to public health, it is a big step. The latter requires a thorough examination of pertinent data sources, clinical expertise, and microbiological understanding in order to choose the best course of model construction.

In this case, the model is considered appropriate if it makes use of the information at hand, can respond to inquiries from decision-makers, and is sufficiently straightforward to allow for the interpretation and understanding of its workings. In the future, to further enhance modeling's efficacy as a public health tool, it will be critical to fortify the connection between sophisticated statistical methods and mathematical modeling.

Further Reading

Bailey (Bailey 1975) is one of the first thorough works on epidemic modeling. Bailey handles and connects stochastic and deterministic models to data. Although it focuses mostly on deterministic unstructured models, Anderson and May's (1991) book is a more contemporary but still classic work on infectious disease modeling. Its strength is a solid connection to facts and discussion of pertinent public health issues.

The mathematical theory of deterministic modeling is presented with several problems for the reader in Diekmann and Heesterbeek (2000). The book focuses on generalizing the basic reproduction number to heterogeneous populations and incorporating population heterogeneity into epidemic simulation. A basic introduction to stochastic epidemic modeling is provided in Andersson and Britton (2000). Advanced statistical techniques for the consideration of the unique features of infectious illness data are described by Becker (1989). Keeling and Rohani produced a recent book that included case examples from applications of epidemic modeling (2007).

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