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Mathematical modelling and prediction in infectious disease epidemiology

A. Huppert[1,*] **and G. Katriel**[2,*]

1) *Biostatistics Unit, The Gertner Institute, Chaim Sheba Medical Centre, Tel Hashomer and* 2) *Department of Mathematics, ORT Braude College, Karmiel, Israel*

Abstract

We discuss to what extent disease transmission models provide reliable predictions. The concept of prediction is delineated as it is understood by modellers, and illustrated by some classic and recent examples. A precondition for a model to provide valid predictions is that the assumptions underlying it correspond to the reality, but such correspondence is always limited—all models are simplifications of reality. A central tenet of the modelling enterprise is what we may call the 'robustness thesis': a model whose assumptions approximately correspond to reality will make predictions that are approximately valid. To examine which of the predictions made by a model are trustworthy, it is essential to examine the outcomes of different models. Thus, if a highly simplified model makes a prediction, and if the same or a very similar prediction is made by a more elaborate model that includes some mechanisms or details that the first model did not, then we gain some confidence that the prediction is robust. An important benefit derived from mathematical modelling activity is that it demands transparency and accuracy regarding our assumptions, thus enabling us to test our understanding of the disease epidemiology by comparing model results and observed patterns. Models can also assist in decision-making by making projections regarding important issues such as intervention-induced changes in the spread of disease.

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Corresponding author: A. Huppert, The Gertner Institute, Chaim Sheba Medical Centre, Tel Hashomer, 52621 Israel
E-mail: amit.huppert@gmail.com

*Contributed equally to the article.

Introduction

Can mathematical models in the field of infectious diseases provide predictions? We argue that they can and do, provided that the scope of the notion of prediction is suitably qualified. Below, we will delineate the concept of prediction as we believe it is understood by mathematical modellers, illustrating it by some classic and recent examples.

A mathematical model is an imaginary microworld consisting of entities behaving according to precisely specified rules. Mathematics provides us with a language for formulating these rules of behaviour in a concise and unambiguous way, thus forcing and helping us to clearly state our assumptions. Once a mathematical model is constructed, mathematical analysis, often combined with computer simulations, helps us to investigate the global behaviour of the model, drawing out the consequences of the assumptions that we have made. Thus, within the context of the model, we can make predictions of the future of our imaginary world and also study how these predictions change as the rules governing the entities described by the model are varied.

Thus, a mathematical model for the spread of an infectious disease in a population of hosts describes the transmission of the pathogen among hosts, depending on patterns of contacts among infectious and susceptible individuals, the latency period

from being infected to becoming infectious, the duration of infectiousness, the extent of immunity acquired following infection, and so on. Once all of these factors are formulated in a model, we can make predictions about the number of individuals who are expected to be infected during an epidemic, the duration of the epidemic, the peak incidence, and, indeed, we can predict the entire epidemic curve, providing us with the expected number of cases at each point in time.

Clearly, for the precise predictions made within the model's virtual world to be relevant to reality, the model itself needs to correspond to or represent what is occurring in the real world —one cannot expect to obtain good predictions from false assumptions. However, modellers are well aware of the fact that all models are, at best, partial descriptions of the mechanisms operating in reality, containing various layers of simplification, idealization, approximation, and abstraction. Indeed, much of the discussion and debate among modellers involves the nature of these simplifications and their appropriateness. Thus, a central tenet of the modelling enterprise is what we may call the 'robustness thesis': a model whose assumptions approximately correspond to reality will make predictions that are approximately valid. If one accepts this general (and admittedly vague) idea, then even highly simplified models—which clearly overlook or even contradict some aspects of reality—can provide some valuable predictions, as long as their assumptions mirror some central aspects of reality. Deciding which of the predictions of a simple model are robust, in the sense that they can be applied with confidence to reality, can be a difficult question. An important procedure that modellers use to test the robustness of predictions made by a mathematical model is to compare different models [1–3]. Thus, if a highly simplified model makes a prediction, and if the same or a very similar prediction is made by a somewhat more elaborate model that includes some mechanisms or details that the first model did not, then we gain some confidence that the prediction is robust. If, on the other hand, a certain prediction is highly dependent on the details of a particular model, then, as we never expect the model to be more than an approximate description of reality, we cannot have much faith in that particular prediction.

The SIR model

Let us illustrate some of the above considerations by reference to the most famous and paradigmatic model in mathematical epidemiology, the simple SIR model of Kermack and McKendrik [4]. In this model, a population is divided into susceptible, infective and recovered individuals, with the functions $S(t)$, $I(t)$ and $R(t)$ denoting their respective fractions in the populations at time t (measured, for example, in days). The evolution of these quantities is described by the differential equations:

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

where the derivatives dS/dt, dI/dt and dR/dt measure the rates of change of the quantities $S(t)$, $I(t)$, and $R(t)$. The transmission parameter β is the average number of individuals that one infected individual will infect per time unit, assuming that all contacts that this individual makes are with susceptible individuals. Thus, a more highly infectious disease has a higher β. The number γ is the rate of recovery, so that $1/\gamma$ is the average time period during which an infected individual remains infectious. The product $\beta S(t)\ I(t)$ is the total infection rate, the fraction of the population that will be infected per unit time at time t. To understand this, note that, if a fraction $I(t)$ of the population is currently infected, then they would infect a fraction $\beta I(t)$ of the population per unit time if all of their contacts were with susceptible individuals, but as only a fraction $S(t)$ of the population is currently susceptible, they will only infect $\beta I(t)\ S(t)$ per unit time.

The ratio β/γ is also known as the basic reproductive number R_0, which is an important index for quantifying the transmission of pathogens. R_0 is defined as the average number of people infected by an infected individual over the disease infectivity period, in a totally susceptible population.

This simple model, which is the basis for many elaborations, turns out to provide some quite striking predictions. By entering the above differential equations into any software for the numerical solution of differential equations, and choosing some values for β and γ together with the initial values $S(0)$, $I(0)$, and $R(0)$, it is possible to generate an epidemic curve corresponding to this model, that is a prediction for the fraction of the population that will be infected on each day of the epidemic. Moreover, analytical tools allow us to draw some general conclusions about the model's solutions. The most important conclusions are as follows:

1. The epidemic threshold: if the inequality $S(0)\ R_0 > 1$ holds, then the number of infected individuals will rapidly decrease; that is, no epidemic will occur. Note that, if $S(0)\ R_0 > 1$, then an epidemic will occur, no matter how small the initial number of infected individuals.
2. The size of the epidemic, when it occurs, will not depend on the initial number of infectives, but it will depend on the initial fraction of susceptibles, $S(0)$, and on R_0. An