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Case fatality models for epidemics in growing populations

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ABSTRACT

The asymptotically homogeneous SIR model of Thieme (1992) for growing populations, with incidence depending in a general way on total population size, is reconsidered with respect to other parameterizations that give clear insight into epidemiological relevant relations and thresholds. One important feature of the present approach is case fatality as opposed to differential mortality. Although case fatality models and differential mortality models are equivalent via a transformation in parameter space, the underlying ideas and the dynamic behaviors are different, e.g. the basic reproduction number depends on differential mortality but not on case fatality. The persistent distributions and exponents of growth of infected solutions are computed and discussed in terms of the parameters. The notion of asymptotically exponentially growing state (as opposed to stationary state or exponential solution) coined by Thieme is interpreted in terms of stability theory. Of some interest are limiting cases of models without recovery where two infected solutions exist.

1. Introduction

Most likely, Anderson and May [2] were the first to discuss the question whether an exponentially growing population can be controlled by an infectious disease. They presented a model based on mass action incidence. Many authors have studied the spread of epidemics in populations of varying size [3–10]. Andreasen [11] mentions specifically exit rates towards immunity and disease-related death. Thieme [1,12] proposed and analyzed a rather general model system in which standard incidence is modified by a factor depending on total population size,

$$\begin{aligned}\dot S &= \nu N - \mu S - \beta C(N)\frac{SI}{N}\\ \dot I &= \beta C(N)\frac{SI}{N} - (\mu+\alpha+\delta)I\\ \dot R &= \alpha I - \mu R\\ N &= S+I+R.\end{aligned} \tag{1.1}$$

Here S, I, R are the classes of susceptible, infected and recovered, N is the total population size. The demographic parameters are the birth rate ν and the natural death rate μ. The epidemiological parameters are the transmission rate β (in case that $C(N)\equiv 1$), the recovery rate α, and the differential mortality (disease-related per capita mortality rate) δ, see Section 2. The case of mass action incidence is included for $C(N)\equiv N$. Throughout the paper we assume that the uninfected population is growing, i.e., we assume $\nu > \mu$.

The incidence is standard incidence, modified by a factor $C(N)$ which in the homogeneous case is $C(N)\equiv 1$ [13]. As in [1] we assume that $C(N)$ is a non-decreasing function, not necessarily bounded.[1]

We discuss the results in terms of case fatality when the model assumes the form

$$\begin{aligned}\dot S &= \nu N - \beta C(N)\frac{SI}{N} - \mu S\\ \dot I &= \beta C(N)\frac{SI}{N} - \gamma I - \mu I\\ \dot R &= (1-c)\gamma I - \mu R.\end{aligned} \tag{1.2}$$

Here γ is the rate at which individuals leave the infected compartment (other than by death from other causes), and c is the case fatality. The two systems (1.1) and (1.2) are mathematically equivalent, case fatality c replaces differential mortality, see Section 2.

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[1] In [1] the parameter β is normalized to 1 and the basic reproduction number is formulated in terms of the function $C(N)$ which is inconvenient since N is variable. The present notation, with a rate β (transmission rate in the standard case) and a dimensionless function $C(N)$, keeps the connection to standard epidemic models.

The results of Thieme [1] are almost exhausting as the dynamic behavior of the system (1.1) is concerned. Consider a solution of (1.2) with $N \to \infty$ and $\lim_{t\to\infty} C(N) = C_\infty < \infty$. The limiting system

$$\begin{aligned}\dot S &= \nu N - \beta C_\infty \frac{SI}{N} - \mu S\\ \dot I &= \beta C_\infty \frac{SI}{N} - \gamma I - \mu I\\ \dot R &= (1-c)\gamma I - \mu R \end{aligned} \tag{1.3}$$

is a homogeneous system, but it is not a special case of (1.2). The typical solution of (1.3) is an exponential solution while the typical solution of (1.2) approximates an exponential solution as N stays finite but goes to infinity.

When the total population size in (1.2) goes to infinity then the limiting exponential solution is not a true solution but only a solution of a limiting system. This feature makes stability analysis complicated. We overcome this difficulty by a transformation such that standard stability theory applies. We recover the overview of [1] of all possible cases in terms of the basic reproduction number and a critical threshold Q that measures the washout effect due to population growth in the presence of the disease.

As has been observed in [1], when $C(N)$ is not constant, upon varying a suitable parameter, there is an interval of stationary points while in the homogeneous case there is only one stationary point.

Finally, we show that the system in the limit case without recovery has two infected solutions. The second solution plays a role in the dynamics in cases of high disease-related mortality.

The paper is organized as follows. In Section 2 the relation between differential mortality and case fatality is further explored. In Section 3 known results on the homogeneous models are presented. In Section 4 we explain asymptotically homogeneous systems and in Section 5 we recast the results from [1] and give short proofs for existence of stationary states and asymptotically exponential solutions. We do not discuss the stability and convergence results in [1]. In Sections 6 and 7 we study the behavior of the homogeneous model for large case fatality, to some extent following earlier results in [14]. The paper closes with a discussion.

2. Case fatality versus differential mortality

The argument for "differential mortality" goes as follows. Uninfected individuals have mortality μ. For infected individuals the mortality is higher. The difference δ is the differential mortality (or excess mortality). The expression $(\alpha+\mu+\delta)^{-1}$ is the mean sojourn time in the infected state. Given the sum $\alpha+\mu+\delta$, the parameter of a sum of three Poisson processes, we cannot tell whether an existing individual has recovered, or has died from natural causes, or from the disease. But within the framework of the compartment model (1.2) we define the proportions of recovered and dead individuals.

The first case fatality model is due to Daniel Bernoulli 1766 (see an abridged translation of the original paper in [15]). This model has been discussed in detail in [16]. In the setting of case fatality the sum $\mu+\gamma$ is the exit rate from the infected state, and $c \in [0, 1]$ is the case fatality probability. The idea behind this model is that individuals leave the infected state and upon exit it is decided whether they are dead or recovered.

The models (1.2) and (1.1) are mathematically equivalent as long as they are seen as compartment models (and not as Poisson processes) by a transformation in parameter space,

$$\delta = c\gamma, \quad \alpha = (1-c)\gamma, \tag{2.1}$$

$$\gamma = \alpha + \delta, \quad c = \delta/(\alpha+\delta). \tag{2.2}$$

The parameter δ is a rate while c is a probability and should not be called a risk because "risk" may be connected to the product of a probability and the resulting damage.

If $\gamma > 0$ and $c \in [0, 1]$ are given, then (2.1) yields $\delta \geq 0$, $\alpha \geq 0$ with $\alpha + \delta > 0$. On the other hand, if such α and δ are given, then (2.2) yields $\gamma > 0$ and $c \in [0, 1]$. The case $c = 1$ corresponds to $\alpha = 0$ and $c = 0$ to $\delta = 0$.

Hence, every differential mortality model is a case fatality model and every case fatality model is a differential mortality model.

The difference between the two models shows up in the basic reproduction numbers for the homogeneous case $C(N) \equiv 1$. In the differential mortality setting,

$$R_0^{\text{hom}} = \frac{\beta}{(\nu-\mu)+\alpha+\mu+\delta} = \frac{\beta}{\nu+\alpha+\delta}. \tag{2.3}$$

It increases with decreasing δ, as was discussed in [17] in the context of treating HIV/AIDS patients, while in the case fatality setting

$$R_0^{cas} = \frac{\beta}{(\nu-\mu)+\mu+\gamma} = \frac{\beta}{\nu+\gamma}, \tag{2.4}$$

it does not depend on c.

In addition to these numbers we shall also use the basic reproduction number for the standard SIR model

$$R_0 = \frac{\beta}{\mu+\alpha+\delta}, \quad R_0 = \frac{\beta}{\mu+\gamma}, \tag{2.5}$$

and the demographic reproduction number

$$R_D = \frac{\nu}{\mu}. \tag{2.6}$$

The authors Day [18], and Ma and van den Driessche [19] discuss whether a case fatality proportion can be defined for a differential mortality model *a posteriori*. In practice, the case fatality proportion gives the proportion of fatal (lethal) cases upon exit from the infected compartment. Usually it is called CFR (case fatality rate) in the literature, although it is clearly not a rate. It may range from small values (0.01 for Asian flu) to very large values as 0.6 for untreated bubonic plague or even 1.0 for rabies. The concept of CFR is not restricted to infectious diseases, but is used for a variety of infectious and non-infectious diseases, from aspergillosis to stroke.

In practice, the estimation of the case fatality proportion is subject to bias because of the uncertainty about the appropriate number of cases in the denominator, see [20,21]. We assume that all model parameters are known. The number $\delta/(\alpha+\delta)$ is the case fatality proportion under the condition that there is no risk of natural death during the infectious period. In practice, with the exception of HIV/AIDS, the natural death rate μ is much smaller than $\alpha+\delta$.

3. The homogeneous model

The homogeneous model is obtained from (1.2) for $C(N) \equiv 1$,

$$\begin{aligned}\dot S &= \nu N - \frac{\beta}{N} SI - \mu S\\ \dot I &= \frac{\beta}{N} SI - \gamma I - \mu I\\ \dot R &= (1-c)\gamma I - \mu R. \end{aligned} \tag{3.1}$$

In [10], Section 3.3, Exercise 3.22, this system (with sterile infected) has been discussed as a model for regulation of the host, there $1-f$ corresponds to the case fatality.

The model (3.1) is a homogeneous dynamical system. The typical "stationary" solution is not a stationary point but an exponential or "persistent" solution, i.e., a solution of the form $(S, I, R)^T e^{\rho t}$