

## Review Article

# Role of Modelling in Emerging Infectious Diseases

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## Abstract

**Background:** Emerging infectious diseases (EIDs) pose significant challenges to public health systems globally. They are diseases that are caused by an infectious pathogen that has evolved in the population in the past two decades, changed pathogenesis, or increased in incidence, geographic, impact, host, or vector range. Most EIDs are of animal origin. Climate change and increased international travel and trade facilitate the rapid spread of infectious agents across borders causing epidemics. Control and prevention strategies of EIDs are complicated and stressful as they require a One Health approach which involves collaboration between human, animal, environmental, and other disciplines. Modelling and prediction of EIDs outbreaks had gained attention due to the advance in big data and machine learning. Modelling is classified into broad categories; compartmental models which divide the population into compartments based on the disease status, agent-based models that simulate the behavior of individual agents, network models which represent interactions between individuals as a network (nodes and edges), and spatial models which incorporate geographic information to study how diseases spread across physical space.

**Conclusion:** Each modelling technique has strengths and limitations, and the choice of model depends on the specific policymaker questions, available data, and computational resources. Integrated approaches combining multiple techniques provide more comprehensive insights into infectious disease dynamics.

**Keywords:** modelling, emerging, re-emerging, infectious agents, communicable diseases

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## Emerging infectious diseases (EIDs)

Emerging infectious diseases (EIDs) are those diseases caused by an infectious pathogen that has newly evolved in the population in the past two decades or has existed but changed pathogenesis or increased in incidence, geographic, impact, host or vector range. <sup>(1)</sup>

A minor group of EIDs was considered major public and global concerns as they caused epidemics or pandemics. For a novel pathogen to become a threat, a contact between animal reservoir and human should occur (zoonotic spillover), then pathogen should be able to transmit from human-to-human.

The World Health Organization (WHO) reports that about 70-80% of EIDs are zoonoses. Vector-borne diseases account for 22.8% of EIDs, causing more than 700 000 deaths annually. For every decade since 1940, there has been a consistent increase in the number of EIDs from wildlife-related zoonosis. The main land hotspots of EIDs were between 30 and 60 degrees north and between 30 and 40 degrees south, mainly in northeastern United States, western Europe, Japan and southeastern Australia. <sup>(2)</sup>

## Classification of emerging infectious diseases

Emerging infections are classified by time and how

humans were involved in the emergence:

Newly emerging infectious diseases – diseases that were not previously described in humans, Re-emerging infectious diseases – those that come back after a major decline due to problems in public health control measures. Deliberately emerging infectious diseases – diseases created by humans for bioterrorism. Accidentally emerging infectious diseases – diseases created or spread unintentionally by humans, such as vaccine-derived poliovirus. <sup>(3)</sup>

In 2024, Centres for Disease Prevention and Control (CDC) reported the first human infection in the United States with an influenza (flu) virus that normally spreads in pigs. The infection with an influenza A (H1N2) variant occurred in a child living near a pig farm in Pennsylvania who had direct contact with pigs prior to illness onset. <sup>(4)</sup>

On 11 June 2024, WHO reported the second detection of Avian influenza (H9N2) in India. Most reported cases of H9N2 have been in China (122 cases). A human case of West Nile virus infection from countries of the European Economic Area was recorded, measles was reported in 22 countries, and 166 cholera cases and two deaths have been reported

in France. <sup>(4)</sup>

Monkeypox is a viral disease, It is categorized into two main genetic clades, Clade I and Clade II. Monkeypox is primarily found in Central and West Africa. On 14 August 2024, countries with documented increased number of cases included the Democratic Republic of Congo (DRC), Nigeria, Cameroon, and Central African Republic. Notable outbreaks occurred in the United States, the United Kingdom, and Denmark. <sup>(5)</sup>

#### Drivers of emerging infectious diseases events

- Climate change There is increased susceptibility to respiratory viral infections due to air pollution. Climatic changes may affect the pathogen's reservoir as the region with the optimal conditions expands. In vector-transmitted diseases: change in temperature and water availability affect transmission-related life cycle traits of the mosquito (biting rate, adult lifespan, population size and distribution) and the pathogen (extrinsic incubation rate).
- Increasing density of the human population and expanding into new geographic areas. As a result, more people live in close contact with wild and domestic animals, both livestock and pets.
- Changes in human demographics and behavior (sexual, cultural, and war). Demographic changes via urbanization may also affect dynamics. Influenza, for example, tends to exhibit more persistent outbreaks in more populous, denser urban regions. A similar pattern was reported in the early COVID-19 pandemic.<sup>(2)</sup>

#### Notable global outbreaks

##### COVID-19 pandemic

For over 3 years, the SARS-CoV-2 SARS-CoV-2 had 7,053,524 confirmed COVID-19 induced deaths worldwide.. A total of 144 waves of SARS-CoV-2 infections were identified in 30 countries. <sup>(3)</sup>

**Zika outbreak (2015-2016):** Zika virus is a mosquito-borne virus first identified in Uganda in monkey. It was the first time in more than 50 years that an infectious pathogen has been identified as the cause of birth defects. Zika was also linked to other problems, such as miscarriage, stillbirth, and Guillain-Barré syndrome. <sup>(6)</sup>

**Yellow fever:** Epidemic prone zoonotic disease caused by an arbovirus. Domestic, jungle, and semi-domestic transmission occurs by bite of aedes aegypti mosquitoes. <sup>(7)</sup>

**Ebola outbreak (2013-2016):** Ebola is introduced into human populations through close contact with the blood and other bodily fluids of infected animals as bats, chimpanzees, gorillas, monkeys. <sup>(8)</sup>

#### Regional situation of emerging infectious diseases

Increased conflict and political instability in WHO Eastern Mediterranean Region (EMR) led to an unusually high number of refugees living in overcrowded. Egypt is one of the most populated countries in EMR region. <sup>(9)</sup>

In last two decades, EIDs have been reported from 18 out of 22 countries in the region. Outbreaks of EIDs in the EMR include CCHF in Afghanistan, chikungunya in Pakistan and Sudan, cholera in Somalia, and Yemen, diphtheria in Pakistan and Yemen, influenza H5N1, and dengue fever in Egypt, leishmaniasis in Pakistan, Syria and Afghanistan, measles in Pakistan and Afghanistan, MERS in Arabian Peninsula, plague in Afghanistan, polio in Afghanistan and Pakistan, and Q fever in Afghanistan and Iraq. <sup>(9)</sup>

#### One Health Approach to Control EIDs

A One Health approach is the appropriate control and prevention strategy of EIDs which mobilizes human, animal, environmental sectors, disciplines and communities and other relevant disciplines to control public health threats and to monitor how diseases spread among human, animals, plants, and the environment. <sup>(10)</sup>

EIDs tend to be widespread and difficult to control, making them uniquely uncertain and unpredictable. Predicting which zoonotic diseases may arise in the future from which geographical areas or animal reservoirs is extremely difficult due to the multifactorial and constantly evolving nature of the risk factors involved. On the contrary, vector-transmitted infections and their associated risk factors can often be monitored as they are strongly influenced by environmental factors. <sup>(10)</sup>

#### Modelling of emerging infectious diseases

##### History of Modelling:

Since 1760, the first disease model of smallpox was developed, numerous mathematical models have been utilized to study disease transmission dynamics, and to predict, assess, and control infectious diseases.

Modern epidemiological analysis and modelling theory began in the late nineteenth and early twentieth centuries. By plotting cholera epidemic cases on a map. It was hypothesized that contaminated water was the predominant contributor to the cholera transmission in London in 1849. Then a discrete-time epidemic model for cholera transmission in 1906 was developed. These early spatial and temporal epidemic research, combined with the progress of biological studies, led to some important discoveries regarding disease transmission. <sup>(11)</sup>

##### Objective of modelling:

For human pathogens, the objective may be simply to minimise the number of individuals getting sick or

dying from infection, whilst for livestock or plant crop diseases, it may be important to minimise the direct cost of an outbreak to the agricultural industry. <sup>(11)</sup>

A model that works in one country is not necessarily successful elsewhere, so policy makers should consider the specific circumstances that are important in their countries but may not be included in models. Modelers and policy makers need to determine in interaction which questions can and should be answered by modelling and what the limitations of models are. <sup>(11)</sup>

### Steps of infectious diseases modelling

The Centers for Disease Control and Prevention (CDC) modelers generally initiate modelling in response to questions from decision makers. The modelers then work closely with the epidemiologists and other experts to answer the questions. The United States Government Accountability Office (GAO) identified four steps of modelling practices<sup>(12)</sup> : Communication between modeler and decision maker, Model description, Verification, and Validation.

### What is a model?

A model is a physical, mathematical, or logical representation of a system, phenomenon, or process that allows a researcher to investigate them in a controlled way. It is a simplified representation of reality expressed through mathematical or logical relationships. <sup>(13)</sup>

The use of mathematics and computer methods to understand the population dynamics of the transmission of infectious agents and the potential impact of infectious disease control program. Exploring health outcomes, and the effectiveness of pharmaceutical and nonpharmaceutical interventions are the core components of a model. By its synthetic nature, modelling for public health allows the integration of and socioeconomic factors to obtain a broad societal viewpoint. <sup>(13)</sup>

Models integrate diverse data like transmission rates, incubation periods, and public health intervention into an interpretable framework, to compare possible scenarios over time, to evaluate interventions, and to estimate the likelihood of different outcomes and their associated costs and benefits. <sup>(13)</sup>

### When modelling is considered not useful:

Modelling may be undesirable when it would take too long to engage the necessary external subject matter experts or when modelling would detract from responding to a disease. <sup>(12)</sup>

CDC did not use modelling when issuing a travel notice for an Ebola outbreak in specific provinces in the Democratic Republic of Congo. Instead, CDC based the travel order on an analysis that considered

disease incidence and prevalence, public health infrastructure, and the availability of therapeutics. <sup>(12)</sup>

### Infectious disease modelling categories:

- Statistical models. This type of model identifies relationships or patterns that can be used to describe what is occurring or predicts what may occur in the future based on what has occurred in the past. <sup>(46)</sup>

Statistical models tend to use a large amount of data, such as past observed events, to forecast future events, such as disease occurrence, but do not require a fundamental understanding of biological processes or human behavior. They can predict outcomes when causes are not known or understood and when scientific understanding of a disease is limited. They tend to use large amounts of data on past events to forecast future events. <sup>(14)</sup>

Statistical models (e.g., models based on regression or Bayesian analysis, or machine learning of data sets) These models test three broad classes: of hypotheses: Disease mapping, disease clustering, and ecological analysis.

- Mechanistic models: They rely heavily on scientific evidence and theory related to infectious diseases, and the understanding of disease dynamics or human behavior from prior knowledge, such as biological processes or interactions between people, to represent known processes. <sup>(11)</sup>

Mechanistic models (e.g compartmental (cohort), agent-based (individual) or combination models (combining elements from both types).

- Gravity models interactions based on Newton's Law of Gravity, which states that attraction between two objects is directly proportional to the product of their masses and inversely proportional to the square of the distance between them. The major criticism of the gravity model and its calibration are its lack of theoretical foundations related to human behavior and neglect of large, random contagious events, such as a super disease carrier traveling to the community. <sup>(11)</sup>
- Network-based models: use graph or networks to represent connections between individuals or groups. These models analyse how the structure of network affects the transmission of disease. <sup>(11)</sup>

### Compartmental Epidemiological models:

Compartmental models (deterministic or stochastic). It is commonly seen in their deterministic versions in which the population is subdivided into a number of mutually exclusive groups and contacts are assumed to be instantaneous and random. Humans flowing from one compartment to another as their exposures, diseases, or other conditions change. <sup>(15)</sup>

The three main elements of compartment models are compartments, transmissions (between compartments), and parameters. Compartmental models are more readily parameterised, but may lack the level of detail needed to answer policy related questions. <sup>(15)</sup>

These categorize individuals into groups based on their infection status:

**The classic Susceptible-Infected-Recovered or "SIR" model** divides a population into three categories: Susceptible to the disease (S), Infected and infectious (I), Recovered or removed from the infected or susceptible population (R). This model uses exploding numbers of equations to determine how many people move between these three categories. However, it largely ignores the effects of global dynamics of infection on local communities as they are well-connected and the assumption that the disease exists only within the community is invalid. <sup>(15)</sup>

#### **Weakness of the classical compartmental model:**

- Individuals in the same compartment are identical. For example, infected individuals transmit the disease to susceptible individuals at an average rate, and each individual has the same importance in the transmission chain.
- Each individual is indifferent without subjective initiative. Individuals will not change their action strategies or formulate nonpharmacological interventions (NPIs, similarly hereinafter) according to the development of the epidemic.
- The compartment is set according to the principle of the epidemic, not the actual observation data. For example, the infected person's compartment is set, but only the confirmed data can be obtained in reality, and the error of approximate substitution is unignorable. <sup>(16)</sup>

#### **SEIR Model (Susceptible, Exposed, Infected, Recovered): Adds an "exposed" state for diseases with an incubation period.**

In compartmental mathematical models, disease transmission occurs by the stochastic infection of a susceptible by a neighbouring infective, and spread takes place when infected individuals mix among susceptible. Thus, at any given time, some individuals from the susceptible segment become infected, while some of those who are infected join the recovered segment. It is assumed that these changes are continuous and can be described by differential equations.

A "SIR" model is a base compartmental model. Extended of SIR models are SIR with diffusion, contaminated environment, several strains of infection, and multiple routes of infection. <sup>(16)</sup>

When SIR is incorporated with an exposed (or latent) compartment model is a SEIR model; and in the cases

in which susceptibility returns after recovery, the model is called an SIS model. More complex mathematical models have been developed from these initial models by taking additional variables into account, such as births, deaths, and migration into and out of the population, or by monitoring the spread of multiple epidemics simultaneously. <sup>(16)</sup>

Compartments as "immune" to the disease may be added in measles models for those babies with maternally derived immunity.

#### **Agent-Based Models (ABMs):**

These simulate individual behaviors and interactions within a population, providing a more detailed picture of disease transmission. Individual (or agent) based micro-simulation models, in which individual agents and their interactions are simulated as a stochastic process with probability distributions describing population heterogeneity and transitions.

**Spatial models:** These consider geographic factors like population density and travel patterns to predict how EIDs might spread geographically. <sup>(11)</sup>

#### **Model parameters and data**

- **Basic Reproduction Number ( $R_0$ ):** Represents the average number of secondary infections produced by one infected individual in a fully susceptible population

If an infected individual averagely produces less than one new infected individual over the course of his/her infectious period, then  $R_0 < 1$  and the infection cannot expand or grow. If each infected individual produces averagely more than one new infection, then  $R_0 > 1$  and the disease can spread in the population. If  $R_0$  is equal to one ( $R_0 = 1$ ), the disease remains stable or endemic in the community, but will not cause an epidemic. <sup>(17)</sup> Value of  $R_0$  is affected by transmission probability, contact rate and duration of infectiousness.

Effective reproductive number ( $R$ ) can characterize the progression of an epidemic in a realistic scenario. It does not depend on the assumption that the population is completely susceptible. <sup>(17)</sup>

#### **Model types according to the parameters used:**

**Deterministic Models:** Use fixed parameters to predict disease dynamics. Chance does not play a role in these models. They define an exact outcome, and provide a clear, consistent prediction of disease spread but may not capture individual variability.

**Stochastic Models:** Incorporate randomness to account for variability in disease spread, particularly useful for small populations or early in an outbreak.

**Hybrid Models:** Combine elements of deterministic and stochastic models to leverage the strengths of both approaches.

### **Current programs for infectious diseases modelling Ebola modelling**

CDC used models to predict the number of Ebola cases that could be expected over time with and without disease interventions such as Ebola treatment units, community care centres, and safe burials. On the basis of this information and other factors, including a United Nations document on Ebola needs, CDC leadership and other U.S. government officials recommended a rapid increase in Ebola response aid. This increase helped to greatly reduce the actual number of cases, compared to the likely number if prompt action had not been taken. <sup>(12)</sup>

### **Zika modelling**

In 2020, a model was designed using parameters of mosquito biting rate, recruitment rate of mosquito, transmission probability per biting of susceptible humans with infected mosquito, rate of awareness in host population, recovery rates of infected human which were the most sensitive parameters of the considered Zika model. The model was validated by fitting with the reported Zika infected human data from 1 to 36-week of 2016 Zika outbreak in Colombia. A compartmental model described the vertical transmission of Zika to the foetus in the early stages of pregnancy in order to estimate the risk of microcephaly due to Zika. Other described the spread dynamics of Zika as both a vector-borne and sexually transmitted disease. <sup>(18)</sup>

### **Pandemic Influenza modelling**

The tool, Google Flu Trends, is a sophisticated Web-based tool for detection of regional outbreaks of influenza in the United States. It is so promising that the CDC is testing it in the United States. Preliminary testing suggests that Google Flu Trends can detect regional outbreaks of influenza 7–10 days before conventional CDC surveillance. The CDC uses laboratory and clinical data to publish national and regional weekly statistics, typically with 1–2 weeks lag in reporting. <sup>(19)</sup>

In response to the H7N9 influenza outbreak in 2017, models were used to determine when doses of influenza vaccine should be delivered and how many doses should be administered in order to mitigate a domestic outbreak. This model found that having a vaccine stockpile could be helpful in preventing disease. <sup>(12)</sup>

In Egypt, highly pathogenic avian influenza subtype H5N1 virus was first reported in poultry in 2006 and was declared to be enzootic in 2008, then during 2014–2015 winter season. Using ecological niche modelling, environmental, behavioral, and population characteristics of H5N1 and H9N2 within Egypt. The distance to live bird markets was a strong predictor of co-infection. <sup>(20)</sup> Another model predicted that targeting day-old chick avian influenza vaccination in industrial and large size hatcheries

would increase immunity levels in the overall poultry population in Egypt and especially in small commercial poultry farms (from < 30 % to > 60 %). <sup>(21)</sup>

### **Yellow Fever modelling**

Model used origin–destination flight data from 2016 and incidence estimates to predict the number of viraemic travellers capable of seeding local transmission in Asia. In high risk locations, a temperature-dependent reproduction number (R<sub>0</sub>) estimates were used and a branching process model to predict the probability of transmission. The model used the population size of each endemic country in 2016, and the average length of stay of international tourists to each endemic country. <sup>(22)</sup>

### **Rift Valley Fever modelling**

Models of transmission dynamics had variable assumptions, assumption was that vector bites hosts at a rate proportional to the number of hosts, and that a host is bitten at a rate proportional to the number of vectors. Other models assume that the rate at which a vector bites hosts is constant across host (reservoir) densities, while the number of bites received by a host is constant across vector densities. <sup>(23)</sup>

### **COVID-19 pandemic modelling**

COVID-19 pandemic has led to intensive and evolving use of alternative infectious disease prediction models. In the early 2020s, the first models used to emphasize the capacity for anticipation to inform policy decisions, in what is usually called “Predictive understanding” based on the theories that scientists place to infer conclusions and to formulate patterns (developing models) to decide the needs to control the outbreak. However, this proved to be scientifically insufficient, as there was a need to an explanatory knowledge to change the model by adapting it to emerging evidence. <sup>(24)</sup>

Develop a pandemic simulator that accounts for two essential aspects of the global spread of EIDs: (i) age-structured disease transmissions and (ii) the pandemic spread across global regions. Based on the simulator, global pandemic evolutions of EIDs and the effect of control measures under a wide range of scenarios was explored. <sup>(24)</sup>

After the outbreak of COVID-19, the three elements of the compartment model faced limitations. These limitations stem from a common cause: the influence of social systems on infectious disease systems. Whether it is nonpharmacological interventions, vaccination strategies, the intensity of population activity, or the age distribution of those infected, these varied effects can each be attributed to a single factor in the social system. <sup>(24)</sup>

### **Creating the initial model for personal protective equipment (PPE) demand for COVID-19:**

The initial population starts in the susceptible

compartment and flows into the infectious compartment at an infection rate  $\beta$ , then moves into the recovered compartment at a recovery rate defined by  $\lambda$  or into the deceased compartment at a mortality rate defined by  $\gamma$ .<sup>(24)</sup>

R(0) of SARS-CoV-2 cases was not traced accurately in the beginning of the pandemic, due to a limitation in resources such as insufficient availability of testing kits.

Historical R(t): was backward computed by searching literature for infection fatality rate (IFR) for SARS-CoV-2

To forecast the future R(t), different pandemic scenarios were generated, each with varying assumptions about public health intervention measures in effect:

**The SARS-CoV-2 containment scenario**—attempts to model a situation where strict public health intervention measures are in place (i.e., lockdowns). Under this scenario, R(t) is always kept under 1.

**The Resurgence Best Estimate scenario**—allows the epidemic to resurge in tandem with the reopening of the economy and allows the R(t) to stay high.

**The Peaks and Valleys Scenario**—allows the epidemic to resurge in tandem with the reopening of the economy until hospital intensive care unit (ICU) occupancy reached 30% of the provincial maximum. Then an intervention plan is triggered to bring the R(t) back down to lockdown level.<sup>(24)</sup>

Although The SIRD model was used until the beginning of 2021 for PPE, as the main epidemiological model for the PPE project until the beginning of 2021. Limitation of this model were the decrease in accuracy and neglect of age structure of the population. These limitations led to the creation of another version of the epidemiological model by using open-source software, for use in the main PPE demand and supply model, with additional compartments that can take more complex characteristics of the pandemic into consideration.<sup>(24)</sup>

### COVID-19 modelling in Egypt

Several Egyptian studies discussed modelling of the COVID-19 epidemic. Researchers from The High Institute of Public Health used cases and deaths in the situation reports of WHO, and the Egyptian Ministry of Health & Population (MoHP) report issued on the 2nd of April 2020. Using IBM SPSS Statistics, survival analysis was carried out to determine the case fatality rate (CFR), where new cases were added, while deaths and recovered cases were subtracted. The death rate among COVID-19 cases with defined outcome was calculated as the number of deaths divided by the total number of cases with defined outcome (either died or cured). Wolfram Player 12 software was used for the Susceptible Infected Recovered (SIR) epidemic dynamics of COVID-19.<sup>(25)</sup>

Another model depending on deep learning was developed for predicting the spread of COVID-19 in Egypt using google population mobility reports, and the number of infected cases reported daily “world in data” website. The suggested model could predict new cases of COVID-19 infection within 3–7 days with the minimum prediction error. The proposed model achieved 96.69% accuracy for 3 days of prediction.<sup>(26)</sup>

### Challenges and considerations

The overriding challenge as with all modelling is to find models that are complex enough to reflect sufficient details of the system, but simple enough not to get lost in the jungle of details.

- Data limitations and uncertainty:
- Behavioral Factors: Different results can be yielded with different spatial and temporal scales, which had proven during the SARS-CoV-2 pandemic.
- Globalization: The movement of people and goods can affect the spread of diseases, requiring models to account for global interactions.
- Challenges around vaccination and emergence of pathogens.<sup>(27)</sup>

### Recommendations and future prospectives

- Machine Learning and Artificial intelligence: Enhancing models with machine learning algorithms to improve predictions and analyze large datasets.
- Real-Time Data Integration: Using real-time data for dynamic updates to models and improving the accuracy of forecasts.
- Genomic Epidemiology: Incorporating genetic data of pathogens to understand mutations and evolutionary dynamics.
- Multi-scale Modelling: Integrating models at different scales (e.g., local, national, global) to capture complex interactions and effects.<sup>(27)</sup>

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