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Time-varying and state-dependent recovery rates in epidemiological models

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ABSTRACT

Differential equation models of infectious disease have undergone many theoretical extensions that are invaluable for the evaluation of disease spread. For instance, while one traditionally uses a bilinear term to describe the incidence rate of infection, physically more realistic generalizations exist to account for effects such as the saturation of infection. However, such theoretical extensions of recovery rates in differential equation models have only started to be developed. This is despite the fact that a constant rate often does not provide a good description of the dynamics of recovery and that the recovery rate is arguably as important as the incidence rate in governing the dynamics of a system. We provide a first-principles derivation of state-dependent and time-varying recovery rates in differential equation models of infectious disease. Through this derivation, we demonstrate how to obtain time-varying and state-dependent recovery rates based on the family of Pearson distributions and a power-law distribution, respectively. For recovery rates based on the family of Pearson distributions, we show that uncertainty in skewness, in comparison to other statistical moments, is at least two times more impactful on the sensitivity of predicting an epidemic's peak. In addition, using recovery rates based on a power-law distribution, we provide a procedure to obtain state-dependent recovery rates. For such state-dependent rates, we derive a natural connection between recovery rate parameters with the mean and standard deviation of a power-law distribution, illustrating the impact that standard deviation has on the shape of an epidemic wave.

1. Introduction

Compartmental models of infectious-disease transmission have proven to be an invaluable tool for the prediction of disease progression and the evaluation of public health policies and interventions. In general, compartmental models describe how an infectious disease propagates throughout a population by characterizing the rates of transition of a populace from states of susceptible to, infected with, and finally recovered from disease. The rate of transition from the susceptible state to the infected state is often called the force of infection or incidence rate (Liu, Hethcote, & Levin, 1987), and the rate of transition from the state of infected with the disease to recovered from disease is called the recovery rate. While classically the

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incidence rate is taken as a bilinear term, there has been extensive theoretical work regarding alternative nonlinear incidence rates. These alternative nonlinear incidence rates are normally developed to account for behavioral characteristics, such as the crowding of infected individuals and the avoidance of exposure to infection (Alexander & Moghadas, 2005; Liu et al., 1987; Liu, Levin, & Iwasa, 1986; Ruan & Wang, 2003; van den Driessche & Watmough, 2000) or to account for multi-stage infections (Krylova & Earn, 2013). In fact, formulations of nonlinear incidence rates can be justified through a first-principles derivation (Ponciano & Capistrán, 2011).

Like incidence rates, recovery rates have received significant attention in regards to their formulations in integral equations (Feng, Xu, & Zhao, 2007; Fowler & Hollingsworth, 2015; Hethcote & Tudor, 1980) and stochastic epidemic models (Ball, 1983, 1986, 1991; Britton, 2010; Clancy, 1999, 2014). Recovery rates have also been generalized in ordinary differential equation (ODE) models, mainly through the method of stages, whereby the infected state is broken into multiple stages, where each stage has a constant recovery rate (Krylova & Earn, 2013; Lloyd, 2001a, 2001b). However, theoretical extensions of recovery rates beyond multiple constants in ODEs have only started to be developed, despite the fact that constant recovery rates based on the mean value of an exponentially distributed infectious period are epidemiologically unrealistic (Bailey et al., 1975; Gough, 1977; Keeling & Grenfell, 1999; Keeling & Rohani, 2007; Lloyd, 2001a, 2001b).

Here we derive time-varying and state-dependent recovery rates for ODE models of infectious diseases. To obtain such novel recovery rates, we use the connection between integral equation models, ODEs and survival functions. First we show how an integral equation model for an infectious disease (Hethcote & Tudor, 1980) is related to more typical ODEs. A key component of this relationship is the probability distribution of the time spent in the infectious class. Most traditional models assume this time is exponentially distributed, and so we review this distribution and its connection to stochastic processes. Next, we show how an alternative probability distribution of the time spent in the infectious class leads to different forms of recovery rates in ODE models.

We validate our work by modeling historical measles outbreaks in Iceland (Cliff, Haggett, Ord, & Versey, 1981). First, we develop a compartmental model with a time-varying recovery rate based on infectious periods that follow the family of Pearson distributions (Pearson, 1893, 1895). The family of Pearson distributions span all possible values of skewness and kurtosis, so we evaluate the sensitivity of model predictions of the timing and magnitude of an epidemic peak with such time-varying recovery rates, relative to the uncertainty in the skewness and kurtosis derived from infectious period data.

Finally, we turn to state-dependent recovery rates, where we compare recovery rates based on power-law distributions to constant recovery rate models. Through this comparison, we demonstrate advantages of recovery rates based on a power-law distribution, including the potential for scaling invariance, the finite contribution of infected individuals to disease spread and the potential for deterministic disease burnout.

2. Methods

We now outline how to obtain state-dependent and time-varying recovery rates η in ODE models. To accomplish this, we illustrate the connection between integral equation models to survival functions and finally ODE models.

2.1. Integral equation models of infectious diseases

We considered a population divided into the proportion of susceptible (s), infected (i) and recovered (r) individuals, with $s+i+r=1$, which follow an integral equation formulation of an SIR compartmental model:

$$\begin{aligned} s &= 1-(1-s_0)\exp\left(-\tilde{b}t\right) - \int_{t_0}^{t} \tilde{\lambda}(x)s(x)\exp\left(-\tilde{b}(t-x)\right)dx, \\ i &= i_0P(t,t_0)\exp\left(-\tilde{b}t\right) + \int_{t_0}^{t} \tilde{\lambda}(x)s(x)P(t,x)\exp\left(-\tilde{b}(t-x)\right)dx, \\ r &= (r_0+i_0-i_0P(t,t_0))\exp\left(-\tilde{b}t\right) + \int_{t_0}^{t} \tilde{\lambda}(x)s(x)(1-P(t,x))\exp\left(-\tilde{b}(t-x)\right)dx. \end{aligned} \tag{1}$$

Here $\tilde{\lambda}$ is the force of infection, $\tilde{b}$ is the population birth rate minus the population death rate, and $P(t,x)$ is the waiting-time distribution for the time spent in the infectious class before recovery, where x is the time of infection.

As $P(t,x)$ characterizes the time waiting in the infectious class before recovery, it also may be interpreted as a survival function. Thereby, $P(t,x)$ possesses all the properties of a survival function, including $1-P(t,x)$ corresponding to cumulative distribution function, $-\frac{d}{dt}\ln P(t,x)$ being a hazard function, and $\int_x^\infty P(t,x)dt$ as the average waiting-time (Arino & van den Driessche, 2006; Rodriguez, 2007).

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