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Reproduction numbers of infectious disease models

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ABSTRACT

This primer article focuses on the basic reproduction number, $\mathscr{R}_0$, for infectious diseases, and other reproduction numbers related to $\mathscr{R}_0$ that are useful in guiding control strategies. Beginning with a simple population model, the concept is developed for a threshold value of $\mathscr{R}_0$ determining whether or not the disease dies out. The next generation matrix method of calculating $\mathscr{R}_0$ in a compartmental model is described and illustrated. To address control strategies, type and target reproduction numbers are defined, as well as sensitivity and elasticity indices. These theoretical ideas are then applied to models that are formulated for West Nile virus in birds (a vector-borne disease), cholera in humans (a disease with two transmission pathways), anthrax in animals (a disease that can be spread by dead carcasses and spores), and Zika in humans (spread by mosquitoes and sexual contacts). Some parameter values from literature data are used to illustrate the results. Finally, references for other ways to calculate $\mathscr{R}_0$ are given. These are useful for more complicated models that, for example, take account of variations in environmental fluctuation or stochasticity.

1. Introduction

Infectious diseases continue to debilitate and to cause death in humans and animals, with new disease-causing pathogens emerging and old pathogens reemerging or evolving. For example, viruses give rise to influenza, measles and West Nile virus, bacteria give rise to anthrax, salmonella, chlamydia and cholera, and protozoa give rise to malaria and trypanosomiasis (sleeping sickness). Disease may be passed directly from person to person by respiratory droplets (e.g., measles), via body secretions (e.g., chlamydia), by biting tsetse flies (e.g., trypanosomiasis) or mosquitoes (e.g., malaria), or by ingestion in food or water (e.g., cholera). Some diseases can be controlled by vaccines, antibiotics, antiviral drugs, reduction in vector populations, increased sanitation or behavioral changes. In order to consider control strategies for a particular disease, it is essential to know features of the pathogen, the mode of transmission and other epidemiological details, since as indicated by the above examples, these differ greatly between diseases.

Mathematical modelling can play an important role in helping to quantify possible disease control strategies by focusing on the important aspects of a disease, determining threshold quantities for disease survival, and evaluating the effect of particular control strategies. A very important threshold quantity is the *basic reproduction number*, sometimes called the *basic reproductive number* or *basic reproductive ratio* (Heffernan, Smith, & Wahl, 2005), which is usually denoted by $\mathscr{R}_0$. The

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epidemiological definition of $\mathscr{R}_0$ is *the average number of secondary cases produced by one infected individual introduced into a population of susceptible individuals*, where an infected individual has acquired the disease, and susceptible individuals are healthy but can acquire the disease.

In reality, the value of $\mathscr{R}_0$ for a specific disease depends on many variables, such as location and density of population. For a few specific diseases, Table 1 gives estimates of $\mathscr{R}_0$ gleaned from data in the literature.

The aim of this review is to elaborate on mathematical ways of finding $\mathscr{R}_0$ for ODE disease models in a population, bearing in mind the epidemiological meaning of $\mathscr{R}_0$, and to demonstrate how this and other reproduction numbers can be used to guide control strategies. Section 2 introduces simple models that establish notation and serve as background for later sections. The next generation matrix method to theoretically calculate $\mathscr{R}_0$ for ODE models is presented in Section 3. In Section 4, the use of $\mathscr{R}_0$ and other reproduction numbers to guide control strategies is shown by defining elasticity indices, and type and target reproduction numbers. Sections 5, 6, and 7 apply these ideas to models specific for West Nile virus in birds, cholera in humans, and anthrax in animals, respectively. As suggested by a referee, Zika models are briefly discussed in Section 8. For these diseases, numerical values for model parameters are taken from the literature, with references given for these and for proofs (which are not detailed here). A final section, Section 9, gives references to other approaches for calculating $\mathscr{R}_0$, in particular for models formulated in other ways. Inevitably the reference list is incomplete as there have recently been many articles on infectious diseases (it has been said that there is an epidemic of disease models), many of which determine a basic or control reproduction number.

2. Simple compartmental disease models

2.1. SIR epidemic model

To begin with a simple model, assume that each member of a population is either susceptible, infectious (infected with the disease) or recovered from the disease with life-long immunity. If the disease is short lived compared with the population lifetime, then demography can be ignored. Such a model may be appropriate as a very simple model for seasonal influenza, ignoring features such as immunity from past infections. Let S, I, R denote the number of susceptible, infectious, recovered individuals at time t. Transmission of influenza is airborne or by respiratory secretions on hands, so this is often modeled by mass action, namely a term βSI, where β is the disease transmission rate constant and βI is the force of infection. Let $1/\gamma$ denote the mean infectious time (about 5 days for influenza), thus $\gamma > 0$ is the recovery rate, and let f denote the fraction of infectious individuals who recover from the disease (thus the fraction $1 - f$ die from the disease). The flow diagram for the disease dynamics with compartments S, I and R is given in Fig. 1.

Ordinary differential equations (ODEs) for this *SIR* model are given by

$$\frac{dS}{dt} = -\beta SI, \quad \frac{dI}{dt} = \beta SI - \gamma I, \quad \frac{dR}{dt} = f\gamma I.$$

Initially $S(0) = S_0, I(0) > 0$ with $I(0) \ll S(0)$, and $R(0) = 0$. There is a disease free equilibrium (DFE) with $(S, I, R) = (S_0, 0, 0)$. Focusing on the I equation, the initial behavior is governed by the sign of $\beta S_0 - \gamma$, or equivalently $\frac{\beta S_0}{\gamma} - 1$. This leads to the definition of $\mathscr{R}_0 = \frac{\beta S_0}{\gamma}$, with the DFE locally asymptotically stable (LAS) if $\mathscr{R}_0 < 1$, but unstable if $\mathscr{R}_0 > 1$. This $\mathscr{R}_0$ is the product of the transmission rate, the mean infectious time and S_0, and clearly fits with the epidemiological definition of $\mathscr{R}_0$ given in the Introduction. Note that $\mathscr{R}_0$ is independent of the fraction dying from the disease. From the dynamics of the system, if $\mathscr{R}_0 < 1$, then the number of infectious individuals decreases monotonically to 0; whereas if $\mathscr{R}_0 > 1$, then this number first increases (before tending to zero); thus $\mathscr{R}_0 = 1$ acts as a sharp threshold between the disease dying out or causing an epidemic.

Table 1
Estimated Mean Values of $\mathscr{R}_0$ from Data.

Disease outbreak and location	$\mathscr{R}_0$	Reference
Smallpox in Indian subcont. (1968–73)	4.5	Anderson and May (1991)
Poliomyelitis in Europe (1955–60)	6	Anderson and May (1991)
Measles in Ghana (1960–68)	14.5	Anderson and May (1991)
SARS epidemic in (2002–03)	3.5	Gumel et al. (2004)
1918 Spanish influenza in Geneva		
Spring wave	1.5	Chowell, Ammon, Hengartner, and Hyman (2006)
Fall wave	3.8	Chowell et al. (2006)
H2N2 influenza pandemic in US (1957)	1.68	Longini, Halloran, Nizam, and Yang (2004)
H1N1 influenza in South Africa (2009)	1.33	White, Archer, and Pagano (2013)
Ebola in Guinea (2014)	1.51	Althaus (2014)
Zika in South America (2015–16)	2.06	Gao et al. (2016)