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Mathematical modelling: Basic concepts & applications in Medical field

Swapna Jaswanth

Introduction

What is mathematical modelling?

A mathematical model is an explicit description of the simplified dynamics of a system. The word simplified is essential because the art and science of modelling require the appropriate selection of information in order to achieve a specific purpose.

A major goal of mathematical model in epidemiology is to develop understanding of the interplay between the variables that determine the course of infection within an individual, and the variables that control the pattern of infections within communities of people.

Mathematical model results help in:

- Determining the plausibility of epidemiological explanations.
- Predict unexpected interrelationships among empirical observations (improve understanding).
- Help predict the impact of changes in the system.

Classifications of models

- **Deterministic models:** the model ignores random variation, and so always predicts the same outcome from a given starting point.
- **Stochastic model:** the model may be more statistical in nature, may predict the distribution of possible outcomes.

Mathematical models are often used to depict the rate of spread or transmission of an infectious agent through a defined human community. For their formulation, three broad classes of information are required:

- The modes (direct/indirect) and rates of transmission (incidence of disease) of the agent.
- The typical course of events within an individual following infection (latent, infectious, incubation period).
- The demographic (age/sex distribution/ birth rate) and social characteristics (close contacts) of the human community.

Compartmental model

When a disease spreads in a population, it splits the population in non-intersecting classes. These typically are:

1. The group of people who can contract the disease under appropriate conditions. These people are called susceptible(S).
2. The group of people who have contracted the disease and are now sick with it. What is more important is that they can transmit the disease after a contact to a susceptible individual. These people are called infectives (I).
3. The group of people who have been removed (by death) or who have recovered and cannot contract the disease again are called removed/recovered individuals(R).

Assumptions in SIR model:

- Population is closed (ignores birth, deaths and migration)
- Considers the whole population to be susceptible
- Once infected, results in lifelong immunity.

The epidemiological models consist of system that describes the dynamics in each class. For example, the rate of change of susceptible individuals

\[ S'(t) = - (\text{number of individuals who become infected per unit of time}) \]

Let N denote the total population: \( N = S + I + R \).

(a) Simple model for infection inducing lasting immunity (E.g. MMR, yellow fever, polio).

Consider one infectious individual. Assume cN– the number of contacts per unit time this infectious individual makes.
S/N – the probability that a contact is with a susceptible individual.

Thus, \( cN (S/N) \) – number of contacts with susceptible individuals per unit of time.

Not every contact with a susceptible individual leads to transmission of the disease. Suppose \( p \) is the probability that a contact with susceptible individual results in transmission. Then \( pcS \) – number of susceptible individuals who become infected per unit of time for one infectious individual.

Denote \( \beta = pc \). Then \( \beta IS \) – number of individuals who become infected per unit of time (incidence).

If we denote by \( \lambda (t) = \beta I \), then number of individuals who become infected per unit of time = \( \lambda (t)S \). The function \( \lambda (t) \) is called force of infection.

The coefficient \( \beta \) is the constant of proportionality called the transmission rate constant, which is made up of two components:

- Rate at which contacts occur between susceptible and infectious person.
- Likelihood that transmission will occur because of contact.

\( \beta \) is dependent on sociology and behavioural factors host factors within the host population (rate of mixing) and the biological properties that determine the infectiousness of the infected person and the susceptibility of the uninfected individuals.

There are different types of incidence depending on the assumption made for the form of the force of infection. This one is called mass action incidence. With this form of the incidence, we obtain the following differential equation for the susceptible individuals:

\[
S'(t) = -\beta IS
\]

The susceptible individuals who become infected move to the class I. Those of the individuals who recover or die leave the infective class at constant per capita probability per unit of time \( \alpha \) called recovery rate. That is, \( \alpha I \) is the number of infected individuals per unit of time who recover. So, \( \Gamma(t) = \beta IS - \alpha I \)

Finally, the recover individuals move to the recovered class. \( R'(t) = \alpha I \)

Thus, the whole model is given by the following systems:

\[
\begin{align*}
S'(t) &= -\beta IS \\
\Gamma(t) &= \beta IS - \alpha I \\
R'(t) &= \alpha I
\end{align*}
\]

This model is called SIR model or SIR system. It is a special type of models called compartmental models because each letter is referring to a ‘compartment’ in which an individual can reside.

Each individual can reside in exactly one compartment and can move from one compartment to another. A diagram often called flow chart schematically describes compartmental models.

The sum of all classes gives the total population size \( N(t) = S(t) + I(t) + R(t) \).

On the other hand, if we add all three differential equations we obtain the differential equation of the total population size, namely \( N'(t) = 0 \). Consequently, the total population size is a constant \( N \).

**Parameters required for model estimation:**

Numerous parameters are necessary to define even the simplest model of direct transmission within a human community. To make the best use of a model it is desirable to have available estimates for each of the parameters for a given infection. Examples like demographic rates of birth and mortality and total population size, can be easily obtained via national census databases (usually finely stratified by age and sex in developed countries). Others, such as the average latent and infectious periods, either must be determined by clinical studies of the course of infection in individual patients (e.g. measures of change in viral abundance during the course of infection) or by detailed household studies of case-to-case transmission. Statistical methodology plays an important role in this instance since, as noted earlier, latent, infectious, and incubation periods are rarely constant from one individual to the next. Statistical estimation procedures have been developed to help derive summary statistics of these distributions (e.g. means and variances).

![Variation in the SIR model](image)

In the above fig, the immunity acquired is transient and individual subsequently return to the susceptible pool (Example: typhoid, cholera, and gonorrhoea)

*IC= infectious carriers

Many infections persist within the host for long period of time during which the infected individual may remain infectious as in case of carriers of Hep B infection. The importance of this is that it enables the perpetuation of such infection in the low-density communities.

In some conditions the immunity developed may be a defence against disease but asymptomatic
reinfection from which new infectious individual arise. (Example: H. influenza and N.meningitidis).

\[
\begin{align*}
S(X) & \rightarrow I(Y) & R(Z)
\end{align*}
\]

The above fig shows the effect of vaccination that is the effect of transferring individual directly from susceptible to recovery class.

**Law of mass action**

Incidence of infection is often assumed to be approximately given by the density (or number) of susceptible, X, multiplied by the density (or number) of infectious persons, Y, multiplied by the probability of an effective (infectious) contact between an infectious person and a susceptible, b (i.e. bXY). This relationship is commonly referred to as the 'law of mass action' by analogy with particles colliding within an ideal gas system. The basic assumption implicit in this concept is that the population mixes in a random manner (often referred to as homogeneous mixing).

Susceptible and infectious individuals behave as ideal gas particles within a closed system with no immigration or emigration and occupying a defined space.

**Basic reproductive rate of infection (R₀)**

A key measure of transmissibility of a infectious agent is given by Basic reproductive rate. The average number of secondary cases of infection generated by one primary case in a susceptible population is simply the number of susceptibles present with which the primary case can make contact (X) times the length of time the primary case is infectious to others, D, times the transmission coefficient, β (rate of mixing and innate contagiousness of the infectious agent). This quantity defines the transmission potential of an infection and is called the basic reproductive rate of infection, R₀ where \( R₀ = βXD \).

The basic reproductive rate is of major epidemiological significance since the condition \( R₀ = 1 \) defines a threshold below which the generation of secondary cases is insufficient to maintain the infection within the human community. For values equal to or greater than one the infection will persist. The threshold defines the problem of control by mass vaccination. To block transmission, sufficient numbers of susceptible people must be immunized such that on average each primary case of infection generates less than one secondary case.

- \( R₀ < 1 \) Eradication.
- \( R₀ = 1 \) Endemic equilibrium.
- \( R₀ > 1 \) Epidemic

**Effective reproductive rate ‘R’**

The average number of secondary cases of infection generated by one primary case in a population containing both susceptible and immunes.

**Sexually transmitted infections**

Epidemiology of sexually transmitted diseases differs from that of common childhood viral and bacterial infections.

- The rate at which new infections are produced does not appear to be closely correlated with population density.
- The carrier phenomenon in which certain individuals harbour asymptomatic infection is often important.
- Many sexually transmitted diseases induce little or no acquired immunity on recovery.

- Net transmission depends on the degree of heterogeneity in sexual activity prevailing in the population and the degree to which individuals in one sexual activity class (perhaps defined in terms of the rate of sexual-partner change) mix with those in the same and in different classes (i.e. 'who has sex with whom').

The basic reproductive rate, \( R₀ \), in its simplest form is determined by the transmission probability \( β \), multiplied by the effective rate of sexual-partner change, \( c \), multiplied by the average duration of infectiousness, D. Heterogeneity in sexual activity is a major influence on the magnitude of transmission success. In general, most people have few different sexual partners and a few have many. The distributions of reported numbers of sex partners per defined period therefore tend to be skewed with a long right-hand tail where a few individuals report many partners. In the case of HIV each component of \( R₀ \) is difficult to measure due to the sensitivity and the practical difficulties associated with the study of sexual behaviour and the long and variable incubation period of the disease AIDS induced by the infection. Over the long incubation period, infectiousness appears to vary widely for an individual and between individuals.

**Principles of control**

The threshold condition for persistence of an infection defined by \( R₀ \), captures the essence of the problem of control.

To eradicate an infection we must reduce the value of \( R₀ < 0 \) by reducing \( β \) that is by altering social and behavioural factors such as reducing overcrowding, IEC for STDs or promote the use of condoms to lower \( β \).
Reduce the density of susceptible by immunization.

Reduce the infectious period by isolation or treatment

**Threshold density of susceptible:**

To maintain the value of R_0>1, the density of susceptible in the population must exceed a critical value XT.

If R_0=1

R_0=βXD

XT= 1/βD

The aim of vaccination aside from protecting individuals is to lower the density of susceptible in the population. If eradication is the aim of control, the density of susceptible must be reduced to less than XT.

**Application of Mathematical model in medicine**

Mathematical models have great potentialities as regards their utility in different disciplines of medicine and health.

- Descriptive models are useful in community diagnosis and other epidemiologic research (natural history of infection, transmission process and how epidemic evolve). Example: mathematical model was used in filariasis to understand the dynamics of infection and development of disease in humans, which was poorly understood so far (LYMFASIM). LYMFASIM simulates the life history of individual person, parasite, dynamics of vector population and the impact of intervention based on vector control, chemotherapy, or a combination of both.
- It is used as a tool for disease forecasting (impending epidemic, magnitude, and preparedness required). They help in predicting the future behaviour of certain diseases. Such models do not take into account unknown forces entering at a future date.

- Operations research models, which depend on various indices such as cost-benefit ratios, suggest how the effectiveness of operations can be maximized.
- Useful in interpretation of the impact of various health programmes using epidemiological parameters like incidence of infection, avg age at infection etc.
- Help in manipulating and analysis of a system using computers rather than experimenting the real system.
- Diagnostic models are formulated by assigning scores to various signs and symptoms as an aid to clinical diagnosis. Rational models are derived in a logical way based on observation, theory, and assumptions about the behaviour of physical components of a system, while empirical models reflect the main features of available data.
- Important areas of application of models in medicine and health include epidemiologic research, prediction, planning, and evaluation of preventive and control measures, measurement of level of health, cost benefit analysis, assessment of risks of illness, patient diagnosis, and maximizing effectiveness of operations.

**Use of Models in the Health System**

Examples:
- Infectious Disease Prevention and Control.
- Non-Communicable Diseases.
- Population Projections.
- Disease Projections.
- Economic Impact.
- Role of Risk Factors and Determinants.
- Health System Planning.
- Impact of Interventions.

**Advantages of mathematical modelling**

- Mathematics is a very precise language. This helps us to formulate ideas and identify underlying assumptions.
- Mathematics is a concise language, with well-defined rules for manipulations.
- All the results that mathematicians have proved over hundreds of years are at our disposal.
- Computers can be used to perform numerical calculations
- Experiments and research which cannot be performed due to various problems can be simplified using mathematical model
- Future prediction in various fields aids decision making (tactical decisions by managers; strategic decisions by planners)

**Limitations of mathematical model**

- Excessive use of symbolism or formal methods of analysis can confuse as opposed to clarify
- Specific guidelines are not available for choosing the number of parameters required for modelling
- A model may be wrong but it may be useful approximation, permitting conceptual experiments that would otherwise be difficult or impossible.
- Most dynamic systems are non-linear (complex) and hence qualitative and quantitative characteristics are not transparent (course of infection in a host)
- Parameters/variables used in models may change with time
- Extrapolating the conditions for interrupting transmission from one population to another is often invalid. E.g., if a small town is able to interrupt transmission of a respiratory infectious disease by immunizing 70% of its population the
same target is unlikely to have the same effect in metropolitan area.

Conclusion

Mathematical models allow better understanding of the disease process and helps in planning and instituting the most effective control measures. Models provide warning about impending epidemics, their magnitude, and preparatory measures required.

Experiments that are not practical to perform due to various reasons can be simulated through mathematical models, which is an alternative and efficient way to explore and test hypothesis.

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