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How population heterogeneity in susceptibility and infectivity influences epidemic dynamics

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HIGHLIGHTS

- We present a new method for analysing epidemic models.
- We consider heterogeneous distributions of susceptibility and infectivity.
- We solve the generalisation of the final size equation.
- We consider the effects of pre-epidemic immunity on the mortality distribution.
- We find the smallest final size and mortality if "children" are vaccinated

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ABSTRACT

An important concern in public health is what population group should be prioritised for vaccination. To this end, we present an epidemic model with arbitrary initial distributions for population susceptibility, and corresponding infectivity distributions. We consider four scenarios: first, a population with heterogeneous susceptibility with a uniform distribution, but homogeneous infectivity; second, a heterogeneously susceptible population with linear heterogeneous infectivity functions, where the most susceptible are either the most or least infectious; third, a bimodal distribution for susceptibility, with all combinations of infectivity functions; finally, we consider the effects of additional pre-epidemic immunity, ostensibly through vaccination, on the epidemic dynamics. For a seasonal influenza-like infectious disease, we find the smallest final size and overall number of deaths due to the epidemic to occur if the most susceptible are vaccinated, corresponding to targeting children.

1. Introduction

Annual epidemics of influenza occur in all temperate regions of the world (Finkelman et al., 2007). Questions of interest to public health practitioners are twofold. For whom should we prioritise vaccination: the most susceptible, least susceptible, the most infectious or least infectious? Then, how do these combinations interplay? We present a model to address these questions that is applicable to any pathogen for which the classic *SIR* structure is appropriate, such as influenza or other influenza like illnesses (ILI). In particular, we assume the individuals in a population to have different susceptibilities to infection prior to the beginning of the epidemic. We also investigate the additional effects of vaccination (or increased immunity achieved by other means such as previous exposure to a similar pathogen) prior to the epidemic.

Perhaps the best-known model for the spread of an epidemic is the so-called *SIR* model. The host population is of constant size, of which proportion S are susceptible to infection, I are infectious, and R are removed either through immunity or death. The proportion infectious, I, is also referred to as the prevalence (of infection). The dynamics may be specified by the scaled (in time) differential equations:

$$\frac{dS}{dt} = -\mathcal{R}_0 SI,$$
$$\frac{dI}{dt} = \mathcal{R}_0 SI - I,$$
$$\frac{dR}{dt} = I, \tag{1}$$

where $\mathcal{R}_0$ is the basic reproduction number (Diekmann et al., 2013; Roberts, 2007).

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The effects of heterogeneity in populations have been well explored in the literature. Several authors have modelled the effect of heterogeneity in susceptibility by either dividing the population into multiple compartments (Hyman and Li, 2005; Bonzi et al., 2011; Ball, 1985; Hsu Schmitz, 2002), or by considering continuous distributions (Katriel, 2012; Boylan, 1991; Dwyer et al., 1997, 2000, 2002; Veliov, 2005). In general, they have found that when susceptibility is the only variable property, the final size of the epidemic is always smaller for a heterogeneous population than for a homogeneous population with the same reproduction number (Katriel, 2012; Boylan, 1991). The final size is the total proportion of the population infected throughout the epidemic (see, for example, Diekmann et al., 2013). Dwyer et al. (1997) found that heterogeneity in susceptibility is important at large and small spatial scales, but that allowing susceptibility to vary randomly over time has no effect on the pathogen dynamics: their model simplifies to the classic *SIR* model. That is, if the population randomly changes its susceptibility over the course of an epidemic, the classic SIR model is appropriate.

Other authors have also considered heterogeneity in both susceptibility and infectivity, again by either dividing the population into discrete compartments (Hyman and Li, 2006; Andreasen, 2011; Clancy and Pearce, 2012; Dushoff and Levin, 1995) or by using continuous distributions (Diekmann et al., 1990; Novozhilov, 2008, 2012). The main findings are that for the same reproduction number, heterogeneity in infectivity alone does not change the mean final size of an epidemic (Clancy and Pearce, 2012), but when susceptibility and infectivity are negatively correlated, the final size is larger than that for the homogeneous case (Andreasen, 2011; Clancy and Pearce, 2012). However, if the reproduction number changes, Novozhilov (2012) found that a variation in infectivity may result in larger epidemics.

Katriel (2012) developed a Kermack–McKendrick model with heterogeneous susceptibility measured by a single parameter with a continuous distribution, resulting in an equivalent model and similar results to Novozhilov (2008, 2012). Katriel derived a final size equation based on the mean and variance of the susceptibility distribution, and found the upper and lower bounds. A major result was that the largest attack rate (final size) for a given mean is found for a homogeneous population: in other words when the variability is smallest. However, infectivity was assumed to be homogeneous. Katriel used the final size equation to determine the effects of vaccination on a population prior to an outbreak, exploring the outcome of complete vaccination and "leaky vaccination" (where the susceptibility of those vaccinated is reduced by a factor $0<r<1$) and a proportion of the population vaccinated. Katriel determined the threshold conditions for these scenarios, showing that the same reduction in the reproduction number can lead to very different attack rates. Katriel also explored the effect of a recurring epidemic, where a proportion of the population had been infected in the previous year, and susceptibility modified accordingly, and found the attack rate to be lower in the heterogeneous population.

Novozhilov (2008, 2012) presented a model similar to the one considered in the present paper, and used moment generating functions to find analytical expressions for a final size. Novozhilov (2012) explored the effect of different variances in an initial gamma distribution of susceptibility on the transient epidemic dynamics, finding that for the same reproduction number, increasing the variance of the distribution results in decreasing the final size, whereas heterogeneity in infectivity exhibits the opposite effect. That is, increasing the variance of the distribution of infectivity (with homogeneous susceptibility) may result in a larger final size. Novozhilov numerically explored heterogeneity in both susceptibility and infectivity, and concluded that since the interaction is nonlinear, the results cannot be predicted by considering heterogeneity in susceptibility and infectivity separately. Novozhilov did not explore the effect of different initial distributions on the transient dynamics, show the effect of the epidemic on the distribution of susceptibility and infectivity over time, or explore the effect of a heterogeneous mortality due to the pathogen. These aspects, together with the vaccination scenario, are the main thrust of the present paper.

Although the final size result has been found by others for similar models (see, for example, Novozhilov, 2008, 2012; Katriel, 2012), those models incorporated heterogeneity in susceptibility only. We present an analytic expression for the final size with heterogeneity in both susceptibility and infectivity, which also gives the resulting distribution of the population.

There are extensive literature on the effect of heterogeneity in contact rates (Novozhilov, 2012; Dushoff, 1999; Andreasen, 2011; Clancy and Pearce, 2012; Dushoff and Levin, 1995; Hethcote and Van Ark, 1987; May and Anderson, 1988; Nold, 1980; Veliov, 2005; Glass et al., 2011) *inter alios*, and it has been found that the final size of an epidemic is larger when mixing is heterogeneous (Dushoff and Levin, 1995). In the present paper we do not explicitly consider variation in contact rates, although these differences are important determinants of the dynamics. However, the transmission rate for the classic *SIR* model incorporates contact rates, and we are altering this with our heterogeneity parameter. Hence there are equivalences with the differences in susceptibility and infectivity that we do explore.

We extend the *SIR* model (1) by allowing susceptibility to vary in the population as a function of a variable θ according to some (initial) distribution. Other authors (Novozhilov, 2012; Hyman and Li, 2006) considered models where there were different parameters for the heterogeneity of susceptibility and infectivity. We assume a single attribute of the individual that dictates both their susceptibility and infectivity. For an ILI, the parameter θ could serve as a proxy for age, with younger people being more susceptible and susceptibility then reducing with age (Glass et al., 2012; Lopez and Huang, 2013; Kimura et al., 2011), but this will not be appropriate for all pathogens. We investigate a single outbreak, so waning immunity and population demography are not factors of interest. We compare results from the heterogeneous model to results from the *SIR* model, where $\mathcal{R}_0$ from Eq. (1) is equal to the basic reproduction number, $\mathcal{R}$, of the heterogeneous model, and where $\mathcal{R}_0$ is equal to the parameter β, which is the median value of $\mathcal{R}$ when the entire population is initially susceptible. It is expected that β would equal the value of $\mathcal{R}_0$ estimated using the homogeneous model, whereas $\mathcal{R}$ would be estimated using the heterogeneous model. Therefore, for a consistent comparison, we investigate both cases.

Roberts (2013) used the methodology outlined here: separation of variables followed by decomposition using basis functions to analyse an *SIR* model with uncertainty about the value of $\mathcal{R}_0$. Here we consider the effect of variation in susceptibility and infectivity in the population, and although we use the language of probability throughout, the model is deterministic. This method is capable of utilising arbitrary distributions, and is illustrated by some numerical examples. A selection of distributions are then used to explore the interaction between susceptibility and infectivity, and the effect of this heterogeneity on immunity gained prior to the epidemic.

Generally, our results agree with others in the literature (see, for example, Katriel, 2012; Boylan, 1991): when only heterogeneity in susceptibility is considered the final size is smaller than that for the homogeneous case. However, we found an exception to this: when the least susceptible are vaccinated prior to the epidemic, the final size for the heterogeneous population (19%) is larger than that for the homogeneous population (15.5%) for both $\mathcal{R}_0=\mathcal{R}$ and $\mathcal{R}_0=\beta$. When both susceptibility and infectivity are heterogeneous